A POLITICS OF YEAST? *SACCHAROMYCES CEREVISIAE*, SYNTHETIC BIOLOGY, AND THE SC2.0 PROJECT

by

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DEDICATION

For Kelli, journeying through this night with me toward the world yet to be.

ACKNOWLEDGMENTS

For many of those who have lived through this time of pandemic, the past few years have been marked by isolation. Yet we are never truly alone; connections between all sorts of organisms and things remain, often hidden in plain sight. All written works like this one emerge from the humus of current and former ideas, people, and relationships. Similarly, this work is the result of collaborations between many minds and voices. While often a deeply individual project, this dissertation would not be possible without the contributions of some key co-laborers and facilitators. I hope that the following pages reflect the best of these group efforts.

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members listed on the title page, Jamie Lorimer has been an intellectual touchstone and inspiration, in addition to playing a critical role in the trajectory of this project. A true committee member, I owe him many thanks for his incisive suggestions, kindness, and willingness to join in this work.

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know. And Jack—thanks for joining in on some of the more recent adventures in fermentation.

My paternal grandparents Sally and Dave have always been an equable source of support and care, valuing education and adventure. My maternal grandmother Maxine was deeply creative, and I know she would be amazed to see what her descendants have carried forth with that spark over the last 23 years. My maternal grandfather Bill inspired in me love for the natural world and a quiet determination that echoes through my life even now. I am who I am because of these people. Thanks be to God.

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LIST OF ABBREVIATIONS

Abbreviation	Description
ANT	Actor-Network Theory
BAG	Build-a-Genome
bp	base pairs
CCYL	Community Cultures Yeast Lab
CRISPR/Cas9	Clustered Regularly-Interspersed Short Palindromic Repeats/CRISPR-associated protein 9
DARPA	Defense Advanced Research Projects Agency
ELSI	Ethical, Legal, and Social Implications
ESC	Embryonic Stem Cell
Gb	Gigabase
GP-write	Genome Project-write
HGP	Human Genome Project
iGEM	International Genetically-Engineered Machine
IRGC	International Risk Governance Council
JCVI	J. Craig Venter Institute
Mb	Megabase
MOOC	Massive Open Online Course
PE	Political Ecology
RRI	Responsible Research and Innovation
Sc2.0	*Saccharomyces cerevisiae* 2.0
Sc3.0	*Saccharomyces cerevisiae* 3.0
SCRaMbLE	Synthetic Chromosome Recombination and Modification by LoxP-mediated Evolution
SGD	Saccharomyces Genome Database
STS	Science and Technology Studies
tRNA	Transfer Ribonucleic Acid
YAC	Yeast Artificial Chromosome

ABSTRACT

Yeast (*Saccharomyces cerevisiae*) is an organism of significant interest to humans; for millennia, humans and yeast have collaborated on a variety of activities ranging from winemaking to brewing to baking (Money, 2018). Various species of yeast have also long been the subject of scientific study. Beginning in the 1970s and accelerating through the end of the 20th century, scientists have taken an acute interest in yeast's potential to act as a "model organism" within the emerging discipline of synthetic biology (Dymond & Boeke, 2012; Langer, 2016). Those working "with" or "on" yeast in laboratory settings tend to apply engineering and design principles in an attempt to elicit desirable genetic outcomes from yeast cells. This epistemic and methodological orientation emphasizes control and a faith in the ability of humans to beneficially manipulate other organisms at the most granular levels. At the same time, these scientists recognize yeast's vitality and "personality" in their work (Calvert & Szymanski, 2020). Yeast's agential status in laboratory assemblages suggests opportunities for thinking across both whole-genome engineering and the "microbial turn" in the social sciences, in which microbes are increasingly recognized as significant components of multispecies assemblages (Paxson & Helmreich, 2014; Szymanski, 2018a).

In this dissertation I explore the development of the first synthetic yeast, Sc2.0, which will also be the first fully synthetic eukaryotic organism. I trace part of the assemblage of actors, technologies, relationships, funds, and knowledge that constitute an emergent scientific imaginary of the present and future and outline how this assemblage has congealed over time and through the efforts of these many agents. This research centers on the Boeke Lab at New York University's Langone Health medical center, as this laboratory has been a sort of epicenter for the synthetic yeast project. Employing a qualitative approach, I draw upon participant observation, textual analysis, and interviews of scientists working with *S. cerevisiae* in this lab to

interrogate the politics and dimensions of yeast-human interactions in the Sc2.0 project. In contrast to this setting, I also conducted interviews and observation at a small yeast lab in San Antonio, Texas with a very different set of priorities and goals. Situated at the intersection of political ecology, science and technology studies, and more-than-human geographies, this work seeks to politicize the use of yeast as an object of scientific research, specifically examining the metaphors and language that shape present and future possibilities for humanity's relationships with other organisms.

This work brings together and builds upon existing academic studies of the rapidly evolving field of synthetic biology and follows the late stages of the Sc2.0 project as it nears completion. My analysis contextualizes how synthetic biologists think about and talk about the organisms they work with and highlights the ways in which scientists use language to normalize and enforce specific understandings of yeasts—and, by extension, microbes in general. Synthetic biologists employ a set of metaphors that reshape scientific practice and work across tensions between commodification and democratization of genetic material. Microbial labor is invoked and masked in these assemblages, and material and semiotic relationships are contested and negotiated despite control-oriented rhetoric. Results gesture away from totalizing narratives that portray yeast as either completely passive or autonomous and toward a more contingent relationship in which spatial context, metaphors, and assumptions matter. From these observations, I propose a cosmopolitics of synthetic yeast that accounts for the processual making of synthetic life and the mutual co-constitution of knowledge about and power over lively, multispecies relations.

keywords: yeast, synthetic biology, science and technology studies, political ecology, more-than-human geographies

1. FOREWORD

"In the beginner's mind there are many possibilities, but in the expert's there are few."

-Shunryu Suzuki, *Zen Mind, Beginner's Mind: Informal Talks on Zen Meditation and Practice*

"Too many bends on a footpath do not prevent one from reaching one's destination."

-Cameroonian proverb

The long and winding road that leads to yeast

When my father received a homebrewing kit for Christmas in 2011, a seed was planted that germinated the following winter. After working as a field organizer for President Obama's reelection campaign in 2012, I returned to my parents' house, unemployed and with nothing particular demanding my attention. There I found the modest starter kit, all but forgotten in the basement. With visions of paternal bonding, I proposed to my father that we put the enclosed liquid malt extract and dry yeast packet to use. In the end, my father's long work hours and my own enthusiasm and ennui led to a solo endeavor, and I became a homebrewer.

Though the ensuing years offered other preoccupations, my interest in this hobby grew. Fascinated by vague notions of *terroir* and a DIY ethic, I stocked the refrigerator with large mason jars full of pungent yeast starters harvested from previous batches of homebrew. A stray craft store coupon helped purchase a basic pasta maker, which when subjected to brute force and retooling became an ersatz grain mill. Hop rhizomes from a farm in Oregon's Willamette Valley were transplanted and trained up an exterior deck attached to the house, then harvested and added to stainless steel stockpots on a gas stove. Honeybees in northern Wisconsin under

the care of my uncle produced honey to sweeten wort and provide carbonation to bottles sealed with a rusty, old manual bottle capper. Mint, basil, and other herbs contributed to unusual brews that were very much of a time and place distinguished by this milieu of people, plants, and microbes.

At the 2015 American Association of Geographers annual meeting in Chicago, my master's thesis advisor introduced me to my current advisor, and we began discussing the possibility of working together in the future. As I wrapped up my master's thesis and moved across the country, I contemplated my next phase of research and the opportunity to somehow tie together my interests in place, landscape, and craft beer. First convinced to apply to and then attend Texas State University, I stepped into what I assumed would be a research plan centered on social and environmental aspects of the craft beer industry as part of regional foodscapes. At Texas State, I was exposed to new ideas and gained an increased interest in critical social theory, which led me to question my initial project ideas.

I spent the spring semester of 2018 as an exchange student at the Université Rennes 2 in Rennes, France. Along with two other Texas State students, we served as guinea pigs of sorts in our home university's efforts toward building a new international exchange between these institutions. Aside from the opportunity to travel (which I can rarely resist), I hoped to improve my language skills and open new research avenues based around my evolving sense of Fermented Landscapes (which tended to translate imperfectly into French as either *Paysages de la Fermentation* or *Paysages Fermentées*, each with its own incomplete connotations) (Myles, 2020). To be sure, any such cross-cultural exchange can be disorienting. A significant aspect of my time abroad was spent navigating the differences between American and French doctoral programs in terms of expectations, division of time, and bureaucratic structures. My hosting department at Rennes 2 graciously afforded me office space and freedom to work on my research, though this

was not clearly understood and communicated until nearly the end of my time in France, in part because of the demands of my coursework and in part because of simple misunderstandings. While I benefited from my experiences there and developed some understanding of the landscapes of local *cidre* production, among other fermentables, it became clear that without sustained funding to offer opportunities to return, any long-term qualitative-based research in such a setting would be exceptionally challenging. Additionally, I would face many difficulties adequately expressing myself and understanding the nuances of participants' comments in a language I didn't speak as fluently as I would have liked.

After this experience, I moved on to finding a new research topic that could be adequately studied domestically. The peculiar structure of graduate assistantships at Texas State—graduate students teach in the classroom every semester—makes field-based research away from campus challenging. While my interest in craft brewing as a socioenvironmental assemblage remained, it became increasingly clear that this subject was less well-suited to the sort of critical approach I was interested in taking with my project. After drawing up conceptual diagrams and scouring geography literature related to the topic, I decided to follow yeast as an organism of interest, to see where it might lead. I was (and remain) intrigued by the use of this microorganism in assigning value and place-based identity to a product at times untethered from any specific place (despite marketing and popular discourse to the contrary): craft beer is typically the result of grain, yeast, hops, and even adjunct ingredients from far-flung places. Of course, the irony is that the resulting product, thanks to the alchemy of fermentation and the logistical hurdle of transporting water long distances, is usually viewed as a quintessential "local" good, imbued with the character and values of a particular place (Flack, 1997). While some brewers do source hyper-locally and may even harvest yeast from their neighboring landscapes, yeast *(Saccharomyces cerevisiae*, usually) more often is shipped from distant

laboratories specializing in starter cultures for breweries. This was all interesting but remained centered on the notion of locality and placemaking, which was becoming less arresting to me.

Eventually I stumbled upon the work of Erika Szymanski and others who were discussing a new development: synthetic yeast. This immediately piqued my interest and led to a deeper investigation into the state of biotechnology efforts related to engineering a "new" life form. The first eukaryotic genome to be fully sequenced, *Saccharomyces cerevisiae* was quickly gaining new associations and affiliations with humans. Further reading pointed to the Sc2.0 project, a multi-sited international endeavor to construct the first fully synthetic eukaryotic organism.

I begin with this biographical sketch to help contextualize this project and illuminate parts of the meandering path I followed in pursuing it. While self-indulgent, I believe that each of these experiences shaped the mental frames and sensibilities that I brought to this work, which is why they bear recounting. What began as a focus on fermented beverages—primarily beer—evolved into something more far-reaching and yet minute, as I sought to identify "matters of concern" related to yeasts as actors in multispecies relationships (Latour, 2005).

Another goal of this preamble is to address the question that I frequently faced during this project: How is this geography? I will be quick to affirm that this is not a typical geography dissertation, but one which could be well-suited to a Science and Technology Studies department. However, this remains a geography dissertation for two main reasons: history and interdisciplinarity. While the project's evolution (discussed above) over time led it further from typical geographic paradigms, it started as an examination of the role breweries play in shaping cultural and physical landscapes, a project intellectually rooted in Carl Sauer's notion of cultural landscape and watered through several academic generations by currents of political ecology. The scion known as "fermented landscapes" (Myles, 2020) gave rise to this project, and it remains thematically connected to Colleen Myles' work through the Fermented Landscapes Lab

at Texas State University.

The other reason for housing this project within geography is precisely the breadth of the field. Though it has led to decades of handwringing among geographers, the discipline's concern with myriad topics and at-times conflicting self-identity makes space for unusual topics like my own that often span social and physical sciences and employ diverse methodologies.

One foundational challenge to this project was (ironically) its seeming lack of spatiality. Notwithstanding the topical oddity of this research in the context of geography as a discipline, the difficulties of doing field-based research in the midst of the COVID-19 global pandemic created a situation of placelessness for the resulting research. Despite the geographic lens guiding this project, it mostly lacks grounding in any particular place. Rather, it is geographically ambiguous, carried through different assemblages of living actors, academic text, and Zoom rooms. Perhaps it fits with a contemporary interest in 'digital geographies,' which explore how digital technologies shape and produce space and yet are themselves "placeless" in the sense that they may lack a fixed, geographic grounding. As much as I'd like to say that this placelessness purposefully echoes that of *Saccharomyces*'—as an organism that exists all over the world and is frequently transported elsewhere by humans and animals—I do regret that this project is not more grounded in a particular locale. While this reality brings clear disadvantages, it reflects the context in which this work was done, constrained by a global pandemic.

On conducting research during a pandemic

The daily rhythms of work—for me, teaching, research, and study—changed dramatically as a result of the COVID-19 pandemic. After the university's spring break in March 2020, all classes were moved online for the remainder of the term. I scrambled to transition my World

Geography students to an entirely new format, replacing in-person discussion and map quizzes with online forums and recorded lectures. Barely a month past defending my project proposal, my research effectively ground to a halt in the uncertainty of those early COVID days. Aspects of fieldwork—particularly qualitative, embodied fieldwork—became especially challenging to navigate, from building rapport with informants to conveying and detecting nuance in (virtual) qualitative data collection efforts.

Even as virality fluctuated and vaccines became available, the uncertainties precipitated by COVID-19 made it difficult to plan and execute fieldwork. My difficulties were compounded by the challenges I faced in recruiting participants to my study; many emails went unanswered and at times weeks dragged on between any meaningful advancement or engagement. Patience may not always be a virtue; in lieu of shifting my proposed field sites and methods in response to prohibitions on in-person research during the spring and summer, I opted to wait out pandemic-related restrictions and focus on teaching and background reading. Unfortunately, as this global health crisis wore on and evolved, I languished, finding the space afforded by social distancing to be at once comfortable and paralyzing. In addition to the academic uncertainties all scholars faced, I also navigated personal life changes (including moving and marrying).

As I will explain further in subsequent chapters, my willingness to "wait and see" about my research was paradoxically both a form of flexibility and a form of stubbornness. Although I attempted and implemented a number of changes to my research methods, I remained committed to my original approach and goals on a fundamental level. Foregrounding a research ethos that acknowledged my own "lace of obligation" to my participants (Derrida, 2016, p. 29), I erred toward an abundance of caution in pursuing my planned interviews and ethnographic field work. Yet coupled with a general slackening of the pace of life during the first year of the pandemic, this caution grew into a general malaise and aversion to moving forward under

suboptimal circumstances (Gailloux et al., 2022).

These pieces of context are relevant at least insofar as they explain the depth of challenge related to conducting this study. Given the rapid pace of change in synthetic biology and genomic engineering in general, parts of this study have begun to feel outdated even as the words are committed to the page. This difficulty has only been exacerbated by the drawn-out process of research and writing during the past two pandemic years. This study lacked discrete data collection and writing phases—not by design, but in and through the realities of its timing. Instead of finding new pathways through which to assemble this work, I continued to attempt to collect data long past my initially proposed timeline in hopes of making up for the lack of data I had hoped to gather earlier. This approach allowed for some iterative revision as I focused more on writing and analysis over time, but my commitment to my initial approach also had drawbacks. Therefore, while the observations and insights offered here seek to speak to the future of yeast-human relationships, they are in some ways more of a chronicle of the near past. However, by acknowledging the temporality of this study—as is true to a degree for any such prolonged effort—I hope the reader will at least be reminded of the limits of knowledge as they relate to the ever-changing, shifting worlds we collectively construct.

2. INTRODUCTION

> "Geographers should avoid considering the earth as the scene on which the activity of man [sic] unfolds itself, without reflecting that this scene is itself living."
>
> -Carl Sauer, *The Morphology of Landscape* (1925, p. 321)

> "Whether or not other organisms "tell stories," they contribute to the overlapping tracks and traces that we grasp as history. History, then, is the record of many trajectories of world making, human and not human."
>
> -Anna Tsing, *The Mushroom at the End of the World* (2015, p. 168)

Yeasty ubiquity

The word 'yeast' is a general term that refers to single-celled microorganisms spanning two different phyla (Ascomycota and Basidiomycota) that collectively form the subkingdom Dikarya in the fungi kingdom. Despite this breadth, 'yeast' is also commonly a synonym for *Saccharomyces cerevisiae*, well-known as brewer's yeast or baker's yeast. The name *Saccharomyces cerevisiae* derives from Latin and Greek, translating as "sugar fungus" (*saccharon*, σάκχαρον, or 'sugar" and *myces*, μύκης, or 'fungus'; *cerevisiae* in Latin denotes "of beer"). This species is a single organism that plays essential roles in the production of a variety of collaborative goods in contexts ranging from baking to brewing to winemaking to pharmaceutical and biofuel development and genomic engineering (Khalil & Collins, 2010; Liu et al., 2022; Money, 2018). From a human perspective, *S. cerevisiae* inhabits various spaces and assemblages as an active agent—as in fermentation—or a receptive reservoir for genetic material in some laboratory settings. Although the word 'yeast' encompasses well over 1,000 different species, in this thesis I utilize it as shorthand for *Saccharomyces cerevisiae* unless noted otherwise.

By some accounts, yeast's labor is the oldest form of biotechnology humans learned to capitalize on and is central to numerous civilizational aspects related to food production, storage, and digestion (Langer, 2016; McGovern et al., 2017). In fermentation, humans discovered a means to make food last longer, taste better, and digest more easily, contributing to our species' historic flourishing (Boekhout et al., 2003). Importantly, fermentation and alcohol have significant cultural and social associations, aiding in ritual and celebration. It is believed that beer has been brewed in some form since the 6th millennium BCE, and it played a visible role in ancient Egyptian society. *Saccharomyces cerevisiae* has been important to so many cultures across the Earth that it seems nearly ubiquitous.

Despite its presence in numerous natural settings, *Saccharomyces cerevisiae* is presently often thought of as a domesticated species due to its proliferation alongside humans in making various fermented comestibles. This collaborative, multispecies relationship is unusual in that humans (particularly in modern, Western contexts) typically view microbes as unwanted intruders and strive to expel them from our lives (Amato, 2000). As Calvert and Szymanski remind, "microorganisms always exist in relation to other organisms, including humans. And yeast is not only a microbe, but a microbe with which humans have an unparalleled relationship, because of its history as a highly domesticated and uncommonly tractable organism that travels through scientific, cultural and industrial worlds" (2020, p. 2).

While humans have relied on the labor of this yeast for millennia, its workings in the biological nature of fermentation have only been apparent to our species for several hundred years. Even as basic understandings of fermentation grew over centuries, it remained a magical phenomenon. Antonie van Leeuwenhoek is commonly credited with 'discovering' yeast in 1680. Observing yeast cells in droplets of beer under a single-lens microscope of his own design, he did not believe that they were alive, understanding fermentation as a chemical, rather than

biological, process (Money, 2018). Indeed, the cell theory would not develop for roughly another century and a half, in 1839, so what van Leeuwenhoek observed was conceptualized very differently from how we think about yeast today (Nanninga, 2010). Van Leeuwenheok described "many small particles" (*seer veel kleyne deeltjens*) in a letter to Thomas Gale of the Royal Society, comparing them in size to red blood cells (which are approximately 7 µm in diameter, compared to 5-10 µm for yeast cells) (Money, 2018; Nanninga, 2010). He also made a wax model of the 'globules' he observed, in one of the first documented attempts of model building for interpreting scientific observations (Figure 1).

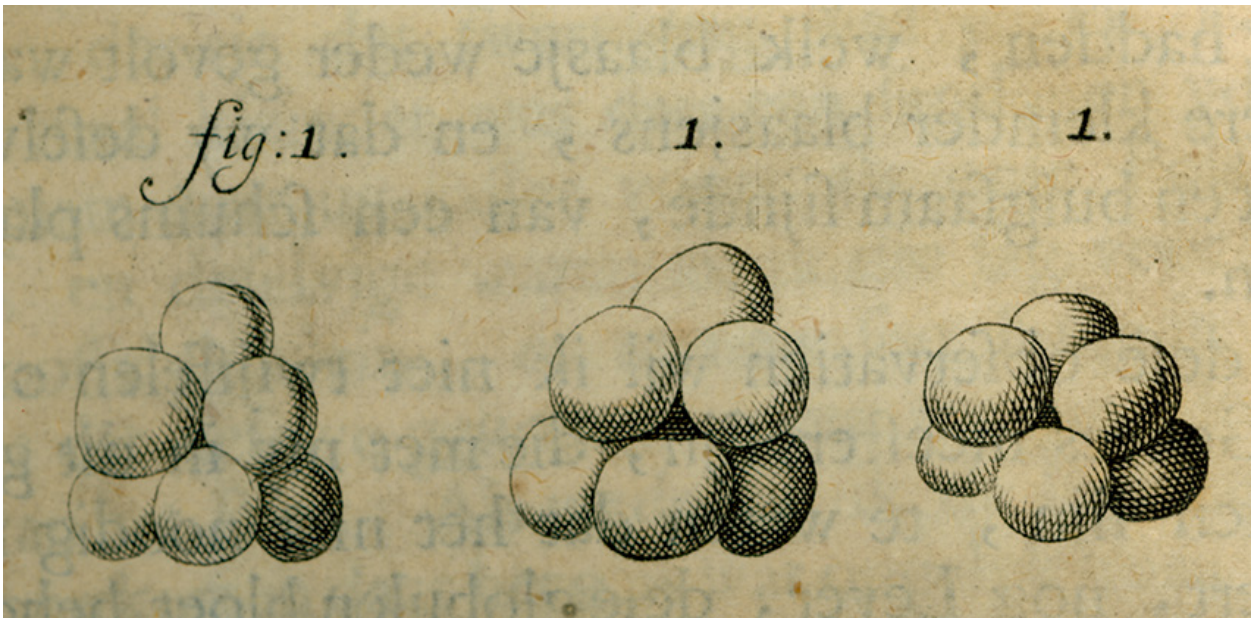

Figure 1: Van Leeuwenhoek's sketch of his wax model of yeast 'globules,' 1680. National Library of Medicine. https://www.nlm.nih.gov/exhibition/fromdnatobeer/exhibition-brewing-mysteries.html

Greater understanding of yeast followed. In the 1830s, Charles Cagniard de la Tour published his observations of samples taken from a brewery in Paris, from which he concluded that fermentation involves the growth of an organism, which he supposed was a type of plant, given that it did not appear to move autonomously (Nanninga, 2010). Friedrich Traugott Kützing and Theodor Schwann came to similar conclusions, but Justus von Liebig, Friedrich Wöhler, and

Jöns Jacob Berzelius maintained that yeast was in fact not an organism. Louis Pasteur would famously later solidify scientific knowledge of the biological nature of fermentation, though debates continued through his lifetime about the degree to which his ideas were truly novel or unique. In 1883, Emil Christian Hansen was the first to isolate a 'pure' yeast cell while working for the Carlsberg Laboratory. In the decades since, human knowledge of yeast has increased exponentially.

The family of organisms known as yeasts is comprised of eukaryotic fungi. In essence, eukaryotes are organisms consisting of a cell or cells in which the genetic material is DNA in the form of chromosomes contained within a distinct nucleus. Like humans, these fungi are heterotrophs, meaning that they obtain nourishment from complex organic substances like plants and animals. "Yeast" is not a taxonomic distinction but rather a description of a diverse set of fungi that is held together as much by what they don't have in common with animals or plants as by what they have in common with each other (Langer, 2016). In fact, current estimates suggest at least 1,500 different species of yeast (Money, 2018). Many yeasts are unicellular, but others are multicellular. They reproduce both sexually (via fusion between a and α mating types) and asexually by budding or fission, displaying a remarkable range of adaptations to environmental conditions (Gasch & Werner-Washburne, 2002). *Saccharomyces* is of particular interest due to its use in fermentation, but not all yeasts are so commensal. For example, *Candida albicans* is a yeast species that can become pathogenic in immunocompromised humans, though it typically co-exists in our gut flora without problems (Erdoğan & Rao, 2015).

Despite the many beneficial uses of yeast in producing foods and beverages, *Saccharomyces cerevisiae* is also a documented human pathogen, albeit a lesser-virulent one (Murphy & Kavanagh, 1999). Thus, context and interspecies dynamics matter in determining whether

health or disease will prevail, and for whom. Boekhout et al. (2003) describe a "fragile balance" depending on "the interplay between various biotic and abiotic factors. In this sense, the study of yeast-food interactions can be really seen as applied ecology…In many cases, yeasts interact with other microbes, such as filamentous fungi and bacteria, in temporarily and spatially differentiated, but balanced, physiological processes" (p. v).

Yeasts do not necessarily need humans to thrive, though their utility in facilitating fermentation has helped forge ecological niches for them in the form of breweries, homes, laboratories, cheese caves, and bakeries (Katz, 2016; Myles, 2020). Humans and yeast have long been co-producers of alcohol, cheese, and bread (Pollan, 2014), yet in terms of research interest and funding dollars, traditional foodstuffs arguably are not where yeast are working in the most interesting ways. One emerging area of research related to food and sustainability is the production of alternative or plant-based proteins, some of which are enabled by yeast (one prominent example is the heme molecule that gives the Impossible Burger its bloody look and taste, which is derived from a soybean gene housed inside a yeast cell). These efforts are part of the broader project of cellular agriculture, which seeks to produce lipids, proteins, and other tissues from cell cultures using a combination of synthetic biology techniques (Mattick, 2018). Increasingly, scientists are working with yeast to produce biofuels and pharmaceuticals while using *Saccharomyces cerevisiae* as a sort of genetic substructure upon which to assemble and test different genes and proteins (Money, 2018). These latter endeavors are increasingly heralded as potential lifelines for coping with energy, health, and environmental crises in a more "natural" way. At the same time, these approaches rely on genomic engineering principles to transcend *Saccharomyces*' current evolutionary status and capabilities. In the face of significant technological change, social scientists interested in the activities of synthetic biologists have raised questions about the role of yeast in these current and emerging assemblages (Szymanski

& Calvert, 2018).

Genetic frontiers in the new millennium

The twentieth century marked massive shifts in understanding of genomes and biology (Keller, 2000a). Humans became more aware of microbiological phenomena and technology developed in response to and as a condition of this increased knowledge. Various species played outsize roles in these developments, aiding in the production of scientific discoveries through the manipulation of their genes and bodies. Working 'up' from what have been understood as simpler organisms like bacteria or mice, scientists increasingly turned their attention toward their own species. In 2000, scientists released the human 'reference genome,' which was missing about 8% of the total sequence (Nurk et al., 2022). The subsequent two decades of this century have seen updated versions of this genome as scientists became aware of omitted base pairs and worked to address gaps in their initial rendering. Only within the last year (2022) has the 'complete' human genome been sequenced. But all of this technological progress accompanied a fundamental shift in mission. As biologists gained knowledge about cells, protein-coding genes, and mitochondrial DNA, they strove to do more than just 'read' (i.e., sequence) genomes, hoping to be able to actively change or 'write' (i.e., synthesize) them, a key goal of the emerging field of synthetic biology.

Synthetic biology is a relatively young field, emerging around 2004 from elements of genomic engineering. This development followed a transition from describing and chronicling DNA sequences to actively manipulating them in the laboratory (syntheticyeast.org). A subfield of synthetic biology, synthetic genomics, seeks to build new, synthetic genomes for various purposes. These goals include creating "platforms" for biotechnological research and addressing

impending energy and environmental challenges.

The technological advancements in synthetic biology over the past several decades have cemented yeast as a "model organism" (Botstein & Fink, 2011). A model organism is a non-human species that is extensively studied in order to understand particular (but theorized and hoped to be potentially universal) biological processes, the acquired knowledge of which is then applied to other species, often humans. Especially in the context of human health, model organisms offer a path around thorny ethical issues involving testing and genetic manipulation. As a prominent model organism, *Saccharomyces cerevisiae* has arguably the most storied scientific life of all the yeasts, but others such as *Pichia pastoris* and *Schizosaccharomyces pombe* also play important roles in laboratory experiments (Langer, 2016). Lessons learned from yeasts have been integral to broader understanding of genomics in humans and other species, from cancer-related cellular division to organelle functions and more. As I'll discuss further in later chapters, yeast is a "model" organism in other ways, too. Its long history as an object of scientific inquiry—from industrial food science to genetics—combined with its adaptability and congeniality to human interests positions it as the beau idéal microbe (Botstein & Fink, 2011).

Early molecular biology was largely synonymous with research on *Escherichia coli*, centered on the gene as a unit of analysis (Langer, 2016). Bacteria like *E. coli* are prokaryotes, meaning that they do not have a nucleus or specialized organelles. Given that yeasts are eukaryotes and ostensibly more similar to 'higher order' organisms, they were seen as a sort of stepping stone to understanding more complex organisms. The use of yeast as a model organism also served as a "conceptual bridge between two transformative processes of the twentieth century: molecularization of the life sciences and biomedicalization of society across the laboratory, industry, and the clinic" (Langer, 2016, p. 16). Nikolas Rose (2007) defines molecularization as

the "reorganization of the gaze of the life sciences, their institutions, procedures, instruments, spaces of operation and forms of capitalization" (p. 44). As biology became more preoccupied with genome-level research, social scientists took note. The "practice turn" of the 1980s-1990s within social studies of science followed this spread of genetic engineering tools and paradigms in biology, as model organisms became more and more visible.

In laboratory spaces, scientists conduct research on yeast genomics to better understand and manipulate this organism for the aforementioned purposes. Scientists working on the frontiers of these applications are compelled to make decisions about how to ethically approach working with another lively organism, including complications surrounding intellectual property and beyond (Delaney, 2001). However, not all laboratories seek the same goals or operate under the same epistemological and ontological paradigms. Instead, the varied spaces of human-yeast collaboration entail different sets of actors engaged in multispecies, metabolic collaborations that exhibit a complex interplay between harnessing and constraining yeast's vitality.

One common goal in contemporary synthetic biology is 'minimizing' genomes, which is to say stripping away DNA that seems unnecessary in order to discover the minimum genes necessary for life. This approach stems from the engineering ethos of synthetic biology and the assumption that life can be treated as modular and reducible. Cho et al. (2009) argue that

> The prospect of constructing minimal and new genomes does not violate any fundamental moral precepts or boundaries, but does raise questions that are essential to consider before the technology advances further. How does work on minimal genomes and the creation of new free-living organisms change how we frame ideas of life and our relationship to it? How can the technology be used for the benefit of all, and what can be done in law and social policy to ensure that outcome?" (p. 2087)

It can be tempting to demonize 'fundamental' research like this. On the other hand, I argue that it is more productive to develop dialogues between scientists and broader publics that render accurate depictions of scientific practice and foreground what is at stake vis-à-vis "key

ethical, religious, and metaphysical questions so that debate can proceed apace with the science. The only reason for ethics to lag behind this line of research is if we choose to allow it to do so" (Cho et al., 1999, p. 2087).

The *Saccharomyces cerevisiae* 2.0 (Sc2.0) project is an international endeavor started in 2011 by synthetic biologists to create a fully synthetic, designer yeast genome, chromosome-by-chromosome (Dymond et al., 2011; Synthetic Yeast 2.0, 2022). When complete, Sc2.0 will become the world's first eukaryotic organism made entirely from synthetic DNA. This organism has been designed *in silico*, meaning that the sequences of its constituent parts were assembled using computers rather than by working with yeast directly under the microscope (*in vivo*). The new Sc2.0 yeast will include several features that are not part of *Saccharomyces cerevisiae*'s "wild-type" genome; these features will in part streamline further, future modifications (Sliva et al., 2015). Currently, the research teams working on this project have successfully synthesized nearly 99% of the genetic material in *Saccharomyces cerevisiae*'s genome (Szymanski, personal communication, 17 December 2019). This new chapter in biological research raises questions regarding the applications of synthetic organisms and the future of yeast, particularly in its associations with humans. Namely, will synthetic organisms pose any unforeseen risks? Will synthetic yeast become a fixture of new, fermented foods? Will it create "crosses" with "wild" yeast, and what will be the outcome? Synthetic biologists lay most of these concerns to rest by clarifying that synthetic organisms like Sc2.0 are primarily models for understanding biologic processes more generally and are lab-bound beings with integrated vulnerabilities that make them ill-suited for life outside the laboratory. At the same time, the scientific imaginary surrounding synthetic organisms is replete with examples of proposed applications, some of which have already leaked out into the "real world" in small ways.

As a part of the broader synthetic biology paradigm, the Sc2.0 project raises potential questions of ownership, authenticity, and power dynamics in human-yeast laboratory assemblages (Cho et al., 1999). Scientists working in synthetic biology point to the promising potentialities of this work for answering big questions, like "What is life?" and tackling daunting challenges, from energy needs to intractable medical conditions (Dymond & Boeke, 2012, p. 170). However, what these developments in genomic engineering will mean for human-yeast associations both in diverse laboratory spaces and in breweries, bakeries, and nature itself is not yet clear. While it seems there is little motivation at present to replace "natural" *Saccharomyces* with its synthetic likeness in food-oriented applications, we as part of the larger public can conceive of various potential futures, both fruitful and perilous.

I suggest that materiality and meaning are foregrounded in these assemblages through intersections of labor, values, and identities arising from the contributions of both *Saccharomyces* and *Homo sapiens*. This is a normative guidepost for this project in that I see both physical and metaphorical facets of bodies as intertwined and integral to the composition of a fermentative and fermentation-inspired politics centered on synthetic yeast—what I call 'zymurpolitics' (Furness, 2022). Part of this orientation stems from the work that both human and yeast bodies do, and I posit that social scientists should seriously consider labor in more-than-human terms as a useful conceptual frame for thinking critically about the intersections between humans, scientific practice, and other species in emerging assemblages shaped by technological advancements in genomic engineering that increasingly blend human and non-human DNA and genetic logics.

Problem statement: Why study *Saccharomyces cerevisiae*?

The rise of yeast as a model organism that is used to test genomic engineering techniques and produce specific proteins in 'cell factories' emerged in tandem with new applications of its labor. As yeast continues to become an ever-more essential collaborator in biotechnological advances, the range of its applications sprawls from the fermentation of comestibles to biofuels, bioremediation, pharmaceuticals, biosensors, alternative proteins, and synthetic vaccines (Heinemann and Panke, 2006). Most broadly, current and future applications of yeast will have significant effects on food systems, energy sources, and pharmaceuticals at societal scales, both directly and indirectly (Murray, 2020). Recent endeavors to use yeast to replace meat, facilitate bioethanol production, and act as a conduit for various drugs demonstrate this phenomenon of transformative potential. More narrowly, scientists working on the frontiers of these applications must make decisions about how to approach working with another lively organism in terms of ethics and intellectual property (Kaebnick et al., 2014).

Synthetic biology aims to create new genetic resources for understanding and managing life at the most minute levels. Its direct, engineered interventions result in new bodies and associations between humans and nature, regardless of its intent. Specifically, *Saccharomyces cerevisiae* is now involved in efforts to create more sustainable futures, and the political and ecological ramifications of the "nature based" solutions of which it is envisioned to be part of are not fully certain (Khalil & Collins, 2010). Synthetic biologists tend to promote notions that yeast will help 'save' the planet through various applications, though questions about nonhuman labor, value, and multispecies relations remain unaddressed.

With all of this at stake, *Saccharomyces* is a worthy subject of social science investigation into scientific practices. In this study, I seek to address the uncertainties surrounding our future

interspecies relations with *Saccharomyces* by drawing on more-than-human, assemblage-inflected and critical feminist political ecological scholarship. This work seeks to destabilize certainties surrounding yeast in contemporary bioscience, problematizing multispecies relationships in laboratory spaces. Problematizing entails naming a problem, showing it to be contingent, and showing old patterns of common sense to be problematic in and of themselves. As a sort of meeting between science and technology studies and more-than-human political ecology, I draw on these different literatures to explain and critique synthetic yeast assemblages as in-process and open to contestation rather than foreclosed and fixed, despite a significant body of scientific discourse suggesting otherwise.

This research morphed over time as I attempted to follow the Sc2.0 project and amended my own initial lack of knowledge about it. In the vast world of synthetic biology research and literature that I continued to stumble upon I see echoes of yeast's own diversity—across species, strains, and (increasingly) genomes. This diversity characterizes the bounds of this study, which varied and 'budded' like yeast cells throughout the research process in ways that were often difficult to anticipate or manage.

Research Goals

Broadly speaking, the goal of this project is to trace and analyze how new technologies of synthetic biology may re-shape relations between society and nature, with an eye toward situations that have the potential to exacerbate social inequalities (Rossi, 2013). In the tradition of political ecology (Robbins, 2011), it seeks to attain the oft-sought but seldom-achieved goal of dissolving the tension between social and ecological concerns, as Ethan Miller (2019) has skillfully begun to do in recomposing economy, society, and environment (Turner, 2016).

Synthetic biology imbricates social concerns in the form of new genetic hopes and fears with ecological concerns in the form of mitigating human-caused environmental challenges and the potential for humans to figure ever-more prominently as co-directors of evolution through new genetic lineages linked to synthetic organisms. Of course, each of these realms of concern is linked to political and economic forces as well.

More specifically, this research seeks to examine how different paradigms and technoscientific assemblages alter yeast-human dynamics in laboratory spaces. The ways in which we and *Saccharomyces* associate has implications for the production of new forms of energy, medicine, and food, and is revealing in terms of how humans relate to other species, particularly microbes, in the (post)Anthropocene. To better understand the interwoven practices and forces reshaping future forms of (synthetic) life, this research aims to:

a. Understand how scientists working with yeast interpret it as an entity in laboratory settings.

b. Scrutinize the politics of synthetic yeast, particularly in emerging associations shaped by technological innovation.

c. Theorize empirically (Swedberg, 2016) about the potential changes synthetic organisms like Sc2.0 may bring to multispecies relationships across space.

Significance and organization of the work

While this project originally aimed to understand scientists' first-hand perspectives and experiences working with yeast, over time it drifted more toward tracing a sort of partial, fragmented and rhizomatic anti-genealogy (Deleuze & Guattari, 1987, p. 11) of synthetic yeast

through scientific literature and other secondary sources. This was primarily due to difficulties in accessing research participants and relevant field sites. As I saw it, each laboratory I might include in the study was an assemblage of actors operating at various, overlapping spatial and temporal scales. From this perspective, connections may be drawn discursively across time and space and scales are contestable rather than ontologically fixed and nested (i.e., increasing in size from "local" to "global").

Throughout this process, I remained committed to tracing and understanding the networks of forces that connect *Saccharomyces cerevisiae*, humans, computers, scientific knowledge, and laboratory equipment, to name a few. These relationships matter and exist in various states of permanence depending on what makes them cohere or come apart. Drawing heavily on Latour's (2005) conceptualizations, I emphasize these "matters of concern" to show why yeasts are actors worthy of consideration in these contexts, not for the sake of novelty but because they *do* things and make things *happen*. As I will discuss at length later, there is a politics of yeast in which power, agencies, ethics, and imagined futures comingle and contest the present.

Thematically, this project owes much to recent work by Erika Szymanski, who has published on the *terroir* of synthetic yeast (2018a), metaphors employed in synthetic biology (2018b), the malleability of the yeast genome and biological identities (Szymanski, Vermeulen, & Wong, 2019), and scientists' sensibilities in laboratory spaces (Calvert & Szymanski, 2020). This work is inspired by and continues these critical examinations of the constructed nature of norms and scientific facts that shape humans' interactions with yeast, with an eye toward tracking with the rapid pace of change in synthetic biology as the Sc2.0 project concludes and the era of synthetic eukaryotes unfolds.

This work makes several contributions to literature on science and technology studies and

more-than-human geographies. First, it follows up on some of the ethnographic work conducted by Szymanski and Calvert on earlier stages of the Sc2.0 project. This was interesting both for the purposes of comparison and frustrating in that many researchers I contacted had begun to move on from Sc2.0 before I really got started with my data collection. Still, my virtual observations of scientists working with synthetic yeast corroborated many of Szymanski and Calvert's earlier findings while also adding additional analysis of specific metaphors and practices employed to enact synthetic yeast as an object of scientific knowledge. Because this research spanned the targeted completion date for Sc2.0 (2020), I witnessed the ongoing pivot beyond yeast and toward subsequent projects involving further genetic modification and "humanization" of microbial and mammalian cells.

Further, this project explores the worldmaking associated with several consequential types of metaphors common in different synthetic biology contexts, at different scales. Most broadly, metaphors of genes-as-information have and continue to reshape understandings of what synthetic organisms like Sc2.0 are, what they should be like, and what they can do. These metaphors have complex interactions with tendencies (many implicit) to commodify nature through intersections with intellectual property and therapeutic applications. These tendencies exist in tension with the open-source ethos and rhetoric broadly embraced within synthetic biology. Information-based metaphors are not unique to synthetic yeast, but they are arguably implemented in new, further-reaching ways than before thanks to technological advances reinforced by emerging conceptions of the promises of whole-genome engineering.

At more intermediate scales, machinic metaphors—like comparing cells to "chassis"—enforce narratives of control, mutability, and universality of cells and genetic material qua replaceable parts. Other metaphors based on software and circuitry have similar, but not identical effects. This is noteworthy because this active casting of nature occurs under and alongside the aegis of

fundamental research that ostensibly describes what life is and how it works at a foundational level in a neutral way. This situation exists alongside the "organism agnosticism" common to synthetic biology and in tension with the "feeling for the organism" described by Calvert and Szymanski (2020) as a way in which scientists still find uniqueness and importance in their particular model organisms, especially those as charismatic as yeast. Additionally, these metaphors entrench human-nonhuman divisions in power differentials that promote anthropocentrism and fail to increase attunement and affinities toward other species, desensitizing scientists to their research subjects.

In a more "local" sense, I observed the use of militaristic metaphors by researchers in the Boeke Lab at NYU-Langone that were either less common or uncommon in extant literature on Sc2.0. I argue that these metaphors are not necessarily intended to weaponize practices and rhetoric involving synthetic yeast, but that they represent a departure from more common discourse that shapes multispecies relationships in the laboratory and therefore are worth following. The full ramifications of this difference, including its staying power, are still playing out.

Finally, much of the contribution of this dissertation is in its synthesis of literature ranging from feminist-inflected STS to more-than-human geographies to political ecology and philosophy. It attempts to draw upon these vast, sometimes overlapping, and sometimes conflicting bodies of research to explore new ways of thinking about and with synthetic organisms, striving toward a cosmopolitics of synthetic yeast, or what I call 'zymurpolitics.' This theoretical contribution extends the recognition that multispecies, microbial-human assemblages are political and laced with power to the emergent realm of synthetic eukaryotes that will surely swell with new species in the years to come.

This dissertation breaks with the common five-chapter monograph format. I wanted the

document itself to embody the multiplicity and ephemerality of yeast, which buds, branches, divides, and borrows from neighboring cells. I have thus written a handful of chapters that attempt to illuminate some of the most salient observations from this project and which overlap and tumble over one another in their efforts to develop and thrive. My hope is that they help sketch the contours of an assemblage but also point to the many unknowns and contingencies held together by it. This form also mimics my understanding of the multispecies relations I write about, which are patchy and open to transformation. This approach is speculative, risky, and yet reflective of the challenges I encountered in writing the dissertation. An additional justification for the work's final form is that the work I ended up accomplishing as I attempted to follow yeasts and humans through social, scientific, and political entanglements did not fit neatly into distinct results and discussion chapters.

The text is divided into several parts. First, I 'step back' to review literature (Chapter 3) that frames this project conceptually and epistemologically. This body of literature and theory is fairly diverse and stakes out the menagerie of ideas that I attempt to bring together in this work. Chapter 4 explains my methodology in detail along with my case studies, providing more context for how I pursued the research goals set forth here. The next part (Chapter 5) draws on existing literature to trace the development of yeast as a model organism and the subsequent development of synthetic biology as an emergent field. In this section, I highlight a number of the assumptions and principles that helped create the conditions for synthetic yeast, which sets up the next part of the work. The following chapter (6) continues the tracing of synthetic yeast from a political ecological standpoint, emphasizing the various ethical, legal, and social forces that intersect with scientific practice in synthetic biology and offering a glimpse into the vast, interconnected and international world of scientific research related to synthetic yeast. Chapter 7 homes in on synthetic biologists' discourse pertaining to synthetic yeast, describing and

problematizing the metaphors used to conceptualize organisms as objects of knowledge production. In this chapter I draw insights from a text corpus of academic literature on synthetic yeast that I gathered, highlighting themes in scientific discourse that offer insight into how ideas about the nature of yeast are produced, propagated, and made durable. The following chapter (8) blends interview data and existing literature to offer sketches of aspects of this 'yeasty' nature, teasing apart themes of labor and biopolitics. A concluding chapter (9) summarizing the contributions, limitations, and potential future directions of this research follows. The final part of the dissertation (Chapter 10) is a brief appendage that highlights the salient characteristics of "zymurpolitics," arguing for a cosmopolitics tailored to the emergent possibilities and contingencies of synthetic life.

3. THEORETICAL FRAMEWORK AND LITERATURE

> "Thinking is neither a line drawn between subject and object nor a revolving of one around the other. Rather thinking takes place in the relationship of territory and earth…involving a gradual but thorough displacement from text to territory."
>
> -Gilles Deleuze and Félix Guattari, *What is Philosophy*? (French original *Qu'est-ce que la Philosophie*?, 1991), trans. Graham Burchell and Hugh Tomlinson (Columbia University Press, 1994)

> "On those stepping into rivers staying the same other and other waters flow."[1]
>
> -Heraclitus of Ephesus

The aim of this chapter is to contextualize this project by outlining the key bodies of literature and the theoretical currents from which it emerges. I focus on some of the critical research conducted by social scientists in recent decades, drawing on key concepts in geography, philosophy, ecology, and other social '-ologies' to address the research questions outlined in the previous chapter. Although I've parceled out these influential coagulations of knowledge under a variety of labels below, this study primarily draws on three major fields of scholarly literature: political ecology, science and technology studies (STS), and more-than-human geographies (Figure 2).

[1] In the revised *Stanford Encyclopedia of Philosophy*, Daniel W. Graham (2021) discusses three quoted fragments attributed to Heraclitus of Ephesus by later writers, noting "It is possible to see Cratylus, a late follower of Heraclitus, supplying the wayward reading" commonly quoted as "No man ever steps in the same river twice." (2021). Accounting for stylistic and dialectical similarities between the fragments and what else is known about Heraclitus, the quotation I've copied above may be truer to his actual musing. Graham continues: "If this interpretation is right, the message of the one river fragment…is not that all things are changing so that we cannot encounter them twice, but something much more subtle and profound. It is that some things stay the same only by changing. One kind of long-lasting material reality exists by virtue of constant turnover in its constituent matter. Here constancy and change are not opposed but inextricably connected. A human body could be understood in precisely the same way, as living and continuing by virtue of constant metabolism… On this reading, Heraclitus believes in flux, but not as destructive of constancy; rather it is, paradoxically, a necessary condition of constancy, at least in some cases (and arguably in all)" (Graham, 2021).

Situating this research across intersections of political ecology, STS, and more-than-human geographies highlights questions of power, biopolitics, ethics, and ecology of the material, living world. While each of these frameworks contributes ideas and sensibilities to this work, their contributions are not necessarily equal. Topically, I follow the contours of STS most closely, but conceptually, assemblage thinking led this project throughout. Assemblage thinking is important in this work because it foregrounds flows and fixities and helps make researchers aware of how processes and encounters might congeal into something lasting and durable. For example, I will argue that scientific discourses about synthetic yeast are made durable through their repetitive use in peer-reviewed literature and conference proceedings. Assemblage thinking may also 'cut' the other way, helping overcome reductive scientific framings through tracing interactions and destabilizing assumptions linked to power and scale.

Assemblages—which may be understood as alliances or ad-hoc groupings of diverse elements—are key to the approach of actor-network theory. Drawing upon Actor-Network Theory (ANT) and feminist critiques of political ecology (Rocheleau et al., 1996) and science and technology studies (STS), I trace synthetic yeast both in logocentric (via discourse) and materialist ways, attempting to draw together and hold in tension various approaches to understanding how it functions as an object of scientific inquiry and how it might reshape human-ecological relations.

In drawing together theoretically-pluralist ideas and approaches, I attempt to hold them together despite tensions between them. Yet, their consolidation and commensurability is not my primary focus. As I wade through the various theoretical and conceptual currents that nourish my thinking, I will point toward subsequent chapters where I develop and apply these ideas in the context of this project.

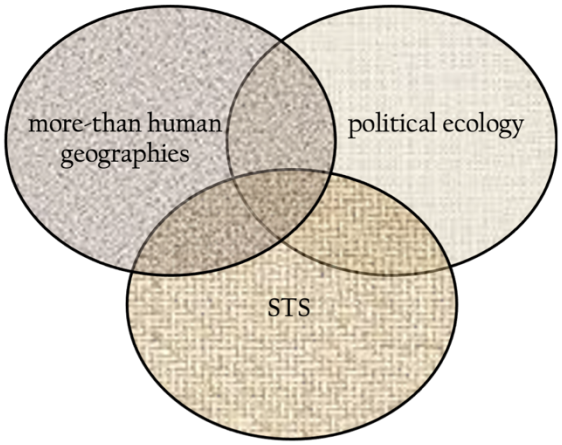

Figure 2: A crude rendering of the dissertation's place in the literature (not to scale).

Political ecology

At the 2019 meeting of the American Association of Geographers, Julie Guthman argued that political ecology is no longer worth classifying as a theory due to its increasing vagueness (April 5). At best, she suggested, it could be thought of as an approach to understanding the interplay of social, political, and environmental forces in assemblages of humans and nonhumans. Working from this critique, I employ political ecology as a general approach within my research. This approach complements other strands in this work (namely, assemblage thinking and multispecies ecologies) and remains useful for understanding processes and power dynamics. While a broader discussion of the strengths and drawbacks of political ecology is beyond the scope of this work, I will briefly summarize some of its key aspects as they influence this project.

Broadly, political ecology (PE) conceives of environmental phenomena as political, complex relations mediated by social and economic forces. In a foundational text, Blaikie and Brookfield (1987) explain that political ecology "combines the concerns of ecology and a broadly defined political economy. Together this encompasses the constantly shifting dialectic between society

and land-based resources, and also within classes and groups within society itself" (p. 17). With roots in political economy, studies of environmental degradation in the Global South, cybernetics and systems theory following the Second World War, cultural ecology from geography, ecological anthropology, and natural hazards research, PE emerged from a variety of fields, which are reflected in its internal tensions (Watts, 2017). As Michael Watts (2017) points out—setting the stage for Guthman's critique—political ecology "never represented a coherent theoretical position" due to contested meanings of its constituent parts (p. 261). Yet, its persistence as a popular framework speaks to its merits, including a focus on how social relations shape practice and the abilities and constraints of exploited and vulnerable populations.

In the decades since the 1980s, PE has evolved and addressed some of its early blind spots, thanks in part to poststructuralist influences that drew attention to the importance of materiality, social construction of the environment, and the need to problematize 'ecology' (Watts, 2017). Poststructuralism also imparted a concern with knowledge and discourse to newer forms of PE (Peet & Watts, 2004). As the world's population became majority-urban, Urban Political Ecology drew attention to cities, which had mostly been overlooked in previous PE research. Swyngedouw and Heynen (2003) applied PE to political and economic processes that contribute to the exploitation of nature, which Peet and Watts (2004) echo in arguing that "the politics of ownership and control must be central to political ecology" (p. 12). Recognizing these "power geometries" (Massey, 1994) lends a critical edge to more-than-human geographies, which have been criticized for failing to adequately account for discrepancies in power and political configurations.

While political ecology acts mostly in the background of this work, I will foreground it in select places. In chapter 6, I will attempt to trace some of the political and economic dimensions

of synthetic yeast, paying attention to aspects of companies, funders, and legalities implicated in Sc2.0.

Science and technology studies

Social studies of science have offered inspiration to geographic research in several key areas. John Law and Bruno Latour's (among others) work on actor-network theory (Latour, 1999a; Law, 2008), Donna Haraway's (1998) feminist approaches to thinking about science, and Isabelle Stengers' (1997) work on the history and philosophy of science have offered critical insight into intersections between humans and other beings (Nightingale, 2014). Science studies and more-than-human geographies share an interest in how knowledge about the world is produced (Greenhough, 2014). In the case of this project, science and technology studies (STS) offers a useful lens for examining emerging tensions between the audacity of engineering approaches to working with life and the speculative hopefulness more common in traditional biological research (Davies, 2011).

A key contribution of feminist political ecology to STS is the destabilizing of Science[2] and scientific knowledge as uncontested entities. As Nightingale (2014) reminds, "science itself, and the privileging of particular kinds of knowledge, is a deeply political process that reflects global power dynamics and the scaling of 'environmental' problems" (p. 128). Thus, STS offers a way to critically engage with the production of scientific knowledge, which is often imbricated with certainties and binary divides between society and nature, objects and subjects, and active and

[2] Here I am intentionally using capital 'S' Science in the same way that Latour (2004) does, denoting the institution of Science which lays claims to objectivity and universality. Lower-case 'science' is an important method and approach to knowledge production that is used by scientists of all sorts, but it is only one means of knowing and understanding the world.

passive entities. Seeing these dualisms as overly simplistic and problematic, STS challenges the notion of scientists as dispassionate observers and demands greater reflexivity from researchers. Science is not a disembodied "view from nowhere" (Shapin, 1998) but always emplaced and translated by humans.

The inevitable shaping of science by social-material environments points to the need to challenge reductionism in science and bring it out of isolation and into conversation with the broader contexts within which it is conducted (Greenhough, 2014). Hinchliffe et al. (2005) note this perceived division between science and politics, writing: "Science has been relied upon to speak of and for nonhumans (what is the matter?) and Politics has been relied upon to decide what is in people's interests (does it matter?)" (p. 644). Understanding politics, law, and nonhumans as contributing to the practice of science helps expand our notions of what matters in the first place and helps us see the world as complex, hybrid, and networked. This goes for humans too, as Haraway (2006) evokes in her figure of the cyborg. Technological advances make hybridized combinations of technological and living things ever more ubiquitous in our world (Nightingale, 2014), and subsequently "We make decisions not as human individuals, but as people who metabolize genetically-modified foods; donate and receive blood, organs, and DNA; cohabit with pets and other animals; and enhance our bodies with visual, auditory and other forms of technologies" (Greenhough, 2014, p. 97).

Critical geography also owes a debt to STS for its influence in deconstructing ecological and environmental representations, avoiding confusion with the objects themselves (Braun, 2000; Demeritt, 1998). In this line of reasoning, Haraway and Goodeve (2018) offer an invaluable example of how genes are abstract concepts constructed to help make sense of complex biological and biochemical processes, arguing that there is danger in forgetting that these abstractions are not "life itself." This is, not to say that physical processes are nonexistent or

meaningless, but rather to take a more agnostic view regarding our understanding of them and to recognize that our understandings are representations of reality (Demeritt, 1998). In sum, "There is an important politics to the making of science that STS highlights, as well as an important politics that derives from such sciences…that political ecologists emphasise, which have different levels and scales of impact" (Nightingale, 2014, p. 131). This making of science and representations is important to this work, and later I will explore how synthetic yeast is constructed through scientific rhetoric at the scale of the laboratory.

More-than-human currents in geography

Twenty-some years into the 21st century, it is abundantly clear that despite the many marvels of science shaping the world, a great deal of public concern is paid to the interface between human and nonhuman encounters. "Natural" hazards, climate change, and zoonotic infections highlight the liveliness of a world presumably under control and the contested approaches taken to address these challenges. Nature was no longer on the other side of the glass, so to speak. Increasingly robust human abilities to reshape our own bodies and bodies other than our own through genetics raised questions about what it truly means to be human and where to draw that distinction. "In short," Greenhough (2014) writes, "it had become very difficult to divide the world (and geographical research about it) neatly into spaces of 'human' and 'physical'/'non-human'" (p. 94).

Revitalized by encounters with social and cultural theory and critical feminist perspectives in the 1980s and 1990s, in the 2000s a cohort of cultural geographers returned to a concern with materiality as a fundamental aspect of human-environment interactions. This shift in focus had roots in studies of material culture that have long existed within geography, including Carl

Sauer's studies of landscape evolution and Kniffen's work on cultural artifacts and vernacular architecture, among others (Jackson, 2000). Spanning urban (Latham & McCormack, 2004), feminist (Nash, 2004), legal (Delaney, 2001), performance studies (Dewsbury, 2003), and more, these currents rippled around "the most enduring of geographical concerns—the vital connections between the *geo* (earth) and the *bio* (life)" (Whatmore, 2006, p. 601). And this "*earthlife* nexus," as Whatmore terms it, has reemerged in creative, new directions after largely disappearing from cultural geography in the latter decades of the 20th century (2006, p. 601). Engagement with philosophy and science and technology studies foregrounded theory as not merely representational but rather actively constitutive of the world (Whatmore, 2006).

As such, this blooming of new materialisms in geography was not so much an abrupt shift as a 'return' to seemingly-familiar 'matters of concern' (Latour, 2004b) through repetitive engagement, a process which Whatmore (2006) likens to turning over pebbles on a beach. Indeed, this return can be contextualized by the collisions of technological and political forces around multispecies interactions in the early 21st century, ranging from debates over GMOs to climate change and conservation (Nowotny et al., 2001). There is an important dimension to this return, however, that sets it apart from previous iterations of material studies. The register of the conversation no longer centered on "the indifferent stuff of a world 'out there', articulated through notions of 'land', 'nature' or 'environment'" but about an "intimate fabric of corporeality that includes and redistributes the 'in here' of human being" (Whatmore, 2006, p. 602). In bringing together ecological matters that (attempt to) transcend some degree of anthropocentrism, these 'new' practices and orientations mark what Whatmore (2002) calls 'more-than-human' approaches.

Thinking in more-than-human terms suggests a decentering of humans as the unquestioned subjects and sole agents in the world. Related to this philosophical shift is a sense of the

importance of *mutual relations* in understanding what distinguishes beings and things from each other. These relational ontologies, developed by thinkers ranging from Spinoza to Whitehead to Deleuze and others, speak to an energized materialism, which is always processual and in the making. As Bennett (2004) puts it, "Humans are always in composition with nonhumanity, never outside of a sticky web of connections or an *ecology* [of matter]" (p. 365; emphasis original). Agency is an important dimension to this web; humans are far from the only 'things' that can actively 'kick back' (Barad, 1998).

The materialist returns of cultural geography in the early years of the 21st century have advanced several research foci in particular. One is a shift away from discourse and toward practice, foregrounding bodily practice and performance and reworking "discourse itself as a specific kind of practice" (Whatmore, 2006, p. 604). Another is an affinity toward affect rather than meaning, which is to say that what things *mean* is no longer as concerning as what they *do*. Affect refers to "the force of intensive relationality—intensities that are felt but not personal; visceral but not confined to an individuated body" (Whatmore, 2006, p. 604). For DeLanda (2002), affect is similar to Gibson's (1979) "affordance." Each of these ideas has connections to the earlier work of the ethologist Jacob von Uexküll (1957) in his rendering of an animal's *Umwelt* (1957). Defining affect as "the actions a body (both human and nonhuman) can practically do in a particular context," Deleuze and Guattari (1987) underscore the centrality of affect to embodied studies, arguing "We know nothing about a body until we know what it can do, in other words, what its affects are, how they can or cannot enter into composition with other affects, with the affects of another body…to destroy that body or to be destroyed by it…to exchange actions and passions with it or to join with in composing a more powerful body" (p. 257). Importantly, the power of a body to affect other bodies carries within it a "corresponding

and inseparable" capacity to *be* affected, in keeping with a relational ontology (Deleuze & Guattari, 1987, p. 257).

Another relevant strand of research emphasizes more-than-human inquiry, which means adding animals and technologies (among others) to the list of agents that can effect socio-material change, while retaining traditional human agency as an important consideration (Wolfe, 2003). Working synergistically with increased emphasis on practice, this broadening of modes of inquiry also pays attention to the entire range of senses and capabilities that co-constitute material worlds, what Wolfe (2003) calls a "bodily sensorium." Dovetailing with poststructuralist political ecology, a focus on the politics of knowledge production responds to this more diversified agency and expertise alongside the reflexive acknowledgement that science and social science play a role in constituting the phenomena they study (Nowotny et al., 2001; Stengers, 1997).

This "ongoing realignment of intellectual energies" (Whatmore, 2006, p. 604) is timely in its preoccupation with life, broadly speaking. Intersections between *bio* and *geo* in an age of socio-technological possibilities and controversies distinctly contextualize how "matter comes to matter" (Barad, 2003)—an outcome of studying social relations through a less-anthropocentric lens—and "are at once about the most mundane and intimate aspects of social life—food, health and kinship—*and* the sites of prolific inventiveness in the life sciences" (Whatmore, 2006, p. 605; emphasis original). 'Life' itself has changed; technologies of genomic engineering increasingly draw humans into the realm of manipulable and commodifiable 'natural resources,' joining the plants and animals that have long been considered part of this assemblage (Whatmore, 2006, p. 605). As I will discuss at length later, synthetic biologists work with a set of priors that understands genetic material as fundamentally commensurate across organisms. This homogenizing of biological differences (which facilitates commodification and

capitalization) may be superficially in keeping with a more-than-human orientation, but there is an important distinction here: it purports to smooth over variance instead of acknowledging and learning from diversity, as more-than-human geographies aspire to.

Vibrant materialism and agential matter

An ontological turn in the social sciences has increasingly rejected the utility of human-nonhuman binaries and the idea that only humans form social structures. Related to the rejection of dualisms, a collection of thought sometimes labeled "vital materialism" draws on monistic understandings of the world expressed in various forms in the work of Lucretius and Spinoza. Monism (in Western philosophy, as distinct from religion) is the assertion that everything from 'mind' to 'matter' consists of a single, universal substance, whether that be "God/Nature" (Spinoza, 2006) or the "primordia" of Lucretius, which today we might call atoms or matter-energy (Bennett, 2010, p. x). The notion of "conatus," which recurs in Spinoza's writing, denotes a striving action or "will to live." As opposed to the cognitive or affective, it relates to purposeful, but not necessarily ultimately rational, action (see Spinoza, *The Letters,* epistle 58).

(Re)Emerging in the 19th century, vitalism responded to mechanistic, deterministic conceptions of life based on advances in chemistry, biology, and physics. Thinkers employing vitalist ideas like Henri Bergson[3] (1907) advocated for direct experience rather than rationalism to understand nature. "Nature was not, for Bergson and Driesch, a machine, and matter was not

[3] Bergson is often considered a proponent of vitalism because of his concept of *élan vital*, but he also criticized vitalism in his book *L'Evolution Créatrice* (1907), writing about the futility of trying to reduce finality to individuality ("C'est donc en vain qu'on pretend rétrécir la finalité à l'individualité de l'être vivant. S'il y a de la finalité dans le monde de la vie, elle embrasse la vie entière dans une seule indivisible étreinte") (p. 38).

in principle calculable: something always escaped quantification, prediction, and control" (Bennett, 2010, p. 63). Bergson (1907) used *élan vital* (roughly, "vital impetus") as a livelier explanation of evolution and humanity's creative impulses. Hans Driesch—whose early work in embryology established the idea of totipotent and pluripotent cells—proposed a revitalized notion of Aristotle's entelechy, connoting a nonspatial, intensive life-force. These (and other) neo-vitalist philosophers grappled with the distinction between life and matter, though for Bergson, "these categories fix what really are but "tendencies" of a cosmic flow" (Bennett, 2010, p. 76). Such an orientation points to an ecological sensibility in which relationality and process ascend to prominence, overshadowing individuality. Echoing and inverting Spinozist monism, Deleuze (2006) conceptualizes this idea as "ontologically one, formally diverse," and Deleuze and Guattari (1987) offer the seeming paradox of "pluralism = monism" (p. 20). These ideas set the stage for later work on vital materiality.

Bennett (2010) introduces her work in *Vibrant Matter* by proposing to "turn the figures of "life" and "matter" around and around, worrying them until they start to seem strange, in something like the way a common word when repeated can become a foreign, nonsense sound. In the same space created by this estrangement, a *vital materiality* can start to take shape." (p. vii; emphasis original). However, Bennett (2010) is quick to distinguish her work from traditional vitalism or what might be called a "life force," emphasizing the equivalence of affect and materiality in her thinking (p. xiii). Bennett (2010) traces a rough equivalence between Spinoza's "conatus," Thoreau's "wild," Foucault's "unthought," Deleuze's "virtual," and her own "thing-power" in staking out her understanding of vibrant matter. Still, "thing-power" belies the un-fixity or stability of material, which arguably may be more accurately conceived of as forces, energies, or intensities. In exploring the politics of (re)arranging landscapes that humans can apprehend, she queries the "abilities" of nonhuman bodies. Notably, her thoughts on vitality borrow from

Deleuze and Guattari's (1987) "material vitalism" explored in their "Treatise on Nomadology," which describes vitality as immanent in 'matter-energy' (Bennett 2010, p. x)[4]. "The point is this: an active becoming, a *creative not-quite-human force capable of producing the new*, buzzes within the history of the term nature. This vital materiality congeals into bodies, bodies that seek to persevere or prolong their run" (Bennett, 2010, p. 118).

Vital materialism has been critiqued by Marxian thinkers for overlooking the crucial ways that human power and social structures have shaped historical materiality. Bennett (2010) contends that vital materialists like Kafka, DeLanda, and Vernadsky "do not claim that there are no differences between humans and bones, only that there is no necessity to describe these differences in a way that places humans at the ontological center or hierarchical apex. Humanity can be distinguished, instead, as Jean-François Lyotard suggests, as a *particularly rich and complex* collection of materials" (p. 11; emphasis original). In this sort of materiality, the world is not flat nor full of myriad actors equal in power, but rather richly contoured. A critical, vital materialism acknowledges that some agents are more powerful or more adept than others at congealing power into durable structures, while considering the agency of even small or less-powerful actors. Bennett (2010) insists, "To put it bluntly, my conatus will not let me "horizontalize" the world completely" (p. 104). The politics of such a critical, vital materialism can be conceived of as the search for a more-connected collective with more channels of communication, what Latour (1999b) calls a more "vascularized" collective (p. 109).

[4] "In sum, when Deleuze and Guattari speak of a material vitality, they do not mean simply to draw attention to a "Hobbesian" movement of bodies in space. Neither are they making the familiar point about the *historicity* of objects, about the way the form and meaning of things change as they age and detach from a social whole or become embedded in new relations with new things. (This is what the "social lives of objects" tradition in anthropology, sociology, and science studies does.) What Deleuze and Guattari set their sights on is something else: a vibratory effluescence that persists before and after any arrangement in space: the peculiar "motility" of an intensity" (Bennett, 2010, p. 56).

Of course, it is difficult to decenter the human perspective—evocative of the observer effect in physics, Bennett (2010) reminds us that "It is easy to criticize this realism: Lucretius quests for the thing itself, but there is no there there—or at least, no way for us to grasp or know it, for the thing is always already humanized; its object status arises at the very instant something comes into our awareness"[5] (p. 18). But perhaps the striving to understand nonhuman others in encounters with lively matter can temper human dreams of mastery over nature, reshaping interests and assumptions in the process. Given the pragmatic reality of partial, situated knowledge, Bennett (2010) suggests that perhaps a measured anthropomorphizing can be good if it serves as a check against anthropocentrism.

Working from this understanding of nonhumans (whether living or not), yeasts and other microbes act and become in the world alongside humans, even if their agentic capacities sometimes elude detection. If one takes Latham and McCormack's (2004) understanding of materiality as "processually emergent," one can conceptualize objects as those things whose "becoming proceeds at a speed or level below the threshold of human discernment" (Bennett, 2010, p. 58). Brian Massumi (1995) describes this notion of liminality as a "pressing crowd of incipiencies and tendencies" (p. 91) with a propensity toward action rather than stability. 'Materiality' itself is troubled by this understanding because the word signifies to us a sort of fixedness that comes into tension with the agential and vibrant conceptions described above. What this suggests is that synthetic yeast is part of this process of becoming, and it is susceptible to change based on human interventions in tandem with its own conatus and evolutionary potential. This is a stark contrast to how synthetic biologists generally conceive of organisms like Sc2.0.

[5] "This is the stroke of genius in [Lucretian]…physics: there is no circle, there are only vortices…spirals that shift, that erode" (Bennett 2010, p. 119). See also Serres, *The Birth of Physics*, p. 58.

Microbial turn

As part of the material turn within human geography, previously underappreciated entities and small things began to loom larger in studies of nature-society relations. Lorimer (2017), Paxson (2012), Simard (2018), and others have highlighted how microbes play vital roles in webs of life, from collaborating to construct gut health to making nutrients available to communities of fungi, trees, and insects. Yet despite these vital roles, microbes are often an afterthought or perceived as a danger, if they are thought about at all. There are, of course, exceptions; certainly, the COVID-19 pandemic of the past several years is illustrative of how something as small as a virus can readily consume our attention and encumber economies and institutions. What these examples illustrate is that ecological thinking (contextualizing instead of essentializing) can help navigate the complexities of health and disease, which are far from a simple binary. It is also critical that social scientists consider the interplay of agencies (human and nonhuman), capital, social structures, laws, and more in examining how complex assemblages of life form and jettison connections.

As humans' technological capabilities for doing new things with yeast have increased, there has also been a greater recognition of the microbial world in the social sciences. Echoing Haraway's notion of the cyborg (1991), Stefan Helmreich (2014) and other STS scholars have introduced the figure of *Homo microbis*, recognizing the "human" as an assemblage that includes microbes on our skin and in our guts as a means to increase our awareness of the mosaic of cells that make us "human." In *Metametazoa*, Dorion Sagan (1992) describes the human body as "an architectonic compilation of millions of agencies of chimerical cells" (p.367), nodding not only toward hybridity but also decentered agency. Assemblage strands in the thinking of Bruno Latour, John Law, Isabelle Stengers, and others offers a practical way to consider these

philosophies and epistemologies.

This sort of assemblage thinking offers a framework through which to follow a thing of interest—yeast, in this case—through its interweavings in our lives. This study positions yeasts as multitudinous collaborators that have long been part of life for many humans, but which are gaining new capacities and affiliations through genetic manipulation. As I will discuss in subsequent chapters, *Saccharomyces* has been an organism of concern for scientists (not to mention brewers and other fermenters) for many years. Yet, new technologies in the emerging field of synthetic biology purport to extend the affiliations and applications of yeast further into engineered worlds.

Nonhuman charisma

Jamie Lorimer (2005) identifies the ways in which ecological affordances[6] of nonhuman organisms intersect with those of humans in forming "charisma" (p. 182). This 'nonhuman charisma' denotes distinguishing properties of an agent that bring it into human awareness[7] (J. Lorimer, 2005, p. 180). It can be further broken into constituent subtypes of charisma, but for the purposes of my work I will leave nonhuman charisma as a conceptual whole that helps

[6] "These affordances determine the *detectability* of the species and the ease with which a researcher is able to tune-in to its behaviour. They include a range of parameters that influence a species visibility, including a species' size, colour, shape, speed and degree of movement. They also include aural characteristics such as the presence or absence of a species' noise, call or song and the frequency and magnitude of this sound" (J. Lorimer, 2005, p. 182).
[7] In some strands of observational biology and especially in birdwatching, this collection of detectable characteristics forms the "jizz" of an organism, a term connoting the character or personality of something as perceived by humans (J. Lorimer, 2005, p. 182). This term was first printed in a column of the 'Country Diary' in the Manchester Guardian paper in 1921 (Greenwood & Greenwood, 2018). The author of this column, Thomas Alfred Coward, claimed to have learned the term from an Irishman who could identify local fauna by their "jizz" or general impression, a term related (if only in sense) to the German *gestalt*. Varied discussions about the origins of the word in Irish English (often spelled 'gizz') connect it to ideas of excitement, spirit, or liveliness. In this way it is perhaps linked to the early slang *jasm*, which possibly gave rise to the modern word "jazz" (Porter, 2018), but of course these meanings are not the same as the biological or birding sense.

contextualize human-nonhuman relationships in laboratory spaces. Following Lorimer's framing of 'dwelling' (Ingold, 2000) vis-à-vis human-environment interactions, the nonhuman charisma of an entity stems from its ecological intersections with humans and other beings over time (J. Lorimer, 2005).

Saccharomyces cerevisiae is arguably a charismatic organism—especially to brewers and other practitioners of fermentation—despite being a microbe. Language used to characterize yeast's affect and 'personality' is particularly common in these arenas. Synthetic biologists also recognize yeast's charms at various points, though arguably with less sentimentality. While yeast's charisma was not a primary attraction for the synthetic biologists I spoke with, several of them noted their interest in fermented comestibles and how these intersecting interests were a sort of bonus of working with *Saccharomyces.* I will return to these ideas of charisma inflected through language more fully in chapter 7. Likewise, other laboratory species like mice have their own charisma that affects how scientists choose to work with (or not work with), nurture, and kill them. I will explore the contours and implications of this claim further in chapter 8 in the context of yeasty bodies, bioethics, and power.

Actor-network theory: Opportunities and risks

Actor-network theory (ANT) is a broad, constructivist approach within social science that seeks to avoid essentialist explanations. In other words, ANT judges the successfulness of a theory or explanation through understanding and accounting for the myriad combinations and interactions of humans and nonhumans, rather than by claiming that a particular explanation is true of false. Its name is somewhat of a misnomer, since ANT is not a cohesive theory on its own but rather an approach to exploring assumptions and connections, emphasizing how everything

is connected to everything else. ANT is a material-semiotic method, meaning that it is concerned both with material relations (between things) and semiotic ones (between concepts). It also seeks to describe states of existence rather than explain them and avoids using 'social' forces as given, preexisting entities that can be used to describe phenomena. Rather, social forces are abstractions that help explain reality only after emerging from the process of description. In an ANT approach, nonhumans are afforded agency (*agencement*), defined as the ability to make things happen. The figure of Latour's (1999a) 'actant'—an entity that modifies other entities in 'trials' and whose competence is deduced from its performance—furthers the notion of distributed agency attached to more-than-human ontologies. ANT therefore offers a way to push back against human tendencies to "classify and categorize, asking instead how such categorizations are achieved" (Greenhough, 2014, p. 96). This can be a laborious, messy process marked by fewer answers than questions, but it foregrounds how "the world is so much more crazily hybridised and networked than the conventional lexicons of academia, politics and policy allow" (Philo, 2005, p. 826).

In his essay "On recalling ANT," Latour (1999a) is quick to point out actor-network theory's shortcomings, not least of which is its name. Lamenting the internet-era boom in usage of 'network,' he notes that "twenty years ago there was still some freshness in the term as a critical tool against notions as diverse as institution, society, nation-state and, more generally, any flat surface, it has lost any cutting edge and is now the pet notion of all those who want to modernize modernization" (Latour 1999a, p. 15). Importantly, the singular word 'network' belies multiple senses; commonplace renderings of 'network' imply on-demand access to boundless information through static configurations, what Latour labels "transport without deformation" (Latour, 1999a, p. 15). Unfortunately, this sense is virtually opposite to the richer, transformation-focused processual sense akin to Deleuze and Guattari's (1987) 'rhizome,' which

I will discuss shortly.

Latour (1999a) points out that the social sciences tend to oscillate between two powerful dissatisfactions even more than between typical tropes like agency and structure (1999a, p. 16). At the heart of these dissatisfactions is a problem of scale: when examining the 'micro' level of interactions (often face-to-face), scientists often realize that a broader view (spatially and historically) is helpful in making sense of otherwise disparate and divergent observations (Latour, 1999a, p. 16). Conversely, when focusing on 'macro'-level structures or cultures, a second but equally powerful dissatisfaction may arise; a nagging feeling that something is missing which could be rediscovered if only we connect back to particular, on-the-ground situations. ANT, as Latour (1999a) reminds, is a useful way for noticing these dissatisfactions and recognizing the need to move between them, weaving around and past these blockages instead of trying to bulldoze them. What if, as he suggests, "the social possesses the bizarre property of not being made of agency and structure at all, but rather of being a *circulating* entity?" (Latour, 1999a, p. 17; emphasis original). Thus, this framing of ANT concentrates on movement, and this movement refers to the "summing up of interactions through various kinds of devices, inscriptions, forms and formulae into a very local, very practical, very tiny locus" (Latour, 1999a, p. 17). For assemblage thinkers, there is an analytical imperative to make constant decisions about which "matters of concern" to pursue immediately, which to keep on the sidelines for now, and which to exclude (Latour, 2004a). These decisions are shaped (in part) by the researcher and are political.

There have been tensions between ANT's 'distributed agency' and the positionality of radically different subjects noted by feminist science scholars (Whatmore, 2002, p. 57). Mol (1999) takes up this critique of ANT as being too flat, both politically and ethically, asking what will come after, now that reality (ontology) can be understood as multiple. Robbins and Marks

(2010) remark on the issue of evaluating and drawing conclusions from different assemblage accounts, given that different actors are unequally powerful: "When material objects and ideas are co-constituted, where do we stand to evaluate the role of each in producing the others?" (p. 191). ANT proponents have also been called out for skimming over their own place in the social life that they purport to study. Criticizing ANT's lack of situatedness, Whatmore (2002) accuses Latour of being

> Too chary of situating his own knowledge practices or risking his intellectual acumen by association beyond the academy to nourish the kinds of connection between analytical adventure and everyday apprehension that are the measure of the 'passionate' mode of enquiry that I am after here. (p. 162)

Assemblages are not the only way to understand materiality in human geography, as Robbins and Marks (2010) argue. They caution that ANT-related approaches run the risk of fizzling out into unfinished projects and incomplete thinking. "The Deleuzian injunction to 'begin in the middle' methodologically, which admirably embraces the reality that all actors and subjects are always already themselves in the middle, is an important one for assemblage geography, but also one ripe for abuse" (Robbins & Marks, 2010, p. 192).

Sayes (2014) contends that Actor-network theory can be a coherent methodology for bringing more-than-human agents into social science accounts, raising the question of how model organisms like yeast might be situated within networks of social and political forces. Law's (2008) emphasis on "relational enactment" underscores the futility of thinking in terms of a "stable prime mover, social or individual, to construct anything" from an ANT perspective (p. 151). This orientation allows social scientists to trace the "material circumstances, social ties, established practices, and bodies of knowledge that make up the networks in which model organisms have functioned as research tools, but it also permits a historical 'thinking with' model organisms as companion species" (Langer, 2016, p. 5). This notion of companion species

originates with Haraway's (2003) work and has been extended to fungi and yeast admirably by Tsing (2012). In assemblages involving companion microbes, scientists and yeast are mutually co-produced via their 'intra-action,' Barad's (2007) notion of relational materialization via practices of boundary drawing (1998), which foregrounds diffraction-like analysis of "patterns of difference that make a difference" (p. 72).

Assemblages and rhizomes

Robbins and Marks (2010) describe genealogical assemblages as a way to contest understandings of science as a machine for clearly answering questions. Hinchliffe (2001), in a study of prions and bovine spongiform encephalopathy, suggests that "sociability" is a way to deal with indeterminacy. In this case, a genealogical assemblage demonstrates that conditions and knowledges are the product of various associations (Robbins & Marks, 2010). Similar to Foucauldian genealogies, this approach considers the role of expertise in shaping cognitive divisions and categories of things in the world while adding in the influence of nonhuman actors (Mitchell, 2002). Robbins and Marks (2010) contend that genealogical assemblages share several critical hallmarks, including:

> 1) that social, technological, or scientific ideas, discourses, and expertise do not precede the encounters of objects and actors in which they are entangled; 2) that the material world is not simply a force or set of conditions that provides friction or resistance to social practices or expertise but instead constitutes these; and 3) that narrating histories as if ideas and objects and the social and material were distinct *is itself* an artifact of the historical force relations of those constituent encounters" (2010, p. 190; emphasis original).

These critical moorings resemble an "ecophysiological" grounds of knowledge, as feminist philosopher Babich (1994) terms it. Rather than the human mind serving as the sole wellspring,

knowledge emerges and comes into being through multi-sided interactions and encounters. Thus, genealogy is a way of tracing parts of assemblages, acknowledging forces that act on its constituents, including the searcher herself. "Put differently, a genealogy traces an assemblage, of which it is a constituent part" (Sarmiento, 2015, p. 33).

Braun (2006) writes about assemblage approaches as key to "the making of socionatures whose intricate geographies form tangled webs of different lengths, density, and duration, and whose consequences are experienced differently in different places" (p. 644). The process(es) of congealing into something assemblage-like brings bodily forces and capacities together, forging something new. Similarly, Deleuze (2006) expresses the idea of coalitions that preserve something of each element as "adsorbsion." Yet the whole is never exactly the sum of its parts, "And precisely because each member-actant maintains an energetic pulse slightly "off" from that of the assemblage, an assemblage is never a stolid block but an open-ended collective, a "non-totalizable sum." An assemblage thus not only has a distinctive history of formation but a finite life span" (Bennett, 2010, p. 24). This sense of a vibrating, buzzing collective evokes bee hives or bubbling yeast slurries, one and plural.

The figure of the rhizome is prominent in Deleuze and Guattari's (1987) 1980 landmark work, *Mille Plateaux* (translated into English as *A Thousand Plateaus: Capitalism and Schizophrenia*). Adapting biological rhizomes, they describe a rhizome as a nonlinear network exhibiting "connections between semiotic chains, organizations of power, and circumstances relative to the arts, sciences and social struggles" without a particular order or hierarchy (Deleuze & Guattari, 1987, p. 7). Deleuze and Guattari (1987) contrast this to the arborescent or tree-like model of thinking, which is characteristic of the Western scientific method. This model suggests linearity between knowledge claims and predetermined, 'fruitful' conclusions. On the other hand, the rhizome is horizontal, changing, and lacks centralizing structure. This rhizomatic form follows

several principles. First, any point can be connected to any other point. Second, it exhibits complete heterogeneity. Third, it exhibits multiplicity. Additionally, the rhizome may be broken, but it can start up again from any point of rupture. Finally, a rhizome is a "map and not a tracing," which is to say that it is oriented toward experimentation in the world (Deleuze & Guattari, 1987). Notably, certain biological phenomena like horizontal (lateral) gene transfer support this conceptualization, troubling more common, arborescent metaphors of evolution (Kirksey, 2018).

Deleuze and Guattari's (1987) concept of "articulation" indicates a complex process of world-making where meaning and materiality are linked (p. 238). Articulations are both *molar* (unifiable, totalizable) and *majoritarian*. Categories tend to be easily ontologized, and variation is often subordinate to similarity. In a similar way, Latour (2005) writes about "composition." Both indicate a move from discrete categorization to processes. As Deleuze and Guattari (1987) argue, "there is no longer a tripartite division between a field of reality (the world) and the field of representation (the book) and the field of subjectivity (the author). Rather, an assemblage establishes connections between certain multiplicities drawn from each of these orders…" (1987, p. 25). In more tangible terms, Tsing (2015) describes how "Some fungi have learned to live in intimate associations with plants, and given enough time to adjust to the interspecies relations of a place, most plants enter into associations with fungi…Fungi are thus world builders, shaping environments for themselves and others" (p. 138).

Collaborative world building can be conceived of as occurring between ontologically distinct, well-defined entities, but it can also be understood as reflexively shaping the entities themselves, resulting in hybridizations that are not easily definable. Deleuze et al. (1994) compare hybridity to learning to swim or learning a foreign language: "…composing the singular points of one's own body or one's own language with those of another shape or element which

tears us apart but also propels us into a hitherto unknown…world of problems" (p. 192). These ideas of hybridity recall human-microbe relations, which are both essential for (human) life and are a crucial aspect of human evolution. So rather than attempting to wall off or disentangle human and nonhuman bodies or energies, a more productive approach may be to engage more civilly and subtly with all members of the assemblages we are also part of. But how to do this? Awareness is one step toward this goal. Deleuze & Guattari's (1987) notion of 'diagramming' or 'writing around' can be used as a conceptual frame to explore new ways of thinking that trouble existing assumptions regarding multispecies interactions. In subsequent chapters, I will return to these questions and attempt to tease these ideas apart further, arguing that synthetic yeast can be understood productively as processually becoming rather than already-defined.

A brief note on landscape

In this project, I deploy 'landscape' both literally and figuratively. In hopes of avoiding confusion, I offer the reader this brief, self-conscious note as a means of explanation. Landscape in this work is conceptualized broadly and encompasses both the physical, material, and natural facets of space in addition to its cultural, political, and semiotic aspects. I am generally working in the tradition of Sauer's (1925) *Landschaft*, though with a looser reading of landscape that is more than the simple outcome of cultural agents acting upon a natural medium (Sauer, 1925) or Daniels' and Cosgrove's (1988) "pictorial way of representing." Notably, both of these "old" and "new" cultural geography approaches to landscape imply the omnipresent influence of humanity in shaping the world. Following the writing of Whatmore, I instead wish to emphasize the multitude of agents, many of them non-human, acting to co-create landscapes that are processual and dynamic. In doing so, 'landscape' can be re-animated, 'the human' can be

appropriately seen as a co-constructed and evolving assemblage, and subjectivity can be decentered (Whatmore, 2006).

Virtually all landscapes can be understood as microbial landscapes, teeming with life that humans often fail to detect or consider. Even bodies—which we have already seen to be multispecies and heterogenous—can be a sort of landscape in this understanding. Laboratory spaces where synthetic bodies are constructed are another kind of landscape, and not just in a cute, metaphorical way, if we take seriously the ideas of "gatherings of ways of being in the making," to borrow an idea from Tsing (2015).

Hopefully the different senses and nuances compressed into the nine letters of 'landscape' will be apparent with context. Though I employ landscape to describe areas of varying scales, I strive to clarify this where necessary. Many of these ideas also descend from and inform the "Fermented Landscapes" research paradigm (Myles, 2020), to which this work is spiritually related, so to speak.

An aside: Fermentation and production of landscape

Fermented foods have been critical parts of the human experience for the entirety of our species' existence. Even before the sweeping societal and livelihood transformations of agriculture and domestication, humans sought and benefitted from fermented foods (Money, 2018). In *Cooked*, Michael Pollan (2014) argues that a key distinguishing aspect of our humanity is cooking, which serves both material and semiotic purposes. In a material sense, cooking food changes its chemical profile, making nutrients more accessible and more digestible while reducing the time and energy needed to process (i.e., chew and digest) its nutritional qualities. Fermentation produces similarly digestible foods, albeit via different means, drawing on the

labor of other species to facilitate these aims. Our yoking together with microbes through fermentation has at times been seen as a threat through the lens of Pasteurianism. Heather Paxson describes Pasteurianism as the indirect control of human bodies through direct control of microbial bodies: a form of biopolitics (2012). On the other hand, post-Pasteurians understand human-microbial relations as a more nuanced negotiation of health, wherein 'bugs' that are understood as contaminants or undesirable in Pasteurian logics are instead collaborators that confer health benefits to humans despite the potential for illness when equilibria are disturbed. Such a post-Pasteurian biopolitics envisions raw ferments as a biotechnology for regionalism, pushing back against the dominance of centralized food systems and standardized organisms.

Pasteurianism facilitates mass production and control of otherwise-volatile microbial bodies, solidifying current capitalist logics that seek to order and homogenize life. In contrast, the unpredictability that living things like yeast exhibit has the potential to disrupt efforts to commodify genomes, microbes, and life in general. Perhaps in the vitalities of microbes like yeast we can envision an antidote to global capitalistic hegemony. If we ascribe to this imaginary, foods explicitly shaped by microbes—like fermented foods—have a democratic capacity. If ferments can be enrolled into solidarity movements that seek greater environmental and social justice, perhaps they can be even more effective agents for constructing more habitable worlds. Yet, these 'specialty' products of human-microbe interaction are also classed and 'raced' entities; they are not neutral parts of an assemblage any more than the bodies of synthetic yeast are neutral chassis.

From a more symbolic point of view, food has played a critical role in social connection, linking humans to humans and humans to nonhumans within the context of the broader environment. Food and fermentation moderate our relationship to other species and ecologies

(Hey, 2017). Unlike bacteria, which are autotrophs (able to proliferate and self-sustain from inorganic material), humans and other eukaryotes (including yeast) are heterotrophs, meaning that we subsist on organic material—the bodies of other species (Hinchliffe et al., 2016). Thus, food and fermentation are visceral links between humans and the other beings we associate with.

The engagements of multiple species modulate the landscapes we co-exist in; they produce landscape as a site of environmental and cultural, consumable materiality. To use a Lefebvrian notion, "the spatial practice of society [which is not limited to humans] secretes its own space" (Lefebvre, 1991, p. 38). These processes leave traces on the land. Food and fermentation—as pervasive elements of multispecies landscape modification—collectively drive landscape change across cultural and environmental modalities.

I say all this not because this dissertation focuses on food or fermentation in particular, but to underscore the role that yeast has played in co-constituting food, culture, and landscape (not to mention providing the initial spark for this work). If we recognize these interconnections, we have a jumping-off point to investigate how synthetic yeast might affect humanity's relationships with other species and ecologies in the future.

At the crossroads: Finding an entry point

Latour's (2005) second source of uncertainty—"action is overtaken'—underscores that we are not always in control when things are set in motion. Despite increasing urbanization and technological innovation that can make humans feel ever-more disconnected from nature, we simultaneously seem to move toward greater entanglement in it, facing intertwining crises of energy, biodiversity loss, climate change, and ecological destruction. In his work *The Three*

Ecologies, Félix Guattari (2000) advocates for a transversal style of thinking that views social relations, the environment, and human subjectivity as different lenses through which to understand human-environment relations broadly. From this perspective, humans are not the only members of 'the public' that affect and are affected by scientific claims and world-building.

Are there nonhuman members of the 'public'? Latour (2005) rejects the categories of nature and culture, favoring "the collective" instead. A public or collective that includes nonhumans recognizes a spectrum of differential tendencies and variable capacities, bridging a divide between "speaking subjects and mute objects" (Bennett, 2010, p. 108). The challenge remains in finding new ways to perceive and consult nonhumans; to listen and respond more carefully. Unfortunately, this work does not directly advance this cause outside of calling attention to this ongoing challenge, but perhaps it indirectly affects capacities for imaginative engagement based on the threads of thought it weaves together in the chapters to follow.

While I argue in this dissertation that synthetic biology alters humanity's relationships toward microbial others, this is not to suggest that human agency has ever been anything other than an enfolded network of human/nonhuman vitalities. Rather, new technologies of synthetic biology have influenced existing technoscientific assemblages to be more engineering and computer science-oriented through an additive process, bringing together information-based understandings of life, computing power, substantive research funding, and scientific claims.

Inspired by the strands of more-than-human geography, science studies, and political ecology outlined above, I seek to bring these theoretical and conceptual approaches to bear on the case of synthetic yeast, which encapsulates technoscientific dreams of solutions to climate, energy, and health crises through biofuels, cancer research, and control of life at ever-more fundamental levels. The way we conceptualize things matters to how we study them. For example, Bennett (2010) notes how "stem cell" is a neologism coined to describe bits of matter believed to be

pluripotent, "that is, able to become any of the various kinds of cells or tissues of the mature, differentiated organism…A stem cell, while pluripotent, is not, however, "totipotent," or able by itself to give rise to a fully differentiated organism"[8] (p. 85). Despite impressive controls at the most minute level, there are still unexpected interactions between synthesized elements of yeast, and they don't work as expectedly as mere 'cogs' in a machine. 'Rational' engineering principles are regularly applied, but often researchers still resort to trial and error in searching for desirable genetic configurations.

Social scientists can contribute to and enrich synthetic biology by engaging with difficult questions and doing empirical research into specific projects like Sc2.0. This work requires commitment to listening and learning. "Not least are the considerable additional skills required to study the detailed knowledge practices involved in the production and circulation of such bio-technological artefacts, if cultural geographers are to get to grips with the *specificity* (as against the originality) of knowledge objects like artificial life forms" (Whatmore, 2006, p. 606). Rather than critique synthetic yeast projects as merely Frankensteinian, I seek to critically engage with scientific claims about *what* synthetic yeast is and what it is *like*. Drawing on vital materialism and assemblage thinking, I argue that synthetic yeast is both socially produced/reproduced and also inflected by discourse and scientific knowledge production through the public's and scientists' own understandings of what it is and what it is for. In the interest of transparency, this effort does lead me toward a good deal of criticism of the assumptions of synthetic biology, but in striving to follow rhizomatic and assemblage thinking, I

[8] Later, Bennett elaborates on this issue of stem cells and perceived divisibility: "If it turns out that there are no 'embryonic stem cells' in vivo, this may be because an embryo is *not* a collection of discrete parts, perhaps not even of protoparts or preformed possibilities, and that it is only in the closed system *of the lab* that what Bergson called the "indivisible continuity" of life allows itself to be sliced and diced into "embryonic stem cells" (2010, p. 92).

make a point to avoid essentializing claims about synthetic biology, recognizing my perspective as partial and limited.

In closing, I'll briefly return to the research goals of the previous chapter in light of this one. Most broadly, this work seeks to explore how scientists who work with yeast understand it as an organism. To what extent does *Saccharomyces*' 'organismness' matter when synthetic biologists are primarily concerned with parts and high-throughput workflows? This goal gets at the intersection of multiple bodies and the outcomes of specific knowledge claims. Building on this, understanding the politics of synthetic yeast entails accounting for the numerous agents, forces, and discourses that shape yeast into an object of technoscientific inquiry. Money, innovation, human health, and more are all at stake here, not to mention the labor and bodies of *Saccharomyces* itself. Working from the ideas discussed in this chapter, a third goal of this project is to theorize empirically (Swedberg, 2016) about what synthetic organisms do and mean, both conceptually and materially. Synthetic biologists make clear that Sc2.0 is not an endpoint but a gateway into 'bigger and better' forms of synthetic life. How will this matter to existing life and to humans' hopes of living with it? To what extent can technological innovation qua synthetic bodies function as a savior to an increasingly inhospitable world (at least from an anthropocentric perspective)? What are the limits of control?

In the next chapter, I discuss my methodology and methods, reflecting on my entry into my study sites and outlining the data that I worked with. I appear prominently in that chapter, in part to acknowledge my presence as a researcher and participant in the groups I sought to study, rather than a disembodied observer with a god's-eye view.

4. METHODOLOGY, SITES, AND QUESTIONS

> "Practicing criticism is a matter of making facile gestures difficult."
>
> -Michel Foucault, *Politics, Philosophy, Culture* (1988, p. 155)

> "This means that ethnography isn't something we go and do. It's a fundamental way of being in the world. If we think of ethnography this way, then we begin to ask different questions. How can I get strangers to talk with me? How can I become more observant? If we approach ethnography as a sensibility, then we can begin cultivating a set of skills or disciplines long before we actually enter the field."
>
> -Matthew Desmond, *Evicted* (2016, p. 404)

To explore a slice of the multispecies relationships engendered in the Sc2.0 project, I focused on the workings of one prominent laboratory conducting cutting-edge synthetic biology research. I will detail further my rationale for this in the paragraphs that follow as I discuss the particular case I focused on, as well as other data sources that informed this project. I will attempt to reflexively tie this description of my methodology to the conceptual and theoretical foundations outlined in the previous chapter, incorporating my own positionality and personal experiences into discussion of my research. Approaching this research through the lens of science and technology studies, I situate my work between political ecology and more-than-human geographies and take a phenomenological approach, drawing upon interviews, textual analysis, and observation of scientists working with yeast to speculate on the (bio)politics and territories of yeast-human interactions in synthetic biology.

This study draws upon interviews of scientists working with *Saccharomyces* in different laboratory settings. One laboratory focuses on culturing yeast for brewing, while the other aims to use yeast to better understand biological systems and more complex genomic dynamics.

While the species of concern is the same in both settings, each differs in the epistemologies and discourses applied to their shared subject. I consider the laboratories where human-yeast collaborations unfold as important spatial contexts populated by assemblages of actors engaged in multispecies interactions that exhibit tensions between harnessing and constraining yeast's vitality. In other words, I argue that laboratory spaces are produced in part through dialogues about and approaches to working with yeast, and because yeasts are alive, that we should consider ethics in these interactions and governance.

Community Cultures Yeast Lab (CCYL) is a small, family-run business in San Antonio, Texas (ccyeastlab.com). Founded in 2016 as the Texas Cultures Yeast Lab, CCYL is a full-service yeast lab that provides pitchable (i.e., ready to add to unfermented wort) yeast cultures to craft brewers in the area, specializing in customized blends involving both widely available commercial yeast strains as well as 'native' strains collected from parts of the American Southwest. In addition to selling yeast cultures, CCYL also offers yeast banking services for breweries, quality control testing, and works with local brewing organizations to provide classes and educational outreach. In their own words, "we are here to support and build the craft beer community with fresh and superior yeast cultures, fast and affordable shipping, full laboratory services, yeast banking, microbiological assistance, contamination resolution, and brewery lab consultation" (ccyeastlab.com/meet-us). Since its inception, CCYL has grown out of the founders' garage into a (dedicated and growing) converted warehouse space abutting railroad tracks in the Beacon Hill neighborhood of San Antonio.

After waiting out earlier phases of the COVID-19 pandemic, I undertook a handful of day-long ethnographic visits to CCYL. These visits were conducted between July 2021-April 2022. While there, I conducted informal interviews with key informants working with yeast, including the owners and two different interns. I supplemented these interviews with observations and field

notes. I later transcribed these interviews and identified emergent themes and matters of concern from the textual data.

My choice to focus on the activities of a relatively small, erudite group of scientists working with significant amounts of funding and resources (in the case of the synthetic biologists, not the laboratory concerned with yeast for brewing) makes this research particularly vulnerable to critiques of its scope and focus on those with substantial power, which have also been used to criticize ANT-oriented work in the past (Gad & Bruun Jensen, 2010; Hetherington & Law, 2000).

Scientific and popular discourses surrounding genomic engineering are political and shaped by media accounts, public fears and excitement, funding institutions and government grants, and scientists themselves. In the context of fermented products, *Saccharomyces* is framed as an active agent whose "yeastiness" is a desirable quality that is both imperative to preserve and part of its (nonhuman) charisma (Lorimer, 2007). In synthetic biology, it is conversely understood to be more of a passive reservoir of genetic material or a neutral "chassis" that invites intervention and modification (Szymanski, 2018b). However, neither rendering is totalizing. These different imaginings and approaches to working with yeast underscore a range of power dynamics and metaphors used to make the microbial understandable.

Methodology

Many human geographers have increasingly scrutinized their research methodologies in light of practical and epistemological questions in the field (McDowell, 1992). An increased focus on methodological aspects of research design was in part informed by critical dialogues with science studies, theoretical challenges arising from post-structuralism, and growing influence of

non-representational theories, alongside important contributions from feminist theory. The upshot of these disciplinary conversations has been that geographers are (hopefully) now more critical of how geographic knowledge is produced and inscribed in knowledge systems, taking into account researcher positionalities (Cloke et al., 2004). Interest in qualitative research methods that emphasize these lessons learned is accordingly on the rise, though far from dominant (Crang, 2002).

Given the theoretical roots from which this project grows, I understand science to be an assemblage comprising relationships between humans, other living organisms, and inanimate objects, technologies, and theories. This goes for social science too, of course. In the interest of reflexivity and transparency, I will readily admit that this research is very partial, fragmentary, and in-process. Nevertheless, my work forms a sort of genealogy (Deleuze, 2006; Foucault, 1980) in that it attempts to trace dynamics of force and meaning in a systematic way with regard to synthetic yeast. Nietzsche's (2006a) conception of genealogy is not especially logocentric (language-oriented), though I found much of the discourse surrounding synthetic biology research to be worth paying attention to and ripe for discussion.

As is customary at Texas State University, the first two years of my doctoral program were spent taking classes full-time and teaching laboratory sections, which justified my funding. While I remained occupied as an instructor of record over the following two and a half years, I was slow to come around to my eventual topic, as mentioned in the foreword. This indecision unfortunately did not confer a clear understanding of the "field" I was proposing to enter. Rather, I found that as I began my fieldwork in earnest (the timing of which coincided almost perfectly with the onset of the COVID-19 pandemic), I became increasingly aware of the degree to which I did not understand the realities of the project I was attempting to study (Sc2.0). While this phenomenon is nearly ubiquitous in research—particularly in inductive, open-ended

approaches like mine—it remained a challenge throughout the project. Due to the timing of my fieldwork and the difficulties I encountered while trying to gain access to the "field," my empirical data collection first stalled, then became an amorphous part of the rest of the reading and writing process. Timelines I had created as part of my dissertation proposal became comically out-of-sync with reality as I found myself languishing, then trying to do all the stages of the project at once. While I do not ascribe to nor expect strict linearity in my research processes, this felt nonsequential to the extreme. Despite the luxurious amount of time I was able to spread my doctoral degree over, the limitations imposed on my fieldwork by COVID-19 ultimately made my data collection much more compressed and anemic than I had hoped. Following Whatmore (2003) and Massey (2003), I anticipated much more of a processual engagement with my field sites and interlocutors than ultimately occurred.

In the following section, I will elaborate on and justify my choice of methods, bearing in mind my own positionality and the constraints posed by logistics and the (largely self-imposed) methodological constraints I was operating under. Namely, I resisted modifying my research approach to become more positivist or more driven by *a priori* assertions, even as I struggled to gain traction in my proposed sites and with my proposed approaches. I prioritized empirical observation and remained committed to certain methods I had chosen prior to starting fieldwork (i.e., interviews and participant observation). The (at times, lack of) opportunities to do field-based data collection redirected my efforts and shaped the resulting project in response to the assemblages I continued to try to unravel and understand. More sensorially-rich methods that relied on physical proximity to yeast and humans in the laboratory were near-universally shelved in response to my inability to effectively visit sites in-person. I undertook several adaptations to move this project forward, which are reflected to an extent in the foreword. This work required me to both trace and construct my own socio-material assemblages, enrolling a

wide range of actors in a project that felt rather disjointed at times. In plainer terms, I had to grapple with my limitations as an outsider to the contexts I hoped to study while trying to draw a thread through information and ideas that didn't always seem to fit well together.

While this project is not autoethnographic, I wish to recognize and make clear my own positionality in doing this research. As a researcher, I have been shaped by formal academic training and my own experiences in the field, including previous experience conducting a hands-on, qualitative study with community gardeners and food pantry clients. Entering (virtually) into the laboratories of synthetic biologists and entrepreneurs, I became part of the assemblage of humans, other species, and materials that compose these spaces. This is true even despite my superficially distant, removed 'gaze' and lack of direct engagement with many of the people I was observing. As an outsider, I tried to enter conversations and presentations with an open mind while acknowledging that my previous experiences and exposure to critiques of anthropocentric, scientific narratives shaped my prior understanding of the positionalities and epistemological orientations of the scientists I studied. Despite the reality of being little more than a 'fly on the wall' on many occasions, I had to learn to be affected by the interlocutors and challenges of this particular project. This required several pivots: relying more on secondary data, tempering my idealized ethnographic approach, and subtly altering the scope of the project to account for the lack of discourse related directly to *Saccharomyces*. It also demanded a general ethos of flexibility.

Originally, I did not anticipate that this project would become so full of biological and technical terminology. As I began to understand the matters of concern surrounding Sc2.0 more clearly, I realized that in order to speak intelligently about the project, it was necessary for myself to change both my approach and upgrade my existing knowledge of synthetic biology principles and terminology, a realization shared by Szymanski (2018a) while conducting similar

research. While I remain far from an expert in these arenas, I strove to understand enough of the science to use terms correctly and understand the general contours of specific techniques and processes.

To be sure, I was researching an elite population of humans: synthetic biologists are largely affluent (excepting graduate students, to a certain extent), intelligent, successful, and privileged professionals funded by large institutional grants. There was nothing in particular that I could offer these folks as compensation for participating in my research. As a social scientist, they had knowledge different from and far surpassing my own vis-à-vis biology in general, not to mention of their specific subfield. As I've alluded to earlier, I had significant difficulty recruiting participants to this project, though those who graciously took the time to speak with me were generous and amiable, for which I am grateful.

Building trust and rapport with my potential interlocutors was something I knew would be a challenge in this project, but I underestimated the degree to which this would be essential and challenging given the realities of trying to conduct research during a global pandemic. Actor-network theorists have not always been particularly reflexive about the process of accessing research milieux or garnering participants' trust and interest (Massey, 2003). I found some degree of superficial interest in my work among those I managed to speak with, though others expressed reticence in engaging with me. Mostly, my numerous inquiries were met with silence. I suspect that a good deal of this was due to the ease with which one can ignore an occasional email, especially from a relatively anonymous sender. Certainly, the researchers whom I requested interviews with were leading busy lives and coping with the pandemic in their own ways. Yet it was difficult to parse when potential interlocutors may have been ignoring messages for other reasons, such as distrust of me, my intentions, or simply a lack of interest. After pursuing one doctoral student whose research was particularly intriguing to me for

months, this researcher finally admitted to me that they just didn't wish to participate in my research, despite the fact that I had suggested other conversation mediums after backing away from my initial-proposed Zoom interview.

Reflecting on the early stages of my fieldwork, I am aware that I discounted some of these challenges, assuming that I would eventually be able to conduct interviews and observe participants in-person, in the lab. As this never materialized, I found myself with little recourse but to try to eke out interviews and scrape together little bits of data wherever I could. Unfortunately, the sort of detachment from a sense of time that some like myself experienced during the COVID-19 pandemic fed a torpid affect that I was long in shaking off.

On the other hand, my interactions with individuals working with yeast in brewing-oriented settings were much freer. Even in the midst of a pandemic, I was eventually able to make field visits to Community Cultures Yeast Lab and several breweries in central Texas and found a greater willingness to submit to interviews and observation than I had with the scientists working with synthetic yeast. Overall, participants were more readily available to talk and share their feelings, politics, and motivations. My own background in homebrewing and my passion for craft beer likely contributed to the rapport-building process in these settings, as I could relate to beer-related terminology and processes more easily. Of course, it is possible that this familiarity could also cause me to overlook potentially important interactions or exchanges (Laurier, 2003). As a relatively young, white male, my various intersecting identities likely made my research simpler than it might have been otherwise. I never felt unsafe in any field sites, virtual or in-person, though I felt very ignorant about much of the work my synthetic biology interlocutors were doing. While, in the context of the synthetic yeast lab, I was at times questioned about what I hoped to learn through this work or why I was interested in synthetic yeast while pursuing a degree in geography, I was never challenged on whether or not I belonged

in laboratory spaces or artisanal breweries in general. I mention this simply to acknowledge and openly situate my positionality in this work as a number of feminist authors have advocated (Haraway, 1991; Harding, 1991; Rose, 1997).

However, this raised an issue that plagued this dissertation throughout its course: what to do with these completely distinct approaches and orientations to working with yeast? Synthetic biologists and brewers have vastly different goals, epistemological orientations, experiences, and assumptions, and simple comparisons between the two groups may be fundamentally problematic except to clearly demarcate these distinctions (Erika Szymanski, personal communication). I feared that simply comparing and contrasting between the two would be at best trite and at worst nonsensical. However, I decided to continue pursuing any opportunities available to me to observe humans' relationships to yeast. This bifurcation in the project persisted in part due to difficulties obtaining access to and information from synthetic biologists through interviews and also because the virtual lab meetings I observed were often less about yeast than I had initially expected. Despite this difficulty collecting primary data, I remained committed to this main focus of the dissertation, sensing that it was important and potentially more profound than a dissertation focused solely on yeast used in craft beer production. In the end, I focused the majority of my attention on how synthetic biology espouses certain understandings of the world, leaving the other aspects of this project as minor appendages to the whole.

I employed critical discourse analysis (Fairclough, 2013) to examine the metaphors used to characterize *Saccharomyces* in each laboratory setting, arguing that the use of language in these different contexts actively produces and shapes the yeast-human relationships that are enacted in space. For Foucault, discourses are more than ways of thinking and producing meaning. They actually constitute the 'nature' of the body, mind, and emotional life of the subjects they seek to

govern (Weedon, 1987, p. 108). So, following a Foucauldian reading of discourse and recent work in more-than-human geographies, I analyze how metaphors serve as tools to produce the nature of yeast as alternately controllable, magical, exploitable, or charismatic, depending on the space(s) within which its interactions with humans occur (Lorimer, 2007; Szymanski, 2018b).

While colorful metaphors stand out in this work, my findings align with Szymanski's (2018b) assertion that scientists possess nuanced understandings of yeast's liveliness if asked the right questions. These results gesture away from totalizing narratives that portray yeast as either completely static or autonomous and toward a more contingent relationship in which spatial and social context matters. Importantly, due to the cutting-edge nature of synthetic biology in general, these relationships are very much in flux and open to unexpected outcomes.

Part of this work was born from my surprise at finding so little literature related to the political ecology of yeast in breweries. As I became aware of Sc2.0 and the aims of synthetic biology in general, this research drifted further away from brewing, but I retained the sense that further reflection on yeasts' role as a more-than-human agent in multispecies interactions was merited, whether these are focused on fermentation or genetic transformation. Rather than static interaction between two completely separate species, I will argue that the process of "making-understandable" (via metaphor and discourse) leads to mutual co-constitution of yeasts and humans in all kinds of laboratory spaces.

Methods

(Virtual) participant observation

Participant observation can bring the researcher into the field in an embodied way, allowing for dynamic encounters with particular practices, actors, and associations. Ideally, it can even

help integrate researchers into the groups being studied, which can help diminish a sense of detachment or otherness in the written product. Given the challenges to travel accompanying the global COVID-19 pandemic over the past several years, my original plans to physically spend time in a synthetic biology laboratory in New York City were shelved in favor of virtual interactions. The lab I was hoping to work with did not reopen to visitors for a very long time after the start of the pandemic, and I had substantial difficulty making connections from afar with my potential interlocutors there. In addition, even as time progressed and the locale became more accessible to me, the projected cost of my fieldwork had risen considerably (mainly because the opportunity I had had for free lodging in New York City had expired), making this field-based work less financially feasible.

As an adaptation, starting in December 2020, I began attending meetings of Jef Boeke's lab at NYU Langone Health, the primary teaching hospital of New York University. These meetings were conducted via Zoom due to the ongoing COVID-19 pandemic. Entering the milieu of this lab group as a relatively anonymous outsider, I faced challenges to establishing trust and familiarity. After defending my dissertation proposal, it took the better part of a year—from spring until December—to gain virtual access to these meetings. Part of this delay was due to broad, societal-level recalibrations to living and operating in a pandemic context, but I also struggled to elicit email replies from lab members. Initially, I had hoped to speak to graduate students and junior researchers first before attempting to contact more senior members of the group.[9] After sustained silence from all but one PhD student, I decided to contact Jef Boeke directly, which led to a brief conversation and an invitation to join the lab's meetings. I also attempted to contact several other labs involved in the Sc2.0 project, but after initial lack of

[9] This strategy was informed by Erika Szymanski's advice (personal communication, 17 December 2019), who had previously spent significant time studying similar groups in-person.

response, gave up on pursuing these efforts further.

Structurally, the Boeke Lab's meetings take the form of research presentations given by lab members, who rotate presentation duties throughout the year. Typically, the group meets once a week for 90-150 minutes, though most meetings last approximately 120-130 minutes. Usually, a solo presenter shares her recent work via a slideshow and off-the-cuff description, though less commonly two presenters will share duties or multiple presentations will be given in sequence by different members. Interruptions from participants are common to ask for clarification of a point, critique a figure, or suggest alternatives. There is often a dedicated time for Q&A at the end of the presentation, which ranges from a formality to a period of lively discussion. There is a clear emphasis on work that is nearing submission for publication, as much of the discussion tends to revolve around which figures best convey the study's findings, the best title to use, or how to strategically position a future paper. Participants include Jef Boeke and members of the lab, including professional researchers, postdocs, PhD students, lab technicians, a lab coordinator, staff members, and occasionally visiting professors or students. Attendance is typically between 20-26 persons, though sometimes this number is slightly higher or lower. The group represents numerous nationalities spanning East, South, and Southwest Asia, Europe, and the Americas, but there were no Black members in the group during my time observing them.

The highly specialized nature of these meetings presented greater-than-anticipated barriers to intelligently interacting with this group. Despite some limited background in biological sciences, I was underprepared for the level of dialogue related to cutting-edge research in synthetic biology, often scrambling to find simplistic explanations of procedures and techniques foreign to me. I amended this deficit through a combination of academic articles, popular science periodicals, and patient attention to lab presentations, which over time painted a more complete picture of the science. However, as already noted, I remain a novice in this field, which I found to

be both disadvantageous (in the sense that I was frequently perplexed by acronyms or genetic engineering techniques and terminology) and advantageous (because this afforded me an alternate perspective on these proceedings, helping make them 'strange'[10] (Kumagai & Wear, 2014).

The modality of these meetings shifted throughout my time with the group. From December 2020 (when I first began attending meetings) to mid-May 2021, the lab group met entirely via Zoom. Though many participants joined from their individual workstations at NYU Langone, others were spread around the country and world. In this way, the pandemic flattened space, affording a window into the lives and interactions of a group otherwise geographically inaccessible to me (Gailloux et al., 2022). During these meetings, most participants remained muted with their cameras switched off unless they were asking the presenter a direct question. At the conclusion of a meeting, many participants would turn on their camera briefly to wave goodbye, but otherwise remained "faceless" (Figure 3). These sorts of virtual settings allow access to many people at once but insulate participants from more direct, visceral connections, allowing them to simply ignore messages if desired. This creates challenges to recruiting participants despite offering them the advantage of minimizing power disparities between themselves and the researcher (Afifi et al., 2020).

[10] The destabilizing force of making things 'strange' has long been employed in arts and humanities, but it is also a useful approach for social scientists studying scientific practice. Fundamentally, 'making strange' promotes critical reflection and creativity. "By forcing us to reconsider familiar ideas, situations, and relationships in new and different ways, this process of alienation and enstrangement frees thought and reflection to pursue entirely new avenues of questioning and discovery" (Kumagai & Wear, 2014, p. 976).

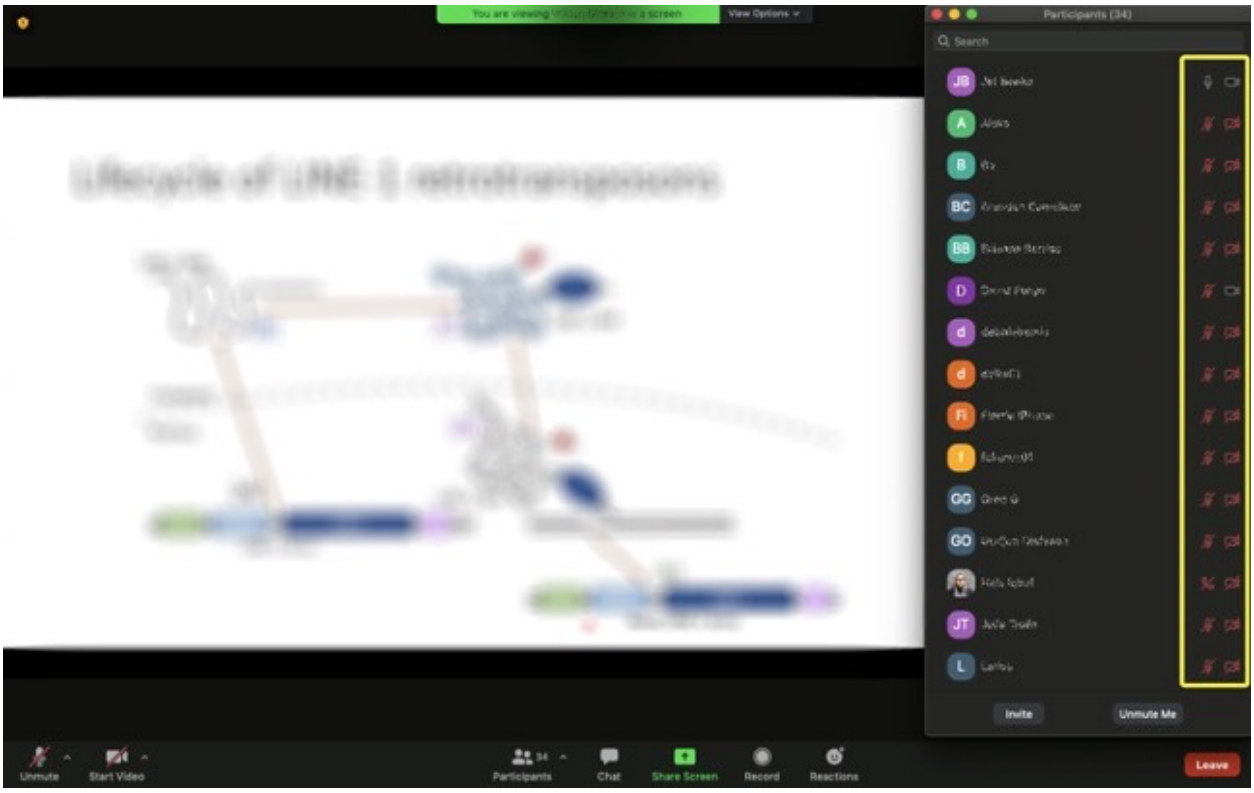

Figure 3: Screenshot of a Zoom window from a virtual Boeke Lab meeting. Note how nearly all participants remained muted with their camera off (highlighted by the yellow box). Image blurred to protect participants' privacy.

On May 19, 2021, I observed the first hybrid meeting of the group, which featured seven members gathered in a conference room with smart cameras and microphones relaying their conversations to the rest of us gathered in the Zoom room. Over time, smaller details have fluctuated—from the number of participants allowed in the room to the presence or absence of food and masks—but the hybrid structure of the meetings persists. As I will describe next, my reliance on and commitment to an epistemology that acknowledges affective complexities and sees participant interaction as emplaced (neither discrete nor disembodied) created challenges to producing rich, shared meaning in the context of virtual lab meetings.

The persistence of these virtually accessible lab meetings opened opportunities for prolonged engagement with this group. While the depth of my interactions with them made my initial

research questions very difficult to answer, I ultimately spent much more time observing this group than I had originally planned. What I had hoped would be intensive, sensorily-rich interactions in laboratory spaces evolved into much more impersonal observations of Zoom rooms. Challenges familiar to those who taught hybrid classes during the past few years are evident in this arrangement: those on Zoom often miss side remarks made in the conference room or struggle to make themselves heard when they wish to interject with a question or comment. Audio quality for those joining remotely diminishes when crosstalk or simultaneous conversation happens in the room, creating an uneven experience based on modality. Microphones "mediated and limited online participants in favor of fully capturing what is happening in the conference room," another example of the "technological glitches that punctuate our virtual lives" (Gailloux et al., 2022, p. 9). Technology enables participation and maintains separation between in-person and remote participants. "Even a high-speed internet connection is not necessarily enough to bridge this divide, since visual cues like body language are less accessible to virtual participants due to fixed camera angles" (Gailloux et al., 2022, p. 9).

Over the 23-plus months that I attended Boeke Lab meetings, I maintained a notebook of observations primarily focused on the role of *Saccharomyces cerevisiae* and related species of yeast in this lab's work. While much of the content of this notebook tries to encapsulate the important points of the presentations I attended, I also recorded interactions between participants (verbal and nonverbal), comments, and frequent motifs (both visual and verbal) in synthetic yeast-related research. My handwritten notes form a significant part of the data gathered for this project. I also took many screenshots of presentation slides to capture important visual representations of yeast and help keep up with the brisk pace of some presentations.

Lab members work on a variety of synthetic biology projects unified by common

epistemology and assumptions but with significant variation in particular topics. Over time, I came to realize that much of this group's emphasis was no longer explicitly synthetic yeast in and of itself—by the time I joined these meetings, initial phases of the Sc2.0 project had been mostly completed. Yet, yeast remains an important background element to much of the group's work, serving as a model organism upon which new techniques and theories are tested. For example, one subset of lab members uses mice extensively in its research, and both the techniques developed to create synthetic yeast and Sc2.0 itself play roles in expressing proteins and manipulating mouse embryonic stem cells (mESCs). Thus, I attempted to focus on the ways in which yeast remained an actor in this assemblage, even if it has been relegated to the background of many projects (i.e., not explicitly mentioned, though used to gauge the success of genomic manipulations). One lab technician shared with me her perspective that some researchers in the lab are "not really yeast researchers" due to their lack of interest in working with *Saccharomyces* specifically (interview, 13 September 2022). This was ostensibly a shift from earlier days, when more folks were explicitly focused on studying *Saccharomyces cerevisiae.*

Presentations varied topically; while some retained a more prominent focus on synthetic yeast (such as addressing remaining challenges to complete synthesis and assembly of the genome), others never mentioned yeast at all, but rather employed tools, processes, and knowledge developed through the Sc2.0 project. Interviews with people involved in synthetic yeast work revealed that not all scientists in the Boeke Lab conceive of yeast in the same way or prioritize it as an organism for its own sake. One research technician I spoke with contended that some 'yeast' projects in the lab were "less honest" because they did not really work with yeast in a meaningful way and that some members were much more committed to yeast as an organism of interest, compared to others. It took significant time for some of these influences to become apparent to me, and this perspective was gained after sustained observation of various projects

and resulting discussions. As I will discuss later, these differences appear to reflect some divergence in not only topical interest, but epistemological foci as well.

As a supplement to my real-time observations of Boeke Lab meetings, I kept a handwritten notebook of detailed jottings and reflections. These notes helped capture my memories of and reactions to interesting occurrences during the meetings. They also played a critical role in helping develop my understanding of the science, as I was able to revisit unfamiliar acronyms and terminology, correcting misconceptions and clearing up confusion. Because many of the presentations were rich with material and contained dozens of slides, I also took screenshots to aid my memory of difficult-to-understand content and prominent visual communication techniques. These screenshots helped ensure that I could accurately capture presentation details while simultaneously paying attention to the dialogue and (eventually once hybrid meetings began) nonverbal communication happening in the room.

Semi-structured interviews

At the outset of this research, my connections to the Sc2.0 project were particularly tenuous, though it took time to realize the extent to which this was true. After some personal communication with Erika Szymanski, who had previously worked alongside some Sc2.0 folks during her postdoc, I decided to contact Jef Boeke with the intent of spending time alongside his lab group, observing day-to-day human-yeast interactions and conducting interviews with scientists working with synthetic yeast. Given COVID-19-related travel restrictions and the need to be especially cautious around the biological integrity of the Boeke Lab's research, I had to conduct my research remotely. I relied heavily on email correspondence to recruit participants, which proved challenging. Connecting to participants and research sites can be challenging under the best circumstances and building rapport in virtual space proved

extremely difficult. Despite an initial introduction to the group at the end of the first meeting I attended, responses to my inquiries and requests for interviews were few and protracted silences the norm. These struggles to gain traction and momentum in the research resulted from and reproduced uncertainties for both me and my interlocutors and our respective relationships to our ongoing work (Gailloux et al., 2022). When I was successful in contacting lab members, they occasionally raised questions about my goals and why I was interested in their work. However, in the context of virtual lab meetings, I remained very much a "fly on the wall," present but merely observing the group's interactions.

Over time and through persistent emails, I was able to recruit a small number of lab members to talk with me, employing snowball sampling and targeting my requests toward lab members who seemed to be working with yeast more prominently than others (Table 1). I drafted a set of 20-some questions that were submitted for IRB approval in April 2020. Over the ensuing two and a half years, I slowly accumulated a few interviewees, though most of my requests for interviews went unanswered. The questions I asked remained mostly the same throughout, though I edited them over time as I learned more about synthetic yeast and the workings of this particular lab. For instance, one of my early questions asked, "Do you think of yeast as something that is 'alive?' How does this affect the ways in which you interact with it?" It did not take long for me to realize that all my interlocutors thought of yeast as alive, and were somewhat perplexed by this question, despite my sense that their discourse surrounding yeast might betray a different opinion. In this way I tried to remain close to the ground (so to speak), tracing the contours of this assemblage and being sensitive to emergent matters of concern, even if they led away from where I had intended to go.

Table 1: Summary of semi-structured interviews. The asterisk denotes interviews that were hybrid or non-standard in some way (i.e., one interview was with a Boeke Lab technician and a postdoc simultaneously, and this lab technician also participated in an individual interview).

Interviewee(s)	Number
Boeke Lab graduate student	1
Boeke Lab postdoc	2*
Boeke Lab faculty	1
Boeke Lab technician	2*
Boeke Lab former member and bio-artist	1
Community Cultures Yeast Lab owners	2

Interviews are often important portals allowing access to actors' primary accounts, which can be both affective and laden with emotion. These interviews were semi-structured; while generally following my interview guide (itself evolving over time), I tried to create a natural conversation in each interview, picking up on interesting comments made by participants and allowing our dialogue to meander topically, following matters of concern. Occasionally an interviewee was not particularly loquacious, and I had to drive the conversation more forcefully, but this was not generally an issue. Most interviews were conducted over Zoom and recorded, when possible, with participants' permission. My initial interview with Jef Boeke was impromptu and was not recorded. Another participant was too busy to meet via Zoom but was willing to answer some questions via email. Regardless, I took handwritten notes during these meetings, though this task was much simpler when I knew I had a recording to compare my notes to and I was able to focus more closely on participants' comments when the need for extensive written notes was obviated.

Stylistically, I tried to tack between a sort of affected naïveté and educated familiarity,

pressing interviewees at times but mostly trying to appear sympathetic. When participants employed technical terms or referenced concepts I did not fully understand, I chose carefully when to ask for clarification and when to simply make a note to learn more about what they were referencing later so as not to disturb the flow of the interview too much or (more importantly, in my view) dislodge them too forcefully from their normal patterns of thinking about and relating to yeast.

I carefully transcribed my interviews to augment my familiarity with the case and the nuances of my interlocutors' accounts. While I relied on some artificial intelligence in the form of voice-recognition software and Zoom's transcript feature to construct a skeleton of some conversations, these tools ultimately proved only mildly helpful, and I listened to and manually transcribed each interview, taking care to try to capture the nuances of the conversation, including non-linguistic verbalizations, inflection, and tone. The advantage of this laborious process was that it allowed time to reflect on the conversations and identify salient themes that emerged. Though it was difficult to trace patterns due to the extremely limited number of interviews I was able to conduct, I annotated transcripts to highlight apparent commonalities and sought to generate meaningful links between them. When possible, I sent transcripts back to interviewees for their review and comments. I did this both to promote transparency in the research process, share power with my interlocutors, and make space for further conversation around key points. As I worked through the transcripts, I corroborated my observations with my notes from each interview and the extensive notes I took during Boeke Lab meetings over the course of a couple of years. This triangulation was useful in triggering memories of illuminating moments during interviews and lab meetings alike and helped paint a more cohesive picture of the lab's particular assemblage. It also helped highlight more affective dimensions of my data that did not readily pop off the page.

In addition to more formal interviews, I held conversations with brewers and the co-owners and employees of a commercial yeast lab. The latter occurred during my series of field visits to Community Cultures Yeast Lab (CCYL). Due to the nature of these visits, recording was unwieldly, as I mostly followed CCYL personnel around while they conducted their usual business and conversations were drawn-out and fragmented due to frequent pauses and interruptions. Meetings with brewers at several craft breweries in south-central Texas were interesting but oftentimes extremely tangential to the main focus of my project.

None of these more informal interactions was recorded, but I took furious jottings when able. Following these conversations, I dictated my reflections and observations into an audio recorder while driving back from the field site. These were later transcribed and used to augment my written notes. I focused not only on what was being said in each conversation but also what seemed to be unsaid, participants' affect and nonverbal mannerisms, and the environmental context of each site.

Textual analysis of documents related to Sc2.0

I compiled a textual corpus of academic literature related to the Sc2.0 project, drawing on internet searches and academic databases. This approach allowed for a broader view of synthetic biology and efforts to synthesize yeast, highlighting important actors and events as well as prominent discourses and framings of objects of scientific inquiry. It also helped aggregate on some level the tiny slice of synthetic biology work that I was privy to through my time with the Boeke Lab. The corpus allowed me to triangulate with some other data I collected, namely extensive notes I took while participating in virtual lab meetings over the past 23-plus months, to see what stands out and what differs between conversations held over Zoom and scientific literature. This corpus includes 88 documents, the vast majority of which are academic articles

written for the purpose of sharing results and progress related to Sc2.0. These documents were published between 2001 and 2023 (Table 2). Using databases like EBSCO, ProQuest, and SCOPUS as guides, I can say that this corpus is extensive, but surely not exhaustive. Synthetic biology is a burgeoning field with an active community of researchers, and the sheer quantity of publications to sift through is daunting. Particularly in ANT-like research, pulling on one thread often leads to many other jumbled knots, and finding a stopping point can be tricky. At times it was very challenging to decide whether a publication merited inclusion in the text corpus or not, as many synthetic biology articles make only a passing reference to Sc2.0 or do not explicitly mention it but clearly deal with and draw upon many of the same ideas, goals, and principles as Sc2.0. Given the constant flow of new academic papers related to genomic engineering in/using yeast, it was challenging to decide when to stop looking, and I am aware that the body of text I assembled is likely already a bit outdated. Much like my field notes taken during Boeke Lab meetings, however, I did reach a point where I felt I was learning little new information about the metaphors used to characterize yeast and conceptual paradigms in synthetic biology writ large. These texts helped attune my senses to the landscape of contemporary synthetic biology research and the public-facing discourse employed by scientists working with yeast in the laboratory. A more detailed discussion of this text corpus and my observations from it can be found in chapter 7.

Table 2: Documents comprising the text corpus, divided by publication year.

Year	Number of publications in the corpus	Year	Number of publications in the corpus
2001	1	2016	3
2003	1	2017	14
2005	1	2018	13
2009	1	2019	8
2011	3	2020	8
2012	2	2021	9
2014	4	2022	11
2015	8	2023	1
		Total	**88**

I used Voyant Tools (Sinclair & Rockwell, 2016), an online open-source textual analysis tool, to analyze this text corpus I assembled. The choice to use this software resulted from two realities. The first was that my epistemological and theoretical stances privilege the use of open-source tools like this that offer a more accessible, democratic user experience. When possible, I have tried to eschew paywalls and expensive software in my research, opting for more open tools. This is for both ideological and practical purposes, namely: as a privileged person researching an elite field, I hoped to promote openness in my research, in any form, and as a cash-poor graduate student, free or inexpensive tools were appealing to me.

In additional to this academic text corpus, I compiled other texts related to yeast and synthetic biology, including popular science articles, press releases, white papers, and records of conference proceedings. I did not conduct a methodical collection or analysis of these documents. Instead, they helped contextualize and frame my findings from the larger corpus.

These documents point to another of the many threads connected to this topic that could be followed extensively, time permitting. Because I turned to them late in my project (having originally planned to focus on interviews and participant observation), I ended up limiting this branch of inquiry in the interest of time.

Affective and non-representational methods

At the same time, I felt frustrated by the distance between myself and one of the primary species I was trying to study—*Saccharomyces cerevisiae*. From talking to scientists, I had some inkling of the experience of working with yeast in a lab to supplement matter-of-fact descriptions of scientific methods in journal articles, but I lacked firsthand knowledge of what it was like to learn to be affected by yeast outside of my own domestic production of fermented foods. I had hoped to engage with more of these embodied, emotional knowledges in this research, but struggled to find avenues to pursue them in the context of COVID-19 and my own geographic detachment from my 'field.' However, a few chance interactions allowed for this sort of non-representational method (Vannini, 2015). Hayden Lorimer (2005) defines non-representational theory as "an umbrella term for diverse work that seeks to better cope with our self-evidently more-than human, more-than-textual, multisensual worlds" (p. 83). Vannini (2015) notes that this approach is a "mosaic of theoretical ideas borrowed from fields as different as performance studies, material culture studies, science and technology studies, contemporary continental philosophy, political ecology, cultural geographies…to name only a few" (p. 3).

While at Community Cultures Yeast Lab, I was able to assist with small tasks like moving hoses during transfer of yeast slurry, fetching miscellaneous items, and viewing colonies under a microscope. Conversations with brewers also permitted up-close, sensorial interactions with yeast. This proximity to another species and technologies used to mediate these embodied

practices invoke a sort of Deleuzian 'becoming' through practice.

In addition to these limited hands-on experiences, I also tried to stretch the text-based data at my disposal in creative ways, drawing on the power of language to access emotional registers. Scholars have noted the potential for creative writing to work on performative dimensions (Latham, 2003; Thrift & Dewsbury, 2000). I applied some of this sensibility to my field notes, attempting to capture light, smells, and other sensations in my dictations and jottings when possible. Outside of my own personal reflections, however, this sort of approach was difficult in practice.

Research questions

My use of the aforementioned methods was guided by the literature framing this project, the opportunities available to me, and a handful of specific questions designed to address the broad concerns outlined in the introduction: how do synthetic biologists understand yeast, what are the politics of synthetic yeast, and how might synthetic organisms like Sc2.0 modulate multispecies relationships? The following questions focus on key concerns germane to the research goals in the theoretical context of assemblage thinking and political-ecological understandings of more-than-human geographies and science and technology studies. I will briefly justify and explicate each of these questions here, but I will also return to them as they connect to subsequent parts of the dissertation.

1. How do scientists in synthetic biology laboratories work with and think about yeast?

This question attempts to uncover how the paradigms of synthetic biology affect humans' understanding of other organisms. Using the Sc2.0 project as an entry point, I sought to trace

connections between conceptions of yeast and spatiality, based on my personal experiences with yeast in brewery contexts, which tend to exhibit a decidedly different set of approaches to working with and thinking about yeast. This question was also a driving force behind the desire to interview scientists and hear their direct reflections on yeast as an organism of interest. By better understanding scientists' own assumptions and goals, a more productive conversation about yeast-human relationships and technology can commence.

2. What are the political and ecological dimensions of synthetic yeast?

An array of actors (not only humans) and things are involved in scientific research on synthetic yeast. This question seeks to sketch some of the contours of this assemblage, paying attention to power differentials between different "enrolled" constituents (Callon, 1986) and focusing on "sources of uncertainty" (Latour, 2005). While the global political ecology of synthetic yeast proved to be too expansive a topic for this dissertation, my examination of particular political and socioecological facets of synthetic yeast as an object of scientific inquiry pointed toward trajectories of power and knowledge production that are neither neutral nor accidental. Funding sources, institutional priorities, scientific discourse, business partnerships, and material circulations congeal and direct forces that produce synthetic yeast in specific ways.

3. How does synthetic yeast challenge or reinforce the politics of human-nature relationships?

As other researchers have argued, emerging synthetic biology technologies offer opportunities to consider how humans interact with other species and what futures may result (Rossi, 2013). As the first fully-synthetic eukaryotic organism, Sc2.0 is a pioneer in a world of contested 'natural' and 'artificial' designations. Value and values are at stake in these labels; there is money

to be made and directed to particular research goals and intellectual property claims to be asserted. Whether synthetic organisms (with their attendant research methodologies and bodies of knowledge) will make the world healthier or 'greener'—and for whom—is a real question that is not predetermined. Rather, understanding the politics of (synthetic) yeast can bring social scientists into fuller conversation with synthetic biologists and society regarding what kind of world(s) we are collectively producing.

Writing up

After long delaying the process of writing up my findings, I began in earnest to forge ahead and make something of the data I had collected so far. As I've already alluded to, my reticence to get started on writing stemmed from my sense that I didn't have enough data to tell a meaningful story, compounded by the nonlinearity of my research process that left me feeling perpetually in 'data collection mode.' Here I attempt to be reflective about this process of writing up, which only (finally) accelerated in the face of external time and job-related pressures. While I am sympathetic to the general advice I received to "just sit down and write," this often felt like a sort of forgery. As Law (1994) has argued, fieldwork (especially when concerned with tracing assemblages) is an open-ended process involving both simplification and translation, since it will never be possible to completely parse an assemblage or disaggregate it into perfect components. My writing, therefore, is very much a partial and modest rendering of scientific discourse surrounding synthetic yeast, situated in a single laboratory at a single point in time. I fully expect that all sorts of unforeseen events or interactions could challenge my interpretations and render them problematic in new ways. In writing, I selected from the data available to me to produce something that I hope is coherent and thought-provoking, and

despite feeling overwhelmed, I found myself constantly wishing I had more data to evaluate and time to dedicate to it. As Jamie Lorimer (2005) insightfully describes, "Given the possibilities of word processing this thesis is very much work in progress—a shifting palimpsest fixed here only temporarily (p. 71).

Conclusions

While I attempted to enter my research sites with an open mind, I think it is worth emphasizing that my academic background and theoretical priors influenced my understandings of and disposition toward synthetic biology research in general. Influential critiques of positivist science developed a certain personal skepticism about the rationalized pursuit of completely synthetic organisms like Sc2.0. Still, I strove to accurately portray the words and viewpoints of the scientists I followed, learning a great deal in the process.

Data remained a troublesome aspect throughout this project. Paradoxically, I faced the (perceived) problem of too little primary data alongside the challenge of a seemingly-endless flow of secondary data in the form of academic writings about synthetic yeast and the ethics and governance of emerging synthetic biology technologies. For well over a year, I strongly resisted adapting my approach to become less reliant on primary data and embrace the significant trove of secondary data available. As mentioned in the foreword, a large part of this decision was based on the hope that COVID-19 would 'end' sooner rather than later. It was also motivated by my desire to write a narrative influenced by the affective dimensions of in-person research with humans and yeast. Where this pseudo-ethnographic approach failed, I had to find new ways to keep moving forward.

Writing about his deep engagement with renters and landlords in Milwaukee, Desmond

(2016) muses, "There's this idea that ethnography is a method…I tend to think of ethnography as a sensibility, a 'way of seeing'" (p. 403). While I do not claim that this project is particularly ethnographic, it resonates with this understanding of an ethnographic sensibility.

I have attempted to adopt this sensibility in my own work, making the best of the data I was able to gather and the partial perspective I was able to gain regarding synthetic yeast. As more astute researchers have previously noted, this sort of partial, situated 'way of seeing' is the path toward objectivity, limited as it may still be. Feminist theorist Haraway (1988) sums up this idea succinctly: "The moral is simple; only partial perspective promises objective vision" (p. 583). I seek to further mobilize this understanding of feminist objectivity through the following chapters, using my very partial perspective on Sc2.0 and synthetic biology more broadly to stake claims to (limited) objective understandings of its political and ecological dimensions.

5. MAKING YEAST SYNTHETIC

> "As with capitalism, it is useful to consider science a translation machine. It is machinic because a phalanx of teachers, technicians, and peer reviewers stands ready to chop off excess parts and to hammer those that remain into their proper places. It is translational because its insights are drawn from diverse ways of life."
>
> -Anna Tsing, *The Mushroom at the End of the World* (2015, p. 217)

> "Ideas and technology…emerged from the mixture and were manufactured in the processes themselves."
>
> -Timothy Mitchell, *Rule of Experts: Egypt, Techno-Politics, Modernity* (2002, p. 52)

Saccharomyces cerevisiae's genome was first sequenced in 1996, meaning that scientists had determined the specific sequence of nucleotides comprising its DNA (Goffeau et al., 1996). This accomplishment marked the first time a eukaryotic genome had been fully sequenced. It was also a calculated decision that surpassed mere curiosity about yeast's genome; specifically, it was a critical step in furthering the development of yeast as a model organism for scientific research. Far from whimsy, contemporary attempts to better understand yeast as an organism originate from humanity's longstanding associations with this species and perceived similarities between its genes and those of humans. For example, in 1997 Foury estimated that almost one-third of human disease-associated genes have functional homologs (equivalents) in yeast (p. 195). As life science research trended toward applications and away from more traditional concerns, function became a dominant organizing principle, and biomedical research related to human health became a sort of Holy Grail of yeast-related research. Thus, yeast models have increasingly been sought after in pursuit of effective treatments for diseases and aging, which conveniently have been used to secure basic biomedical research funding in the United States

(Langer, 2016). "Model organism" is no longer a purely descriptive term, but also a prescriptive one that drives laboratories toward certain research paradigms in pursuit of grants (Slack, 2009). Ankeny and Leonelli (2011) note that *Saccharomyces* is an archetypal model organism in both a technical (i.e., pragmatic) and social (i.e., cultural-relational) sense, while questioning whether any organism subject to experiments should be considered a 'model.' In the Sc2.0 project, yeast's heritage as a model collides with the reality that scientists are no longer really using it to better understand biological principles so much as to *model* specific practices of building synthetic genomes (Calvert & Szymanski, 2020). For yeast, becoming a model organism preceded becoming synthetic.

While humans in synthetic biology contexts typically emphasize the ease and usefulness of manipulating yeast, it can sometimes disrupt this narrative of control by acting in unexpected, "lively" ways (Bennett, 2010). Indeed, yeast's agential and organismal status in these laboratory assemblages suggests opportunities for thinking across both whole-genome engineering and the "microbial turn" in the social sciences, in which microbes are increasingly recognized and investigated as significant components of multispecies societies (Paxson & Helmreich, 2014; Szymanski, 2018a). Scientists working in synthetic biology point to the utility of this work for answering big questions ("The synthesis of a minimal genome would be extremely valuable as a genetic answer to the question, 'What is life?'") and tackling daunting challenges, from energy needs to intractable medical conditions (Dymond & Boeke, 2012, p.170). As Langer (2016) summarizes, "This yeast model is an engineering ideal representing the potential of molecularized biology to predict and control evolution through human programming" (p. 440).

A model organism

Saccharomyces cerevisiae has been an object of scientific inquiry since Leeuwenhoek's microscope observations in 1680. Over the next few centuries, interest in the phenomenon of fermentation grew, particularly from a chemical perspective, as chemists examined the composition of the "broth" in which yeast apparently acted (Lavoisier, 1790). The French chemist Louis Jacques Thénard (1803) argued that this pursuit could lead to a "fertile source of new reflections and truths," underscoring the weight that scientists had already given to their work with yeast (p. 134). This optimism was not limited to the walls of the academy, either. In 1818, English poet John Keats wrote to a friend in the spirit of lively yeast metaphors, suggesting that men are "propelled to act, to strive, and buffet with Circumstance" through a sort of "spiritual yeast" that drove the "ferment of existence."[11]

This understanding of yeast as active continued to propagate. By the 1830s, European scientists affirmed that it was in fact a living organism, which led to Franz J. F. Meyen's (1837) coining the name *Saccharomyces cerevisiae*, which combined the sense of "sugar fungus" and "beer" (Langer, 2016). Thus, yeast was already becoming defined by its chemical and environmental associations (ethanol production, brewing, etc.). By the mid 19th-century, industrial brewers began emphasizing technical elements of fermentation, which led to further explorations of yeast's origins, which were still generally considered to develop spontaneously from rotting plant matter.

As noted in the introduction, Louis Pasteur was not the first person to recognize that yeasts were living, but his experiments demonstrating that contaminants traveled through air (but

[11] John Keats, "X.X.X.I. - to Benjamin Bailey (January 23, 1818)," in *Letters of John Keats to His Family and Friends*, ed. Sidney Colvin (London: MacMillan and Co., 1891), 61.

were not air itself) laid the groundwork for subsequent developments in fermentation science, refuting ideas of spontaneous generation and affirming germ theories (Langer, 2016). Importantly, Pasteur demonstrated how yeast acted differently based on its environmental conditions: when oxygen is scarce, yeast mostly produces carbon dioxide and alcohol, but when well-aerated, yeast reproduce rapidly, budding and dividing.

In the 1870s, the Carlsberg Brewery in Copenhagen opened a laboratory to complement its existing commercial operations (www.carlsberggroup.com). Seeking to develop greater scientific understanding of yeast to better control and manage fermentation, Carlsberg pursued a transformation of brewing from an art to a perfected science. Tracing this development, Langer (2016) writes, "The brewers' art could be made into a science of perfection in the 1870s by borrowing from a statistical tradition that brought population thinking together with yeast "types" to allow comparisons between groups of individual cells. Statistics offered the mathematical rigor of a science" (p. 43). Although yeast 'breeding' programs had not yet begun in earnest, these statistical logics served the purpose of accounting for uncertainty surrounding yeast "types" and preserving ideas of species stability (Langer, 2016, p. 43). As Latour (1993) notes, brewer's yeast became an exemplar of microbial life: "one instance of a whole class of phenomena" (p. 135).

Due in part to the Carlsberg laboratory's work with different yeast types (driven by Emil Christian Hansen's development of "pure cultures"),[12] conceptions of yeast evolved from primordial "broths" to various subtypes of yeast with attributed origins, characteristics, and purposes. Increasingly, the realization of yeasts' variability caught the attention of research

[12] "One and the same yeast does not suit all breweries.... there are several species or races of culture yeast... [and] these give beers dissimilar in their character... Every brewer therefore must select, according to a definite plan, a species which suits his brewery." In Hansen, *Practical Studies in Fermentation: Being Contributions to the History of Microorganisms*, 21.

scientists and yeast became more than an industrial collaborator. Once in the laboratory, its constant replication provided the biological grist for various technoscientific dreams. In a passage worth quoting at length, Langer (2016) draws a thread between scientific research with yeast and social-political agendas:

> …yeast science traversed the many entangled relationships between academia and industry to show not just the pursuit of knowledge at the frontiers of science but its exploitation in many different kinds of applications in society…practical knowledge of yeast heredity entered, existed, and returned to the laboratory in a cycle shaping pertinent research questions and future opportunities for extramural support. Rather than maintaining a false boundary between the laboratory and an "external" sociological world…both academic and industrial scientists have contributed to modern laboratory science with yeast and the contemporary notion of "research translation." (p. 3)

By the middle of the 20th century, a Yale Ph.D. student named Seymour Pomper (1949) finished his degree in microbiology on a fellowship from Standard Brands, the parent company of Fleischmann's Yeast. Following stints at Oak Ridge National Laboratory and the University of California, he ended up directing Fleischmann's laboratories, contributing to the company's brand of baker's yeast (Langer, 2016). Pomper's (1949) career exemplifies the process of "research translation" that increasingly occurred between academic and industrial science in the latter part of the last century. Yeast-related research grew in prominence as biomedically oriented research gained political and social currency in the late 1970s, transforming "an earlier anthropomorphization of molecules to a new project of 'molecularizing humans' which continues in our own time" (Langer, 2016, p. 2). This shift marked a change in the foundational goals of biology from the pursuit of knowledge at disciplinary frontiers to the application and exploitation of this knowledge in society, leveraging cultural and economic forces in the process. The intersection of technology and infrastructure along with huge federal contracts allowed for these massive shifts and transformation of yeast into a model organism; a nonhuman species that could presumably be studied to elucidate biological phenomena and apply them more broadly

(Judson, 1979).

Efforts to understand and control variation in yeast led to heredity becoming a measurable property. Model organisms were part of this development, reflexively shaping the consortia of scientists that studied them. Langer (2016) casts this as a sort of intentionality: "Model organisms themselves are meant to serve as disciplinary tools. As stabilized material, they are expected to transfer technical and conceptual standards from local, specific sites of production to wider research communities" (p. 21-22).

Viewing model organisms in their historical context focuses a lens on scientific practice and the attendant institutional affiliations, funding schemes, and disciplinary paradigms that undergird the production and distribution of scientific knowledge. Ankeny and Leonelli (2011) argue that not all organisms used in experimental research should be thought of as model organisms and that material and epistemic features matter in shaping these designations. Typically, model organisms are estimated to be docile and inexpensive to work with, but this can obscure facets of species that did not fit this narrative when they were first brought into the laboratory. Model organisms also tend to check certain boxes for researchers "that are closely related to their power as genetic tools: they typically have small physical and genomic sizes, short generation times, short life cycles, high fertility rates, and often high mutation rates or high susceptibility to simple techniques for genetic modification" (Ankeny & Leonelli, 2011, p. 316).

Model organism research is characteristically (but not monolithically) collaborative and encourages the free exchange of ideas and data (see Ankeny, 2000, p. S262; Griesemer & Gerson, 2006, p. 366; Kohler, 1999, p. 345). These norms may exist in part to encourage uptake of a particular biological standard, but they also facilitate cooperation necessary for some large-scale genomic engineering projects that take place across multiple laboratories and continents. As I

will explain further in subsequent sections, this commitment to open-source principles ties together model organism and synthetic biology research. Model and synthetic organisms and the communities of scientists, technicians, and funders that coalesce to create them all develop in tandem (Kohler, 1999). Leaders in the field strive to build communities of 'users' that share norms and principles related to information accessibility and biosafety assumptions alongside technical developments like "BioBricks" and cell "chassis" (Calvert, 2010). Jasanoff (2006) points out that this is an example of how both natural and social orders are co-constructed. Or, as Braun and Castree (1998) state, "it is abundantly clear that technoscience and its artefacts are central to remaking society and nature simultaneously" (p. 29).

Synthetic biology

Originally associated with early attempts to search for artificial life in the first decades of the 20th century, "synthetic biology" in the 21st century evolved from earlier genetic engineering initiatives and work with recombinant DNA (Keller, 2000b). Various contested labels were applied near the turn of the century—"intentional biology," "constructive biology," "natural engineering," "synthetic genomics,"[13] and "biological engineering"—but scientific discourse increasingly coalesced around "synthetic biology" (Balmer & Martin, 2008, p. 6). Borrowing its key adjective from the Greek *súnthesis*, synthetic biology grew from referring to the assembly of

[13] Synthetic genomics is not just an ersatz term for synthetic biology, however. In a 2019 paper, Tom Ellis argues that while synthetic genomics owes much to and shares much with synthetic biology, it represents a broader concern with understanding how genomes work as compared to implementing specific, engineered modifications. "[M]ost synthetic genomics projects right now aim to deliver new knowledge of genome coding, content and organization—aspects that are hard to determine by other approaches. By tackling these interesting questions using a new synthetic approach to genome manipulation, these projects both push and pull the development of new technologies that one day will enable broader use of synthetic genomics within research or applied synthetic biology" (What is synthetic genomics anyway?, p. 7).

functional biological modules into a broad body of scientific research and institutional priorities that masks a number of different approaches (O'Malley et al., 2007). Drew Endy and his colleagues at MIT, along with George Church at Harvard, Jay Keasling at the University of California, and Craig Venter at the National Institutes of Health were all instrumental in developing and institutionalizing this emergent field in the early 2000s. These innovators drew inspiration from many of the fields reflected in early, alternate names for synthetic biology, including engineering, computer science, biotechnology, and modelling, while assuming the necessity of design and reduction of biological complexity to gaining full control over biological processes (McLeod & Nerlich, 2017; O'Malley et al., 2007, p. 57).

Broadly concerned with engineering life, synthetic biology can be difficult to succinctly define because it consolidates biological sciences with an engineering sensibility in the quest to produce 'synthetic' biological entities 'from scratch,' an approach that is often called *de novo* (Ball, 2004; Calvert, 2010). In addition to *de novo* synthesis, synthetic biologists also modify existing organisms through genomic redesign. This notion of creating novel biological organisms forms a cornerstone of synthetic biologists' efforts to distinguish their field from older (and somewhat negatively received in the public imagination) genetic engineering methods that are still an important part of synthetic biology (Arkin et al., 2009). Ellis (2019), a leading researcher in the field and member of the Sc2.0 consortium, portrays its ultimate goal as "tailoring cells as technologies for specific tasks" (p. 6). Scale also plays a role: synthetic biology increasingly invokes engineering at the systems level, compared to the individual "component" level of genetic engineering (Calvert, 2010). At one time, syntheticbiology.org defined the field as "the design and construction of new biological parts, devices, and systems and the re-design of existing, natural biological systems for useful purposes" (Calvert, 2010, p. 96). This website no longer exists, but syntheticbiology.com—hosted by a biotechnology company called Ginkgo

Bioworks—poses questions like "What if we could grow everything?" to readers on a splashy home page. Perhaps implying that wondrous things are to come, synthetic biology invites parallels to the early days of computer engineering, which portended technological transformations (Barrett et al., 2006).

Calvert (2010) describes three main approaches within synthetic biology. The first is concerned with "principles of standardization, decoupling and abstraction with the objective of developing biological components which are interchangeable, functionally discrete and capable of being combined in a modular fashion, along the lines of 'plug and play'" (Calvert, 2010, p. 97; Isaacs & Collins, 2005). Another is the minimization and synthesis of entire genomes, which is seen as increasingly feasible and desirable. The third approach concerns the development of 'protocells' from simpler components (Calvert, 2010). Similarly, O'Malley et al. (2007) deconstruct synthetic biology into three realms of "semi-independent schools of research": DNA-based 'device' construction, genome-driven cell engineering, and "protocell" creation (p. 57). Each of these, they argue represents nuanced assumptions, approaches, and relationships to regulation and knowledge claims.

Synthetic biology's broad goals stem from the vision of making natural life 'better,' whether in reference to organisms themselves or the outcomes of the applications they will be part of. Before it ceased to exist, each page of syntheticbiology.org contained a footer with the tag line "making life better, one part at a time" (syntheticbiology.org, 2017). Clearly, this is a value-laden notion that deserves greater explanation. "From the perspective of a synthetic biologist, making life 'better' is making it easier to engineer" (Calvert, 2010, p. 101). Synthetic biologists have developed biological 'analogs' to electrical parts, including oscillators and logic gates (which act like an 'on/off' switch) in hopes of replicating the successes of electrical and computer engineering (Calvert, 2010; Hartwell et al., 1999). Essential assumptions about the equivalency

between cells and circuits underpin these synthetic biological creations. Pottage and Sherman (2007) contend that "the image of synthetic biology as an exercise in 'engineering' building blocks and programmable logic gates synthesized from inanimate materials extends the mechanical and instrumental vision of nature into the deep texture of life" (p. 545). However, as Loettgers (2007) notes, these assumptions of electromechanical-biological equivalence have not been proven.

As a model organism par excellence, *Saccharomyces cerevisiae* has played a significant role in the development of synthetic biology. Its decades spent as a constructable, fungible body of genetic information helped create the conditions for synthetic biology to extend conceptions of yeast as a programmable manufacturing system to other organisms (Langer, 2016). Picking up these mechanistic metaphors that had long been used to characterize nature, scientists began referring to cell "factories" (Fujio, 2007). Factories were desirable models for laboratory organisms because of their association with replaceable parts and uniformity. In "genome transplantation experiments," the "cell factory" is celebrated because "the program replicates (makes identical copies of itself), whereas the cell reproduces (makes similar copies of itself)" (Danchin, 2012, p. 2129). Somewhat surprisingly, Danchin (2012) seems to sense the need to remind readers that "we also must recognise a specific property of living cells, that differentiates them from standard machines: they make a young progeny, and being young implies a noteworthy difference between the parent and its offspring…The program has been replicated, the host chassis has been reproduced. During reproduction something has been conserved, an information, which is beyond the matter of the chassis" (p. 2133). The language used here to characterize cells is both machinic ("chassis") and computational ("program"[14] and "information"). Unlike 'natural' cells,

[14] Synthetic biologists often refer to the genome as the cell's "operating system" (Ellis, 2019, p. 7).

genetically modified synthetic cells can be manipulated to either minimize or maximize variation as they reproduce. They can also have genes and segments of their DNA replaced by synthetic ones, which are typically conceived of as 'modules.' Over time, as parts of the organism are replaced by synthetic ones, a process evocative of Theseus' boat in Greek myth unfolds. After all aspects of a yeast cell are replaced or modified, is it still a yeast cell?

One may fairly wonder to what degree this sort of work is still 'biological.' During a Zoom interview with a postdoc in the Boeke Lab, my interviewee turned the tables on me, asking "Which do you think is more important, 'synthetic' or 'biology'?" I interpreted this question to mean which part of that phrase was most relevant to my work. A little perplexed, I answered "Synthetic," reasoning that it spoke more clearly to the goal of my research into synthetic yeast. Perhaps this was a misunderstanding, aggravated by a choppy internet connection. To my surprise, my interlocutor launched into an animated defense of why "biology" was the more important part of that phrase, arguing that the work they were doing in the lab was fundamentally biological, despite the "synthetic" label. This interaction struck me because it emphasized biology more than engineering and design and because later in the conversation, this same researcher spoke about yeast as almost an afterthought, suggesting that now that scientists had synthesized *Saccharomyces*, they could move on more completely to mammalian cells. Thus, to this researcher, 'biology' seemed to be divorced to a degree from specific biological organisms like yeast. Rather, biology was the stuff of cellular components and nucleotides that collectively serve as replaceable, editable parts of a new biology, synthetic or not.

Modularity

A 'module' can be defined as "a functional unit that is capable of maintaining its intrinsic properties irrespective of what it is connected to" (Sauro, 2008, p. 1). Borrowed from engineering, 'modularity' is a key part of synthetic biology's ontological conception of the world. Engineering in synthetic biology is both literal and metaphorical, tacking between a sort of epistemological orientation and an overarching framework. "In this context, engineering moves from being an analogy of the rational combination of genes—as in standard molecular biology and biotechnology—to becoming a veritable methodology with which to construct complex biological systems from first principles" (de Lorenzo & Danchin, 2008, p. 822).

Early synthetic biologists developed structures to aid in this quest for standardization and modularity. The International Genetically Engineered Machine (iGEM) Foundation, an "independent, non-profit organization dedicated to the advancement of synthetic biology, education and competition, and the development of an open community and collaboration" (iGEM Foundation, 2022), was founded by electrical engineers and early internet pioneers Tom Knight and Randy Rettberg at MIT in 2003 as an independent study course (iGEM Foundation, 2019). Over time, this course morphed into a summer synthetic biology competition for students. iGEM maintains the Registry of Standard Biological Parts (parts.igem.org), a database of over 20,000 "standardized genetic parts" that conforms to the BioBrick™ standard. BioBricks™ are "composable" (units that are compatible and connectable), "interchangeable parts, developed with a view to building biological systems in living cells" (iGEM, n.d.). These BioBricks can theoretically be used like LEGO bricks (an analogy previously employed by iGEM) to construct an infinite number of modular 'parts.' Such 'parts' are not merely reimagined existing biological structures, but, increasingly, 'unnatural,' alternate versions. The possibility of

making modularity more successful drives these developments: "The idea here is that 'orthogonal' [in the sense of statistically independent] parts could be designed, which perform the same function as their natural counterparts but which, because they are not naturally found in the cell, do not interfere with the existing cellular context and thus are more likely to be easily separable and manipulable" (Calvert, 2010, p. 102). Interestingly, the biological 'modules' or 'parts' that increasingly populate laboratories and databases are very much like model organisms more broadly because they also serve as reliable, predictable entities on lab benches.

Proponents of modularity also suggest that it could make synthetic organisms safer by incorporating failsafe mechanisms or dependencies on certain nutrients not easily obtained outside the laboratory into the organism's DNA (such organisms are called auxotrophic). Perhaps counterintuitively, the suggestion is that by making organisms less natural, they are being made safer because they are more separate from the natural world (Calvert, 2010). Whatever the outcome of this argument, the "epistemic ideal of modularity is [being] imposed on the materiality of living things" (Calvert, 2010, p. 109). At present it seems that synthetic biologists are likelier to change nature to fit their models than the other way around, echoing Heidegger's notion that technology leads science.[15]

The mechanical chicken or the theoretical egg?

A critical question in this moment is whether this modularity actually reflects or describes the reality of nature, or whether this is just an anthropocentric framework that 'life' is shoehorned into (Arkin & Fletcher, 2006). Calvert (2010) writes, "The key question here is

[15] "For Heidegger, technology is not simply the practical application of natural science. Instead, modern natural science can understand nature in the characteristically scientific manner only because nature has already, in advance, come to light as a set of calculable, orderable forces — that is to say, technologically" (Blitz, 2014).

whether biological systems are actually comprised of functional modules, or if they are simply best understood as such by the engineering approaches that are adopted in synthetic biology," stating that "There is no consensus on this issue" (p. 99). Modularity does seem to be observed to a degree in structures like cells and ribosomes, for example. This observation underpins the assumption that therefore, useful and 'engineerable' design principles exist (Arkin & Fletcher, 2006, p. 2). Yet even proponents of the abstractions that divide the things and beings of synthetic biology into parts and modules admit that "Abstraction hierarchies are a **human** invention designed to assist people in engineering very complex systems by ignoring unnecessary details. If the process to design a biological system was to write down the string of nucleotides, it would immediately become untenable even for experts to design anything but very simple systems" (Openwetware, 2005; emphasis in original). Examined closely, this situation offers little more than ambiguity about the degree to which nature is mechanical/modular or merely understandable via abstraction, leading into questions of infinite regress, with complexity "all the way down."

My observations of Boeke Lab meetings suggest that most scientists in that group tend to think that the modularity enlisted in their design processes reflects some degree of modularity in nature. This tends to become most evident in the spontaneous discussions arising during presentations, when lab members raise questions about particular assembly techniques or design choices related to specific parts used. Of course, modules can mean different things to different specialists (Calvert, 2010) and organisms have evolved to survive, not to be conveniently categorizable or fulfilling a human desire for understanding or ordering. A functional module from a cell's perspective may be different from a functional module to a synthetic biologist. As Calvert (2010) notes, "Although…functioning primarily as heuristic tools at the moment, in the process of doing synthetic biology these heuristic tools become material

constructions" (p. 101). In short, epistemology may be confused with ontology "because the reshaping of nature in synthetic biology is tied up with scientists' own epistemic practices" (Calvert, 2010, p. 101).

The remodeling of nature in engineering terms evokes Rabinow's (2005) concept of "biosociality." This reversal of "socio-biology" (which suggested that culture is modeled on a metaphor of nature) turns typical suppositions about the relationship between nature and culture on their heads. Franklin (2000) renders this idea as "culture becomes the model for nature instead of being 'after nature', as if a kind of successor project" (p. 194–195). In a synthetic biology version of this arrangement, biodiversity results not from evolutionary forces but rather from design decisions. Rheinberger (2000) describes how "an extracellular representation of intracellular configurations" characterized early attempts to understand cells, but after recombinant DNA technology, "a radical change of perspective ensued. The momentum of gene technology is based on the prospects of an intracellular representation of extracellular projects – the potential 'rewriting' of life" (p. 19). This is notable because ideas about what nature could or should be suddenly had to the potential to actually influence intracellular environments:

> The very essence of our being social is not to supersede, but to alter our natural, that is, in the present context, our genetic condition. We come to realise that the *natural* condition of our genetic makeup might turn into a *social* construct, with the result that the distinction between the 'natural' and the 'social' no longer makes good sense. (Rheinberger, 2000, p. 29; emphasis original)

While the idea of modularity is still key to synthetic biology world-building, Calvert and Szymanski (2020) note that when working with an organism's entire genome (as in synthetic genomics), opportunities may arise for thinking about microbes differently. As concern shifts toward the entire genome, phenotypic expression becomes increasingly important compared to individual genomic constructs. Whole-genome "writing" projects like Sc2.0 are increasingly

common, suggesting that social scientists interested in intersections between human-environment relationships and technology ought to devote greater philosophical and critical energies toward examining them. The very notion of synthesis transcends sequencing, or determining the primary structure of a genome; synthesis invokes not only revealing the order of nucleotides but also editing and designing that order to be different in some way:

> Unlike the sequencing of whole genomes—which involves determining the order of nucleic acids—synthesis provides opportunities for creativity and novelty since it allows scientists and engineers to completely reimagine and re-design existing genomes. The synthetic yeast project, as the largest whole-genome synthesis project so far, is the ideal starting point for analyzing these ambitious endeavors." (Calvert & Szymanski, 2020, p. 2)

Articulating life in the image of computers

As previously noted, synthetic biology tends to draw upon informatic and computational metaphors, describing genetic material as "information" or "code," genomes as "operating systems," sequencing as "reading," and synthesis as "writing." By the 1980s, Hal Abelson, Gerry Sussman, and Tom Knight (the latter went on to co-found Ginkgo Bioworks and iGEM) estimated that the computing power of a simple organism outstripped the most advanced chips they could envision at the time (Bennett, 2017). "The question was whether the analogy between information processing in computers and the information processing of living things could be made literal" (Bennett, 2017, p. 180). Integral to this informational imaginary was an emphasis on a design sensibility that emphasized know-how and collaboration to further link information and communication.

In the early 2000s, researchers at MIT's Artificial Intelligence Lab and Berkeley's Molecular Sciences Institute began applying computer science principles to molecular biology. Among these principles were assumed equivalencies between cells and circuits and DNA and computer

code (Bennett, 2017). Another key to this emerging biotechnical paradigm shift was the understanding of living material as replaceable, standardized parts. Understanding life as modular made comparisons to standardized, reusable, software 'code' more facile. The growing influence of computer science imparted a sense of limitlessness to information in synthetic biology. As Bennett (2017) elaborates,

> This helped generate a cultural situation in which the functions of living beings could be talked about and imagined without reference to the living beings themselves. The vision of cells-as-assembled-components entailed an ontology wherein the living being was assumed to be nothing but a series of contiguous juxtapositions across multiple interactive scales. (p. 180)

Information itself was foregrounded in this framing, making the living organism and its biology almost an afterthought or obstacle to be conquered. While the vitality of organisms (presumably) attracted biologists to their professions in the first place, this vitality has been increasingly externalized and held up as something to be contended with in experimental trials that seek genome-level control (Bennett, 2017). Still, the presumption of equivalence between living things and digital things requires effort to maintain. As I will argue, discourses in synthetic biology help to prop up this equivalence through publications and presentations that normalize and canonize life in the image of computers.

Synthetic biologists are in many ways programmers working with genetic "code," which is often conceptualized as information—an abstraction that creates both the conditions for progress in contemporary synthetic biology and a governing ethos rooted in inspiration (literally, "breathing in"), which has an unmistakable sense of vitality that is seemingly limited only by the imagination.

Prior to the discovery of DNA, biologists conceptualized information as a sort of hypothetical physiological equivalent to the soul that first helped navigate vitalistic and mechanical

metaphors and later established itself as a material reality contextualizing life in linguistic and mathematical terms (Bennett, 2017). "With the discovery of the structure of DNA, and the proposition that the key to both heritability and development lay in the ordering of a finite number of chemical bases, life was reimagined on the metaphors of information theory—programs, codes, and instructions" (Bennett, 2017, p. 177). As the metaphor of information became more associated with the reality of life, it became applied ever more broadly.

The interactions of an organism with its environment contain information, since a living thing's actions co-constitute its *Umwelt*, or experience of the world (Schroer, 2021). Yet in a developing synthetic biological sense, ecological interactions came to be seen as regulated by the immanent code of the organism itself. "Metaphors of code thus allowed life to be imagined, studied, and encountered as a series of communicative operations wherein code is made manifest as non-living chemistry" (Bennett, 2017, p. 177). Understanding life as variable and responsive could still be tethered to a notion of infinite possibility arising from finite starting conditions, which fits cleanly with a theory of a handful of nucleic acid bases in DNA giving rise to the diversity of all life. Thus, the materiality of DNA itself came to be "an ensemble of informational bits that could, in principle, be taken up as discrete, predictable, and interoperable" (Bennett, 2017, p. 178). The mutability of this materiality was nevertheless "reliable" enough to attract engineering approaches that would direct variation.

Digital biology

While synthetic biologists have increasingly looked to computers for models of how biology works, a subset of 'digital biologists' have embraced equivalency, explicitly treating living things like digital code. As Bennett (2017) explains,

> Digital biology can be thought of as gene editing taken up on the level of the whole

> genome, i.e., editing involving the whole complement of DNA in an organism. What makes it "digital" is that it names a mode of synthetic biology that holds that the long-standing scientific task of understanding how life works can now be productively sublimated to the technical task of building computers powerful enough to make life work differently. (p. 171)

This move toward digitization of the living runs counter to more vibrant materialities that locate agency in nonhuman actors (Bennett, 2010). Bennett (2017) argues that a key aspect of the biotechnical imaginary is that it treats the living world as disenchanted (i.e., passive and mechanical). Of course, this portrayal of the nonhuman world is hardly new; since the Enlightenment, predominantly Western, hetero-masculine visions of the Other have cast nature (and even fellow humans) in this mold (Tsing, 2015). In some ways, this orientation toward other species in synthetic and digital biologies is the continuation of a throughline that has endured for centuries.

In this 21st-century framing of an old idea, biology is thought of as the material basis for a manifest technological revolution. Underpinning this frame are two important assumptions that are so self-evident that they coalesce as facts. First, it is presumed that there are deep connections between biological and computational principles. Second, it is held as fact that digital and living logics are *fundamentally commensurate*. "This assumption is not philosophical. It is, rather, part of the operative rationality of laboratory life: living things are approached by way of sequence information, made available through online databases, and recapitulated in labs around the world through synthesis. Living code is being managed as digital code— "bits to bytes to bits," as one bioengineer put it" (Bennett, 2017, p. 173).

However, actual experimental work in laboratories reveals diverse modes of relating to living things. Rather than solely *a priori* conceptualizations of life as digital, scientists remain open to and cognizant of the ways in which life can be unpredictable and evade simple categories. On

one hand, the labor that contributes to building customized, synthetic organisms is largely conceptualized as digital and carried out on computers. On the other hand, it remains very experimental, driven by trials and failures as much as by pre-programmed successes. The need for control in these experimental settings is clear to experienced laboratory technicians who are well aware of the unpredictability of life. As Bennett (2017) puts it, "The computational and the biology may be getting synthesized, but on experimental grounds the biological continues to frustrate the computational" (p. 173).

As has proved the case with birds and mammals (Leder, 2012), attempts to force microorganisms like yeast into production-centric lifecycles are sometimes derailed by the organism's own drive to survive or its eventual death. Thus, digital conceptualizations of life clash with the reality of responsive engagements in the laboratory. In a way, the analogy of life-as-information pushes back as "an "analogy of being" begins to run the other way: "life is not only understood in terms of digital logics; digital logics must also be reimagined under the pressure of the logic of life, a logic that makes itself known through a refusal of cooperation" (Bennett, 2017, p. 182). Clearly, experimentation remains integral to biotechnology in spite of technoscientific dreams of infinitely-editable and 3D-printable life. This is not a slight, but rather an observation. A research scientist in one hybrid Boeke Lab meeting expressed his frustration with the challenges of genotyping synthetic "hypervariants," lamenting that "this allele-specific qPCR is a bitch" (field notes, 14 July 2021). He also noted that "not all the clones are perfect" for their intended use. In fairness to the synthetic biologists, experimentation nearly always precedes "perfection." Yet, current scientific discourse suggests that such control of outcomes has already been achieved, all while day-to-day laboratory practice indicates much greater contingency. Despite significant automation in synthetic biology labs that allows researchers to process hundreds of yeast colonies in rapid succession, these "high throughput"

(e.g., Mitchell et al., 2015) approaches function in part by casting a wide net to ensnare desirable mutations, rather than by engineering them precisely, as is typically promoted. This tension is a testimony to what Peirce (2009) called the "outward clash" between humans and that which lies beyond their forms of representation.

Complexity and reductionism

Despite the influence of systems biology, which foregrounds the immense complexity of living systems, synthetic biology seeks parsimony and reduced complexity. Some synthetic biologists even deem complexity a barrier to synthetic biology's goals: "As the complexity of existing biological systems is the major problem in implementing synthetic biology's engineering vision, it is desirable to reduce this complexity" (Heinemann & Panke, 2006, p. 2793). Ball (2004) quotes prominent synthetic biologist Tom Knight concurring that "an alternative to understanding complexity is to get rid of it" (p. 625). Another pioneer in synthetic biology suggested, "You focus on parts of the science that you do understand and clean out the parts that you don't understand" (George Church, quoted in Breithaupt, 2006, p. 22–23). These sentiments convey a sensibility of tearing down and starting over. The term 'refactoring,' borrowed from computer science, conveys much of this sense; dispensing with the "unnecessary detritus" that organisms have accumulated over millions of years (Calvert, 2010). Dupré (2010) argues that "the traditional notion that complex systems, such as those found in biology, can be fully understood from a sufficiently detailed knowledge of their constituents is mistaken" (p. 32). Cho et al. (1999) see this as an unsurprising outcome of the pervasive idea of nature's simplicity, writing "The attempt to model and create a minimal genome represents the culmination of a reductionist research agenda about the meaning and origin of life that has

spanned the 20th century" (p. 2087).

Of course, all knowledge production and perhaps even perception involves a sort of reductionism in order to make life understandable (Barnes & Dupré, 2008). However, the degree to which synthetic biology engages in reductionism may further entrench human-nature divisions while paradoxically claiming the opposite; i.e., that all life is modular, composable, and interoperable. In this framing, humans still occupy a privileged position as the subjects and arbiters of life, an old trope of the nature-culture binary. Of concern in the present is that by attempting to "eliminate complexity and contingency, synthetic biologists might end up losing sight of the emergent properties that define living systems, which are themselves historical accumulations" (Calvert, 2010, p. 103).

Steps toward synthesis

Saccharomyces cerevisiae holds the distinction of being the first eukaryotic genome that humans managed to fully sequence (Goffeau et al., 1996). Researchers released it into the public domain on April 24, 1996. (Goffeau et al., 1996). At approximately 12.1 million base pairs (bp), its DNA sequence is long enough to challenge researchers and offer significant potential for editing, but short enough to remain feasible for a coordinated consortium of early 21st-century scientists to tackle. These 12.1 million base pairs comprise 6,275 genes spread across 16 chromosomes (Goffeau et al., 1996).

Alongside this sequencing achievement, microbiologists were beginning to set their sights on transcending 'mere' description. In 2002, researchers synthesized a strain of poliovirus (a form of *Enterovirus C*), and the following year a form of bacteriophage *phi*-X174 joined the ranks of synthetic viral genomes (Calvert & Szymanski, 2020). In 2008, the J. Craig Venter Institute

(JCVI) synthesized *Mycoplasma genitalium*, a bacterium, followed by *Mycoplasma mycoides* in 2010. This latter achievement was promoted as the development of "synthetic life" in bacteria (Bennett, 2017). Six years later, JCVI released a 'minimized' version of *Mycoplasma mycoides*' genome, the "smallest self-replicating organism known" (Nature Biotechnology, 2016, p. 673). This creation involved stripping away what was considered excess or "junk" DNA and reconstituting or "booting up" a new organism *in vivo*. Both this approach and its adopted terminology helped serve as a proof-of-concept for future synthetic biology efforts (Gupta & Jaiswal, 2014). *Escherichia coli* was also synthesized with changes to its codons in 2016. However, *Saccharomyces cerevisiae*'s genome is an order of magnitude larger than these bacteria and required much more time and effort to synthesize.

Emmanuelle Charpentier and Jennifer Doudna first published their pioneering work in DNA editing in 2012 (Jinek et al., 2012), and subsequent applications of these "genetic scissors" changed the face of biology irrevocably, leading to their Nobel Prize in Chemistry in 2020. The development of CRISPR (clustered regularly interspaced short palindromic repeats) as a technology for gene editing radically altered the landscape of genome manipulation and associated scientific imaginaries. Evocative of the mass-production/mass-consumption principles of Fordism, CRISPR allowed faster, more predictable gene editing for less money. Ethical, legal, and ecological questions lagged in the wake of these rapid advances (Braverman, 2017b). As a result, genome engineering and synthetic biology are arguably under-regulated and under-theorized. However, this project joins in a recent uptick in interest among social scientists studying synthetic biology.

The seeming elegance of CRISPR lies in part in its biological origins. Strictly speaking, CRISPR is a "naturally occurring system by which prokaryotes such as bacteria defend

themselves against viruses" (Braverman, 2017b, p. 3). "It does this by capturing genetic material from invading viruses and passing it on to its immune system for future use" (Bennett, 2017, p. 175). Remnants of previous infections, these fragments of DNA are left behind by bacteriophages, then used by the infected cell to prepare defenses against subsequent infections. These CRISPR sequences thus play a key role in antiviral acquired immunity for cells and are found in nearly half of sequenced bacterial genomes and 90% of archaea (Braverman, 2017b). In this way, CRISPR is simply another function of an agential organism, but when applied with the speed of computer-aided evolution, it can become something more, reterritorializing life.

CRISPR-associated protein 9 (Cas9) plays a critical role in the functionality of CRISPR. By "cutting" DNA strands like a pair of "genetic scissors," Cas9 catalyzes a response from cells, which typically attempt to repair DNA at a break point by "sealing up the broken ends, often deleting or inserting a few bases (i.e., adenine, cytosine, guanine, or thymine) in the process, which can disrupt the function of the gene" (Braverman, 2017b, p. 3). As with CRISPR, scientists have learned how to harness this biological process. Using a synthetic DNA sequence as a repair template, desired strings of base pairs (bp) can be incorporated into a gene at a specific location (Braverman, 2017b). Citing a personal conversation at a gene editing symposium, Braverman (2017b) relates how one geneticist explained that "All CRISPR does is cut the DNA…Everything else is the cell repair system, and that's what we're hitching on to" (p. 3). Scientists tend to run with the cutting metaphor, frequently employing scissor icons in their diagrams to denote the location of Cas9-caused disruptions in the genetic code. CRISPR itself is sometimes considered to be essentially a "find-and-replace" tool for DNA editing, in keeping with dominant language paralleling computer science (Regalado, 2015).

Though basic laboratory skills are necessary to perform CRISPR, its relative ease is part of its appeal (Cohen, 2016). A sense of "effortless editing" leads to ostentatious claims like "any idiot

can do it" (Braverman, 2017b, p. 3). In the years following its initial development, other varieties of CRISPR have emerged, with particular applications: CRISPR-Cpfl, CRISPR-C2c2 (which operates on RNA instead of DNA), CRISPR-CasX, and CasY, resulting in *Science* deeming this string of advances a "CRISPR revolution" (Braverman, 2017b, p. 3). The proposed implications of this "revolution" are myriad, from cancer therapies to radically altered crops (Regalado, 2015). The United States Department of Agriculture (USDA) has thus far declined to regulate CRISPR-modified crops in any way, viewing the process simply as an accelerated form of traditional breeding. Restrictions on transgenic plants (where DNA is taken from another species) are still in place. However, this does not apply outside the realm of food, where scientists are modifying yeast and mice with "humanized" genes (Laurent et al., 2016). One needs only a cursory grasp of history to understand that living things frequently transgress national boundaries, raising questions about how such organisms will be viewed under the Cartagena Protocol of 2000 on Biosafety and the Nagoya-Kuala Lumpur Supplementary Protocol of 2010—which are both attached to the United Nations Convention on Biological Diversity (CBD)—when they inevitably cross borders (Braverman, 2017b, p. 6). CRISPR also has the advantage of stealth; it can operate on helices without leaving traces of foreign DNA behind. "This characteristic poses a challenge for existing regulations, which are often based on the presence of such foreign DNA" (Braverman, 2017b, p. 4).

It seems fair to wonder about the utility of restrictions on transgenic organisms at a time when species boundaries seem specious and in light of vague and shifting historical understandings of species differences. For scientists who view genetic material as "information" or "code," how meaningful are species-level distinctions anyway? All of this points to increasing opportunities for blurring the lines separating bacteria, mammals, plants, and fungi. For instance, is "humanized" yeast still yeast? Will this shift disrupt traditional nature-human or

environment-society dualities? Will it paradoxically cement them as humans continue to embody the ideals of engineering-based solutions to climatic and biological catastrophe?

CRISPR unlocked earlier "gene drive" technology that promised to further accelerate genomic changes across populations (Burt, 2003; Champer et al., 2016). Like CRISPR, gene drives are naturally occurring phenomena that have become harnessed by humans in new ways (Oye et al., 2014). Operating on the population scale, gene drives override "normal" inheritance rules in sexual reproduction, ensuring certain genes are passed on from one generation to the next, reducing variability. An example of this technology that has permeated the broader societal consciousness is proliferating a mutation in mosquitos to eliminate parasitic diseases like malaria (Braverman, 2017a). Burt suggested this application in 2003, but it took years before CRISPR made this proposal feasible. Other potentially beneficial applications of gene drive technology include controlling invasive species, augmenting crop yields, and promoting climatic adaptations (Braverman, 2017b). Aided by short generation times in many species of interest, gene drives can work in tandem with CRISPR to effect rapid changes in many individuals of a species. Significant funds have been invested in gene drive technologies, including by the Bill and Melinda Gates Foundation for malaria control (Regalado, 2016) and the Defense Advanced Research Projects Agency (DARPA) of the United States Department of Defense (Neslen, 2017).

Like many technologies of the "genetic turn," gene drives are full of future imaginaries and promises. And while the bioethics of specific applications or principles are very much open to debate, it is clear that gene drives are another force nudging public discourse away from conversations about changing destructive behavior and toward engineering adaptability (Braverman, 2017b). Reflecting on gene drives' potential to promote conservation efforts, Sandler (2017) links their use to a paradoxically expansive-but-narrow future imaginary where engineering is the only way forward: "It is evolution by artificial selection among engineered

variations: a full embrace of the Anthropocene" (p. 49). Indeed, the meaning of "conservation" seems dubious if we are more invested (literally and metaphorically) in engineering the world rather than conserving it.

Inflecting life with CRISPR is powerful because it draws upon organisms' ability to act in a way that is neither predetermined nor completely random. Bennett (2017) describes CRISPR-induced mutation as a form of piggybacking, riding "on the back of [an organism's] ability to sense their environments, discriminate, move, communicate, relate, adapt, coordinate, and choose" (p. 175). In this sense, CRISPR is superficially very foreign to control-driven narratives of synthetic biology. However, closer reflection reveals a paradoxical elision that smooths out this active-passive dualism. There is, therefore, a tension between these modes of understanding and relating to lives outside our own.

In this way, a theory of life becomes linked to a theory of power, where software for rational design and machines for its implementation become the goals of "the masters of the digital world" (Bennett, 2017, p. 172). Following paradigms of the computer age, scientists strive to transcend "read"-only models of genomic understanding in favor of projects that envision humans' ability to proactively edit genetic code with mere keystrokes. Notably, these metaphors are no longer primarily linked to text but to code. "Writing" and "editing" evoke new technological futures in which entrepreneurial creators will revolutionize living organisms much in the way that our own lives have been radically changed by smart phones, cloud storage, and wearable technology. Confidence in this approach reflects the subsumption of biology's traditional concerns into the purview of computer engineering (Bennett, 2017).

The mobilization of CRISPR under a hybridized bio-tech paradigm works to "reinforce the already-diffuse sense that biological engineering has become a digital designer's playground" (Bennett, 2017, p. 176). Notably, this was not the inevitable outcome of CRISPR-Cas9

technology. "Where CRISPR began as a story of technical capacity keyed to the experience of living things, it was quickly remade into a story of the reification of the regnant conception of life underwriting digital biology" (Bennett, 2017, p. 176). Once different in sensibilities and approach, computer engineering and biology have grown together around the *sine qua non* of the digital in biological futures (Bennett, 2017).

Digital biology can be seen in this light as both a contraction and an exit. It is a contraction because, while it recognizes that genomic information is an accretion of lived histories, it takes up those lived histories as if they can be recapitulated in the form of digital annotations, characterizations, and quantification— a useable synchronic remainder. It is an exit, because that synchronic remainder, it is believed, can be expressed as the encoded basis for the composition of something that will begin a new history" (Bennett, 2017, p. 184).

Sc2.0

Given the potential afforded by CRISPR and computer modeling, synthetic biologists have continued to scale up their efforts to synthesize entire organismal genomes. In 2008, this was accomplished on the "megabyte" scale (roughly one million-plus base pairs or Mb) through the synthesis of a bacterium (Gibson et al., 2008). A decade later, a synthetic version of the *E. coli* genome—about four times larger—was announced (Fredens et al., 2019). Synthetic biologists saw eukaryotic organisms (those whose genetic material is DNA in the form of chromosomes inside a distinct nucleus) as the next target worth synthesizing. The common yeast *Saccharomyces cerevisiae* was chosen to be the first eukaryotic organism with a redesigned, completely synthesized genome. Its 12-megabase (Mb) genome, spread across 16 chromosomes,

represents a more sweeping challenge to synthetic biologists, even as its completion looms. The relative enormity of this genome compared to those synthesized previously has all but necessitated a coordinated, distributed approach.

The result of this is the Sc2.0 project, an international endeavor to create a fully synthetic, designer yeast genome, chromosome-by-chromosome (Richardson et al., 2017). 'Sc' stands for the project's central organism, *Saccharomyces cerevisiae*, and '2.0' is a nod to the next generation of something in the language of computer software. In technical terms, Richardson et al. (2017) describe the "complete design of a synthetic eukaryotic genome…a highly modified *Saccharomyces cerevisiae* genome reduced in size by nearly 8%, with 1.1 Mb of the synthetic genome deleted, inserted, or altered" (p. 1040). Introduced in 2011, this project also serves as a stepping stone between the synthesis of smaller organisms and dreams of engineering gigabase (Gb) sized genomes of other eukaryotes in the future (Boeke et al., 2016). Sc2.0 is a 'platform' or proof-of-concept for studying other eukaryotic genomes. Though its epicenter is arguably Jef Boeke's lab at the Institute for Systems Genetics at New York University's Langone Medical Center, the project is somewhat decentered, "with chromosome synthesis distributed across a consortium of nine laboratories in the UK, the USA, Australia, Singapore, and China, with another two laboratories in France and Germany analyzing the completed synthetic chromosomes" (Calvert & Szymanski, 2020, p. 7) (Figure 4). Eventually, the individual synthetic chromosomes "will be consolidated into a single strain by "endoreduplication intercross."" (Calvert & Szymanski, 2020, p. 7). To date, this final combination of all 16 synthetic chromosomes (the 16 naturally occurring in *Saccharomyces cerevisiae* will be reduced to 15 with the combining of chromosomes I and III, and a 17th "neochromosome" containing relocated tRNA genes will be added (Calvert & Szymanski, 2020)) is yet to occur.

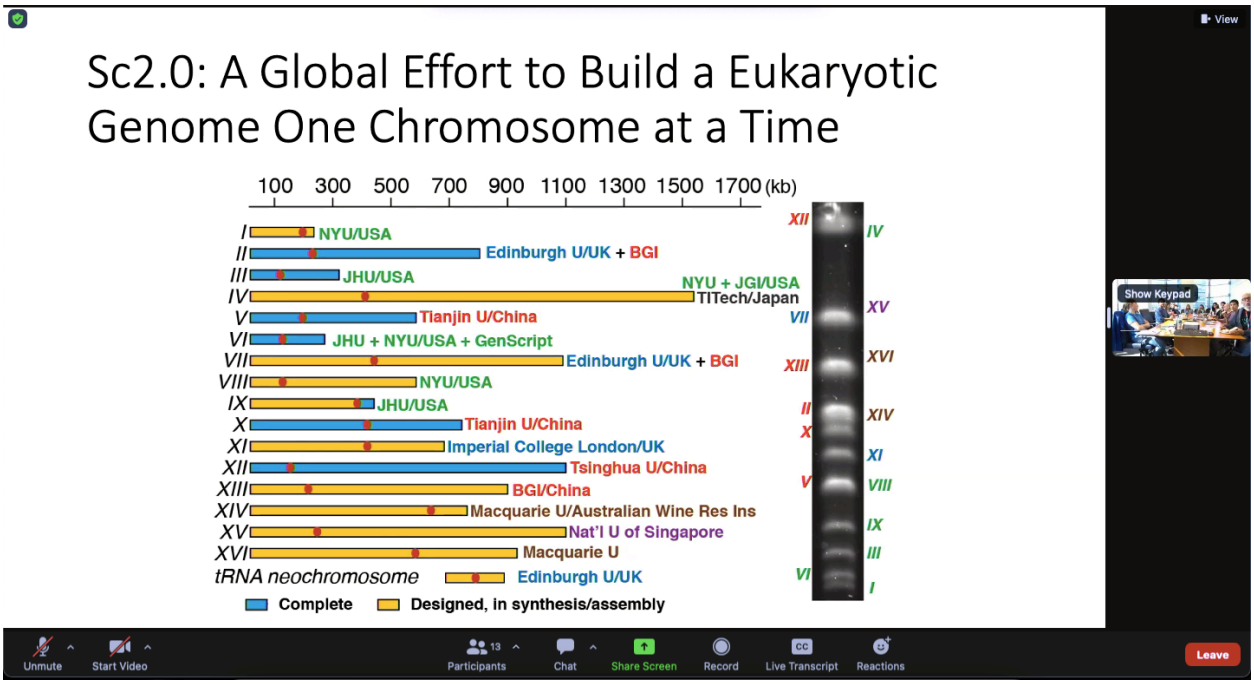

Figure 4: Screenshot from a Boeke Lab meeting in May 2022 demonstrating the division of labor between numerous labs working on different Sc2.0 chromosomes. Although the project was originally supposed to be completed in 2020, at the time this screenshot was taken some chromosomes are still unfinished, and a single cell containing all chromosomes is yet to be shown to be viable.

Describing their approach, synthetic biologists noted the dozens of lab groups that were enrolled in seeing this project to fruition (Richardson et al., 2017). The project relies on a suite of software to accomplish various tasks, from designing and rendering genetic sequences to communicating and presenting their results. BioStudio, an open-source software for eukaryotic genome design, has been instrumental in this work (Richardson et al., 2017). Unsurprisingly, this project has relied on consistent collaboration between genetic specialists and computational specialists. Other computational and technological resources also played an important role, including "a major database employing experts working with the larger community to maintain its annotation. As updates are made to the wild-type reference sequence and annotation, the substantial investment in existing infrastructure, such as the SGD database (www.yeastgenome.org), is critical to success" (Richardson et al. 2017, p. 1043). As the project

progressed, it continued to embrace computer science paradigms, integrating version control: "To enable participation of multiple genome designers within multiple groups…Version control software allows incremental "rollbacks" to previous designs when errors or other problems are encountered. It also permits asynchronous, distributed document manipulation by tracking the person responsible for each version and permitting authorized designers to accept or reject proposed changes to the Sc2.0 genome" (Richardson et al., 2017, p. 1043).

Interestingly, the spatial configuration of yeast's chromosomes, like that of other eukaryotes, lends itself to a distributed effort toward its synthesis, making the tools of synthetic biology more readily applicable *in situ*, in contrast to bacteria, which typically have a single, circular chromosome (Calvert & Szymanski, 2020). Also of importance is the diversity of this large consortium: "Across this large and geographically diverse group, the scientists involved bring with them a range of different interests and expertise. Some are self-defined synthetic biologists who have been active in parts-based approaches to the field and see the Sc2.0 project as a proof-of-principle of large-scale synthetic biology. Others are experts in yeast genetics and want to use constructive techniques to find out more about their favorite organism" (Calvert & Szymanski, 2020, p. 7). Each laboratory working on this project shares some common orientations and assumptions, but each also exhibits somewhat different approaches and goals (Szymanski, personal communication, 17 December 2019).

The Sc2.0 consortium reported that it had completed the first synthetic yeast chromosome, synIII, in 2014. This was the same year that Jef Boeke moved from The Johns Hopkins University to New York University. At Johns Hopkins, Boeke, Joel Bader, and collaborators had developed an undergraduate course model known as "Build a Genome" (BAG) (Cooper et al., 2012; Dymond et al., 2009). In these intensive courses, students engaged in hands-on laboratory work that directly contributed to the Sc2.0 project's goals of creating a "stronger, leaner, and more

agile genome (Langer, 2016, p. 439). BAG courses were a form of outreach and recruitment; one of the lab members I interviewed specifically mentioned the influence of this course on his current career trajectory:

> So I was an undergrad at Johns Hopkins, where Jef used to be. And Jef ran a course called Build a Genome…the idea was basically—especially early on when building synthetic DNA was a lot of like, sort of manual labor, and you could outsource it to companies, but it was—the cost was prohibitive for—in the early stages of the project, especially when you want to build a lot of DNA. And so Jef had the idea to basically outsource it to undergrads who would be paid nothing, but would get a valuable sort of research experience. And they would learn a bunch of stuff, but also contribute to the sort of more menial, if you can call it that—more sort of laborious part of the project. And it would be split up over hundreds of people rather than two people doing it over and over again for five years, right? So you could do it both faster and cheaper, potentially. And so my roommate at the time had taken the class and said, "Oh, man, this is super interesting. It's also like an easy A," you know, "You should totally do it next semester, it would be good for you." And, yeah, so that was in the fall semester of my junior year of college. So I've been trying to get that easy 'A' for the last like seven years now [laughing]. So basically started with the Build a Genome course, and then I worked for a little bit in Jef's lab at Hopkins, and then Jef moved to New York and then I started graduate school in New York, joined the lab, and then worked a little bit on the synthetic yeast stuff when I first started in the lab… (interview, 23 June 2020).

As genome size has increased, so too have the interventions scientists have implemented, completely modifying typical aspects of the genome. One of these interventions is known as "watermarking," which uses polymerase chain reaction (PCR) tags "to specify pairs of primers specific to either the wildtype or synthetic version of that gene" (Richardson et al., 2017). Other edits in Sc2.0 include removing "retrotransposons, subtelomeric repeats, and introns; eliminating and relocating all tRNA [transfer RNA] genes to a "neochromosome" (Richardson et al., 2017); and swapping all TAG stop codons to TAA" (Dai et al., 2020, p. 1). "Freeing up" the TAG codon allows for reassignment to help synthesize an additional, non-native amino acid that can be used to study the evolutionary effects of genetic code expansion (Sliva et al., 2015). Representative of synthetic biologists' far-reaching visions for their work, "The neochromosome's design audaciously transgresses organismal boundaries by incorporating DNA

from nine different yeast species, with only 10% of the sequence from *S. cerevisiae*. This eclectic range of species is used because the scientists are designing the neochromosome to operate independently of the rest of the genome" (Calvert & Szymanski, 2020, p. 9).

Teams working on Sc2.0 chromosomes typically start with small 'chunks' of DNA and append them to other sections of DNA piece-by-piece. As Sliva et al. (2015) explain,

> One bottom-up approach has been to start with oligonucleotides of 60–70 bp, ordered from DNA synthesis companies and assembled into building blocks (~750 bp) *in vitro* by PCR and subsequently molecularly cloned in bacteria. The building blocks are stitched together first into minichunks (~3 kb) and then into larger chunks (~10 kb) by the method of *in vivo* yeast assembly followed by bacterial plasmid recovery for sequence verification. Finally, the chunks are ligated *in vitro*, and the resulting megachunks (30–50 kb) are integrated into the yeast genome, replacing endogenous chromosomal material with the new synthetic version. (p. 1024-1025)

Relying on techniques like SCRaMbLE (Synthetic Chromosome Recombination and Modification by LoxP-mediated Evolution) and CRISPR-Cas9, scientists engineer a sort of biodiversity through rapid evolutions *in silico*, which means that computer simulations rapidly test and provide feedback on novel genetic combinations as opposed to working under the microscope in a more traditional way, or what is sometimes called *in vitro*. Richardson et al. (2017) describe the "assembly" strategy of Sc2.0, which "exploits the endogenous homologous recombination [the exchange of genetic material between two similar molecules of DNA] machinery to replace individual 30- to 60-kb segments of each wild-type chromosome with the corresponding synthetic sequence" (p. 2). In plainer language, scientists are leveraging *Saccharomyces*' existing ability to reshuffle parts of its genetic sequence to insert their own custom-made segments of DNA. A technology called "SwAP-In" allows this segmental assembly, dividing chromosomes into "megachunks" (30 to 60 kb long), which can be further divided into "chunks" (typically ≤10 kb in length), "minichunks" (2-4 kb), "building blocks" (~750 bp) and

overlapping oligonucleotides (Richardson et al., 2017; Sliva et al., 2015). "Chunks can be assembled into megachunks by restriction enzyme cutting and ligation in vitro, and the megachunks are subsequently integrated into the host genome, replacing the corresponding wild-type segment" (Richardson et al., 2017, p. 2). Scientists aim to 'modularize' the genome assembly process itself, in keeping with broader synthetic biology sensibilities.

Sc2.0 researchers orient the project around two key goals. First, they attempt to maintain an organism that is phenotypically similar to "wild type" yeast, primarily in terms of reproductive fitness. Second, they strive to incorporate "inducible genetic flexibility" while "minimizing sources of genomic instability resulting from the repetitive nature of native yeast DNA" (Richardson et al., 2017). To this end, thousands of "LoxPsym" sites (basically, site-specific locations where genetic recombination can occur) have been added at synthetic "landmarks" via "synthetic chromosome rearrangement and modification by loxP-mediated evolution" (SCRaMbLE) (Dymond et al., 2011). As its convoluted name suggests, SCRaMbLE was designed "to permit on-the-fly genome rearrangements leading to a combinatorially diverse population of cells with a corresponding selectable phenotypic diversity…A large number of strains also contained duplications, providing additional useful variation to evolve new phenotypes" (Richardson et al., 2017, p. 3). In other words, scientists have inserted special nodes into the synthetic yeast genome that promote radical recombination, leading to forced genetic diversity. In a 2020 interview, Jef Boeke shared that a significant goal for Sc2.0 is compiling all its essential genes onto a single chromosome without LoxP sites, which will "never be lost or altered" as a form of safeguarding the 'wild type' genes. At the same time, this approach would ostensibly provide more flexibility for SCRaMbLE and a more comprehensive "universe of possible SCRaMbLE events" (presumably by allowing scientists to induce even more-radical evolution without fear of damaging the 'essential' parts of the organism) (J. Boeke, interview, 24 October

2020).

The insertion of SCRaMbLE sites into the synthetic yeast genome will, some claim, permit "on demand," rapid evolution due to the possibility for genomic changes on a scale unseen in nature, permitting unnatural experimental trajectories (Calvert & Szymanski, 2020). Transposons, also known as "jumping genes," are chromosome segments that may undergo transposition, moving elsewhere in the genetic sequence.

> Virtually all sequenced genomes contain transposons; the *S. cerevisiae* genome has five families (and overall, about 50 copies) of retrotransposons[16] called Ty elements that are bounded by long terminal repeat (LTR) sequences; recombination between the two LTRs has led to formation of hundreds of 'solo LTRs' in the genome. Bottom-up design of a synthetic yeast genome allows removal of every base pair of retrotransposon and LTR repeats, producing a potentially more stable genome free of mobile elements. (Richardson et al., 2017, p. 4)

This lengthy excerpt demonstrates a key goal of these alterations: greater genomic stability (i.e., ensuring that human-modified genomes will replicate and act according to their engineers' wishes), ironically achieved through recombination gone wild. Synthetic biologists argue that more stable genomes will both help elucidate essential conditions for life while also serving as a sturdy 'platform' from which to launch future modifications.

Several design principles guide these changes. Parsimony is nearly synonymous with virtue as scientists attempt to "streamline" and minimize the size of genomes by eliminating "junk" DNA, meaning sequences deemed to be useless or redundant byproducts of previous evolution (Langer, 2016). This notion resembles the concept of vestigiality.[17] Much to scientists' delight, many cells are surprisingly tolerant of gene-level edits to their genetic structure (Dai et al., 2020). Yeasts in particular seem to be masters of homologous recombination. This tolerance

[16] A transposon whose sequence is similar in position or structure (i.e., exhibits homology) to that of a retrovirus, which is an RNA virus that can insert a copy of its genome into a host cell to replicate. HIV is one infamous retrovirus.
[17] A famous example is the human appendix, though scientific assessment of its vestigial status has shifted in the past several decades.

seems to jibe with the hypothesis that organisms in general and yeast in particular have highly redundant elements within their genomes that can be transposed almost at will and ideally streamlined into a much more compact genome (Dai et al., 2020).

Importantly, this process is very much an educated form of trial-and-error. Despite rhetoric of control and design elegance, researchers take a stepwise approach, testing for "bugs" in an iterative way. "The fitness of the resulting recombinant semisynthetic strains is assessed, and any substitution that proves lethal or leads to a measurable fitness defect can be corrected, typically by reverting the sequence to wild-type ('debugging')" (Richardson et al., 2017). While this strategy establishes a basic blueprint for assembling Sc2.0, scientists have devoted significant time to developing and testing new pathways for scaling up genome synthesis (usage of the metaphor "pipelines" cropped up repeatedly in Boeke Lab meetings, as recorded in my field notes on numerous occasions throughout 2021-2022). Ideals of time and cost-related efficiency tend to take center stage in these discussions, underscoring the engineering mindset that directs much of this work.

In addition to collaborators at various academic and commercial research centers, Sc2.0 drew upon the labor of DIY scientists in Los Angeles (biohackers.la; though note that as of 2022, this group appears to be defunct; see Fig 4) and high school students at The Dalton School in New York City (Sliva et al., 2015).

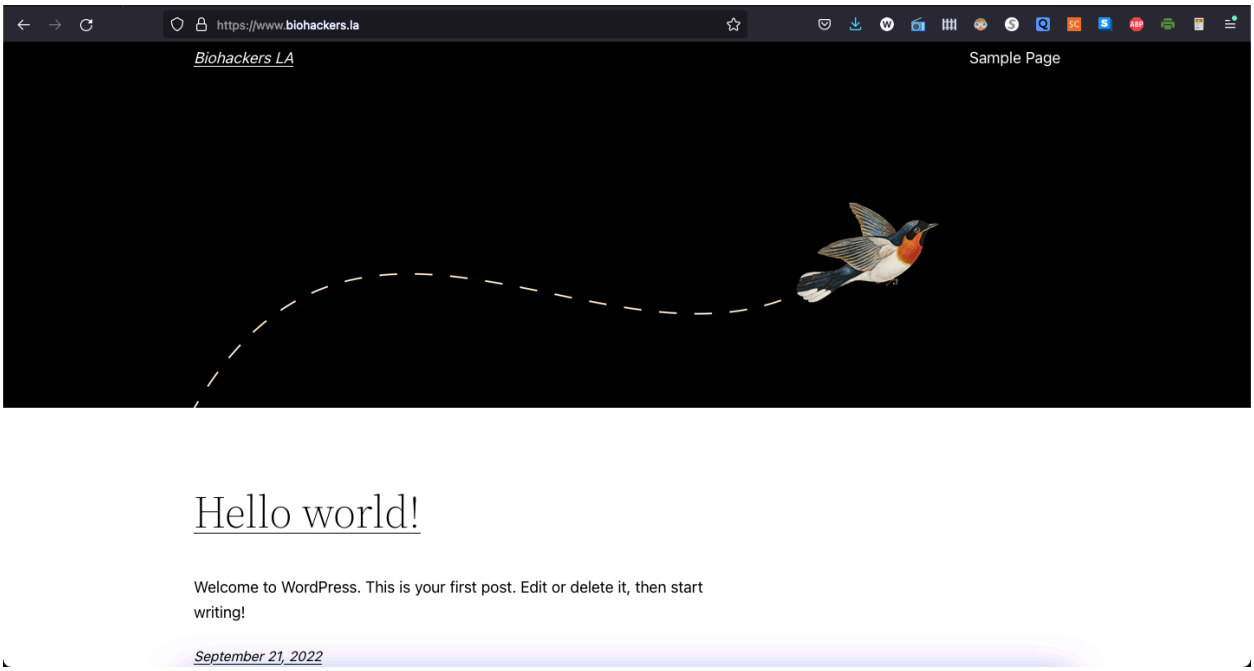

Figure 5: Screenshot of the apparently defunct Biohackers LA website. Despite appearing in Sliva et al. (2015), as of 2022, Biohackers LA seems to be no longer active.

As mentioned above, build-a-genome (BAG) undergraduate courses taught by scientists affiliated with Sc2.0 have been a recruiting tool and source of labor for this project as well, as some of my interviewees noted. Yet while Sc2.0 scientists tout this diverse network of collaborators, it became evident over the course of this project that many of the lesser-resourced actors engaged with Sc2.0 did not persist over time. That is, those actors not attached to prominent research centers with large pools of grant funds to draw upon have tended to sprout up and fall by the wayside relatively quickly as this project has evolved over the past decade. Part of this turnover is simply related to the fact that Sc2.0 is nearly finished, but I speculate that another factor is the lack of capital that speeds the unraveling of these actors' involvement.

As Sc2.0 nears completion, it raises the possibility of deeper human-yeast entanglements like the swapping of genetic material between our species (Laurent et al., 2015). My observations of Boeke Lab meetings quickly revealed that although work on Sc2.0 was ongoing in late 2020, it

has continued to slow as more members have shifted to working on other initiatives like the Dark Matter Project (thedarkmatterproject.org), which uses yeast cells as a 'platform' to engineer mammalian DNA, much of it in the form of mouse embryonic stem cells (mESCs) (Laurent, 2016). By late 2022, Sc2.0 has been mostly relegated to the background of this lab group's work, and the primary researcher working on its final stages (including assembling all synthetic chromosomes into a single cell) declined to speak with me individually. These observations make clear that although yeast-as-organism may have attracted some individuals to work with it in the first place, most of these folks have moved on from it, even as the work remains technically unfinished. This signals a vision of yeast as a model for *other* synthetic biology research rather than an end in itself. It also demonstrates the pressures research scientists are subjected to in following funding, which has reinforced conceptions of yeast-as-model in pursuit of human health-oriented applications that may not have any special need for yeast.

Sc2.0 Ethics/Governance

Following the First International Meeting on Synthetic Biology, held in Beijing in April 2012, the Sc2.0 team agreed to draft a document outlining its ethics and policy principles, which was circulated prior to the Second International Meeting on Synthetic Biology held in July 2013 (Sliva et al., 2015). The resulting ethics and governance document was once available at syntheticyeast.org, but its page is no longer maintained (see https://syntheticyeast.github.io/sc2-0/ethicsandgovernance/). However, I saved a copy of this document (dated 24 November 2013) earlier in the research process. Sc2.0's ethics and governance statement "enjoins researchers to work for the benefit of humankind; be open and transparent; comply with relevant national and local regulations; avoid providing materials to

those with nefarious intent; embrace an ethos of personal and environmental safety; undertake ethics training; and have a commitment to open sharing of intellectual property" (Appendix B). Societal benefit, intellectual property, safety, and self-governance form four key aspects of the project's ethics and governance statement (Sliva et al., 2015), which frame the 11 key statements that make up the document.

Although novel organisms in the United States are nominally regulated by the Environmental Protection Agency (EPA), Sc2.0 scientists practice self-regulation with regard to safety measures. In their laboratories, multiple species intertwine as yeasts, bacteria, mice, and humans collaborate and facilitate synthesis of DNA strands. While these sorts of interactions may sound unnerving to the uninitiated, they are quite common within biological research in general. Scientists do acknowledge that despite their efforts to create organisms that cannot thrive outside of controlled laboratory settings, they cannot guarantee that a "streamlined" yeast genome would be unviable in the wild (Sliva et al., 2015). Thus, one focus of the Sc2.0 project has been designing engineered vulnerabilities that could be exploited in case of accidental release.

Key actors within Sc2.0 highlight its emphasis on innovation and beneficial uses for its technology, claiming:

> ...the project is about the creation of a public resource—a platform—for asking questions about evolutionary biology and developing solutions to global problems, such as the need for sustainable energy sources and alternatives for the diverse small molecules that are currently obtained from petroleum. Members of the project agree that no intellectual property rights or restrictions on data and materials sharing should be exercised on the clones used to generate novel strains, intermediary strains, or the final Sc2.0 strain. These strains will be available to the broader community at cost through a central repository. (Sliva et al., 2015, p. 1025)

Still, my observations of scientists working on Sc2.0 and subsequent initiatives like the Dark Matter Project, which seeks to understand the function of non-coding DNA, reveal that they are

rather concerned with typical research-related worries, like poaching, publishing novel findings first, and generally staking out their intellectual territory. This does not discredit an orientation toward transparent science and nonexclusive intellectual property claims, but it does complicate the picture of altruistic, public-funded efforts painted above.

The 'unnaturalness' of synthetic organisms like Sc2.0 has been used as an argument for their safety, but it can also be leaned on when making intellectual property claims. If a synthetic organism is not a 'product of nature,' then it may evade the limitations imposed by the landmark 1980 Diamond v. Chakrabarty (447 U.S. § 303) decision in which a divided U.S. Supreme Court ruled that human-made bacteria could be patented. "Since synthetic biology aims to de-complexify and improve on natural biological systems, its creations are clearly different from what is found in nature, so an argument can be made that they are human inventions, and that they deserve the reward of a patent" (Calvert, 2010, p. 107). Some scientists have deliberately staked out intellectual property space in their work with synthetic genomes. Craig Venter notably added his own name alongside his collaborators' as a 'watermark' on a minimized bacterial genome, using codons to produce proteins corresponding to specific letters of the alphabet (Highfield, 2008).

It is possible to see all intellectual property law as the result of the persistent distinction between the natural and the artificial. "When something becomes intellectual property it is moved out of the realm of the natural into the realm of the artificial; it becomes an artifact" (Calvert, 2010, p. 107). Of course, the presupposition underlying this divide is rife with issues; if this is the case, what stable concept of 'nature' can we cling to in this era of synthetic biology? Where does culture end and nature begin? Franklin (2000) explains that "The twentieth-century transformation of life itself has had the consequences that the grounding or foundational function of nature as a limit or force in itself has become problematic and lost its

axiomatic, *a priori*, value as a referent or authority, becoming instead a receding horizon (p. 190).

Public engagement through a website (syntheticyeast.org) and public lectures offer opportunities for broader publics to learn about synthetic yeast research. Compliance with Sc2.0's Statement of Ethics and Governance requires collaborators to hold at least one public engagement event each year. However, given the current state of the Sc2.0 website and the lack of continuity with some preexisting partnerships, it seems that these public engagement efforts suffer either from lack of resources, will, or both. Sliva et al. (2015) note that synthetic biology benefits from the presence of do-it-yourself (DIYbio) laboratories, in which citizen scientists contribute to new developments in a rapidly growing field. At the same time, these community science labs typically fall outside of existing regulatory structures, which tend to lag behind advancements in synthetic biology in general anyway. In light of bifurcated public fascination and fear surrounding synthetic biology, this "suggests that scientists working in the field bear the unique responsibility of ensuring that the work they are contemplating or conducting is carried out in a way that maximizes the opportunity for benefit while minimizing the risk for harm" (Sliva et al., 2015, p. 1021).

Members of the Sc2.0 team see their self-regulatory efforts as part of a continuum that includes pioneers of recombinant DNA (rDNA) research in the 1970s and the 1975 Asilomar Conference (Department of Health and Human Services, 2012). They also advocate for case-by-case oversight and regulation of synthetic biology projects (Sliva et al., 2015). In keeping with the dominant narrative of cutting-edge science and technology, scientists tend to point out that policy flags in rapidly developing fields like synthetic biology. Policy makers are perceived to be too slow-acting and not knowledgeable enough to make informed regulatory decisions about synthetic biology. Stricter regulations are also interpreted as stymying the pace of development, so synthetic biologists prefer to self-regulate whenever possible. Sc2.0 researchers acknowledge

that project-level regulation is imperfect and patchy but contend that it helps fill gaps in existing regulatory structures while modeling beneficent, transparent science. The Boeke group also advocates for managing risk on a case-by-case basis, avoiding blanket oversight to all synthetic biology research. As Maurer (2012) suggests, both self-regulation and institutional and government oversight can mutually inform and benefit one another.

Programs focused on ethical, legal, and social implications (ELSI) tend to reinforce rather than challenge the credibility of promises made by synthetic biology (Balmer et al., 2016). From a critical standpoint, this undermines the utility of these frameworks for ensuring equitable distributions of benefits and risks. One intervention social scientists can make is in questioning foundational assumptions, like the general equivalence between cells and machinery or computer code. These assumptions do work; they have arguably helped catalyze discoveries and innovation in synthetic biology, which will lead to various medical (and other) applications. At the same time, how these applications will be implemented and made available to different populations is uncertain. Even more pertinent to this project, the assumptions grounding synthetic biology have both perpetuated typical anthropocentric relations toward the nonhuman world and extended paradigms of human control in new ways. From this perspective, no longer are humans merely 'masters' of extant bodies and heredity, but engineers of new bodies and new understandings of life itself.

GP-write: Humans up next?

The Genome Project-write (GP-write) is another international research project working with many of the same assumptions and approaches as Sc2.0 (Boeke et al., 2017). On Halloween 2015, a group of scientists convened at New York University's Langone Medical Center to discuss the

potential for a synthetic human genome. (Center of Excellence for Engineering Biology). This initiative became known as HGP-write (Human Genome Project-write) and sought to build upon the previous successes of HGP-read—the sequencing of the human genome—which had been accomplished nominally in 2003 but was not fully complete until March 31, 2022 (genome.gov). Much like HGP-read—the world's largest collaborative biological project, HGP-write was envisioned as highly interdisciplinary endeavor.

The first dedicated "Human Genome Project-write" meeting took place at Harvard in 2016 and provoked immediate negative reactions from bioethicists, synthetic biologists, and others, who expressed concerns about potential ethical ramifications (including human cloning and germ-line modification) and the lack of prior public consultation (e.g., Endy & Zoloth, 2016). The idea of a theoretical Homo sapiens 2.0 immediately elicits a response, perhaps because is hard to be organism agnostic when we are talking about our own species (Calvert & Szymanski, 2020, p. 13).

In the face of editorial and logistic headwinds and potential further public outcry, the leaders of HGP-write changed tack, renaming their endeavor GP-write and focusing broadly on the synthesis of other genomes (Calvert & Szymanski, 2020). Yet, the sensibilities and motivating forces behind the original project persist, likely because they are linked to the multiple forces that have held together synthetic biology assemblages so far. Oriented by assumptions and goals similar to its predecessor's, GP-write's mission is "To understand the Blueprint of Life" (Figure 5).

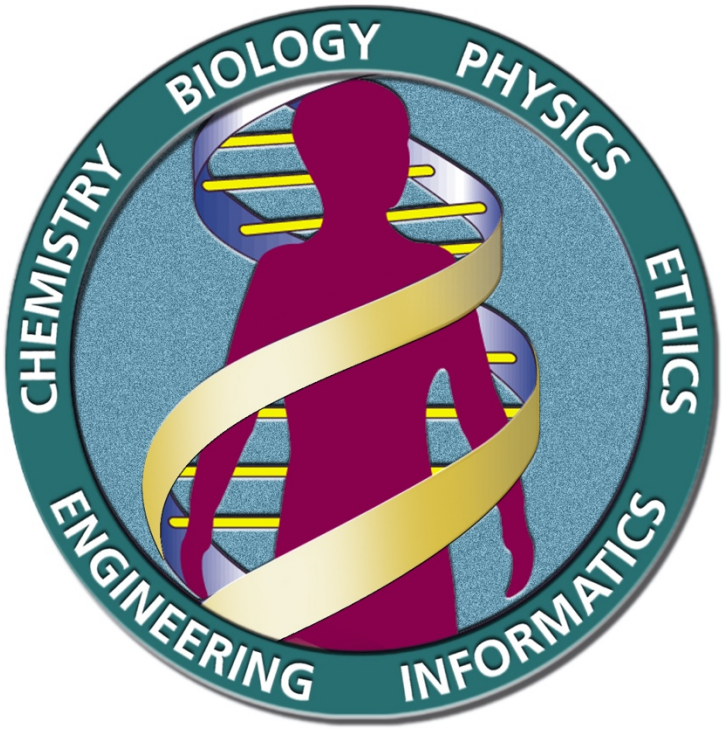

Figure 6: The logo of the Human Genome Project. Retrieved from https://www.wikiwand.com/en/Human%20Genome%20Project

This project furthers an emphasis on whole-genome synthesis that began with earlier synthetic biology initiatives. To accomplish this, a primary goal of the project is to economize the engineering of large genomes over the next decade in an effort to speed "whole genome engineering of human cell lines and other organisms of agricultural and public health significance" (Center of Excellence for Engineering Biology). The Center of Excellence for Engineering Biology (CEEB) emphasizes that special ethical, legal, and social implications of human genome modification will be considered throughout this project. One such consideration is restricting the project to operating on cells and organoids (artificially-grown, organ-like masses of cells and tissues) for the present (Center of Excellence for Engineering Biology). Citing the need for more complete understanding of the human genome and the potential benefits of that knowledge to humanity, GP-write claims that "Many scientists now believe that

to truly understand our genetic blueprint, it is necessary to "write" DNA and build human (and other) genomes from scratch" (Center of Excellence for Engineering Biology).

For the scientists associated with GP-write, the active modification of genomes is key to a more prosperous future and appears to be a moral imperative, or nearly so. The rhetoric used gestures toward sweeping goals and global problems and moving beyond "observation to action" (Center of Excellence for Engineering Biology). In addition to public funds in the form of federal research grants, GP-write has brought commercial collaborators into its work. Featured partners in GP-write include Autodesk, Hughes Hubbard & Reed, Labcyte, Twist Bioscience, ANSA Biotechnologies, Agilent, Lattice, Inscripta, Nancy J Kelley + Associates, DNAScript, Bhakti Creative, Signal Group, Indie Bio, and Catalog (Center of Excellence for Engineering Biology). The many linkages between this often publicly-funded research and a host of private corporations reveals the blurring of public-private distinctions in GP-write as well as synthetic biology more broadly, as companies and investors anticipate opportunities to capture value and capitalize on emerging, lively commodities.

Synthesizing a human genome is a much bigger challenge than synthesizing a yeast one, though this has not kept scientists from anticipating it (see Ellis, 2019, p. 6 for a clear example). A good deal of this challenge stems from the "sheer length of the human genome, which has three billion base pairs compared to yeast's 11 million" (Nature Biotechnology, 2016, p. 673). Some geneticists and observers contend that "The huge effort and money spent on creating a full complement of 23 synthetic human chromosomes may be a matter of diminishing returns" (Nature Biotechnology, 2016, p. 673). Others warned that the success of the Sc2.0 project should not necessarily lead to the conclusion that other genome sequencing projects would be equally productive. In a 2017 conference presentation, Richardson argued that the Sc2.0 project has been successful because "yeast loves us back." She suggested that before taking on the synthesis of

another genome it is advisable to "step 50 feet back and ask: is it as familiar and friendly to us as yeast?" (Calvert & Szymanski, 2020, p. 14). Anthropomorphism aside, this emphasis on the particularity of species is stands out in contrast to organism agnosticism typical of synthetic biology. Where the Sc2.0 project has raised questions about which design decisions will be made, which values will they reflect, and how and by whom will they be made, a potential synthetic human genome raises the profile and stakes of each of these questions.

Sc3.0?

In the last several years, DNA editing and synthesis advancements have allowed for greater scrutiny of the connections between genotype and phenotype. Building on the successes of the Sc2.0 project and its anticipated completion, Junbiao Dai, Yizhi Cai, and Jef Boeke have proposed "Sc3.0," the next generation of synthetic yeast (Dai et al., 2020). With each "version" of synthetic *Saccharomyces*, genes are categorized as "essential" or not and potentially refactored into more desirable configurations that mesh with the logics of synthetic biology. The proponents of Sc3.0 envision a similarly distributed model for the project's implementation, relying on the laboratories that participated in assembling the 16 chromosomes of Sc2.0 (known as synI-synXVI) to provide the labor for this new generation. Chromosomes may be added or deleted in this process; nothing is "off the table," so to speak (Luo et al., 2018; Mitchell et al., 2017; Shao et al., 2018). However, scientists recognize that gene interactions may arise in a single, large yeast chromosome that may prove fatal to the cell (Dai et al., 2020). To manage this risk, Dai et al. (2020) propose building and exploiting "the eArray, a circular centromere-containing DNA containing all of the essential genes, or a linear chromosome derived from it, synE" (p. 2).

This innovation will theoretically circumvent some of the barriers to viability and position scientists to iterate *Saccharomyces*' genome even more freely. Because SCRaMbLE (much like CRISPR) operates via stochastic or random deletions and other edits, the visionaries behind Sc3.0 hope that by moving all essential genes and their attendant regulatory sequences onto a centromeric plasmid (Dai et al., 2020), SCRaMbLE can operate freely on the remaining "nonessential" genes without risking lethality, which is much more likely in wild-type *Saccharomyces*, where roughly 1,000 genes deemed to be essential are spread throughout the genome (Shen et al., 2018). Theoretically, this walling-off of essential genes from non-essential ones will further enable ever-more radical deletions and modifications. Here it is worth pointing out that this novel structure is another example of (synthetic) life being shaped into an image predetermined for it by design-minded scientists. The eArray exists because scientists have rationalized its existence as a necessary component of more docile, predictable yeast.

Sc3.0 envisions a complete *de novo* (from scratch) rebuild of all genes to test and permit further modifications (Dai at al., 2020). Transcription promoters from related species of yeast may be imported into the new design, fulfilling computer science dreams of "versioning" yeast and readily distinguishing between native, Sc2.0, and Sc3.0 forms of genes. This endeavor is suffused with dreams of increasing control and "rational" design: "Since SCRaMbLE is largely random, multiple rounds of SCRaMbLE will be needed. Sc3.0 thus represents the ultimate tool for driving to the most minimal of minimal *S. cerevisiae* genomes" (Dai et al., 2020, p. 3).

Sc3.0's proponents speculate that further editing ("reprogramming") could be done even after genome minimization. Specifically, they lay out three principles to guide this approach. First, synonymous recoding of open reading frames (ORFs) will reduce the number of codons (a unit of genetic code in DNA) in the genome. Second, replacement of various regulatory parts of the

genome with fully-synthetic sequences or those borrowed from related species will allow reduction of intergenic (between-genes) sequences. Lastly, rearranging genes by function will aid in streamlining the genome overall (Dai et al., 2020). These reorganization principles demonstrate the mutual co-constitution of yeast and humans in synthetic biology through strong forces of desire. Yeast is re-made in specific ways that make sense to humans, while humans are re-made—perhaps through their perception of yeast as obliging these transformations—into subjects who increasingly conceive of yeast as the mechanistic, bare-bones 'chassis' that they desire it to be.

Sc2.0 helped achieve the dream of ontologically fixing yeast by removing "mobile" elements like retrotransposons from its genome, which allowed scientists to experiment with genomic stability (Dai et al., 2020). Sc3.0 attempts to go even further, prioritizing genome minimization and modification to non-coding regions of DNA in an attempt to probe "redundancies" in wild-type yeast and answer questions about the "minimum" genome necessary to support life under given conditions. Sc3.0's designers remain aware of their partial knowledge of the yeast genome and its regulatory mechanisms, but most of this concern seems to be geared toward ensuring cell viability and keeping their technologically-mediated evolutionary apparatuses running smoothly rather than reflecting on the broader implications of attempting to control life at this level of granularity. At the present, a significant amount of uncertainty revolves around interactions and co-regulation among different genes, which complicates visions of genes as discrete and interchangeable.

Moving forward

Decisions about how to regulate and dialogue with synthetic biology projects matter to broader human-environment relationships in the present and future. Synthetic biologists envision technoscientific solutions to crises as diverse as energy, food, and health, which aligns their projects with similar visions already circulating in centers of government and industry. These assemblages are made durable by their complementary visions for the future of multispecies interactions. Yet, social scientists and concerned others can still interject their own dreams and desires for the future into these spaces, potentially deterritorializing them and allowing new configurations of becoming. What will promote (responsive, responsible) research, human benefit, and innovation while simultaneously decentering humans a bit? Emerging technologies present particularly profound challenges for responsible stewardship because humans' understanding of the potential benefits and risks is incomplete, preliminary, and uncertain (Carlson, 2011). How do we ensure fair distribution of benefits and risks from synthetic biology? For example, in transitions from research spaces to health spaces and private/industrial applications, what paradigms and norms will dominate or endure "downstream?" How democratic will new applications of synthetic biology be?

My observations of the Boeke Lab suggest that most synthetic biologists do not have (nor are they trying to have) a 'relationship' with yeast in the sense that they are affected by its capacities and agency. Mostly, they seemed perplexed when I alluded to such an idea. Rather, it is clear that yeast is a proxy for advancing "basic" biological research at the molecular scale, and humans' interactions with it are almost incidental, or at least below a register that most humans detect. Promoting reflexivity and discussion among scientists may help stave off tunnel vision and keep more equitable futures in view. This can help transcend the reductionism of "human

health," which has come to dominate the *raison d'être* of synthetic biology insofar as current projects are increasingly partnered with and preoccupied by health-oriented organizations.

Still, discussions with synthetic yeast scientists reveal nuances in their understandings; sometimes yeast is portrayed as extremely controllable or compliant, but other times its vitality and ability to make things happen beyond the expected is acknowledged (oftentimes the unexpected result is failing to live and thrive despite a rational design that should theoretically work). One graduate student grappling with the challenges of assembling various components of the synIX chromosome (some of which had been redesigned and rebuilt several times) related the difficulties of "trying to make this a healthy yeast strain that behaves like a wild-type" (field notes, 23 November 2021). Qualitative interventions into these technical operations, when done well, may open space between technoscientific jargon and lived experiences. Species entangled in scientific practices—like yeast—are part of the 'equation' and affect the knowledge produced in the lab because they affect what humans think and do (Latimer & Miele, 2013, p. 24). STS scholars propose that a re-enchantment of life is fundamental to questions of governance and unsettling the dominant imaginary of synthetic biology. Bennett (2017) argues that "the power of biotechnology cannot be successfully regulated if dealt with only in a piecemeal fashion. Biotechnology needs to be governed at the level of the broad cultural imaginaries that govern it" (p. 169). A misalignment of principles and practice in synthetic biology speaks to the need for further inquiry. Social scientists can help by taking critical theoretical stances and understanding the science well; otherwise, they risk irrelevance.

Conclusion: Biotechnology and the social imaginary

As Taylor (2002) puts it, "the social imaginary is not a set of ideas; rather it is what enables, through making sense of, the practices of a society" (p. 91). Much like cultural and social institutions, biotechnology plays an active role in shaping our sense of how life itself is ordered and the possibilities it offers for the future. This framing of biotechnology renders visible some implicit, foundational assumptions of synthetic biology. These assumptions form the necessary background for scientists to develop biotechnological imaginaries that elevate or relegate forms of life (see Jasanoff, Hurlbut, & Saha, 2015, p. 26-27). These imaginaries shape everyday decisions for scientists, but they also shape collective futures when they are drawn on as cultural reserves.

Aristotle postulated that life is defined by immanent activity; that is, nature defines its own nature. Spinoza subsequently espoused the notion of *Natura naturans* ("nature naturing"), arguing for a self-referential and self-driving character of life (Lord, 2010, p. 37). Canguilhem, on the other hand, rightly points out that sometimes life does not replicate or iterate itself with complete fidelity, citing diversity and abnormalities. These failures of allostasis may be nonetheless durable and survivable (Bennett, 2017). From this perspective,

> ...it is never enough for the sciences of life to be based on a concept of life. The sciences of life must also be based on an experience of life. The combination of these two—the concept and the experience—generates a situation in which biology can never quite free itself from what has been called "vitalism"...[which] refers to the way in which the living thing functions as a unified being that has an intrinsic capacity to act in the world in a way that is neither predetermined nor random. Living things are not just bundles of passive mechanisms; they are also agents. (Bennett, 2017, p. 174-175)

At the risk of sounding pedantic, it is worth noting that at a foundational level, biologists still hold *a priori* that living organisms are alive (life-as-concept), and that this understanding persists

despite centuries of conceiving nature as mechanical/passive and more recent trends toward understanding life via information metaphors (life-as-experience). There is seemingly an aporia between these modes of life (experience vs. concept).

The older concept of an "analogy of being" assumes that one living thing is so much like another living thing that they share a "participatory ontology." For synthetic biology, digital and living things are linked by information in a similar ontology (Bennett, 2017). If this analogy between conceptualizations of life remains flexible, there is the possibility for experimental and philosophical evolution. On the other hand, analogies can become "so deeply internalized into the rhythms of laboratory life that infrastructures—from buildings to habits, processes, concepts, machines, and business plans—were designed to actualize and thus reify them" (Bennett 2017, p. 183). DNA and information may be similar in some ways, but similarity has begun to ossify into identity in synthetic biology. This understanding underpins contemporary synthetic biology and allows for its subsequent analysis.

6. A POLITICAL ECONOMY OF SYNTHETIC YEAST

> "Politics is an art, and an art has no ground to demand compliance from what it deals with. It has to create the manners that will enable it to become able to deal with what it has to deal with."
>
> -Isabelle Stengers, "The Cosmopolitical Proposal"
>
> "If we have any dreams of handing a livable world to our descendants, we will need to fight for the possibilities of resurgence. The biggest threat to resurgence is the simplification of the living world as a set of assets for future investments."
>
> -Anna Tsing, "A Threat to Holocene Resurgence is a Threat to Livability."

Much like other, earlier biotechnologies, synthetic biology works by "extending the reach of human manufactures into the texture of life itself" (Pottage, 2007, p. 324). In an important sense, then, synthetic biology is much like other technologies humans have developed and relied on for years, including crossbreeding and fermentation. The difference is that instead of 'domesticating' nature, organisms themselves are being remade.

Beginning in the late 1960s, yeast molecular biology was a crucial part of "academic and industrial biomedical research on the world stage" (Langer, 2016, p. 430). In the 1970s, this manifested in the development of genetic engineering methods and the beginnings of the biotech industry. The era of recombinant DNA technology that began in the 1970s allowed scientists to directly manipulate yeasts on levels that had been previously achieved only with prokaryotes like *E. coli*. This reality has been described as yeast becoming "prokaryoticized" (i.e., made manipulable in ways similar to prokaryotes), while biology itself was becoming "eukaryoticized" (i.e., more concerned with eukaryotes as organisms of study and models of how life itself works (Langer, 2016, p. 429). Yeast was increasingly studied in genetic terms, and genes were a sort of

consolidating force through which biology writ large was standardized, with the help of model organisms (Ankeny & Leonelli, 2011). Advances in synthetic biology developed in response to funding opportunities. "These tools had been engineered to molecularize humans in a broader effort to reap societal benefit from American public investment in science and to fuel the economic engine of research as an industry in its own right" (Langer, 2016, p. 430). Lessons learned from yeast cell biology were extrapolated to other organisms.

Yeast artificial chromosomes (YACs) developed in the 1980s helped researchers study malfunctioning nucleus divisions during mitosis (a type of cell division yielding two 'daughter' cells with the same number of chromosomes as the 'parent' cell), which could be applied to understanding conditions like birth defects (Sullivan, 1983). These YACs were also used in early cloning technologies to map the yeast genome. By the end of the 1980s, the initiation of a yeast genome sequencing project opened the door to a number of additional ways for yeast science to model and engineer human health and disease" (Langer, 2016, p. 430).

Increasingly, genomic research has been emphasized over other forms of "basic" research (whether in epidemiology, psychology, cognition, or other fields), making clear the United States' federal prioritization of clinical and commercial applications over alternate interventions in health (Woolf, 2008). Arguing for more "basic" biological research (i.e., genomic research deemed to be at the base of all life), Botstein (2012) explicitly linked this work to interest in human health outcomes among scientists, suggesting that their curiosity was critical to the success of these "translational" research agendas.

Model organism-centered research in synthetic biology has shaped biomedical visions of the future, including ordering research priorities and emphasizing "translatable" applications and analogies while incorporating private foundations, public grants, not-for-profits, and corporations into its technoscientific imaginaries. "The prioritization of genomic research over

other types of "basic" research in epidemiology, behavioral science, psychology, communication, cognition, social marketing, economics, and political science, for example, has made clear the federal emphasis on clinical and commercial outcomes over other types of health interventions" (Langer, 2016, p. 435).

Yeast is increasingly implicated in precision medicine as a sort of surrogate for human cells due to its presumed functional homology with human genes (Langer, 2016). Oncologists have studied the effects of tailored chemotherapy drugs on mutated yeast cells, while synthetic biologists push toward various forms of "humanized" yeast via the Dark Matter Project, among others. In one Boeke Lab meeting on this topic, a postdoc wrote in the chat that "Genetics in humanized yeast is a pain! But its [sic] possible." Laurent et al. (2016) envision personal, yeast "avatars" that will aid in identifying optimal treatment pathways through specific expressions of combinations of genes (p. 7).

Proponents of yeast model research have argued that its development will, over time, reduce the need for animal bodies to serve as screening mechanisms for new drugs before they are tested on humans. However, Roberts and Oliver (2011) point out that animal testing rates have not declined, despite a burgeoning body of yeast-related work. My own conversations with synthetic biologists support this assertion. Researchers in the Boeke Lab increasingly view yeast as almost a "stepping stone" to more direct work with mammalian cells. While *Saccharomyces* is currently used to develop specific parts of molecular pathways in mammalian cells, one researcher I interviewed expressed his hope that eventually they would be able to abandon working with yeast in favor of more-complex organisms, including working directly with non-chimerical (non-hybridized) human cells.

All these efforts mark a shift in the relationship between biological models and the phenomena they seek to explain:

> Rather than determining if or how yeast models may be generalized given their differences with humans, these practices show how yeast models are seen as already relevant. The question now becomes how to most accurately engineer yeast to justify these extrapolations since yeast has become both a model technology and a technology of modeling." (Langer, 2016, p. 436)

Current yeast models not only offer potential analogues for studying human disease; they also generate valuable "functional, comparative, and systems level data," which synchronizes with current emphases in biological innovation (Langer, 2016, p. 436). Because yeast genes can be "deleted, mutated and reintroduced into yeast cells, overexpressed, tagged and thoroughly studied," Foury (1997) contends that yeast offers matchless instruction in understanding how disease associates with human gene functions (p. 8).

While much synthetic biology discourse emphasizes how its work is 'solving' big challenges, it is not always clear where the solutions start and the amassing of data stops. One laboratory technician alluded to this situation while relating a conversation they had with a supervisor in the lab. Asking the supervisor whether he thought they were making good progress in their work (in hopes of securing an extension to a large grant they've been working under), the supervisor replied,

> It's complicated...in a lot of ways we've achieved a lot, but in a lot of ways we haven't achieved a lot, and most of our promises to advance research about disease have not come to fruition. We've developed technology in a really awesome way. We've studied some basic science...and we've made strides in that. But the human disease research that we kind of promised we were going to do in the initial grant [did not materialize]. (interview, 13 September 2022)

Of course, shortfalls in research are ubiquitous (including in this project), but what this interviewee seemed to be suggesting is that in the daily realities of conducting this sort of work, the revolutionary leaps promised in much public-facing discourse do not align with the situation in the lab, where scientists are forced to contend with the limits of their control.

In this chapter, I argue that an assemblage approach provides a workable frame for moving

between the most extreme scales of yeast-human relations, from the microgeographies of individual laboratories to the global political economy of the synthetic yeast industry. Along the way, I identify important agents and matters of concern in this assemblage, paying attention to the ways in which power shapes dimensions of the yeast lab and the entities co-constructing it.

Organismic capital

Advances in genetics are blurring distinctions between nature and culture, leading to an increasingly entwined bio-sociality. "Biotechnology, biodiversity, bioprospecting, biosecurity, biotransfer, and other things bio – draw novel lines of property and protection around organisms and their elements (e.g., genes, organs), which now circulate in new ways as gifts, as commodities, and as tokens of social belonging or exclusion" (Helmreich, 2016, p. 1). Aiming to stabilize and standardize life, scientists apply similar principles to both model organisms and new synthetic organisms. By developing more standardizable forms of life, synthetic biologists seek organisms and parts of organisms that are exchangeable. But the same properties that make model organisms and synthetic organisms useful laboratory subjects—uniformity and predictability—also make them more easily commodifiable and subject to intellectual property claims (Calvert, 2010).

Plants preceded microbes in this arena. The 1930 Plant Patent Act in the United States paved the way for plant varieties to be patentable, since asexually reproducing plants were deemed not to vary (Pottage & Sherman, 2007). Plant breeders were understood to be crucial agents in these plants' propagation and "to normalise the abnormal, to stabilise and standardize nature's deviants, mutations and aberrations" (Pottage & Sherman, 2007, p. 559). The theme of eliminating difference and homogenizing a 'product' lives on in contemporary crop breeding

programs and synthetic biology projects. "The catalogues that plant breeders produced so that their wares could be bought as replicable copies bear strong similarities to the 'catalog of parts and devices' that can be found on the BioBricks website" (Calvert, 2010, p. 106; https://parts.igem.org/Main_Page).

It is increasingly clear that data about organisms does more than simply offer a neutral overview of their populations, distributions, and tendencies. Rather, databases and institutions contributing to data infrastructures of living things are crucial to understanding environmental governance in the 21st century, and "data has become a significant site in which contemporary environmental politics are waged and socionatures are materialized" (Nost & Goldstein, 2022, p. 3).

Economies of scale in synthetic biology

Synthetic biology is of course concerned with life on a scale smaller than what is visible to the unaided eye, but it has also become a powerful mode of knowledge production and resource capture on a global scale. Laboratories around the world (largely in the Global North at the moment) have incorporated the sensibilities and practices of this emergent field into more durable associations simultaneously shaped by and solidified through scientific practice. More than the speculative cellular manipulation of its earlier days, in the 2020s synthetic biology is a set of infrastructures enrolling many actors—human, nonhuman, living, inanimate—in institutions, grant-funded projects, and countless bytes of data. These data, especially, form a significant site where new biological politics, ethics, and socionatures vie for recognition and dominance. Like the biological entities they purport to represent, data are material and semiotically rich. Yet, the nature of data suggests disembodiment and global circulation in

tandem with urban capital flows, even as it still "inhabits" a particular geography of servers, labs, and private corporations. Synthetic biology operates across many scales at once, and only by flitting between some of its curdlings and slackenings will more complete conceptualizations of its totality emerge.

A series of Sc2.0 and synthetic biology conferences have played an important role in institutionalizing and advancing synthetic yeast over the years. In 2012, the First International Synthetic Yeast Genome Meeting was held in Beijing, China, followed by the Second in London the following year. The Third International Synthetic Yeast Genome Meeting took place in Taormina, Italy in summer 2014, in tandem with the International Synthetic and Systems Biology Summer School (2014). The synthetic yeast project website partly documents these early conferences, which ostensibly provide

> …critical 'face time' for all researchers involved in the project to directly interact, in particular the students and postdocs who are the frontline 'chromosome builders'…these meeting [sic] attract members from the synthetic biology community, yeast research community, plus representatives from industry. The yearly meeting provides an important opportunity to discuss downstream uses of the synthetic genome and collaborations with groups wishing to get involved in using Sc2.0 strains. (Synthetic Yeast 2.0, 2022)

In 2015, the 4th Annual Sc2.0 and Synthetic Genomes Conference was held in New York City and co-sponsored by NSF Science Across Virtual Institutes (SAVI), NYU Langone Medical Center, and Nancy J Kelley + Associates (https://events.bizzabo.com/SynGenome2015/home). After three iterations of conferences that had focused primarily on the Sc2.0 project, this meeting marked a shift in synthetic yeast researchers' orientation toward what was seen as the work of the future. As the organizers explained, "This year we are expanding the conference to include a focus on Synthetic Genomes and Engineering Biology. This is a hot topic and we are thrilled to announce that this year's program will include two panel discussions: 'Genome Engineering and Society' and 'What's the Next Big Genome to be Synthesized?'…The meeting

will also feature panel speakers and demonstrations from the lab automation and DNA synthesis industries and a poster session" (bizzabo.com, 2015). As a bonus feature, the conference included an "in-depth technical, gustatory and social analysis of yeast products of the liquid kind (coffee, beer and wine)…Conference attendees will have the unique opportunity to taste several beers for which the 'genotype-phenotype' relationship of the brewing yeast has been characterized" (bizzabo.com, 2015). Photos shared on the website of Nancy J Kelley + Associates (2023), a biotech company that helped organize and sponsor the meeting, display some of these sensorial aspects of the meeting (Figure 7).

Figure 7: A table of taster glasses proudly displays a yeast cell-shaped logo made up of interlocking puzzle pieces. Brewed with yeast that scientists claimed to have discovered the connections between its genotype and phenotype, this comestible contributed to the materiality of the conference. Photo from https://nancyjkelley.com/case/sc2-0-synthetic-genomes-conference

Nancy J. Kelley's (2023) website for the event proudly centers a quote by Jef Boeke encapsulating the conference and the company's role in realizing it: "The 2015 Sc2.0 conference was the biggest and the best meeting to date. Nancy J Kelley + Associates took the event to an entirely new level of professionalism and prominence, attracting nearly 200 scientists from over 8 countries and numerous new sponsors." The company highlights how the meeting was featured in multiple scientific publications and far-reaching news outlets. An "Operating budget of $70K was managed effectively, resulting in a profit of $10K (15%+)" (Nancy J. Kelley + Associates, 2023). Clear themes of growth, profit, and private capital are evident in this iteration of a once-niche subfield of biological research.

Walker and Cai (2016) document the Fifth Annual Sc2.0 and Synthetic Genomes Conference, held in Edinburgh, Scotland. Signs of synthetic biology's expansion beyond yeast as the focus of the meeting included Jef Boeke's presentation on HGP-Write. With regard to yeast, Boeke "reported that all 16 synthetic yeast chromosomes have been assigned to laboratories located in the USA, China, the UK, Australia and Singapore, with successful integration of approximately 60% of the overall synthetic yeast genome" (Walker & Cai, 2016, p. 920).

From this point onward, overlaps between the Sc2.0 conferences and other synthetic biology-focused meetings proliferated. The 6th Annual Sc2.0 Meeting was tacked on to the end of SB7.0, the Seventh International Meeting for Synthetic Biology at National University of Singapore in 2017 (Eventbrite, 2023). This large event was co-sponsored by the BioBrick Foundation and SynBioBeta, "the premier innovation network for biological engineers, innovators, entrepreneurs, and investors who share a passion for using biology to build a better, more sustainable planet" (SynBioBeta, 2022a). SynBioBeta also hosts an annual Global Synthetic Biology Summit, which returned to an in-person event in 2022 at the Oakland Marriott City Center after two years of virtual meetings due to the COVID-19 pandemic (SynBioBeta, 2022b).

In an obvious political reference, the conference website proclaimed, "we're bringing synthetic biology's leading community of innovators, investors, engineers, entrepreneurs, scientists, thought leaders, policy makers and academics together to *Build Back Better With Biology!*" (SynBioBeta, 2022b; emphasis original). The same page also emphasized a certainty about the success of the young field: "Synthetic Biology is taking on the world's biggest problems and winning!" The conference is slated to return to its home in Oakland in May 2023.

Though I could find almost no information about it, the 7th International Yeast 2.0 and Synthetic Genomes Conference was held in Sydney, Australia from November 26-28, 2018 (SGDWiki, 2022). The 8th Annual Sc2.0 Meeting was co-billed as the Genome Project-Write meeting and hosted at NYU Langone health in 2019, demonstrating the importance of the Boeke Lab to these projects. The Yeast Genetics Meeting, held in even years around the United States, is another conference series with ties to this project, holding its most recent meeting in August 2022 at UCLA (https://genetics-gsa.org/yeast-2022/). Like any international-scale research conference, these meetings provide opportunities for exchanging knowledge, connecting with business and publishing interests, and coalescing of popular discourses and approaches.

Aside from these events, technological innovation in synthetic biology processes and techniques has played a role in scaling up this research. Increasing automation and more efficient workflows have substantially reduced the cost of DNA sequencing and synthesis. This in turn has opened new possibilities for working with larger genomes on faster time scales (including the human genome, for example). Attempting to account for the cost of the Sc2.0 project, Richardson et al. (2017) note,

> Further improvements in both the software and DNA synthesis technology, with current synthesis costs for Sc2.0 averaging approximately US$0.10 per base pair, mean that genome-wide synthesis projects like this one will become routine. At this price, the overall cost for the Sc2.0 DNA, accounting for required overlaps, the synthesis of URA3 and LEU2 markers that are incorporated and then deleted, and errors in synthesis that

> require resynthesis of segments, is estimated to be approximately US$1.25 million. The total costs of the project, including labor for assembly, genotyping, sequencing, evaluating fitness and phenotypes, debugging and correcting bugs, developing and maintaining software and servers, and other activities and associated indirect costs will be, of course, considerably higher. The next design frontier could involve living systems that will be less and less similar to native genomes and more like de novo designs." (p. 1044)

These sums are not insignificant but considering the array of funders willing to support this kind of research, laden as it is with promises of potentially lucrative pharmaceutical, biofuel, and other applications in the future, it seems like that *Saccharomyces cerevisiae* will be only the first of many eukaryotic organisms with a synthesized genome.

As the center of the Sc2.0 project, the Boeke Lab is very well-resourced. When asked to describe the lab, one of my interlocutors noted,

> ...our lab is fairly large, even for sort of an academic medical center. So we have a floating, sort of, population between 20-30 people at any one time, and this includes graduate students, postdocs, staff...and, of course, the PI. That's Jef Boeke. And because it's in a academic medical center, we, you know, we're, I think generally pretty well resourced. We have a lot of core facilities, which are basically shared facilities that are provided to us by the institution that provide all sorts of services that make our sort of day-to-day research experience a lot easier. So in terms of like, you know, washing your dishes or, you know, preparing certain solutions that you might need or you know, like the person I was just on the phone with handles our mice and makes mice for us and things like that. So...so that's, that's again, it's pretty nice. (interview, 23 June 2020)

As this passage makes clear, researchers in the Boeke Lab are supported by a host of technicians, facilities staff, and outside vendors who provide equipment and supplies, living organisms like mice for experimentation, and conducive lab space maintained by support staff. Though I could not observe this more closely than through the small (Zoom) windows of access I had from afar, even this convivial lab group exhibits aspects of a hierarchical power structure. Laboratory technicians and junior graduate students provide significant assistance to more senior students and professional researchers, who in turn support the sweeping goals of a

handful of primary investigators. Knowledge and power are co-constitutive here. Experience and conscientiousness evince some of these power strata of the lab; less-experienced members who frequently deal directly with supplies and equipment seemed more likely to commit errors in its handling. On this latter point, the Lab Supervisor frequently chimed in at the end of weekly lab meetings to admonish the research team for their conduct and use of laboratory resources ("We need to talk about dry ice packages! $4,000 in materials just goes to trash" (field notes, 14 October 2022)). Whether it was leaving dry ice out or failing to properly clean up benches, close freezer doors, or submit requests to re-stock reagents, this staff member often expressed mild frustration with the students and postdocs, though this never seemed to escalate into anything more significant than metaphorical slaps on the wrist. On rarer occasions, Jef Boeke himself joined in chastising unnamed members publicly, lamenting in one meeting that "people are being horrible lab citizens!" for offenses including opening multiple packages of plates at once and failing to reorder spent reagents (field notes, 25 August 2021).

What is a 'wild type'?

Largely due to its long associations with humans, *Saccharomyces cerevisiae* is a highly domesticated microbe, found more often in fermentation tanks, laboratories, and vineyards than in "the wild" (Gallone et al., 2016). This long history of domestication and cohabitation with humans is held up by synthetic biologists working with yeast in laboratory settings as rationalization for further genetic modification; if humans have already been selecting for certain yeasts at the colony level over millennia, perhaps DNA-level manipulations are more a difference in degree than in kind.

What makes a strain of yeast 'wild' or not is context dependent. In the synthetic biology lab,

"wild-type" signifies specific strains of domesticated *Saccharomyces* that have been previously selected for their desirable, well-known properties. These wild-types serve as controls in experiments targeting specific genes, for example. However, to the brewer, "wild" yeast is explicitly not *Saccharomyces cerevisiae*, but rather numerous other species of yeast that have been traditionally viewed as undesirable for "clean" beer production. In either case, wildness serves to differentiate yeast in some way, though even in the lab, what is "wild-type" can theoretically change with population structure over time: the most common phenotype of a species is usually afforded "wild-type" status. Wildness is often synonymous with "natural," though these frequently collocated words can also sow confusion.

What makes a strain of yeast "wild," then? In some ways, wildness becomes defined by exclusion. Wild-type yeasts lack deliberate, human-induced genetic alterations.[18] When genes are "knocked out" or yeast DNA is transfected with a foreign plasmid, yeast loses its wildness. But such wildness can be preserved when employing less technologically advanced or more traditional methods. The irony of this definition is that "tools" like CRISPR-Cas9 are "natural" in the sense that they are part of the cell's existing capabilities, wild-type or not. Yet by harnessing and manipulating these natural functions, humans can banish wildness from yeast. Two observations follow. First, this understanding necessarily situates wildness as a temporal, non-fixed definition (because what is considered "wild-type" is the historical product of human-yeast interaction), and second, this conceptualization is linked to scale because changes made at micro scales (i.e., the level of base pairs or homology arms) disqualify wildness, while more

[18] Though technological modality seems to be of importance here. For instance, a brewer manually selecting specific colonies of yeasts for favorable characteristics over many generations would likely still be considered to be working with "wild-type" (albeit not "wild") strains, even though the result of these deliberate selections presumably makes the yeast less "wild." This is evocative of animal breeders or farmers making intentional choices about how to optimize their animal populations. On the other hand, scientists using a variety of gene-editing tools (including "natural" ones like CRISPR) would likely be considered to no longer be dealing with wild-types but rather with a non-wild, experimental strain.

macro-scale changes (i.e., selecting or discarding certain yeasts because of some phenotypic or functional characteristic) can preserve it.

To further muddy the waters, yeast function, or what the organism can actually do, seems to work across both scales (e.g., a wild-type/experimental-type yeast can rearrange elements of its DNA naturally with CRISPR/unnaturally with human-induced CRISPR). While wild-type yeasts have a set of well-known capabilities and functions, "natural" changes to these via evolution (whether helped along by humans or not) is possible. On the other hand, experimental strains of yeast have demonstrated numerous "non-natural" capabilities and functions, including the ability to survive in unfavorable conditions or to express specific proteins. Therefore, function alone may not be an especially useful criterion for delineating wildness or lack thereof. This observation might both delight and frustrate synthetic biologists, who tend to face headwinds when their work is cast as "unnatural" or Frankensteinian. A conceptualization of genetically modified yeast as "natural" or all yeast as not "wild" levels distinctions based on naturalness. Yet, working with this understanding essentially invalidates the concept of a wild-type microorganism entirely, rendering that distinction meaningless. The intersecting strata of scales and technologies at play here complicates straightforward classification of yeasts.

Still, the concept of a 'wild type' remains nearly omnipresent in discussions of synthetic yeast because it provides a point of reference, however fraught, for comparing obviously synthetic organisms against (Figure 7). Despite its continued use, geneticists increasingly acknowledge the contingency of this archetype. "In nature, there is no wild type, rather, all phenotypes are quantitative traits…beyond some arbitrarily defined point along a spectrum" (Hartman et al., 2001). Calvert and Szymanski (2020) concur, noting that "While the phrase "wild-type" is employed to describe the yeast that serves as the template for engineering in the synthetic yeast project, this "wild-type" is, in fact, a highly domesticated laboratory strain" (p. 6). Roberts and

Oliver (2011) raise the question of whether any strain of yeast can function as a standard type, since "noise in cellular transcription or translation processes" produces "phenotypic individuality" even when grown from a single colony under constant environmental conditions (p. 481-482). When other methods of genetic shuffling like lateral/horizontal gene transfer are added to the mix, it becomes even more clear that rigid understandings of wild types and standard strains are too narrow to usefully reflect the nature of reality (Gonçalves & Gonçalves, 2022). In my field notes, I recorded an interesting exchange related to this difficult terminology. Perhaps thinking though some of these ambiguous meanings, Jef Boeke addressed a PhD student's use of "wild-type" in their research on the synIX yeast chromosome: "We try not to use 'wild-type' —we try to use 'native.' Or just 'IX' instead of that" (25 May 2022). In the same meeting, the student was advised to describe suboptimal yeast cells as "unfit" or "unhealthy" instead of "sick."

Thus, distinctions between 'natural' and 'unnatural' are muddy from the start and only get more abstract as synthetic biology continues to work on yeast. Synthetic biologists have already incorporated genes found in different strains of *Saccharomyces* into a more pluralistic genome, and it is believed that a more diverse "gene pool" of genetic resources may benefit full-genome synthesis projects. Still, given its centrality in synthetic biology presentations and experiments, it is important to consider the yeast designated as the "standard strain."

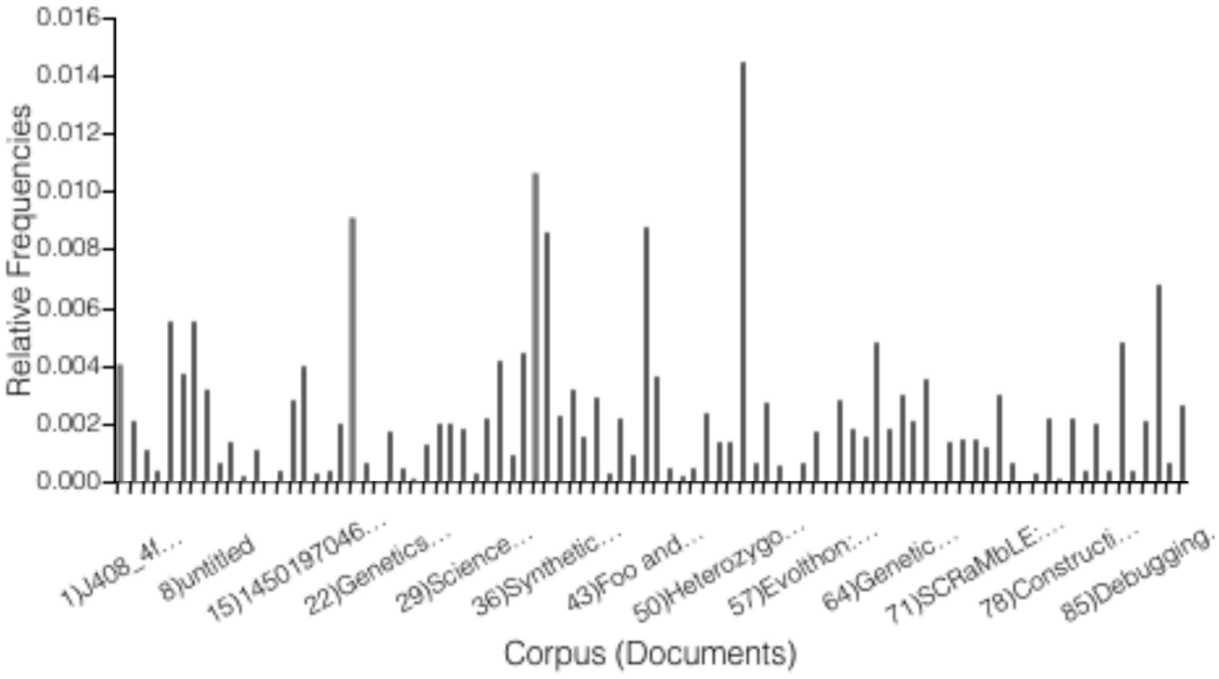

Figure 8: Relative frequencies of the phrase "wild*type" in the text corpus. The asterisk is a wildcard character; use of this term captures discrepancies between "wild type" and "wild-type," as they are used interchangeably. The x axis is organized chronologically, while the y axis displays relative frequencies. While there is no clear trend, use of this phrase is common across most of the texts.

S288C[19]

As microbiological techniques became more sophisticated, yeasts were reorganized into taxa based not only on their origins but their uses in various products and ecological relationships. In the late 1930s, yeast scientists sought to create a "breeding stock" with which they could hybridize and catalog the range of yeast species in circulation at the time (Langer, 2016, p. 139). But combining desirable traits from different strains into a single, superior strain proved to be exceptionally difficult. Researchers at the Carlsberg laboratory and Washington University in St. Louis reported that "yeasts were refusing to mate, or that they would not form spores, or that

[19] For a much more in-depth (and excellent) account of S288C and the "standard strain" of *Saccharomyces*, see Chapter 2 of Langer, 2016.

their spores were dying quickly…Some investigators reported hybrids offering a perfect reflection of their parents; others found offspring behaving wildly unexpectedly. Conflicting observations led to conflicting explanations, and the disagreements about yeast appearance and behaviors led to more disagreements about the yeasts' hereditary mechanism" (Langer, 2016, p. 140). This chaotic situation did not lend itself to scientific ideals of sustained progress. In the 1950s, scientists (led by Robert Mortimer at the University of California-Berkeley) collaborated on a compromise solution: "S288C, a shared laboratory strain of the industrial baker's yeast *Saccharomyces cerevisiae*, which served as an experimental "wild-type" in the decades which followed" (Langer 2016, p. 140). Decades later, Mortimer coauthored an account of the genealogy of the S288C strain, tracing its parentage to six progenitors, of which "approximately 88% of the gene pool of S288C is contributed by strain EM93" (Mortimer & Johnston, 1986, p. 35). This organism became a standardized part of laboratory sciences, fulfilling the role of a docile, knowable body that would be amenable to future interventions in its genome. In this way, S288C became a part of scientific material culture (Shapin & Schaffer, 1985, p. 25) and a sort of holotype, which is a single specimen that stands in for an entire species through its description and characteristics.

Throughout the latter half of the 20th century, S288C became ubiquitous in yeast research, challenging traditional distinctions between 'natural' and 'artificial.' Because of its storied life in the lab coupled with its persistent 'wild type' designation, this "standard strain" begged questions of its very identity. Langer (2016) writes,

> It was argued that *S. cerevisiae* is essentially a human artefact, maintained in domestication. Despite this artificiality, S288C was a natural choice for a standard at midcentury because it included many of the ideals and compromises of the first generation of yeast geneticists. If it had become subsequently "artificial" that was only because it was so widely used." (p. 214-215)

The coalescence of forces that led to the elevation of a seemingly arbitrary strain of baker's yeast demonstrates how scientific knowledge is produced through the interaction of multiple (and multidirectional) agents and movements.

> Organisms are part of this multidirectional traffic. They are co-opted and deployed by scientists in the support and defense of particular amalgamations of theories, beliefs, and practices. And, in the process, organisms are themselves transformed into symbols, embodying the theories and traditions that first put them on the map" (Mitman & Fausto-Sterling, 1992, p. 176).

But these symbols are no longer the same; they are hybridized and reterritorialized in an image of the forces that deterritorialized them in the first place. Thus the 'wild type' strain S288C exhibits a hybridity "as both a participant in a Latourian network of 'nature-culture' and as the cohabiting and interdependent model organism with which to molecularize humans in the sense of Haraway's collapsed duality and contracted term 'naturecultures'" (Langer, 2016, p. 353).

Efforts to sequence the S288C genome got underway in 1989. By 1996, project leaders announced the completion of the world's first eukaryotic genome sequence, comprising 6,000 genes (Goffeau et al., 1996). This effort involved 600 scientists at over 100 laboratories across Europe, Japan, Canada, and the United States (Langer, 2016). At the time, it was the world's largest decentralized experiment, made possible in part by emerging computer and internet technologies. Beyond accomplishing their stated goal, this group of scientists saw their project as a model for future, "open and cooperative" research endeavors (Botstein & Fink, 2011, p. 1442). Yeast itself became an emblem of coordinated sequencing efforts working with, storing, and managing large, distributed datasets. This would set the stage for future collaborations that led to the Sc2.0 project.

> The Sc2.0 design was specified relative to the *S. cerevisiae* reference sequence on the basis of derivatives of the S288C strain [sequence last updated by the Saccharomyces Genome

> Database (SGD) on 3 February 2011]…Edits are densely spaced, with a mean distance between clusters of edits of 400 base pairs (bp) when mapped back to the reference genome. (Richardson et al., 2017, p. 1040-1041)

According to its entry in the SGD, S288C was specifically selected for its non-flocculent tendencies and minimal set of nutritional requirements. It neither forms pseudohyphae (elongated 'buds' that do not break away from the rest of the cell during cell division) nor is suited for mitochondrial studies due to a mutated copy of the transcription factor HAP1 (https://www.yeastgenome.org/strain/S000203483).

After the S288C "standard" yeast genome was sequenced, yeast geneticist Herskowitz (quoted in Langer, 2016, p. 433) proposed that scientists working with yeast should move in new directions, focusing more on human health applications and less on biology as it had been conducted previously: "We yeast people must deliver, that is, contribute to learning about disease." The National Human Genome Research Institute (NHGRI) circulated a call for proposals that would advance large-scale functional analysis of yeast genomes—what became known as "functional genomics" (2022). While public research funding had done much to advance knowledge about genome sequences and create infrastructure for their study, functional information about genomes was scarce (Kumar & Snyder, 2001, p. 302). The NHGRI hoped that *in vivo* experimental modifications of yeast could deploy some of the trove of information that had been gathered so far in the service of cancer and human health research more generally (Botstein & Fink, 2011).

One of the resulting projects, the Yeast Gene Deletion Project, focused on analyzing gene functions in a set of "knockout mutants" through function loss (a gene 'knockout' is a technique in which a specific gene is rendered inoperative so that inferences can be made between 'knockout' and 'normal' organisms). As the Human Genome Project developed simultaneously,

yeast mutants were understood as analogs and homologs of human genes (Langer, 2016). Scientists created and maintained the Saccharomyces Genome Database (SGD) as a technology for cataloguing and sharing ever-growing datasets of yeast genetic samples and sequences (yeastgenome.org). It is worth noting that the SGD is a digital database and does not contain physical yeast samples but rather informational representations of their genetic 'code.' This simulacrum of yeast bodies increasingly elides distinctions between genes-as-material and genes-as-information. Leonelli and Ankeny (2012) note that the SGD was also key to the development of the Gene Ontology Consortium, which seeks to create a "species independent" 'vocabulary' to translate gene products to cell parts, biological processes, and molecular functions. This is yet another example of attempts to standardize and functionalize genetic material, key aims of so-called "translational" research.

S288C was proposed as a model organism in tandem with the Human Genome Project because it was presumed to offer insight into how human genes work, largely because working with yeast offered opportunities for functional experiments that could not be performed on humans (Langer, 2016). Additionally, information on yeast genes had already begun to be compiled in data libraries over the preceding decades; historical momentum was on its side. As biological research has shifted to become more computational and big-data focused, traditional practices have fallen out of favor. The 'wild-type' S288C genome was once lauded for its genetic stability, but this same quality now renders it "phenotypically atypical" in an era of CRISPR-Cas9 evolution, relegating it to an "artifact of the laboratory" (Langer, 2016, p. 437-438).

BY4741

For the purposes of this project, the BY4741 yeast strain is also worth tracing briefly. The SGD notes its descent from S288C: "BY4741 is part of a set of deletion strains derived from S288C in which commonly used selectable marker genes were deleted by design in order to minimize or eliminate homology to the corresponding marker genes in commonly used vectors without significantly affecting adjacent gene expression" (Stanford University, n.d.). Though it first descended from FY2 (itself a descendant of S288C), for most intents and purposes, variations between S228C and BY4741 are "miniscule" (Stanford University, n.d.). BY4741 is perhaps best known for its use as the parent strain for the "international systematic *Saccharomyces cerevisiae* gene disruption project" (Stanford University, n.d.).

But BY4741 is noteworthy in the context of this project because Jef Boeke was one of its designers (Brachmann et al., 1998), and its origins demonstrate a continuity in thought between the "designer strains" of the late 1990s and the "designer genomes" of the 2020s. Given this history, it is unsurprising that the Boeke Lab presents itself in language of discovery, its home page proclaiming, "We reveal the secrets of the genome using synthetic, systems, and genetic approaches" (Grossman School of Medicine, 2023a).

BY4741 is frequently used in Boeke Lab experiments, making appearances on presentation slideshows. This strain, alongside innumerable others, is available for purchase through American Type Culture Collection (ATCC), a "private, nonprofit, global biological resource center and standards organization that provides scientists with the biomaterials and resources they need to conduct critical life science research" (American Type Culture Collection, 2022). In late 2022, an ampoule of frozen viable yeast cells retails at $269.00 on ATCC's site and has a rating of 94/100 "Bioz Stars." Genomic DNA from the BY4741 strain in an isolated nucleic acid

form may also be purchased for $360.00.

Commercial interests

The Boeke Lab utilizes a combination of in-house and external resources and labor. While many of the technical aspects of experiments are conducted by graduate student and postdoc researchers, lab technicians, and staff (often in collaboration), the team also hires companies outside the university to complete routine sequencing tasks. My field notes from one lab meeting in March 2021 record the group discussing "Qinglan" (Qinglan Biotechnology, http://www.sxqlbio.com/eng/index.asp), a Chinese company they contract with to provide sequencing services for bacteria and other DNA samples for lab experiments. "Interrupting a presentation, Jef animatedly admonishes the group to 'check Qinglan's work,' noting that they should be doing this anyway as a matter of good practice. A few minutes later, Jef asks the group whether they 'bank' the bacteria they receive from Qinglan and suggests that the group consider 'centralizing all [our] stock that we get from Qinglan'" (field notes, 26 March 2021). Boeke then proceeded to discuss the "microbial conundrum," as he called it, by saying "You want to pick a single colony, but the risk is that the colony can be unstable" (field notes, 26 March 2021), leaving all the eggs in one basket, so to speak. This exchange offered brief insight into the tensions between a powerful drive for a systematized, standardized Sc2.0 genome and the risks and paradox of so little diversity amongst theoretically infinite, CRISPR-mediated variation.

Other companies involved in the Sc2.0 project include Gen9, Inc., which specifically worked on the synIX chromosome, and GenScript, which was hired in November 2011 to "complete the synthesis of a bulk length special yeast chromosome arm using GenScript's technology platform" (genscript.com, 2012). In the same press release, the company proudly proclaimed that

"GenScript is the only commercial entity to be invited to participate in this large-scale project. "GenScript is very proud to be a part of the Synthetic Yeast Genome Project," said Dr. Frank Zhang, CEO and Chairman of GenScript. "Dr. Jef Boeke is leading a very significant and far-reaching research project. The ultimate goal is to generate an ideal model organism, and to design a synthetic biological system for the production of drugs, fuels, and other materials. GenScript is excited for the opportunity to contribute towards this goal'" (genscript.com, 2012).

As alluded to by one of my interviewees, a number of lab members have commercial interests in addition to their academic research careers. One prominent example is illustrative: Boeke and a former postdoc, Leslie Mitchell, collaborated with Joel Bader (one of Boeke's former colleagues at Johns Hopkins) to co-found Neochromosome, a company that explicitly links itself to the Sc2.0 project on its website (neochromosome.com). Neochromosome bills itself with the tagline "Designed genomes powering novel therapeutics," in an explicit nod to biomedical applications. Since its founding, the company has been acquired by Opentrons, a large biotech company that focuses on selling automated lab equipment with the goal of "democratizing" processes and robotics (Opentrons, 2023). The multiplying intersections between academic-medical research, commercial interests, and future applications suggests the need to understand the legal landscape as it relates to synthetic organisms. In the next section, I'll take up this subject and discuss elements of synthetic yeast and the law.

Nonhumans and the law

As new objects of scientific knowledge (like synthetic yeast or human-mouse chimeras) emerge, social questions and anxieties beg to be addressed. Though *Saccharomyces cerevisiae* grows quickly and robustly, it is broadly recognized as 'safe' in laboratory settings, as its genes don't

overlap across chromosomes like those of some bacteria (Calvert & Szymanski, 2020). Both the biological "artifacts" themselves and the intellectual property claims to them are subject to law (Delaney, 2001), and social scientists have contributed an exploratory spirit to these evolving questions through methods that transcend familiar talk and text-based approaches. A spatial twist on intellectual property can bring together the concerns of law and geography as bodies are governed and mapped (through genome sequencing, for example) across the world and in the microgeographies of laboratory spaces. As the basis for modern law, property is key to notions of the self and other, establishing the zone of the 'exterior' (Deleuze & Guattari, 1987). Interestingly, genes-as-information trouble longstanding distinctions between physical and intangible property. "Not until the 1980s…did legislation and case law, led by the U.S. Supreme Court, begin to shift these ontological coordinates by making a new cut between biological and microbiological knowledge practices and objects that admitted biochemical 'in(ter)ventions' and genetic entities into the company of patentable things" (Whatmore, 2002, p. 109).

Science and technology and property and law exhibit parallels in their ordering of things: "…law, like science, is inclined to efface its own practices, masquerading its fabrications as self-evident accomplishments" (Whatmore, 2002, p. 61). More simply, scientific practices are frequently hidden behind a veil of objectivity that obscures their workings. Whatmore (2002) references the example of Monsanto presenting rDNA modification of seeds as a straightforward extension of traditional breeding and selection practices, which is dishonest. Rather, "this disarming concatenation belies the arduous business of experimental trial and error that perturbs any veneer of 'controlled precision'" (p. 132).

Advancements in recombinant DNA (rDNA) research in the 1970s led to the development of the *NIH Guidelines for Research Involving Recombinant DNA Molecules* (Talbot, 1980), which helped regulate rDNA research funded by the United States' National Institutes of Health. A form of

this document—now known as the *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules*—remains the primary guide for synthetic biology research in the U.S. Organisms and nonliving compounds in laboratory spaces are classified according to a biosafety level (BSL) schema. Thus far, the United States National Institutes of Health (NIH) has handled hybrid novel organisms by defaulting to the risk category of the 'riskiest' organism making up part of the novel one (Bar-Yam et al., 2012). Yet, the nature of some synthetic biology experiments transcends this framing because molecular parts and modules are increasingly dissociated from their original organismal source (Sliva et al., 2015). Clearly, synthetic biologists and affiliated policymakers have devoted substantive thought to the ethical and legal implications of emerging research in the field. But at minimum, it seems the guidelines currently in place do little more than rubber-stamp existing approaches and protocols.

Hierarchies of research risk and biosafety categorizations stem from this framework, shaping human-microbial relations (Department of Health and Human Services, 2013). Current Department of Health and Human Services (DHHS, 2010) guidelines lack substantial specificity and recommend company-level voluntary screening for potentially nefarious customers as well as any toxic or harmful agents resulting from specific DNA sequences and maintaining records of intended end uses of genetic products (2010). Even more broadly, synthetic biology generally considers the 1992 United Nations Convention on Biological Diversity as a guide toward ensuring even distribution of benefits from genetic resources (United Nations Environment Program, 1992). Another UN conference on biodiversity was held in October 2014, which examined questions surrounding the "environmental release of synthetic biology products" and emphasized the need for appropriate risk assessment prior to authorization of field testing for synthetic organisms (Antonich et al., 2014; Sliva et al., 2015). Two supplemental documents have further delineated the space of synthetic biology regulation: the Cartagena Protocol on Biosafety

(Secretariat of the Convention on Biological Diversity, 2000) and the Nagoya Protocol (Secretariat of the Convention on Biological Diversity, 2010). The former focuses on biosafety, while the latter focuses on fair distribution of benefits arising from synthetic biology research (Sliva et al., 2015). Scientists have produced their own white papers and publications attempting to formalize best practices within the field (see Maurer, 2012; Maurer et al., 2006). One of the key points in the 2006 white paper by Maurer et al.—that scientists should take care to procure DNA only from companies whose synthesis followed DHHS guidelines—helped solidify the political economic structures of the industry and field, where untold billions of cells are cultured, sold, and shipped alongside pallets of essential laboratory equipment, much of which is single-use. Other advice includes establishing a confidential hotline for reporting biosecurity concerns (Sliva et al., 2015). Yet it is unclear how effective these particular measures are or will be. Aside from scientific integrity on the individual or laboratory scale, these indeterminacies throw up barriers to regulation of genome-wide synthesis.

Challenges to regulation

Sliva et al. (2015) contend that a lack of regulatory leverage points in the synthetic biology industry are one reason why oversight remains fragmented and vague. Both the interdisciplinarity of the science and the breadth of its potential applications complicate attempts to define, much less manage it from the top-down (Kronberger, 2012). Carter et al. (2014) have expressed concern that existing regulatory mechanisms like the United States Environmental Protection Agency's (EPA) review of applications for new microbes will not be able to keep pace with multiplying applications in the future. Further, as technical and capital barriers to do-it-yourself synthetic biology wane, it is unclear how decentralized and less formal labs will be monitored and kept in compliance with existing regulations. Fears of "dual use" (i.e.,

applications with nefarious intent) circulate in these contexts. While admonitions against potentially harmful, unconventional uses of synthetic DNA linger in synthetic biology literature (see Garfinkel et al., 2007; Sliva et al., 2015), the material and financial barriers to DIY synthesis are often downplayed. Even so, doing synthetic biology still requires a degree of *savoir faire* and specialty equipment beyond the reach of the general public.

Often, synthetic DNA sequences are sourced from companies focused on DNA synthesis, which are typically more visible and in theory more regulable than DIY actors (Sliva et al., 2015). Proposals for requiring registration of DNA synthesis machines (synthesizers) offer potential for more formalized tracking of synthetic sequences. Regulation efforts must navigate international law, as the collaborative nature of much synthetic biology research spills over national borders and affects imports and exports (Bar-Yam et al., 2012).

CRISPR legalities

Humans' relationships with other species and the environment are filtered through legal, cultural, and societal institutions and norms. Debates over the place of CRISPR in the worlds we are building are situated at the heart of many of these intersections. "In this sense, CRISPR, gene drives, and other gene editing technologies are not only enabled and governed by law, but also constitute regulatory platforms" in a mutual process that Jasanoff (2014) refers to as "co-production" (Braverman, 2017b, p. 7).

The legalities surrounding genetically engineered organisms often center on notions of arithmetic and provenance. In 2016, the USDA approved a CRISPR-engineered mushroom designed to not turn brown (ostensibly extending its shelf life) on the grounds that genetic material was deleted, not added, and because the mushroom didn't contain any "foreign" DNA

from viruses or bacteria. (Waltz, 2016)

> In effect, one might suggest that the mushroom is an outlaw: it stands outside of the law. As such, it illuminates the existing regulatory assumptions that only unnatural additions constitute a "regulatable" change. In this way, not only does the mushroom's classification as a fungus rather than an animal, and its proposed alteration as natural rather than unnatural, impact its regulatory supervision by the USDA rather than by the Food and Drug Administration (FDA), but the law also allows the mushroom population to indeed mushroom as it applies no legal restrictions on its biological life. (Braverman, 2017b, p. 7)

When it comes to gene-related patent law, "natural" and "artificial" labels are highly significant yet sometimes poorly delineated. In 2013, the United States Supreme Court ruled that "naturally-occurring" DNA sequences are not patentable (Association for Molecular Pathology v. Myriad Genetics, Inc.). Even in lower-stakes settings, there is a tendency for an all-or-nothing approach to defining and regulating nature, which fails to acknowledge complex hybridities and identities that defy simple categorization.

Engineering animals for human consumption is another arena where definitions blur. The United States Food and Drug Administration (FDA) approved "AquAdvantage" salmon in 2016, labelling it an "animal drug" application (Meghani, 2014). These fish are expressly designed for human consumption: all are female, and all are supposedly sterile. The bodies of these fish are policed by workers and physically separated from wild fish and open water by physical barriers and geographic distance.

> Here, again, the natural-artificial distinction raises its head (or fin) and is thus policed through scientific means, supposedly establishing and maintaining clear boundaries between wild and human-created life to ensure that the artificial "product" can safely circulate to global markets without poising a risk to natural populations. (Braverman, 2017b, p. 11)

Paradigms of containment thus rely on the distinct demarcation of wild and artificial, even though this distinction is blurred in piscine bodies.

In a 2017 report, the National Academies of Sciences, Engineering, and Medicine expressed concern about the "patchy regulatory regime pertaining to gene editing in the United States," noting the risks gene drives pose in the face of no effective legal oversight (Braverman, 2017b, p. 10; National Academies of Sciences, Engineering, and Medicine, 2017, p.7). The most common response to these concerns is that organisms native to laboratories cannot survive "in the wild." This promise of biological containment relies on the foundational assumption that life can be controlled and governed at will, a notion that underpins much of synthetic biology, but which is less than ironclad when examined up-close.

Scientific discourse tends to amplify the gulf between rationalistic, human-centered design of genomes and organisms' natural evolutionary state, which often includes many genes deemed as "junk" due to their apparent lack of function in contemporaneous metabolic processes. This dichotomy between parsimony and "sloppy" excess simultaneously privileges researchers' more reasoned approaches over natural evolution while justifying manipulations of genomes by emphasizing that lateral gene transfer and genetic exchange through various forms of reproduction have been ongoing for millennia. Under this configuration, new technologies simply accelerate and streamline what has already been happening without human intervention for a long time (Braverman, 2018).

> In the ecology of powers, regulatory operations that implant norms into the field of emergence constitute exercises of *biopower*. **Scholium.** Biopower exerts a force of *normalization*. It attempts to direct what is arising from the field of emergence down regulated channels. To succeed in revaluing value, fully reaffirming the differential intensity of the field of life, the postcapitalist future will have to decouple value from normativity. It will have to grapple with disciplinary power and biopower. (Massumi, 2018, p. 62-63)

What paradigms might be useful for thinking about biopower and governance in yeast-related research? Aldo Leopold, Arne Næss, and others' ecological approaches are one alternative to neoliberal conceptualizations of nonhumans as subjects. Social scientists have also proposed

"rights of nature" in response to the challenges of binaries like property/personhood. An orientation toward metabolic relationships may allow us to defetishize legal dualisms (like personhood/property, etc.) and foreground belonging and dependence. We could also pluralize our attachment to "society" in the singular, emphasizing mixed and overlapping societies, evocative of Haraway's cyborgs (1991). Rights and personhood are slippery concepts when it comes to microbes, however. As I will discuss later, labor is likely a more productive frame for thinking across synthetic biology, ethics, and the law.

Governance happens through technologies of documentation, classification, reproduction, and control. "In all its guises, actual or aspirational, technology functions as an instrument of governance" (Jasanoff, 2016, p. 8). These are all essential facets of genomic engineering in yeast; gene editing makes and shapes worlds, just as laws themselves do. Given the pace of advancement in synthetic biology, scientists often find themselves in the position of self-governance due to flagging legal guidelines, though STS scholars rightly point out that legal guidance need not be merely retrospective (Braverman, 2018). Indeed, the legal landscape forms the present and future that science and technology exist within. Instead of seeing science as an entity that governs and is governed by the law, we can understand technological innovation in a more nuanced way that accounts for the ways it is co-productive with the law (Braverman, 2017b, p. 14).

Specific skills and expertise are often required to make sense of multispecies relationships, and those typically come with familiarity. However, familiarity can also engender close-mindedness. Storytelling (advocated by Greenhough and Lorimer, among others) can help avoid desensitization. So, bringing bioethics to bear more effectively on yeast-human lab interactions might look like engaging in technical yet creative conversations with scientists who are intimately familiar with yeast, and also seeing labs as co-constructed and therefore changeable.

The development of a culture of professionalism was underway long before synthetic biology became a reality. Human-yeast collaborations have increasingly tilted toward this paradigm, beginning in the industrialization of Western economies in the nineteenth and early twentieth centuries as brewing and breadmaking fell increasingly under the purview of specialists and home economists (Bobrow-Strain, 2012). As with healthcare, "baking was to be a terrain of control and expert measurement rather than art and aesthetics" (Bobrow-Strain, 2012, p. 60). Since the middle decades of the twentieth century, there has been a resurgence in amateur and artisan production of goods, but the influence of technoscientific approaches lingers and certainly remains prominent in biological and laboratory-based sciences.

Democratization?

The greater accessibility of gene editing tools over time is often touted as a "democratization" of science. Modularity has the advantage of facilitating open-source collaboration, as one scientist can more easily pick up where another left off if there are standard 'parts' in place that can be reused in other research projects (Calvert, 2010). With published DNA sequences and techniques like CRISPR, independent "biohackers" can make custom genetic modifications to their own bodies or wreak havoc as bioterrorists, at least in theory.[20] Of course, labor, knowledge, and resources congeal in ways that stratify power dynamics between vigilante

[20] For more on transcending human limitations, see the work of Nick Bostrom (2005) on transhumanism as "the bold view that humans should exploit technological inventions that improve, lengthen, and yes, possibly change the lives of human kind" (p. 3). Transhumanism shares some assumptions with synthetic biology: namely, a deep confidence in emergent technology and the possibility and imperative of using this technology to its fullest potential, which is why I find it instructive to mention here. A podcaster named Dave Asprey runs a popular show called The Human Upgrade that frequently deals in these sorts of questions as well (for one prominent example, see episode #913, "Controlling genetic destiny with synthetic biology, part 1" (https://daveasprey.com/andrew-hessel-913/)).

environmentalists and well-funded research labs, for example. The United States' Pentagon Defense Advanced Research Projects Agency (DARPA) is increasingly interested in synthetic biology interventions and is one of the largest public funders of some of these efforts (Braverman, 2017b). Programs like Safe Genes have been implemented to mitigate fallout surrounding any potential "genetic spills" into the environment in case of unintended releases of modified organisms, and many researchers are quick to point out that such engineered organisms are unlikely to survive outside of their native laboratory settings (Moe-Behrens et al., 2013). "The promise of biological containment—that lab organisms would not be able to survive "in the wild"—has allayed fears for decades…but it is founded upon and underpinned by the assumption that biological life is thoroughly controllable and governable" (Braverman, 2017b, p. 10). Yet, unresolved debates about the tradeoffs between increasing public access to these tools continue. For instance, concerns linger about the potential for "dual use" applications like bioterrorism if synthetic biology tools are open-access or easy to use (Cirigliano et al., 2017). In the grand scheme of things, many of them are, but as noted in chapter 5, some scientific acumen and access to material resources is still necessary. Synthetic biology projects like Sc2.0 (re)shape the politics of multispecies interactions by rendering genetic material like genes and chromosomes as information. This disembodied information has the potential for commodification, depending on the intellectual property claims made. Certainly, many other industries in the 21st century have demonstrated the power and desirability of data as a commodity. On the other hand, we could imagine a more democratic approach to thinking about information and its free distribution among the public, like open-source tools. How we handle this has implications for social inequalities (Rossi, 2013).

Education, ethics, and responsibility

Education has also been a pillar of the ethics and governance guidelines for synthetic biology (Schmidt, 2008). Sliva et al. (2015) note that,

> Even though biosafety training is generally not required for individuals or laboratories working with organisms such as *S. cerevisiae* that are generally regarded as safe by the U.S. Food and Drug Administration, individuals working on Sc2.0 receive training on the risks of dual-use technologies through lecture, the use of the National Science Advisory Board for Biosecurity's educational module for individual learning, and group discussions. (p. 1026)

Debra Mathews, a pioneering researcher of synthetic yeast, also heads a massive open online course (MOOC) hosted by Coursera titled "Engineering Life: Synbio, Bioethics, & Public Policy" that seeks to introduce these themes to the broader public (https://www.coursera.org/learn/synbioethics?). In order to familiarize myself with Sc2.0's public-facing efforts, I took this course online in 2022. These efforts—both internal and externally-facing—seek to develop a curriculum of sorts for synthetic biology education and best practices.

Still, in light of the field's emerging nature and lack of formal structures, it is uncertain how effectively this "synthetic biology curriculum" will be delivered. One informant in this project pointed out that his degree is "in the general biomedical sciences because we…have an umbrella program, and then we have sort of individual training tracks that…you choose rather than are assigned to. My particular one is called cell biology, which is just a very—again, very blanket/umbrella term for all sorts of genetics or anything to do with cells, which is most biology when you think about it" (interview, 23 June 2020). Academic programs in synthetic biology are trending, however, and will likely become more common with time. Given the transformative potential of this work, establishing an ethical framework to guide the

development and stewardship of these programs is arguably needed.

Several institutions are guided by the mission of securitizing synthetic biology research protocols. One of these, the Woodrow Wilson International Center for Scholars, oversees the Maps Inventory project, initiated in 2009 (Woodrow Wilson International Center for Scholars, 2014a). This project maintains a world map of academic and commercial laboratories working with synthetic organisms as well as the Synthetic Biology Applications Inventory (Woodrow Wilson International Center for Scholars, 2014b) and a scorecard for researchers, institutes, policymakers, and industry stakeholders (Woodrow Wilson International Center for Scholars, 2014c). However, this site was last updated in 2016, and my personal inquiries into its current status have gone unanswered.[21]

The Hastings Center started a separate project in 2009 with the goal of examining ethical questions in synthetic biology, focused on parsing potential risks and benefits (Kaebnick et al., n.d.). The following year, the U.S. Presidential Commission for the Study of Bioethical Issues published a report in response to J. Craig Venter's announcement of the creation of the first cell with a fully-synthetic genome (Presidential Commission for the Study of Bioethical Issues, 2010). This commission concluded that no moratoria or new laws regulating synthetic biology were needed at the time, recommending only "prudent vigilance" and strong communication between scientists and the public (Presidential Commission for the Study of Bioethical Issues, 2010).

In 2010, the International Risk Governance Council (IRGC) contributed another set of guidelines for the field, addressing biosafety and biosecurity, public engagement, and interdisciplinary policy discussions (International Risk Governance Council, 2010). Alongside

[21] Additionally, attempting to access the Center's world map returns a 404 error in 2022 (https://www.synbioproject.tech/sbmap/).

recommended safety audits, the guidelines promoted engineered fragility as a built-in safeguard against accidental releases of synthetic organisms.

Jefferson et al. (2014) noted a tension between perceptions of risk based on the accessibility of synthetic biology to lesser-skilled persons. When experts emphasized the "de-skilling" of science, the risk of so-called "dual-use applications" (i.e., nefarious uses of genome engineering) is perceived to be high. However, when scientific knowledge and skills needed to perform synthetic biology are emphasized, risk is perceived to be lower, a phenomenon dubbed the "synthetic biology/engineering conundrum" (Sliva et al., 2015).

Conclusion: Multispecies relationships

Yeast-human relationships modulate depending on the spatial context of different laboratory spaces, whether a high-powered synthetic biology lab or a humbler regional yeast lab or an unassuming kitchen space. Instantly, it seems clear that it is too simplistic to attempt a typology wherein a single discourse or approach to working with/on yeast characterizes any given type of space. At the same time, there are real epistemological differences between these spaces that may allow or close off certain futures or ways of interacting with the microbial world. It is advantageous to live and work in this tension, understanding multispecies assemblages as rife with asymmetries in terms of agency and power but nevertheless multidirectional and capable of opening into new territories.

Humanity's conception of our 'selves' influences these understandings. It seems that the orientation of the Sc2.0 project, despite its rhetorical emphasis on multispecies encounter, seeks ultimately to prioritize and impose an anthropocentric relationality onto microbial life. What would more thoughtful engagement with other lives look like? Which postures should we take

to do this effectively, learning to be affected? Some may find the answer to this in a world where humans can engineer and orchestrate other lives comprehensively to their advantage under the guise of symbiotic relationships, but I contend that we should instead seek more creative ways to associate with, listen to, and sense (with) other organisms (Hird, 2009). Metaphors matter—those that prematurely shut down possibilities for interspecies intra-action (Barad, 2007) risk limiting the material-semiotic relations possible in these assemblages, recalling Latour's notion of premature unification. And unexpected things like a global pandemic can interject, swiftly altering our relationship to the microbiome on a societal scale.

An aside: The case of CCYL

As noted in chapter 4, I made connections with more-local interlocutors as the COVID-19 pandemic unfolded and my original research plans foundered. From summer 2021 through spring 2022, I conducted several site visits to Community Cultures Yeast Lab (CCYL) in San Antonio, Texas. I also conducted several interviews over Zoom with the owners. This fledgling family business specializes in providing yeast starters to craft breweries across the state. While their epistemological orientations (and certainly their goals) are largely polar opposites, I retain this brief sketch as a counterpoint to the aspirations of synthetic biology at the heart of this dissertation. I want to be clear that in no way am I suggesting a sort of analytical utility in comparing the Boeke Lab to CCYL (though both yeast labs in a sense, practically nothing about them is similar); rather, aspects of this latter company's experiences reveal some small and very different facets of a political economy of yeast.

Like many small businesses, CCYL survives on the sweat of its owners and occasional interns. Growing out of the owners' garage, by the time I visited them in person, CCYL had moved into

an old warehouse space next to the tracks in San Antonio's Beacon Hill neighborhood (Figure 9). CCYL also functions as a resource and education center for brewers and homebrewers, offering classes and meeting space from time to time. When the brewing schedule is particularly onerous, the co-owners have crafted a small loft in the back of the building with a bed, TV, and a window AC unit for late nights paired with early mornings.

Figure 9: Exterior view of Community Cultures Yeast Lab. Photo by author.

Experiences with yeast in this lab are very visceral. In the summer, most of the building is not air-conditioned and working among the tanks in the back is a sweaty experience. Mountains of flasks and equipment await washing, tanks must be sanitized between batches, and sticky wort has to be scrubbed off surfaces. Styrofoam boxes used to ship yeast orders lined

a storeroom during my first visit, where I witnessed a few orders being packed by hand. These material objects are important figures in the day-to-day operations of the lab, protecting yeast colonies and their accompanying ice packs from the South Texas sun.

Conversations with the co-owners of CCYL painted a picture of evolving goals and priorities as the company took shape, grew, struggled briefly during COVID-19, surged back, and found more stable rhythms of production and sales. Early on, the founders prioritized their "native yeast" program, compiled from samples of yeast found in nature on flowers, bark, and other inconspicuous places and aided by citizen scientist partners. The home page of their website (ccyeastlab.com) still evokes this sense of adventure and terroir that they tried to meld with a more traditional yeast lab business model. Always short on time to devote to their 'native' strains, the owners strove to balance the demanding hours of their young business with their passion for place and nature. Perhaps paradoxically, as they grew more financially successful and gained clients, they ended up reducing their focus on their native yeast program even further. One of the co-owners expressed her desire to make a map locating the different 'wild' yeast strains they had collected during their camping trips across the Southwest ("Mapping out different yeast geographies, essentially," interview, 20 May 2020), but this never materialized due to lack of time and expertise. Becoming more business-like entailed website and general aesthetic improvements alongside a focus on fewer different (but more commercially popular) strains of yeast. In interviews, one of the co-owners in particular expressed disappointment at this turn of events; she had presumed that with more financial success they would have more time, not less, to spend on their passion projects. In a way, the agential capacities of the business alongside obligations to customers and opportunities to earn more affected them, reshaping their assemblage of DIY and hand-me-down equipment, erratic and flexible schedules, and trajectories of growth. Of course, their yeast colonies are very much present in these assemblages

as well (Figure 10).

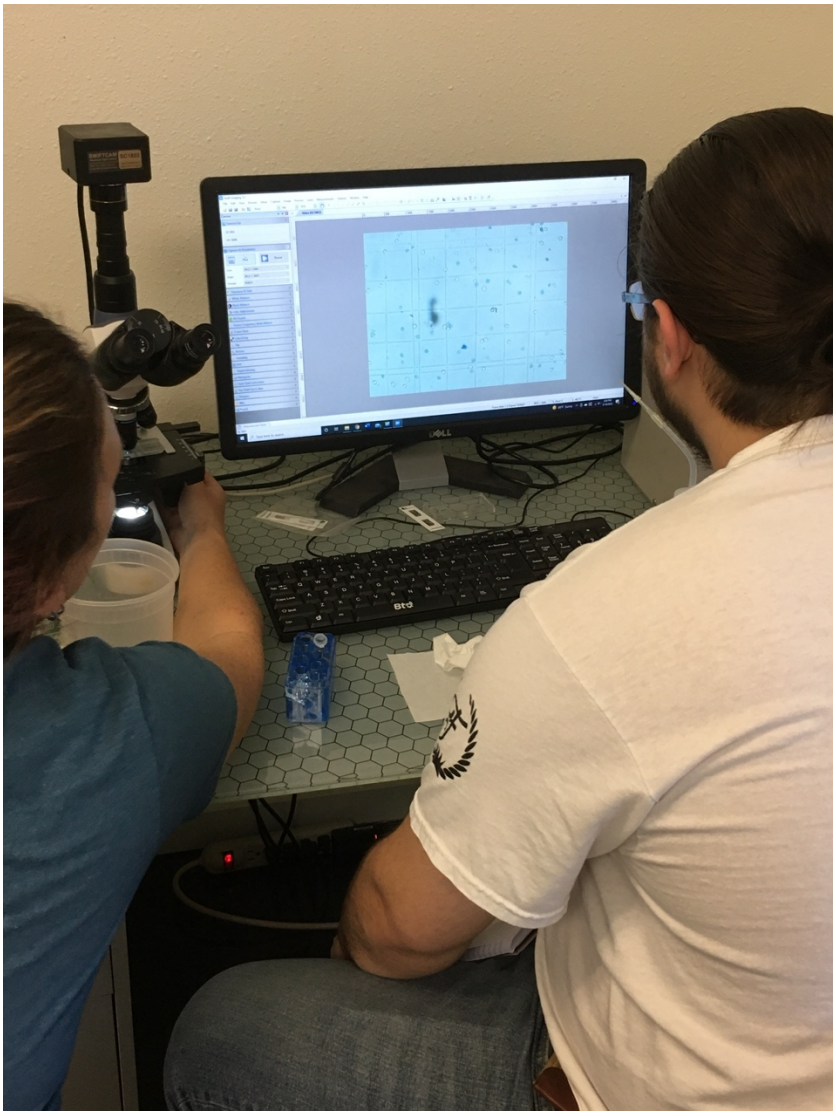

Figure 10: Counting yeast cells under the microscope at CCYL. One of the founders of the company has a background in biochemistry and has always taken a scientific approach to their cultures. Still, with increased professionalization and commercialization, tools like microscopes figure ever more prominently in the lab's daily operations.

This case illustrates an arc of enchantment to disenchantment, as the founders' initial attraction to working with yeast and financialization of their existing hobbies were taxed, changed, and became something new. Despite owning a successful (albeit small) business, they remain responsible for nearly all of the daily, tedious work required to keep it alive. During a couple of my site visits, I interacted with two different interns who were students at local

colleges and who helped with some of the lab tasks, but their roles are small compared to those of the founders. The paradox of CCYL is that its increased (incremental) success as a business foreclosed aspects of its founders' early yeasty enchantment, demanding (or at least suggesting) further financial success despite not being beholden to a board or shareholders. Over the course of several interviews and field visits, I observed a rhetorical shift from idealism to pragmatism, including a reduction in focus on wild cultures and a concomitant increase in production of popular, bestselling yeast starters, reflecting capitalist tendencies in the yeast economy. Even though neither of its founders seem particularly fixated on generating wealth, the business itself seemed to pressure them into modes of being attuned to new speeds of circulation more conducive to growing capital.

Despite this, CCYL retains connections to *Saccharomyces cerevisiae*'s affective registers and personality. The owners variously personified yeast as "ornery," "finnicky," and compared its behavior to that of cattle or honeybees (interview, 25 June 2020). As we will see in the next chapter, metaphors like these have effects in synthetic biology labs too, though the ones that tend to be used in breweries and labs like CCYL inhabit their own distinct ontological and practical coordinates.

During a site visit, I observed one of CCYL's co-founders "transferring a yeast culture from a conical fermenter to prepare it for shipping to a brewery. Despite her caution and attentiveness, a little of the liquid yeast slurry spilled out underneath the fermenter" (Furness, 2022, p. 42) (Figure 11). This small loss did not negatively affect the product going out the door, but her reaction to it was noteworthy: "It always makes me a little sad to see that there, because it is alive…it's more than just a raw material" (Furness, 2022, p. 42). Moments later, while cleaning up the spill, she again expressed regret over those cells not being able to "continue [their] short life and fulfill [their] evolutionary purpose…all natural organisms have evolved to eat and

reproduce and science shows that when organisms are not able to do these things, they are unhappy" (Furness, 2022, p. 42). Though the anthropomorphizing strands of thought are clear in this quote, her attentiveness toward yeast engenders new multispecies relations and values forged through time and familiarity with another organism and presents a contrast to some of the more aggressive postures synthetic biologists sometimes take toward microbes.

Figure 11: Spilled yeast slurry at CCYL. This loss elicited regret from the worker transferring the yeast cells to another container for sale. The smallness of this loss mirrors the worker's attentiveness toward the smallness of her yeast collaborators and care for their wellbeing.

7. DISCOURSE AND METAPHOR IN SYNTHETIC YEAST

> "Language is the amber in which a thousand precious and subtle thoughts have been safely embedded and preserved."
>
> -Richard C. Trench
>
> "It is not an easy task to transform the inarticulate mutterings of a multitude of entities that do not necessarily want to make themselves understood."
>
> -Bruno Latour, *Politics of Nature* (2004, p. 168)

Synthetic biology is, broadly, a collection of approaches to working with DNA that emphasizes a parts-based disposition toward cells and genomes. As part of the process of turning life into 'parts,' scientists have developed metaphors and language for making their laboratory subjects more understandable and subject-like. In this chapter, I focus on these metaphors and how they territorialize knowledge production and relations of power in synthetic biology. Instead of mere linguistic flourishes, I see the language used to characterize yeast as alive with consequential political, legal, and ethical reverberations. McLeod and Nerlich (2017) argue that metaphors "are fundamental tools for thinking about the world and acting on the world…They need to be used 'responsibly'" (p. 1), and Szymanski (2018b) notes how "metaphors bring microorganisms into being in the synthetic biology lab as 'experimental partners' with certain characteristics patterned by what they are described as being like, and of which certain expectations are therefore reasonable" (p. 2).

Of course, words do not perfectly represent some fundamental expression of reality. They do not stand alone, nor do they emanate fully formed from the void. Rather, they are constituents of assemblages that act on and are acted upon by other forces. They are mutable

and their meanings may be contested. The ways in which they are deployed in different assemblages matter, forming more or less durable relations. Their use is inflected by culture and geography. With this understanding of language in place, we can study and critique its usage, gaining useful insights into its role in shaping reality while avoiding the trap of logocentrism, which is the tendency within Western thinking to emphasize the written (or spoken) word over the thing it signifies or refers to (Fincher, 2015).

This chapter attempts to further important dialogues already happening between synthetic biologists and social scientists about "how language shapes both emerging meanings of life…and emerging meanings of responsibility" (McLeod & Nerlich, 2017, p. 2). Language and technology have operated as complementary forces shaping assemblages of humans, yeast, laboratory equipment, and research funds, deserving greater attention in socially-oriented studies of science and technology. Unfortunately, the research I was able to conduct lacked an important element of collaborative exchange, given the constraints of the time during which it was completed. As substitute, I had to rely on existing accounts by synthetic biologists to augment the meager interviews and disembodied observation that made up my primary data collection.

Textual analysis of synthetic yeast scholarship

To supplement my observations of and interviews with Boeke Lab members, I collected scholarly texts related to synthetic yeast and the Sc2.0 project in particular. In compiling this text corpus, I had to make decisions about where to draw boundaries. For example, a ProQuest 61-database search of the keywords "synthetic" and "yeast" yielded approximately 22,150 results, a staggering number to try to digest. Limiting the search to the phrase "synthetic yeast" narrowed the results to 380. Searching for "Sc2.0" yielded a much more manageable 143 results,

when last checked in late October 2022. Documents were not included if they made only a passing reference to Sc2.0 or if the project was not the main focus or source of their work. Some of these results were removed from the final text corpus, which includes 88 documents. Documents were excluded for several reasons. First, a few dozen of them were not actually related to the Sc2.0 project but appeared in the search due to incidental combinations of letters and numbers in the text. Another few dozen results were duplicates of articles in another databases. A handful of results were not included because I was not able to access the full text through any database available to me, including through Texas State's library, public databases like Google Scholar, and paywall-circumventing sites like sci-hub. A couple of results were excluded because they were written in Mandarin, and I suspected that any automatic web-based translation into English would not be useful for such a logocentric analysis. Another text was written in German and was similarly excluded. Most of the corpus documents are published journal articles. A smaller subset are preprints or working papers, and two are doctoral dissertations.

As a result of this filtering process, the articles in the text corpus are all written in English. While this certainly excludes some academic writing about synthetic yeast (as noted above), it seemingly captures a significant portion of the research related to Sc2.0, given the location of consortium members and the overarching bias toward the English language in synthetic biology literature. Most of the articles I included are scholarly, peer-reviewed journal articles, though a smaller number are science journalism pieces written for a more general audience and several are Ph.D. dissertations, many of which were authored by the same scientists who later published related scholarly articles in journals.

I also collected various news articles and press releases related to Sc2.0. These journalistic sources were not a primary focus of my data collection but served as useful guideposts in finding

other sources and understanding scientists' public-facing discourse related to synthetic yeast. Within these articles, yeasty metaphors remained prominent, suggesting that there is not an attempt to conceal these renderings of complex biological processes. Whether this reflects a lack of self-consciousness by the researchers or an intentional effort to make complicated ideas more understandable, I am not sure.

The production of nature

Synthetic biology's aspiration to construct nature 'from scratch' challenges ideas of 'natural' and 'artificial' (Calvert, 2010). It is literally constructing nature through developing new biological entities and metaphorically constructing nature by influencing dialogue about what is 'natural.' Synthetic biologists at times stress that their work improves upon nature while at other times emphasizing how their creations are in fact 'unnatural' and therefore more patentable. 'Synthetic' itself as a descriptive word for this field not only means 'artificial' but also carries the sense of *synthetizing* elements into novel genetic entities. "The standardized, modular, decomplexified creations of synthetic biology will inevitably start to infect our understandings of what is 'natural', which, as we have seen, is itself a 'receding horizon' defined primarily in terms of what it is opposed to" (Calvert, 2010, p. 108).

The reconstructing/restructuring of nature on synthetic biology's terms plays an important role in instrumentalizing nature. In other words, life is made simpler and streamlined in order to make it more 'useful.' As Braun and Castree (1998) write, "the world 'outside' the laboratory comes to mirror the world inside" (p. 27). Wynne (2005) sees synthetic organisms as the product of an "instrumentalist epistemology of modern scientific culture overall" (p. 77), which privileges research that can further prediction, control, and exploitation. Certainly, synthetic

biology is not novel in this push to 'tame' nature, but as Calvert (2010) explains, "there are a confluence of different factors which all push in the same direction, and which include engineering, modularity, scientific practices, model organisms, standardization, exchangeability, intellectual property, and even open source" that distinguish the contemporary synthetic biology program from previous human efforts to shape nature in the image of culture (p. 108). Yet, efforts to control organisms often proceed in fits and starts, and microbial vitality can frustrate even carefully designed experiments. Even in small ways, the nonhuman projects its agency into spaces of interaction, creating moments of tension between control and unpredictability. This tension seems to tantalize synthetic biologists, whose epistemological and ontological foundations suggest that complete mastery over nature is only a matter of time and funding. I suggest that this conclusion is not foregone, and that the assemblage is still subject to the agency of the collective of beings comprising it. Such an ontological politics foregrounds these contested negotiations to ask of each articulation,

> What are its effects? What does it open and what does it foreclose? What relations of power does it affirm and express? How does it *fail* to become the singular shape of reality (always remaining one partial articulation among others)? What multiplicity does it express beyond its hegemonic forms? What are its "lines of flight" (Deleuze and Guattari, 1987, p. 203) that unravel it toward other becomings? What other worlds are clamoring, beyond its reach, to be born? (Miller, 2019, p. xvii)

Metaphors of responsibility

The 1975 Asilomar Conference mentioned in chapter 5 served as a focal point for early efforts toward assessing regulatory restraints on the use of recombinant DNA research, with particular emphasis on potential biohazards (McLeod & Nerlich, 2017). Two decades later, another framework emerged. Ethical, Legal, and Social Implications (ELSI, a program funded by the National Institutes for Health in the United States) or Ethical, Legal, and Social Aspects (ELSA)

sought to define the responsible conduct of genomics research (Zwart et al., 2014). Zwart et al. (2014) note that these labels did not emerge from amongst scientists themselves so much as from government and funding agencies in a "top-down" manner. Nevertheless, ELSI/ELSA gained traction as a paradigm for conscientious research practice. In more recent years, a new label has emerged in a similar way. Responsible Research and Innovation (RRI) is a framework for the governance of science in keeping with ethical and socially conscious principles (McLeod & Nerlich, 2017). Zwart et al. (2014) contend that,

> At first glance RRI is *not* a radical departure from ELSA, and that, in the process of further developing the RRI approach, the inclusion of ELSA's heritage may well prove essential. Yet, we do see a new emphasis emerging in RRI in comparison with ELSA, namely the focus on socio-economic benefits and collaboration with private and industrial partners. (p. 12)

Like its predecessor, RRI began as a signifier that actively shaped and preceded the research strategies it purported to describe (the signified, in this case) (Zwart et al., 2014). Publishers contributed to this neologism too—Taylor and Francis founded the *Journal for Responsible Innovation* in response to the shift toward RRI terminology.

In addition to adapting to funding mandates, scientists emphasize RRI to underscore the beneficial aspects of their work to humanity, broadly conceived. This emphasis has grown in the face of increasing pressure on researchers to demonstrate responsibility with regard to new, awesome powers of whole-genome engineering (Szymanski, Smith, & Calvert, 2021). Still, much can be elided by an acronym: responsible to whom? Responsible/response-able how? As I have discussed in previous chapters, insights drawn from multispecies, more-than-human geographies (including relationality and care) can benefit a more expansive form of RRI that must grapple with microbial ecologies and perhaps the impossibility of caring "for everyone equally all the time" (Szymanski, Smith, & Calvert, 2021, p. 4).

Yeasty metaphors

As I noted in previous chapters, synthetic biologists approach their work with microorganisms from an engineering mindset, emphasizing their ability to control and design living bodies that do not always comply. Synthetic biologists hold closely ideas of genes-as-information and genes as replaceable parts; this metaphor also scales up to the level of the organism, suggesting equivalence between different microbes and applicability of lessons learned in one microbial context to others.

Metaphors linked to yeast are not new and have been used to shape biological and chemical identities of yeast of hundreds of years. As Langer (2016) notes, "Literature of the nineteenth century shows us that yeast's fermenting and leavening activities were images with popular appeal" (p. 32). However, the metaphors of synthetic biology extend this history in a new direction, employing metaphors to shape a new organism and make it understandable rather than evoking particular emotions through art and literature.

Compared to traditional biologists, synthetic biologists tend to be generalists, working across species lines. (Calvert & Szymanski, 2020). Part of this orientation stems from notions of equivalence and replaceability prominent in this field. Instead of focusing on the peculiarities and nuances of a particular species, researchers in synthetic biology attempt to construct 'toolkits' and modular components that can be (ostensibly) applied to many different species based on need, repudiating the idea that species-specific knowledge is of critical importance (Calvert & Szymanski, 2020). Despite the ubiquity of these ideas in much of synthetic biology, Calvert and Szymanski (2020) suggest that as whole-genome synthesis projects become more commonplace, specific organismal properties will be taken into account, leading toward an "attentiveness" to certain organisms.

Information, circuits, and software

In a world increasingly captivated by 'big data' and machine learning, information waxes in importance. Actors of all kinds mobilize to capture data as an asset, raising questions of ownership, privacy, and security. With genomes and DNA now generally accepted into the stable of organizable and capitalizable information, it is worth asking how this biodata will be used, owned, and deployed. Tensions persist in synthetic biology research, where scientists are incentivized to use intellectual property claims to demarcate their work but where they also often ascribe to open-source ideals as part of Responsible Research and Innovation (RRI) norms. In one lab meeting in January 2021, a postdoc in the Boeke Lab paused mid-presentation to ask for "confidentiality with the next slides," as he felt that a certain individual not in the meeting was a "scoop risk," meaning that this person might use the presenter's work to gain a competitive advantage and publish first.

Living things have been subject to intellectual property claims before; Monsanto's seed patenting designs are perhaps the most infamous examples in contemporary imagination, but adrenaline and insulin are other, older examples, among many (Murray, 2020). The landmark 2013 United States Supreme Court decision in *Association for Molecular Pathology v. Myriad Genetics, Inc*. drew some basic boundaries around gene patents, basing their permissibility on whether an isolated gene can be found in nature, or not. Notwithstanding the numerous unanswered questions this designation engenders about nature and whether this division will matter in patentable applications, this ruling was intriguing because it broke with historic precedent that generally allowed gene patents, casting doubt on thousands of existing ones. It also sparked a lively debate about whether gene patents promote innovation (as patents purportedly do in general) or squash it and the free exchange of ideas, as the plaintiffs argued. In this unfolding discussion—shaped by public opinion, the judiciary, money, and scientific agendas—a sort of

blueprint for synthetic biology's approach to intellectual property took shape. If life cannot be patented per se, synthetic organisms ought to reflect this, which we can see in organizations like the BioBricks Foundation. Still, scientists are protective of their research, wary of poaching and eager to publish their ideas first. This points to ongoing tension between synthetic biology's commitment to open-source ideals and researchers' unsurprising cageyness about their cutting-edge work.

So how will genes-as-information be treated in synthetic biology in an era of whole-genome synthesis? On one hand, current rhetoric suggests a democratic approach to thinking about information and its free distribution via open-source tools. On the other hand, with substantial stakes connected to therapeutic applications, the limits to free exchange of ideas may be tested. Rossi (2013) suggests there is an opportunity to "document and analyze how this new technology reshapes these socionatures" and that social scientists can "intervene in situations where the products and processes of this technology potentially create or exacerbate social inequalities" (p. 1140).

In typical synthetic biology rhetoric, genetic expression equals software and cellular structures equal hardware, but this is a flawed equivalence. The conceptualization of genes-as-information is theoretically linked to scientists' ability to "write DNA" (Calvert, 2010, p. 105). This metaphor is ubiquitous in synthetic biology. 'Reading' (via sequencing) and 'writing' (via synthesis) are understood as fundamental aspects of a synthetic biology approach (Villalobos et al., 2006). Cells are conceptualized as factories that produce desired products while shunting away waste, but also as computers that can receive and execute software programs. Danchin (2012) makes explicit connections between cells, computers, and genes-as-information, writing about a "remarkable feature of the cell factory: the program replicates (makes *identical* copies of itself), whereas the cell reproduces (makes *similar* copies of itself), placing in the limelight the

role of informational maintenance" (p. 2129; emphasis in original). These visions of what cells are like often fail to address discrepancies raised by their own characterizations (i.e., is a cell a computer or a factory? Neither is alive, but cells are).

Calvert and Szymanski (2020) argue that *Saccharomyces*' "personality" and the affective relationship between it and humans challenges this "organism agnosticism" of synthetic biology. Here "agnosticism" carries a sense similar to its meaning in computer science, denoting an object that is compatible with multiple systems. "Organism" is attached to "agnosticism" mainly in the context of computational tools used to manage DNA, including comparative genome browsers and bioinformatics tools. The term is found in the synthetic yeast project with respect to software developed for genome design (GeneDesign and BioStudio). Although this software was made specifically for designing yeast genomes, it is described as "open source, organism-agnostic, and freely available to the public, in the expectation that the algorithms and standards it introduces will be useful to other large scale synthesis projects" (Richardson, 2011, p. 52).

Presentations, published work, and everyday conversations in synthetic biology frequently invoke metaphors that evoke replaceable parts and software applications. For example, the International Genetically Engineered Machine (iGEM) competition names modified genetic building blocks "BioBricks," which "are standardized DNA widgets that can ostensibly be used in downstream applications" (Sliva et al., 2015). Tom Knight proposed this "BioBrick standard" in 2003 to further the goal of developing standardized, biological 'parts.' Shetty, Endy, and Knight (2008) envision a conglomerative world of these biological bricks:

> The key innovation of the BioBrick assembly standard is that a biological engineer can assemble any two BioBrick parts, and the resulting composite object is itself a BioBrick part that can be combined with any other BioBrick parts. The idempotent physical composition standard underlying BioBrick parts has two fundamental advantages. First, the BioBrick assembly standard enables the distributed production of a collection of compatible biological parts. Two engineers in different parts of the world who have never interacted can each design a part that conforms to the BioBrick assembly standard,

> and those two parts will be physically composable via the standard. Second, since engineers carry out the exact same operation every time that they want to combine two BioBrick parts, the assembly process is amenable to optimization and automation, in contrast to more traditional *ad hoc* molecular cloning approaches. (under "Background" section, no page number)

Scientists in the Boeke Lab often discuss the use of "barcodes" to automatically identify specific cells (e.g., field notes from 31 March 2021 record an argument between two lab members about how certain "payloads" are "barcoded"). Invoking UPCs, this framing also flattens inter-cell variation by assuming that all cell constructs of a particular type can be assigned a barcode that encapsulates their form and function. This metaphor also overlaps with others; one member discussed the implementation of a "small barcoded payload" in their experiments. Lab members also used more simple, spatial metaphors to describe aspects of the DNA they were working with, including "loops" and "hairpins," which were often sites of interest for manipulating genes.

Other metaphors are borrowed from computer science and engineering: "debugging," "versioning," and "refactoring" (Richardson et al., 2017) are all commonly used in these discourses, implying a process of rationalizing and cleaning up software. Each of them tends to downplay differences between organisms (Calvert & Szymanski, 2020). In a 2020 conversation, Boeke described how as the Sc2.0 project nears completion, focus has shifted toward "debugging and choosing which errors to fix" (interview, 24 October). Scientists often discuss "reprogramming" organisms (e.g., Gallivan, 2007) without reflecting on the differences between cells and computer programs (for a more nuanced exception, see Ferber, 2004). Boeke Lab members also discussed various "hacks" from time to time, invoking a sense of computer hacking in their work (field notes from 14 April 2021 include mentions of "sequencing hacks to skip gel purification" and the humorous hashtag "#labhacks").

Much like in other laboratory spaces, the word "bugs" is used, but with a different connotation. In the kitchen, bugs are often thought of as affectionate critters, though they can

certainly also carry negative associations (Greenhough et al., 2018). In the yeast propagation laboratory, they can be desirable or undesirable microbes, depending on the selected starter culture. In the synthetic biology lab, bugs are kinks or issues in the genetic code that do something unexpected or cause a failure of some sort, much as a software engineer would use the term. This difference points to the notion of control and its importance in certain lab spaces. My field notes from June 2, 2021 record a conversation about where bugs come from; answers ranged from changes in the reference sequence from the initial design to unintended errors during assembly to synthetic features with unexpected consequences. None of the explanations seemed to suggest that there were errors in the initial design of the synthetic construct.

In particular, completing the synIX chromosome has involved a significant amount of "bug mapping" or "resolving" issues between various assembled pieces that initially took shape at different laboratories. Frustrated with the seemingly endless hurdles, Boeke quipped that "[It] would have been easier to start from scratch" (field notes, 2 June 2021). The following week (10 June 2021), another researcher repeatedly described bug-related sites as "troublemakers." Launching into a creative tangent, Boeke expressed interest in writing a paper titled "My bug collection" or "A taxonomy of Sc2.0 bugs" that would create a typology of these "synthetic bugs" (field notes, 10 June 2021). All of these "buggy" framings of yeast precipitate design choices regarding its genome and how to achieve the goal of streamlining it or making it "tidier" (Calvert & Szymanski, 2020).

To be sure, many brewers and bakers are also concerned with control too—a bad fermentation can ruin an entire batch. One of the co-owners of Community Cultures Yeast Lab, who has a background in microbiology, expressed his interest in doing his own genetic manipulations of yeast for brewing, though it was not currently possible for him given the time and resource constraints he was operating under. Specifically, he told me that his idea was to

"implant" a copy of a kveik yeast into a Chico[22] strain to achieve a "fast fermentation with crisp, clean flavors" (interview, 20 May 2020). This individual's fascination with genetically manipulating yeast for brewing was not especially typical of people I spoke with in the brewing industry, but it is not unique either (Figure 12).

Figure 12: "Atomic Punch Bowl" IPA, brewed by McMenamins' Cornelius Pass location in Hillsboro, Oregon. This beer used a genetically altered yeast strain from Omega Labs in Chicago, IL (a large provider of yeast cultures for craft breweries). Named "Cosmic Punch" yeast, this strain is a CRISPR-thiolized version of a London Ale strain. According to Omega, "The Thiolized® process enhances a yeast's ability to biotransform compounds found in malt and hops to unleash thiols — flavor- and aroma-active compounds reminiscent of grapefruit, passion fruit, and guava" (https://omegayeast.com/all-about-our-thiolized-yeast-series). Omega is not the only yeast company making genetically modified strains for brewing. Berkeley Yeast is another competitor with similar offerings. Photo by author.

[22] Kveik is an umbrella term for a group of yeasts traditionally used in Norwegian farmhouse brewing. Typically, this yeast was harvested and maintained by each brewer and shared as necessary between farms to maintain strong, desirable ferments. Kveik appears to be geographically unique to western Norway (Garshol, 2020), but it has recently experienced a surge in popularity among craft brewers in the United States who desire its ability to ferment wort quickly at higher than usual temperatures without producing 'off' flavors.

Chico is arguably the "driving force behind the craft beer boom we all find ourselves in today" (beermaverick.com). Popularized by the Sierra Nevada Brewing Company (whose original taproom was located in Chico. California), this strain apparently came from Ballantine Brewery in Newark, New Jersey. In the late 1970s, the founders of Sierra Nevada received a sample of this yeast, which they began using in their signature pale ale (beermaverick.com). A blog at anspachandhoday.com suggests that the strain used by Ballantine originated in northern England, but this is unproven. Chico has become one of—if not the—most commonly-used strains of brewer's yeast in the United States, particularly in classic IPA styles.

Machinery: The chassis as a mental and functional frame

Scientific writing about *Saccharomyces* largely constructs it as a neutral body with near-infinite ability for manipulation. These qualities are often taken as evidence that cells can be understood as machinery. The parts-based ontology of synthetic biology is particularly useful for viewing cells as a collection of modifiable components. Commonly employed metaphors for yeast in synthetic biology include "platforms," "chassis" (as in the structural framework of an automobile or computer; e.g., Dymond & Boeke, 2012, p. 170), and "operating systems" (e.g., Cameron et al., 2014; Dietz & Panke, 2010). 'Chassis' in particular connotes a neutral, minimal body upon which components can be "bolted on." Calvert and Szymanski (2020) note that "In much synthetic biology, the cell that provides the context for engineering a genetic pathway of interest often goes unmentioned or is described as a "chassis," a neutral frame into which engineered constructs can be inserted" (p. 2). These terms are used to make the small understandable and cast it as 'neutral frames' rather than living, agential organisms, which also serves to smooth over species' differences and distance the organism from "organism-ness" (Calvert & Szymanski, 2020). The chassis metaphor emerges from and facilitates efforts to design a 'minimal' genome devoid of anything deemed unnecessary to evolutionary fitness, or at least to surviving long enough to provide useful experimental results (for a recent example, see Xu et al.'s 2023 paper titled "Trimming the genomic fat…"). Seeing a cell as a chassis and strands of DNA as functional modules that can be added or subtracted at will sets up life to be very instrumental and mechanical.

For synthetic biology, the chassis is a virtuous construction, allowing maximum flexibility to researchers while proving their notions of cells qua machinery. Thinking in terms of chassis and seeking their practical attainment has become an important part of genomic engineering. Examining the text corpus I assembled reveals that 'chassis' is common throughout the body of

literature related to Sc2.0, but it is also disproportionately represented in a few key publications (Figure 13). Antoine Danchin (2012) emphasizes the importance of the cell's chassis as the basis for the "cell factory." In the same paper, other mechanistic structures are invoked, from "scaffolds" (as in a temporary structure used to aid construction of a building) to "safety valves" ("An engineer would propose a safety valve: once reaching a threshold level the valve opens and excess metabolite is expelled out of the cell") (Danchin, 2012). Interestingly, Danchin (2012) argues that synthetic biology has not been sufficiently engineering-oriented in its conceptualizations of "cell factory" functions, despite metaphors of "nanomachines" that describe cellular components.

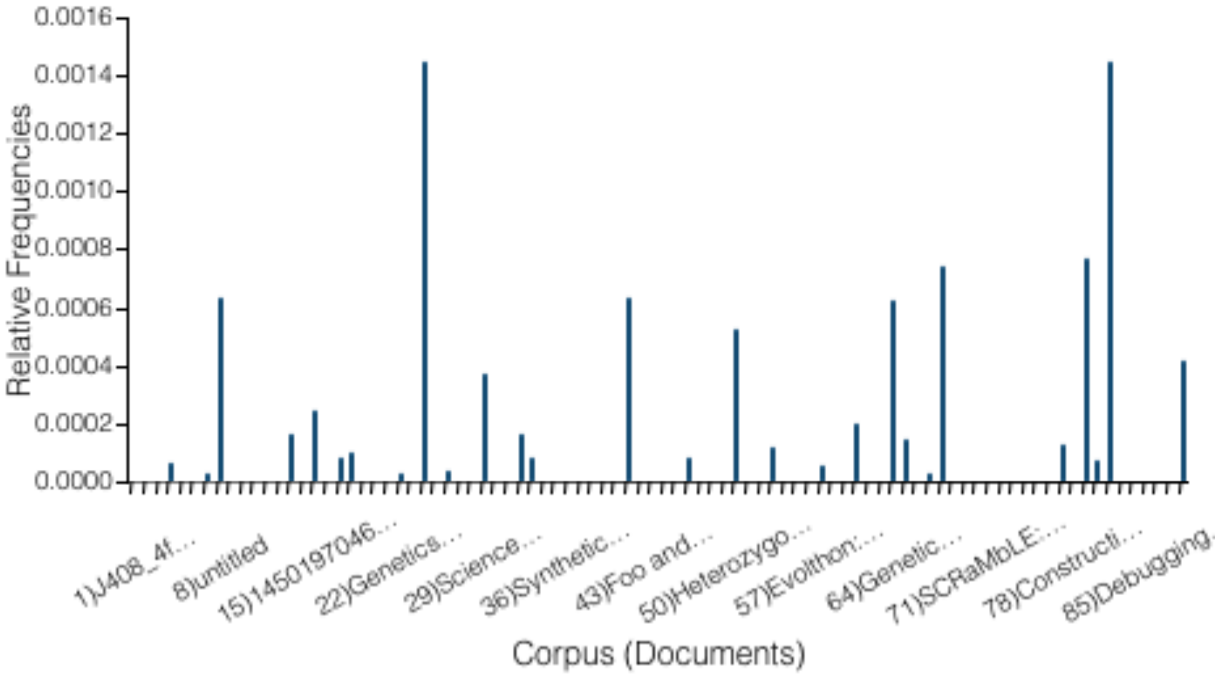

Figure 13: Relative frequencies of the term "chassis*" in the text corpus. The asterisk is a 'wildcard,' capturing potential variations of this term. The x axis is organized chronologically, while the y axis displays relative frequencies.

Metaphors of violence and militarism

In my own observations of Boeke Lab meetings, I noted the consistent use of metaphors with militaristic overtones. Research presentations by lab members frequently describe "landing pads," "launch pads," and "platforms" onto which "payloads" of genetic material can be delivered ("…delivery of a landing pad, overwriting the landing pad, and delivery of the payload;" field notes, 23 November 2021). One presenter described a "battlefield" of genetic carnage left behind from millions of years of evolution[23]. While this latter metaphor was rare, "landing pads" and "payloads" are used frequently to describe designated sites for gene integration/recombination (Bourgeois et al., 2018) and vectors for delivering genetic material (Gaidukov et al., 2018). "Knockouts" (and "knock-ins") are common frames for describing the replacement of one gene or stretch of DNA with another. In an April 2021 lab meeting, one member said, "It makes me hopeful that you can really 'torture' the kinetochore" (a complex of proteins associated with the centromere of a chromosome). Frequent discussion revolves around whether a genetic modification is "non-scarless" or "scar-less," meaning whether or not the operation leaves behind evidence of it having taken place. The former is considered to be more efficient (faster), but not always desirable depending on the context.

I suspect these metaphors are being used unwittingly, but I contend that their use nevertheless frames the possibilities and realities of yeast-human interaction in this laboratory space. During a lab meeting held on May 16, 2022, a researcher underscored just how instrumental most cells are seen to be: "For episomal editing, do we really care about the health

[23] For an earlier use of this term, see Johnson, N. A. (2010). Hybrid incompatibility genes: Remnants of a genomic battlefield? *Trends in Genetics, 26(7), 317–325.* doi:10.1016/j.tig.2010.04.005. It is worth noting, however, that the term appears only in the title and nowhere else in the article. Subsequent articles have adopted the term "ecological battlefield," in particular several authored by Nerve Zhou (e.g., Zhou, N., Katz, M., Knecht, W., Compagno, C., Piškur, J. (2018). Genome dynamics and evolution in yeasts: A long-term yeast-bacteria competition experiment. *PLoS ONE 13*(4): e0194911. https://doi.org/10.1371/journal.pone.0194911).

of the whole strain? We're just going to kill them anyway" (field notes, 16 May 2022). The bluntness (and perhaps flippancy) of his comment elicited chuckles from the group. It would be unproductive to argue at length here about the travesty of mass cell killings (which are apparently outside the purview of RRI), as countless yeast cells have reproduced and died during the writing of these words alone. And yet, the mindset evinced above coexists with existing chimeras like humanized yeast cells, humanized mice, and designs to synthesize bigger and more complex genomes on the horizon. These framings will have consequences for how we view what is responsible research and who gets to decide what it means and encompasses. In this way, metaphors of violence and militarism are revealing, even if inadvertent. Will they become more durable through the scientific literature, or will their moment pass?

Synthetic biologists use all kinds of other colorful names and acronyms in their work. One member described a "Hyperactive Sleeping Beauty Transposase." Others compared DNA of unknown function to "space junk." Different "cassettes" are frequently part of experiments, delivering small packages of genetic material to specific locations. "General housekeeping genes" made numerous appearances in discussions of tidy genomes. "Libraries" to store volumes of genetically distinct strains and parts and "backbones" to build components around are other common metaphors. "Grass" is used to describe stretches of low, consistent peaks on PCR graphs. Yet another tool-related metaphor that cropped up from time to time was the idea of "ratchets" working on yeast cells.

The iconography of synthetic biology

In addition to the metaphors used to help make synthetic yeast understandable, synthetic biologists deploy a sort of iconography in their presentations. One of the most common icons is

the scissor, which stands in for the "cutting" that CRISPR does (Figure 14). This icon is ubiquitous in the lab meetings that I observed and was used consistently over time. It also meshes with the common characterization of "cutting and pasting" used in lab meetings. In a lab meeting in May 2021, Boeke expressed his desire for "well-behaved" promoters that would predictably function as "cutters" and "non-cutters." On rarer occasions, a "Pac-Man" icon is also deployed in a similar fashion, suggesting chewing up and digesting certain DNA fragments to allow for integration of new genetic material at a site of interest (Figure 15).

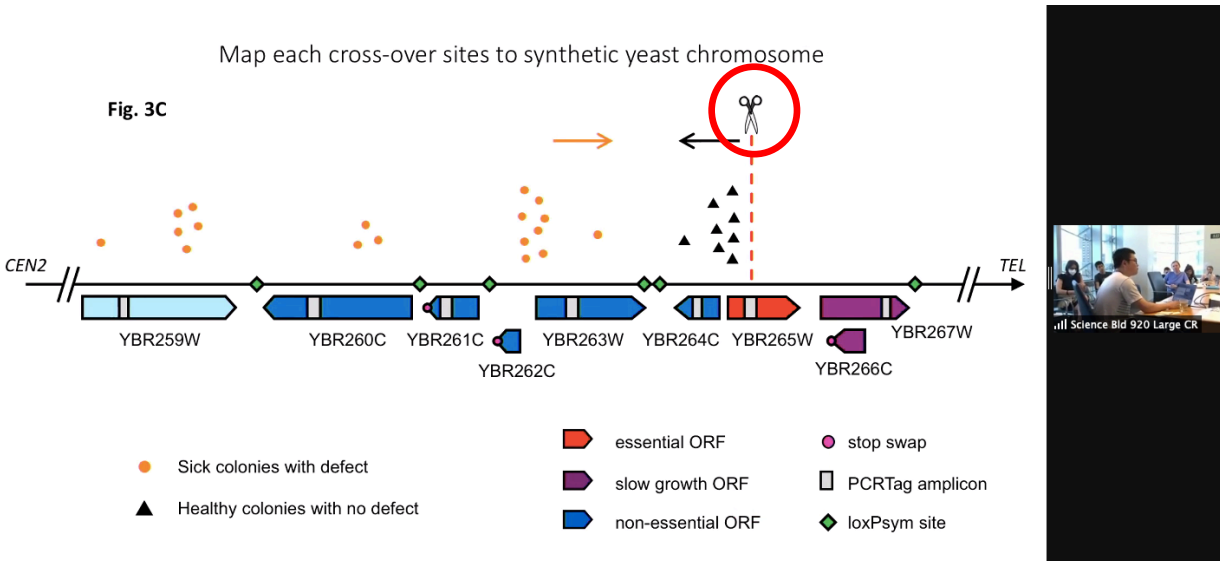

Figure 14: Screenshot from a Boeke Lab meeting displaying a slide with a scissor icon (circled in red).

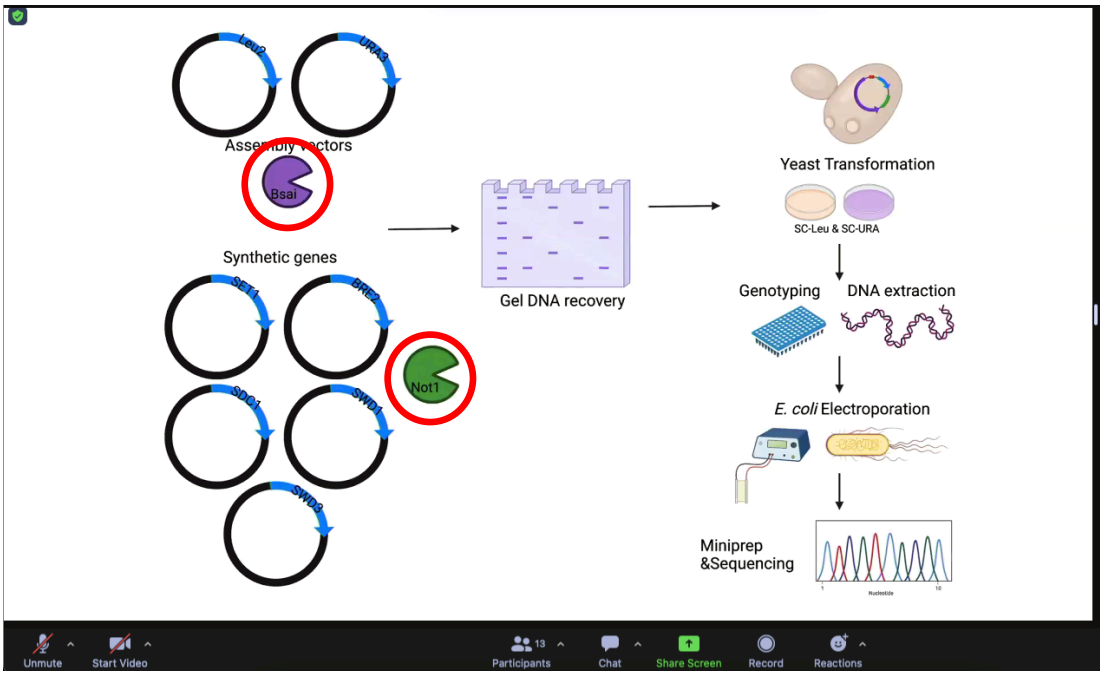

Figure 15: Screenshot from a Boeke Lab meeting displaying a slide with "Pac-Man" icons (circled in red).

Gears and ratchets form part of the iconography of synthetic biology as well. Though less common in Boeke Lab presentations, gears often appear on websites devoted to synthetic biology projects and invoke mechanistic understandings of cellular functions and interactions (Figure 16, Figure 17, Figure 18). Aside from enforcing these renderings of microbial life, it is unclear what understandings are conferred by equating biological processes like CRISPR-Cas9 to bolts and cogs.

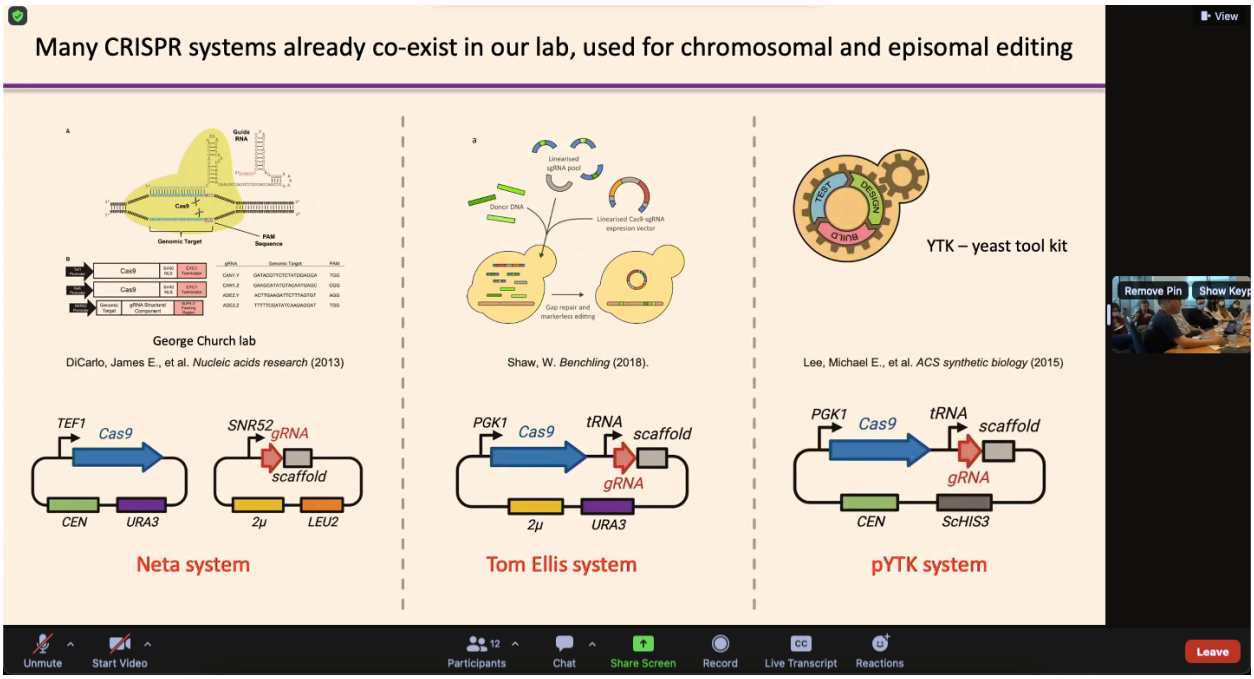

Figure 16: Screenshot from a Boeke Lab meeting portraying yeast as a set of interlocking gears. The words "design," "build," and "test" form the interior of the yeast "cog," reminding the audience of the dominant engineering approach to developing synthetic yeast.

Figure 17: Banner from syntheticbiology.org artistically depicting a yeast cell morphing into a cog. This website is no longer available, but the paradigm it portrays is alive and well.

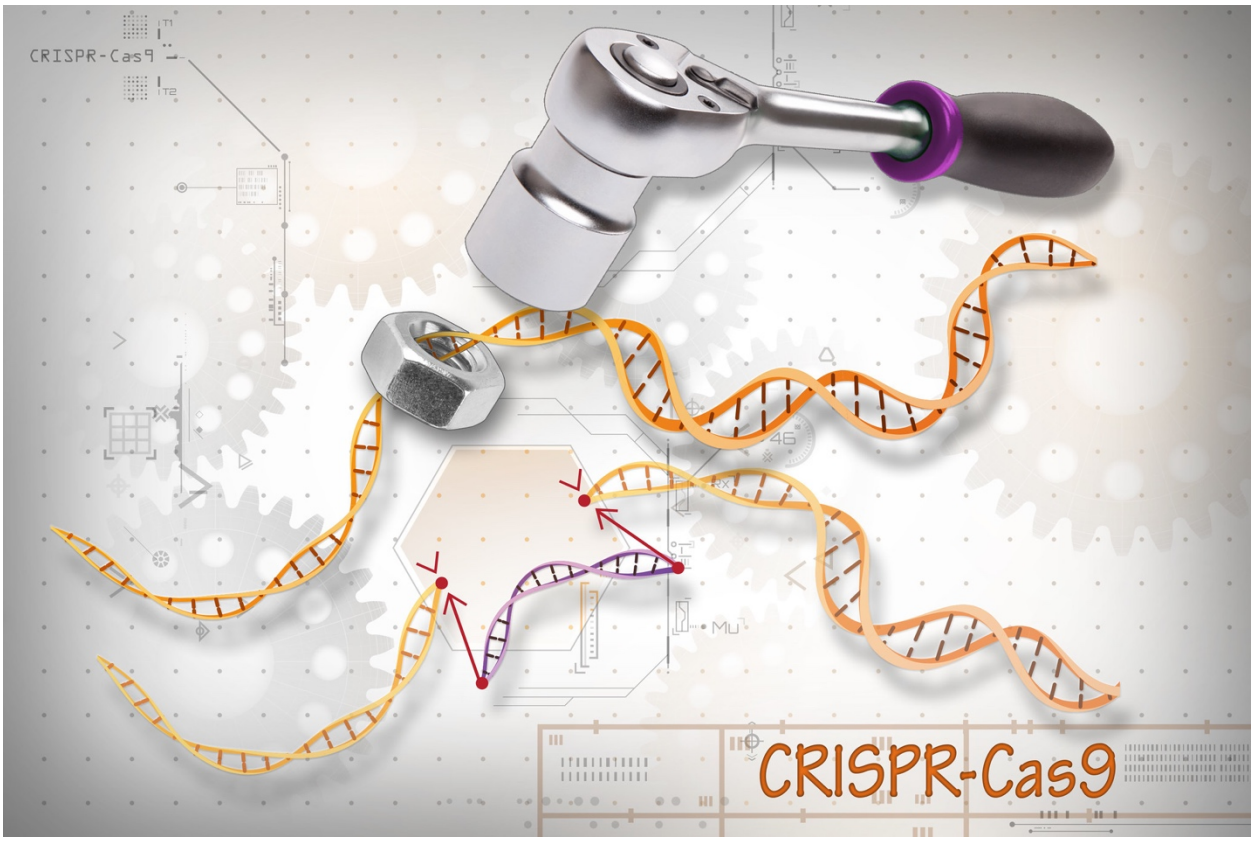

Figure 18: A depiction of CRISPR-Cas9 as a ratchet. Image by Ernesto del Aguila III, National Human Genome Research Institute.

Design and rationality

As noted previously, design is a central organizing principle within synthetic biology in general, which allows scientists to invoke novel, future imaginaries. Design invokes and reveals values in its quest to make things 'better,' and the resulting cornerstones of the Sc2.0 project—fitness, genomic stability, and genetic flexibility—are no exception. As Calvert and Szymanski (2020) note, these three principles are somewhat incongruous in that the latter two specifically reference properties of the genetic material, while the first is concerned with the organism's overall reproductive health:

> Tellingly, this first principle is sometimes expressed by the phrase 'do no harm to the yeast.' … although the design, engineering and construction in this project are all focused on the DNA, the scientists judge the success of their genetic changes by assessing the fitness of the whole organism. And the way in which they assess its fitness is phenotypically –usually by looking at whether the yeast grows as rapidly as would be expected on agar plates or in liquid-media cultures. (Calvert & Szymanski, 2020, p. 8)

Thus, the organism (and specifically its phenotypic expression) writ large is still significant in the Sc2.0 project. Boeke identified evolutionary fitness as "the most important thing" (interview, 24 October 2020). In the Sc2.0 project, consequential decisions about the best way to shape a synthetic genome "that could teach us biology" were made early on (Calvert & Szymanski 2020, p. 8). Boeke himself admitted that the design involved "a laundry list of arbitrary decisions," spanning a significant planning period (Boeke, 2016).

Despite the sensibilities lacing synthetic biology research, there are (perhaps small) openings for constructing the nature of yeast differently, recognizing its vitality and agency. I argue that current discourse exists in tension between these imaginaries—control and agency. Scientists working with yeast in the Sc2.0 project seem to acknowledge its 'yeastiness,' emphasizing the organism in a way that offers glimpses into meetings between massive-scale genomic engineering and the "microbial turn" in social sciences (Boeke as cited in Urquhart, 2014; Paxson & Helmreich, 2014).

Szymanski (2018b) notes that metaphors invoking mechanical passivity tend to dominate discourse in synthetic biology, which renders microbes as non-participants in the research process. She suggests that using different metaphors that construct microbial life as active and collaborative may open new possibilities for 'working with' and 'learning from' them (Szymanski, 2018b). This envisioned approach emphasizes uncertainty and a different scale of things; in working 'with,' we might work toward the *organism* rather than toward the molecule.

Finally, preserving "yeastiness" is also a concern that modulates based on spatial context.

Yeastiness may be thought of as the almost-magical qualities of yeast to bakers or brewers (from hobbyists to professionals, at times), but to synthetic biologists and yeast scientists it indicates the evolutionary fitness of a culture. "The synthetic yeast project centers on a microorganism that we have come to see as particularly charismatic, but we argue that yeast's distinctive features come to the fore in this project in large part because it involves engineering a whole genome rather than a discrete part or pathway." (Calvert & Szymanski, 2020, p. 3). Boeke himself expressed that to him, 'yeastiness' is equivalent to fitness (interview, 24 October 2020).

If *Saccharomyces* affects human responses to it in some way based on its distinctive character and the centuries-old associations it is entangled in, then perhaps the Sc2.0 assemblage echoes a form of what Evelyn Fox Keller (1983) termed "a feeling for the organism" in her biography of Barbara McClintock. Keller (1983) was describing the special familiarity McClintock had with her organism of interest (maize), developed through lengthy engagement with it as well as her own perspective as a woman in a male-dominated field. Building on this idea, Calvert and Szymanski (2020) offer their interpretation of synthetic biologists' "feeling for the (micro)organism" as an opening for investigating how microbes like yeast might be cast differently than mechanical objects (McLeod et al., 2017). Scientists at times express this feeling for yeast through multiple senses. Boeke described a desire to preserve the "beautiful smell" of yeast in an interview (24 October 2020). Another researcher described a "beautiful pattern" in their visualizations of yeast colonies (interview, 8 December 2022).

What do these metaphors *do*?

In keeping with new materialist foci, I am not just interested in what these metaphors and discourses *mean*, but rather the work they *do* in composing the worlds of synthetic organisms.

Through allusions to machines, code, computers, and violence, these metaphors shape scientific imaginaries in specific ways, emphasizing engineering and design principles explicitly and control implicitly alongside a digitization of life. Biology is brought more and more into the realm of computer science and life is increasingly articulated in binary. These metaphors shape the world of synthetic organisms, which is rapidly growing beyond just yeast.

Publications, conferences, and lab meetings are sites where the metaphors and logics discussed in this chapter recur and become durable. There is a reflexive element to this scientific discourse; an almost-circular quality that is self-referential and self-perpetuating. This preserving, maintaining force is an example of territorialization in the Sc2.0 project. Territorializing discourse in synthetic biology acts as a sort of centripetal force and part of a refrain (*ritournelle*) (Deleuze & Guattari, 1987, p. 312). A refrain (in Deleuze and Guattari's usage) is a tripartite process of fixing "a fragile point as a center," organizing a "pace (rather than a form)" around that point, and launching "out of itself" (1987, p. 312). These three processes are aspects of the refrain, rather than moments of evolution. Thus, the refrain is a territorial assemblage that tightens and slackens around processes of becoming more stable (territorialization) and transforming into something else (deterritorialization). The metaphors employed in Sc2.0 and synthetic biology more broadly become expressive and form a territory in which yeast is understood as a chassis-like object that is completely (or nearly so) programmable and tractable. Like the yeast cell reproducing or re-executing a block of 'code' that it's been transfected with, there is a rhythm—a periodic repetition—to the repetitive use of machinic and informatic metaphors. But mutations occur, even in synthetic yeast (and we have yet to learn how a yeast cell with all 16 synthetic chromosomes will act). When they do, the territory and rhythms are destabilized and transformed; the new cells form new milieus that may again territorialize differently, and the metaphors are vulnerable to intrusions of new

meanings and logics. These same metaphors can open into new regions created by their own circles of territory and be taken up by a deterritorializing movement, releasing a machine. For Deleuze and Guattari (1987), a machine is "like a set of cutting edges that insert themselves into the assemblage undergoing deterritorialization, and draw variations and mutations of it" (p. 333). Here it is productive to remember that despite the current power of these discourses, synthetic biology is a young field actively being shaped by groups like the Boeke Lab. As surely as synthetic biology emerged from coagulations of recombinant DNA technology and model organism research, drawing upon their rhythms and vibratory milieus, its existing motifs will be overtaken by counter-motifs as a machine opens it to other assemblages. How durable will current metaphors prove to be?

Metaphors emphasizing control reinforce human agency while minimizing yeast's vibrancy in a move that builds on traditional nature-culture divides. In one lab meeting, Boeke pushed back against some members' skepticism regarding a certain approach, claiming, "It's just the yeast genome…we can do whatever we want. We own it" (field notes, lab meeting 21 January 2021). This may well be true on a *certain* level (ownership aside!), but it also fails to acknowledge the times when "rational" design doesn't account for nonhuman agency and yeast's unpredictable responses to parsimonious genome editing. At times Boeke himself recognizes these ruptures between discourse and reality, but the control paradigm remains dominant in lab meetings, conference proceedings, and academic literature. As Babich (1994) (speaking of Nietzsche's rejection of ultimate knowledge) puts it, "One assumes constancy and identity by suppressing—forgetting but not explaining—"minor" differences" (p. 90).

Ruptures and pinholes

> "Insofar as people become the words and metaphors they use, are we witnessing the formation of a new mind, and thus a new people?" (Amato, 2000, p. 162)

Discourse matters. In the case of synthetic biology projects like Sc2.0, academic publications, scientific knowledge claims, and corporations (re)shape the politics of multispecies interactions by rendering genetic material like genes and chromosomes as discrete chunks of information—LEGO-like bricks of 'code,' if you will. What is the result of this framing? Is it merely a convenient way to make minute things understandable? Is a new imagination of life already forming in highly resourced and esteemed institutions? What work might this metaphor of interchangeability and constancy do in the context of synthetic life? One can envision the potential for commodification or privatization. In general, synthetic biologists have hewed to open-source ideals thus far, though ruptures in these ideals are readily apparent, with some prominent Sc2.0 researchers linked to private biotech firms. The connections between academic research units and private companies like Neochromosome, which are clearly invested in turning a profit from their synthesis work, loom large.

I want to be clear that synthetic biologists who work with yeast are not monolithic in their opinions or approaches, though the reader might be led to this conclusion by the preceding pages. Rather, throughout this chapter and the dissertation as a whole, I wish to highlight dominant discourses within the field of synthetic biology that shape human understanding of what yeast—and by extension, microbial and macroscopic life in general—is and how it works.

Babich (1994) discusses the thorny but deceptively simple question "Is it raining?" to examine Nietzsche's critique of nature as a discernable continuum, noting that what may appear delimited and classifiable is "a chaos rendered continuous by the discerning process itself" (p.

117). She continues:

> To fix our selective parameters we may ask how many drops it takes to make it "rain"…indeed, what precisely counts as a drop? Just a drop of water? Must it be a drop of rain? Is there a difference? What distinguishing details are important, viewed from the differing perspectives of a meteorologist, a special-effects technician, or indeed, the research scientist *simulating* rain (causing rain for the purposes of a meteorological study or the effects of rain-absorption by plants)? Is simulated rain involving a shower of water more *rainlike* than the visual effect of slashed sheets of mylar waved across the stage to the audio accompaniment of falling raindrops in a theater production or even the pure simulacrum of the video-effect addition of shimmering or fuzzy electronic rain "falling" on the video-monitor "before" or "on" TV-studio/video performers as safe from rain as they are from sun or cold? (Babich, 1994, p. 117-118)

What distinguishing details, therefore, are important about synthetic yeast? Is synthetic (simulated) yeast more *yeastlike* than "natural" or "wild-type" yeast? If the effects/behavior we humans are looking for from yeast are either totally predictable to the point of lacking vibrancy or totally customizable to the point of yeast being capable of any synthesis, "torture," or genetic gymnastics, perhaps synthetic yeast better fits our desires for a companion organism than its non-synthetic ancestor. *Saccharomyces cerevisiae* seems to exist and thrive somewhere in between these poles, however. Through the pinholes in scientific practice offered by this dissertation, we can see daylight.

More diverse and perhaps subversive perspectives lurk around the corners, as demonstrated through the literature and interactions with scientists discussed here. Some synthetic biologists recognize that what humans perceive as uncertainty may be an intrinsic aspect of 'individual cell behavior' (Andrianantoandro et al., 2006) and attempt a middle path between the extremes of unmanageable complexity and universal modularity. Yet, these more nuanced understandings of yeast remain marginal because they confound the central principles and assumptions of synthetic biology. Perhaps more vibrant, agential renderings of microbial life that seek understanding over mastery are just a thorn in the side of synthetic biology's purported improvements to life on earth. Or maybe there is something worth paying attention to here;

something that fundamentally conflicts with our reality of a damaged but resilient world that may outlast us and that has already been long subjected to our technological 'improvements,' with dubious results.

In the next chapter, I focus more precisely on the role that yeasts play in doing 'work,' using labor as a conceptual frame to map how work-related metaphors further entrench human ideas of yeastiness but in contrasting ways. I argue that labor is an important part of making yeast into an organism that has contributed so much to human endeavors, from brewing to genomic engineering.

8. ATTENDING TO THE SMALL THINGS: LABOR AND BODIES

> "The tiny creature replied that he was commanding all the weeds to rise up, because the king chose all the creatures of the "Wraith-Island" town but left him out, although he was the smallest among all, but he had the power to command weeds etc. which had been cleared to grow up as if it was not cleared at all. But the king said that he had just forgotten to choose him with the rest and not because of his small appearance. Then the king made excuses to him, after that he went away. This was a very wonderful tiny creature."
>
> - Amos Tutuola, *The Palm Wine Drinkard*

> "My suspicion is that we might nurture responsibility with and for other animals better by plumbing the category of labor more than the category of rights, with its inevitable preoccupation with similarity, analogy, calculation, and honorary membership in the expanded abstraction of the Human."
>
> -Donna Haraway, *When Species Meet*

Although metaphors equating yeast cells to factories, machinery, and computers populate the world of synthetic biology (McLeod et al., 2017), the fact remains that yeasts have bodies that actively make things happen. When they die, those forces cease. Their effects in the laboratory can be modified and guided by human designs, but also predate humanity's awareness of their existence. In this chapter I examine these effects through the lens of labor, conceptualizing yeast's agency as different aspects and forms of work. Microbial labor is, to some degree, a misleading anthropomorphizing of natural processes and desires—of wills to thrive, for example.

> Intention and functionality are immanent to the labor process, rather than the imposition of prior design upon an external substrate—the difference, Karl Marx (1976) argued, between the labors of the architect and those of the bee. Divisions between productive and reproductive labor are a moot point here, for animals are simultaneously bodily technologies and living commodities. Furthermore, animal work is porous, performed relationally with an entourage of actors that cross-cut animal–human divides. (Barua, 2018)

To understand synthetic yeast in this framing, it is useful to revisit literature dealing with bodies, metabolisms, and subjectivities that tend to blur species-level distinctions. Across these concepts, power remains a lodestone pointing toward differences in how bodies and labor are valued or not and how relationality is produced not out of thin air, but through processes over time. "Inequality in the lab is, in short, not of a humanist kind, whether religious or secular, but of a relentlessly historical and contingent kind that never stills the murmur of nonteleological and nonhierarchical multiplicity that the world is. The questions that then interest me are, How can the multi species labor practices of the lab be less deadly, less painful, and freer for all the workers?" (Haraway, 2008, p. 77).

Metabolism and *Homo microbis*

Metabolism—which in my usage here transcends a strict biological definition to include more Marxian and metaphorical readings of the processes through which yeast enacts "fermented landscapes" imbued with materiality, semiotics, and values (Myles, 2020)—is a useful framework in that it is processual. In a similarly imaginative and critical way, geographers and theorists have stretched Marx's original conceptions of metabolism, applying it to food networks, cities, and assemblages of actors in various senses to better understand how more-than-human ecologies operate. In the context of emerging synthetic biological technologies, metabolism can be a powerful framing for thinking about global energetic flows related to fuel and food, of which yeast promises to be an important part in the future (McLeod et al., 2017).

One of the advantages of thinking with metabolism is that it also carries connotations of reciprocity, flows, and kinship—what Kyle Powys White describes as "being in networks or

coalitions" (2020). When metabolism points to kinship, it invokes a sense of mutual responsibility and needs, consent, and trust. Yeasts and humans are both near and distant kin.[24] They are near in that they have related and lived together for millennia, but they are distant because they are types of beings that do not easily communicate on typical human terms. These situations point to the need to relate differently to yeasts from a human perspective.

The revelation that human bodies are not ontologically-pure entities but rather are composed of more 'alien' (i.e., bacterial) cells than 'human' ones has demanded reexamination of our notions of selfhood and agency (Hird, 2009). Studies attempting to apply a ratio to the numbers of human and nonhuman cells making up our body have landed on different values, but it seems clear that roughly half or more of 'our' cells are not what are commonly conceived to be human. This ontological reorientation asks us to reexamine our interspecies relations and attentiveness toward other bodies with which we associate as a result. To echo Barad (2007), "to be one is to become with many." We can therefore utilize the figure of *Homo microbis* (Helmreich, 2014) to understand the human as an assemblage that includes microbes on our skin and in our guts. We can approach this more expansive character through practices of relationality and becoming; an ontology of processual associations as opposed to static notions of being. This move allows ethnographers of the microbiome to slip into the mutable world of microbes, which defies positivist scientific or commonsense notions of gender, species differentiation, and individuation (Kirksey, 2018). Lateral gene transfer, Lamarckian modes of expression/inheritance, and helminthic regimes of control favor 'diagramming' or 'writing around' these figures and tracing connections between actants of all kinds by noting what they do, as opposed to what they are (Deleuze & Guattari, 1987; Latour, 1988; Lorimer, 2017).

[24] Here I am thinking of Donna Haraway's "odd kin" (2015).

While the extension of our sensory capabilities via technological innovation (i.e., microscopes, gel electrophoresis) has opened up new ways of understanding and exploring microbial lives, the realization of this cosmos beneath our noses and nails does not engender a predetermined future but rather multiplies paths we might follow in responding. Though possible futures are surely multiple, for simplicity's sake I could conceptualize this as a sort of binary (at my own peril!) between a neoliberal mode of relating to newfound microbial partners that seeks to enroll them in various anthropocentric projects of world-building—including, notably, biosecuritization—in the old mores of capitalist accumulation vs. a more attentive, approach that attempts to de-center the human and think of "becoming hosts" à la the symbiogenesis of Hinchliffe et al. (2016).

Critical social scientists have argued that the former mode of relating to the microbiome is prone to overexcitability at the prospect of the near-ideal commodity that the (synthetic) microbe represents (Paxon & Helmreich, 2014). Microbes are at once mutable "on their own" and via the engineering of synthetic biology; powerful but 'controllable' (Latour, 1988); mobile—circulating across borders and regimes (Barker, 2015); and seemingly ownable and scalable, if the pharmaceutical industry is any indication. This new frontier for capitalist accumulation qua linear scientific 'progress' promises to bring in research funds and prestige while enabling the 'good Anthropocene' (a contradiction, according to Haraway (2008)) of better human health and freedom from chronic gastrointestinal diseases and afflictions of absence, like allergies. This 'microbiomania' (Paxson & Helmreich, 2014) echoes in proliferating research and interest among STS scholars, critical geographers, and anthropologists. However, overselling the microbiome risks perpetuating damaging ways of relating to nonhumans, not to mention co-

constructing less-livable worlds. Critics of 'microbiomania'[25] cite numerous examples from fads to clinical health research trials that contain a seed of novel microbial revelation, yet (over)extend the claims sprouting from it in unmerited directions. Such proscriptions, though perhaps not theoretically intricate, are rightly indignant (Eisen, n.d.).

The latter mode of relating to microbes emphasizes attunement and networks of care (Krzywoszynska, 2019; Puig de la Bellacasa, 2015). Adequately paying attention to the (often powerful) humans acting in multispecies assemblages while also tracking/tacking back and forth between scientific practices and the spaces that tiny actants often inhabit[26] is necessary to account for the various registers at play (Greenhough et al., 2020). Tsing's work in particular offers ways to think about living "amongst the ruins" and attending to what survives capitalism—the "third nature" (2015). Perhaps one way in which critical social science can navigate the hype of microbiomania is to focus on "pericapitalist" spaces where refuge can be found from hegemonic capitalist paradigms (Tsing, 2015). These spaces allow for critique and attempt to avoid fetishizing economic modalities that have become the background to our quotidian ways of being/interacting. They do not presume the subsumption of Capitalism but view these spaces as occurring in tandem, though perhaps spatially differentiated (Tsing, 2015).

However, we should take care to familiarize ourselves with the active side of microbiomania—that of hope and promise. Whatmore's invocation to view the future as commons instead of a common future might help guide us (2002). A more expansive notion of what it means to be human or what it means to be healthy helps destabilize our thinking about multispecies relationships and offers points of departure or ruptures from which to take up a

[25] Jonathan A. Eisen of the University of California-Davis maintains an excellent blog with examples of egregious microbiomania claims at https://phylogenomics.blogspot.com/p/blog-page.html
[26] Here I am thinking of Latour's (1988) scientists in their enacting of praxis.

renewed task of world-building. Such a co-constitutive conceptualization reminds us that alternative futures are possible and are always already coming into existence. How humans navigate the reality of *Homo microbis* and ally with or distance our 'selves' from other lives has generative power. Here Mol's (2002) 'theorizing empirically' is instructive, reminding us that critical social scientists and synthetic biologists are not merely representing different perspectives on the same thing, but rather describing (generatively) different things and situations altogether (Greenhough et al., 2020).

Co-domestication and care

A common narrative in spaces of human consumption of fermented products is one of domestication, but the relationship in question is typically seen to be unidirectional (i.e., humans domesticating yeasts). However, a more relational ontology troubles this notion, drawing our attention to the vast landscapes humans have dedicated to feeding yeast (e.g., vineyards, barley fields) and the temples we've built to fermentation, including gleaming breweries, state-of-the-art laboratories, and industrial bakeries. While not quite universal, our propensity as a species for the products of fermentation—whether alcohol or healthful, lively foods like kimchi—belies our dependency on microbes and their domestication of humans as willing conveyors of nutrients and careful midwives of subsequent generations. It seems incontrovertible that, even at this point in our coevolution, yeasts do not need humans to thrive, though they have certainly benefitted from the infrastructures we have constructed for their proliferation. On the other hand, we as humans stand to benefit (not just culinarily) from considering how we can attend to the task of enacting more livable worlds that specifically promote interspecies collaborative efforts (Tsing, 2017). This may require reevaluating our

needs and wants and how they align (or not) with others' in the hope of finding a synchronous rhythm we can collectively vibrate within.

A good deal of anthropomorphizing takes place in spaces of fermentation, where earnest bakers may name their sourdough starters or describe their quirky "personality" traits, including but not limited to smell, color, texture, and fermentative activity. Even outside of homes and less formal spaces, an ethic of care is sometimes invoked. At a craft brewing conference, one presenter proclaimed, "TAKE CARE OF YOUR YEAST AND IT WILL TAKE CARE OF YOU" (Erway, 2015). These approaches to working "with" yeast emphasize that it plays an agential role in its relationship to humans and that there is a co-productive, co-laborative dynamic at work.

Likely owing to their epistemological training and cultivated sense of objectivity, scientists and technicians working with yeast by and large did not readily voice these sorts of affective, emotional registers, instead speaking in a manner in keeping with positivistic knowledge production in natural sciences, where emotions are typically perceived as capricious and decidedly unscientific. For example, many of the researchers I spoke with were complicit either directly or indirectly in killing significant populations of mice and countless yeast colonies in pursuit of their research goals. While I rarely drew attention to this reality of their research, I observed how participants spoke about this aspect of their work. One researcher acknowledged (unprompted) that his work involved killing many yeasts but exhibited a dispassionate response, justifying it by adding, "There isn't really this sense of like, 'What does the yeast feel?' or 'What does it think?'" He continued, "I think there is a big difference in that kind of research [referring to working with and killing macroscopic organisms, like mice]…I think we're just much more likely to say, 'Okay'"—to accept that those losses are part of the cost of doing research, whether with yeast "or even bacteria." His conception of the work required is: "Let's

grow like 10 liters of this stuff and just kill all of them for the sole purpose of producing the DNA that we want" (interview, 23 June 2020). Even though most scientists are far from devoid of reflexivity and affective capacities toward microbes, their milieus engender certain mentalities of detachment that form part of the laboratory assemblage.

Domestication creates new relations, often unforeseen. Human-domesticated strains of yeast used in industrial wine fermentation seem to pose dangers to indigenous yeast microbiota due to their high fitness and presence in areas where native yeast populations are scarce (Viel et al., 2017). Perhaps human domestication both homogenizes yeast strains and situationally boosts their resilience, but this also runs counter to the idea that yeasts specialized for laboratory applications (in this case, industrial fermentation) generally are less competitive "in the wild," where growing conditions are less optimal and more variable.

Does 'taming' yeast in the lab for the purpose of standardizing processes and bolting on "parts" enact a sort of homogenization that allows *Saccharomyces* to operate in new contexts? If so, this runs counter to the more common notion that lab organisms like synthetic yeast will not be fit for conditions outside their controlled habitats and that reducing genetic diversity creates significant vulnerabilities for populations. Synthetic yeast troubles this framing because it is subject to extreme diversification through serial, induced mutations via CRISPR while also exhibiting striking genetic similarity across the many "wild-type" samples of the standard strain maintained as experimental controls. This raises questions about the importance of biodiversity in the age of synthetic genomics.

The domestication of synthetic yeast is facilitated by scientific discourse and practice. Although synthetic biologists spend significant time in the presence of their model organisms, working with yeast genomes *in silico* is a somewhat disembodied experience. Rather than

working *in vivo* with all its tactile and sensory encounters, working *in silico* (while still involving bench days and hands-on experience with yeast) is more akin to programming or running computer simulations. The Sc2.0 project conducts its chromosome-by-chromosome synthesis in chunks[27] of base pairs that are designed, tested, and assembled in a virtual environment, using software. While the *in silico* approach is a powerful mode of working with DNA, it is important to be aware of the leap we make between different modes of working with yeast and the reductionism we may practice in assuming that partiality and abstraction map perfectly onto yeasty bodies outside software windows. Made pliable as chassis and platforms, Sc2.0 is also equipped with new capacities (at least theoretically) and may strike out in powerful new directions if it manages to be carried away to assemblages more conducive to its diffusion.

Thinking with new materialisms (Bennett, 2010; Braun, 2015), yeast-human assemblages can be more than forms of neocolonialism, where capitalist paradigms extend to the microbial realm as an outpost for accumulation of biocapital. I hesitate to suggest that this mode of value capture will be or can be completely overcome. Rather, the co-construction of landscapes of fermentation in which production and consumption entwine via the metabolic action of more-than-human life emerge as gatherings of ways of becoming. These gatherings, or 'moots' (to use an arcane but apt word), deterritorialize traditional notions of domestication as linear and irreversible (Deleuze & Guattari, 1987; Latour, 2005; Tsing, 2015).

[27] My field notes record lab members debating the proper, current terminology for various lengths of base pairs. On May 25, 2022, Jef Boeke commented on a doctoral student's presentation, asking her to change some of this verbiage: "The blue and red squares [referring to symbols in a diagram] are actually mini and megachunks…What we used to call building blocks…we're kind of getting away from that now."

From subject to collective

More recent students of nonhuman natures point to the individual as a complex of multiplicities, "becoming host" to the plethora of organisms that make up a human (Hinchliffe et al., 2016; Hird, 2009; Lorimer, 2017; Paxson, 2012). The notion of symbiogenesis is a useful frame for dismantling narratives of individualism and ontological purity. Put simply, symbiogenesis is a theory based on microbiological evidence that the organelles in our cells descend from individual single-celled organisms that were incorporated long ago into human cells via a symbiotic relationship. Post-Pasteurian values (i.e., not all 'germs' are bad) welcome assemblages of nonhumans into the body's (personal, human) space, blurring the distinctions between human and nonhuman. A sort of "ecopoiesis" emerges here, emphasizing co-constructed ecologies and immunocompetencies that ask how and with what kinds of bodies we can associate; with whom can we affiliate and learn to be affected by? Symbiogenic conceptualizations of subjectivity view the subject as a collective, always already coming into existence and generating its conditions of being in multispecies negotiations. Instead of a subject/object divide, we can speak of a subject/subject entity when it comes to human-microbe relations.

Such an agnostic framing of yeast-human concessions and negotiations suggests that we become attuned to yeasty bodies and subjectivities through attentiveness toward and "networks of care" (Krzywoszynska, 2019). This is easier said than done but may be realized most effectively in acknowledging our positionality and situatedness within rhizomatic power networks which foreground the asymmetric but sociable aspects of nature and life itself. Becoming attuned and learning to listen to organisms with whom we do not communicate well may involve "speaking nearby," diagramming, or "writing around" (Deleuze & Guattari, 1987;

Minh-ha, 1994). It is much easier to write for or about species than to write with them or to let them "speak for themselves," but working from the standpoint of a more collective subjectivity demands that we find new ways to communicate, sense, and extend this difficult work (Latour, 2005). In this way, this project offers insights into another dimension through which to help advance our abilities to think and communicate more collectively.

This orientation meshes with the notion of microbiopolitics (Braun, 2015; Chandler, 2018; Paxson, 2008; Sarmiento, 2020; Spackman, 2018), which foregrounds how and in what ways a host of microbes make possible and collaboratively co-produce the world, which is modulated by power dynamics and affectivities or capacities (Carolan, 2013). Synthetic biology projects like Sc2.0 apply an engineering approach to essentialize the genetic code of a fellow eukaryote into permutable and ownable biological information-as-capital. Despite its seemingly self-evident focus on yeast, Sc2.0's anthropocentric epistemological grounding may create blind spots in understanding the ways in which human knowledge is limited and constrained, apotheosizing rational design principles. A more useful approach would follow the matters of concern and assemblages populated by yeast through the twists and turns of their chthonic worlds (Haraway, 2015). Perhaps, as beings that pre-exist humans and our dreams of control, they know something that we do not yet (Sarmiento, 2015).

(Micro)Biopolitics

The modes of control through which life is managed in synthetic biology speak to the Foucauldian concept of biopolitics. Foucault (2007) conceived of biopolitics as the population-level regulation and securitization of bodies. These efforts to control vitality rely on specific techniques and knowledges to develop mechanisms for managing life. Social scientists have

applied biopolitical concepts to microbial bodies, a synthesis resulting in the notion of microbiopolitics (Braun, 2015; Paxson, 2008; Spackman, 2018). "Such biopolitical ecologies of fermentation and health arguably bring a new dimension to Foucault's notion of *micropolitics*, expanding the 'capillaries' of power relations to the microscopic realm…" (Sarmiento, 2020, p. 315). In addition to extending biopolitical concepts to the microbial scale, microbiopolitics offers ways to think with microbes about how they co-constitute our material existence, specifically through embodiment. We are not, Jane Bennett argues, merely embodied but "*an array of bodies*, many different kinds of them in a nested set of microbiomes…if we were more attentive to the indispensable foreignness that we are, would we continue to produce and consume in the same violently reckless ways?" (2010, p. 112-113; emphasis original). This move foregrounds "relationality, rather than individuality, as the axiom of social life" (Whatmore, 2002). Micro-geographies of laboratory spaces reveal assemblages of actors engaged in relational, metabolic collaborations that exhibit a complex interplay between harnessing and constraining yeast's vitality (Latour, 2004; Szymanski, 2019).

These assemblages invoke Foucault's concept of 'heterotopia' (*hétérotopie*), which signifies spaces that are 'other' or contradictory (2002, p. 12). In the context of contemporary synthetic biology, animal bodies such as *Saccharomyces cerevisiae* and mice may be understood as one example of heterotopias; they approximate utopian dreams of control and manipulability. They are ordered by technologies and classification schemes drawing on the currency of genes as informational capital (Whatmore, 2002).

In the 21st century, microbiopolitics is not just for microbes. The human microbiome has increasingly emerged as an object of scientific knowledge over the past half century, during which time it has also become a trans-scalar site of global struggle entangling privacy concerns,

intellectual property, and debates about the extent to which humans should genetically modify our own species. As scientific knowledge of the human microbiome grows, questions remain about how microbes and ferments will articulate with the objects of technoscience regarding power, agency, public policy, and health (Greenhough et al., 2020).

Rights?

Should synthetic organisms (or microbes in general, for that matter) be afforded certain rights? Whatmore (2002) and other feminist writers like Liz Grosz (1994) and Luce Irigaray point toward a 'relational ethics' that deconstructs individual rights-based arguments in favor of an embodied situatedness that might transcend the old binaries of nature-culture and human-non-human through returning theory to material bodies. Further extensions of rights may be based on notions of 'being in the world,' like Whatmore's (2002) "earth others," yet the challenge of representing and 'speaking for' remains. At this perceived impasse it is worth remembering that we humans have always been intertwined with the extra-linguistic world, though this often does not mesh well with modern scientific knowledge production. Haraway (1991) ponders these questions in thinking through how to avoid "terms in which the best the non-human can get out of [it] is to be permanently represented [by 'us'] as lesser humans" (p. 86). Shifting from relational 'being' to relational 'becoming' echoes the Heraclitan sentiment of constancy through change, wherein a fluidity of understandings that privileges processual relationships over fixed ontologies and rights can stick with the constantly-evolving species we interact with and are ourselves. These notions reverberate through Nietzsche's eternal return and the refrain of Deleuze and Guattari.

To return to the question, it would be a tall order to argue for individual rights for yeast, for example. However, principles and ethics currently being applied to yeast research may "spill

over" species boundaries, as hybridized cells are designed to mediate between human and yeasty bodies. Thus, these questions have relevance for what it means to be human and for the future of policy and governance. Law is its own kind of technology that sorts non-human populations, prioritizing organisms depending upon their work (Collard & Dempsey, 2013). Critical geographers have increasingly noted the work that nature does and the ways in which it can be appropriated by capitalist accumulation (Barua, 2019; Battistoni, 2016; Besky & Blanchette, 2018; Braun, 2015; Collard & Dempsey, 2013). Despite rhetoric and semblance of total control over yeast in the laboratory, it occasionally acts unpredictably, seeming to resist (com)modification. For example, field notes from March 26, 2021 record an exchange that Jef Boeke labeled a "cautionary tale" because he had told two students that a particular deletion in a gene would be easy to make when in reality, it proved a major challenge. The scientific practices that trigger regulatory interventions and the nonhuman bodies that are deemed worthy of legal protections emerge as important questions in this regard, revealing the rich potential in studying the interrelations of "law in action" and "science in action," as Latour (1988) puts it. Rights aside, bodies offer another lens through which to examine relational ethics: labor.

Nonhuman Labor

Many small things, like soil bacteria, resist being cultured in the laboratory (Granjou & Phillips, 2018). Yeasts may be similarly stubborn at times, as scientists note. Yet oftentimes this agentic power to cooperate or resist is lost in our conceptions of nonhumans. One example is illustrative: evaluations of the labor of nonhumans as ecological services mask power dynamics and agential capacities of the assemblage (Barua, 2018). Here a political economy approach may be instructive, so long as we take care not to essentialize either work itself or the microbes that

seemingly undertake it (Paxson, 2018). As Haraway argues, "To notice how material-semiotic labor is done does not vitiate it ethically or politically but locates it culturally and historically, within which nonreductive judgment is possible" (2008, p. 125).

Seeing modern (Western) conceptualizations of work as "natural" imposes certain norms and values onto nonhuman life. Besky and Blanchette (2018) note the naturalization of nature as working as a form of capitalist expansion into the newly-accessible microbiome. Barua (2018) points out that naturalizing work does work itself. As they and others argue, there is nothing necessarily natural about working in this common sense. Some feminist scholars have demonstrated how labor may be more accurately conceptualized as a hybrid/distributed/collective undertaking (Battistoni, 2016). Social scientists and synthetic biologists alike could benefit from denaturalizing—perhaps by practicing a rhizomatic anti-genealogy (Deleuze & Guattari, 1987, p. 11)—nature as natural capital or ecosystem services or even the notion of work itself as somehow natural (Barua, 2018). "Animals are workers in the shadows of capitalism: their labors remain or are rendered invisible, but become pivotal when actual practices of value extraction are taken into consideration. Animals, however, are not self-directed creatures exchanging alienable labor in the marketplace of their own volition" Barua, 2018). Denaturalizing the work of nature may offer helpful ways out of fetishizing our current social-environmental-economic paradigms (Miller, 2019).

The notion of sympoiesis offers a way to synthesize human and microbial labor as neither mere exploitation nor apolitical, neutral cooperation, but rather as a complex negotiation of species' needs and wants within a co-constructed ecology; one that is nevertheless sensitive to power dynamics and structures while avoided fetishizing them (Carolan, 2013). Drawing upon the notion of 'immunocompetence,' in which health is seen not as the opposite of disease but as the ability to effectively associate with a variety of other bodies

(similar to Spinozan affect), we might imagine how human-yeast assemblages can redirect our gaze toward more collaborative theorizing (Enticott, 2003). If associating with yeast can help shepherd the arrival of a new *dispositif* (Braun, 2014), scientific practice may benefit from this re-alignment and take up the challenge to broaden its abilities to sense via playful methodology and methods, think with, and bring yeast more fully into its Parliament of Things (Latour, 2005). While contemporary human-yeast ecologies are deeply intertwined, *Saccharomyces* seems to have profited from other trans-species associations for millennia before humans metaphorically adopted it[28] and will likely continue to do so long after contemporary modes of being cease to exist, recalling Tsing's (2015) "emergence in postcapitalist ruins."

The Sc2.0 project offers an interesting case of labor across human and more-than-human registers. Its simultaneous existence as a pedagogical tool (enrolling undergraduates and other students in performing the labor of synthesizing segments of genetic material through Build-a-Genome courses) and open-source dissection of a model organism draws on both human and microbial labor to achieve its goals. A cynical reading of these facets of Sc2.0 might suggest that they seek to dampen any public concerns related to associations with more controversial and high-profile genetically-modified organisms, like Monsanto's stable of genetically modified seeds. Whether or not there is truth to this, a more affirming reading of this laboratory assemblage highlights exciting possibilities for re-visioning multispecies futures. In whatever research humans undertake, we should be cognizant of both the labor of our fellow humans—undergraduates working within the Build-a-Genome component of the Sc2.0 project in this case—and of fellow nonhumans like *Saccharomyces cerevisiae*. While the potential benefits to undergraduates participating in Sc2.0 are numerous, the researchers involved should still

[28] For one example, see the work wasps do in harboring yeast in their guts (Stefanini et al., 2012).

consider how the profits—literally and metaphorically—and burdens of this work are distributed. This is not so much a strident critique as it is a cautionary admonishment.

The Sc2.0 project draws on laboratory labor around the globe, with teams collaborating on synthesis, chromosome by chromosome. While it remains to be seen what kinds of landscapes synthetic yeast will produce once it is unleashed (Szymanski, 2018a) and what kinds of associations it will make with other vibrant materialities (whether comestibles or not), seeing Sc2.0 as laboring can provoke reflection on what kinds of worlds we want to live in and which lives/deaths we valorize. To put it differently: Which kinds of worlds are most livable? To answer this, we can take a sympoietic approach, affirming and exploring agencies and associations rather than conceiving of microbes as shiny bio-cogs or sleek chassis (as depicted in the previous chapter) in a superficially novel but fundamentally dominant growth machine (Chandler, 2018). Visions of *Saccharomyces cerevisiae* as laborer offers the potential to re-think how our lives depend on others and to re-politicize and re-animate the landscapes we share, from laboratories to breweries to kitchens. Whether this labor is valued or discounted is another matter. Valuing the labor of yeast would change our notions of ownership, as co-production is foregrounded in place of quasi-ecological service/servitude.

As with soil (Puig de la Bellacasa, 2015), a driving force behind understanding yeast at the smallest levels has been desires to pace its (re)productive capacities with human demands. A key concern in some areas of synthetic biology is the design of "high throughput" systems (Mitchell et al., 2015) that maximize efficiency not only of experiments but also of the cell factories they seek to optimize. Forcing organisms to transcend their habitual capacities and affects is an accumulation strategy with high risk of negative outcomes. As Boyd (2001) demonstrates with industrialized chickens, unintended consequences tend to follow any "program of biological intensification" (p. 662). Thus, speed of bodily circulations matters

(McLeod et al., 2017). In Sc2.0, speed obscures the metabolic labor of yeast, "the body-work of animals that is at the heart of contemporary biocapital, as commodities and modes of production" (Barua, 2018). An "anatamo-politics of capital" emerges from the demands of labor on the cells of living bodies that circulate through metabolic, ecological, and affective landscapes of liveliness and livelihoods (Barua, 2018; Battistoni, 2016; Collard & Dempsey, 2013). Conversely, becoming attuned to yeast means increasing our productive associations with microbial bodies while tempering human dreams of control and purity (Bobrow-Strain, 2012).

As applications of *Saccharomyces* multiply in pharmaceuticals, bioremediation, cancer research, and emerging organisms like Sc2.0, it is perhaps not saying much to posit that indeterminacy lies ahead. Such a reading acknowledges the unpredictable and multiple nature of Nature and re-opens prematurely unified scientific facts that shape our perception of nature's compliance with human designs, many of which figure prominently in Sc2.0 (Latour, 2004; Latour, 2005).

The workhorse, the lab rat

Discourse related to labor intersects with microbes in specific ways. Yeast is commonly conceived of as a 'workhorse,' meaning that it efficiently and obediently carries out the tasks asked of it, laborious as they may be. Scientists frequently use this term when describing yeast's labor (Figure 19), but unlike some of the other common metaphors employed by synthetic biologists and discussed in the previous chapter, 'workhorse' is also used in other laboratory spaces and texts (Boekhout et al., 2003, p. v). This is one area where I observed significant overlap between the metaphors of synthetic biology and those of the brewing industry.

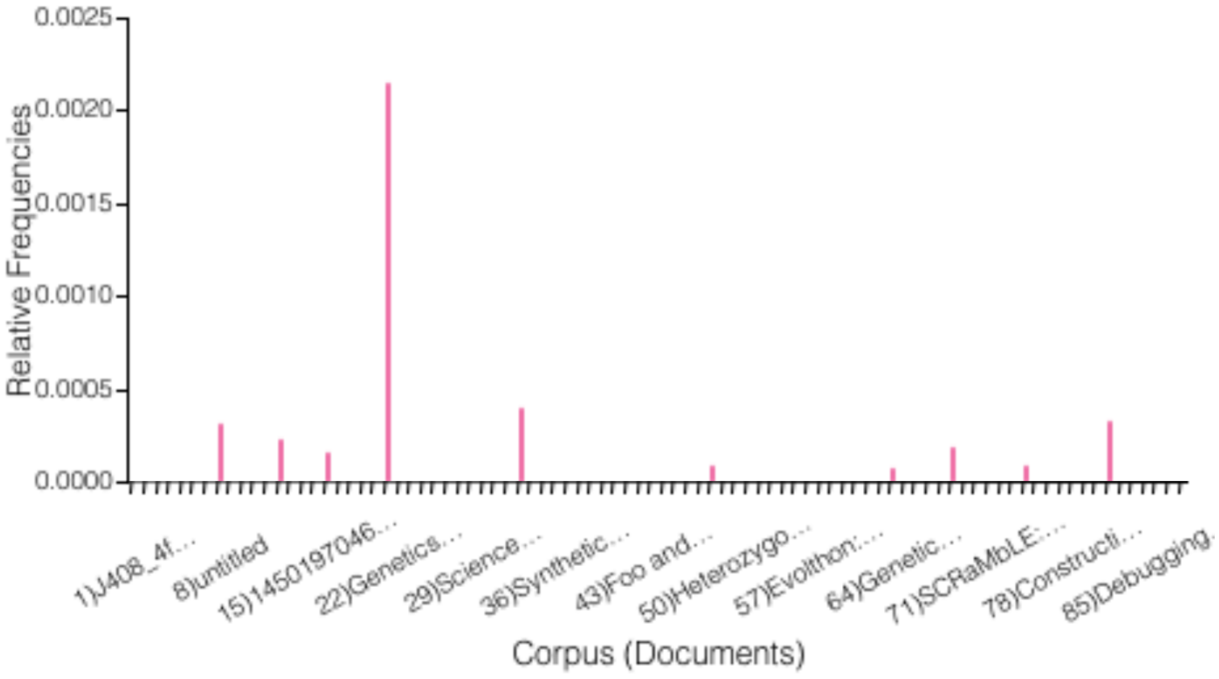

Figure 19: Relative frequencies of the term "workhorse*" in the text corpus. The asterisk is a 'wildcard,' capturing potential variations of this term. The x axis is organized chronologically, while the y axis displays relative frequencies. In this case, it is clear that one publication in particular (Mitchell et al., 2016) is responsible for a disproportionately high usage of this metaphor.

The design choices made in the Sc2.0 project are aggressive and were not certain to succeed at the outset of the project. Jef Boeke, the PI of the Sc2.0 project, wondered aloud in one presentation at just how much "torture" the cell could withstand (Boeke, 2011). More recently, he was again quoted marveling that "It is amazing how much torture the yeast genome can take and still be happy and healthy" (Boeke as cited in Holmes, 2017). Mitchell (2015) and others have repeatedly expressed surprise at the flexibility and adaptability of *Saccharomyces*, measured in terms of its ability to continue to reproduce under variable genomic configurations. One prominent scientist working with synthetic yeast put it this way: "We know a lot about it, we love it, we test all molecular biology and biochemical tools on it, it's very familiar, it's a "go to", it's a good buddy, it's such a good buddy we make mushy toys of it; it's quite the friend. And what do you do when you have such a good friend for so long? Do you mess with its genome

even more? Because that's what we did" (Richardson, 2017).

Although it was never foregrounded, discussions of yeasts' labor cropped up in Boeke Lab meetings. Notes from April 6, 2022 record Jef Boeke suggesting that "Maybe we should just let yeast do the heavy lifting for us" in regard to a tedious procedure. Later, he reiterated: "Let yeast do the hard work" (field notes, 6 April 2022).

Interviews with scientists involved in Sc2.0 reveal that researchers do ascribe personality traits to yeast, not completely unlike brewers or other 'lay' fermenters. Boeke has also reiterated a desire to maintain "healthy, happy yeast" (as cited in Duhaime-Ross, 2014). This outcome is measured by the look of yeast and its general phenotypic presentation as "normal."
At times, yeast seems to be both an *object* to be worked *on* and a *subject* to be worked *with*. Its identities as partner, machine, tool, etc. coexist in and through different laboratory settings simultaneously in an uneven and patchy, relational way. McLeod, Nerlich, and Mohr (2017) found similarities in relationships between humans and bacteria, which were alternately construed as "machines" or agents deserving of respect and care (see also Lorimer (2017) on hookworms). This sort of complex relationship may not be unique to yeast, but it is noteworthy because of the dramatic manipulations *Saccharomyces* is currently subject to against the backdrop of millennia of human-yeast coproduction of landscapes and comestibles.

While it is tempting to portray engineering approaches as purely extractive and self-serving, Calvert and Szymanski (2020) argue that "the synthetic yeast project shows that intervening and manipulating can be combined with appreciation, and that engineering does not imply a straightforwardly exploitative relationship to living things" (p. 12). In my interviews, some scientists expressed amazement at yeast's adaptability and potential for new applications, exuding sentiments not unlike reverence.

One form of adaptability that yeast excels at is genetic flexibility. Homologous

recombination, "a type of genetic recombination in which nucleotide sequences are exchanged between two similar or identical molecules of DNA," can be interpreted as a division of labor between the humans ostensibly directing its course and the yeast cells conducting the actual gene shuffling (Sidransky, 2022). At the moment, the importance of this homologous recombination ability cannot be overstated; it constrains the biological imaginary to the extent that some scientists suggest it will be necessary to assemble future synthetic genomes of other species in yeast cells. "Homologous recombination is essential to building a synthetic genome, making the yeast's abilities crucially important to the project…" (Calvert & Szymanski, 2020, p. 11). Scientists at times refer to the "awesome power of yeast genetics," acknowledging the importance of this flexibility to their work (Calvert & Szymanski, 2020, p. 11). One prominent Sc2.0 scientist explained that since yeast "does take up DNA so well…we're working in collaboration with our organism essentially, in the way that we're able to integrate our DNA" (Mitchell, 2017). In these quotes there are hints at decentered agency, even if they are not recognized as such.

In 2016, the J. Craig Venter Institute (JCVI) undertook the minimization of the *Mycoplasma* genome, stripping the organism down to its "essential" elements. "Working out what constituted an "essential" gene proved to be more complex than anticipated, however, and the conclusion that the researchers eventually drew was that there was no one minimal genome" (Calvert & Szymanski, 2020, p. 12). Calvert and Szymanski (2020) argue that as an alternative, a focus on the entire model organism opens new ways of understanding:

> Engaging with the whole organism seems to drive synthetic biology to become more biological; the organism assumes a character and significance that makes it difficult to treat as merely another entity to be engineered. In whole genome engineering, the 'hopeful contingencies of biology' (Davies, 2011, p. 439) reassert themselves. (p. 15)

At the 7th International Meeting on Synthetic Biology in Singapore, synthetic biologist

Christopher Voigt raised the question "Now that we have the ability to synthesize anything, what do we build, what do we design with that capacity?" (2017). This statement seems to echo notions of limitless possibility on Ginkgo Biowork's home page mentioned earlier in the dissertation. However sweeping humans' abilities to "synthesize anything" end up becoming, this power raises questions of access and inequality. "As whole-genome projects proliferate, and value-laden design decisions are made, it is important that a diverse range of people become involved these discussions. Whole-genome synthesis not only compels us to reconsider our relationships to existing organisms, it also challenges us to engage with what they may become" (Calvert & Szymanski, 2020, p. 15).

What do yeasty bodies *do*?

Bodies are ethico-political sites operating at the scale of individual experience. Yet, even when referring to humans, individualistic assumptions have limitations, as noted above. When it comes to microbes, it is productive to think communally. Researchers and brewers talk of 'colonies' of yeast, and microbes engage in all sorts of communal actions like lateral gene transfer and quorum sensing that stretch our conceptions of the body and what it can do. Latour's "networked nature-culture" and Haraway's "naturecultures" offer possibilities for multispecies mappings that transcend the bombastic claims in some corners of synthetic biology ("Now that we have the ability to synthesize anything…" and "We can do whatever we want") by acknowledging interconnectedness/interdependence and *still* embracing the significant advances in DNA-based technology that are reshaping what is possible, for better and worse.

Distributed agency acknowledges how bodies of all kinds have capacities to make things happen by highlighting what they do in trials rather than what they are. Annemarie Mol, in

questioning the unity of the body, notes how varied accounts of corporeality are not merely 'different perspectives on the same thing,' but rather generatively compose different bodies through discourse (2002; 2008). This reorientation necessarily shifts our conceptions of responsibility, freedom, and unfettered decision-making. In the context of working with other species, these ideas can help us move beyond an understanding of small agents like yeast as passive or even as mechanical novelties and toward a more attentive conceptualization attuned to the labor and collaborative efforts of others.

The kinds of subjects we create depends upon our discourse and practice. The ontologies and meanings that we assign to humans or microbes affects how we discipline bodies, attribute individual responsibility, and understand feedback (Wakefield, 2018). In the rhizomes and refrains of Deleuze and Guattari, subjectivity is a process of tightening and slackening moments, moving between territorialization and deterritorialization. Bennett (2010) continues the deterritorialization of the individual subject, filling the air with all kinds of vibrant things and calling us beyond the agency of objects to the vitality of all matter. Material objects are no mere props for performance, but parts and parcel of hybrid assemblages endowed with diffused personhood and relational agency. "The human body"—Thrift tells us—"is what it is because of its unparalleled ability to co-evolve with things" (Vannini, 2015, p. 10). Not unlike *Saccharomyces cerevisiae.*

When it comes to small beings like yeast, our depictions and representations matter. Many people may never interact with *Saccharomyces* in a more purposive way than unwitting encounters with food. Yet synthetic biologists are one group who do, and this suggests the need to be reflexive about our subjectivity in relation to other species and power. The body acts as a contested site of power and is acted upon by forces, even as it itself is forceful (Grosz, 1994; Haraway, 2008; Mol, 2002).

9. CONCLUSIONS, CONTRIBUTIONS, AND REFLECTIONS

> "Genomics is at once a body of knowledge and a technology; it is a culture carried by specialists who both know things and do things, and the knowing and the doing cannot be understood independently of each other…Idealized visions of scientific fields, which present their knowledge abstractly as a revelation of how the world really is, may inspire the imagination in one way but they impoverish it in another. As beautiful as some of them may be, they are static visions, in which the human activities that are the springs of change of knowledge lie hidden, and of course not all of these idealized cosmological visions are even beautiful."
>
> -Barry Barnes and John Dupré 2008, p. 243

> "Everything ties together in an asymmetrical block of becoming, an instantaneous zigzag."
>
> -Gilles Deleuze and Félix Guattari, *A Thousand Plateaus: Capitalism and Schizophrenia* (1987, p. 307)

The Sc2.0 project reflects both a longstanding trend and a particular moment in scientific research. The trend is a movement toward ever more-granular forms of manipulation vis-à-vis bodies and genetic material. At the same time, a particular moment under various banners—synthetic biology, synthetic genomics, whole-genome synthesis—has congealed due to forces combining informational understandings of DNA, engineering mindsets ported into biological research, funding for human health research at the level of molecular genetics, and sensibilities that prioritize model organisms as a crucial and profitable tool to understand biological processes in general.

Understanding yeast as a model organism—and synthetic yeast as a model for synthetic organisms—builds upon and co-produces shifts in biological and medical research that simultaneously emphasize eukaryotes as a set of equivalencies useful for explaining and confirming biological abstractions (like genomes as code) while connecting them to human

health at the molecular level. If yeast as a model and stepping stone to other models with longer genetic sequences becomes more important than understanding what specific organisms are like and what they do, then preserving the 'yeastiness' of yeast, which as I have discussed roughly equates to evolutionary fitness, can be seen as a process more concerned with power and control than with specific characteristics of *Saccharomyces cerevisiae*. How will synthetic biology inspire or impoverish our future imaginaries of co-habitation in an era of sweeping climatic and technological transformations?

In this concluding chapter, I offer a summarization of the key points of the dissertation, connecting them back to the original research goals and questions. I subsequently reflect on the limitations of this work, framing them by discussing potential future directions for this research and offering thoughts on the broader contributions of this work.

> It remains to be seen how more recent computational methods and engineering culture will transform yeast biology, but it seems likely that work with the organism will continue to attract biomedical funding and infrastructure in the years to come. While in the past, basic research support was made available for study of the yeast organism, today most resources allocated to yeast research in the name of human health and disease are earmarked for its use as a model technology. This is a fulfillment of the biomedical "molecularization" of humans that could find applications for the "eukaryoticization" of biology (Langer, 2016, p. 440).

Goals and key points

Looking out from the tangle of the previous chapters, I will briefly summarize some of the key findings that emerged from the warp and weft of this work. This project morphed over the course of its execution as important actors and themes came into greater focus and certain questions became more or less relevant. As a result, some research goals waned in importance as I learned more about the Sc2.0 project and synthetic biology more broadly.

The first goal of this project was to understand how scientists working with yeast interpret it

as an entity in laboratory settings. It quickly became clear that the synthetic biologists I spoke with had a fairly instrumental view of yeast in their laboratory experiments. Discourse emphasizing control and ease of working with yeast underscored this point. However, some interviewees expressed particular affinities for yeast due to its capacities to quickly reproduce and survive a variety of conditions, in addition to its longstanding cultural associations. Anecdotally, some lab members even experimented with using some of their synthetic yeast cells in homebrews—demonstrating an affective connection to and curiosity about their species of concern—though I was unable to talk to any of these individuals. Entering the field, I had anticipated more of a focus on yeast as an organism and wanted to find out how scientists thought about it in and of itself. I came to realize that any particular yeasty characteristics told only part of the story of why *Saccharomyces cerevisiae* has become the first synthetic eukaryotic organism, and that a collection of historic and institutional forces played an even more important role in its development.

Second, I sought to scrutinize the politics of synthetic yeast, particularly in emerging associations shaped by technological innovation. The Sc2.0 project proved to be a useful starting point for analyzing these political dimensions of synthetic biology. Yet, the timing of my research complicated my efforts, as scientists I spoke with increasingly looked beyond synthetic yeast as a foregone conclusion and old news, so to speak, despite the technically incomplete nature of the project. This was clear in observations of Boeke Lab meetings, which were much less explicitly about yeast than I had hoped and expected. On the other hand, this situation also afforded opportunities to examine how scientists discussed and understood their work in a linear arc that assumed progress toward more granular levels of molecular manipulation while simultaneously scaling up across genomes. For example, lessons learned from manipulating yeast chromosomes were increasingly applied to mice, presaging mammalian genome synthesis.

Broadly, this goal directed me toward an assemblage-inflected tracing of the connections between various actors, knowledges, and funding sources that have made Sc2.0 and subsequent, related projects possible. More specifically and importantly, it shed light on the metaphors of synthetic biology and the work they do in shaping scientific imaginaries and socionatures.

Finally, I aimed to theorize empirically about the potential changes synthetic organisms like Sc2.0 might bring to human-environment relationships in the Capitalocene (Haraway, 2015). This goal led me into the realm of bioethics and the sociology of scientific knowledge production. As the preceding chapters demonstrate, broad dreams of technological solutions to environmental and human health issues permeate synthetic biology research, but their application can be murky in the context of daily scientific practice. Instead, what seemed to come to the forefront again and again was a general acceptance of the utility of synthetic biology research as a tool to better understand life, reduced to a chemical and physical level of causation in which an infinite combination of finite base pairs and 'parts' form the building blocks of biology. These realities point toward a view of synthetic organisms as anchors for the aforementioned scientific imaginaries. In other words, synthetic organisms seem to confirm that we humans are on the 'right track' to engineering solutions to environmental and health challenges. Their materiality—in the form of genetic 'code' and sequences stored in databases—is poised to emerge as an important force in many more areas of life, territorializing scientific practices and visions of human-nonhuman relations. And this materiality has already 'escaped' the laboratory. For example, genetically modified yeast is already playing a role in brewing a small number of beers. Yet, a critical examination of ontological categories (Miller, 2019; Mol, 1999) reveals that synthetic and wild-type or natural or any number of other labels are partial and overlapping designations that at best offer only a glimpse into the complex negotiations happening between actors in these assemblages. Social scientists can critically engage with the

philosophical and empirical dimensions of synthetic organisms, offering another perspective to that of the dominant one within synthetic biology. By doing this, lines of flight (Deleuze & Guattari, 1987) toward different territories of scientific practice and knowledge production radiate and become anew.

In the context of these goals, some key points emerged during the course of this study. In no particular order:

Saccharomyces' status as a model organism is not a historical inevitability but rather the result of forces that may become more or less durable over time.

It appears yeast's role in synthetic biology research may not be limitless, but this is still indeterminate and dependent on multiple forces. Many synthetic biologists seem content to move beyond studying yeast specifically as an organism, taking the lessons learned from it and leaving behind the material remainder. If their efforts are successful, this might mark an end to the era of yeast as a model organism. In this case, yeast would be temporally bounded, being very much of a specific time, beyond which the forces keeping it emplaced as a model organism deterritorialize and reconstitute, encircling another territory. But given all that is still unknown about non-coding DNA and multi-gene interactions, perhaps yeast will retain a role in future synthetic biology experiments. The accumulation of decades of knowledge about this organism weigh down on efforts to find the next big thing in model organism research. Further, the remaining challenges to adding a tidy bow to Sc2.0 suggest that despite enormous progress in decomposing the *Saccharomyces cerevisiae* genome and gaining insight into modes of protein expression and more, the envisioned timelines and effortlessness of Sc2.0 have not yet come to pass.

Militaristic and machinic metaphors in the Sc2.0 project extend notions of human control over nature, a characteristic of the Anthropocene in general.

Though likely unintentional, synthetic biologists' use of metaphors with militaristic undertones maintains a status quo in positivistic research that emphasizes control, via violence if necessary. "Landing pads," "payloads," and "battlefields" populate the discourse of synthetic biology lab meetings, and to a lesser extent, academic journals. Cells are scarred and tortured. Well-behaved cells resemble factories that reliably produce desired compounds. Yeast cells are envisioned as sleek chassis and platforms ready to accommodate bolted-on modules and parts to extend or constrain their functionality according to rational design principles. It can be tempting to overstate the importance of these words, but I argue that they nevertheless represent durable forces in the Sc2.0 project, and based on its perceived success, might sustain future ideas about what life is like and how we humans should think about working with organisms. This includes *Homo sapiens*, as synthetic biologists continue to strive toward working more directly with human genomes.

Informational paradigms expedite the commodification of genes and genetic sequences

In addition to renderings as factories and platforms, microbes are understood to be functionally and ontologically similar to computers and circuits. These conceptualizations facilitate an equating of genetic material like DNA and tRNA to information, data, and computer code. Functions associated with these types of objects are then projected onto cells: reading, writing, editing, copy/pasting, and executing software programs are now the purview (and necessary skillsets) of synthetic biologists because they are also capabilities of the cells themselves. This mode of transferring capacities and functions masks some aspects of scientific

practice and privileges abstract revelations of "how the world really is" (Barnes & Dupré, 2008, p. 243). Furthermore, genes-as-information are more available to capture by intellectual property claims proliferating through a cadre of biotech companies that have drawn upon the fundamental research undertaken at the heart of synthetic biology. Genes and genetic sequences are vulnerable to commodification as biocapital as a result. To think and write productively about this biocapital in the 21st century, social scientists should employ a tripartite structure encompassing use value, exchange value, and *encounter* value, without over-privileging human exceptionalism (Haraway, 2008, p. 46).

There are spatial differences to the materiality and circulation of yeast bodies.

There is an interesting difference in materiality between work conducted with yeast in synthetic biology and in other settings geared toward comestible production. Both settings exhibit forms of metabolism. In the case of Community Cultures Yeast Lab, a physical yeast slurry is shipped out the door in Styrofoam boxes on a regular basis and transported to craft breweries by couriers like UPS and FedEx. Yeasty bodies exit the lab and enter breweries, where they multiply, metabolize, and die, though some might persist to be used in future batches or take up residence elsewhere, inside or outside the brewery walls.

In synthetic biology laboratories, yeasts circulate in more constrained spatial trajectories, moving between automated liquid handlers, automated work cells, many-welled plates, acoustic droplet ejection robots, thermal cyclers, and other lab machines that facilitate human-designed experiments. The process of analyzing yeast colonies to isolate and assemble specific chromosomes (e.g., "building big DNA") illustrates this form of metabolism. In a video on the Institute for Systems Genetics' website, Boeke narrates how with the help of automated robots, scientists are able to perform "up to 30,000 genotyping reactions per day, at a cost of 7.4 cents

per reaction" (which comes to $2,220/day) (NYU Grossman School of Medicine, 2023b). Once the yeast cells' DNA has been transmuted into genetic code, their circulation is complete. "At the end of this, the plate is discarded, because the information that is needed has been captured on a computer and is analyzed to tell us which colonies contained the correct chromosome" (NYU Grossman School of Medicine, 2023b). Metabolisms of synthetic biology not only move at incredible speeds (editing, culturing, processing, genotyping, discarding many colonies per day), but they also transform material bodies into data. The use of *in silico* techniques emphasizes this point.

Despite action and application-oriented rhetoric, much synthetic biology work is still concerned with compiling data and making incremental progress toward its fundamental goals.

As noted earlier, researchers are at least somewhat reflexive about this, recognizing that their projects have not always fulfilled every promise they've made. Opportunities to observe lab meetings and speak with Sc2.0 project members afforded glimpses into quotidian research practices that rely heavily on trial and error and experimentation rather than parsimonious "design-build-test" workflows. In this way, synthetic biology is perhaps not as different from earlier biological research approaches than it represents itself to be. In other ways, the discourse driving this field has severed it from these moorings, launching new scientific imaginaries that seek not just to understand but to control life.

Again, enormous advances have been made in understanding and applying cellular functions through synthetic biology projects, but sweeping claims often outpace their progress. Nevertheless, a proliferation of actors circulates around and through these claims. Alongside researchers conducting synthetic biology experiments, a large and growing biotech industry continues to develop and implement synthetic biology technologies and paradigms, which

tangle with legal and bioethics issues.

Ontological categories of 'yeast' and 'human' are mutually co-constituted through the practices of synthetic biology.

Saccharomyces cerevisiae is a lively, agential organism that makes things happen in multispecies assemblages, from well-studied pathways of fermentation to less-obvious effects on scientists themselves. Through its propensity for homologous recombination and its history of association with humans as a model organism, yeast plays a role in shaping how scientists envision their own research goals and capacities. Each moment of accumulation that made yeast more of an experimental model—from visualizing it under a microscope to understanding it as biological to classifying it into taxa to isolating 'pure' cultures to developing a standard strain to nominating homologs to human genes to sequencing its genome to synthesizing its genome—nudged what came after it in important ways. Of course, many actors and forces (certainly not 'only' humans and yeast) converged in these moments, including research funding, lab equipment, desires and fears related to human health, and more.

Importantly, this understanding of yeast allows it to be seen as more than a passive, subservient 'lab rat' or genetic reservoir waiting to be tapped. Instead, synthetic yeast illustrates the sort of "transversal" interaction that Deleuze and Guattari (1987) write about in their example of the wasp and the orchid. Male wasps of the Thynnidae family are attracted to petals of orchids in the Drakaea genus, which mimic flightless, female Thynnidae wasps. To successfully attract a wasp, the orchid has to be attuned to aspects of its environment and possess some inkling of a wasp motif, even if its *Umwelt* does not explicitly include the wasp. In attempting to fly away with part of the flower (which they perceive to be a mate), the wasps

may inadvertently pick up pollen, later transferring it to another flower via a similar interaction. In this process of becoming, both the wasp and the orchid are "liberated from their own reproduction" (Deleuze & Guattari, 1987, p. 293). "The orchid deterritorializes by forming an image, a tracing of a wasp; but the wasp reterritorializes on that image. The wasp is nevertheless deterritorialized, becoming a piece in the orchid's reproductive apparatus. But it reterritorializes the orchid by transporting its pollen. Wasp and orchid, as heterogeneous elements, form a rhizome" (p. 10).

Synthetic yeast is shaped by scientific knowledge production and assumptions, but it also shapes them by how it 'acts' in the laboratory. As similarly heterogeneous parts of an assemblage, synthetic yeast and humans share moments of territorialization and deterritorialization that might carry them away toward another trajectory of becoming. In fact, a truer understanding of Deleuze and Guattari's model of rhizomatic thought might blur and fade the organismal subjects (yeast or human) in favor of a modality of becoming that forms and works as an assemblage. From this perspective, I agree with synthetic biologists that there are many exciting and as-yet-unknown developments on the horizon for synthetic organisms, but I contend that this uncertainty stems from these (de)territorializing forces rather than from a foreclosed arrangement wherein humans will linearly march toward the solutions to their questions and desires.

Limitations

The limitations of this work coalesce around several themes. First, the evidence and arguments presented here are logocentric, focusing on the words and texts of elite scientists directed at an audience of similarly situated researchers, funding agencies, and to a much lesser

extent, the general public. This was largely the result of the methods chosen and the constraints of conducting research during a pandemic with interlocutors I had only tenuous connections to. As a result, more affective dimensions of the assemblages I studied are conspicuously absent; nonverbal and unwritten registers are disadvantaged. While this is not invalidating in and of itself, it is worth noting that a more ethnographic project likely may have produced different sorts of interactions with scientists and, subsequently, different observations.

Second, for a study emphasizing the futility of a "god's eye" perspective and the importance of situatedness and embodiment to conducting research, this work is fairly detached from particular spaces and experiences. Most of the data collection happened through the mediating pixels, cameras, and microphones that connected the screen through which I write these very words to the screens and virtual rooms of my interlocutors. Aside from ubiquitous challenges like picking up on nonverbal cues and navigating choppy video/audio streams, this reality created (perceived) incongruencies between my theoretical foundations and the research I ended up conducting. Primary data were scarce from the outset of this project to its conclusion. As a result, much of this dissertation's contribution is in the syncretism of different bodies of literature and preexisting, excellent scholarship on yeast in synthetic biology (Figure 20). To be sure, one important aspect of research is reexamining and reevaluating previous studies. This paper works in tandem with recent work by Erika Szymanski (2018; 2019), Jane Calvert (2010), and others (Hey & Szymanski, 2022; Rossi, 2013), building upon, reaffirming, and reframing their insightful studies of synthetic biology and the Sc2.0 project. It also picks up (in some ways) where Erika Langer's comprehensive dissertation (2016) on the history of yeast model organism research leaves off. The final pages of that study sketch some of the contours of earlier stages of Sc2.0, when the project was still the central focus of many of the scientists in the Boeke Lab. Given the rapid pace of change in synthetic biology, the years since offer opportunities to

further trace emerging trajectories from this work as scientists shift their focus to mammalian cell research, including the human genome.

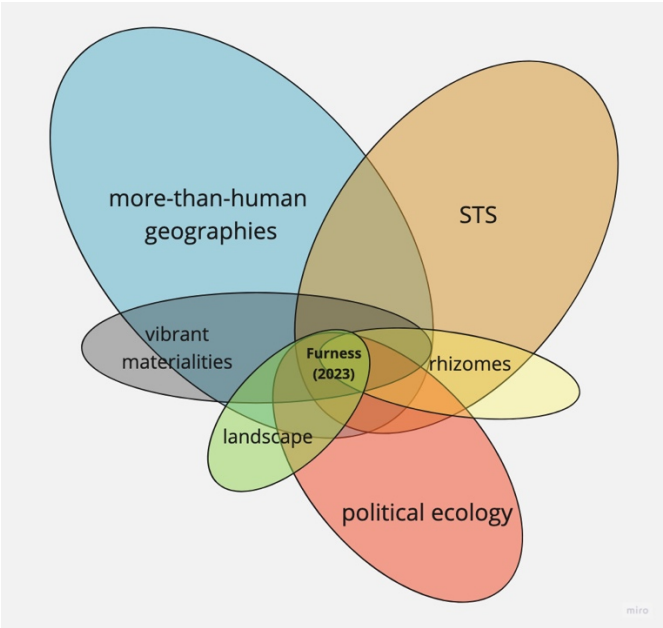

Figure 20: A rendering of the dissertation's place in the literature (roughly to scale).

Future directions

While he is bullish about the prospects for synthetic biology and synthetic genomics, the influential synthetic biologist Tom Ellis (2019) recently acknowledged the limitations of the science alongside its accomplishments:

> However, the true synthetic biology version of a synthetic genome, a genome designed and built using first principles from a kit of modular parts, is still a long way off, looming as a grand challenge that could even take another couple of decades to achieve. Right now, we simply don't know enough about all the genes and genetic regulation that is required to direct a cell to grow and perform a cell cycle, and so we cannot yet write a genome from scratch. (p. 7)

In this acknowledgment, we can see glimpses of difference and heterogeneity that run counter to the dominant narratives of control and facile genome-level editing. More work

remains to be done in this area, as scientists continue to strive toward a fully assembled-from-scratch yeast genome that incorporates all of the design changes made to individual chromosomes into a complete, 'yeasty' cell that functions as desired and expected. And more voices can be part of this unfolding future. Most broadly, social scientists can contribute critical insight to discussions of synthetic organisms and human-environment interactions as synthetic biology technologies continue to develop. On the level of this research study, many more scientists could join in the work of critically examining the assumptions and goals of Sc2.0 and projects deriving from it. A more systematic study of the different, international laboratory settings within which Sc2.0 took shape could offer opportunities for more geographic differentiation. On a smaller scale, a similar study conducted with another synthetic yeast group might open new lines of inquiry into the degree to which different laboratory spaces offer the same or dissimilar discourses. Certainly, more in-depth and face-to-face interaction could offer richer nonrepresentational and affective elements to this work. These remain open-ended conclusions. This study captures a fleeting snapshot of some aspects of two particular laboratories through an unusual, pandemic time. Yet, this narrow look offers perspective on scientific endeavors that might reshape life in dramatic ways. Scholarship on synthetic organisms does not have to be another rubber stamp on efforts to re-engineer life according to dreams of control, nor merely a reactionary, clarion call to return to an idealized past free of genetic chimeras and CRISPR yeast. Instead, it can be something more subtle and more powerful, pointing toward contingent futures laced with multispecies power and contested meanings. To hear synthetic biologists talk of it, the conclusions are mostly foregone. Still, in the midst of this dominant rhetoric, currents of uncertainty and possibility for difference run under the surface.

10. APPENDAGE: TOWARD A ZYMURPOLITICS

> "An ecosystem is not a machine, where the various components mindlessly fulfill their functions as a reflection of the external mind of the engineer. Ecosystems are incredibly complex articulations of innumerable, sentient subjects, engaging each other through the lenses of their own subjective worlds."
>
> -Alf Hornborg 2001, p. 125

"Critique *is* dangerous, and *so is our refusal of it*."

-Ethan Miller 2019, p. 27

A neologism and some limits

What are we left with after considering this partial investigation into the scientific practices and discourses surrounding the first fully synthetic yeast? What can be claimed or learned from the messy assemblage of ideas, bodies, base pairs, institutions, and pages, especially when there is still much to unravel? As a sort of appendage in development or "appendage-ing," here I briefly discuss my own notion of 'zymurpolitics,' conceived of as a politics of synthetic yeast and modeled after Stengers' (2010) "cosmopolitics." Haraway (2008) notes that "Stengers' cosmopolitical proposal…is that decisions must take place somehow in the presence of those who will bear their consequences. Making that 'somehow' concrete is the work of practicing artful combinations…To get "in the presence of" demands work, speculative invention, and ontological risks. No one knows how to do that in advance of coming together in composition" (p. 83).

Narrower than the cosmos of cosmopolitics, the specific territory of this concept is zymurgy or zymology, meaning the study or practice of fermentation. This 19-century coinage from the Greek ζύμωσις + ἔργον ("the workings of fermentation") is an imperfect label, much like many

of the products of and associations involving fermentation. This is because my aim in coining 'zymurpolitics' is *not* to propose a unifying theory of the politics of fermentation, but rather to address the more specific case of the politics of synthetic yeast, specifically the Sc2.0 project and what it might reveal about other synthetic organism assemblages. Unsurprisingly, I find the term 'zymurpolitics' to be a more convenient and pleasant shorthand for these ideas than "synthetic yeast politics" or "the politics of Sc2.0."

Fermentation is an attractive frame in many ways, signifying both material and semiotic change related to edibility, durability, values, and even landscapes (Myles, 2020). Yet like many of the metaphors discussed in this dissertation, when used in broader senses beyond its strict biochemical definition, it can also elide important differences in context, goals, and power differentials while blurring the particularities of the material and semiotic changes it effects. An undiscerning application of fermentation to represent transformation writ large risks fetishization (Murray, 2020).

Furthermore (accepting for now the broader/looser metaphorical senses as I have in this dissertation), fermentation is multifaceted. It neither encloses a singular way of relating to microbes nor of knowing them[29]. It is used toward different ends, across all kinds of scales. Among brewers alone, a vast range of sensory approaches is used to characterize and relate to yeast. Some of these are scientific and use specialized equipment, while others rely on basic senses. Among synthetic biologists, sensorial understandings of yeast are understandably downplayed in favor of those mediated by computer software and high-end laboratory machines, but they are often still present. To be sure, scientists working on Sc2.0 are not directly concerned with fermentation per se, but fermentation arguably remains an important

[29] Not to mention that the scientifically constructed term "microbe" belies an incredible diversity of life that is linked primarily by the fact that it is generally too small to be seen by the unaided human eye (Evans, 2021).

backdrop to their associations with yeast: the promise of material transformation and (later) genetic recombination is precisely the reason why *Saccharomyces cerevisiae* has become so deeply affiliated with and studied by humans. Even in conversations where participants were not particularly reflective about their interests in working with yeast, the history and facility with which *Saccharomyces* and humans interact was held up as reason enough for its use as a model organism. The point is that fermentation in this less-technical sense is epistemically and pragmatically diverse and therefore any claim to a broadly generalized politics of fermentation ought to be scrutinized (Evans, 2021).

So, if 'zymurpolitics' is not an overarching politics of fermentation, what is it? Much as cosmopolitics treats specific groupings of entities as emplaced by their own "habits" (Whitehead, 1968, p. 154), qualities, and possibilities, 'zymurpolitics' takes as a given the complex interplay between laws and phenomena as they relate to the ecologies of synthetic yeast. These ecologies are more than material relations between Sc2.0 and its laboratory environment, however. From this vantage point, synthetic biologists' ecologies of practice always work (perhaps unwittingly) to produce values and meanings (Stengers, 2010, 34). Semiotics inhere in these ecologies of practice and form complex, asymmetric topologies. The lab (being a product of human invention and paradigms of rationality) arguably makes it harder to address trans-species relationality in a symmetric way, as power strata involving both humans and nonhumans privilege certain ways of knowing and relating. Would it be easier to see synthetic organisms in relation to humans in a clinical setting, for example? This too could be highly stratified and asymmetric.

Synthetic biology labs prioritize a certain form of discovery of an *a priori* ilk, where exploration is confirmation of existing design principles that "should" work. A mode of discovery based on observation and experimentation is arguably more scientific. As Haraway

asks, "do we want predictable or surprising com-panions?" (2008, p.33). This too is a cosmopolitical query, after Stengers.

This understanding transcends dominant epistemic paradigms in synthetic biology. When researchers like Jef Boeke or organizations like the National Science Foundation[30] strive to discover the "rules of life," they are not necessarily anticipating the ecologies of practice that 'zymurpolitics' foregrounds. Instead of complex, interacting practices that produce values that help repeat and prop up certain practices, synthetic biology by and large remains committed to a neat division of knowledge—in the form of laws—and practice—in the form of experimental phenomena. The sustained commitment to information metaphors for genetic material among researchers working on the frontiers of synthetic organisms creates an enticing nexus of knowledge and power that promises infinite manipulability, but this knowledge is not seen for the powerful link that it is, tying together multiple species. "Knowledge attaches and entangles rather than clarifies and separates; it multiplies relations between beings, and foregrounds the way concepts and ideas capture researchers just as much as it is researchers who produce concepts and ideas" (Robbert & Mickey, 2013, p. 4).

Here I am suggesting that the scale and novel nature of synthetic genomics create the conditions to influence human ecologies of practice in new, specific ways that go beyond the throughline of cosmopolitics I've been following. 'Zymurpolitics' addresses these new promises and potential affiliations between humans and synthetic nonhumans, with Sc2.0 in the vanguard. It is thus a more limited incarnation of cosmopolitics that seeks to apply its paradigm shifts to new modes of existence, if indeed Sc2.0 is just the start of the synthetic menagerie.

[30] Understanding the Rules of Life. https://www.nsf.gov/news/special_reports/big_ideas/life.jsp

What might zymurpolitics do?

With that foray into zymurpolitics, I will conclude with a few thoughts about why it might matter and what it might add to multispecies geographies and STS. First, despite my efforts, much of the preceding discussion remains firmly human-centric. Considering much recent emphasis on the condition of the Anthropocene in geographic and science studies literature, zymurpolitics pushes toward a decentered *anthropos* to give significant roles to microbes like yeast and other non-human actants. Nonhuman agency is real, and we should pay attention to it. Of course, a multispecies cosmopolitics already addresses many of these concerns. Zymurpolitics innovates by extending the implications of this accounting to the potential ruptures opened by whole-organism synthesis, which as we have seen reveal slippages between ownership and democratization, discourse and practice, organism agnosticism and specificity, and equivalencies between life and computers.

More specifically, zymurpolitics seeks to account for discursive transformations made possible by synthetic, fermentative agents—Sc2.0 in this case—while attending to the *power relations* that inhere in these assemblages. Synthetic yeast and humans are not collaborating in laboratory spaces void of power relations, domination, or anthropocentrism. Rather, information metaphors and scientific practices recursively shape emergent (synthetic) multispecies worlds by binding together knowledge and power in a double move of increasing understanding and control. Technologies play a significant role in these assemblages too, acting almost as species that contribute their own values and possibilities to the mix. Ideas are "themselves technologies for pursuing inquiries. It's not just that ideas are embedded in practices; they are technical practices of situated kinds" (Haraway, 2008, p. 282). Again, this

framing conflicts with scientific imaginaries that cast CRISPR and other genomic engineering tools as value-neutral.

Lastly, zymurpolitics might provoke some humility and empathy, if we can grok the implications of the previous points. Viewing synthetic yeast through a lens of "care for" (Krzywoszynska, 2019) and "attentiveness toward" allows for a more compassionate and ethical approach to the intersection of human and non-human lives. Attending to (being attentive toward) other species' needs is a way to interact more response-ably and responsibly with non-humans who make much of our daily lives possible, whether or not they are readily perceived as doing so.

Zymurpolitics might stand to make a contribution if it can get us humans thinking more carefully about the engagement needed to account for the many, complex relations and encounters comprising a cosmos that includes synthetic organisms. This sort of thinking might spur us to account for not only laws and facts but values and the ways in which natures and cultures are constantly contested and negotiated in emerging fields like synthetic genomics.

Coda

The proposition of zymurpolitics is a risky critique because it attempts to describe current territorializations of synthetic yeast while anticipating deterritorializing forces that may open toward processes of becoming not yet in focus. "A Whiteheadian proposition, says Stengers, is a risk, an opening to what is not yet. A proposition is also an opening to become with those with whom we are not yet" (Haraway, 2008, p. 93). Becoming with synthetic yeast requires a more nuanced approach than much of synthetic biology currently exhibits. It means being more critical about metaphors and their power to shape scientific imaginaries and practices. It means

a commitment to exploration and experimentation and risky inquiries. It means understanding synthetic yeast as multifaceted and dynamic, like light glinting off shards of broken glass, digitized but offering analog edges that don't quite fit its pixels; linked to humans through evolution, time, and practice (Figure 21). With this reflexivity comes new powers—power to be affected by another organism and form productive affiliations with it that hearken to long-existing rhythms of association with yeast.

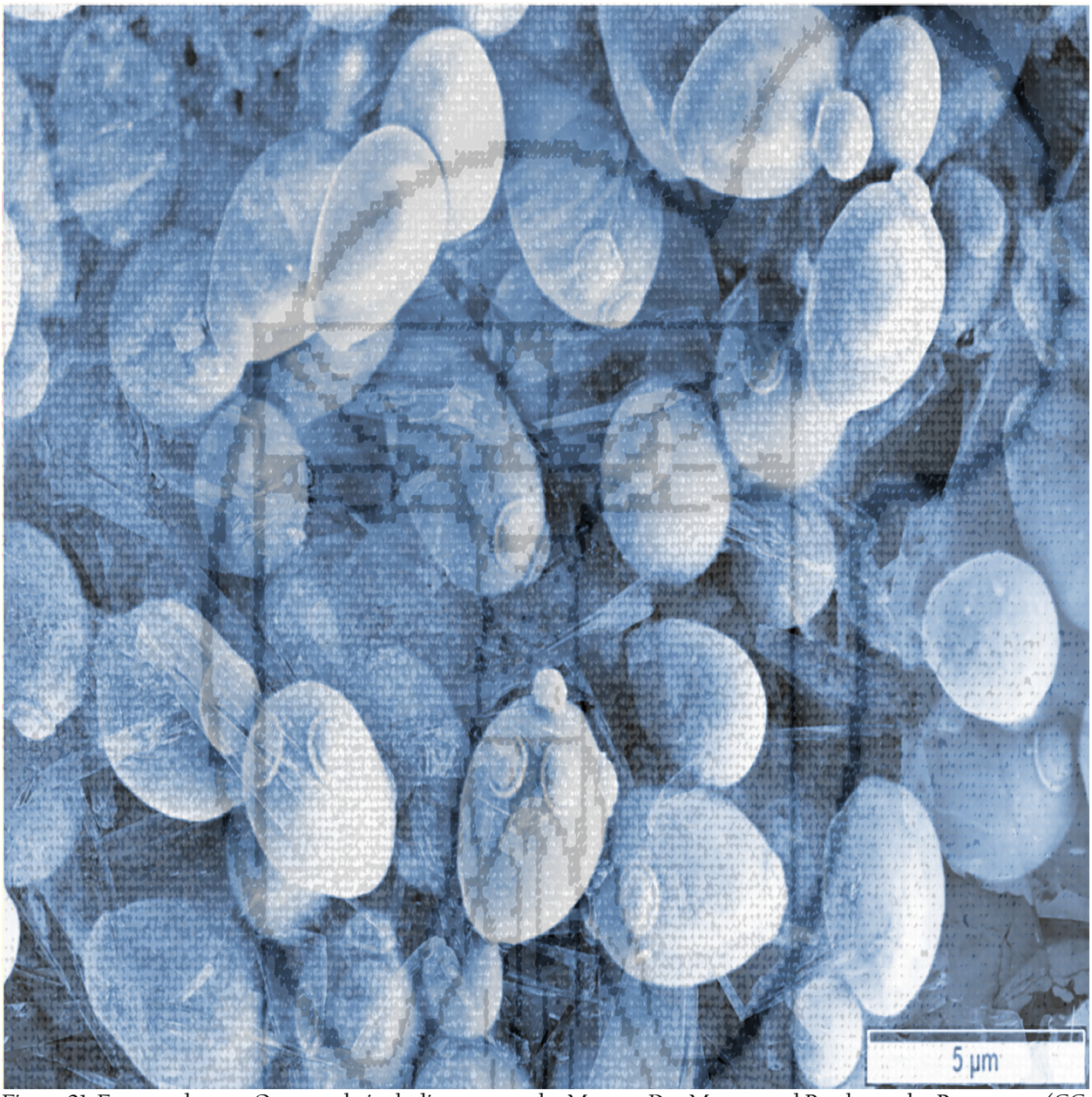

Figure 21: Fractured yeast. Own work, including content by Mogana Das Murtey and Patchamuthu Ramasamy (CC BY-SA 3.0, https://commons.wikimedia.org/w/index.php?curid=52254246), *Vitruvian Man* yeast art by Jasmine Temple (yeastart.org; used with permission of the artist), and photography by Walter Furness.

APPENDIX SECTION

Appendix A: Guide for Semi-structured Interviews

Date/time _____ Location _____

Interviewee _____ Consent form signed? ☐

Interview Guide

Thank you for taking the time to speak with me today. This project attempts to better understand multispecies relationships between humans and yeast in laboratory settings. We hope to gain insight into how new technologies shape humans' relationships with other species and the potential changes synthetic organisms like Sc2.0 may bring to multispecies relationships across space. As noted in the consent form, I will be recording our conversation today and may take additional notes from time to time. Do you have any questions for me before we begin?

[Introductory/warm-up questions]

What is your name and title? What is/are your affiliation(s)? What is your disciplinary/academic background?

How did you become involved in this work?

How long have you worked in this capacity?

[How do scientists in the laboratory work with and think about yeast?]

What does your day-to-day work look like? With yeast, specifically?

What are some of the outcomes/goals you/your team are seeking in your current work?
Who are collaborators in this project?

What aspects of working with/studying yeast are particularly challenging?

Has your focus or approaches to working with yeast changed over time? How?

Misconceptions about your work?

Why are you interested in working with yeast?

[What are the political and ecological dimensions of human-yeast interactions in laboratory spaces?]

What future applications for yeast do you envision?
Is there anything you are particularly excited about or concerned about?

Bottlenecks?

[How does yeast's liveliness affect human-yeast relations in different laboratory settings?]

Have you ever worked with yeast in another laboratory or in a different way? How did that compare to your current work?

Are there special precautions that you have to take when working with another organism like yeast?

[How does synthetic yeast challenge or reinforce the politics of human-yeast relations?]

At a fundamental level, how is synthetic yeast is different from 'regular'/'natural' yeast?

How do you think synthetic yeast might change our relationship to nature in general or other species in particular?

[Concluding questions]

Is there anything else you'd like to tell me about your research or experiences with yeast?
What else should I ask you about that I've left out?

Whom else should I speak to about this?

Appendix B: Sc2.0 Ethics & Governance Agreement (2013)

Societal benefits

1. We will conduct and promote our work on *Sc2.0* for the benefit of humankind.
2. We will participate with the project's efforts to engage with the public and be transparent and open about our work on *Sc2.0*.

Intellectual property

3. Intellectual property rights will not be taken on *Sc2.0* once created, nor on the intermediary clones and strains generated as part of the project.
4. Data and materials generated by this project will be made available to other researchers.

Safety

5. All sequence providers generating sequences for use in *Sc2.0* shall be in compliance with the U.S. Department of Health and Human Services' *Screening Framework Guidance for Providers of Synthetic Double-Stranded DNA*.
6. Members of the Sc2.0 project will assess individuals requesting Sc2.0 Project data/materials prior to shipment of any such materials to help reduce the chance that we are distributing materials to those with nefarious intent.
7. Our laboratories, practices, and methods will have at their core an ethos of safety for both laboratory workers and the communities outside our institutions.
8. All personnel will receive training in biosafety, dual-use concerns, and other ethics issues, as appropriate.
9. Our work on *Sc2.0* is in compliance with national and local laws.

Governance

10. The Sc2.0 Executive Committee will address any issues that may arise with regard to safety or compliance with this agreement.
11. We will revisit this agreement as the project and the technologies it uses develop to ensure that any risk posed by this work is appropriately matched to the oversight it receives.

(originally from syntheticyeast.org; no longer available)

REFERENCES

Afifi, R. A., Abdulrahim, S., Betancourt, T., Btedinni, D., Berent, J., Dellos, L., et al. (2020). Implementing community-based participatory research with communities affected by humanitarian crises: the potential to recalibrate equity and power in vulnerable contexts. *Am. J. Community Psychol.* 66, 381–391. doi: 10.1002/ajcp.12453

Amato, J. A. (2000). *Dust: A history of the small and the invisible*. University of California Press.

American Type Culture Collection. (2022). *About us.* https://www.atcc.org/about-us

Andrianantoandro, E., Basu, S., Karig, D. K., & Weiss, R. (2006). Synthetic biology: New engineering rules for an emerging discipline. *Molecular Systems Biology*, *2*(1). https://10.1038/msb4100073

Ankeny, R. A. (2000). Fashioning descriptive models in biology: Of worms and wiring diagrams. *Philosophy of Science*, *67*(S3), S260-S272.

Ankeny, R. A., & Leonelli, S. (2011). What's so special about model organisms? *Studies in History and Philosophy of Science*, *42*(2), 313-323. https:// 10.1016/j.shpsa.2010.11.039

Antonich, B., Kantaim, T., Kosolapova, E., Malan, S., Monfreda, C., Paul, D., Tsioumani, E., & Tsioumanis, A. (2014). Summary of the twelfth meeting of the Conference of the Parties to the Convention on Biological Diversity and the first meeting of the Parties to the Nagoya Protocol on Access and Benefit-sharing, *Earth Negotiations Bulletin*, *9*(645), 1-34.

Arkin, A. P., & Fletcher, D. A. (2006). Fast, cheap and somewhat in control. *Genome Biol*ogy, 7(8), 1-6. https://doi.org/10.1186/gb-2006-7-8-114

Arkin, A., et al. (2009). What's in a name? *Nature biotechnology*, *27*(12), pp. 1071-1073.

Babich, B. (1994). *Nietzsche's philosophy of science: Reflecting science on the ground of art and life.* University of New York Press.

Ball, P. (2004). Starting from scratch. *Nature*, *431*(7009), 624–626. http://dx.doi.org/10.1038/431624a

Balmer, A., Bulpin, K., & Molyneux-Hodgson, S. (2016). *Synthetic biology: A sociology of changing practices*. Springer.

Balmer, A., & Martin, P. (2008). Synthetic biology: Social and ethical challenges. *Biotechnology and Biological Sciences Research Council (BBSRC)*. https://research.manchester.ac.uk/files/28770312/FULL-TEXT.PDF

Barad, K. (1998). Getting real: Technoscientific practices and the materialization of reality. *Differences: A Journal of Feminist Cultural Studies*, *10*(2), 87-91. https://doi.org/10.1215/10407391-10-2-87

Barad, K. (2003). Posthumanist performativity: Toward an understanding of how matter comes to matter. *Signs: Journal of Women in Culture and Society*, *28*(3), 801-831. http://dx.doi.org/10.1086/345321

Barad, K. (2007). *Meeting the universe halfway: Quantum physics and the entanglement of matter and meaning*. Duke University Press. https://doi.org/10.1215/9780822388128-002

Barker, K. (2015). Biosecurity: Securing circulations from the microbe to the macrocosm. *The Geographical Journal*, *181*(4), 357-365. https://doi.org/10.1111/geoj.12097

Barnes, S. B. & Dupré, J. A. (2008). *Genomes and what to make of them*. University of Chicago Press. https://doi.org/10.7208/chicago/9780226172965.001.0001

Barrett, C. L., Kim, T. Y., Kim, H. U., Palsson, B. Ø., & Lee, S. Y. (2006). Systems biology as a foundation for genome-scale synthetic biology. *Current Opinion in Biotechnology*, *17*(5), 488-492. https://doi.org/10.1016/j.copbio.2006.08.001

Barua, M. (2018, July 26). Animal work: Metabolic, ecological, affective. *Society for Cultural Anthropology*. https://culanth.org/fieldsights/animal-work-metabolic-ecological-affective

Barua, M. (2019). Animating capital: Work, commodities, circulation. *Progress in Human Geography*, *43*(4), 650-669. https://doi.org/10.1177/0309132518819057

Bar-Yam, S., Byers-Corbin, J., Casagrande, R., Eichler, F., Lin, A., Oesterreicher, M., Regardh, P., Turlington, D., & Oye, K. (2012). The regulation of synthetic biology: A guide to United States and European Union regulations, rules and guidelines. *SynBERC and iGEM*, Version 9.1. NSF Synthetic Biology Engineering Research Center. https://doi.org/10.1177/0090591716638389

Battistoni, A. (2016). Bringing in the work of nature: From natural capital to hybrid labor. *Political Theory*, *45*(1), 5-31. https://doi.org/10.1177/0090591716638389

Bennett, G. (2017). Digital enchantment: Life and the future of gene editing. In I. Braverman (Ed.), *Gene Editing, Law, and the Environment* (pp. 168-185). Routledge. https://doi.org/10.4324/9781315168418-10

Bennett, J. (2004). The force of things: Steps to an ecology of matter. *Political Theory*, *32*(3), 347-372. https://doi.org/10.1177/0090591703260853

Bennett, J. (2010). *Vibrant matter: A political ecology of things*. Duke University Press.

Bergson, H. (1907). *L'évolution créatrice* [Creative evolution]. Felix Alcan, Paris.

Besky, S. & Blanchette, A. (2018, July 26). The naturalization of work. *Society for Cultural Anthropology*. https://culanth.org/fieldsights/series/the-naturalization-of-work

Blaikie, P., & Brookfield, H. (1987). *Society and land degradation*. Tavistock, London.

Bizzabo.com. (2015, July 16-17). *4th Annual Sc2.0 and synthetic genomes conference.* https://events.bizzabo.com/SynGenome2015/home

Blitz, M. (2014). Understanding Heidegger on technology. *The New Atlantis*, *41*, 63-80. https://www.thenewatlantis.com/publications/understanding-heidegger-on-technology

Bobrow-Strain, A. (2012). *White Bread: A Social History of the Store-Bought Loaf*. Beacon Press.

Boeke, J. (2011, June 15-17). The synthetic yeast project [Conference presentation]. The Fifth International Meeting on Synthetic Biology, Stanford University, United States.

Boeke, J. (2016, July 8-9). Overview of the Sc2.0 project [Conference presentation]. The Fifth International Sc2.0 and Synthetic Genomes Conference, Edinburgh, Scotland.

Boeke, J., Church, G., Hessel, A., & Kelley, N. J. (2017, May 9-10). *Genome Project-write: A grand challenge using DNA synthesis, gene editing and other technologies to understand, engineer and test living systems* [Meeting summary]. GP-write, New York, New York, United States. http://engineeringbiologycenter.org/wp-content/uploads/2017/10/GP-write-2017-summary.pdf

Boeke, J. D., Church, G., Hessel, A., Kelley, N. J., Arkin, A., Cai, Y., Carlson, R., Chakravarti, A., Cornish, V. W., Holt, L., Isaacs, F. J., Kuiken, T., Lajoie, M., Lessor, T., Lunshof, J., Maurano, M. T., Mitchell, L. A., Rine, J., Rosser, S., … Yang, L. (2016). The Genome Project-write. *Science*, *353*(6295), 126–127. https://doi.org/10.1126/science.aaf6850

Boekhout, R., Phaff, H., & Robert, V. (2003). *Yeasts in food: Beneficial and detrimental aspects.* Woodhead Publishers.

Bostrom, N. (2005). Transhumanist values. *Review of Contemporary Philosophy*, 4(1-2), 87-101. http://www.nickbostrom.com/ethics/values.pdf

Botstein, D. (2012). Why we need more basic biology research, not less. *Molecular Biology of the Cell*, *23*(21), 4160-4161. https://doi.org/10.1091/mbc.e12-05-0406

Botstein, D., & Fink, G. R. (2011). Yeast: an experimental organism for 21st century biology. *Genetics*, *189*(3), 695-704.

Boyd, W. (2001). Making meat: Science, technology, and American poultry production. *Technology and Culture*, *42*(4), 631-664. https://doi.org/10.1353/tech.2001.0150

Braun, B. (2000). Producing vertical territory: Geology and governmentality in late Victorian Canada. *Ecumene: A Journal of Cultural Geographies*, *7*(1), 7- 46. https://doi.org/10.1177/096746080000700102_

Braun, B. (2006). Environmental issues: Global natures in the space of assemblage. *Progress in Human Geography*, *30*(5), 644-654. https://doi.org/10.1177/0309132506070180

Braun, B. (2014). A new urban dispositif? Governing life in an age of climate change. *Environment and Planning D: Society and Space*, *32*(1), 49-64. https://doi.org/10.1068/d4313

Braun, B. (2015, January). The 2013 Antipode RGS-IBG lecture: New materialisms and neoliberal natures. *Antipode*, *47*(1), 1-14. https://doi.org/10.1111/anti.12121

Braun, B. & Castree, N. (1998). *Remaking Reality: Nature at the Millennium*. Routledge.

Braverman, I. (2017a). Editing the environment: Emerging issues in genetics and the law. In *Gene Editing, Law, and the Environment: Life Beyond the Human*, Irus Braverman, ed. (Routledge July 2017)., University at Buffalo School of Law Legal Studies Research Paper No. 2017-005, Available at SSRN: https://ssrn.com/abstract=3032590

Braverman, I. (Ed.) (2017b). *Gene editing, law, and the environment: Life beyond the human.* Routledge. https://doi.org/10.4324/9781315168418

Braverman, I. (2018). Law's underdog: A Call for More-than-human Legalities. *Annual Review of Law and Social Science*, *14*(1), 127-44. https://doi.org/10.1146/annurev-lawsocsci-101317-030820

Breithaupt, H. (2006). The engineer's approach to biology. *EMBO Reports*, *7*(1), 21–24. https://doi.org/10.1038/sj.embor.7400607

Burt, A. (2003). Site-specific selfish genes as tools for the control and genetic engineering of natural populations. Proceedings. *Biological Sciences*, *270*(1518), 921–928.

Callon, M. (1986). Some elements of a sociology of translation: Domestication of the scallops and the fishermen of St. Brieuc Bay. In J. Law (Ed.), *Power, action and belief: A new sociology of knowledge?*, 196-233. Routledge.

Calvert, J. (2010). Synthetic biology: Constructing nature? *Sociological Review*, *58*(1), 95-112. https://doi.org/10.1111/j.1467-954x.2010.01913.x

Calvert, J. & Szymanski, E. (2020). A feeling for the (micro)organism? Yeastiness, organism agnosticism and whole genome synthesis. *New Genetics and Society*, *39*(4), *385-403.* https://doi.org/10.1080/14636778.2020.1736537

Carlson, R. (2011). Staying sober about science. *Hastings Center Report*, *41*(4), 22–25. https://doi.org/10.1002/j.1552-146x.2011.tb00119.x

Carolan, M. S. (2013). The wild side of agro-food studies: On co-experimentation, politics, change, and hope. *Sociologia Ruralis*, *53*(4), 413-431. https://doi.org/10.1111/soru.12020

Carter, S. R., Rodemeyer, M., Garfinkel, M. S., & Friedman, R. M. (2014). Synthetic biology and the U.S. biotechnology regulatory system: Challenges and options. *J. Craig Venter Institute*. https://doi.org/10.2172/1169537

Champer J, Buchman A, Akbari, O. S. (2016). Cheating evolution: Engineering gene drives to manipulate the fate of wild populations. Nature Reviews. *Genetics*, *17*(3), 146–59.

Chandler, D. (2018). *Ontopolitics in the Anthropocene: An introduction to mapping, sensing and hacking*. Routledge. https://doi.org/10.4324/9780203703434.

Chen, N. N. (1994). Speaking nearby: A conversation with Trinh T. Minh-Ha. *Visualizing Theory: Selected Essays from Visual Anthropology Review, 1990–1994*. Routledge.

Cho, M. K., Magnus, D., Caplan, A. L., & McGee, D. (1999). Ethical considerations in synthesizing a minimal genome. *Science*, *286*(5447), 2087-2090. https://doi.org/10.1126/science.286.5447.2087

Cirigliano, A., Cenciarelli, O., Malizia, A., Bellecci, C., Gaudio, P., Lioj, M., & Rinaldi, T. (2017). Biological dual-use research and synthetic biology of yeast. *Science & Engineering Ethics*, *23*(2), 365-374. https://doi.org/10.1007/s11948-016-9774-1

Cloke P., Cook, I., Crang, P., Goodwin, M., Painter, J., & Philo, C. (2004). *Practising human geography*. Sage. https://dx.doi.org/10.4135/9781446221235

Cohen, J. (2016). A reporter does CRISPR. *Science*, *354*(6312), 541. https://doi.org/10.1126/science.354.6312.541

Collard, R.C. & Dempsey, J. (2013). Life for sale? The politics of lively commodities. *Environment and Planning A*, *45*(11), 2682-2699. https://doi.org/10.1068/a45692

Cooper, E. M., Müller, H., Chandrasegaran, S., Bader, J. S., & Boeke, J. D. (2012). The build-a-genome course. In J. Peccoud (Ed.), *Gene Synthesis* (pp. 273-283). Springer Link. https://doi.org/10.1007/978-1-61779-564-0_20

Coursera Inc. (2023). Engineering life: Synbio, bioethics & public policy. https://www.coursera.org/learn/synbioethics?

Crang, M. (2002). Qualitative methods: The new orthodoxy? *Progress in Human Geography*, *26*(5), 647-655. https://doi.org/10.1191/0309132502ph392pr

Dai, J., Boeke, J. D., Luo, Z., Jiang, S., & Cai, Y. (2020). Sc3.0: Revamping and minimizing the yeast genome. *Genome Biology*, *21(*205), 1-4. https://doi.org/10.1186/s13059-020-02130-z

Danchin, A. (2012). Scaling up synthetic biology: Do not forget the chassis. *FEBS letters*, *586*(15), 2129-2137. https://doi.org/10.1016/j.febslet.2011.12.024

Daniels, S. & Cosgrove, D. (1988). Iconography and landscape. In S. Daniels & D. Cosgrove, (Eds.), *The iconography of landscape: Essays on the symbolic representation, design and use of past environments* (pp. 1-10). Cambridge University Press.

Davies, D. (2011). Playing dice with mice: Building experimental futures in Singapore. *New Genetics and Society*, *30*(4), 433–441. https://doi.org/10.1080/14636778.2011.606175

DeLanda, M. (2002). Deleuze and the Use of the Genetic Algorithm in Architecture. *Architectural Design*, *71*(7), 9-12.

Delaney, D. (2001). Making nature/marking humans: Law as a site of (cultural) production. *Annals of the Association of American Geographers*, *91*(3), 487-503. https://doi.org/10.1111/0004-5608.00255

Deleuze, G. (2006). *Nietzsche and philosophy*. Columbia University Press.

Deleuze, G., & Guattari, F. (1987). *A thousand plateaus*: *Capitalism and schizophrenia*. (B. Massumi, Trans.). University of Minnesota Press.

Deleuze, G., & Guattari, F. (1994). *What is philosophy*? (H. Tomlinson & G. Burchill, Trans.). Columbia University Press.

Demeritt, D. (1998). Science, social constructivism and nature. In B. Braun & N. Castree (Eds.), *Remaking reality: Nature at the millennium* (pp. 173-193). Routledge. https://doi.org/10.4324/9780203983966

de Lorenzo, V., & Danchin, A. (2008). Synthetic biology: Discovering new worlds and new words. *EMBO Reports*, *9*(9), 822–827. https://doi.org/10.1038/embor.2008.159

US Department of Health and Human Services. (2011, April 14). Screening framework guidance for providers of synthetic double-stranded DNA. *Federal Register*, 75(197), 1-28.

Department of Health and Human Services (DHHS). (2013). NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules. *National Institutes of Health*, Washington, DC.

Derrida, J. (2016). Force of law: The "mystical foundation of authority". In D. Cornell, D. G. Carlson, & M. Rosenfeld (Eds.) *Deconstruction and the Possibility of Justice* (pp. 3-67). Routledge.

Desmond, M. (2016). *Evicted: Poverty and profit in the American city*. Crown Publishers.

Dewsbury, J. D. (2003). Witnessing space: 'Knowledge without contemplation'. *Environment and planning A*, *35*(11), 1907-1932.

Driesch, H. (1914). *The history & theory of vitalism*. Macmillan and Company, limited.

Duhaime-Ross, A. (2014, March 27). Scientists just took a major step toward making life from scratch. *The Verge*. http://www.theverge.com/2014/3/27/5553044/first-functionaleukaryoticchromosome

Dupré, J. (2010). It is not possible to reduce biological explanations to explanations in chemistry and/or physics. In F. J. Ayala & R. Arp (Eds.) *Contemporary Debates in Philosophy of Biology* (pp. 32-47). Wiley Blackwell.

Dymond, J. S., Scheifele, L. Z., Richardson, S., Lee, P., Chandrasegaran, S., Bader, J. S., Boeke, J. D. (2009). Teaching synthetic biology, bioinformatics and engineering to undergraduates: The interdisciplinary build-a-genome course. *Genetics*, 181(1), 13–21. https://doi.org/10.1534/genetics.108.096784

Dymond, J. S., Richardson, S. M., Coombes, C. E., Babatz, T., Muller, H., Annaluru, N., Blake, W. J., Schwerzmann, J. W., Dai, J., Lindstrom, D. L., Boeke, A. C., Gottschling, D. E., Chandrasegaran, S., Bader, J. S., & Boeke, J. D. (2011). Synthetic chromosome arms function in yeast and generate phenotypic diversity by design. *Nature*, *477*(7365), 471–476. https://doi.org/10.1038/nature10403

Dymond, J. S. & Boeke, J. D. (2012). The Saccharomyces cerevisiae SCRaMbLE system and genome minimization. *Bioengineered*, *3*(3), 170-173. https://doi.org/10.4161/bbug.19543

Eisen, J. A. (n.d.) Microbiomania. *The Tree of Life*. https://phylogenomics.blogspot.com/p/blog-page.html

Ellis, T. (2019). What is synthetic genomics anyway? *The Biochemist*, *41*(3), 6-9. https://doi.org/10/1042/BIO04103006

Endy, D., & Zoloth, L. (2016). Should We Synthesize a Human Genome? *Cosmos Magazine*. May 12, 2016. https://cosmosmagazine.com/society/should-we-synthesise-a-human-genome.

Enticott, G. (2003). Lay immunology, local foods and rural identity: Defending unpasteurised milk in England. *Sociologia Ruralis*, *43*(3), 257-270. https://doi.org/10.1111/1467-9523.00244

Erdoğan, A., & Rao, S. S. (2015). Small intestinal fungal overgrowth. *Current Gastroenterology Reports*, *17*(4), 1-7. https://doi.org/10.1007/s11894-015-0436-2

Erway, J. (2015). Practical yeast care. 2015 Craft Brewers Conference, Portland, Oregon.

Evans, J. (2021). Frontiers of fermentation: Three proposals for a multispecies ethics. https://www.researchgate.net/publication/354687578_Frontiers_of_Fermentation_Three_proposals_for_a_multispecies_ethics

Eventbrite. (2023, June 17). 6th annual Sc2.0 meeting, Singapore. https://www.eventbrite.sg/e/6th-annual-sc20-meeting-singapore-tickets-32810369699

Fairclough, N. (2013). *Critical discourse analysis: The critical study of language (2nd ed.)*. Routledge.

Ferber, D. (2004). Microbes made to order. *Science*, *303*(5655), 158–161. https://doi.org/10.1126/science.303.5655.158

Fincher, W. (2015). Logocentrism. In *The Blackwell encyclopedia of sociology*. Wiley Online Library, https://doi.org/10.1002/9781405165518.wbeosl055.pub2

Flack, W. (1997). American microbreweries and neolocalism: "Ale-ing" for a sense of place. *Journal of Cultural Geography*, *16*(2), 37–53. https://doi.org/10.1080/08873639709478336

Foucault, M. (1980). *Power/knowledge: Selected interviews and other writings, 1972-1977*. Vintage.

Foucault, M. (2007). *Security, territory, population: Lectures at the Collège de France, 1977-1978* (G. Burchell, Trans.). Picador/Palgrave MacMillan. https://doi.org/10.1057/9780230245075

Foury, F. (1997). Human genetic diseases: A cross-talk between man and yeast. *Gene*, *195*(1), 1–10.

Franklin, S. (2000). Life itself: Global nature and the genetic imaginary. In S. Franklin, C. Lury, & J. Stacey (Eds.), *Global nature, global culture* (pp. 188–227). Sage. https://doi.org/10.4135/9781446219768.n7

Fredens, J., Wang, K., de la Toreed, D., Funke, L. F., Robertson, W. E., Christova, Y., Chia, T., Schmied, W. H., Dunkelmann, D., Beranek, V., Uttamapinant, C., Llamazares, A. G., Elliott, T. S., Chin, J. W. (2019). Total synthesis of Escherichia coli with a recoded genome. *Nature*, *569*(7757), 514–518. https://doi.org/10.1038/s41586-019-1192-5

Fujio, T. (2007). Minimum genome factory: Innovation in bioprocesses through genome science. *Biotechnological Applications of Biochemistry 46*(3), 145-146.

Furness, W. W. (2022). Making space for yeast: Toward a "zymurpolitics." *The Geographical Bulletin*, *63*(1), 39–47. https://doi.org/10.2307/j.ctvwh8f20

Gad, C., & Bruun Jensen, C. (2010). On the consequences of post-ANT. *Science, Technology, & Human Values*, *35*(1), 55–80.

Gaidukov, L., et al. (2018). A multi-landing pad DNA integration platform for mammalian cell engineering. *Nucleic Acids Research*, *46*(8), 4072–4086. https://doi.org/10.1093/nar/gky216

Gailloux, C., Furness, W. W., Myles, C. C., Wiley, D. S., & Collins, K. (2022). Fieldwork without the field: Navigating qualitative research in pandemic times. *Frontiers in Sustainable Food Systems*, *6*. https://doi.org/10.3389/fsufs.2022.750409

Gallivan, J. P. (2007). Toward reprogramming bacteria with small molecules and RNA. *Current Opinion in Chemical Bio*logy, *11*(6), 612–619. https://doi.org/10.1016/j.cbpa.2007.10.004

Gallone, B., Steensels, J., Prahl, T., Soriaga, L., Saels, V., Herrera-Malaver, B., Merlevede, A., Roncoroni, M., Voordeckers, K., Miraglia, L., Teiling, C., Steffy, B., Taylor, M., Schwartz, A., Richardson, T., White, C., Baele, G., Maere, S., & Verstrepen, K. J. (2016). Domestication and divergence of Saccharomyces cerevisiae beer yeasts. *Cell*, *166*(6), 1397-1410. https://doi.org/10.1016/j.cell.2016.08.020

Garfinkel, M. S., Endy, D., Epstein, G. L., & Friedman, R. M. (2007). Synthetic genomics: Options for governance. *Industrial Biotechnology*, *3*(4), 333-365. https://doi.org/10.1089/ind.2007.3.333

Gasch, A. P. & Werner-Washburne, M. (2002). The genomics of yeast responses to environmental stress and starvation. *Functional & integrative genomics*, *2*, 181-192. https://doi.org/10.1007/s10142-002-0058-2

GenScript.com. (2012). GenScript to synthesize yeast genome with Johns Hopkins scientists. Press release. 20 August. PRNewswire-Asia. https://www.genscript.com/press_release/genscript-to-synthesize-yeast-genome-with-johns-hopkins-scientists/

Gibson, J. J. (1979). The theory of affordances. The ecological approach to visual perception. *The people, place and, space reader*, 56-60.

Gibson, D. G., Benders, G. A., Andrews-Pfannkock, C., Denisova, E. A., Baden-Tillson, H., Zaveri, J., Stockwell, T. B., Brownley, A., Thomas, D. W., Algire, M. A., Merryman, D., Young, L., Noskov, V. N., Glass, J., Venter, J. C., Hutchison III, C. A., & Smith, H. O. (2008). Complete chemical synthesis, assembly, and cloning of a *Mycoplasma genitalium* genome. *Science*, 319*(5867)*, 1215–20. https://doi.org/10.1126/science.1151721

Goffeau, A., Barrell, B. G., Bussey, H., Davis, R. W., Dujon, B., Feldmann, H., Galibert, F.., Hoheisel, J. D., Jacq, C., Johnston, M., Louis, E. J., Mewes, H. W., Murakami, Y., Phippsen, P., Tettelin, H., & Oliver, S. G. (1996). Life with 6000 genes. *Science*, *274*(5287), 546-567. https://doi.org/10.1126/science.274.5287.546

Gonçalves, P., & Gonçalves, C. (2022). Horizontal gene transfer in yeasts. *Current Opinion in Genetics & Development*, *76*, 101950.

Graham, D.W. (2021). Heraclitus. In E. N. Zalta (Ed.), *The Stanford encyclopedia of philosophy* (summer 2021 edition), Stanford University. https://plato.stanford.edu/archives/sum2021/entries/heraclitus/

Granjou, C. & Phillips, C. (2018). Living and labouring soils: Metagenomic ecology and a new agricultural revolution? *BioSocieties*, *14*(3), 393-415. https://doi.org/10.1057/s41292-018-0133-0

Greenhough, B. (2014). More-than-human geographies. In R. Lee, V. Lawson, R. Kitchin, & N. Castree (Eds.), *The Sage handbook of human geography* (pp. 94-119). Sage. https://dx.doi.org/10.4135/9781446247617

Greenhough, B., Dwyer, A., Grenyer, R., Hodgetts, T., McLeod, C., and Lorimer, J. (2018). Unsettling antibiosis: How might interdisciplinary researchers generate a feeling for the microbiome and to what effect? *Palgrave Communications*, *4*(149). https://doi.org/10.1057/s41599-018-0196-3

Greenhough, B., et al. (2020). Setting the agenda for social science research on the human microbiome. *Palgrave Communications*, *6*(18). https://doi.org/10.1057/s41599-020-0388-5

Greenwood, J. & Greenwood, J. (2018). The origin of the birdwatching term 'jizz.' *British Birds*, *111*(5), 292-294.

Griesemer, J. R., & Gerson, E. M. (2006). Of mice and men and low unit cost. In *Making mice: Standardizing animals for American biomedical research, 1900–1955*. Karen A. Rader, ed. Princeton University Press. ISBN 0-691-01636-4.

Grosz, L. (1994). *Volatile bodies: Toward a corporeal feminism*. Indiana University Press. https://doi.org/10.4324/9781003118381

Guattari, F. (2000). *The three ecologies*. (I. Pindar & P. Sutton, Trans.). The Athlone Press. (Original work published 2014). https://doi.org/10.5040/9781350354531

Gupta, P. K., & Jaiswal, V. (2014). Synthetic genomics: From synthesis of prokaryotic genomes to synthesis of a fully functional eukaryotic chromosome. *Current Science*, *107*(12), 1975-1982.

Guthman, J. (2019, April 5). Entangled pathologies in the California strawberry assemblage [Conference presentation]. *AAG Annual Meeting*. Washington, D.C., United States.

Haraway, D. (1988). Situated knowledges: The science question in feminism and the privilege of partial perspective. *Feminist Studies*, *14*(3), 575-599.

Haraway D. (1991). *Simians, cyborgs, and women: The reinvention of nature*. Routledge. https://doi.org/10.4324/9780203873106

Haraway, D. (2003). *The Companion Species Manifesto*. Prickly Paradigm Press.

Haraway, D. (2006). A cyborg manifesto: Science, technology, and socialist-feminism in the late 20th century. In S. Stryker & S. Whittle (Eds.), *The transgender studies reader* (pp. 103-118). Routledge.

Haraway, D. (2008.) *When species meet*. University of Minnesota Press.

Haraway, D. (2015). Anthropocene, Capitalocene, Plantationocene, Chthulucene: Making kin. *Environmental Humanities*, *6*(1), 159-165. https://doi.org//10.1215/22011919-3615934

Haraway, D. J., Goodeve, T. N. (2018). Gene: Maps and portraits of life itself. In D. J., Haraway (Ed.), *ModestWitness@Second Millennium. FemaleMan_Meets_OncoMouse: Feminism and Technoscience* (pp. 131-172). Routledge. https://doi.org/10.4324/9780203731093

Harding, S. G. (1991). *Whose science? Whose knowledge?: Thinking from women's lives*. Cornell University Press. https://doi.org/10.7591/9781501712951

Hartman, J. L., Garvik, B., and Hartwell, L. (2001). Principles for the Buffering of Genetic Variation. *Science*, *291*(5506), 1001-1004.

Hartwell, L. H., Hopfield, J. J., Leibler, S., & Murray, A.W. (1999). From molecular to modular cell biology. *Nature*, *402*(6771), C47-C52. https://doi.org/10.1038/35011540

Heinemann, M., & Panke, S. (2006). Synthetic biology—putting engineering into biology. *Bioinformatics*, *22*(22), 2790–2799. https://doi.org/10.1093/bioinformatics/btl469

Helmreich, S. (2014). Homo microbis: The human microbiome, figural, literal, political. *Thresholds*, *42*, 52-59. https://doi.org/10.1162/thld_a_00076

Helmreich, S. (2016). *Sounding the limits of life: Essays in the anthropology of biology and beyond*. Princeton University Press. https://doi.org/10.1515/9781400873869

Hetherington, K., & Law, J. (2000). After networks. *Environment and Planning D: Society & Space*, *18*(2), 127-132. https://doi.org/10.1068/d216t

Hey, M. (2017). Making-do/making spaces: Exploring research-creation as an academic practice to study fermented foods. *Commposite*, *19*(3), 79-95.

Hey, M., & Szymanski, E. A. (2022). Following the organism to map synthetic genomics. *Biotechnology Notes*, *3*, 150-153. https://doi.org/10.1016/j.biotno.2022.07.001

Highfield, R. (2008). "Watermarks" written in first artificial genome. *Telegraph*. 1 Feb.

Hinchliffe, S. (2001). Indeterminacy in-decisions – Science, policy and politics in the BSE (Bovine Spongiform Encephalopathy) crisis. *Transactions of the Institute of British Geographers*, *26*(2), 182-204. https://doi.org/10.1111/1475-5661.00014

Hinchliffe, S., Kearnes, M. B., Degen, M., & Whatmore, S. (2005). Urban wild things: A cosmopolitical experiment. *Environment and Planning D: Society and Space*, *23*(5), 643-658. https://doi.org/10.1068/d351t

Hinchliffe, S., Bingham, N., Allen, J., & Carter, S. (2016). *Pathological lives: Disease, space and biopolitics*. Wiley Blackwell. https://doi.org/10.1002/9781118997635
Hird, M. (2009). *The origins of sociable life: Evolution after science studies.* Palgrave MacMillan. https://doi.org/10.1057/9780230242210

Holmes, B. (2017). Five designer chromosomes bring synthetic life a step closer. *New Scientist.* https://www.newscientist.com/article/2124052-five-designer-chromosomes-bringsynthetic-life-a-step-closer/

Hornborg, A. (2001). Vital signs: An ecosemiotic perspective on the human ecology of Amazonia. *Σημειωτκή-Sign Systems Studies*, *29*(1), 121-15

iGEM Foundation. (n.d.). Registry of standard biological parts. https://parts.igem.org/wiki/index.php?title=Help:An_Introduction_to_BioBricks&redirect=no

iGEM Foundation (2019, September). What is iGEM? (part 3): Insights from iGEM's History. https://blog.igem.org/blog/2019/9/18/what-is-igem-part-3

iGEM Foundation. (2022, March). About. https://old.igem.org/About

Ingold, T. (2000). Bush base: Forest farm: Culture, environment, and development. In E. Croll & D. Parkin (Eds.), *Culture and the perception of the environment* (pp. 39-56). https://doi.org/10.4324/9780203036129

International Risk Governance Council (IRGC). (2010). Guidelines for the Appropriate Risk Governance of Synthetic Biology. Switzerland. https://irgc.org/wp-content/uploads/2018/09/irgc_SB_final_07jan_web.pdf

Isaacs, F. J., & Collins, J. J. (2005). Plug-and-play-with-RNA. *Nature Biotechnology*, *23*(3), 306–307. https://doi.org/10.1038/nbt0305-306

Jackson, P. (2000). Rematerializing social and cultural geography. *Social & Cultural Geography*, *1*(1), 9-14.

Jasanoff, S. (2006). *States of knowledge: The co-production of science and the social order*. Routledge. https://doi.org/10.4324/9780203413845

Jasanoff, S. (2016). *The ethics of invention: Technology and the human future*. WW Norton & Company.

Jasanoff, S., Hurlbut, J. B., & Saha, K. (2015). CRISPR democracy: Gene editing and the need for inclusive deliberation. *Issues in Science and Technology*, *32*(1), 25-32.

Jefferson, C., Lentzos, F., & Marris, C. (2014). Synthetic biology and biosecurity: How scared should we be? King's College London. https://www.researchgate.net/publication/263162191_Synthetic_Biology_and_Biosecurity_How_scared_should_we_be

Jinek, M., Chylinski, K., Fonfara, I., Hauer, M., Doudna, J. A., & Charpentier, E. (2012). A programmable dual-RNA–guided DNA endonuclease in adaptive bacterial immunity. *Science*, *337*(6096), 816-821.

Judson, H. F. (1979). *The Eighth Day of Creation: Makers of the Revolution in Biology*. Simon and Schuster.

Kaebnick, G., Murray, T. H., Parens, E. (n.d.). Ethical issues in synthetic biology. *The Hastings Center*. http://www.thehastingscenter.org/Research/Archive.aspx?id=1548

Kaebnick, G. E., Gusmano, M. K., & Murray, T. H. (2014). The ethics of synthetic biology: Next steps and prior questions. *Synthetic Future: Can We Create What We Want Out of Synthetic Biology?*, *special report*, *Hastings Center Report 44* (6): S4-S26. DOI: 10.1002/hast.392

Katz, S. E. (2016). *Wild fermentation: The flavor, nutrition, and craft of live-culture foods*. Chelsea Green Publishing.

Keller, E. F. (1983). *A feeling for the organism: The life and work of Barbara McClintock*. W. H. Freeman.

Keller, E. F. (2000a). *The century of the gene*. Harvard University Press. https://doi.org/10.4159/9780674039438

Keller, E. F. (2000b). Models of and models for: Theory and practice in contemporary biology. *Philosophy of Science*, *67*(3), S72-S86. https://doi.org/10.1086/392810

Khalil, A. S., & Collins, J. J. (2010). Synthetic biology: Applications come of age. Nature Reviews. *Genetics*, *11*(5), 367-379. https://doi.org/10.1038/nrg2775

Kirksey, E. (2018). Queer love, gender bending bacteria, and life after the Anthropocene. *Theory, Culture & Society*, *36*(6), 197-219. https://doi.org/10.1177/0263276418769995

Kohler, R. E. (1999). Moral economy, material culture, and community in Drosophila genetics. In M. Biagioli (Ed.), *The science studies reader* (pp. 243-257). Routledge.

Kronberger, N. (2012). Synthetic biology: Taking a look at a field in the making. *Public Understanding of Science*, *21*(2), 130–133. https://doi.org/10.1177/0963662511426381

Krzywoszynska, A. (2019). Caring for soil life in the Anthropocene: The role of attentiveness in more-than-human ethics. *Transactions of the Institute of British Geographers*, 44(4), 661-675. https://doi.org/10.1111/tran.12293

Kumagai, A., & Wear, D. (2014). "Making strange": A role for the humanities in medical education. *Academic Medicine*, 89(7), 973-977. https://doi.org/10.1097/acm.0000000000000269

Kumar, A., & Snyder, M. (2001). Emerging technologies in yeast genomics. Nature Reviews. *Genetics*, *2*(4), 302-312. https://doi.org/10.1038/35066084

Langer, E. (2016). Molecular ferment: The rise and proliferation of yeast model organism research. [Doctoral dissertation, University of California, San Francisco]. ProQuest Dissertations Publishing.

Latham A. (2003). Research, performance, and doing human geography: Some reflections on the diary-photograph, diary-interview method. *Environment and Planning A*, *35*(11), 1993-2017. https://doi.org/10.1068/a3587

Latham, A., & McCormack, D. P. (2004). Moving cities: Rethinking the materialities of urban geographies. *Progress in Human Geography*, *28*(6), 701-724. https://doi.org/10.1191/0309132504ph515oa

Latimer, J., & Miele, M. (2013). Naturecultures? Science, affect and the non-human. *Theory, Culture & Society*, *30*(7-8), 5-31.

Latour, B. (1988). *The pasteurization of France*. Harvard University Press.

Latour, B. (1993). Pasteur on lactic acid yeast: A partial semiotic analysis. *Configurations 1(1)*, 135.

Latour, B. (1999a). On recalling ANT. *The Sociological Review 47*(1), 15-25. https://doi.org/10.1111/j.1467-954X.1999.tb03480.x

Latour, B. (1999b). *Pandora's Hope: Essays on the Reality of Science Studies.* Harvard University Press.

Latour, B. (2004a). How to talk about the body? The normative dimension of science studies. *Body & Society*, *10*(2/3), 205-229. https://doi.org/10.1177/1357034x04042943

Latour, B. (2004b). *Politics of nature: How to bring the sciences into democracy*. Harvard University Press. https://doi.org/10.4159/9780674039964

Latour, B. (2005). *Reassembling the social: An introduction to actor-network theory*. Oxford University Press.

Laurent, J. M., Young, J. H., Kachroo, A. H., & Marcotte, E. M. (2016). Efforts to make and apply humanized yeast. *Briefings in Functional Genomics*, *15*(2), 155-163. https://doi.org/10.1093/bfgp/elv041

Laurier E. (2003). Participant observation. In N. Clifford & G. Valentine (Eds.), *Research methods in human and physical geography* (pp. 133-148). Sage.

Lavoisier, A. (1790). *Elements of chemistry*, (Trans. Robert Kerr. Edinburgh). William Creech.

Law, J. (1994). *Organizing modernity: Social ordering and social theory.* Blackwell.

Law, J. (2008). Actor network theory and material semiotics. In B. S. Turner (Ed.), *The New Blackwell companion to social theory* (pp. 141-158). Wiley Blackwell.

Leder, D. (2012). Old McDonald's had a farm: The metaphysics of factory farming. *Journal of Animal Ethics*, *2*(1), 73-86.

Lefebvre, H. (1991) *The production of space.* (D. Nicholson-Smith, trans.) Blackwell.

Leonelli, S., & Ankeny, R. A. (2012). Re-thinking organisms: The impact of databases on model organism biology. *Studies in History & Philosophy of Biological & Biomedical Sciences*, *43*(1), 29-36. https://doi.org/10.1016/j.shpsc.2011.10.003

Liu, Z., Wang, J., & Nielsen, J. (2022). Yeast synthetic biology advances biofuel production. *Current Opinion in Microbiology*, *65*, 33-39. https://doi.org/10.1016/j.mib.2021.10.010

Loettgers, A. (2007). Model organisms and mathematical and synthetic models to explore gene regulation mechanisms. *Biological Theory*, *2*, 134–142. https://doi.org/10.1162/biot.2007.2.2.134

Lord, B. (2010). *Spinoza's* ethics: *An Edinburgh philosophical guide.* Edinburgh University Press. https://doi.org/10.1515/9780748634514

Lorimer, H. (2005). Cultural geography: The busyness of being "more-than-representational." *Progress in Human Geography*, *29*(1), 83–94. https://doi.org/10.1191/0309132505ph531pr

Lorimer, J. (2005). Biodiversity? An investigation into the scope of UK nature conservation. [Doctoral dissertation, University of Bristol]. EThOS.

Lorimer, J. (2007). Nonhuman charisma. *Environment and Planning D: Society and Space*, *25*(5), 911-932. https://doi.org/10.1068/d71j

Lorimer, J. (2017). Parasites, ghosts and mutualists: A relational geography of microbes for global health. *Transactions of the Institute of British Geographers*, *42*(4), 544–558. https://doi.org/10.1111/tran.12189

Luo, J., Sun, X., Cormack, B. P., & Boeke, J. D. (2018). Karyotype engineering by chromosome fusion leads to reproductive isolation in yeast. *Nature*, *560*(7718), 392–396. https://doi.org/10.1038/s41586-018-0374-x

Massey, D. B. (1994). *Space, place, and gender*. University of Minnesota Press.

Massey D. (2003). Imagining the field. In R. Pryke & S. Whatmore (Eds.), *Using Social Theory: Thinking through Research* (pp. 71-88). Sage.

Massumi, B. (1995). The autonomy of affect. *Cultural Critique 31*(2), 83–109. https://doi.org/10.2307/1354446

Massumi, B. (2018). *99 Theses on the Revaluation of Value: A Postcapitalist Manifesto*. University of Minnesota Press.

Mattick, C. S. (2018). Cellular agriculture: The coming revolution in food production. *Bulletin of the Atomic Scientists*, 74(1), 32-35. https//:doi.org/10.1080/00963402.2017.1413059

Maurer, S. M. (2012). Taking self-governance seriously: Synthetic biology's last, best chance to improve security. University of California, Berkeley Goldman School of Public Policy Working Paper No. GSPP12-003. https://doi.org/10.2139/ssrn.2183306

Maurer, S. M., Lucas, K. V., & Terrell, S. (2006). *From understanding to action: Community based options for improving safety and security in synthetic biology*. University of California-Berkeley.

McDowell, L. (1992). Doing gender: Feminism, feminists and research methods in human geography. *Transactions of the Institute of British Geographers*, *17*(4), 399-416. https://doi.org/10.2307/622707

McGovern, P., Jalabadze, M., Batiuk, S., Callahan, M. P., Smith, K. E., Hall, G. R., Kvavadze, E., Maghradze, D., Rusishvilli, N., Bouby, L., Failla, O., Cola, G., Mariani, L., Boaretto, E., Bacilieri, R., This, P., Wales, N., & Lordkipanidze, D. (2017). Early neolithic wine of Georgia in the South Caucasus. *Proceedings of the National Academy of Sciences of the United States of America*, *114*(48), E10309–E10318. https://doi.org/10.1073/pnas.1714728114

McLeod, C., & Nerlich, B. (2017). Synthetic biology, metaphors and responsibility. *Life Sciences, Society and Policy*, *13*(1), 13. https://doi.org/10.1186/s40504-017-0061-y

McLeod, C., Nerlich, B., & Mohr, A. (2017). Working with Bacteria and Putting Bacteria to Work: The Biopolitics of Synthetic Biology for Energy. *Energy Research & Social Science*, *30*, 35–42. https://doi.org/10.1016/j.erss.2017.06.017

Meghani, Z. (2014). Risk assessment of genetically modified food and neoliberalism: An argument for democratizing the regulatory review protocol of the Food and Drug Administration. *Journal of Agricultural and Environmental Ethics*, *27*, 967-989. https://doi.org/10.1007/s10806-014-9511-1

Meyen, J. (1837). Jahresbericht Über Die Resultate Der Arbelten Im Felde Der Physiologischen Botanik V. D. Jahre 1837," *Archiv fur Naturgeschichte 4*(2), 100.

Miller, E. (2019). *Reimagining livelihoods: Life beyond economy, society, and environment*. University of Minnesota Press. https://doi.org/10.5749/j.ctvdtphm5

Mitchell, L. A., Phillips, N. A., Lafont, A., Martin, J. A., Cutting, R., & Boeke, J. D. (2015). qPCRTag analysis – A high throughput, real time PCR assay for Sc2.0 genotyping. *Journal of Visualized Experiments*, *99*, e52941. doi:10.3791/52941

Mitchell, L. (2017). How we build and de-bug Sc2.0 chromosomes [Conference presentation]. *SB7: The Seventh International Meeting on Synthetic Biology, National University of Singapore, Singapore*. https://www.biospace.com/article/releases/national-university-of-singapore-nus-release-7th-international-meeting-on-synthetic-biology-takes-fresh-look-at-opportunities-and-challenges-/

Mitchell, L. A., Wang, A., Stracquadanio, G., Kuang, Z., Wang, X., Yang, K., Richardson, S., Martin, J. A., Zhao, Y., Walker, R., Luo, Y., Dai, H., Dong, K., Tang, Z., Yang, Y., Cai, Y., Heguy, A., Ueberheide, B., Fenyö, D., . . . Boeke, J. D. (2017). Synthesis, debugging, and effects of synthetic chromosome consolidation: SynVI and beyond. *Science, 355*(6329), 1-11. https://doi.org/10.1126/science.aaf4831

Mitchell, T. (2002). *Rule of experts: Egypt, technopolitics, and modernity*. University of California Press. https://doi.org/10.1525/9780520928251

Mitman, G., & Fausto-Sterling, A. (1992). Whatever happened to Planaria?: C. M. Child and the physiology of inheritance. In A. E. Clarke & J. H. Fujimura (Eds.), *The Right Tools for the Job: At Work in Twentieth-Century Life Sciences* (pp. 172–197). Princeton University Press. http://www.jstor.org/stable/j.ctt7zv5cv.10

Moe-Behrens, G. H., Davis, R., & Haynes, K. A. (2013). Preparing synthetic biology for the world. *Frontiers in microbiology*, *4*(5). https://doi.org/10.3389/fmicb.2013.00005

Mol, A. (1999). Ontological politics. A word and some questions. *The Sociological Review*, *47*(1), 74-89. https://doi.org/10.1111/j.1467-954X.1999.tb03483.x

Mol, A. (2002). *The body multiple: Ontology in medical practice.* Duke University Press. https://doi.org/10.1215/9780822384151

Mol, A. (2008). I eat an apple. On theorizing subjectivities. *Subjectivity: International Journal of Critical Psychology*, *22*(1), 28-37. https://doi.org/10.1057/sub.2008.2

Money, N. P. (2018). *The rise of yeast: How the sugar fungus shaped civilization.* Oxford University Press.

Mortimer, R. K., & Johnston, J. R. (1986). Genealogy of principal strains of the Yeast Genetic Stock Center. *Genetics 113,* 35-43.

Murphy, A. & Kavanagh, K. (1999). Emergence of *Saccharomyces cerevisiae* as a human pathogen: Implications for biotechnology. *Enzyme and Microbial Technology*, *25*(7), 551-557. https://doi.org/10.1016/s0141-0229(99)00086-1

Murray, A. (2020). Zymurgeography? Biotechnological ferments and the risks of fermentation fetishism. In C. Myles (Ed.), *Fermented landscapes: Lively processes of socio-environmental transformation* (pp. 273-300). University of Nebraska Press. https://doi.org/10.2307/j.ctvwh8f20.17

Myles, C. C. (2020). Fermented landscapes: Considering the macro consequences of micro(be) processes of socio-environmental transformation. In C. Myles (Ed.), *Fermented landscapes: Lively processes of socio-environmental transformation* (pp. 3-20). University of Nebraska Press. https://doi.org/10.2307/j.ctvwh8f20.7

Myles, C. C. (Ed.). 2020. *Fermented landscapes: Lively processes of socio-environmental transformation.* University of Nebraska Press. https://doi.org/10.2307/j.ctvwh8f20

Nancy J. Kelley + Associates. (2023). *SC2.0/synthetic genomes conference.* https://nancyjkelley.com/case/sc2-0-synthetic-genomes-conference/

Nanninga, N. (2010). Did van Leeuwenhoek observe yeast cells in 1680? In M. Schaechter (Ed.), *In the company of Microbes: Ten years of small things considered* (pp. 72-75). https://doi.org/10.1128/9781555819606

Nash, J. C. (2004). From lavender to purple: Privacy, black women, and feminist legal theory. *Cardozo Women's LJ*, *11*, 303.

National Academies of Sciences, Engineering, and Medicine. (2017). *Human Genome Editing: Science, Ethics, and Governance*. Washington, DC: The National Academies Press. https://doi.org/10.17226/24623

National Human Genome Research Institute. (2022). Homologous recombination. In *National Institutes of Health*. Retrieved October 14, 2022, from https://www.genome.gov/genetics-glossary/homologous-#H

National Library of Medicine. (2012). Risk, regulation, and scientific citizenship: The controversy over recombinant DNA research. *The Maxine Singer Papers.* https://profiles.nlm.nih.gov/spotlight/dj/feature/regulation

Nature Biotechnology. (2016). Editorial: Rewriting our Future. *Nature Biotechnology 34*(7), p. 673. https://doi.org/10.1038/nbt.3640

Neslen, A. (December 4, 2017). US military agency invests $100m in genetic extinction technologies. *The Guardian*. ISSN: 0261-3077.

Nietzsche, F. (2006a). *On the genealogy of morals* (D. Smith, Trans.). Oxford University Press. (Original work published 1887)

Nietzsche, F. (2006b). *Thus spoke Zarathustra* (A. Del Caro, Trans.). In R. Pippin (Ed.). Cambridge University Press.

Nightingale, A. J. (2014). Nature-society. In R. Lee, V. Lawson, R. Kitchin, & N. Castree (Eds.), *The Sage handbook of human geography* (pp. 120-147). Sage.

Nost, E., & Goldstein, J. E. (2022). A political ecology of data. *Environment and Planning E: Nature and Space*, *5*(1), 3–17. https://doi.org/10.1177/25148486211043503

Nowotny, H., Scott, P., & Gibbons, M. (2001). *Rethinking science: Knowledge, and the public in an age of uncertainty*. Polity.

Nurk, S., Koren, S., Rhie, A., Rautiainen, M., Bzikadze, A., Mikheenko, A., Vollger, M., Altemose, N., Uralsky, L., Gershman, A., Aganezov, S., Hoyt, S. J., Diekhans, M., Logsdon, G. A., Alonge, M., Antonarakis, S., Borchers, M., Bouffard, G. G., Brooks, S. Y., & Caldas, G. V. (2022). The complete sequence of a human genome. *Science*, *376*(6588), 44–53. https://doi.org/10.1126/science.abj6987

NYU Grossman School of Medicine. (2023a). *Boeke lab.* https://med.nyu.edu/research/boeke-lab/

NYU Grossman School of Medicine. (2023b). *Institute for systems genetics.* https://med.nyu.edu/departments-institutes/systems-genetics/

O'Malley, M. A., Powell, A., Davies, J. F., & Calvert, J. (2007.) Knowledge-making distinctions in synthetic biology. *BioEssays*, *30*(1), 57–65. https://doi.org/10.1002/bies.20664

Opentrons. (2023). *Our mission.* opentrons.com/about

Openwetware. (2005, December 22). *Synthetic biology: Abstraction hierarchy.* https://openwetware.org/wiki/Synthetic_Biology:Abstraction_hierarchy

Oye, K. A., Esvelt, K., Appleton, E., Catteruccia, F., Church, G., Kuiken, T., Lightfoot, S. B-Y., McNamara, J., Smidler, A., & Collins, J. P. (2014). Regulating gene drives. *Science*, *345*(6197), 626–628. https://doi.org/10.1126/science.1254287

Paxson, H. (2008). Post-Pasteurian cultures: The microbiopolitics of raw-milk cheese in the United States. *Cultural anthropology*, *23*(1), 15–47. https://doi.org/10.1111/j.1548-1360.2008.00002.x

Paxson, H. (2012). *The life of cheese: Crafting good and value in America*. University of California Press. https://doi.org/10.1525/california/9780520270176.001.0001

Paxson, H. (2018). The naturalization of nature as working. *Society for Cultural Anthropology.* https://culanth.org/fieldsights/the-naturalization-of-nature-as-working

Paxson, H. & Helmreich, S. (2014). The perils and promises of microbial abundance: Novel natures and model ecosystems, from artisanal cheese to alien seas. *Social Studies of Science*, *44*(2), 165–193. https://doi.org/10.1177/0306312713505003

Peet, R., & Watts, M. (2004). *Liberation ecologies: Environment, development and social movements*. Routledge. https://doi.org/10.4324/9780203235096

Peirce, C. S. (1867). "On a new list of categories." Presented 14 May 1867 to the American Academy of Arts and Sciences. Published 1868 in *Proceedings of the American Academy of Arts and Sciences 7*.

Philo, C. (2005). Spacing lives and lively spaces: Partial remarks on Sarah Whatmore's *hybrid geographies. Antipode*, 37(4), 824-833. https://doi.org/10.1111/j.0066-4812.2005.00529.x

Pollan, M. (2014). *Cooked: A natural history of transformation.* Penguin Books.

Pomper, S. (1949). The biochemical genetics of yeast. [Doctoral dissertation, Yale University]. ProQuest Dissertations Publishing.

Porter, L. (2018, February 26). *Where did 'jazz,' the word, come from? Follow a trail of clues, in Deep Dive with Lewis Porter*. WBGO.org. https://www.wbgo.org/music/2018-02-26/where-did-jazz-the-word-come-from-follow-a-trail-of-clues-in-deep-dive-with-lewis-porter

Pottage, A. (2007). The socio-legal implication of the new biotechnologies. *Annual Review of Law and Social Science*, *3*, 321–344. https://doi.org/10.1146/annurev.lawsocsci.3.081806.112856

Pottage, A., & Sherman, B. (2007). Organisms and manufactures: On the history of plant inventions. *Melbourne University Law Review*, *31*(2), 539–568.

Powys White, K. (2020, March 7). Redefining energy justice through consent of nonhuman relatives [Conference presentation]. *Environmental Justice in Multispecies Worlds Conference*. Madison, Wisconsin, United States.

Presidential Commission for the Study of Bioethical Issues. (2010, December). *New directions: The ethics of synthetic biology and emerging technologies*. U.S. Government Printing Office. https://bioethicsarchive.georgetown.edu/pcsbi/sites/default/files/PCSBI-Synthetic-Biology-Report-12.16.10_0.pdf

Puig de la Bellacasa, M. (2015). Making time for soil: Technoscientific futurity and the pace of care. *Social Studies of Science*, *45*(5), 691-716. DOI: 10.1177/0306312715599851

Rabinow, P. (2005). Artificiality and enlightenment: From sociobiology to biosociality. In J. X. Inda (Ed.), *Anthropologies of modernity: Foucault, governmentality, and life politics* (pp. 179-193). Blackwell Publishing. https://doi.org/10.1002/9780470775875

Regalado, A. (2015, October 8). DuPont predicts CRISPR plants on dinner plates in five years. *MIT Technology Review*. www.technologyreview.com /2015/10/08/109790/dupont-predicts-crispr-plants-on-dinner-plates-in-five-years/

Rheinberger, H-J. (2000). Beyond nature and culture: Modes of reasoning in the age of molecular biology and medicine. In M. Lock, Young, A., & Cambrosio, A. (Eds), *Living and working with the new medical technologies: Intersection of inquiry* (pp. 19-30). Cambridge University Press. https//:doi.org/10.1017/CBO9780511621765.002

Richardson, S. (2011). Computer assisted design for synthetic biology. [Doctoral dissertation, Johns Hopkins University]. ProQuest Dissertations Publishing.

Richardson, S. (2017, June 13-16). Principles of genome design [Conference presentation]. *SB7: The Seventh International Meeting on Synthetic Biology*. National University of Singapore, Singapore.

Richardson, S. M., Mitchell, L. A., Stracquadanio, G., Yang, K., Dymond, J. S., DiCarlo, J. E., Lee, D., Huang, C. L. V., Chandrasegaran, S., Cai, Y., Boeke, J. D., & Bader, J. S. (2017). Design of a synthetic yeast genome. *Science*, *355*(6329), 1040–1044. https://doi.org/10.1126/science.aaf4557

Robbert, A. & Mickey, S. (2013). Cosmopolitics: An ongoing question. Paper delivered at The Center for Process Studies, Claremont, CA. *Political Theory and Entanglement: Politics at the Overlap of Race, Class, and Gender*. October 25. https://knowledgeecology.files.wordpress.com/2017/03/claremont_cosmopolitics.pdf

Robbins, P. (2011). *Political ecology: A critical introduction*. John Wiley & Sons.

Robbins, P. & Marks, B. (2010). Assemblage geographies. In S. Smith, R. Pain, & S. Marston (Eds.), *The Sage handbook of social geographies* (pp. 176-194). Sage. https://doi.org/10.4135/9780857021113.n8

Roberts, I. N., & Oliver, S. G. (2011). The yin and yang of yeast: Biodiversity research and systems biology as complementary forces driving innovation in biotechnology. *Biotechnology Letters*, *33*(3), 477-487. https://doi.org/10.1007/s10529-010-0482-7

Rocheleau, D. E., Thomas-Slayter, B., & Wangari, E. (1996). *Feminist political ecology: Global issues and local experiences*. Routledge. https://doi.org/10.4324/9780203352205

Rose, G., (1997). Situating knowledges: Positionality, reflexivities and other tactics. *Progress in Human Geography*, *21*(3), 305-320. https://doi.org/10.1191/030913297673302122

Rose, N. (2007). *The politics of life itself: Biomedicine, power, and subjectivity in the twenty-first century*. Princeton University Press.

Rossi, J. (2013). The socionatural engineering of reductionist metaphors: A political ecology of synthetic biology. *Environment and Planning A*, *45*(5), 1127-1143. https://doi.org/10.1068/a45195

Sagan, D. (1992). Metametazoa: Biology and multiplicity. In *Incorporations: Fragments for a History of the Human Body*, Jonathan Crary and Sanford Kwinter, eds, Zone, pp. 362–385.

Sandler, R. (2017). Gene drives and species conservation: An ethical analysis. In I. Braverman (Ed.), *Gene editing, law, and the environment* (pp. 39-54). Routledge.

Sarmiento, E. R. (2015). Umwelt, food, and the limits of control. *Emotion, Space, and Society, 14*, 74-83. http://dx.doi.org/10.1016/j.emospa.2013.08.008

Sarmiento, E. R. (2020). Raw power: For a (micro) biopolitical ecology of fermentation. In C. C. Myles (Ed.), *Fermented landscapes: Lively processes of socio-environmental transformation* (pp. 301-318). University of Nebraska Press. https://doi.org/10.2307/j.ctvwh8f20.18

Sauer, C. O. (1925). The morphology of landscape. In T. Oakes & P. L. Price (Eds.), *The cultural geography reader* (pp. 96-104). https://doi.org/10.4324/9780203931950

Sauro, H. M. (2008). Modularity defined. *Molecular Systems Biology, 4*(1), 1-2. https://doi.org/10.1038/msb.2008.3

Sayes, E. (2014). Actor–network theory and methodology: Just what does it mean to say that nonhumans have agency? *Social Studies of Science*, 44(1), 134-149. https://doi.org/10.1177/0306312713511867

Schmidt, M. (2008). Diffusion of synthetic biology: A challenge to biosafety. *Systems and Synthetic Biology 2*, 1-6. https://doi.org/10.1007/s11693-008-9018-z

Schroer, S. A. (2021). Jakob von Uexküll: The concept of umwelt and its potentials for an anthropology beyond the human. *Ethos, 86*(1), 132-152.

Secretariat of the Convention on Biological Diversity. 2000. Cartagena Protocol on Biosafety to the Convention on Biological Diversity. United Nations Environmental Programme, Montreal, Canada.

SGDWiki. (2022, April 27). *Meetings.* https://wiki.yeastgenome.org/index.php/Meetings

Shapin, S. (1998). Placing the view from nowhere: Historical and sociological problems in the location of science. *Transactions of the Institute of British Geographers, 23*(1), 5-12. http://dx.doi.org/10.1111/j.0020-2754.1998.00005.x

Shapin, S. & Schaffer, S. (1985). *Leviathan and the Air-Pump: Hobbes, Boyle, and the Experimental Life. Including a Translation of Thomas Hobbes, Dialogus Physicus De Natura Aeris by Simon Schaffer*. Princeton University Press.

Shao, Y., Lu, N., Wu, Z., Cair, C., Wang, S., Zhang, L., Zhou, F., Xiao, S., Liu, L., Zeng, X., Zheng, H., Yang, C., Zhao, Z., Zhao, G., Zhou, J-Q., Xue, X., & Qin, Z. (2018). Creating a functional single-chromosome yeast. *Nature, 560*(7718), 331–335. https://doi.org/10.1038/s41596-019-0192-0

Shen, M. J., Wu, Y., Yang, K., Li, Y., Xu, H., Zhang, H., Li, B.-Z., Li, X., Xia, W.-H., Zhou, X., Mitchell, L. A., Bader, J. S., Yuan, Y., & Boeke, J. D. (2018). Heterozygous diploid and interspecies SCRaMbLEing. *Nature Communication*, *9*(1934), 1-8. https://doi.org/10.1038/s41467-018-04157-0

Shetty, R. P., Endy, D., & Knight Jr., T. F. (2008). Engineering BioBrick vectors from BioBrick parts. *Journal of Biological Engineering*, *2*(5). doi:10.1186/1754-1611-2-5

Sidransky, E. (2022). *Homologous Recombination*. National Human Genome Research Institute. https://www.genome.gov/genetics-glossary/homologous-recombination#:~:text=Homologous%20recombination%20is%20a%20type,or%20identical%20molecules%20of%20DNA

Simard, S. W. (2018). Mycorrhizal networks facilitate tree communication, learning, and memory. In F. Baluška & M. Gagliano (Eds.). *Memory and learning in plants* (pp. 191-213). Springer.

Sinclair, S., & Rockwell, G. (2016). *Voyant tools*. http://voyant-tools.org/

Slack, J. M. W. (2009). Emerging market organisms (review of *Emerging Model Organisms: A Laboratory Manual*). *Science*, *323*, 1674–1675.

Sliva, A., Yang, H., Boeke, J. D., & Mathews, D. J. H. (2015). Freedom and responsibility in synthetic genomics: The synthetic yeast project. *Genetics*, *200*(4), 1021-1028. https://doi.org/10.1534/genetics.115.176370

Spackman, C. C. W. (2018). Formulating citizenship: The microbiopolitics of the malfunctioning functional beverage. *BioSocieties*, *13*(1), 41-63. https://doi.org/10.1057/s41292-017-0051-6

Spinoza, B. (2006). *The essential Spinoza: Ethics and related writings*. Hackett Publishing.

Stanford University. (n.d.). *Strain: BY4741*. https://www.yeastgenome.org/strain/S000203456#resources

Stefanini, I., Dapporto, L., Legras, J-L., Calabretta, A., Di Paola, M., De Filippo, C., Viola, R., Capretti, P., Polsinelli, M., Turillazzi, S., & Cavalieri, D. (2012). Role of social wasps in Saccharomyces cerevisiae ecology and evolution. *Proceedings of the National Academy of the Sciences*, *109*(33), 13398-13403. https://doi.org/10.1073/pnas.1208362109

Stengers, I. (1997). *Power and invention: Situating science*. University of Minnesota Press

Stengers, I. (2010). *Cosmopolitics I*. (R. Bononno, Trans.). University of Minnesota Press

Sullivan, W. (1983). First synthetic chromosome reported made. *The New York Times*, September 18.

Swedberg, R. (2016). Before theory comes theorizing or how to make social science more interesting. *The British Journal of Sociology*, *67*(1), 5-22. https://doi.org/10.1111/1468-4446.12184

Swyngedouw, E. & Heynen, N. C. (2003). Urban political ecology, justice and the politics of scale. *Antipode*, 35(5), 898-918. https://doi.org/10.1111/j.1467-8330.2003.00364.x

SynBioBeta. (2022a). *About SynBioBeta.* https://www.synbiobeta.com/about

SynBioBeta. (2022b, April 12-14). *Conference.* https://www.synbiobeta.com/attend/conference-2022

Synthetic and Systems Biology Summer School. (2014, June 15-19). *International synthetic and systems biology summer school: Biology meets engineering and computer science.* https://ssbss2014.taosciences.org/

Synthetic biology: Abstraction hierarchy. https://openwetware.org/wiki/Synthetic_Biology:Abstraction_hierarchy Accessed 19 October 2022

Syntheticyeast.org Synthetic Yeast 2.0. (2022). *International Meetings.* https://syntheticyeast.github.io/savi/international-meetings/)

Szymanski, E. A. (2018a). What is the *terroir* of synthetic yeast? *Environmental Humanities*, *10*(1), 40-62. https://doi.org/10.1215/22011919-4385462

Szymanski, E.A. (2018b). Who are the users of synthetic DNA? Using metaphors to activate microorganisms at the center of synthetic biology. *Life Sciences, Society and Policy*, *14*(15). https://doi.org/10.1186/s40504-018-0080-3

Szymanski, E. & Calvert, J. (2018). Designing with living systems in the synthetic yeast project. *Nature Communications*, *9*(1), 2950. https://doi.org/10.1038/s41467-018-05332-z

Szymanski, E., Smith, R., & Calvert, J. (2021). Responsible research and innovation meets multispecies studies: Why RRI needs to be a more-than-human exercise. *Journal of Responsible Innovation*, *8*(2), 261-266. https://doi.org/10.1080/23299460.2021.1906040

Szymanski, E., Vermeulen, N., & Wong, M. (2019). Yeast: One cell, one reference sequence, many genomes? *New Genetics and Society*, *38*(4), 430-450. https://doi.org/10.1080/14636778.2019.1677150

Talbot, B. (1980). Introduction to recombinant DNA research, development and evolution of the NIH guidelines, and proposed legislation. *University of Toledo Law Review*, *12*, 804–814.

Taylor, C. (2002). Modern Social Imaginaries. *Public Culture 14*(1), 91-124. https://www.muse.jhu.edu/article/26276.

Thénard, M. (1803). A memoir on vinous fermentation. In Nichols (Ed.), *The Repertory of Arts, Manufactures, and Agriculture* (pp. 67-130). J. Wyatt.

Thrift, N. J. (2008). *Non-representational theory: Space, politics, affect*. Routledge.

Thrift, N. & Dewsbury, J. D. (2000). Dead geographies—and how to make them live. *Environment and Planning D: Society and Space*, *18*(4), 411-432. https://doi.org/10.1215/22011919-3610012

Tsing, A. L. (2012). Unruly edges: Mushrooms as companion species. *Environmental Humanities*, *1*(1), 141-154.

Tsing, A.L. (2015). *The mushroom at the end of the world: On the possibility of life in capitalist ruins*. Princeton University Press. https://doi.org/10.1515/9781400873548

Tsing, A. L. (2017). A threat to Holocene resurgence is a threat to livability. In M. Brightman & J. Lewis (Eds.). *The anthropology of sustainability: Beyond development and progress* (pp. 51-65). Palgrave Macmillan.

Turner, M. D. (2016). Political ecology II: Engagements with ecology. *Progress in Human Geography*, *40*(3), 413-421. DOI: 10.1177/0309132515577025

United Nations Environment Programme. (1992, December 22). Convention on Biological Diversity. Montreal, Canada.

Urquhart, J. (2014, March 26). *Synthetic yeast chromosome is fully functional.* Chemistry World. https://www.chemistryworld.com/news/synthetic-yeast-chromosome-is-fully-functional/7222.article

Vannini, P. (2015). Non-representational research methodologies: An introduction. In P. Vannini (Ed.), *Non-Representational Methodologies* (pp. 1-18). Routledge. https://doi.org/10.4324/9781315883540

Viel, A., Legras, J-L., Nadai, C., Carlot, M., Lombardi, A., Crespan, M., Migliaro, D., Giacomini, A., & Corich, V. (2017). The geographic distribution of *Saccharomyces cerevisiae* isolates within three Italian neighboring winemaking regions reveals strong differences in yeast abundance, genetic diversity and industrial strain dissemination. *Frontiers in Microbiology*, *8*, 1-15. https://doi.org/10.3389/fmicb.2017.01595

Villalobos, A., Ness, J. E., Gustafsson, C., Minshull, J., & Govindarajan, S. (2006). Gene designer: A synthetic biology tool for constructing artificial DNA segments. *BMC Bioinformatics*, 7, 285-288. https://doi.org/10.1186/1471-2105-7-285

Voigt, C. (2017, June 13-16). Genetic circuit design [Conference presentation]. *SB7: The Seventh International Meeting on Synthetic Biology*, National University of Singapore, Singapore.

von Uexküll, J. (1957). A stroll through the worlds of animals and men. *Instinctive Behavior*. International. University. Press.

Wakefield, S. (2018). Infrastructures of liberal life: From modernity and progress to resilience and ruins. *Geography Compass*, *12*(7), e12377.

Walker, R. S. K., & Cai, Y. (2016). The Fifth Annual Sc2.0 and Synthetic Genomes Conference: Synthetic genomes in high gear. *ACS Synthetic Biology*, *5*, 920-922. DOI: 10.1021/acssynbio.6b00227

Watts, M. (2017). Political ecology. In E. Sheppard & T. J. Barnes (Eds.), *A companion to economic geography* (pp. 257-274). Blackwell Publishing. https://doi.org/10.1002/9780470693445.ch16

Weedon, C. (1987). *Feminist Practice and Post-Structuralist Theory*. Oxford: Basil Blackwell.

Whatmore, S. (2002). *Hybrid geographies: Natures, cultures, spaces.* Sage. https://doi.org/10.4135/9781446219713

Whatmore S. (2003). Generating materials. In M. Pryke, G. Rose, & S. Whatmore (Eds.), *Using social theory: Thinking through research* (pp. 89-104). *Sage*. https://doi.org/10.4135/9780857020253.n5

Whatmore, S. (2004). Humanism's excess: Some thoughts of the "post-human/ist" agenda. *Environment and Planning A*, *36*(8), 1360-1363. https://doi.org/10.1068/a37127

Whatmore, S. (2006). Materialist returns: Practising cultural geography in and for a more-than-human world. *Cultural Geographies*, *13*(4), 600-609. https://doi.org/10.1191/1474474006cgj377oa

Whitehead, A. N. (1968). *Modes of Thought.* The Free Press.

Wolfe, C. (2003). *Animal rites: American culture, the discourse of species, and posthumanist theory.* University of Chicago Press. https://www.bibliovault.org/BV.landing.epl?ISBN=9780226905129

Woodrow Wilson International Center for Scholars. (2014a). Maps Inventory: Updated Map Tracks Global Growth of Synthetic Biology. Washington, DC. https://www.synbioproject.tech/inventories/maps-inventory/

Woodrow Wilson International Center for Scholars. (2014b). Library: Synthetic Biology Applications Inventory. Washington, DC. https://www.synbioproject.tech/cpi/

Woodrow Wilson International Center for Scholars. (2014c). Synthetic Biology Scorecard. Washington, DC. https://www.synbioproject.tech/scorecard/

Woolf, S. H. (2008). The meaning of translational research and why it matters. *JAMA: Journal of the American Medical Association*, *299*(2), 211-213. https://doi.org/10.1001/jama.2007.26

Wynne, B. (2005). Reflexing complexity: Post-genomic knowledge and reductionist returns in Public science. *Theory, Culture and Society*, *22*(5), 67–94. https://doi.org/10.1177/0263276405057192

Zwart, H, Landeweerd, L., & van Rooij, A. (2014). Adapt or perish? Assessing the recent shift in the European research funding arena from 'ELSA' to 'RRI'. *Life Sciences, Society and Policy*, *10*(11), 1–19. https://doi.org/10.1186/s40504-014-0011-x