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Organs and Humans on Chips: Translation, Biomedical Models, and the Political Economy of Innovation

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Organs and Humans on Chips: Translation, Biomedical Models, and the Political Economy of Innovation

by
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CONTRIBUTIONS

Some of the arguments laid out in this dissertation have been developed in published in sole-authored manuscripts by the author. Chapter 5 is published as the following article:

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Organs and Humans on Chips:

Translation, Biomedical Models, and the Political Economy of Innovation

Melanie Jeske

ABSTRACT

In 2010, a team of researchers published a paper in *Science* claiming to have created a "chip" platform that recapitulated a human lung. They claimed this technology, because it used *human* cells, provided a more accurate way to model the human body and its responses than animal models, like mice, rabbits, hamsters, and dogs. The scientists predicted that these technologies could overcome translational barriers in pharmaceutical and toxicity research, by introducing human-based models into the earliest stages of safety and efficacy testing. In doing so, they suggested that "organ chips" would eliminate the failure of translation between non-human animal models and humans, while also making pre-clinical testing stages more efficient and cheaper. Less than two years later, the US National Institutes of Health National Center for Advancing Translational Sciences devoted extensive federal research funding to launch the Tissue Chip Program. Since then, organ chip research and development and public and private investment in these technologies have greatly expanded.

Drawing on interviews with organ chip researchers and funders, ethnographic observations of laboratories, scientific conferences, and educational settings, and document analysis of scientific publications and policy and regulatory documents, I document how organ chips, as technological artifacts, emerge as productive and valuable tools, and trace how they are imagined and brought into fruition by a diverse set of actors across government, industry, and academic sectors. I begin the dissertation with an analysis of the discursive construction of the translational crisis, arguing that the failure to translate biomedical discoveries from "bench to

bedside" is constructed as a problem of an inefficient research pipeline and misaligned infrastructure of academic biomedical research. I show how constructions of the crisis of translation in biomedicine fuel particular formations of research teams, funding structures, and the prioritization of particular kinds of health interventions, that together make organ chips the 'right' tool for resolving the translational crisis. Following, I offer a social worlds analysis, exploring how organ chips become constructed as the right tool for particular jobs, analyzing the sociotechnical conditions of possibility alongside the actors and networks that leverage them to position organ chips as 'doable' and 'right' technologies. I then turn to the models themselves, to surface the social nature of model making. I contend that organ chips are rendered "human enough" through social processes of scientific negotiation and show how market forces shape the technical design of these technologies. Thus, I argue that the interests that elevate these technologies and their value also shape their very design, in ways that may fundamentally transform how we model human health and disease. Finally, in response to the historical moment in which this dissertation research was conducted, I offer an empirical analysis of how COVID-19 disrupted laboratory science. Turning my gaze to scientific labor and organization, I show how the pandemic exacerbated institutional pressures, leading laboratory workers to launch critiques of academic science and to articulate the conditions of their estrangement.

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CHAPTER ONE: INTRODUCTION

In 2010, a team of researchers published a paper in *Science* announcing the creation of a "chip" platform that modeled human, organ-level lung function. They claimed this technology, because it used *human* cells, provided a more accurate way to model the human body and its responses than animal models like mice, rabbits, hamsters, and dogs. The scientists predicted that these organ chip technologies could one day replace animal models in pharmaceutical and toxicity research, by introducing human-based models in the earliest stages of safety and efficacy testing, and also make these stages more efficient and cheaper (Huh et al. 2010). For a biomedical research infrastructure that has long relied on animal models, this was a bold and potentially transformational proposition.

Less than two years later, the US National Institutes of Health National Center for Advancing Translational Sciences (NIH NCATS) established the Tissue Chip Program.[i] Together, NCATS and the Defense Advanced Research Projects Agency (DARPA) committed $145 million in federal research funding over a five-year period to fund the development of organ chip platforms representing the major organ systems of the body as well as integrated human-on-a-chip platforms. Since then, organ chip research and development and public and private investment in these technologies have greatly expanded. What accounts for this rapid ascent, swift uptake, and significant investment in these nascent technologies? How is it that organ chips became the right tool for the job (Clarke and Fujimura 1992) of overcoming translational failure, and making pharmaceutical testing more efficient and cheaper?

Sociologists and science and technology studies (STS) scholars have long demonstrated that technologies are social artifacts, shaped by the sociohistorical circumstances in which they emerge (Winner 1980; Cowan 1985; Braun 2014). Developments in science and technology

depend not only on their technical characteristics, but also on their social positioning, as valuable and worthwhile endeavors. Joining this literature, this dissertation uses the case of organ chips to explore key empirical questions: (1) How do particular research problems come to be seen as worthy of concentrated funding, attention, and efforts to establish whole new fields? (2) How are problems, jobs, and rightness co-constructed such that particular technologies become understood as the right tools for the job? And (3) how do sociopolitical and market forces shape the construction of scientific tools?

In this dissertation, I offer a sociological account of organ chips that links macro-level trends influencing twenty-first century academic science to the construction of biomedical technologies used to produce knowledge about the human body. I document how organ chips, as technological artifacts, emerge as productive and valuable tools, tracing how they are imagined and brought into fruition by a diverse set of actors across government, industry, and academic sectors. I show how constructions of the crisis of translation in biomedicine fuel particular formations of research teams, funding structures, and the prioritization of particular kinds of health interventions, that together render organ chips the 'right' tool for resolving the translational crisis. Thus I argue that the interests that elevate these technologies and their value also shape their very design, in ways that may fundamentally transform how we model human health and disease.

Theoretical Framings and Contributions

This dissertation draws on several theoretical frames to analyze the political economy and construction of organ chips. I approach these frameworks as sensitizing concepts (Blumer 1954, 7) that draw attention and heighten awareness to particular areas of inquiry, suggesting

"directions along which to look" when approaching my empirical situation. Sensitizing concepts are not overly prescriptive; when applied, they allow analysts to seek nuance and divergence from the extant literature. I draw on theories across STS and medical sociology scholarship. Specifically, I use extant theoretical work that examines the production of scientific and biomedical knowledge, including theories of capital in academic science, biomedicalization, and laboratory tools and infrastructures.

Capital in Academic Science

Social scientists have shown that the rise of *academic capitalism* has greatly shaped university science. Over the past several decades, boundaries between academic and industry science have blurred, wherein market forces now shape research agendas, academic scientists routinely engage in relations with industry, and academic scientists are encouraged to commercialize scientific discoveries through patenting and start-up ventures (Hoffman 2017, 2021; D.R. Johnson 2017; Berman 2012a; D.L. Kleinman and Vallas 2001; D.L. Kleinman 2003a). Indeed, while STS scholars have shown that science is always *interested*, meaning that science has never been apolitical, since the 1970s there has been a concerted increase in markets overtly shaping academic science practices. This shift has occurred across academic science fields, but are concentrated in particular disciplines like the biological sciences, engineering, and biomedicine that lend themselves to market applications (Berman 2012a; Hackett 2005, 1990; D.L. Kleinman and Vallas 2001; Rasmussen 2014).[ii]

In his article, *Science as Vocation,* Hackett (1990, 251) described how universities were responding to transformative pressures at this time:

> Universities today are receiving an ambivalent message from the society at large. On the one hand they are to preserve traditional values (and to cling onto classic texts and

> themes: witness the uproar when major universities change their core curricula), but on the other hand they are to conduct themselves in a more businesslike fashion, controlling costs and responding to national needs and the economic environment.

Hackett and others wrote about increased research loads, the establishment of divisions devoted to innovation and product development, and the rise of technology transfer offices within academic institutions (Baldini 2006; Berman 2008; Slaughter, Archerd, and Campbell 2004). Critical scholars argue that academic capitalism is emblematic of a broader neoliberalization in higher education (Moore et al. 2011), and that these shifts shape how researchers and fields pursue particular agendas, research questions, and methods while leaving others left undone (Frickel et al. 2010; Jeon 2019; Hoffman 2017). Scholars have also traced how academic capitalism has shaped knowledge production practices through the organization of scientific teams and restructuring of advanced training in the siences (Hackett 2005; D.R. Johnson 2017; Sacco 2022). Taken together, these studies shed light on how scientists navigate the changing landscape of academic research and learn to be successful in the climate of academic capitalism, through the pursuit of commercialization and industry partnership endeavors (Hoffman 2017; D.R. Johnson 2017; D.L. Kleinman and Vallas 2001).

These shifts in the constitution of academic science have led scholars to investigate the impacts of industry relations and influence in academic science. This work has primarily focused on the politics surrounding conflicts of interest and what such conflicts mean for the production and dissemination of knowledge. Conflicts of interest (COI) are defined as instances where individuals hold concurrent positions that may give rise to interests that compete with their primary role (here, of producing “objective” knowledge). This scholarship underscores the notion of corporate influence as a threat to academic science, for instance showing how research

funded by pharmaceutical companies is associated with results favoring sponsor interests (Sismondo 2008, 2009; Resnik 1998, 2000).[iii]

As COI disclosure is now requisite across many settings, scholars have examined the unintended consequences associated with the ritualization of disclosure, such as the public perceiving researchers with disclosed conflicts to be more trustworthy, presumably on the basis of their transparency. In effect, this literature demonstrates that disclosure might enable a moral licensing, in which "anything goes" so long as it has been disclosed (Grundy et al. 2018), posing new challenges for COI governance. Despite consensus that COI are problematic, they have become ubiquitous in biomedical sciences, and particularly so in the new field of translational medicine. In 2019 alone, over 70% of research articles published in *JAMA*, *Nature Biotechnology*, and *Science Translational Medicine* were written by authorship teams with COI to disclose (Jeske 2021a).

In the dissertation, I build on this literature in three ways. I add to the scholarship on how trends of academic capitalism shape the pursuit of particular lines of research, and how the development of organ chips is situated within this sociohistorical context. The case of organ chips is undoubtedly marked by the character of academic science that scholars in this area have noted: one in which capitalism and neoliberalism shape in profound ways what science is valued, and increasingly how scientists perform their work. The laboratories I observed and researchers I interviewed for this dissertation were all situated at academic institutions, but they typically received some industry funding, and were engaged in efforts to patent their discoveries and/or had already launched businesses from their work. Throughout the dissertation, I show how market forces shape the construction of organ chips, and unpacking the imprints of industry interests in the very design of basic biomedical technologies.

I also consider how the crisis of translation, which re-aligns the priorities of government funding agencies, academic researchers, and industry in new ways, renders existing COI governance inadequate in different ways than articulated by past research. I argue that in the pursuit of translational goals, translation has come to be synonymous with commercialization. In other words, *conflicts* of interest are no longer understood as such, by many actors in the arena, precisely because the interests are aligned.

Finally, much literature on academic capitalism has focused on those in relative positions of power in academic science. In Chapter 5, I attend to gaps in this literature created by its emphasis on "studying up," and narrow focus on those with power in academic settings. I foreground the experiences of low-status laboratory workers, and examine how these macro-level trends shape the day-to-day experience of laboratory work in biomedical science.

Biomedicalization and Allied Concepts

This dissertation is greatly informed by biomedicalization theory, as theorized by Clarke, Shim, Mamo, Fosket, and Fishman (2003). Biomedicalization posits that the technoscience of the late twentieth century reorganized and reconstituted medicine, and that previously developed social theories that attended to medicine were no longer sufficient to describe these profound transformations.[iv] They contend that the transition from medicalization to biomedicalization is a the result of major "technoscientific" changes in medicine, in which there is a "shift from enhanced control over external nature to the harnessing and transformation of internal nature" of the body (Clarke et al. 2003:164). Biomedicalization is co-constituted through five interrelated processes: 1) political economic shifts, 2) a focus on health, risk, and surveillance biomedicines, 3) technoscientization, 4) transformations of production, distribution, and consumption of

biomedical knowledges, and 5) the transformation of bodies and identities. The crux of biomedicalization, as Clarke and colleagues write, is that "biomedicine broadly conceived is today being transformed from the inside out through old and new social arrangements that implement biomedical, computer, and information sciences and technologies to intervene in health, illness, healing, the organization of medical care, and how we think about and live 'life itself'" (2010:2). Organ chips, as a technoscientific development, are emblematic of multiple biomedicalization processes, namely political economic shifts in biomedicine, technoscientization, and transformation of knowledge production.

Technoscientization, the third process of biomedicalization, is manifest in three overlapping areas: 1) computerization and data banking; 2) molecularization and geneticization of biomedicine and drug design; and 3) medical technology design, development and distribution. In each of these, biological and biomedical phenomena are being examined using new tools, embedded within which are new ways of knowing, changing assumptions of what types of data are possible to collect, and new visions of what technologies are possible to design, all of which in turn change what it is that we can know. Thus, Clarke and colleagues write that "theorizing these technoscientific transformations of biomedicine requires that their meanings *and* their material forms and practices, including embodied corporeal transformations and manifestations, be conjointly studied and analyzed as co-constitutive" (2010:71). In our recent update (Clarke et al. 2021), we identified additional domains in which technoscientization manifests—data technologies, biomedical technologies used in the clinic and at home, and laboratory technologies—and examine the empirical scholarship that attends to these. This dissertation excavates how organ chips are made possible through technoscientific developments in the late twentieth century alongside the political economic circumstances that allowed them to

be seen not only as technically "doable," but also desirable and valuable biomedical technologies.

Since the publication of Clarke and colleagues' initial analysis of biomedicalization in 2003, allied concepts such as pharmaceuticalization have served to deepen our understanding of different but related processes at hand in twenty-first century biomedicine. Pharmaceuticalization, in particular, is useful for this dissertation because it has attended to the economic and political dimensions and increasing power of the pharmaceutical industry in biomedical research (S.E. Bell and Figert 2015). Pharmaceuticalization (Nichter 1996; Williams, Gabe, and Davis 2008) is the "process by which social, behavioral or bodily conditions are treated, or deemed to be in need of treatment/intervention, with pharmaceuticals by doctors, patients or both" (Abraham 2010, 290). For example, scholars have examined the ever-increasing list of conditions made treatable by pharmacotherapies (Dumit 2012; Fishman 2004; Greene 2007), the emergence of the clinical trial industry (Fisher 2006, 2007, 2009; Petryna 2005), and the construction of an ethics infrastructure for human subjects testing (Stark 2011).

This literature has largely concentrated on the markets and economies produced by the making of treatable diseases and problematized the trend of conceptualizing social problems as individual ones, and in turn, treatable with a pill. Similarly, this literature has also focused on end products—pharmaceuticals—and much less so on the research tools and technical infrastructures needed to conduct pharmaceutical research and development.[v] This dissertation attends to this gap through an exploration of technologies that are poised to become basic tools in pharmaceutical testing infrastructures. As pharmaceutical companies look for ever-more drug markets, they seek technologies and processes that make research and development cheaper and more efficient. Examining how organ chips figure in this quest, then, deepens our understanding

of how these market forces play a role in shaping basic biomedical technologies used in these settings.

Laboratory Studies & Scientific Tools

Laboratory ethnographies are a hallmark of STS scholarship, and have generated foundational knowledge about how scientific practice is thoroughly social (H. Collins 1991 [1985]; Fujimura 1987; Knorr-Cetina 1979, 1981, 1999; Latour and Woolgar 1979; Lynch 1985; Traweek 1988). Laboratory settings, tools, and infrastructures—themselves the products of sociohistorical contexts—shape the construction and negotiation of scientific facts. Critically, this scholarship has brought attention to the social negotiations that occur in scientific spaces, complicating narratives of scientific objectivity and technological determinism (Fujimura 1987). Scholars have documented how scientists come to *see* through their training and the technical and tacit knowledge they acquire (H. Collins 1991 [1985]; Zenzen and Restivo 1982). Only through articulation between sites of scientific work—in laboratories, universities, and broader fields—do scientific problems become doable (Fujimura 1987).

In their volume, Clarke and Fujimura (1992) contend that scientific tools, jobs, and rightness are co-constructed. They highlight that technoscientific advancement is not inevitable, but constructed at each turn among human and non-human actors. This work is as much methodological as it is empirical, calling laboratory studies scholars to attend to the various elements and sites at play. Explaining how to analyze this co-construction, Clarke and Fujimura write:

> What needs to be taken into account in order to understand a situation in which scientific work is being done? ***Everything in the situation,*** broadly conceived. […] The elements of the situation generally include *workplaces* (laboratories or other work sites and their basic infrastructure); *scientists* (including their individual career issues); *other workers* (graduate students, technicians, clerical staff, artists, computer programmers); *theories,*

> *models,* and *other representational entities* (both tacit and explicit); *research materials, instruments, technologies, skills and techniques,* and *work organization* (of the immediate work site, of the larger local administrative unit such as a university or federal agency, and of disciplines and specialties through professional organizations and other means of communication); *sponsorship and its organization* (of both intramural and extramural fiscal support); *regulatory groups* (local, national, and international); and both desired and unintended *audiences and consumers* of the work. (1992, 5, bold emphasis added)

Scholarship in this vein has traced how organisms have become scientific tools (known as model organisms), and how knowledge about basic biological processes and human disease are generated through their use (Creager et al. 2007; Kohler 1994). In particular, the development of model organisms has enabled researchers to transform nature into standardized, manipulable, laboratory tools for studying basic biological processes (Bolman 2021; Kohler 1994; Rader 2004). More recent literature on non-human animal models has shown that animal models come to be understood as "good enough" through social processes of scientific negotiation (Lewis et al. 2012), and how knowledge is transposed and translated between research settings (Friese and Clarke 2012; Shostak 2007). Others have focused not on the translation from model organism to human, but rather on the specific construction of scientific claims made in experimental work. Nelson (Nelson 2013, 2018) for instance has focused on the claims about the capacities of animal models as knowledge generating tools rather than the translational elements of this work.

In the dissertation, I take Clarke and Fujimura's situational approach seriously, systematically analyzing the various elements that bring organ chips into being. I draw on insights from laboratory studies to examine how organ chip researchers build the case for organ chip technologies through their simultaneous downgrading of scientific evidence produced by animal models, and promotion of knowledge produced by engineering advances in cellular technologies. Moreover, I explicitly show how market forces shapes the technical construction of these models.

Research Methods

In this dissertation, I draw on constructivist grounded theory (Charmaz 2014) and situational analysis (Clarke 2005), both qualitative, inductive methodologies that guide data collection and analysis. Constructivist grounded theory encourages ground-up, interpretive analysis and is carried out through iterative data collection and analysis, gathering rich data through interviews and observation, then analyzing by coding, memoing, and returning to the field until theoretical saturation (when additional data collection no longer offers new insights about the situation of inquiry) is reached. Constructivist grounded theory—signaled through the inclusion of "constructivist" in its very name—fundamentally challenges the notion that researchers 'discover' data and theories. Instead Charmaz argues that researchers are an integral part of the research process, and the resulting data and theories that it produces. She claims that researchers "construct our grounded theories through our past and present involvements and interactions with people, perspectives, and research practices" (2006, 10) and thus produce an *interpretive* analysis of the social world.

As a methodology, constructivist grounded theory was well suited for this project because it centers social action and process and allows for multiple forms of qualitative data to be analyzed collectively. In this study, I examine social action happening in scientific social worlds, and use multiple data collection methods to capture the complexity of these worlds and attend to the social processes of scientific work. Just as I elucidate the active participation of actors in bringing organ chips into being, and constructing their rightness, I too am an ever-present actor, constructing and situating my data through my particular lens.

Situational analysis extends constructivist grounded theory in multiple ways, as Clarke puts it, "being pulled by and pushing [it] further around the postmodern turn" (Clarke 2005, 2). Situational analysis offers an approach consonant with constructivist grounded theory that enables researchers to examine discourses, agency, action, structure, imagery, and history (Clarke 2005). Situational analysis draws explicit analytic attention to nonhuman entities (i.e., discursive formations, documents, tools) and the relationships humans may have with them. Situational analysis was well suited for this study because it takes as its unit of analysis the arena in which multiple social worlds come together and interact—here to enable the emergence of organ chips—and attends to the heterogeneity of actions, positions, and power dynamics within and among social worlds.

Organ chips remain nascent, emerging technologies, meaning that their futures are quite uncertain and there were few clear cut "consequences" to point to. Studying technologies in the making presents both strengths and challenges. One strength is that it enables social scientists to have a window into the design and development of technologies in real time, before they become routinized and taken for granted. The processes of claims making are perhaps more visible. During my time in the field, many events occurred that shaped how organ chip researchers pitched their technologies, directed efforts, and imagined futures. For instance, while the Theranos scandal played out in Silicon Valley and later in the courts, it was often referenced in presentations and conversations about ethics in biomedical engineering (Jeske 2020). The scandal hinged on a defunct microfluidic technology, and so it hit close to home (I return to this issue in Chapter 3). I observed how researchers actively distanced themselves from this scandal and how they leveraged it to talk about their own ethics. Later, when COVID-19 hit, organ chip researchers were quick to demonstrate how these technologies could be valuable in pandemic

times. I observed how some researchers galvanized around this moment, eager to show what organ chips could do for future pandemics.

While I do not attempt to evaluate the impacts of these events on organ chip research or researchers, they were noteworthy occurrences to see how public perceptions and framings of future value are managed in order to bring a particular future into vision. Certainly, the emergent nature of these technologies also presented methodological challenges for me: where to draw boundaries about who to "count" as an organ chip researcher as researchers were quickly jumping on the organ chip bandwagon (Fujimura 1988), how long to include new publications that seemingly emerged every week, and how to trace the field that was quickly shifting from the development of these technologies to their application for modeling physiological functioning and diseases. Drawing on insights from field formation literature (Clarke 1998; Frickel 2004; Shostak 2013) and the social worlds approach I deployed, I made the methodological decisions described below.

Data Collection

In this dissertation, I integrate three qualitative methods: 1) ethnographic observation, 2) in-depth, semi-structured interviews, and 3) content analysis. This study was submitted to the UCSF Human Research Protection Program's Institutional Review Board (IRB) and deemed "not human subjects" research.[vi] Despite this designation, I still protect the identities of participants in this study to the extent possible. Any names used to refer to participants or sites in the text are pseudonyms. During data collection for this dissertation, the COVID-19 pandemic hit. Consequently, I needed to halt in-person data collection in March 2020. This methods section is thus arranged in two parts. First, I describe the methods used in the first three empirical chapters dissertation (Chapters 2, 3, and 4). I then briefly describe the methodological

implications of COVID-19 for this dissertation, and my decision to launch a supplemental study, the Disruptions to Laboratory Life (DLL) Study, that could be safely conducted using remote methods. I describe the methods I used in the DLL study, which provides the dataset for the analysis presented in Chapter 5.

In-depth interviews

I conducted 30 in-depth interviews with principal investigators, research staff, trainees, and other stakeholders involved in the production of organ chips. Through interviews, I explored how actors designed their technologies, thought about the value of organ chips, navigated industry-academic boundaries, and their experiences working in academic biomedical engineering. I conducted these interviews throughout my observations as well as after, and when possible, I used the interviews to explore themes that emerged during my observations.

To be eligible for interviews, participants needed to be principal investigators or laboratory staff (e.g., research scientists, lab technicians, postdoctoral researchers, graduate students) working in organ chip laboratories or stakeholders involved in the development of organ chips. I identified an initial set of eligible participants based on the NCATS Tissue Chip Program awards. These researchers were early organ chip developers, and I had hoped to get a sense of the development of the field from them. Many of these researchers did not grant my requests for interviews (only four investigators from the original eleven groups consented to be interviewed), and as such I expanded to reach out to organ chip researchers I observed at events and whose publications I came across during my document analysis. I was also introduced to some participants through academic networks.

When recruiting, I sent emails that described the project and invited researchers to participate. If they were willing, we then scheduled an interview time and I sent an informational sheet about the project. When feasible, these interviews were conducted in person, the rest were conducted over video or phone. In the laboratories I observed, I conducted multiple interviews with the principal investigators of the labs, along with informal conversations. When I was conducting in-person observations in laboratories, I did not send formal email interview requests. In these instances, I asked researchers working in the laboratories if they had time to talk with me during my observation periods and made their availability the priority. In most of these cases, I recorded interviews and transcribed them for analysis. Some interviews were not recorded because we were in lab settings where it was inappropriate to record, or because the interviewee asked to not be recorded; in those instances, I took detailed notes during and following the interviews.

Ethnographic Observation

I conducted over 200 hours of ethnographic observations over a three-year period. These observations consisted of both in-person (prior to the pandemic) and virtual observations. My ethnographic observations brought me into the myriad spaces where organ chips are created and also where they are put on display. These spaces, from laboratory benches to podiums in crowded conference halls, require continual claims making. The types of claims that are made in these spaces vary, but they are all critical for constructing organ chips as the right tools for particular jobs. Altogether, I conducted observations in laboratories, educational settings, and at conferences and symposium.

Laboratory ethnography is a longstanding tradition in STS as discussed above. Extended period studying laboratory life provides a window to the day-to-day operations, the mundane, daily grind of work to construct scientific knowledge and technologies. It was in these spaces that I observed tinkering (Knorr-Cetina 1979), problem solving and troubleshooting, articulation tasks (Fujimura 1987), and optimizing of technologies. When seeking laboratories for observation, I navigated entrée by conducting interviews with the PI of the laboratory. In these cases, I used a portion of our interview to ask questions about the size and flow of their lab (e.g. the number of collaborators and post docs, graduate students, and other trainees), and how the organ chip project(s) fit into their overall research program as a way to determine if it may be a generative site for observation. If principal investigators were willing to consider observations, I sent them a project overview and description of what I was interested in observing. While I originally planned to conduct a longer period of observations in two laboratories, this was altered due to the pandemic. I conducted ethnography in one laboratory at Valley University, over a four-month period. During my time at Valley University, I typically went to the lab a few days per week, one of which included the weekly lab meeting day. During these visits, I also conducted formal and informal interviews with lab members. Additionally, I conducted what I call short site visits at two other laboratories where organ chip technologies were being developed. One visit was just an afternoon, and the other visit was a week-long stay in the laboratory.

I also conducted observations in two training settings. The first was a semester-long undergraduate bioengineering course in which students learned how to design, manufacture, and test microfluidic devices and nanoplasmonic biosensors for medical and biological applications. This course was delivered at a large public university with a highly ranked bioengineering

department and was geared toward advanced undergraduate bioengineering majors. I received permission to audit the course from the instructor, and received laboratory safety training from the lab manager of the classroom laboratory space. I observed weekly lectures as well as lab sessions. Students taking this course were divided into project teams, and each team collectively pitched a technology to develop over the semester. Over the course of fifteen weeks, they designed, fabricated, and tested their devices. The semester ended with team presentations.

As an observer, I was not on any of the student teams, but I attended lab sessions with them as they developed their projects and learned the techniques for fabricating devices. Observing this course provided critical contextual information about the construction of these technologies, information that enabled me to understand more of what I was seeing in laboratory ethnography and hearing in interviews. I often had informal conversations with students during their lab sessions, and had many conversations with the graduate student instructor who was in charge of the lab sessions I attended.

The second training setting I observed was a quarter-long course on ethics and the responsible conduct of research, a required course for graduate students and postdoctoral scholars who are funded by the NIH. Based on the extensive interfacing between academic researchers and industry representatives I observed in the conference observations and understanding the relations of many investigators I interviewed, I was curious to understand how junior researchers were socialized in this landscape and what they learned about research conduct. I attended this course at a large public university. The weekly sessions covered topics including scientific misconduct, record keeping and data management, human subjects, animal welfare, publication practices, conflicts of interest, and mentorship.

I also observed over 25 scientific conferences, research symposium, and webinar events. Scientific meetings and presentations offer insight into how technologies are presented outwardly in public settings to varied audiences. Given the nature of bureaucratized 'big science,' in which national and transnational teams work collectively on research projects, even prior to the pandemic many events I attended were virtual. Often talks happening physically in one geographic location were livestreamed for interested researchers elsewhere. Virtual conferences and research talks provide a way for communities of researchers who are located across the world to meet and disseminate research. Prior to the pandemic, these observations also included in-person events that ranged from large disciplinary conferences to more niche organ-chip focused conferences. In-person conferences were typically multiple days long (ranging from two to four days in duration). Though academic conferences, some of these conferences were held in high-end resorts in vacation-worthy locations. I registered for all these events as a member of the public, using my student affiliation at UCSF, and paid any associated fees with attendance using research funds. Emblematic of the industry involvement in conference settings, following my participation in these events I would often get emails and phone calls from biotechnology companies asking if I wanted to talk further about using these technologies in my own work, effectively asking if I was interested in becoming a customer. In these cases, I explained that I was a sociologist studying these technologies and was not interested in purchasing them.

During observations across these spaces, I took detailed fieldnotes. Sometimes these were initially taken by hand (particularly when in the lab and classes) and other times, when appropriate, using my laptop. Handwritten fieldnotes were later typed up. I took extensive notes on the setting of the event, the actors present in the space (e.g., lab members, students, audience

members), and the content of the material being presented. Nearly all conferences I observed were a blend of academic researchers, government funding agency representatives, and pharmaceutical and biotechnology industry members. When I could discern this information, I took notes about it.

Each of the settings offered different kinds of insights about organ chips that were useful for my analysis, and in the empirical chapters that follow, my observations across these spaces are woven throughout. Being in the field for an extended period of time profoundly shaped the questions I ended up pursuing in this dissertation. For instance, observing how common industry relations were and how they were discussed opened up new questions for me about the political economy of the biomedical research. Hearing claims about the rightness of organ chips and the problems they could solve made me attentive to the importance of hyping work and how this varied given the audience. Simply put, observations offered a window into critical elements of the situation that I would not have known to probe without having spent time in the physical and virtual spaces that academic biomedical engineers inhabit. Since leaving the field formally, I have continued to attend virtual events to keep my finger on new happenings. Observations during this time have been conducted in the same way as during formal fieldwork, wherein detailed fieldnotes are taken during observations. Some data from this period is included in the dissertation.

Content Analysis

I analyzed a broad set of documents and media that spanned three categories: scientific publications, policy and regulatory documents, and media representation. I had initially intended to do a review of the universe of organ chip publications, but due to the extensive expansion of

research in this area, this quickly became unmanageable. Therefore, I used the NCATS Tissue Chip Program awardees to identify an initial set of publications, and I used this group of papers to do forward and backward citational analysis, that is, tracing how papers were cited moving forward in time, as well as the previous works listed in those papers' citations. I also relied on disciplinary journals, as well as review articles and pieces assessing the state of the field written by respected researchers in the field (Frickel 2004). Often these articles recapped researchers' accounts of major accomplishments, offered descriptions of foundational theories and building blocks that made recent advances possible, and paid tribute to individual scientists and researchers who shaped the knowledge field. Taken together, the scientific documents I analyzed (n=150) helped elucidate the construction of organ chip technologies as well as to chart the broader landscape of the knowledge field in which organ chip research is published.

While I initially planned to analyze policy and regulatory documents only in relation to organ chips, the questions pursued in Chapter 2 led me to expand this analysis to conduct a selective historical analysis of translational priorities in biomedicine (Clarke 2005; Shim 2014). I therefore analyzed policy and regulatory documents published between 1990 and 2019 by US health-related government institutions (n=40). As with scientific publications, I identified key documents, and used these to work backward and forward in time to trace other documents involved in discussions of translational priorities, and to elucidate connections between translational research and organ chips.

Finally, media representations were an important site of analysis for this project because they reflect and also co-constitute the discourses that motivated the shift toward translational research and also the hype surrounding organ chips. Article headlines, such as those that open Chapter 3, point to just a few examples of how scientific and popular media play a role in the

hyping of emergent technologies. This was a convenience sample, comprised of media items that researchers in the field mentioned to me in interviews or were discussed in observations, as well as things that I came across on my own. In addition to online and print media articles (n=15), I also included radio segments that discussed organ chips and invited organ chip researchers. In these cases, I had audio segments transcribed and used the transcriptions for analysis (n=5).

Data Analysis

Both grounded theory and situational analysis are characterized by flexible, iterative, inductive approaches to data collection and analysis. Procedurally, this means that data collection and analysis take place simultaneously. As observation and interview data are collected and analyzed, that interview questions, participant selection, and selection of observation events were modified in order to clarify initial findings and to elicit new insights. Iterative memoing enabled me to move between data collection and coding of data, and to pick up on patterns and concepts as they emerge in the data, and to identify ways to follow these threads.

I coded fieldnotes, interview and radio transcriptions, and documents, using Dedoose, a qualitative research software. In this method, codes, or meaningful labels, are assigned to segments of data. Using grounded theory principles, I conducted open coding followed by focused coding. In grounded theory, coding is the "pivotal link" (Charmaz 2006, 46) between data collection and developing analysis, and is the process in which researchers define what is happening in the data and begin to analyze what it means. I conducted open coding through a close reading of the data and labeled segments of data with "codes." The open coding process is unstructured: there are not set codes or limits to what codes can be. Instead, I remained open to theoretical possibilities. I used the codes generated during open coding to create a set of focused

codes, which followed the most salient themes in the data. I organized these codes into categories or "families" that coalesce around a particular theme. Codes were constructed so that they captured heterogeneity of a given quality, rather than applying specific codes for positive or negative valences (or discrete categories). I did this to focus on the social processes rather than the outcome. Analysis memos were written throughout the research process. Often following interviews and observations, I would make voice recordings on my phone to capture new analytic insights. I used these to then write analytic memos. These analysis memos helped to identify findings as they emerged from the data and to adjust interview questions, attend to new hunches, and build larger classes of codes. These larger classes of codes, or categories, grouped codes around themes.

Following situational analysis (Clarke 2005; Clarke et al. 2017), I created positional and social worlds/arenas maps as "analytic exercises" (Clarke 2005, 83) to better understand the empirical situation at hand. Situational maps visually lay out the human and nonhuman, discursive, historical, cultural, political, and symbolic elements in a given research situation. Social worlds/arenas maps lay out the collective actors and discursive arenas. Arenas may contain multiple social worlds in them, and emerge where social worlds meet. Social worlds and arenas are concerned with meso-level action, structures, and discourses. Thus social worlds/arenas maps include not only individual actors who participate as individuals and members of social worlds, but also the practices, collectivities, and discourses produced that circulate in and among social worlds. Positional maps lay out positions taken (and, importantly, not taken) by individual and collective actors along particular "axes of variation and difference, focus, and controversy" found in the situation (Clarke 2005:xxxv). These mapping exercises

were utilized throughout data analysis, as a productive strategy to clarify positions and to articulate the actions, actors and actants (including non-human) at play.

Methods for the Disruptions to Laboratory Life (DLL) Study

Chapter 5 takes the form of a standalone journal article based on the separate DLL Study dataset and is forthcoming at *Science, Technology & Human Values.* When the pandemic hit, I needed to stop in-person data collection and rethink my strategy for how I would conclude data collection efforts for the dissertation. Given my time conducting observations in laboratories, I knew that the nature of laboratory life would be hard to navigate with pandemic restrictions. Laboratories are spaces where the hustle of bustle of work means crowded spaces: workers are constantly running around to share equipment, and leaning over microscopes and computers together. While many academic labs shut down for short times in the early days of the pandemic, labs largely resumed limited in-person work for six to eight weeks after the onset of the pandemic, long before vaccines were available for workers, and when guidelines for safety were still "in development." I was curious about how my interlocuters were navigating this challenging time, and from anecdotal reports I knew that the shutdown had felt chaotic to many laboratory workers. I decided to supplement my main dissertation study with an empirical, interview-based investigation of how COVID-19 disruptions changed the nature of laboratory work, and how the pandemic impacted laboratory workers. I was granted ethics approval from the UCSF IRB (#20-31573).

Semi-structured, in-depth interviews were conducted with biomedical research trainees (advanced doctoral students and postdocs) who spent 70% or more of their daily work time (pre-pandemic) at the bench, over an eight-month time period. Initial interviews (T1, n=39) were

conducted in September-October 2020, approximately six months into the pandemic. Follow-up interviews (T2, n=36) were conducted in February-March 2021, approximately six months following the first interview, and eleven months following widespread shutdowns. Biomedical trainees represented multiple disciplines within biomedicine, and were at a range of universities and research institutes with high research activity in the United States (often referred to as R1 institutions).

T1 interviews ranged from 45-90 minutes, and asked about trainees' background and training, COVID-19 disruptions and consequences for their research projects, work experiences during the pandemic, mental health and wellbeing, and reflections on their role in science, future plans, and career goals. T2 interviews ranged from 30-75 minutes, and followed up on each of the areas discussed in T1 interviews, gathering information on how laboratory work progressed between T1 and T2, new challenges and experiences, and reflections on their work and future plans. All interviews were audio recorded and transcribed for analysis. I wrote analytic memos for each interview, following both T1 and T2 interviews. All transcripts and memos were imported into MAXQDA for analysis. Analysis procedures followed constructivist grounded theory practice outlined above (Charmaz 2014). Further details on data collection and analysis are presented in Chapter 5.

"I'll give you my blood!": Navigating the Social Arena of Organ Chip Research

The underlying epistemological commitments of this dissertation embrace that researchers are not detached, neutral observers, but instead that our subjectivities are part of our analyses. As researchers, we come to our empirical sites and research questions as people who have been shaped by the social worlds around us, and our positionality inevitably shapes the

research we produce, as well as how we enter and are accepted (or not) in the social worlds we study. This means that the analysis presented in this dissertation is necessarily situated and partial, and it presents the "view from here" (Haraway 1988).

When I embarked on interviews and fieldwork, my UCSF affiliation provided key capital for gaining entrée. UCSF is well known in the biomedical research arena, and in some ways I felt that when I spoke with researchers, I was treated as if I was already "one of them" and part of their scientific community. Additionally, biomedical engineers at UCSF helped to make connections with organ chip researchers in their social circles and alerted me to observation opportunities. This affiliation likely made entrée much easier than it otherwise would have been, and even with it, I still found it hard to gain entrée in the broader organ chip arena.

My role as a social scientist was often opaque to the researchers I interviewed and observed; many put me in a science communications or journalism bucket. In the labs that I observed, some staff members equated themselves to "mice" or "cells" when trying to situate me, using their own work on their own objects of study as a metaphor for what they understood I was trying to do, in relation to them and to their own ways of doing research. I recall on one occasion at Valley University, a postdoc asked me how my observations were going and whether I was getting what I needed. She said that the lab members had been talking about me, and trying to understand what it was I was doing. After a bit of back and forth, she exclaimed, "We're like your cell samples!" I was amused by this and generally agreed.

Through ethnography, I also became very aware of the labor that my presence in this space required. While I had not felt particularly extractive during initial interviews with principal investigators, when I began ethnography in the spaces where research staff, postdoctoral trainees, and graduate students worked, I began to notice this. And even then, it was not until after I

conducted the Disruptions to Laboratory Life study during the pandemic that I grappled with its extent (as I discuss further in the Preamble to Chapter 5). In general, principal investigators were the ones who granted my access to their laboratories, but it was the research staff—staff scientists, lab managers, postdocs, and graduate students—who were the ones who managed my presence there. They were the ones I interacted most with, following them around in their days, observing their experimental work, asking incessant questions. I recall an experience early on in my fieldwork, when I learned that some of the samples used in one particular lab came were acquired through blood donations from lab members. They would, quite literally, go to another lab, have their blood drawn, and then bring it back for their research. I was elated to learn this, and perhaps a little too inquisitive as it sparked extensive discussions about their ethics approval to do so. But without thinking much about it, I excitedly volunteered. With a big smile I interjected, "I'll give you my blood! Do you need me to donate?" While we all chuckled, I realized that my eagerness to do something I had no desire to actually do was rooted in my wanting to give back to my participants. They were providing so much for me, and I was doing nothing for them in return. On that particular day, my blood was not needed. While I never ended up donating blood in that lab or others, this experience was important in my own recognition of my place, and the burden of my presence, in this space.

Finally, my position as a white woman also shaped my experiences navigating the social worlds of organ chip research. While gender disparities in science, technology, math and engineering (STEM) are widely recognized (Valantine 2017), biomedical engineering is a field in which there is substantially higher representation of women (Gutierrez et al. 2017). While gender parity has not been achieved, women make up about 40% of biomedical engineering degree recipients at the bachelor's and master's level and 38% of recipients at the doctorate

level. (Unlike gender, representation of "minority" racial and ethnic groups in biomedical engineering are substantially worse than other engineering disciplines. In general, engineering as a field remains quite homogenous (Chesler 2019).) I was most aware of the gender gap when conducting interviews with principal investigators, who were more senior researchers and tended to be men. Similarly, at conferences, those giving podium presentations tended to be leaders of the lab, and thus while their laboratory groups may have been more diverse, the laboratory leadership was largely a homogenous group. In the laboratory spaces I observed, as well as outlets where trainees and junior researchers to present work (such as poster sessions), there were many women.

OVERVIEW OF THE DISSERTATION

A central theme of this dissertation is examining how biomedical technologies become collectively understood as useful and valuable. I am concerned with the politics that undergird investment in particular types of technologies and streams of research, especially when they are in their infancy, and how researchers and developers actively construct technological futures. I explore different dimensions of these issues throughout the dissertation.

In Chapter 2, I trace the construction of the "translational crisis" in biomedicine. This chapter examines the social construction of the 'job' that organ chips come to be seen as a (but not the only) right tool for. I argue that this particular discursive framing of both the "crisis" and the proposed solutions provide critical social context for understanding the emergence of organ chips as a key tool for solving certain translational problems. Drawing primarily on document analysis, the chapter begins with an analysis of the framing of "translation" as an acute problem in biomedical research, and excavates what is framed as its causes, consequences, and potential

strategies to ameliorate them. I then turn to the infrastructure building work conducted in the service of these solutions, elucidating how industry has become an integral—and desirable—partner in solving the translational crisis. I argue that the hype surrounding the translational crisis fueled and legitimized the establishment of national centers, federal and local funding streams, and training programs geared toward breaking down boundaries between academic research and industry, encouraging an ethos that pushes academic biomedical researchers to always already be thinking about the commercial potential (i.e., anticipating the translational value) of their scientific work. I then turn to the consequences of this shift for the governance of conflicts of interest, contending that under translational values, the very meaning of "conflict" has shifted.

In Chapter 3, I analyze how organ chips researchers and funders position organ chips as 'the right tool' (Clarke and Fujimura 1992) for solving a key aspect of the translational crisis: the high rates of failure when moving from non-human animal models to human clinical studies. Often accounts of becoming the right tool have a certain historical nature, wherein the object of analysis has indeed become the right tool—adopted, accepted, and its rightness and utility taken for granted (Bolman 2021; Cowan 1985). This chapter offers a different story, one that is unfolding and in progress. The first part of the chapter analyses the sociotechnical conditions of possibility for organ chips to become both technologically possible, or 'doable' (Fujimura 1987). I then turn to the social arena in which organ chips emerge, showing how state and industry actors place a central role in positioning organ chips as doable and right. While much scholarship has shown how individual researchers navigate multiple levels of articulation—the experiment, laboratory, and field—to render scientific problems doable and worthy of investment, I show how this also happens in more "top down" ways and is influenced by state and industry actors. Later in Chapter 3, I turn to the critical role of *hyping* in the construction of doability and

rightness. I show how the nature and function of hyping work varies. Depending on audience and goal, hyping entails generalized claims of the disruptive and performative potential of organ chips as well as claims of technical legitimation and superiority. Finally, I turn to the challenge that regulation poses for organ chips. I argue that in heavily regulated spaces standardization emerges as a key part of achieving rightness.

Chapter 4 draws on STS scholarship on model organisms and model construction. I bring the reader "into the lab" to investigate the social nature of scientific decision making and the construction of organ chips. I begin with a discussion of how model organisms are used in biomedical research, and how building the case for organ chips requires first generating skepticism about the accuracy of model organisms for predicting human response. I then detail how organ chips are made, highlighting the role of state actors in shaping design choices. I focus on the issue of cell sourcing to show how researchers use varying cell types—primary donor cells, induced pluripotent stem (IPS) cells, and cell lines—to produce different kinds of knowledge using organ chips. Organ chip researchers choose cell types based on their research questions and decisions about the competing tradeoffs, between physiological relevance, reproducibility, and scaling, that are necessary, worth the compromise, and preserve their potential market value. Then, using two cases, the lung chip and Evatar (the female reproductive system on a chip), I show how organ chips come to be collectively understood as "human enough" by researchers and others working in this arena, as well as how market forces shape the technical design of organ chips. The shaping power of market forces takes a different form in the lung and Evatar examples. For the lung, market forces result in the creation of a standard device that can be used not only to model the lung, but several different organs. For Evatar, market

forces result in the inclusion of the liver in the model in order to harness the potential for pharmaceuticals.

Chapter 5 is a product of the COVID-19 pandemic. Here I shift focus to attend to the ways COVID-19 disrupted laboratory life. I begin with a brief preamble that offers reflections on my pivot to study the ways in which COVID-19 impacted laboratory environments. I describe why and how I decided to launch the Disruptions to Laboratory Life Study, and offer reflections on my experience conducting this study and writing the chapter. The remainder of Chapter 5 is the article that is forthcoming in *Science, Technology & Human Values*. Drawing on interviews with biomedical research trainees, Chapter 5 demonstrates how laboratory life during the pandemic was marked by emergent stratifications and inequities in access to sufficient lab time, increased stress around productivity, and frustrations with the culture of academic science. I show how the loss of social interaction, and the ensuing lonely scientific struggles, made visible the importance of sociality in science for workers. Finally, I contend that pandemic disruptions not amplified and exacerbated existing social inequities in lab settings, but also resulted in workers' estrangement from science itself.

While the dataset Chapter 5 relies on is separate from the main dissertation, it is informed by the work I conducted throughout the dissertation. There, I bring together literatures on the institutional pressures that have come to mark twenty-first century academic science in the US: academic capitalism, bureaucratization, and neoliberalism. While these have largely been described at the macro level, describing broad trends in the academy, I build on this literature by linking these transformative, structural pressures to the day-to-day experiences of laboratory workers. I foreground the experiences of those in lower-status positions in academic science, and

show how the exogenous shock of the pandemic, in many ways, exacerbated the conditions of their estrangement that had long been bubbling under the surface.

I conclude the dissertation by summarizing the findings and theoretical contributions of this work. I discuss plans for future work and offer reflections on the process of studying an emerging technology.

CHAPTER 2: A "CRISIS" OF TRANSLATION

Introducing the keynote speaker (a senior biomedical engineer at a prominent research institution in the Midwest) a former student speaks of his mentor's success. Effusively, he describes his mentor's commitment to lifelong learning, mentoring, and effecting change. His career, the audience is told, is marked not only by an impressive publication record, but also several successful patents and start-ups. On the screen behind the two men, we see the title slide. Listed at the bottom, under "disclosure" are five biotech firms. The speaker describes these disclosures—which have historically been understood to be conflicts of interest—instead as "ventures" that prove that he has been committed to actively getting his work "out there," beyond the walls of academia.

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At an evening session about commercialization, an audience member asked panelists why they decided to commercialize the technologies being developed in their laboratories. A senior biomedical engineer at a prominent research institution on the West Coast with multiple successful start-ups and spin-offs, answers: "We're spending all this federal money to have things that only we [academic laboratories] would have [access to] – instead, I see this as a way for my technologies to have a larger impact."

(From fieldnotes of two separate observations at a 2018 biomedical engineering conference)

Introduction

Scenes like this—moments in which academic researchers embraced and celebrated the commercialization of their laboratory developments—were commonplace throughout my ethnography. These moments highlight how academic biomedical engineers are navigating a situation in which the boundaries between academic research, industry, and entrepreneurialism have blurred, and exemplify how commercialization has become a valued part of what it means to be successful and even *responsible* academic biomedical researchers in the United States (US). At most of the conferences that I observed, nearly all presenters, who held academic appointments in a wide range of biomedical fields such as biomedical engineering, pharmacology, oncology, internal medicine, and toxicology (among many others), had at least

one and many had multiple conflicts of interest to report. Yet these were rarely viewed as jeopardizing the integrity of their research or even in an unfavorable light.[i]

How is it that activities that once were understood as conflicts of interest and therefore cause for concern, are now seemingly valued and viewed as markers of success in academic biomedicine? In this chapter, I show how a "crisis" of translation (between bench research and patient bedsides) has been discursively constructed, in ways that create spaces in academic biomedicine where industry involvement and the commercialization of science on the one hand, and the integrity of academic science on the other—once competing priorities—are no longer seen as such. As a result, commercial conflicts of interest have paradoxically become celebrated indicators of academic capital. This shift has been gradual: science and technology studies (STS) scholars have shown that since the 1970s industry involvement in academic research and academic entrepreneurship has increased (Berman 2012b; Etzkowitz 1989, 2001; Stuart and Ding 2006; Rasmussen 2014). Such scholarship highlights how norms in academic science have changed in the sense that they have become more accepting of industry involvement, particularly in fields related to the biomedical sciences and biotechnology development. Others have shown that academic science has taken on many characteristics of industry research and development so much so that the current era of academic research has been termed "academic capitalism" (Hackett 1990, 2005; D.L. Kleinman and Vallas 2001; Lee and Walsh 2021). And indeed, as I witnessed time and again in my ethnography, commercialization of academic biomedical engineers' discoveries signaled success for and commitment to solving translational bottlenecks.

Through an analysis of the discursive construction of the *crisis of translation* at the turn of the twenty-first century, this chapter attends to the new logics, values, and practices that have emerged in its wake. How problems are framed and discursively constructed matters, at least in

part because their particular construction leads to the type of interventions that are seen as possibilities (Conrad and Barker 2010; Jeske 2021b; Shostak 2013). This chapter primarily draws on examination of federal health agency documents such as strategic plans, mission statements and charters, annual reports, position statements, and funding announcements, as well as published scientific journal articles and editorials on translational medicine published between 1990-2020. Such agenda-setting documents—such as strategic plans, institute establishment charters, annual reports, funding announcements—are important not only because they outline potential formations of these relations, but because they guide and legitimize the infrastructures that support them. Specifically, I was interested in understanding how issues of commercialization, relationships with industry, and the role of industry as a stakeholder in translational research efforts and programs were discussed in these documents.

I begin this chapter with an analysis of the framing of "translation" as a crisis in biomedical research, excavating what is framed as its causes and potential solutions. I then attend to the ways in which translational medicine advocates built a new infrastructure in the service of these solutions, elucidating how industry has become an integral—and desirable—partner in solving the translational crisis. I document how hype surrounding translation has led to the establishment of national centers, federal and local funding streams, and training programs that are geared toward breaking down boundaries between academic research and industry, encouraging an ethos that pushes academic biomedical researchers to always already be thinking about the commercial potential (i.e., anticipating the translational value) of their scientific work. I argue that the proposed solutions to the translation crisis instill industry values as a central part of what it means to do successful, efficient, and effective biomedical research, contesting previous ideas about the appropriate and *separate* role of industry in academic science. I close

the chapter by attending to new issues these findings raise, particularly concerning the governance of conflicts of interest and the public interest. In sum, this chapter provides critical social context for understanding the emergence of organ chips as a key means to address the translational crisis in biomedical research.

Constructing the Crisis of Translation

In the decades since the invention of recombinant DNA technology in the mid 1970s, the early development of tissue engineering in the 1980s, and the mapping of the human genome in the 1990s—just to name a few—investment in biotechnology and biocapital has boomed, and these advancements have profoundly shaped what we imagine biomedicine can and should achieve (Clarke et al. 2003; Clarke et al. 2021; Rajan 2006). The potential for hedging disease risk, growing (and later, bioprinting) artificial tissue and organs, and developing personalized therapeutics through precision medicine have boasted great promise for what the future of biomedicine *might* hold. Seeing these great advances, many believed such discoveries would result in the prompt translation of bench-side discoveries to bedside, or market, applications. At the outset of this period of rapid biotechnology innovation in the 1970s and early 1980s, recognizing the potential for academic researchers and institutions, then-President of Yale University, Angelo Giamatti, wrote of the promise of linking scientific concepts to application:

> In this century, the time lag between the creation of a new scientific concept and its general application is usually measured in decades. Occasionally, however, the gap is compressed as a new theoretical insight moves swiftly to the stage of application, and hence of wide practical dissemination. We are now in the throes of such a movement. (Giamatti 1982, 1278)

Indeed, there was a real sense that things were different particularly in new fields like bioengineering and biotechnology, and that these scientific advances both required and

contributed to changes in the relations between academic researchers and industry. Yet, as has been well documented, promissory language like this has fueled widespread anticipation and hype around biotechnological advances, where the public is primed for promises that biomedicine often ultimately leaves unfulfilled (Adams, Murphy, and Clarke 2009; Kenney and Mamo 2020; Thompson 2013). The development of technologies to visualize and *know* the body in deeper, more molecular ways enabled more and new kinds of information to proliferate; however, an inability to translate this knowledge into effective therapies in humans persists (Marincola 2003b; Zerhouni 2003). Thus, following the doubling of the National Institutes of Health (NIH) budget that occurred from 1998-2003, questions were raised as to what successes the biomedical research community had to show for it. Where, and *what*, was the return on this vast public investment?

Since the late 1990s, this refrain and concern about biomedical researchers' inability to bridge the gap from basic research to bedside therapies was repeated by prominent leaders at the NIH and the Food and Drug Administration (FDA), as well as researchers in the broader scientific community. The NIH estimates that 30% of new, promising pharmaceuticals shown to be effective in pre-clinical, animal studies fail in human clinical trials because they are found to be toxic in humans. An additional 60% fail in clinical trials because they are not effective in humans (NCATS 2011). Thus, taken together, around 90% of novel drugs effective in mice and other non-human animals are ultimately deemed unsuitable for use in humans (Mak, Evaniew, and Ghert 2014; Marincola 2003a). This chasm between translating laboratory bench success to products proven effective in human clinical trials is often referred to as the "valley of death," so coined by past NIH Director Elias Zerhouni in 2003. As Figure 2.1 depicts, the "valley of death" is imagined a deep and dangerous valley, where bench scientists are on one side of the chasm,

and clinicians and their patients are on the other. Bench scientists and clinicians are linked by a rickety bridge desperately in need of repair. Along the floor of the valley is a skeleton, perhaps representing the patients who died waiting for therapies to reach them or the potential therapeutics that unsuccessfully tried to walk the bridge.

Figure 2.1: Depiction of the "Valley of Death." Source: Declan Butler (2008) in Nature

Translating basic research to applied bedside therapies and tools is not a new problem; scholars have shown that efforts to address translational problems have been happening at since at least the mid-twentieth century, for example, in cancer research at the National Cancer Institute (Aviles 2018). However, hype surrounding the purported valley of death in pharmaceutical and medical device development ignited new efforts beginning in the early 2000s to fund translational research itself, including its institutionalization as a priority in federal health research (Robinson 2019; Solomon 2015).[ii] In 2003, then NIH Director Elias Zerhouni launched the "NIH Roadmap" which included a number of initiatives to explicitly fund translational research. Similarly, in 2004, the FDA released a report titled *Innovation/Stagnation: Challenge*

and Opportunity on the Critical Path to New Medical Products (hereafter referred to as the "Innovation/Stagnation Report"), which launched their Critical Path Initiative. The Critical Path Initiative is the FDA's national strategy aimed at "transforming the way FDA-regulated medical products are developed, evaluated, and manufactured" (FDA n.d.-a) . In the Innovation/Stagnation Report, the FDA wrote that the translational crisis centers on the poor "yield" of the "inefficient" and "costly" product development pipeline:

> New basic science discoveries that have been made in recent years may not quickly yield more effective, more affordable, and safe medical products for patients. This is because the current medical product development path is becoming increasingly challenging, inefficient, and costly. […] If the costs and difficulties of medical product development continue to climb, innovation will continue to stagnate or decline, and the biomedical revolution may not deliver on its promise of better health. (FDA 2004, i)

Later, they noted that "many accomplished scientists in academia, government, and industry are working on these challenges," but that the "fact remains that the pace of [product] development work has not kept up with the rapid advances in product discovery" (ibid., iii).

Indeed, documents like this position translation as such a fundamental problem embedded within the very infrastructure of academic biomedical research, that a whole new field—that of translational medicine—and a new set of actors and practices were deemed necessary to attend to the constituent causes of the "valley of death." In general, translational medicine and its allied fields are concerned with solving the problems that inhibit discoveries made in basic biomedical research from making it to the frontlines of health care delivery in the form of pharmaceutical development, diagnostic devices, as well as community health interventions and prevention programs (Solomon 2015). A number of terms have been used to label the emergent field that seeks to tackle this issue of "translation:" translational medicine, translational science, and clinical translation among others.

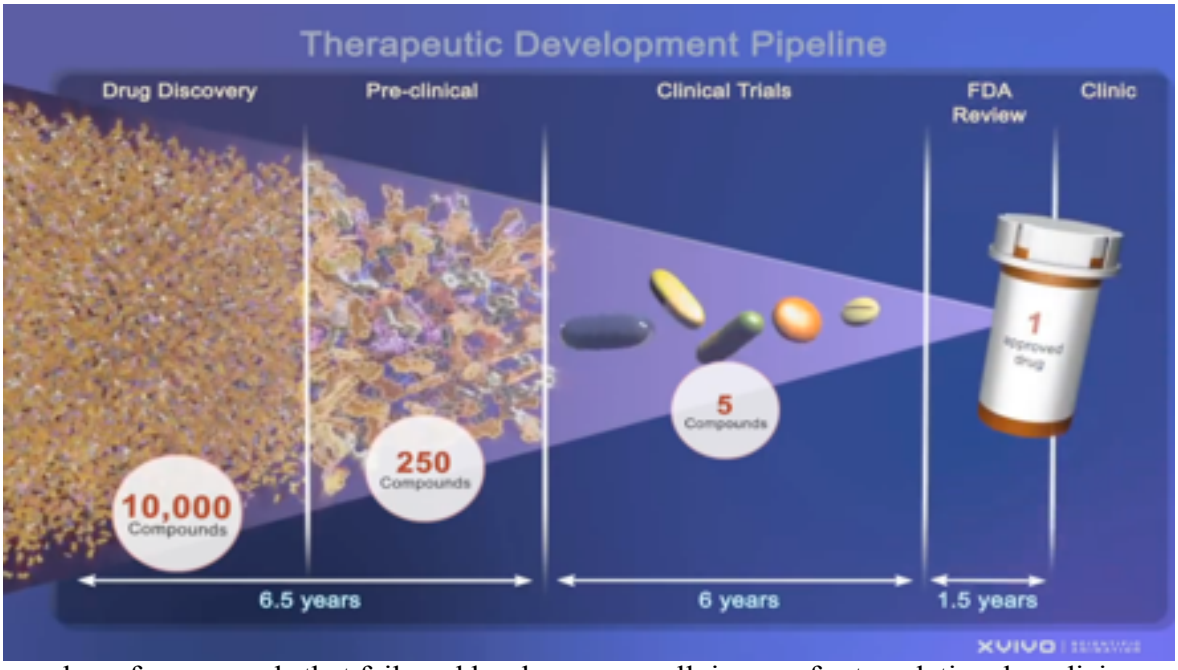
One area where this construction of the crisis of translation and the attendant solutions of translational medicine was particularly ubiquitous was in organ chip research and development. Images and representations like Figure 2.1 (also Figure 2.2 described below) often were leveraged at the beginning of organ chip presentations and figures estimating pharmaceutical development timelines and cost projections were cited to open organ chip publications, emphasizing the problem that translational medicine is here to solve. Often images of rodents were placed alongside images of pharmaceuticals and piles of money, with commentary on the high rates of failure when moving from non-human animal models to human models. For instance, at a webinar I observed, one slide featured four images: petri dishes, pills, a mouse, and US dollars. The slide included the following bullets:

- *Cost to develop and approve a new drug >$3 billion*
- *Animal studies take years to complete*
- *Innumerable animal lives are lost*
- *>70% don't predict clinical responses!*

Slides like this were routinely used to underscore the severity of the translational crisis and positioning organ chips as a key technology that could intervene. Throughout my time in the field such rationales were *always* present (as I discuss further in Chapter 3), and audience members often nodded in agreement; that is, the translational crisis was never contested.

Similarly, across scientific publications, strategic plans and state reports, the prevailing framing of translation situates the high costs and high rates of failure associated with crossing the "valley of death" as the result of an inefficient research-to-market pipeline. In this framing, the inability to effectively translate is discussed in economic terms as a poor return on investments:

billions of dollars are being invested in a rather inefficient and ineffective research infrastructure (Mankoff et al. 2004; Mak, Evaniew, and Ghert 2014). The indications of this inefficiency include the estimated 10-15 years to bring a new drug to market, and the $2.6 billion it costs to do so given high rates of failure (PhRMA 2016). The economic framing underscores how the consequences of a leaky and slow translational pipeline are measurable not only in terms of dollar costs, but also in terms of time. Figure 2.2 below depicts the long, arduous timeline and



number of compounds that fail, and has become a rallying cry for translational medicine advocates.

Figure 2.2: Therapeutic Development Pipeline. Source: NIH Director's Blog 2013.

Figure 2.2 and others similar to it are commonplace in translational medicine documents and in presentations I observed. Figure 2.2 analogues are typically animated in presentations to underscore the significant narrowing that occurs in the inefficient therapeutic development pipeline. Such figures illustrate the costly, and extensive time horizon it takes to determine whether a drug is a good candidate to move beyond the pre-clinical phase, and to shift from

using animal models to human trials.[iii] In the next section I deconstruct how the causes of this crisis is defined, to lay the groundwork for how this framing has led to particular interventions intended to reform critical aspects of the infrastructure of biomedical research.

Defining the Causes: an inefficient pipeline and misaligned infrastructure

What causes these high rates of failure, substantial costs, and long time horizons for pharmaceutical development? Translational medicine documents construct the cause of this crisis is an inefficient pipeline and misaligned biomedical research infrastructure. Their critiques, as I describe below, center on how biomedical science upholds the use of well-established, but often inaccurate, scientific models and tools, as well as the very infrastructure of academic biomedical research: its norms, incentive structure, publishing practices, and organization. Documents addressing the translational crisis position key components of academic biomedical infrastructure as inherently *misaligned* with translational goals, and as such in need of realignment.

Widespread recognition of the inadequacy of non-human animal models in pharmaceutical development has become a major motivation for developing new, human-cell based models like organ chips. Put simply, "animal experiments, test tube analyses and early human trials do simply not reflect the patient situation well enough to reliably predict efficacy and safety of a novel compound or device" (Wehling 2008, 1). In 2004, the FDA Innovation/Stagnation Report claimed that 92% of pharmaceuticals that succeed in pre-clinical testing phases fail to make it to market. (In 2012, NCATS claimed a similar estimate of 90%, as noted above.) These statistics, and others like them, have become ubiquitous in the "alternative model" social world, underscoring the need for in vitro and computational modeling technologies that promise to be more accurate than existing non-human animal models. In a 2005 opinion piece in the *New England Journal of Medicine*, then NIH Director Zerhouni wrote, it has

"become clear that available animal models of human disease are often inadequate, necessitating even more research on human populations and biologic samples" (Zerhouni 2005, 1622).

The inconsistent relevance of non-human animal studies and their unpredictable translatability to humans is not a new issue. Those working with animal models, for instance, have long acknowledged the limitations of animal systems for modeling the human body (Vagtborg 1968).[iv] What is noteworthy about the current moment, however, is that translational research advocates have been able to mobilize this critique in order to attract investment toward new, innovative modeling approaches, such as computational simulation techniques believed to more accurately represent humans, as well as the introduction of human-based models earlier into testing processes. As will be examined in Chapter 3, organ chips are just one example of this, where the problem of non-human to human translation has been leveraged extensively to attract investment and generate hype about the potential of these technologies.

Translational research proponents position the issue of translational failure between non-human animal model to humans not only as an problem of model inaccuracy, but as an infrastructural issue: their critique of animal model reliance and inadequacy is directed at the deeply entrenched practice of using model organisms in biomedical research. Historically, biomedical research has heavily relied on the use of animal models, so much so that it is hard to imagine contemporary biomedical research without animal models (Creager et al. 2007; Nelson 2018; Rader 2004). As will be addressed in Chapter 4, many fields in biomedicine rely on model organisms to understand human reaction to exposures and the molecular basis of disease. Model organisms—such as nematode worms, zebra fish, mice, rats, rabbits, and dogs—fill buildings at research institutions, and are a staple of understanding human physiology, pathology, and behavior. Put simply, animal experimentation is a fundamental part of the "machinery of

contemporary biomedicine" (Nelson 2018, 2). While they may not predict human response as accurately as biomedical researchers (and translational medicine advocates, in particular) would like, they are a standard and ubiquitous tool that has been embedded throughout biomedical research.

Because such models have long been the norm and thus have an established body of scientific evidence can be called upon, translational advocates claim that journals and funders privilege evidence generated by "traditional" models, like animal models as well as two-dimensional (2D) cellular models (*in vitro* cultures typically done in petri dishes) (Marincola, 2003b). For those developing novel modeling technologies, like organ chips, this created a challenge when their work is reviewed. Organ chip researchers frequently discussed how journal and grant reviewers often ask them for comparative data using animal or 2D models, despite compelling evidence of their inadequacy. Discussing this challenge, one researcher explained that three-dimensional (3D) models like organ chips were easier for reviewers to criticize, saying,

> [3D] is more difficult to control, more difficult to get your end points out, more difficult to increase your Ns. So, more things are statistically significant. I mean the list goes on and on and so it's, it's just easier to criticize. It's ironic. I think 2D sort of has been around for so long, that I can criticize 2D all I want, but it seems like it just slides off like teflon. It's like, [humans] are totally not 2D, what are you doing? It's just standard and it's so easy to do when you have super good control over it. So, you can do these super clean experiments, but it doesn't really mean anything. It's kind of analogous to doing these super interesting, clean experiments in mice.

This researcher explained that 3D models introduce more complexity and thus the findings generated using them can be more challenging to interpret, but that they also more accurately reflect the human body. Even though "humans are totally not 2D," 2D models are the "standard" and offer "good control" and "super clean experiments." This excerpt provides one example that leads translational medicine advocates argue that prevailing research and publishing standards do

not encourage translational research. They argue that while that translational work would perhaps be less "clean" and "pristine" compared with animal models or 2D cultures, it would also be more analogous to what is seen in humans. In fact, some go so far to suggest that the current infrastructure of scientific metrics and peer review fundamentally *discourages* researchers from designing innovative models that better translate to humans. Instead, the infrastructure incentivizes researchers to focus on matching the current standards expected and even required by journal and grant reviewers (Marincola 2011). Such debates point to one way advocates argue the infrastructure must be fixed in order to achieve translational goals.

Finally, and relatedly, incentive structures for professional advancement in academia are not perceived as being aligned with bringing biomedical discoveries (products) to the clinic or bedside (potential markets). Traditionally, academic researchers have been rewarded for quality and quantity of scientific publications; scientific journals, and especially high-ranking publication outlets, often require novel discoveries and are less willing to publish studies that do not advance knowledge or demonstrate positive findings. This perceived bias towards publishing positive findings has come under fire by advocates of translational medicine who argue that this results in an information disparity in biomedical research: they claim that negative findings are just as critical to solving translational bottlenecks as positive results. Put simply, knowing what has not worked for other researchers can help the community to move forward more quickly. As Marincola wrote in the launch of *The Journal of Translational Medicine,* the first journal devoted to this field:

> Often scientists that designed new potential therapies based on fundamental scientific breakthroughs are not inclined to learn why things did not work as well in humans as they did in the pre-clinical settings because there is no room in prestige journals for negative results. Indeed, the scientific community is not generally interested in negative results. In addition, difficulty in publishing results derived from phase I studies is compounded by the fact that often data are of compromised quality and not of the pristine quality

achievable in the pre-clinical setting. (Marincola 2003b, 2)

Indeed, because translational medicine advocates believed mainstream journals did not see the value and purpose in publishing the kinds of research most useful for translation, they needed to create their own high-profile scientific journals devoted to publishing translational research. Thus they established several journals, including *Journal of Translational Medicine* (established in 2003), *Science Translational Medicine* (established in 2009), the *American Journal of Translational Research* (established in 2009), and *Clinical and Translational Science* (established in 2008). These journals specifically seek to publish translational advances and aim to be widely disseminated; as such several of them are open access publications.

As this section has shown, advocates of translational medicine have discursively constructed the high rates of failure and consequential economic costs as the result of a misalignment between the infrastructure of academic research and the priorities of translational medicine. They posit that fundamental aspects of the scientific infrastructure are at fault for this misalignment, suggesting that academic science is more concerned with producing prestigious science than with advances that improve the health of the public (Marincola, 2003). Crucially, as I detail next, while traditional academic and government regulatory processes are constructed as the problem, industry is largely absent. As I will show, industry and the private sector come to be framed as a valued and trusted expert and part of the solution.

Building an Infrastructure for Translational Research

Translational research advocates argue that building an infrastructure supportive of translational priorities requires (1) the weaving of industry—its logics, values, and practices—into the very fabric and infrastructure of biomedical research and (2) the breaking down of sector and

disciplinary siloes. Importantly, translational medicine explicitly reframes the role of industry in biomedical research, formally and overtly inviting industry into these spaces and elevating the status of industry expertise as a trusted, valued, and necessary form of expertise. This represents a departure from past scientific practice, in which industry affiliation was something which biomedical researchers needed to manage and distance themselves from, an issue I turn to later in the chapter. In my document analysis, visions for new relations between government agencies, universities, and industry abound, and relations that once would have constituted conflicts of interest are now key strategies to achieve translational priorities. I now turn to how translational research documents position industry as critical player in solving the translational crisis. Then, I turn to specific ways translational medicine institutionalizes interdisciplinarity.

Bringing Industry Formally into the Fold

The rise of translational medicine is made possible by broader shifts in the capitalization of academic science (Hackett 1990; Kleinman & Vallas, 2001, Johnson 2017, Lee & Walsh 2021). STS scholars have examined the ever-changing relations between universities and industry, with particular attention to the rise of academic capitalism. This literature has demonstrated how increasing commercial investment shapes the larger social environment in which scientific practice takes place and the consequences for the production of scientific knowledge (Berman 2008; D.L. Kleinman 2003a). The intertwining of academic and industry science has a long history, in which the relations between commercial entities, the state, and the university have shifted throughout time (Mirowski and Sent, 2008). While private interests have never been absent from academic research, many scholars agree they have significantly increased and become more explicit since the 1970s. This shift was the result of universities'

ability and desire to pursue intellectual property, alongside the downsizing of corporate in-house research, which is increasingly outsourced to academic and hybrid settings (Croissant and Smith-Doerr 2008; Mirowski and Sent 2008; Mirowski 2011). Importantly, since the 1970s, universities have come to recognize the economic value of commercialization and solidified practices to extract this value (Berman, 2012b). These broader shifts have in part led to industry involvement in academic biomedical research becoming commonplace as well as the adoption of industry practices in many academic research settings (Kleinman & Vallas 2001, Johnson 2017).

Here I focus primarily on efforts undertaken at the NIH. Strategic plans, as well as mission statements and annual reports for the National Center for Advancing Translational Sciences positioned stronger, more intertwined *relations* between academic researchers, industry, and government as a solution. Indeed, the introduction of industry, more purposeful collaboration, and goal alignment *across* such boundaries is framed as the key to breaking down barriers for translation. As I will show, translational medicine advocates have explicitly worked to change the infrastructure of biomedical research to align the needs, requirements, and priorities of academic researchers, industry representatives, and government agencies, forging new relations among them throughout the research and development process.

In the wake of the hype surrounding the valley of death and translational problems in the early 2000s, then NIH Director Elias Zerhouni launched translation initiatives through the NIH Roadmap in 2003 introduced above.[v] Endorsed by Congress in 2006 under the NIH Reform Act, the Roadmap served as a strategic plan to launch a number of initiatives geared toward translation, and toward funding innovative approaches to conducting biomedical research (Zerhouni 2003). This document laid out visions for embedding industry interest in the shaping of research agendas and as collaborators in the regulatory process. It created a formal place at the

table for the private sector to play a role in shaping the agenda, and put commercialization as an explicit goal of NIH efforts. Significantly the programs and initiatives launched through strategic plans normalized industry partnerships as an important part of developing an infrastructure to support translational research. For instance, the Roadmap called for "vastly different" research teams, in which collaborations between academics and private industry would become the new normal:

> The private sector will play an essential role in this new paradigm, and federal agencies will be required to do more collaborating with industry and each other. We recognize that the research teams of the future will look and feel vastly different from their predecessors. (2003, 64)

Though the Roadmap did not explicitly specify what roles industry would play, it frames the private sector as "essential" to successful research teams of the future and that extensive collaboration with industry will be necessary to achieve translational goals. Similarly, the FDA's 2004 Innovation/Stagnation Report, highlighted the need for effective collaboration, to realize translational goals, and to overcome the challenges of bringing drugs and medical devices from bench to bedside:

> Through scientific research focused on these challenges, it will be feasible to improve the process for getting new and better treatments to patients … We are confident that, with effective collaboration among government, academia, and the private sector, these goals can be achieved. (FDA 2004, p. iv)

Here the FDA posits that effective collaboration across government, academia, and private sectors is key to translation and to the kinds of scientific research that can facilitate translation.

While the exact nature of industry-academic-government relations are left unspecified in many of these documents, what is visible across these documents are powerful calls for the increased involvement of industry in the production of translational research, highlighting the

value of industry as a partner in biomedical research. This is notable because industry affiliation and collaboration previously has been understood as something that needs to be policed, or at least minimized to the extent possible, because of its potential to corrupt the production of biomedical research (Relman 1984; Resnik 1998, 2000, 2015; Resnik and Shamoo 2002; Steinbrook, Kassirer, and Angell 2015). Under the logic of translational medicine, industry is viewed as a critical and valued stakeholder and indeed, industry partnership and collaboration emerge as *essential* to translational success.

Breaking Down Silos and Institutionalizing Interdisciplinarity

Bringing industry formally into the fold requires the active breaking down of traditional silos between sectors as well as scientific disciplines. Calls for interdisciplinarity are not unique to solving the crisis of translation; as STS scholars have shown, acknowledgement of disciplinary silos led to widespread calls for interdisciplinarity initiatives, centers, and training programs at the turn of the century (Frickel, Albert, and Prainsack 2016). In the translational medicine space, however, this critique extends beyond critiques of disciplinary siloes, to include sector (government, industry, and university) silos. Institutionalizing interdisciplinarity has been positioned as key way to solve translational bottlenecks. The Roadmap, for instance, claimed that "to devise and use the state-of-the-art technologies" developed through Roadmap initiatives, they would need "the expertise of nontraditional teams of biological scientists, engineers, mathematicians, physical scientists, computer scientists, and others" (Zerhouni, 2003, 64). Indeed, while the Roadmap and its various initiatives made clear the potential value of bringing experts from ranging sectors and disciplines together, the 2012 establishment of the National Center for Advancing Translational Sciences (NCATS) became a key node for institutionalizing interdisciplinarity at the NIH and for, as its name states, advancing translational research.[vi]

NCATS was created by the Consolidated Appropriations Act in 2012 (Public Law 112-74). NIH established NCATS as a new center at NIH devoted to "transform[ing] the translational science process so that new treatments and cures for disease can be delivered to patients faster" (NCATS 2020b). Unlike other NIH Institutes that focus on a specific disease area (e.g., specific infectious diseases, cancer, diabetes and kidney diseases), organ system (e.g., eye, lung, blood), or field (e.g., nursing, genomics, environmental health sciences), NCATS focuses instead on the *process* of translating scientific discoveries at the NIH to improve care. Principally, NCATS is concerned with making the translation process from bench to bedside more efficient and less costly. As Francis Collins, then NIH Director, explained at a press event when NCATS was founded,

> Simply put, NCATS's mission is to catalyze the generation of innovative methods and technologies that will enhance the development, testing, and implementation of diagnostics, therapeutics, and devices across a wide range of human diseases and conditions. (F.S. Collins 2011)

NCATS "emphasizes innovation and deliverables, relying on the power of data and new technologies to develop, demonstrate and disseminate improvements in translational science." Its mission is explained through the "3Ds": 1) *d*eveloping new approaches, technologies, resources, and models, 2) *d*emonstrating their usefulness, and 3) *d*isseminating data, analysis, and methodologies (NCATS 2020b). Emphasizing the interconnectedness of disciplines, agencies, and organizational practices to solve translational problems, NCATS adopted an ecosystem approach that requires a shared focus on multiple diseases, connecting with stakeholders early in the research process, collaborating across NIH institutes and with the FDA (NCATS 2011).

NCATS conceptualizes translation as *a scientific and organizational problem*. As Christopher Austin, the first director of the Center, wrote in the 2012-2013 annual report:

> The science underlying the translational process is poorly understood, leading to the current high failure rate of translational projects. But roadblocks also are caused by organizational, educational, incentive and policy issues that often thwart success. […] NCATS is distinct in many ways. It serves as an "adaptor" to connect basic, clinical and public health research and as a convener for disparate organizations that play roles in the long, complex process from discovery to health improvement. The Center focuses not on what is *different* about diseases but on what is common to them and the translational process. Because successful translation requires teamwork, every NCATS initiative is a collaboration with partners in the public, private, government or nonprofit sector. (NCATS 2014, i, emphasis in original)

This except again highlights that the private sector is an important "partner." Noteworthy here too, is that Austin explicitly claims that the "high failure rate of translational projects" is not just about science, but that "roadblocks are also caused by organizational, educational, incentive and policy issues." As such, NCATS' solutions are not only about advancing the science of translation but also addressing the organizational elements that were perceived to be the crux of the translational problem, by eliminating disciplinary and agency silos, and changing incentive structures in academic research (NCATS, 2014). Consider the following excerpt, where NCATS outlines how it plans to navigate such complexities:

> Developing a potential therapy to the point of regulatory approval can require expertise in molecular biology, medicinal chemistry, compound synthesis and formulation, pharmacology and toxicology, technology transfer, clinical science, regulatory science, and entrepreneurship, as well as the integration of patient perspectives. However, academic advancement and tenure structures and professional and cultural barriers can make teamwork difficult to navigate. For this reason, NCATS places high value on innovation in team science and partnership development, and it designs and tests novel partnership structures that cut across traditionally siloed scientific disciplines, organizations and sectors. (NCATS 2016, 25)

In this excerpt, NCATS pairs the myriad forms of expertise needed to bring a potential therapy to the point of regulatory approval along with the organizational "barriers" to doing so. Put another way, NCATS links the issue of academic "professional and cultural barriers" to disciplinary

siloing and the challenges it poses for "teamwork," thus offering a critique of the traditional organization of expertise within the academy. It poses that "novel partnership structures," which invite industry explicitly into the fold, will enable them to overcome such barriers to drug and device development. By listing myriad forms of expertise needed, which range from scientific disciplines, to "regulatory science," and "entrepreneurship," NCATS makes the case for interdisciplinarity and "novel" partnerships. Such novel partnerships encompass federal regulatory (such as the FDA) and research agencies (e.g., NIH), as well as product development and commercialization experts. Indeed, this is a strategy taken up in the development of organ chips, which will be further discussed in Chapter 3.

As NCATS has operationalized its efforts, fixing these inefficiencies has also redistributed *where* particular parts of research and development of potential pharmaceuticals and medical devices happen. Importantly, parts of the process with the highest costs and risks have historically been footed by both private industry as well as the federal government. As Robinson (2019) has aptly articulated, in responding to the constraints this financial burden has presented for pharmaceutical and biotech industry, the "riskier" parts of research and development have been shifted to the state. High-risk research is increasingly funded by the federal government and carried out by academic researchers, effectively "de-risking" development pipelines (Robinson, 2019). This is no secret; as Francis Collins, past director of the NIH, wrote in 2010:

> If [moving from development to market] were easy, drug companies would not be struggling with languishing new-drug pipelines. What can the NIH do with this center [NCATS] that the pharmaceutical giants aren't already doing? It most certainly will not be easy. But there has been a recent deluge of discoveries about the molecular pathogenesis of disease. This has revealed hundreds of new potential drug targets. For rare and neglected diseases, economic considerations will limit private-sector interest; but NIH-funded researchers can explore the earlier stages in the drug-development pipeline to 'de-risk' projects that would otherwise lie untouched. Similarly, for common diseases,

> many of the new molecular discoveries are of uncertain value for drug development, but NIH investigators can valid ate these drug targets and develop promising lead compounds, as well as carrying out process engineering on the pipeline itself. The goal will be to bring each project just far enough to become of interest to the private sector to pick up."

Here, Director Collins outlines how the NIH can intervene in the pipeline to shoulder some of the burden of the costs associated with drug development. He suggests that the NIH can serve the needs of industry and, ultimately, the public by getting new drugs to market by de-risking the development pipeline.

In the years since these calls and the establishment of these programs and institutes/centers devoted to translational efforts, we have seen the visions for public-private collaboration unfold in multiple ways, including the inclusion of industry representatives on advisory boards, steering committees, as well as the creation of public-partnerships in funding research programs. Ultimately, the new norm of early engagement with industry and investors in the development of research programs and programmatic oversight imbues industry representatives with a powerful position in the shaping of publicly-funded research agendas. For instance, NCATS engages with its "stakeholders" to shape the direction and goals of the Center. They include, as expected, the NIH, FDA, and other government agencies, academic institutions, patient organizations and nonprofits—but also representatives and leaders of pharmaceutical, biotechnology, and venture capital firms. Consider the current makeup of NCATS advisory council, which includes two industry representatives, two disease foundations, and two academic researchers, one of whom is a professor of finance (NCATS 2020a). With this composition, industry representatives play a potentially substantial role in helping to decide what are worthwhile translational endeavors for NCATS to pursue and define the goals and priorities of the Center. Moreover, while translation broadly conceived encompasses all sorts of

interventions, it is a specific slice of translation that is taken up NCATS: its portfolio has consistently privileged rare disease research, as well as the development (and repurposing) of pharmaceuticals and biomedical devices and development of tools that can be used in pharmaceutical development (NCATS 2022). I return to this issue in the conclusion of the chapter.

Instilling a Commercial Ethos

Successfully shifting the infrastructure to attend to translational priorities also requires redefining productivity for academic biomedical researchers. Whereas academic capital has typically consisted of publications and research grants, new goals and metrics of commercialization and entrepreneurial pursuits need to be seen as valuable, worthy endeavors for individual researchers. Investigators need to be overtly encouraged to think about the commercial potential of their research and technologies, equipped with the funds, tools, and networks to pursue paths toward commercialization, and rewarded for their progress and success in commercialization. In effect, researchers need to envision themselves as not only researchers, but as potential entrepreneurs developing and shepherding discoveries into products and toward markets. In this section, I consider how academic researchers are encouraged to engage in commercialization and industry partnership. I then return to the observations that opened this chapter, and explore the tensions activities raises for potential conflicts of interest.

Retooling Researchers as Entrepreneurs

A key aspect for achieving translational priorities requires that academic researchers see value in engaging in the commercialization of their scientific work. Thus opportunities needed to

be established for academic researchers to: 1) engage, early in the development of their technologies, with potential industry partners, and 2) seek formal training in commercialization and entrepreneurship. Opportunities for formal training in entrepreneurship include federal initiatives, through the creation of programs like Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR), as well as more localized efforts driven by universities, research institutes, and their technology transfer offices. While these efforts are not unique to translational research, they are leveraged as key pieces of its revised infrastructure. Throughout my ethnography, researchers often spoke about the utility of these programs and the pivotal impact of their participation in them. Scientific conferences have become a key site where structured networking across academic and commercial sectors and researcher-industry engagement occur, as well as where the commercial ethos is put on display and promoted. At the 2018 conference from which I shared the vignettes that open this chapter, for instance, special sessions were held for researchers to learn about the SBIR and STTR programs. Biomedical engineers who had participated in these programs shared stories about their experiences and how their participation shaped future research and commercial endeavors.

The SBIR and STTR programs were established in 1982 and 1992, respectively, across multiple US federal agencies with large extramural research budgets.[vii] The SBIR and STTR programs are used to fund small businesses, including academic researcher led start-ups, with technologies under development that have a "strong potential for technology commercialization" (SBIR n.d.). SBIR grants are available to academic researchers as well as researchers employed by non-profit research institutions (such as private, non-profit institutes established in partnerships with universities). At NIH, both of these programs move awardees through a three-phase program where they demonstrate the feasibility and proof of concept of their technologies

and research (Phase I), move forward research and development (Phase II), and commercialization (Phase III). In Phase I and Phase II, awardees can apply for additional assistance programs such as the Niche Assessment Program, I-Corps™ (Innovation Corps), and the Commercialization Accelerator Program. In each of these, investigators learn skills essential to commercializing technologies such as how to conduct a market study and interpret the findings, networking with biotechnology sector experts, build commercial relationships, and identify revenue opportunities. These assistance programs provide training for investigators to become entrepreneurs and foster successful start-ups. I-Corps™, for example, bills itself as an "innovative program to develop and nurture a national innovation ecosystem that builds upon biomedical research to develop technologies, products and services that benefit patients"[viii] and that offers investigators the opportunity to gain "years of entrepreneurial skills in only weeks" (NIH n.d.).

The purpose of these programs and grant opportunities may be interpreted as twofold: they actively push an ethos of commercialization throughout the biomedical research ecosystem and pipeline, and do so by imbricating commercialization into the already accepted incentive structure and metrics of evaluation in academic research. Grants and awards such as those detailed above bring revenue into universities, and importantly, count towards tenure and promotion.[ix] These training avenues are critical to embedding the ethos of commercialization into traditionally academic spaces. Like establishing journals where the allegedly antagonistic practices of academic publishing are minimized, these avenues shift the infrastructure to be more welcoming to commercialization efforts where it may previously have raised concerns about the integrity and objectives of biomedical research.

Shifting Values, Persistent Tensions: Governing Conflict of Interests

> To change the reward system, one must first change the mind-set of leaders and senior faculty in academic institutions. Some faculty members believe that drug discovery and development are antithetical to academia. Intellectual curiosity and love of teaching more likely attracted them to academia than a desire to commercialize technology. Although their perspectives need to be fostered in academic institutions, the translation of research discoveries to benefit patients is also a critically important and worthy academic endeavor. Fear of corporate interests tainting academic research is unwarranted. (Parrish et al. 2019, 412)

As values in biomedicine shift with translational priorities, tensions emerge among key actors and institutions. As the above excerpt highlights, there are deep tensions between those who believe in utility of corporate interest and participation in academic biomedical research and those who find such relations problematic. While translational medicine advocates accept the value of commercialization as a worthy endeavor and a legitimate way to achieve translational goals, others question the consequences such values and relations may have for the production of biomedical knowledge. In this section, I turn to this enduring tension.

Since the 1980s, scientific journals have held policies for the disclosure of conflicts of interest. In 1984, when the *New England Journal of Medicine* was among the first journals to adopt a conflict of interest (COI) disclosure policy, then editor-in-chief Arnold Relman remarked,

> Connections between industry and academic medical scientists are not new. It has long been common practice for manufacturers of pharmaceuticals and medical devise to retain the services of academic scientists as consultants or to subsidize their research studies – particularly clinical trials of marketable products in which the company is interested. But in recent years, as the commercial possibilities of new biomedical discoveries have become increasingly attractive, these connections have become more pervasive, complex, and problematic (Relman 1984, 1182).

Editors like Relman recognized that relations between academic scientists and industry were becoming even more intricate in the wake of the commercial *potential* that accompanied biomedical discoveries in the late twentieth century and that scientific journals needed to act. Such policies were motivated by ensuring transparency and maintaining public trust in science (Hauray 2021).

Notably, alongside the rise of translational priorities I have discussed in this chapter, new tensions around COI reporting have surfaced: ones that question how this reporting aligns with translational priorities and the consequences, not of conflicts of interest themselves, but of disclosure policies and reporting requirements. Scientific journals have historically been key arbiters of COI disclosure policies, requiring authors to disclose competing interests in order to publish their work. Yet in this moment even they seem to reluctant to fully embrace disclosure policies: alongside COI disclosure policies, journals make note that such policies are not intended to discourage academic-industry relationships. Indeed, journals actively work to *normalize* financial interests and industry relations, suggesting that these relations are both expected and accepted, and not a barrier for publication.

High profile journals often comment on the purpose of these policies, reassuring potential authors that such the disclosure of such relations will have minimal impact on their decision. For instance, the Royal Society of Chemistry, which runs a collection of over forty journals in the chemical sciences, biology, biophysics, engineering, medicine and materials science—fields that tend to conduct translational research—writes the that they should be informed of any "significant conflict of interest that editors, authors, or reviewers may have." Immediately following, they normalize these relations, writing "conflicts of interest are almost inevitable and it [the disclosure policy] is not intended to attempt to eliminate these." Implicit here is the notion

that COI disclosure operates to chastise research conducted by researchers with COI. Similarly, after clarifying disclosure policies across the Nature journals (Nature 2004), *Nature Cell Biology* went so far as to offer commentary on the intended purpose of such policies and to reassure contributors of their excitement to publish such application-oriented research:

> The aim is to add transparency to the increasingly elaborate net of financial interests that pervades not only industrial and biotechnology research, but also academia — both at the institutional and personal level. It is not our aim to castigate research with a profitable bottom line — far from it. […] We hope it is self-evident that the aim of this policy is not to denigrate application-oriented research; rather, it is to foster transparency, particularly at this exciting time of ever-increasing and ever-more intricate affiliations between academia and industry, and the increased level of public scrutiny this has precipitated. (Nature Cell Biology 2004, 67)

Thus, journals almost equivocate between enforcing and tightening their policy around the disclosure of competing interests, while also making it clear that they are interested in publishing the very work that might be most vulnerable to such conflicts: that which is translational, or "application oriented." This normalization—and arguably enthusiasm for—industry partnership and translational oriented work is a noteworthy loosening of previous conflict of interest concerns. COI disclosure now seems to be a moot point: in 2019, at least 70% of original research articles published in the *Journal of the American Medical Association (JAMA)*, *Science Translational Medicine,* and *Nature Biotechnology* were written by researchers with conflicts of interest to disclose (Jeske 2021a).[x] Such statistics emphasize the extent to which private interests have become enmeshed in the production of biomedical knowledge. They suggest that competing interests are no longer an obstacle for those working in academic biomedical research—certainly, COI are not a barrier to publishing in prestigious journals—and raise critical questions about how else the role and influence of industry and private interests in the conduct of biomedical research in the US might be governed.

And yet, this is by no means a settled issue. Tensions surrounding scientific publishing and translational medicine values and priorities came to the fore in an editorial series published in the *New England Journal of Medicine* (NEJM) in 2015. Jeffrey Drazen, then editor-in-chief, solicited a series of essays that re-examined COI disclosure policies. In both his editorial and the three subsequent pieces by Lisa Rosenbaum, national correspondent for the journal, they posited that anti-industry bias in scientific publishing is dangerous. In his editorial that launched the series, Drazen tells the story of Selman Waksman, a soil microbiologist practicing in the 1940s. Waksman won the Nobel Prize for the discovery of streptomycin, used to treat tuberculosis. As Drazen recounts, "Waksman realized that if his discovery was to be of value to the world, he needed a partner capable of manufacturing adequate amounts of the material under conditions that would make it suitable for use in humans" (Drazen 2015, 1853). That partner happened to be Merck, a major pharmaceutical company. Drazen used this example, and drew on other institutional proponents of translational medicine who have articulated similar examples of academic-industry partnership, to emphasize the *social value* of such academia-industry relations and their ability to commercialize laboratory discoveries into clinical interventions. Rosenbaum's essays note that the goals of industry and academic science are in fact aligned given their "shared mission" of fighting disease. She argues the "collective conscience" that has brought public and scholarly attention to COI in biomedical research has had negative consequences and that that "charged debates" about the importance of COI are getting in the way of getting treatments to patients (Rosenbaum 2015a, 2015b, 2015c). That these arguments were aired in such a high-profile platform is remarkable. While the NEJM had been among the first scientific journals to adopt a conflict-of-interest disclosure policy, the 2015 series of essays suggest that such a firm stance has very much eroded.[xi]

However, this series of essays was met with harsh criticism. Perhaps most scathingly was the criticism from previous senior editors of NEJM, who wrote in *The British Medical Journal*, that "in a series of rambling articles, Lisa Rosenbaum, supported by editor-in-chief Jeffrey Drazen, tried to rationalize financial conflicts of interest in the medical profession." They called out the "colorful language" and "fanciful notions," alongside the lack of empirical evidence for such claims. And in fact, there is much evidence that speaks to the contrary (for example, Cosgrove, Bursztajn, and Krimsky 2009; Grundy, Bero, and Malone 2013; Sismondo 2008). The criticism countering overt attempts to normalize conflicts of interest, and make the case that interests between academic researchers and industry are in fact aligned, underscore that skepticism still remains.

This section has highlighted the ways in which an infrastructure for translational medicine has been established has woven industry values, interests, and representatives more deeply into the fabric of biomedical research. Conceptualized as a way to overcome the "valley of death," translational research advocates have reframed the role of industry in biomedical research, explicitly inviting industry into these academic research spaces and elevating its status as a trusted, integral expert. Researchers participating in translational research also needed to see the value of commercialization. Thus, building an infrastructure for translational priorities required not only bringing industry experts into the fold, but also redefining incentives for academic researchers. And yet, these shifts introduce critical questions about whose interests are at play in translational research and what types of research are pursued in the name of translation. Ultimately, the particular formation of translational medicine raises questions about how we imagine what the public stands to benefit from investment in translational medicine.

Conclusion: Translation, Commercialization, and Public Good

This chapter has shown that while the discourses and politics surrounding translational efforts embed industry interests into the very fabric of academic research, defining what translation means and the logics of how it is to be achieved. Commercialization of biomedical research is embedded within the very building of translational infrastructure itself, with commercialization positioned as a unifying goal to solve the translational problems of academic incentive structures, its slow and meandering pace, and its disciplinary and sector silos. Under the logic of translational medicine, commercialization is co-constitutive of translation, and its achievement is what is trumpeted as translational success. Concomitantly, we have moved from policies policing the disclosure of conflicts of interest to acknowledgments that normalize (and indeed seem to almost vaunt) not just their existence but also their pervasiveness and inevitability.

Translational medicine advocates for and legitimizes commercialization as a social good. It does so by arguing that it is the primary way that the public can "realize" its investment in federally-funded biomedical research in the US. Critiques about the scientific process often center on the purpose of this research and its ties to public health as a social good. Constructed in this way, shifting the infrastructure (including norms and incentive structure, publishing practices, and organizational structure) of academic research is arguably in the mission of serving the public. As a member of NIH leadership involved in translational programs explained succinctly to an audience at a conference I observed in 2019, "our constituents, the American people, say 'we don't care about papers, we want drugs.'" More formally, Marincola writes,

> The scientific process is meant, after all, to alleviate human misery and this ultimate goal could be facilitated by connecting basic scientists with the reality of human disease and making translational research more than an interesting concept (2003, 1).

Sentiments like these call into question the accountability of biomedical researchers to the public, suggesting that those who are more interested in "papers" or "interesting concepts" are not working to "alleviate human misery." Thus, translational medicine advocates are able to position the inefficiencies and misalignments of academic biomedical research infrastructure as being against the public interest, thereby garnering acceptance of the increasingly intertwined relations of industry interests and biomedical expertise.

Scholars have demonstrated that such commercial pressures result in the prioritization of some types of scientific endeavors while leaving other research areas "undone," reproducing inequalities along the way (Frickel et al. 2010; Hess 2016; Moore et al. 2011). Taking seriously how embedded industry is in translational medicine, we might question the nature of the public good that translation can achieve as it is currently defined and bounded. It is telling, for instance, that the NCATS portfolio is not centered on public health initiatives which could also be construed as "translational research"; its research portfolio is instead dominated by searches for pharmaceuticals for rare diseases, technology development, and molecular target identification, reflecting applications of limited societal impact compared to others, perhaps less profitable but that may greatly impact public health.

If translation is understood as commercialization, we must consider the deep inequities and stratification of benefit that the market-driven healthcare system in the US has already enabled (Clarke et al. 2021) and question who stands to benefit most from the construction of translation-as-commercialization. Under the logic of translational medicine, what will happen to research that may greatly benefit the health of the public, but for which a "market" might not

exist, and where industry and public-private partnerships do not see a potential for return on investment? This chapter has highlighted how the values and infrastructure needed to achieve translational goals in biomedicine legitimate industry involvement in all corners of biomedical research, not only in the development of pharmaceuticals, but also in the tools and technologies that become basic tools in biomedical research and in the ethos of researchers themselves. As it has been constructed, translational medicine promises a social good that is difficult to critique: getting biomedical advances into the hands of the public. But choices about *how* this is accomplished are obscured; the embedding of industry more deeply in the infrastructure of biomedical research is not the only and inevitable pathway. The very notion that industry is necessary to solve and save biomedical research is a particular framing. Under the logic of translational medicine, beliefs about the appropriate role of industry in biomedicine, alignment of government, academia, and industry, and pathways to achieving broader impact, prioritize private interests in the name of public health. It is in this moment that we must reflect on our tools to make power relations visible in this infrastructure, and to govern and potentially reclaim it. As the meaning of the work biomedical researchers conduct has shifted under the logic of translational medicine, so too must the ways we conceptualize industry involvement in biomedical research, the interests that are served, and what is ultimately at stake for the public.

CHAPTER 3: BECOMING THE RIGHT TOOL

Figure 3. 1:National Geographic Magazine Cover, January 2019

"The future of biomedicine: virtual humans"
NBC, March 17 2008

"Lung-on-a-chip could be used to predict the effects of toxins or drugs: The lung-on-a-chip device mimics a human lung and allows living tissue to be studied without opening up people or animals"
The Guardian, June 24, 2010

"Organs-on-a-Chip for Faster Drug Development: New devices may help bring drugs to market faster"
Scientific American, March 1 2011

"The 'Human Body on a Chip' Project that Could Change Biological Warfare and Medicine"
Slate, July 25 2012

"Goodbye, Animal Models?"
Genome Web, 2017

"Menstrual Cycle "on a Chip" Offers a New Window into Female Physiology"
Scientific American, June 1 2017

Introduction

The media headlines and magazine cover (Figure 3.1) above paint organ chips as a disruptive, innovative technology that will become "the future of biomedicine." Since the publication of the 2010 Science paper reporting the lung chip technology (Huh et al. 2010), organ chips have been touted as the technology that will make drug development faster and more efficient, transform biological warfare, and offer a new window into physiology. How did organ chips become a technology equipped to tackle so many different issues, including the translational crisis? How do certain tools materialize as the right tools for multiple jobs?

This chapter shows how organ chips researchers and funders position organ chips as the right tool for solving a key aspect of the translational crisis: translating non-human animal models to human clinical studies. Often accounts of becoming the right tool have a historical nature, wherein the object of analysis has indeed become the right tool; it has been adopted, accepted, and its rightness and utility are largely taken for granted (Clarke and Fujimura 1992; Cowan 1985). This chapter tells a different story, one that is emergent and in progress. At the time of writing this dissertation, organ chips remain at the margins of biomedical research: their developers are still trying to make the case for why they are indeed the right tool for the job. They are still seeking to win over regulators and other researchers who remain unconvinced of the validity, accuracy, and reliability of organ chips. Yet at the same time, the public profile and promissory potential of organ chips—as evidenced by proliferating media reports—suggest something of an accelerating bandwagon. While their future remains to be seen, this is a particular time in which the negotiations and construction of *rightness* (or wrongness) are overtly worked on and therefore acutely visible. In this chapter, I draw on STS scholars who have analyzed how particular technologies become the right tools for the job through social

negotiations, rather than any inherent technical superiority, as well as through the *articulation* of "doable" scientific problems (Fujimura 1987). How technologies emerge as the right tools are not inevitable, but rather are the result of technical, economic, and political decisions "made by complex social institutions over long periods of time (Cowan 1985, 202). Clarke and Fujimura write that "tools, jobs, and rightness are each and all constructed in, and therefore can only be understood as part of, a situation" (Clarke and Fujimura 1992, 6). In order to understand the particular situation of a tool and its rightness, they contend that the *elements* of a situation must be analyzed. For Clarke and Fujimura, these elements include:

> ***Everything in the situation****,* broadly conceived. […] The elements of the situation generally include *workplaces* (laboratories or other work sites and their basic infrastructure); *scientists* (including their individual career issues); *other workers* (graduate students, technicians, clerical staff, artists, computer programmers); *theories, models,* and *other representational entities* (both tacit and explicit); *research materials, instruments, technologies, skills and techniques,* and *work organization* (of the immediate work site, of the larger local administrative unit such as a university or federal agency, and of disciplines and specialties through professional organizations and other means of communication); *sponsorship and its organization* (of both intramural and extramural fiscal support); *regulatory groups* (local, national, and international); and both desired and unintended *audiences and consumers* of the work. (1992, 5, bold emphasis added)

This chapter takes up this analytical approach, examining the assemblage of material, social, and discursive elements that developers and stakeholders collate to construct organ chips as the right tool. This chapter begins with a discussion of four trends that I call the *sociotechnical conditions of possibility*. These trends are critical elements of the situation that provide the necessary conditions for organ chips to both be technologically possible, or doable, *and* socially valuable. I then turn to a discussion of the actors and networks involved in the production and elevation of organ chips, analyzing how these various actors come together to collectively conduct articulation work (Fujimura 1987). In the case of organ chips, I show how articulation work is necessarily a collective enterprise, does not always occur at the level of scientists alone, and can

take different forms depending on the investment and formation of social worlds. I then turn to analysis of the hyping work requisite for positioning organ chips as the right tool. I contend that hyping is a critical type of articulation work that organ chip proponents must engage in. I examine how hyping work is performed by organ chip researchers and stakeholders, as well as in dialogue with outsiders, and how the nature of this work changes depending on the audience. Finally, I contend that the very job organ chips are purported to perform, that is, to disrupt extant pharmaceutical testing practices, creates a formidable obstacle to becoming the right tool due to heavy regulatory oversight in pharmaceutical testing. Thus, whether or not organ chips may emerge as the right tool is highly dependent on the collective articulation work that unfolds not only among funders, academic researchers, and industry, but also with regulators.

Situating the Emergence of Organ Chips

Four broad trends happening in the biomedical sciences in the late twentieth and early twenty-first centuries pave the way for organ chips to become a sociotechnical possibility: 1) the translational crisis, 2) growing discontent with the inadequacy of non-human animal models, 3) the rise of cell culture technologies and *in vitro* experimentation, and 4) the integration of engineering approaches in the life and biomedical sciences. The former two provide the social context in which organ chips come to be seen as valuable tools worthwhile of investment, and were explored in Chapter 2. Below, I examine the latter two trends that provide the scientific and technological conditions necessary for organ chips to be technologically and scientifically feasible. These four trends, of course, occur in the broader context of shifting norms in academic research that others have described as academic capitalism and bureaucratized science, as

explored in Chapter 2 (Hackett 1990; D.L. Kleinman 2003a; D.L. Kleinman and Vallas 2001; Berman 2012a).

Cultivating life outside the body: in vitro experimentation and cell culture

That cells could live in perpetuity outside animal bodies transformed the biological sciences in the twentieth century. The advent and rise of *in vitro* experimentation in the twentieth century has been well-documented (Landecker 2007). *In vitro* experiments are those in which biological molecules, cells, and microorganisms are conducted outside their biological context, relying on the ability to culture, or grow, cells in petri dishes. The shift from *in vivo* (within the living) experimentation to *in vitro* (within the glass) experimentation, in which human and non-human animal bodies—in fragmented and detached forms—could be brought into the lab to understand and experiment, changed the potential of what the biological sciences could do.

Cell culture is a scientific process whereby cells are taken from living organisms and are cultivated to live in an artificial environment outside the body using media, or liquid carrying nutrients, to sustain them. Early methods of cell culture were developed in the early 1900s, and over the course of the twentieth century became a key technology of biology. As Landecker explains, cell culture technology brought into being "cellular life that was autonomous, external, and dynamic" (Landecker 2007, 67) for biology.[i] Simply put, cell culture technology fundamentally changed the methods through which scientists understood animal life at the molecular level. Landecker contends that cell culture gave rise to

> a new way of thinking about, seeing, and experimenting on the cells of complex organisms. The body was not replaced by the cell, nor reduced to it; rather this technique substituted an artificial apparatus for the body and generated new views of the autonomy and activity of cellular life." (Landecker 2007, 33)

Mediated through technologies such as microscopes, imaging technologies, and cell counters, life scientists could see and know the body in new ways. Because cells live outside their bodily environments, they can be manipulated to grow in specific ways, allowing researchers to make inferences about the molecular basis of normal cellular function as well as disease pathology.

Moreover, the development and use of cell lines in cell culture were paramount in biology because they enabled cost effective, "unlimited" supply of cellular material. Cell lines are collections of cells developed from a single cell and so have a uniform genetic makeup. When kept in growth medium, they continue to reproduce indefinitely. They are considered "pure" populations of cells, which enable consistency in samples and reduce reproducibility concerns (Kaur and Dufour 2012). Cell lines are highly regarded because they are cost effective and easy to use (largely in part because the scientific community has developed them to be so). Because cell lines reproduce without mutation, they are reliable, stable tools: they are easily mobilized in a wide variety of laboratory settings. Cell lines are also well characterized and have become a critical laboratory tool in the biosciences.

The utility of cell lines has also in part depended on the perception that they bypassed the ethical concerns associated with obtaining cells directly and immediately from human samples (Kaur and Dufour 2012; Thompson 2013). However, this position overlooks the deeply problematic origins of where and how human cell lines were first developed. The first human cell line that could be shared easily across laboratories were HeLa cells, developed from cells taken without consent from Henrietta Lacks, a young black woman who sought care for advanced cervical cancer at a Johns Hopkins clinic (Skloot 2010). Her cells became the first immortal cell line and have been used for decades in scientific advances across the biomedical sciences. The HeLa case since has become a key case in understanding how the biomedical

sciences have been developed through the harms to marginalized communities. HeLa cells are just one example of many cell lines whose origins became obscured as part of the process of becoming routine laboratory materials, an issue I return to in Chapter 4.

Since the early 2000s, another cellular development has been critical to *in vitro* experimentation: the development of induced pluripotent stem cells, or IPS cells. IPS cells derive from primary adult skin or blood cells that have been "reprogrammed" to an embryonic-like state. From there, cells can be programmed to become specialized cells characteristic of a specific organ that is of interest. The first IPS cells were developed in Shinya Yamanaka's lab at Kyoto University in 2006, using mouse models. Human IPS cells were then developed by Yamanaka in collaboration with James Thomson's lab at University of Wisconsin, Madison in 2007.[ii] IPS cells have since become widely used in biomedical research and are regarded as an important tool for modelling and investigating human diseases and for drug screening so much so that some refer to them as a "lab workhorse" (Scudellari 2016). As I discuss more fully in Chapter 4, IPS cells are used in organ chips and are a critical tool for their standardization and scaling. Advances in cell culture and cellular technologies described above are critical for organ chips, which require tissue-specific cells to live and maintain function on the chip platform for an extended period of time (at least four weeks).

Integrating engineering approaches in the life and biomedical sciences

The final sociotechnical condition of possibility for organ chips is the entrenchment of engineering approaches in the life and biomedical sciences. As described above, *in vitro* experimentation and the development of cell cultures and cell lines are integral for the sustaining of cellular life and modeling of particular organ cells, but the platform itself—the "chip"—relies

on engineering advances. Here, I turn to the increasingly prominent role of engineering in biomedicine and discuss three developments—tissue engineering, microfluidics, and lab-on-a-chip devices—that provide the requisite technological advances for organ chips.

Broadly conceived, engineering is the application of science and mathematics principles to "design or develop structures, machines, apparatus, or manufacturing processes" (Smith 1999). Formalized training in engineering dates to at least the eighteenth century, in specialties like mechanical, civil, and chemical engineering, though the earliest engineers recorded date to ancient times, with the construction of step pyramids in Egypt (Diemar 2021).[iii] Engineers and researchers have been integrating engineering approaches in biomedical science over the course of the twentieth century, as they developed technologies designed for medical purposes, such as nuclear magnetic resonance (NMR) later used to develop the MRI (Joyce 2008), isotope medicine (i.e. fluorine 19 which is used to separate isotopes to make medicines), kidney dialysis technologies, and cardiac technologies like heart valves and pace makers (AIMBE n.d.) . Undoubtedly, the integration of engineering approaches in the life sciences in the late twentieth century is fundamental to the technoscientific shifts indicative of biomedicalization (Clarke et al. 2003).

Once engineering approaches were recognized to have value for biomedicine, there was a concerted effort to institutionalize the field. The first formalized training programs were established in the late 1960s (Peppas and Langer 2004). Bioengineering brings together principles from engineering and biology to construct applications, models, and technologies for the life sciences and medicine. Bioengineering is often referred to as an interdiscipline by experts in the field, wherein expertise from many engineering and biological areas are retooled.[iv] According to one prominent historical account, it is thought to be rooted in chemical

engineering, or industrial chemistry, and builds on two major advances in late twentieth century bioscience: molecular biology and genomic biology. As one account puts it, "these two revolutions made it possible to identify and manipulate the mechanistic components of living systems and to accelerate the rate of analysis" (MIT n.d.), thus making living systems a new domain for engineers to claim jurisdiction over and explore. Though often used interchangeably, bioengineering and biomedical engineering are slightly different in scope. Biomedical engineering specifically focuses on applications of bioengineering to biomedical research and therefore can be considered a sub-area of bioengineering.

Against this backdrop, in the 1980s researchers working at the intersection of biology and engineering began developing "biological substitutes" that maintain tissue and organ architecture and function. Early founders of "tissue engineering" engineered blood vessels, vascular tissue, skin, muscle, and bone. Tissue engineering, like cell culture, offered a new way of seeing, conceptualizing, and experimenting on tissues outside the body. This technique did not replace the body, but it created an apparatus for understanding the body and the functioning of tissues, as well as creating artificial bodily materials that could be implanted into the body. In doing so, tissue culture and engineering paved the way for major advances in *in vitro* experimentation at the tissue level, for understanding the structure and function of tissues, requisite advances for organ chip technologies.

Another set of engineering advances, in microfluidics and "lab-on-a-chip" devices, were critical to making organ chips a technical possibility (Azizipour et al. 2020). Microfluidics is the manipulation of very small amounts of fluids in channels with dimensions in the tens to hundreds of micrometers. According to one account, microfluidics emerged from multiple motivations including molecular analysis, biodefense, molecular biology, and microelectronics (Whitesides

2006). Organ chips are microfluidic devices; indeed to the naked eye, one can barely see the reservoirs and channels etched into the device. Similarly, a "lab-on-a-chip" device is technology that integrates some analysis onto a miniaturized, chip platform. Such analyses would typically be done in a lab, hence the name, and these devices allowed assays (or investigative tests or procedures) to be run on tiny devices in single laboratory. The first lab-on-a-chip device was developed in 1979 at Stanford University, and was used for gas chromatography. The design and technical specifications of lab-on-a-chip devices rely on soft lithography, which was highly successful in silicon microelectronics (Casquillas, Houssin, and Durieux 2020). In part, this is where the "chip" aspect of the name organ chip comes from: participants explained that "organ-on-a-chip," the term used early in the development of the field, was in part an homage to the lab-on-a-chip developments of the late twentieth century. In the 1990s, researchers began using lab-on-a-chip devices to experiment with microfluidics in cell biology applications, including the application of polymerase chain reaction (PCR) in a microfluidic device in 1998 (Ahrberg, Manz, and Chung 2016). Since then, the application of microfluidic lab-on-a-chip devices for biomedical applications has greatly expanded. Organ chips fundamentally rely on the engineering techniques of tissue engineering, microfluidics, and lab-on-a-chip: they are microfluidic technologies that support the development of cell cultures that mimic tissue and organ level physiology over a period of time, and are used to perform specific analyses.

These four sociotechnical conditions of possibility—the development of cell culture and rise of in vitro experimentation, the integration of engineering approaches in the biomedical sciences, as well as the translational crises and growing discontent with animal models discussed in Chapter 2—are each key technical and sociopolitical elements for organ chips to become a

"doable" technological pursuit. In the next section, I turn to the actors and networks involved in constructing organ chips as the right tools for particular jobs.

Mapping the Landscape of Organ Chip Research in the US

While the sociotechnical conditions described in Chapter 2 and above enable organ chips to be a social and technical possibility, they are insufficient in and of themselves to make organ chips the right tool. It is through actors and networks, and the power relations that shape their interactions, that these conditions come to have social force and can be leveraged to make the case for the rightness of organ chips. In this section, I describe some of the key actors and networks at play in the organ chip arena, and how they come together to position organ chips as the right tool for multiple jobs. Critical to constructing this rightness is the articulation of doable, and desirable, scientific problems. Fujimura's concept of *articulation* captures how researchers construct doable problems across three levels of work: the experiment, the laboratory, and the broader social world in which science is situated (Fujimura 1987).

Given that organ chips come out of developments in biological science and engineering developments in academic science, academic researchers are expected actors in this arena.[v] In Chapter 4, I center these particular actors, and explore their interests and participation in the construction of organ chips more fully. Here, I focus on two other categories of actors that make the organ chip arena an interesting site of analysis: state actors and industry actors. My analysis adds complexity to existing STS scholarship on articulation that has typically taken individual researchers and laboratories as the primary site of analysis and social action, and the more common focus on scientists' agenda setting, navigation of scientific work, and articulation processes (Hoffman 2021; Jeon 2019; Fujimura 1987). In this chapter, I show in the case of organ chips that articulation work happens in both top-down and ground-up ways: while

individual scientists do some of the work of articulating organ chips as doable and right, much of this work is shared and even instigated by state actors. Indeed, overt efforts by government funders themselves to shape organ chips as right and providing funding for them have been integral and added momentum to constructing organ chips as the right tool. I then turn to industry actors and their role shaping organ chips as the right tool, an outcome and manifestation of the embedded role of industry and commercial ethos in this arena, as described in Chapter 2.

State Actors: Structuring the NCATS Tissue Chip Program

From the outset, government funding agencies have been involved in organ chip research, allocating funds for their development and overseeing the progress of this work. Indeed, government funders have played a key and overt role in shaping the trajectory of organ chips in the US. In its inaugural year in 2012, NCATS launched the Tissue Chip Program in partnership with DARPA (Defense Advanced Research Projects Agency) and the FDA, to develop technologies and tools that would make the "therapeutic development process faster, cheaper and more accurate." (NCATS 2014). As discussed in Chapter 2, the Tissue Chip Program positioned organ chips as solving a key aspect of the translational crisis: by introducing human-based models in the earliest stages of pharmaceutical and toxicology testing, advocates suggested that organ chips could overcome the high rates of translational failure when moving from non-human predictive models to human trials. In the excerpt that follows, NCATS leadership describes the promise of organ chips, explaining that the program would

> Develop 3-D human tissue chips that accurately model the structure and function of human organs, such as the lung, liver and heart. These devices will enable researchers to predict harmful health effects of new drugs more accurately, thus addressing one of the main reasons that drug studies so often fail. (NCATS 2014, ii)

DARPA and NCATS provided financial support on the order of $75 million and $70 million respectively. DARPA supported the developments of two research teams working on ten-organ human-on-a-chip platforms at the Wyss Institute at Harvard University and at Massachusetts Institute of Technology. Indeed, early work at the Wyss Institute, where the lung model was developed, inspired the establishment of the entire Tissue Chip Program (National Public Radio [NPR] 2015).

NCATS' $70 million investment funded eleven groups for the first phase of the project to develop 3D cellular microsystems.[vi] These eleven groups covered the ten organs of interest that would eventually be combined to create a full human-on-a-chip model. Table 3.1 below outlines the projects funded as part of the first phase of the Tissue Chip Program.

Table 3.1: NCATS 2012 Tissue Chip Awards

Organ(s)/tissue	Project	Investigator& Institution	Commercial Activities
Heart, liver	Integrated Heart-Liver-Vascular Systems for Drug Testing in Human Health and Disease	Columbia University	TARA Biosystems, Inc.: Biotech company that produces predictive tissue models
Nervous, circulatory and gastrointestinal tract systems	Microphysiological Systems and Low-Cost Microfluidic Platform With Analytics	University of Central Florida	Hesperos, Inc.: Biotech company specializing in organ chip technology
Skeletal muscle and blood vessels	Circulatory System and Integrated Muscle Tissue for Drug and Tissue Toxicity	Duke University	
Vascular system	Human Cardiopulmonary System on a Chip	Harvard University	
10-organ model	All-Human Microphysical Model of Metastasis and Therapy	Massachusetts Institute of Technology	
Neural system	Human Induced Pluripotent Stem Cell and Embryonic Stem Cell-Based Models for Predictive Neural Toxicity and Teratoenicity	Morgridge Institute for Research at the University of Wisconsin-Madison	
Female Reproductive System	Ex Vivo Female Reproductive Tract Integration in a 3-D Microphysiologic System	Northwestern University	

Organ(s)/tissue	Project	Investigator& Institution	Commercial Activities
Heart, liver	Disease-Specific Integrated Microphysiological Human Tissue Models	University of California, Berkeley	
Heart (cardiac muscle) and solid tumor	An Integrated In Vitro Model of Perfused Tumor and Cardiac Tissue	University of California Irvine[vii]	Aracari Biosciences: Biotech company specializing in organ chip technology
Liver	A 3-D Biomimetic Liver Sinusoid Construct for Predicting Physiology and Toxicity	University of Pittsburgh; Rutgers University	
Kidney	A Tissue-Engineered Human Kidney Microphysiological System	University of Washington, Seattle	Nortis: Biotech company specializing in organ chip technology
Brain (neurovascular unit)	Neurovascular Unit on a Chip: Chemical Communication, Drug and Toxin Responses	Vanderbilt University	

Critically, these awards were funded as "U awards," which are designated as "research project cooperative agreements." This designation is important because it structures funding and engagement with the NIH in particular ways: U awards are used when "substantial programmatic oversight is anticipated" between the awarding institute and the investigators (N.I.o.H. NIH 2019). There are typically specific outcomes that are expected that must be met for subsequent funding to be made available. In the case of organ chips, researchers were expected to meet particular benchmarks—essentially to demonstrate that their organ chips were functional, successful platforms—in order to move onto later funding rounds. This is just one way in which state actors, funding agencies in this instance, played an overt role in shaping the trajectory of organ chips and both constructing them as and producing them into the right tools for the job.

Additionally, government agencies built the Tissue Chip Program as an explicitly interdisciplinary effort, overseen by the Trans-NIH Microphysiological Systems Working Group.

This group is comprised of approximately sixty program officials across the NIH who represent over fifteen Institutes and Centers. They meet monthly to discuss the project awards and their progress (NCATS 2021). This move is emblematic of NCATS commitment to breaking down interdisciplinary silos as a necessary ingredient for the twinned development of organ chip technologies and their potential to solve the translational crisis, as discussed in Chapter 2.

At the outset, DARPA's and NCATS' research in this area has been described as "separate but parallel" (Tagle, 2013): they had a shared vision of creating better *in vitro* testing platforms, but for different jobs. The program at DARPA was called the Microphysiological Systems (MPS) Program, established to develop platforms to test the safety and efficacy of novel countermeasures. Countermeasures are used against, or to treat, a wide range of weaponized health threats, including infectious disease outbreaks, and chemical or biological attacks.[viii] Testing countermeasures is challenging because it is both "unethical and impractical" to evaluate through the usual mechanism of human clinical trials (DARPA, n.d.). Historically, countermeasures have been developed akin to pharmaceuticals, relying on non-human animal testing data. In contrast, as discussed above, NCATS needed organ chips for a different purpose: to solve translational failure when moving from non-human animal models to humans for the purposes of developing pharmaceuticals.

Finally, the FDA has played a more indirect but nonetheless critical role in shaping how organ chip researchers and funders construct rightness. Because organ chips are articulated as both interventions and solutions to existing challenges in pharmaceutical and toxicology testing, which is a heavily regulated space, their doability and rightness has always required ongoing consideration of regulatory oversight. While the FDA did not provide funding for organ chip research and development, it was involved from the very beginning as a key stakeholder to

ensure that organ chip researchers would be proactively thinking about regulatory requirements and designing their technologies with the regulatory requirements in mind. This is a core issue, and obstacle for the construction of organ chips' rightness, that I return to later in this chapter.

Industry Actors

Constructing organ chips as doable and right strongly relies on ensuring that industry will become consumers of these technologies. Industry actors in this space range from pharmaceutical companies and contract research organizations (companies that provide support to the pharmaceutical and biotechnology industries for clinical trial management, validating technologies, and so on), who are seen as the potential "end users" of organ chip technologies, to biotech companies looking to expand their product profile, as well as interest groups that bring together representatives from industry. From the beginning, NCATS has formally worked with the International Consortium for Innovation and Quality in Pharmaceutical Development (IQ Consortium) to test and develop devices, as well as "discuss marketability and other industry logistics (NCATS 2021). The IQ Consortium is a not-for-profit group of pharmaceutical and biotechnology companies. It defines its mission as "advancing science and technology to augment the capability of member companies to develop transformational solutions that benefit patients, regulators and the broader research and development community (IQ Consortium, n.d.) . The consortium's Board of Directors includes a representative from each member company. Major pharmaceutical and biotechnology companies like AbbVie, GlaxoSmithKline, Eli Lilly, Gilead, Genentech Johnson & Johnson, Merck, Novartis, Pfizer, Sanofi, Biogen, and Amgen, are among the forty-some members. There are leadership groups, working groups, and affiliates. The IQ Consortium was often listed as a collaborator on organ chip activities at NCATS.

The IQ Consortium has an "Affiliate" group for microphysiological systems (MPS, which includes organ chips), which functions like a subgroup for special initiatives.[ix] The IQ MPS's mission is to "facilitate the industry implementation and qualification" of MPS models. While they do not endorse specific models, they are interested in facilitating the integration of MPS into practice. The IQ MPS Affiliate has been very involved in the organ chip arena, and member companies were often present at conferences I attended. Moreover, they have been quite active in engaging with the FDA to better position MPS developments for speedy and expeditious integration into regulatory policies and infrastructures (Baran, 2022).

For industry, organ chips are only the right tool if they are cheaper and more accurate than animal models (thus leading to cost savings) and—perhaps more importantly—can be used as evidence-generating tools for FDA approval. Put simply, industry holds immense power in the development of organ chips—perhaps eclipsed only by the FDA, as I explore later in this chapter.

Promising Potential: Hyping Organ Chips

The promissory language found in the media excerpts that opened this chapter are indicative of the critical role of hyping when actors construct doability and rightness. Such hype rarely—if ever—questions whether these technologies are in fact doable, obscuring the uncertainty that marks science. Instead, they focus on constructing organ chips as a valuable, disruptive technology that can transform pharmaceutical testing, and thus as a significant benefit not only among for participating in the organ chip arena, but also for other biomedical researchers, regulators, industry and investors, and ultimately, the public and society at large.

Thus, hyping work happens in myriad settings and is aimed at multiple audiences: in popular media, NIH press conferences, scientific publications, and at scientific conferences.[x]

Throughout my fieldwork and document analysis, the work of hyping organ chips emerged as a prominent theme. I often found myself surprised by how repetitious this work was: the same statistics, stories, images, and logic were used time and again to underscore why organ chips were a critical technology and the right tool.[xi] This hyping work tapped into the translational crisis, discussed in Chapter 2, and paired the crisis narrative with a vision for what organ chip technologies could do to intervene and solve the problem. Upon closer examination, I came to understand that hyping work took on different purposes in its varied settings. In this section, I offer an analysis of some of this hyping discourse, excavating its role in constructing both organ chips as doable technologies and the multiple jobs for which they are the right tools. I contend that two types of hyping work are integral to the construction of their rightness: (1) generalized constructions that are more superficial, surface-level hype, and (2) legitimations of specific technical aspects of organ chips. I then show how researchers question and push back on this hype, and how this skepticism serves to demonstrate their commitment to scientifically sound work, key to organ chips doability and rightness.

Generalized Constructions of Organ Chips as Disruptive Technologies

Early organ chip publications touted the disruptive potential of organ chip technologies. For example, the following excerpt is from a 2012 publication from the team who created the first lung chip at the Wyss Institute:

> [Organ chips'] potential to predict response in animals and humans is tremendous, and if successful, this disruptive technology could have profound effects on drug development as well as chemical and nano-toxicology testing. Future success will require academic

> investigators to collaborate with industry and regulatory agencies to develop appropriate biomarkers, clinically-relevant endpoints, and linked computational PK/PD (pharmacokinetic and pharmacodynamics) models that will be necessary for system validation and extrapolation to humans." (Huh et al. 2012)

The authors underscore the "tremendous" potential of organ chips, hyping their potential for multiple jobs: not only drug development, but also chemical and toxicology testing. This excerpt also highlights the actors in the social arena who will be necessary for organ chips to be successful. In fact, they claim that future success depends on the collaboration of academic, industry, and regulatory actors. This is a precise place in which the co-construction of jobs and tools is made visible, and made possible through the explicit mobilization of groups and particular relations who advocate for and endorse organ chips as the right tool.

Upon the launch of the NCATS Tissue Chip Program, then NIH Director Collins claimed the Program was "an unprecedented opportunity to speed development of effective therapies, while saving time and money." Leveraging the translation crisis, he continued,

> We know the development pipeline has bottlenecks in it, and everyone would benefit from fixing them. What we need are entirely novel approaches to translational science, to take full advantage of the deluge of new biomedical discoveries that have been made in recent years. (NIH 2011)

Collins explicitly links the translational crisis to the introduction of "novel approaches" like organ chips. He continues on to underscore that undetected (in animal models) toxicity as a common reason why "promising compounds" fail, and that organ chips would fix this key point in the translational pipeline, allowing researchers to discern which compounds are safe and effective earlier in the process.

These generalized assertions about organ chips, which construct them as transformative technologies, routinely were made in the introduction of scientific publications, as well as in presentations, in essence priming audiences to see them as disruptive and novel, yet necessary

because of these qualities. Often when I observed scientific conferences where organ chip researchers were present, presenters would have a slide early on that explained what inspired and impelled their work. I came to call this the "motivation slide" in my fieldnotes. The motivation slide offered an explicit framing of the problem that the persenter's technology—whatever it was—was poised to solve. This slide would often include things like economic costs, number of lives lost to a particular disease (or procedure), and would underscore that the problem, in case the audience did not yet know it, was absolutely dire, and something that society urgently needed a technological fix to solve. (The inclusion of this motivation slide and framing was not specific to organ chips, as I witnessed it throughout biomedical engineering. In the undergraduate class I observed, for instance, students all included this piece in their presentations, suggesting that is a practice that biomedical engineers are socialized to take up as an important practice for justifying—and I would argue hyping—their work.)

For organ chip researchers, the motivation slide included a set of statements about pharmaceutical development costs and failures and the inadequacy of animal models for predicting toxicity and efficacy (like the one referenced in Chapter 2). By the third or fourth presentation on organ chips, researchers would pull up the ubiquitous "motivation" slide, and quickly note that the "audience had heard it all before" from other researchers that day. Indeed, it seemed significant that the framing of this crisis never seemed to vary, but yet it continued to be important to note. In a sense, this hyping was routinized, serving to establish and subsequently reinforce to audiences how right these tools are. These generalized constructions were just that—general—and did not acknowledge or parse the complexity of what integrating a technology as "disruptive" as organ chips into the biomedical research infrastructure would entail. While there

were more nuanced conversations about the scientific potential of organ chips and their limitations, as I discuss later, such conversations rarely were aired publicly.

Technically Specific Legitimations of Organ Chips as Superior Technologies

In contrast to the big-picture and generalized claims about how organ chips may improve the efficiency of biomedical research, in this section I show that hyping work also includes claims-making about aspects of the technologies themselves, that ostensibly make them superior to their animal counterparts and to two-dimensional (2D) *in vitro* models. Consider the following excerpt, which positions organ chips as superior to animal models, and then lists a number of technical features that substantiate their superiority:

> We need real human organ-like devices that are superior to animal models. Organ-on-a-chip may be a good solution, which has minimal functional units that use primary human cells, rather than animal cells, like a real human organ. The ideal methods will not only use human cells but also mimic 3D architecture and flow conditions within real human organs. Microfluidic devices seeded with human cells and perfused with cell culture media in a physiologically relevant manner have already been developed to provide a minimal functional unit to mimic real organs. The small size allows easy flow control and requires few cells and only small volumes of samples and reagents. Parallel experiments with large numbers of samples at the same time can also be realized. An additional advantage of the devices is optical transparency that allows visualization, at the cellular level, of the whole drug response process, something that is difficult to do in actual living organs. (Kim and Takayama 2015, 166)

This excerpt itemizes multiple aspects of organ chips that purportedly make them technologically superior: they use "few" human cells, mimic 3D cellular architecture and flow conditions, and are optically transparent.[xii] These features also undergird the construction of organ chips as *physiologically relevant.* The authors couple these technological features of rightness with economic ones that further buttress their case: organ chips are cheap and efficient because they require only small volumes of cell samples and reagents (substances and compounds that

facilitate reactions). Other documents discuss what comparisons directly to humans that organ chips enable:

> Because these tissue chip systems will closely mimic human function, scientists can probe the tissue chips in ways that they aren't able to do in people, and the knowledge gained may provide critical clues to disease progression and insights into the development of potential therapeutics." (NIH 2014)

Here, organ chips are positioned to offer knowledge that can't be ascertained in other ways, because organ chips can be "probed" or manipulated and tweaked in specific and detailed ways that are not ethically or technically possible to do to human bodies. They offer the physiological relevance of humans without the risk and messiness of human subjects research. Critically this was a key motivator for DARPA, which was interested in using organ chips and microphysiological systems for the development and testing of countermeasures.

But organ chips have also promised other advances related to this no-consequence probing: in the context of precision medicine initiatives (which aim to develop targeted therapies and diagnostics for individuals and population groups), chips are increasingly used to model rare genetic disorders that impact particular organ systems in the hopes of developing targeted therapies for them, or repurposing existing drugs for secondary (or beyond) use. Recent work has hyped their capacity to model specific "sub populations," positioning organ chips to be useful for precision medicine initiatives. In multiple conferences I observed, researchers talked about the future potential of organ chips to do precisely this, an issue I return to in Chapter 4.

Testing the Constructions of Organ Chips as Disruptive and Better Technologies

While both types of hyping work discussed above were performed in public-facing venues like press releases, scientific publications, and presentations, organ chip researchers often spoke behind closed doors about pushing back on this hype. Some of this pushback came from

critics, but many researchers who themselves work on and believe in organ chips also aired similar concerns. Organ chip researchers I interviewed were acutely aware that part of the work of ensuring the success of novel biomedical technologies is convincing biomedical researchers—and regulators—who have long used other, more entrenched methods like animal models and 2D disease models, that organ chips are a valid and rigorous way to test pharmaceuticals and predict human response. Yet, as I will show, rather than substantially undermining the case for organ chips being the right tool for the job, these critiques and reservations served to circumscribe and focus in on the jobs that organ chips *could* do, and as a result, paradoxically buttressed the case that organ chips were capable of replacing non-human animal studies in pre-clinical pharmaceutical testing.

Acknowledging the hype around organ chips, I would often ask researchers if they thought the claims of *replacing* animal models were realistic. Much media reporting and generalized constructions of organ chips as disruptive, transformative technologies would make broad claims that organ chips would "replace animals" in biomedical research. When I pressed interviewees about the odds of organ chips actually accomplishing this and what it would entail—typically after they expressed unbridled enthusiasm for the technology— they then spoke in more measured ways about how organ chips might intervene in biomedical research, offering a more circumscribed vision of where and how organ chips might disrupt existing research practices. Consider the following excerpt from a researcher who explained multiple cases where he thought organ chips would be more and less useful:

> I think we could replace some but not totally replace all [animal models]. I mean, I think I know the situation quite well in the genome editing space, moving away from toxicology. I'm interested in developing new genome editors, um, like provide some sort of therapy to muscular dystrophy. Let's say that's the case study. So, to find where else in the human genome, these editors could potentially edit, so called off-target effects, that's very hard to model in a different [non-human] genome. So I think that's one limitation of

> the animal models in terms of genomic structure that's different. There's certain things that you could potentially do in nonhuman primates that are close, but you know, 99.9 percent the same, those other. small differences matter a lot for some of these genomic editors. So in that case, I don't think you can go to a non-human system to answer that question of specificity. So people are working with human cell lines with the human IPS [induced pluripotent stem] cells. We have a project of working with human IPS cells in the eye. And we put in another [grant] that's looking at human heart tissues from IPS cells. I think the major advantage there is that you can test the exact sequences that you want to put into patients, at least target inpatients and what happens.

In this excerpt, the researcher constructs organ chips as right, underscoring the advantages of working in a human-based model. He explains that there are genomic questions that must be asked using human systems, because "small differences matter a lot" for some genomic editors. Using human based models, he could introduce genetic sequences and trusted that these results would better predict what might happen when they would be put into human patients. But he then continued on to explain that there are some questions for which their "humanness" matters less, and for which animal models are requisite:

> But then there's fundamental questions about toxicity and safety that we can't address in the human tissue systems [including organ chips]. Once you inject, let's say the genome into the muscle at the kidney, will it hit the liver, will [it] hit the brain, the heart? You can make a micro physiological system where you have little kidney tissue, neuro tissues all kind of clumped together, but that's not going to be how it really circulate inside a human body. And that's where, you know, where we look to animal system. So our questions about where things go and how they get absorbed well by different tissues are best done in a living, breathing, arguably best done in a nonhuman primate, but there's limitations to that, where there is an alternative to not have to use nonhuman primates, I think the field wants to go there.

This researcher noted where and how organ chips and other human tissue systems can and cannot answer the questions they were asking in their research. Of particular note was his description of how chemical compounds move throughout the body, and how this could not be replicated in human tissue systems.

Indeed, while organ chip researchers plan to eventually connect various organs to create full human systems (and have been funded to do so), moving chemical compounds throughout the model is unlikely to capture what actually happens, particularly the unintended "side effects" on other organ systems *in vivo*. Investigators were careful to note that while organ chips are able to predict some human physiological responses (e.g., possible toxicity to a specific organ), they were not sufficiently reflective of the human bodies they are meant to stand in for to convincingly accomplish other jobs (e.g., tracking multiple-organ side effects) that full system models, like animal models, can do. In the latter cases, investigators explained that there were just simply some jobs that animal models can do that new technologies like organ chips cannot. Another researcher explained that there were many jobs that organ chips were not, and would never be, right for:

> I really do believe that organ-on-chip studies can overcome a lot with animal models, but perhaps there are small things that you just can't capture fully. We'll need those models. I think, [if] you do a whole body knockout of some gene [a technique in which a particular gene in an organism is made inoperative], you're still going to need animal models for that to really get a sense of how everything's all connected. But once you have that hypothesis around what happens when you knock out one gene or something, I think from then on you can kind of then migrate into 3D or organ chip models. Yes, there's some things that you're still going to need mouse models for. So it wouldn't kill the [mouse] industry, it would just be one corner of it. And [it's] lucky for the people doing that, [knockouts] were the most expensive models. So, they'll be in good business, the most expensive part of their business would stay intact.

This investigator's explanation highlights how the rhetoric of replacement in surface level hype overpromises the transformative potential of organ chips. At the same time, she also makes the case that even where organ chips are "wrong" for some jobs, they could still be "right" for other jobs further down the line. Both researchers quoted above qualified the notion of replacement as a complex question—far more complex than surface level hype would make it seem—and

whether organ chips could be the "right" tool was fundamentally about the specific research questions at hand and what exactly researchers were trying model and measure.

For others, critique of the hype was often aired in the context of the term "organ chips." As I have mentioned, organ chips are microfluidic models; technically speaking, they are more formally termed "microphysiological systems." But other than in publications, this terminology was rarely used, and even when invoked in presentations and publications, it was often used interchangeably or elaborated with the terms "organ chip" or "organ-on-a-chip." Yet, despite these terms' ubiquity and seeming normalization, many investigators told me in interviews and researchers giving presentations would note that they felt discomfort with using them. In presentations, sometimes they would air such sentiments by mimicking with their fingers scare quotes around the phrase "organ chips" while others would outright state their concerns. In an interview with me, one researcher explained his discomfort with the term this way:

> 'Organ-on-a-chip" is kind of the lay term that has quickly permeated many levels of our society. I mean, I think my mom and dad, my in-laws, almost could understand what "organ-on-a-chip" means. It's a dangerous word. It implies that you have literally an organ on a chip and so unless you're in the field…. I think it promises too much really. I mean we are mimicking just tiny features of organs on chips. And so it's a little bit of a misleading term, but I think it's a little sexier term that is easier… people just sort of latched onto it.

One presenter at a 2018 conference said to a room full of researchers conducting organ chip research, "I prefer to call them 'organotype models' because we are a-ways away from an 'organ-on-a-chip.' We can debate about this later." In two presentations later that day, researchers referenced this person's talk as they stated, "we're an organ chip lab,"[xiii] and then qualified it in one way or another, explicitly attending to the skepticism that the first presenter had shared. For instance, one agreed that the research community is a long way off from an "organ on a chip." The other made an offhand comment about his "feelings" regarding the term.

Both acknowledged the hype surrounding this term, and were sure to distance themselves from it, albeit performatively.

Critically, these exchanges were not aired in more public spaces or to the broader scientific community. Instead, they occurred at conferences attended by experts and insiders who were well versed in the limitations of what these technologies can do. While they seem to be breaking down the generalized and technical hype, I contend that this is also important hyping work: in conceding that organ chips and the discourse surrounding them perhaps promise too much, researchers are then able to detail the specific scientific features of the organ chips and what they are able to do using them. It also signaled that an approach to their scientific work that was realistic, sober, and clear-eyed. By distancing themselves from the surface hype, they signal that they are doing important and *scientifically sound* work, a key element for constructing doability and rightness. This was particularly important given several biotechnology scandals that hinged on microfluidic devices like organ chips. As I explore separately (Jeske 2020), the highly publicized Theranos scandal, in which a biotechnology company lied to investors and the public about the functionality of its microfluidic device, loomed large in biomedical engineering communities, and especially for those developing medical devices like organ chips.

Regulatory Infrastructure & Scaling and Standardizing Organ Chips

For organ chips to succeed as a pharmaceutical testing platform, they must additionally integrate successfully into the existing regulatory infrastructure of the FDA. The existing regulatory infrastructure and ecosystem pose a formidable challenge for organ chips at the national and international scale. Replacing animal models in early-stage pharmaceutical testing requires that regulatory agencies like the US FDA and the European Commission (because the

pharmaceutical industry is global) accept safety and efficacy data produced using organ chips. As such, in recent years organ chip developers and stakeholders—particularly those who have launched companies focused on these technologies, and who participate in the IQ Consortium (described above)—have been involved in the regulatory space. This involvement has taken the form of advocacy to "modernize" the language in the Food, Drug, and Cosmetic Act that has written the use of animal models into law, and to shift regulatory agency standards so that organ chips become regarded as a valid way to produce pharmaceutical safety and efficacy data. As I explore below, these changes require amendments to existing legislation as well as shifts in scientific practice.

The FDA Food, Drug, and Cosmetic Act requires the use of animal studies of potential new drugs prior to testing in humans. Animal testing is used to make several measurements (and predictions about safety and efficacy in humans): drug absorption in the blood, its chemical breakdown in the body, toxicity of is metabolites, and the time it takes for the drug to be excreted (FDA 2015). In 2021, the FDA Modernization Act was introduced in Congress with bi-partisan support. The Bill amends a subsection of Section 505 of the Federal Food, Drug, and Cosmetic Act that mandates the use of animal testing in preclinical studies. The proposed amendments strike specific places in the Act where "animal testing" has been explicitly named, and instead insert "nonclinical tests or studies" which are defined as

> a test or study that is most likely to predict human response based on scientific evidence and occurs before or during the clinical trial phase of the investigation of the safety and effectiveness of a drug. Such test or study may include the following: (1) cell-based assays, (2) organ chips and microphysiological systems, (3) sophisticated computer modeling, (4) other human biology-based test methods, and (5) animal tests.

Effectively this widens the types of scientific studies that can be used to produce pre-clinical data about a new drug. If passed, this means that experimental drugs will no longer have to be tested

in non-human animals before clinical trials in humans can be approved. Data produced using organ chips, among the other types listed above, would be acceptable, which would be quite impactful for market uptake.

The passage of this Act could prove critical momentum for organ chips to become the right tool. But novel technologies must also prove their validity, and regulators at agencies must feel "confident" in evaluating data from novel methods. Without the social processes of scientific negotiation around the models themselves—their accuracy, validity, and reliability—regulators will not consider data produced using organ chips as valid, robust scientific evidence. In that case, organ chips will have limited value for pharmaceutical companies and contract research organizations; there will be far fewer jobs for which they will be the right tool. Thus, from the launch of the NCATS Tissue Chip Program, the FDA was included in discussions about how to best develop organ chips. Representatives from the FDA, including its Center for Drug Evaluation and Research, Center for Biologics Evaluation and Research, and the National Center for Toxicological Research, have been tapped to provide expertise and guidance to organ chip researchers. These regulators therefore hold substantive power over whether and if organ chips will become the right tool; accordingly, organ chip developers and interest groups, like the IQ MPS Affiliate, actively work to engage regulators in the development of organ chips and move the field toward practices that are more accepted among regulators.

When pharmaceutical manufacturers submit application packages to the FDA for approval to move to clinical testing of an investigational new drug (IND), they are required to submit specific types of data that include animal pharmacology and toxicology studies that generate pre-clinical data on whether the IND is reasonably safe in humans (FDA n.d.-b). These data typically include:[xiv]

- Dose levels or exposures at which no adverse effects are observed
- Determine safe first-in-human doses
- Identify potential target organs for toxicity
- Identify potential developmental and reproductive toxicity
- Identify potential carcinogenicity
- Identify and understand factors that may affect different responses by sub-populations

While it is not required that every analytic is produced through animal studies, typically this has been the main method used, and for which the most robust validation and reliability data exist (Baran et al. 2022). In other words, while translational advocates and organ chip researchers point out that animal testing does not reliably predict safety and efficacy in humans (as discussed in Chapter 2), it does produce reliable data in the model organisms themselves, and data that regulators are reliably comfortable interpreting and accepting. Thus, novelty works against organ chips: while they introduce complexity that more closely mimics the body, they also introduce uncertainties about the data produced using them, particularly whether and how regulators find those data trustworthy enough to accurately show the safety and efficacy of the chemical compound itself, and not something else, such as an interaction between the chemical compound and the testing platform.

One key area where regulator concerns have been leveraged to shape the design of organ chips is the material that is used to create the platform of the chip. (A second example of regulatory impact is on the type of human cells used, which will be discussed in detail in Chapter 4.) Many organ chips are created using Polydimethylsiloxane (PDMS), a common type of silicone widely used in soft lithography (as discussed above). PDMS has been used in many microfluidic applications, and is highly regarded for having particular properties, including its ability to create molds with extremely small etched channels (just a few nanometers), oxygen permeability, and optical properties that make it ideal for imaging (which, as described above,

are touted as important technical features of organ chips for physiological relevance and for using the device). But when used in organ chip platforms, PDMS was shown to leach into the samples as well as to absorb small molecules, raising questions about the reliability of the data produced using organ chips (Carter et al. 2020). What results could be attributed to the reactions that researchers were actually trying to measure versus the impact of the PDMS platform leaching and absorption?

This concern led industry to seek out other materials, like hydrogels elastomers and thermoplastic polymers, in order to avoid this problem (Campbell et al. 2021). Industry became critical of academic researchers who were continuing to use PDMS, launching organ chip researchers to investigate the effects of PDMS absorption, develop ways to discern what is attributable to PDMS versus the chemical compounds being introduced into the model, and, when they decide to continue using it, to justify doing so (Grant et al. 2021). Indeed, when researchers I interviewed used PDMS in their platforms, they often noted that "industry had since moved on" or at least acknowledged that they were made well aware of the potential issues with using PDMS. Concerns like this presented by regulators also created pressure for organ chip developers to standardize organ chips so that they can be more readily integrated into the regulatory science infrastructure. That is, to produce data deemed trustworthy and acceptable by drug regulators, organ chips must fit into an infrastructure that requires a high degree of standardization. If some organ chips are made using PDMS, while others are not, then regulators must be prepared to evaluate different data submission packages that detail the safety and efficacy of a compound, but potentially also data that shows the effects of the platform.

Another effect regulatory concerns have had on organ chip design has focused on their specific applications or "contexts of use" which standardize the bounds of what organ chips can

be used for. This is a key place where conversations between regulators and interest groups have ensued. In conference proceedings from a 2020 workshop with IQ MPS Affiliate and the FDA, they wrote "a number of challenges remain before these cellular technologies can be fully incorporated into drug discovery and development, with one of the most critical being establishment of robust qualification packages built around specific contexts of use" (Baran et al. 2022, 2). Context of use is an FDA term that refers to specifications of the particular and appropriate use of a given technology, including the circumstances under which something is qualified. Of course, these considerations are also social processes of negotiation. Thus interested groups have worked to define the context of use for organ chips that satisfy regulator concerns.

Because organ chips are poised to intervene in a highly regulated space, standardization is inherently tied to their doability and rightness. This is a noteworthy departure from how standardization is thought about in biomedical innovation, as novelty and standardization are often seen as competing goals. Fujimura's conceptualization of articulation is indicative of this tension. She writes, "standardization increases the doability of a particular set of problems until a certain point, when it begins to work directly against novelty, thus marketability and doability" (1987, 282). In this case, organ chips only become marketable, doable, and right for the jobs state and industry actors care about if they are in fact standardized; unless proponents can successfully demonstrate organ chips possess this quality, they are unlikely to be accepted by regulators as valid and reliable tools for knowledge production.

Conclusion: Rendering Tools Right for Certain Jobs

Since the publication of the lung chip paper in *Science* in 2010 (Huh et al. 2010), there has been a rapid proliferation of organ chip technologies and investment in their development. In the scientific community, publications went from one paper in 2010 to several hundred publications in 2020 and 2021.[xv] In 2016, organ chips made the World Economic Forum's list of top ten emerging technologies, alongside Blockchain, autonomous vehicles, and nanosensors (Cann 2016). Since its launch in 2012, the Tissue Chip Program has gone on to fund multiple new lines of research, moving organ chip work into new phases of development. Such efforts include establishing initiatives for standardizing and scaling organ chips (as will be discussed further in Chapter 4), and launching programs to study specific diseases using organ chip platforms, and sending organ chips to the International Space Station to study aging.[xvi] Such developments suggest that organ chips are indeed on their way to becoming the right tool for particular jobs.

The term *becoming* in the title of this chapter signals that organ chips are not yet the right tool for particular jobs, but rather that they are in the process of being shaped as so. Thus, this chapter offers an examination of the construction of rightness during a phase of development when this articulation work is particularly critical and visible. Following Clarke and Fujimura's conceptual framework, I offered an analysis of the elements of the situation, particularly the sociotechnical conditions of possibility (including the research materials, technologies, skills and techniques, as well as social trends) and the landscape of actors. I showed how different and new categories of actors coalesce around organ chips to construct their rightness and to shape their trajectory in particular ways. The social worlds that come together to work on organ chips include academic biomedical researchers, who are traditionally recognized as experts, but

increasingly other actors too, like funders, regulators, pharmaceutical and biotechnology development companies, and investors. I demonstrated how the work of articulation (Fujimura 1987) occurs collectively, in which various actors exert power in shaping the trajectory of organ chip development.

Throughout, I demonstrated the various jobs for which organ chips are positioned as right. Organ chips are positioned as solving the problem of *scientific* translation, of moving from non-human animal models to humans, a point at which failure is all too common and exceedingly costly. But organ chips also solve other problems, particularly those of interest to pharmaceutical companies: they are potentially much cheaper than animal models which, in addition to the cost of purchasing (or developing), require breeding, housing, and maintenance which represent significant costs for laboratories. Additionally, organ chips also offer a way to make go/no go decisions exceptionally early in the development of a pharmaceutical product. Simply put, organ chips are positioned as saving a tremendous amount of time and substantial capital.

I then turned to the critical work of hyping that occurs in multiple spaces to position organ chips as doable and right. Hype is defined as "to promote or publicize (a product or idea) intensively, often exaggerating its benefits" (Oxford n.d.) and is typically invoked when the benefits are not self-evident, not yet achieved, or less than anticipated. In this case, however, I showed that generalized, or surface level, constructions of transformative potential and more technical legitimations perform essential work for constructing the organ chips as both doable and right. I demonstrated that questioning this hype, too, enables researchers to legitimate these technologies. These varieties of hyping serve particular functions in constructing rightness for particular audiences, and for establishing credibility of scientists.

Finally, I turned to the role of regulation, arguing that a critical element of constructing rightness requires that organ chips count as a valid and reliable technology that can produce trustworthy safety and efficacy data. Because they intervene in a highly regulated space, coordination and collaboration with regulators has been key throughout their development. While standardization is often thought to work against marketability, I show that in this case standardization is a requisite piece of rightness. In Chapter 4, I take a deeper dive into the construction of organ chips, further tracing how market forces shape the technical design of organ chips.

CHAPTER 4: MODEL NEGOTIATIONS: MAKING ORGAN CHIPS MARKET-READY AND HUMAN ENOUGH

All models are wrong, but some are useful.

-George E.P. Box

Introduction

Scientists have long used models to understand the world. Models can be mathematical, computational, and physical; whatever their form they are mobilized as tools that help to render something knowable: to grasp how a biological mechanism works, to predict how a disease impacts one part of the body, to project how climate is changing. Models offer simpler renditions of complex phenomenon: they are tools that, at best, provide partial information. They preserve particular features of the original, while purposefully simplifying, discarding, or neglecting other features.[i]

Models come to be useful tools for different jobs; as they do so, they are imbued with power. Some models, and the knowledge produced using them, are contested. In other cases, that knowledge is regarded as if it were not derived from models at all, but rather as reflections of the complex phenomena they are meant to render or simplify. While scientists readily observe that models do not, and are not intended to, capture the complexity of what they represent, they still come to be *useful* and *right* tools for particular jobs (Clarke and Fujimura 1992) as I have shown in Chapter 3. In this chapter, I turn to the construction of organ chips, excavating the social nature of scientific decision making. I begin by showing generally how organ chips are made and how the human cells used in these models are sourced. I then follow two cases, the lung chip and the female reproductive system, to trace how organ chips become collectively understood as "human enough," and how market priorities explicitly shape the design of organ chips. I

highlight not only how these negotiations are shaped by scientific concerns, but also how the organ chip development is driven by the political and economic forces that demand scalable models.

Model Organisms in Biomedical Research

Historians of science and STS scholars have examined how animal models became fundamental tools for biomedical research and built the foundation for much of our knowledge about the human body (Nelson 2018; Creager et al. 2007; Rader 2004; Sismondo 1999). Recent estimates suggest that nearly 95% of non-human animals used in biomedical research are rodents (Stanford Medicine n.d.).[ii] Social studies of animal models have shown how model organisms became highly standardized and manipulable laboratory technologies, and essential tools for bioscience (Kohler 1994; Lewis et al. 2012). The staying power of mouse models, in particular, is sustained through many justifications often presented in a neatly rationalized package: First, mice are inexpensive and considered "mild tempered" and "docile," making them easy to care for and handle in the laboratory, all of which are important economic considerations for biomedical labs. Second, mice have a short lifespan and reproduce rapidly, meaning that the time from when a mouse is born to when it reaches desired maturity for testing is relatively short. Third, mice share important similarities with humans, namely much of our genomes are similar as are the genes associated with particular diseases (NIH 2014b). Finally, their genetic, behavioral, and anatomical features are well characterized, given that they have been used for over one hundred years in biomedical research.

The STS literature has examined how, particularly in the US, institutional and political support for mice breeding programs in the twentieth century, along with commitments to genetic

theories of causation, resulted in the mouse's transformation into the standard laboratory organism (Gaudillière 2001; Rader 2004). More contemporary studies of the role of mouse models in biomedical research show how deeply rooted mice are in the infrastructure of contemporary scientific research. Nelson (2018) argues that its institutionalization strips the mouse from the places and historic circumstances that constructed and standardized it as the right tool for biomedical research. Nelson and others have shown that mice straddle the line between human and artificial, embodying characteristics of both: "the mouse's status as a living being that shares an evolutionary history with humans imbues it with epistemic authority of the natural world, and the way it has been altered to function as a scientific tool gives researchers opportunities to design experiments that would be impossible with human subjects" (Nelson, 2018:4).

This literature has largely focused on how animal models are used to make epistemic claims and how they come to be understood as "good enough" to provide meaningful data about the humans they represent, highlighting the ways in which knowledge produced using models always requires social negotiation and judgment (Lewis et al. 2012).Thus sociologists and STS scholars have been concerned with the ways model organisms are used to produce knowledge about basic biological processes (Ankeny and Leonelli 2021, 2011) and how researchers navigate translating findings across species, and from non-human animal model to humans (Friese and Clarke 2012; Lewis et al. 2012). Historians of biology have also taken up questions of how model organisms come to be right for particular jobs,[iii] focusing on organism choice and scientific work using model organisms. Recent scholarship has emphasized the political economy of laboratory organisms, bringing attention to the role of capitalism and the "economic and financial situations" (Akeny and Leonelli 2021: 270) in which model selection, sourcing,

dissemination, and standardization take place (Bolman 2021, 2022). However, the literature examining market forces has not gone so far as to analyze how the construction of the very models themselves.

In a parallel literature, reviewed in Chapters 1 and 2, sociologists and STS scholars have examined how academic science increasingly adopts industry practices and celebrates the commercialization of scientific work. This scholarship has attended to the ways capitalism shapes the institution of academic science, particularly in its turn toward market-like activities, in which university employees, including researchers, engage in industry partnerships and consultancies, patenting, and other activities meant to generate external revenue (Hackett 1990; Nickolai, Hoffman & Trautner 2012). In this chapter, I show how political economic forces and the commercial climate imbuing academic research also come to shape the very construction of biomedical models, highlighting how the potential market value of technologies for particular jobs influence the development of highly technical aspects of their construction.

Organ Chips and Model Organisms

In the case of organ chips, building the case for novel models requires the simultaneous breaking down of the deep institutionalization of non-human animal models. As discussed in Chapter 2, despite the longtime and routine use of the mouse and other animal models in biomedical research, the relatively poor rate of translation from non-human animal models to humans presents a persistent problem particularly for pharmaceutical safety and efficacy testing. Thus, there is growing consensus among translational medicine advocates that animal models should be replaced or supplemented by others that more reliably predict toxicity and efficacy in humans (cf. Mak et al 2014; Marincola 2003a, 2003b). Organ chip researchers have galvanized

around the potential of organ chip models to offer better, more accurate predictions about human response to pharmaceuticals, as well as insights into pathophysiology.

According to organ chip researchers and funders, organ chips differ from routinely-used biomedical models in multiple ways that make them advantageous. First, organ chips are models made from the species and tissue it is intended to model, and therefore is a clear departure from predecessor models (Bolker 2009). Organ chip developers think of organ chips as replacements for surrogate models, which are proxy organisms that are used when the target species is inaccessible, unethical, or difficult to study.[iv] Researchers developing organ chips consider them as potentially better than existing surrogates because they include human cells and thus remove a key translation—from non-human animal to human—where many previous surrogate models fail. Second, through the integration and linking of various organ chips in sequence, researchers can observe the effects of, for example, introducing a chemical on multiple organ systems in the body. Surrogate models already offer this, but they do so in a non-human model (though Chapter 3 complicated this). Third, organ chips offer the ability to test chemical compounds without "risk": with organ chips, there is no risk of toxicity to non-human animal life, let alone human life; the only potential casualty are cells. In this way, organ chips offer a "consequence free" way to conduct safety and efficacy testing in which the only potential risk is financial. This capacity has been highly sought after for some time but has yet been unachievable until the development of organ chips.

Thus, a key justification for investment in organ chips is that they are human-based models, and this humanness is regarded by those in the field as inherently better.[v] Across interviews, in observations, and in the published record, this fact is taken for granted; for instance, when I asked researchers what made organ chips better than traditional models, they

often began with phrases like, "well they're human, of course." Indeed, whereas other cases of emergent technologies have highlighted how novel technologies rely on the cumulative credibility of previous, precursor technologies (Lynch et al. 2008), the case for organ chips relies on skepticism about their predecessors. Repeatedly, they are treated as a solution to the problems stemming from preexisting models' inability to dependably produce knowledge that can be directly translated to, and is applicable for, humans. This inability is incredibly costly in terms of time and resources, as discussed in Chapter 2. What makes organ chips' justification so self-evident, and what makes their human-ness so advantageous, is because the return on investment—in using organ chips as surrogate models in biomedical research as well as in the development of organ chip technology itself—can potentially be much higher than using animal organisms. By introducing human cells earlier in the pharmaceutical testing processes than they historically have been, organ chip funders and researchers suggest that they can overcome translational failure by providing more reliable data, thus making decision making cheaper and eventual products more profitable.[vi]

However, while organ chips may introduce the human earlier in the testing of pharmaceuticals and offer human-based testing in areas where this has previously not been possible (e.g., testing of countermeasures), they still require translations in order to extrapolate data produced using organ chips to humans. In the next section, I turn to the construction of these technologies.

Constructing Organs on Chips

Midway through our interview, the investigator abruptly stands up and starts looking around his office. "Have you seen one of them before? They're pretty fun." He digs around in a cardboard moving box and hands me a sheet of flexible clear material. The clear object fits in the palm of my hand, with multiple "chips" printed onto it, waiting to be cut apart. He explains that each

chip is its own model, but it's economical to do the photolithography on a whole plate rather than one chip at a time. Each model measures no more than an inch long. The object bends, and tiny holes are etched onto it, connected by even tinier channels, under just the right light they are barely visible to the naked eye. I look at it slowly, contemplating what can be seen and known using this object.

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How does this object, about the size of a flash drive, come to stand in for a human? How is it that researchers trust a technology comprised of polymer, fluids, and some human cells to model the human body and provide accurate and valid information about its predicted responses? In this section, I examine how organ chips are constructed and the ways in which researchers make decisions about what fragments and functions of organs to model, in order to be considered "human enough." I focus on one of the central concerns of organ chip researchers: where to source human cells.

In Chapter 3, I detailed the 2012 launch of the NCATS Tissue Chip Program and DARPA's MPS Program, which together funded the first group of organ chip researchers to develop various different systems as well as integrated human-on-a-chip systems. These funding programs stipulated multiple metrics that organ chips must meet in order to be deemed successful (and also, to be funded in later phases of the Tissue Chip Program). Such benchmarks included lifespan—NCATS stipulated that organ chips must offer an *in vitro* model that maintains tissue viability for a minimum of four weeks—and that they must recapitulate specific organ functions across the lifespan. They also required that they be 3D microfluidic models (as opposed to 2D[vii]), and modular, so that they could be combined with other organ chips (Tagle 2013). But beyond these specifications, there are many design choices that are left up to organ chip developers. For instance, what material should the platform be made of? What type of human cells should be used? How should the chambers be arranged? What is the best way to

move fluid throughout the model? Each of these questions represents a decision point that shapes how the model works—how aspects considered to be essential about a specific human organ are recapitulated in its model, experimental form—and has implications for what can be ascertained from the model. Regulatory concerns dictate some choices, such as the debate around platform material discussed in Chapter 3. Here I discuss another feature of organ chip construction, sourcing human cells. In this case, I document how both experimental intentions and scaling for the market shape decisions about what type of cells to use. Moreover, I show how state actors have again played a central role in moving toward market ready technologies.

Sourcing Cells

Part of the promise of organ chips is derived from their use of human cells. This is the feature that much hype surrounding these technologies hangs on: organ chip researchers believe they are superior models because they are made of the same stuff as humans are. In presentations and publications, organ chips are called "human-based models" and there are multiple types of human cells that can be used to construct organ chip models. But not all human cells are equally physiologically relevant to *in vivo* cells in human bodies, and the various human cell types that can be used—primary donor cells, induced pluripotent stem (IPS) cells, and cell lines—introduce compromises. In making decisions about what type of cell to use, organ chip researchers must make key tradeoffs between physiological relevance (do the in vitro cells correspond to what the expected biological functioning is under particular conditions, thus best predicting human response?), reproducibility (can this experiment be repeated in another setting, or by other researchers, and still yield the same results produced in the original laboratory?), and scalability (can this technology be manufactured in large quantities, to become a commercially available

laboratory tool?). Table 4.1 below offers an overview of the various sources of human cells that can be used in organ chips and their relative advantages and disadvantages, as characterized by organ chip researchers.

Table 4. 1: Human Cell Types Used in Organ Chips

Cell type	Description & Sourcing	Tradeoffs
Primary Donor Cells	Donor cells are acquired through donations from patient surgeries (e.g., hysterectomy), lab member donations	While researchers agree these are most physiologically relevant, they are hard to come by and sustained supply not guaranteed. When concerns around scaling up, specifically to scale these technologies for the market, this route of cell supply is problematic. For rare disease studies, primary donor cells preferred.
Induced Pluripotent Stem (IPS) Cells	Derived from adult skin or blood cells, that are reprogrammed to an embryonic state and then matured to tissue of interest IPS cells can be derived from patients, or purchased from commercial vendors	Consistently available and scalable, highly manipulable, amenable to gene editing. Researchers think these are not usually "mature" enough to be physiologically relevant, even when differentiated. Simply put an IPS cell, when differentiated to be an adult kidney cell is not the same as an *in vivo* adult kidney cell. As one researcher put it, "they are neonatal at best."
Cell Lines (human and non-human animal)	Immortalized cells propagated in vitro (e.g., HeLa cell line)	Easily commercially purchased, and are highly regarded for their robust characterizations and reproducibility. Cell lines are the least physiologically relevant or functionally optimal – researchers note that cell lines rarely behave like in vivo cells.

In what follows, I discuss each cell type and how organ chip researchers I interviewed and observed used them for particular experimental purposes. In doing so, I elucidate how each kind of cell enables different types of knowledge production. Most labs used a combination of all three cell types, and the particular phase of their model development they were in, the goals of a particular experiment, and resource constraints dictated the type of cells they used.

Primary Donor Cells and the Pursuit of Physiological Relevance

Primary donor cells were most often used when researchers were trying to create models that recapitulated what is observed in cells living in human bodies. If researchers were asking questions about particular diseases, for instance, they often preferred to have primary donor cells. Primary donor cells were sourced in two main ways: from lab member donations and from patient samples acquired through medical centers. For instance, in one lab I observed, one project was developing models of vascular tissue and atrial fibrillation, a cardiac disorder. Fresh blood was the gold standard for maintaining physiological relevance for their experiments, and often they used donations from lab members in order to have the "freshest" blood possible. This was not an uncommon practice; many labs had institutional review board (IRB) approval for protocols that enabled them to take "in-house" samples. Often, one or more persons in the lab would have completed phlebotomy training. Quite literally, lab members walked upstairs to another lab to have their blood drawn, and then walked back down with the fresh blood to begin processing. In another lab I observed, the group had a blood draw scheduling sheet for the lab, and lab members would donate blood when it was their "turn."

Lab members I spoke with about this considered it normal practice and knew of many labs in which this was standard practice. But at least on one occasion I witnessed how such practices could be coercive: it was new lab member's "turn" to give blood; she was a bit nervous and told me that she "hated needles," that phlebotomists often had a hard time finding her veins. Ultimately, she did end up donating that day, but her anxiety was palpable during the experience. In another exchange, with a lab member who was trained to do blood draws, she noted that donation turns were not equitably distributed in her lab: because she was the only one who could

safely do blood draws, she rarely donated herself. Like Thompson (2013) has shown, primary cell sourcing for biomedical research remains a place where ethical questions frequently arise. In the lab setting, such bodily donations often seemed to be rationalized as part of doing scientific work.

Many labs relied on cell donations from affiliated academic medical centers, where principal investigators typically had research relationships with clinical researchers, or formalized procedures common at academic medical centers through which researchers are able to ask for consent, prior to procedures, for using biological material for research (this was the case with Evatar, discussed later in this chapter).[viii] This was a particularly important source of cells for modeling rare diseases, important patient groups for precision medicine efforts. In all of these cases, however, researchers recognized that donor cells were vulnerable to being in short supply. Thus, reliance on primary donor cells introduced some problems when it came to scaling, as will be seen in the next section.

IPS Cells and the Pursuit of Market Ready Technologies

For other goals like scaling, IPS cells were typically the preferred choice. Over the time I was in the field, NCATS increasingly promoted IPS cells as the preferred cell source for model validation because of their scalability, reproducibility, and standardization goals. As discussed in Chapter 3, these goals are paramount for NCATS, because platform validation and standardization are critical for organ chips to become readily integrated into the market and for regulators to accept organ chips as a valid and reliable way to produce safety and efficacy data for pre-clinical pharmaceutical testing, a purpose with extremely high economic stakes.

As such, in 2016 NCATS established three Tissue Chip Testing Centers at academic institutions to independently validate organ chips.[ix] Tissue Chip Validation Centers functioned as external, independent validation centers where organ chip researchers could send tissue chips for evaluation of functionality, reproducibility, robustness, and reliability (NCATS 2018). Several of the initial projects funded in the Tissue Chip Program (Chapter 3, Table 3.1) sent their organ chips to the Texas A&M Center for validation. The first to do so was the team that developed the kidney chip at University of Washington. In a press release following this effort, NIH explained key findings noting that cell source was an important consideration. The original studies done by the team that had developed the model had used primary human kidney cells from patients. At the testing center, they used cells from the developer lab as well as commercially supplied IPS human kidney cells in order to test the impacts of cell source (Sakolish et al. 2018). They explained,

> The scientists also found that the source of kidney cells mattered. There were enough differences in the original study [which used donor cells], including in cells' abilities to metabolize vitamin D and generate ammonia, that the scientists recommended using a commercially available source of cells, including stem cells when possible. Many tissue chip systems already employ induced pluripotent stem [IPS] cells, which can develop into any type of cell and are a renewable resource. (NCATS 2019)

The researchers found that cell source "mattered" for reproducibility purposes, and recommended using a "commercially available source of cells" to mitigate such problems. Findings like this have been leveraged to promote wider adoption of IPS cells among organ chip researchers and are another example of the power that NCATS, and leaders of the Tissue Chip Program, hold in shaping the trajectory of organ chips.

However, researchers often discussed the drawbacks that IPS cells introduce. They discussed these in presentations and often in interviews. One researcher I spoke with noted that

IPS cells, despite being a game-changer for the field of tissue engineering, still had significant limitations:

> I mean that technology [IPS cells] completely transformed the broader field of tissue engineering, tissue engineering. Honestly, when you look back on it, it was like the stone age. It was just like kind of stupid what we were doing. You're trying to generate tissues by these really kind of archaic methods and um, and then you have these like IPS cells that came about and WOW. I mean they have problems. You have problems as you try to differentiate them into sort of certain tissues, trying to get the cells mature enough and stuff. And there's a lot of challenges there, but you can manipulate the parent cell.

This researcher explained that there were challenges trying to get IPS cells to mature to what they would be in an adult human. As another researcher put it, IPS cells mature to be "neonatal at best." And yet, while they are not as physiologically relevant as primary donor cells, organ chip researchers told me IPS cells are far more physiologically relevant than the other alternative cell source, cell lines.

Sourcing Cells for Particular Research Questions

Researchers used different cell types depending on the research problem at hand. In fact, none of the researchers I interviewed or observed claimed that one cell type was inherently superior to the others. Instead, they offered nuanced descriptions of how and why they use particular cell types for different problems. As I explore below, researchers choice different cell sources depending on what kinds of knowledge they were trying to generate.

Cell lines proved to be a valuable cell source when optimizing the technology itself. Because cell lines are robustly characterized, researchers often used cell lines to help validate and optimize the platform. In other words, while not relevant to human physiology in the same way that primary donor cells could be, cell lines were valuable for learning about how the tool was working (or not working), as well as producing knowledge about basic biological processes.

For instance, I observed researchers using cell lines to draw inferences about the platform's functionality. Cultures from cell lines would be inserted into the chip platform and if the cell line cells behaved as expected per the literature or previous experiments in the lab (e.g., in petri dishes), researchers concluded that the platform was functioning appropriately. If, however, the cells behaved otherwise, researchers then investigated what went wrong: Were channels and reservoirs etched properly? Was the platform material interacting with the cells or chemical compounds? Cell lines were also used for producing knowledge about basic biological processes using organ chips. Akin to model exemplary model organisms discussed above, non-human animal cell lines were often used for this purpose. Like human cell lines, these are robustly characterized and have been developed as key scientific tools in the biological sciences.

Researchers explained that their experimental questions drove cell choice. One investigator developing kidney chips explained that his lab used both primary patient cells as well as IPS cells derived from kidney organoids depending on the experimental question at hand. When I asked how his team makes the decision, he put it this way:

> It depends on the experimental question that you're asking, which cell type to use. There are advantages to both. The primary cells are mature cells; they really replicate human physiology well. IPS cells tend to be more immature, but have the advantage—it's easier, you know, they're a scalable resource coming from a stem cell and we can do a lot of gene editing for disease modeling, for genetic diseases [with those]. So it really varies with what we're trying to accomplish in a given experiment.

Despite pressure to use IPS cells in the broader organ chip arena from NCATS, many researchers I spoke with continued using primary patient cells in their work depending on their experimental questions and goals of their modeling efforts. Another researcher, working on adipose tissue models, sourced primary donor cells from an affiliated academic medical center. Like many researchers I spoke with, she had a collaboration with clinicians at academic medical centers. In

this case, she collaborated with a clinician-researcher there who performed elective surgeries. She explained,

> Some have Type 2 diabetes. Some are formerly obese and have lost weight and now we're getting their extra fat [adipose tissue], like body contouring patients, so people who are undergoing elective surgeries. We get their tissue and then we isolate our cells from it. But we do, we have the ability under our IRB to track, you know, some of their medical, um, like things like their disease state, their gender, their age, like we actually have access to that information.

When I asked if what the lab did with comorbidity and demographic data attached to the cells, she said they currently were not using that information. But, as in the broader field, there was often a sense that *someday* this type of information would be relevant and could be important for organ chips to be leveraged for precision medicine initiatives. I turn to the issue of donor data next.

Donor Data

Notably, while cell source was discussed widely when it came to decisions between IPS cells, cell lines, and donor patient cells, there were major silences surrounding the sociodemographic information attached to donor cells. Typically, sociodemographic information of any kind was not noted in scientific publications or presentations, perhaps for patient privacy purposes, but when coupled with explicit discussions about the future utility of donor data—along race and sex lines, for example—for precision medicine research, this omission was curious.

Indeed, over my time in the field many presentations I observed talked about their capacity to create models for specific groups. Sometimes this was not explicitly stated, but rather implied. For instance, one presentation I observed in 2018 about developing models of female reproductive system in order to "reverse engineer" diseases like polycystic ovary syndrome, the

presenter included an image on the slide of three groups of women: white, Black, and brown. While nothing was explicitly said about racial groups, the image implied that racial categories were meaningful for biomedical models of the female reproductive system. In another presentation, a researcher spoke of "personalized clinical trials" and showed an image that showed four groups of people: women, babies, elderly people, and Black women and men. Similarly, in their presentations some researchers referenced "sub populations." Indeed, the NCATS Tissue Chip Program included "genetic diversity" as a goal of the program. (Though as is emblematic of much discourse surrounding diversity, what constituted meaningful dimensions of "diversity" was left open for interpretation.) In multiple conferences I observed, researchers talked about the future potential of organ chips to achieve precision and personalized medicine goals. In future work, I plan to follow developments in the field along these lines.

In sum, for organ chip researchers, the question of where to source cells was about the scientific questions at hand. In deciding what kind of cells to use, researchers are often optimizing for different questions. Does the platform work as intended? Do the results produced using the organ chip match what is seen in humans? Can these results be reproduced in another lab? These questions were at times about translation, but at others they were not. Much of the literature analyzing model organisms has focused on scaling models: moving from non-human to human, specific to general, wherein researchers develop generalizations through iterative experimentation. Nelson (2013) contends, however, that for biomedical research, models are often developed to study particular phenomena, and do not attempt to move from specific to general, but rather from specific to specific. Similarly here, organ chip researchers make choices about what cells to use that make these models useful for different purposes. When validating a model—the platform itself—researchers may select less physiologically relevant cells, like cell

lines. Other researchers (or the same researcher but for a different experiment) may elect to use primary patient cells in order to make a more "physiologically relevant" model. These nuances are lost when organ chips are simply talked about being "human-based" models. In the next section, I follow two examples—a lung chip and the female reproductive system—to highlight specific additional areas of negotiation.

Human Enough

Sourcing cells is just one of many scientific decisions that must be made when creating organ chips. Other decisions include considerations about what aspects of organ architecture to model, and what "counts" as the minimum functions that an organ chip must recapitulate. These decisions also shape how physiologically relevant a given organ chip is, and critically, what kinds of interpretations and extrapolations must occur and be accepted for researchers to translate their findings to humans. I now turn to two cases in which I unpack how organ chips are constructed, explicitly tracing various design aspects. Following Lewis and colleagues (2012) who have shown how animal models come to be "good enough" equivalence to humans through social negotiations, I document various points of social negotiation to surface the social nature of scientific decision making. I then turn to specific ways that potential market value is explicitly attended to when designing organ chips to be "human enough."

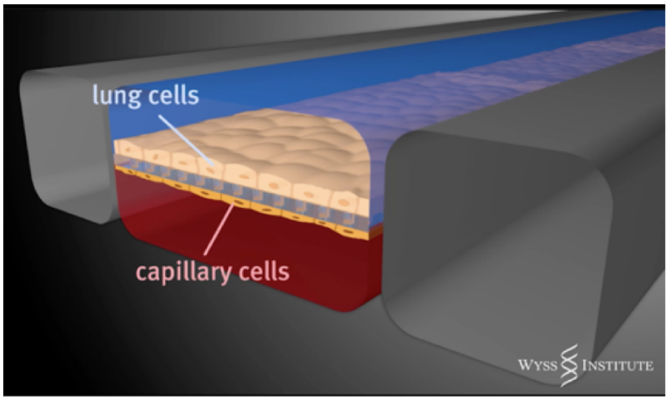
Case 1: The Lung Chip

The lung chip model was developed by researchers at the Wyss Institute for Biologically Inspired Engineering at Harvard University. It is considered the first organ chip model developed, and debuted in the 2010 *Science* paper that launched the field. The lung chip became

the flagship product of the start-up company, Emulate, which was founded in 2012 as a spinout from the Wyss Institute.[x] The lung chip is the most iconic of the organ chip technologies: it has graced the covers of many science magazines (for example, the National Geographic issue shown in Chapter 3) and has been featured many times on National Public Radio (NPR) (2010, 2012, 2015). While many other organ chips have made it to market (shown in Table 3.1), Emulate is arguably the most prominent organ chip company and has been extremely active in promoting these technologies to be mainstream tools for use in laboratories and pharmaceutical research and development, and advocating for regulatory changes to support continued uptake. Since launching its lung chip in 2012, it has continued to expand and now markets a number of organ chip products and a "human emulation system" that combines these tools with analysis software. Below, I provide an overview of how the lung chip is constructed and made to work, and then turn to some key decisions that make this model "human enough."

Figure 4.1 below shows the cross section of the lung chip. In the figure, the middle chamber is divided into two with a perfused layer of PDMS, the contested material that is used to create many of these platforms, as discussed in Chapter 3.[xi] The sheet of PDMS is punched with holes to allow exchange between the two chambers it creates. The top of the PDMS is layered with cultured human lung cells. On the bottom of the PDMS are cultured capillary, or blood, cells. The blue chamber above the lung cells represents an airway, where air flows through the device, introduced at designated entry points (where the tubes are hooked up, as shown in Figure 4.2). The red chamber, below the capillary cells, represents blood flow. Other media (as well as pathogens and pharmaceuticals) can also be introduced into the model, in the "airway" or into the "blood stream." For example, researchers might introduce a virus through the airway in order to model how the human lung responds to a virus. This model also mimics the mechanical

functioning of the lungs. Two square grey channels on the left and right sides of the middle chamber on Figure 4.1 are vacuum channels. When in use, these enable the breathing simulation.



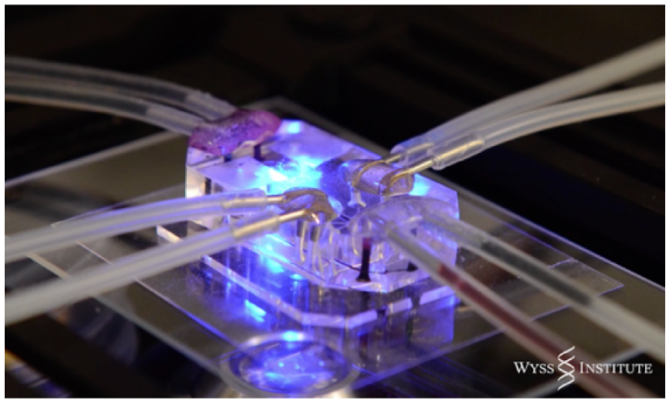


Figure 4. 1: Cross section of lung-on-a-chip (Wyss Institute). Figure 4. 2: Image of the lung chip when in use (Wyss Institute).

In this example, there are multiple negotiations that must be navigated about what makes a model accurate and relevant for humans. In the case of the lung chip, here are some of the negotiations:

- The model must include human cells differentiated to cell types relevant for the lung model. As discussed, these cells may come from one of the three sources: primary donor cells, cell lines, or IPS cells.
- The model must include the appropriate cell types for given functional unit, as they would be arranged, and in proper ratios in the human organ.
- The model must simulate the exposures a normal lung would be subject to – blood and air flow.
- The model must account for the primary mechanical functioning of the organ.
- The model must "live" for 4+ weeks.

Each of these decisions has implications for how physiologically relevant the chip will be. The second bullet in particular is an interesting feature. The cells must include appropriate cell types for a given functional unit, but not all cell types present in any given organ need to be present in the model. This is a key place where the tradeoff between functional value and representational detail (Lewis et al. 2012) is visible. For the lung chip, the functional unit might include the

alveolus (this is the tiny air sac at the end of the air passages), or it might just be the airway; a lung chip need not include cells from both. (This is not unique to the lung chip: in other cases, such as the kidney chip, a researcher explained how complex the kidney was, with forty different cell types. They distilled the "complex architecture" of forty different cell types present in the kidney to three: peritubular microvascular endothelial cells, peri vascular cells (which are part of the capillary network) and the proximal tubule cell.) For Emulate, modeling the sub-units led to the development of two different models. They now market an alveolus chip and a small airway chip. But in each case, this underscores that organ chips are still very much *models* in which the complexity and real worldness—even at the organ level—is made simpler. Yet the language of "organ chip" obscures this sub-organ specificity, just as the marketing organ chips as "human-based" models obscures the tradeoffs of choosing certain types of human cells and not others.

As the field of organ chips has expanded, many projects that were funded through the NCATS Tissue Chip Program have made it to market (see Chapter 3, Table 3.1 for some examples). Often these companies were start-ups that emerged from lab developments, like Emulate's launch from the Wyss Institute. This very platform is now being used for various organs. This is a noteworthy move: it erases difference in the design of these technologies around particular organs and their unique features. Individual organ chip researchers funded through the NCATS Tissue Chip Program had developed models that included design features specific to the architecture of different organs, for instance through the arrangement of chambers and channels on the platform, the ways that fluid flows through them, and the application of mechanical force. Emulate now offers multiple organ models using the same chip, including two lung models (alveolus and airway, mentioned above), two intestine models (duodenum and colon), a kidney, a liver, and a brain model. Offering a technology "kit" that just needs to be loaded with cells in the

end user lab—with nothing unique or special to attend to for specific experiments—eliminates one step in an already complex process, a key component for marketability and scalability. In fact, being able to transport an organ chip to another laboratory, to be used by a different team with limited training (or none) from the creator lab, was a one goal of the Tissue Chip Validation Center I discussed in Chapter 3. This was seen as a key step toward successful commercialization, and encouraged the streamlining and simplifying of devices in multiple ways.

But many organ chip researchers I interviewed aired concerns about this move toward a "one-device-fits-all" approach, highlighting the tensions that emerge between market value and the scientific tradeoffs that scaling, in particular, requires. In interviews, many researchers felt conflicted about this tradeoff. While they critiqued the strategy, ultimately they described this as a difference in goals. Here, a researcher who was building adipose tissue, or fat, models explained,

> There are definitely people that are [are doing a] sort of 'plug and chug' model, and they almost want one platform system that can be used for a bunch of different tissues. It's really just a minor tweak and then it can be used for something else. Whereas my goal is very different. I'm not trying to do every tissue, I'm just trying to do the best fat model that we can do. I think it's very different mindset.

She explained that building better—here, in the sense of more physiologically relevant—models required attention to aspects of the bodily environment that are unique to a given tissue. For adipose tissue, this included things like considering the microenvironment that surrounds adipose tissue. In obese states the cellular environment stiffens, and lab built their model to mimic this. Another researcher highlighted this tension more pointedly, claiming that it was between a market approach and a scientific one. He was building models of vascular tissue. He put it this way,

> People kind of call it, building widgets.[xii] So Emulate has this. You can buy this prefab [pre-fabricated] shape and then you kind of load it yourself and do it and try to do whatever that platform will let you do. Then the other approach, which is definitely what my lab does, is… well, I call it doing science. *[Laughs]* Maybe doing science the right way, which is find the problem first and then design your device and technologies and stuff to solve that problem. I think that's how science should be done.

He explained that for this reason his lab did not use many "prefab" technologies because of their limitations. His position was that such devices were "probably more useful for commercial purposes" than in academic laboratories and would be unable to answer the kinds of questions he was interested in pursuing. These researchers highlight what they see as a tension between doing "good" science, building the best, most human models, versus prioritizing about the market potential of their technologies. They actively distanced themselves from the highly commercialized organ chips, positioning themselves as being more concerned with the scientific integrity of their models. This is not to say that they were not interested in the commercial potential of their technologies, too, but they thought this could be done while still achieving the scientific goals of building better models. Indeed, they both had patents for their technologies, and one of them had founded a startup company focused on organ chips.

Case 2: Evatar or the Female Reproductive System

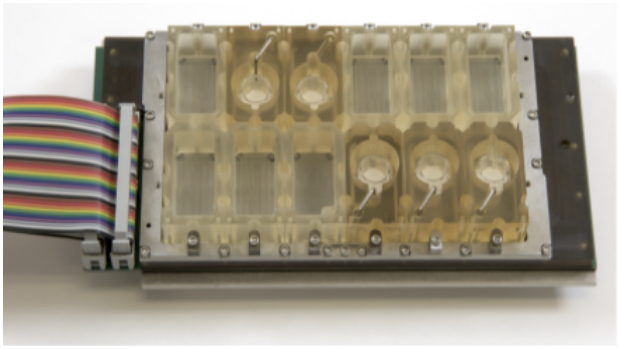
Funded under the initial Tissue Chip Program at NCATS in 2012, a group of researchers at Northwestern University developed a model of the female reproductive system called "Evatar." Evatar links together several organ models, and it is physically larger than other organ chips. Researchers often referred to it as a microphysiological system rather than an organ chip, because of its size and linkage of multiple organ models. Though it may appear more complex than the single organ chips because it integrates multiple organs (see Figures 4.3 and 4.4 below),

the underlying technology is the same microfluidic technology that all organ chips utilize. The lab promotes Evatar as "the mother of all microhumans" and on their website, they explain the model like this:

> She's innovative. She's three-dimensional. She's made out of human cells. She can tell you how a drug may affect fertility in women, or if it is toxic to the liver. And she fits in the palm of your hand. She's the future of drug testing in women and personalized medicine, and her name is Evatar.

The evident hype in this description derive from Evatar's technological advancement ("she's innovative"), as well as its humanness ("she's made out of human cells"), and future value ("she's the future of drug testing…and personalized medicine"). As I unpack the construction of this model in what follows, we see how the potential value of Evatar is built into its very design.

The Evatar model is comprised of five individual organ modules (Figure 4.3). The first four are the ovary, fallopian tube, uterus, and cervix that comprise the female reproductive system; the fifth is the liver. The figure below (Figure 4.3) shows five modules, each representing the one of the five organs. The wells house layers of cells of the particular organ of interest, and on this platform, the bottom plate is hooked up to a pump that brings nutrients to cells, introduce blood flow, and pharmaceuticals. Next to the device is an image of the conceptual model. Each organ model is connected by channels that enable flow of media, pharmaceuticals, and so on to move through the model (powered by the pump).



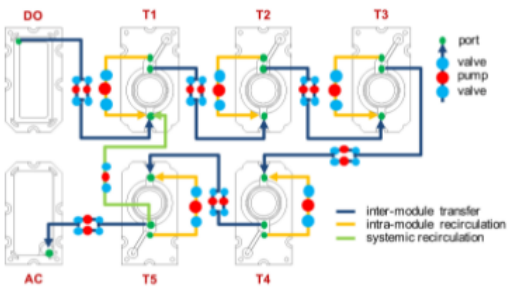


Figure 4. 3: Evatar (Xiao et al. 2017). Figure 4. 4: Conceptual model of Evatar (Xiao et al. 2017).

For Evatar, here are some of its design elements that rendered it "human" (or in this case, "female") enough to be accepted as a model of the female reproductive system:

- The model must live for 4+ weeks, in this case to complete a full 28-day hormone cycle.
- It must produce and respond to hormones, specifically follicle stimulating hormone (FSH) and luteinizing hormone (LH).
- The cycle itself must map onto observed follicle development and hormone levels seen in a "normal" or expected cycle of human females.

Evatar completes a full 28-day hormone cycle. In this case, it becomes evident how ideas about standard humans and normalcy are built into organ chips models. Evatar's hormone cycle is the "normal" length of 28 days, even though this does not match what many female humans experience. (In fact, a recent study found that only 13% of people who menstruate have a 28-day cycle (Bull et al. 2019).)

With both Evatar and the lung chip, there are two key negotiations common to the construction of all organ chips: model accuracy and value. Earlier in this chapter, I explained how different types of cells could be selected for inclusion in a given model, but that the key commonality was that they were *human* cells. In the case of Evatar, a new wrinkle emerged for researchers when determining which kinds of cells to use in this model: Evatar developers prioritize primary donor cells because of their physiological relevance, and they typically acquired these from patient donations during routine surgeries. For many of the organ models in Evatar (e.g., fallopian tube, uterus, and cervix), researchers explained that it was relatively easy to get patient samples of healthy and diseased cells. They had established institutional connections and networks to get these. In fact, there was a member of the lab whose job it was to broker these relations.[xiii] But Evatar's developers were unable to get human cells for the ovary. Thus, while Evatar is marketed as a "human cell-based model," the ovary cells were actually

sourced from mouse ovaries. I asked a researcher on the team about this seeming anomaly, and he explained:

> We don't get healthy ovarian tissue for, you know, obvious reasons… When a woman comes in for a hysterectomy, you typically leave the ovaries. And women of reproductive age, of course, are not getting their ovaries taken out, unless it's in the case of ovarian cancer, or a terrible case like that… For the most part the ovary plays such an important functional role that it's not tissue that we get as much of. The other tissues, we can get a uterine tissue, Fallopian tube tissue, you know, hysterectomies are done all the time. And so it's not hard to get ahold of that tissue. But in terms of the human ovary tissue it's a little bit harder.

In this case, because of the scarcity of getting healthy ovarian tissue, the substitution of mouse ovary cells was rendered to be good enough. Additionally, extant scientific work establishing the *sameness* of mouse and human ovary cells was leveraged to defend their inclusion in this model (Skory et al. 2015). Together, then, these constraints and justifications for this exception from the use of human cells and the substitution of mouse cells are understood and agreed by researchers as preserving the relevance of Evatar as a model for the human female reproductive system.

There are also key decisions that deal with the value of this model. What organ chips include, in terms of the organs they represent and the functional design of the technology, are also shaped by the intended purpose of the model and their potential value. This is what makes the inclusion of the liver in the Evatar model noteworthy: Evatar only becomes valuable for pharmaceutical applications when it also includes the liver. When I spoke with a researcher from this team about why the liver was included in the model, they explained to me:

> We have the liver in there because we think really the power of these systems … is going to be drug discovery, drug testing. And so it's essentially just proof of concept, right? Showing that we can have this liver component in there, that it was producing albumin and that potentially could be used—if we introduced the drug to the system, we can not only see how that drug itself effects potentially the function and health of those tissues, but also the metabolites of it pass through that liver and is metabolized.

The point the researcher makes about the power of this technology – its value – underscores the point that what makes these models right is not just about their human relevance, but also their future value. Evatar is made valuable when it includes the liver, because then the system can be used to show metabolization of pharmaceuticals, a key aspect of testing novel drugs. Indeed, the group that developed Evatar says that "In the future, we will connect even more organs to Evatar, making it possible to give her a heart, lungs, and other vital organs." They note that "this will allow the study of interactions between organ systems, and the human body as a whole. Maybe one day Evatar will even become a new standard for pre-clinical testing of drugs." This excerpt underscores the future potential of organ chip technologies like Evatar, in which multiple organ systems of the body will be connected to model the human body. It then projects a future in which this type of technology becomes a new standard—a new future of biomedical modeling in which data from human-based studies such as organ chips will replace animal model testing currently required in order to move to human trials—because of their superiority, their *humanness*. This excerpt is then followed with the following promise: "Just as Eve is thought to be the mother of all humans, Evatar is the mother of all microHumans… Of course, in this case, we will have to give her a partner in crime…**HE**vatar. Stay tuned." The coupling of the success of the current model, Evatar, with the promise of how it will expand to become even more human (a full female human model) with its male reproductive counterpart[xiv] highlights the constant presence of the promissory nature of organ chips—not only for solving one aspect of the translational crisis in biomedical research, but as commercial products in their own right with seemingly open-ended potential—an issue I now I turn to in the conclusion.

Conclusion

Figure 4. 5: Emulate landing page. Source: Emulate, 2022

Models are simplified renditions of complex phenomenon, technologies that promise to teach us things, and to render new insights, that otherwise is left unknown. The webpage image above (Figure 4.5) offers a snapshot of the promissory nature of organ chips as biomedical models of the human body. Technologies the size of a flash drive have the potential, it tells us, to "ignite" a new era in human health. Indeed, the promise of organ chips does not stop with their potential to better model the human body than non-human animal models, but rather to change the very ways we understand human health. Once neatly packaged, the constructed and uncertain nature of the models themselves becomes *invisible*.

Yet it is through social action that models are brought into fruition and become regarded as "human enough," and in this chapter I have foregrounded these social processes. By exploring how organ chips are built, I elucidated the various points at which organ chip researchers must make design choices. Throughout, I showed how these decisions shape the kinds of knowledge that can be produced: researchers make design choices for the experimental questions at hand. Drawing on the example of cell sourcing, a key component of organ chips and their purported

"humanness," I showed cell sourcing decisions shape what kinds of knowledge can be generated with a given model, and how researchers make tradeoffs between physiological relevance and scalability.

Using two cases, I then explored how market forces shape the design and trajectory of specific organ chips, building on STS scholarship that examines the political economy of models. In the case of the lung chip, I showed how marketing 'organ chips' as such obscures that they in fact model sub-units of organs, thus requiring translation first to the full organ, and then to humans. I next followed how one company, Emulate, transformed the platform intended to model the lung into a platform capable of modeling multiple different organs. I then examined the case of Evatar, the female reproductive system chip platform, to showcase a different way that market forces shaped the design of organ chips. While the female reproductive system is comprised of four organs—the ovary, fallopian tube, uterus, and cervix—Evatar's developers chose to add a fifth organ to the model, the liver, in order to harness its potential value for drug testing and discovery. I contend that these two cases demonstrate that scientific negotiations are shaped not only by scientific concerns, but also by the market forces driving organ chip development, building them with their end users in mind (pharmaceutical companies and contract research organizations). Building better, or more human, models is not only about the concerns of recapitulating, and predicting, human response better than animal models, but is also about achieving viable, scalable, and marketable laboratory tools.

PREAMBLE TO CHAPTER 5

In March 2020, as institutions across the US halted most in-person activities and principal investigators of academic science laboratories were instructed to shut down their labs, it was clear that the ethnography portion of this dissertation could not continue as planned. At the time, I had completed a long period of observations at Valley University and many conferences and symposia, and had been taking a break from observations to catch up on data analysis and think through what further data I needed, and what observations, if any, should come next. I wondered about the researchers and labs I had been following, and how my interlocuters were navigating this stressful time.

I remembered a story I had been told by one lab member at Valley about a time when the power in their building went out on a weekend evening. As a staff scientist and the lab's manager, he coordinated their emergency response to get the generators going and save as many samples they could. At the time an important experiment had been underway, and it was quite the crisis. Even when he told me the story, long after it had occurred, the stress of the situation remained palpable. I wondered how laboratory workers were approaching this moment, in which the very structure of their laboratory environments was at odds with public health guidance: laboratories are confined spaces, with lots of workers buzzing around, looking at samples together, sharing equipment, and working in close quarters. In open lab settings in which multiple lab groups share a common room, each lab "owns" a section of narrow benches typically called "bays." In each bay, lab workers typically have a few baymates who are located in the same section. The crowded nature of the lab space, and the need to move around freely in the space to access equipment were two major hurdles that would prove challenging to navigate during the pandemic. How was science getting done?

And so I made plans to pivot data collection. I applied for ethics approval and began recruiting participants for the Disruptions to Laboratory Life (DLL) Study in August 2020, and began conducting interviews over Zoom with lab workers. I initially thought of it as a primarily methodological study: For those of us who rely on in-person observations as a core data collection method, how could we reconceptualize our methods for studying scientific work during this time? How might laboratory ethnographies—and the scientific studies that we study—change due to pandemic restrictions? Would scientific studies from this period be carried out differently than how they might have otherwise have been?

When I began data collection for the DLL Study, I was prepared to ask participants about their scientific work, and to have them walk me through how their projects were changing in light of the pandemic. I was prepared to talk about the science. Quite quickly, it became clear that this was not the most important story for me to attend to because my participants rarely wanted to talk about their experimental work when they were experiencing so many other difficulties just trying to get their work done. The initial interviews I conducted with participants, in September and October 2020, were filled with anxiety and stress, but these feelings were accompanied by a momentum to, as Aimee put it, "just get through it." Participants had been working shift schedules and long hours for months, and they told me that they hoped it would only be *just a little longer*. As one participant, Isabel, put it "I just keep telling myself it will be better by spring." But, as we now know two plus years into the pandemic, it was not just a little bit longer. For most of my participants, one year into the pandemic things were not better. They were worse. I conducted follow-up interviews in February and March 2021 and at that time, these interviews held a different weight. Most of my participants were on edge, extremely frustrated with their working conditions, lab leadership, and utterly exhausted. My participants

felt invisible; the exploitative nature of academic capitalism was weighing heavy on them. I worried about some of them who seemed to be at their breaking points, feeling helpless, overworked, and, as Lena put it, "miserable." Trying to hold back tears, she said, "I know that sounds dramatic, but I'm completely miserable."

What I learned through embarking on the DLL study made me think about the laboratory space from a new angle, one that was not present in my analysis previously. My dissertation had been focused on the technoscience constructed in laboratory settings—the models, the science of organ chips, the knowledge, and capital—but not so much on the organizational aspects of the laboratories where technoscience is produced and the labor that goes into it. The social worlds approach (Clarke 2005) present in this dissertation had, from the outset, attended to the people in these spaces and their varying positions and power, as well as the reproduction of inequalities produced *through* biomedical science and its practices. Yet it failed to attend to the organizational dynamics of laboratory labor itself. Thus for me and my research, the DLL study opened up new questions about the organizational structure and working conditions of laboratory labor, key social pieces of the scientific space that is co-constitutive of the science produced, but often not the focus of laboratory ethnographies.

Moreover, questions about inequality and ethics became apparent when I started to think through the possibility and implications of my own return to the lab as an ethnographer: it became clear that being in a laboratory setting to collect data would be undue burden on lab workers. Many of my DLL study participants reported that their scientific collaborations that required personnel from other laboratories to be in the same space had halted during the pandemic precisely because it felt unfair to ask someone else in their lab to give up their time in order to enable an outside scientist to come into the lab. Given the various obstacles that

participants detailed in interviews, alongside the exhaustion of navigating lab work during the pandemic, I was unsure when I would feel comfortable asking to be present in these spaces again. But more pointedly, I realized that while permission for my laboratory observations was granted by the principal investigators (PIs) of those labs, the work, and burden, of my presence fell on the shoulders of the laboratory workers. In these observations, the people whose labor it was to show me around, allow me watch their experiments and ask them incessant questions was not the PI, it was those working in the lab setting in the lowest-status and lowest-paid positions: staff scientists, postdocs, and graduate students. It was the same workers who now were having to navigate a million things in order to work safely in the laboratory space, who were picking up work for others who could not safely (relatively speaking) be on site, figuring out how to mentor more junior lab members amidst the uncertainty, and trying to stay on top of their own experiments all while working with severely restricted time in lab and with chaos unfolding all around.

In the midst of follow-up interviews, I felt like I did not have the tools to give my participants what they needed. I am not a trained therapist, and at the end of most interviews, I felt deeply uncomfortable when participants thanked me for what "felt like a therapy session." Perhaps just a turn of phrase for some, but in the heaviest of interviews I worried whether my participants had qualified therapists and close connections to turn to in these times. When I was nearly finished with data collection, I told a colleague about how depleting these interviews had been for me. I told her about the challenges participants were facing and how emotional interviews had been. She found it surprising and remarked that when science is the object of inquiry, we do not expect it to be emotional. This comment struck a chord: society rarely expects—or creates space for—scientists to struggle, or at least not to openly talk about it. This

division, between science and society and scientists and whole people, was precisely what my participants found so alienating during this time. Indeed throughout the pandemic, the boundary work of separating "science" and "society" had been hyper visible for sociologists. But, as I show in Chapter 5, it also was illuminated for many participants in in this study—not only the construction of this boundary—but also the management work that goes into enforcing and maintaining it.

In the chapter that follows, I present findings from the DLL study in an article length manuscript. The manuscript builds on the extant literature, offering an analysis of the experiences of biomedical research trainees in an era of bureaucratized academic capitalism during a particularly tumultuous time. Just as the pandemic highlighted the inequalities in the social world, it did in academic science settings too. The chapter examines how laboratory life during the pandemic was marked by emergent stratifications and inequities in access to sufficient lab time, increased stress around productivity, and frustrations with the culture of academic science. I show how the loss of social interaction, and the ensuing lonely scientific struggles, made visible the importance of sociality in science for workers. Finally, I contend that pandemic disruptions not amplified and exacerbated existing social inequities in lab settings, but also resulted in workers' estrangement from science itself. This chapter is forthcoming at *Science, Technology & Human Values*. As such it will not be part of the future book project.

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The COVID-19 pandemic changed many things in our lives collectively and also in profoundly stratified ways. For sociologists, it opened up conversations about many topics we talk about in our classrooms to a broader public: health inequality, racism, inequity, and the myriad reasons why strictly technological solutions will never be able to fix deeply social

problems. The relevance students saw created waitlists in my undergraduate "health, biomedicine, and inequality" seminars—students were excited for timely courses, and I received emails from students majoring in biomedical engineering, biology, and other science and engineering fields who were eager to take my seminars. There was a sense of resolve, and a desire to meet the moment. I too felt an urgency around my work, as well as pressure to do *something* in a moment where it felt like sociologists and STS scholars were uniquely positioned to contribute, even if it seemed that most of society was not ready to listen.

Writing this chapter was a smoother experience than writing other pieces of the dissertation: being engulfed in my participants' experiences and stories created a sense of urgency to get their words out into the world. But it was also challenging to float around this situation of inquiry, as if I too was not experiencing some of the same difficulties and emotions as my participants. The looming uncertainties that impacted them were impacting me, too, even if our daily working environments looked different. Alongside their failures, I experienced my own. As they described waves of motivation and exhaustion, I knowingly nodded. Similarly situated as an academic researcher, our shared experiences created the right conditions for rapport building and incredibly rich interviews. But this project also challenged my own understanding of my place and participation in academic science and opened my eyes to new dimensions of how power operates in this space, which previously had been missing in my work.

CHAPTER 5: SCIENCE ESTRANGED: COVID-19 DISRUPTIONS, POWER, AND INEQUITY IN LABORATORY LIFE

Introduction

In March 2020, academic research laboratories across the country and world shut down in response to the SARS-CoV-2 (COVID-19) pandemic. The key recommendations to slow the spread of COVID-19 were to distance from one another and avoid contact in indoor settings, exceptionally challenging guidance to adhere to in most laboratory settings. Save for those doing COVID-19 research and other essential projects, institutions instructed principal investigators (PIs) to shut down research operations.[i] Halting ongoing experiments, culling animal colonies, and preparing samples and animals for storage were cumbersome and costly feats (Nowogrodzki 2020; Thurston et al. 2021). When research activity resumed—for many, weeks or months later—the nature of laboratory life had changed. Time in lab became a scarce resource: working safely in lab through the pandemic and its multiple surges meant a new experience of compressed time, shift work, and little, if any, socialization. With this new mode of laboratory life, the routine ways and workflows of "normal science" that had been taken for granted by laboratory workers were gone. In their place emerged new stratifications and inequities in access to sufficient lab time, stressors around productivity, and exacerbated frustrations with the structure and culture of academic science.

Sociologists and science and technology studies (STS) scholars have demonstrated how disasters, such as weather events, epidemics, and economic crises amplify and exacerbate existing social inequities (Tierney 2012; Quarantelli 1998; Petryna 2013; Adams 2013; E. Kleinman 2003b). As COVID-19 played out on the national and global stage, participants in this

study witnessed how the pandemic exposed the vulnerabilities of our social safety nets, enduring health inequities, and racial injustices. Lab workers drew parallels to their experience in academic science. In the lab setting, they highlighted how the pandemic intensified existing problems within the structure and culture of academic science. They expressed deep frustrations with power and inequality in their labs and institutions, problems they were aware of long before the pandemic began but that were amplified in its wake. The pressures to produce throughout the pandemic, set against formidable working conditions, highlighted misaligned values between lab workers and their PIs led them to question their participation in academic science. Participants were aware of such misalignments and power dynamics long before the onset of the pandemic; yet against the backdrop of crisis, these critiques became more visible and the disconnects more jarring.

Drawing on in-depth interviews conducted with biomedical research workers in academic laboratories during the COVID-19 pandemic, this article offers an account of how the pandemic impacted laboratory workers. For many laboratory workers, the pandemic underscored the importance of *time*—that is, time to do science in the ways participants enjoyed and are necessary to produce "good" scientific work. Time in lab became a scarce resource, leading to inequity in shift work and scheduling, loss of joy in work, and increased stress around productivity. I then show how the loss of social interaction, and the ensuing lonely scientific struggles, enabled workers to understand the importance of sociality in their science not only for their personal fulfillment but also for the benefit of their science. Throughout, I show that the ways institutional and lab leadership responded to the pandemic exacerbated existing inequities in academic science laboratory work. Consequentially, workers' experiences during this time

brought about structural critiques of the "culture" of academic science and its policing of boundaries between science and society.

Academic Capitalism and the Bureaucratization of Science

STS scholars have documented the transformative pressures facing academic science in the late twentieth century, including the capitalization and bureaucratization of academic science and their concomitant institutional changes (Hackett 1990; D.L. Kleinman and Vallas 2001). Academic capitalism captures universities' turn toward market-like activities, in which university employees are increasingly encouraged to engage in activities meant to generate external revenue (Hackett 1990; Nickolai, Hoffman, and Trautner 2012). Such work has shown how the boundaries between academic science and industry have blurred, markets increasingly shape academic research agendas, and scientists are encouraged to think like entrepreneurs (Kleinman and Vallas 2001; Hoffman 2021; D.R. Johnson 2017; D.L. Kleinman 2003; Popp Berman 2012). This literature has focused on the knowledge that is produced in these spaces and the practices through which such knowledge is produced, including how researchers and fields pursue particular research agendas and questions and work to articulate doable research problems (Jeon 2019; Frickel et al. 2010; Hoffman 2017, 2021; Fujimura 1987).

Others have attended to how the organizational structure of scientific teams has changed, documenting their increasing size and that they function as small shops or quasi-firms (Milojević 2014; Wuchty, Jones, and Uzzi 2007; Etzkowitz 1983). They contend that academic capitalism and bureaucratization have created a class of "academic marginals," which Hackett defines as scientists who hold positions in academic institutions but are not on faculty (similarly, Lee and Walsh (2021) include "supporting scientists" such as staff or contract scientists and "permadocs"

in this category). Hackett and others attribute the rise of academic marginals to the aforementioned structural changes in academic science, in which scientific teams are getting larger (Milojević 2014; Wuchty, Jones, and Uzzi 2007) and there is a growing mismatch between the production of new scientists and number of permanent positions in academic science (Gaughan and Bozeman 2019; Hackett 1990).

Scholarship in this tradition has examined institutional inequity that lower-ranking workers (e.g., staff scientists, trainees including postdoctoral researchers and doctoral students, and lab technicians) are subjected to and under these macro-level shifts (Gaughan and Bozeman 2019; Hackett 1990). Such work has also documented the increased specialization of doctoral and postdoctoral training, leading to many critiques that doctoral training in scientific fields no longer leads to independent, integrated scientists but rather skilled technicians who need further training following the completion of the doctorate (Lee and Walsh 2021; D.R. Johnson 2017). These now structural features seemingly sustain the model of requiring long postdoctoral fellowships prior to the *potential* acquisition of permanent academic positions.

Recently, researchers have theorized how the bureaucratization of science and the shifts toward large teams in science have led to alienation among researchers (D.R. Johnson 2017; Lee and Walsh 2021). Such work attends to the infrastructure of academic science and how these macro-level trends shape the conditions under which scientists can feel fulfilled in their work (or not). However, less attention is paid to the interpersonal dynamics of the laboratory environment and the experiences of low-ranking laboratory workers. In the case presented here, I link these structural forces to lived experience, foregrounding the experiences of those in lower-status positions in academic science, and show how the exogenous shock of the pandemic, in many ways, illuminated the conditions of their estrangement.[ii] As will become clear in the analysis,

workers not only recognized and articulated their estrangement, they also leveraged critiques of the academic science infrastructure that shaped their realities and, through these critiques, imagined how science—and the ways that laboratory groups are organized and managed—might be otherwise.

This study builds on the extant literature, offering an analysis of the experiences of advanced doctoral students and postdoctoral researchers, often termed "trainees," in an era of bureaucratized academic capitalism during a particularly tumultuous time. Trainees occupy liminal roles in academic science: they are at once pursuing advanced training (e.g., doctoral degrees and postdoctoral training), but also operate as workers in labs sustaining the model of lab organization in which one PI builds a lab comprised of multiple graduate students, postdocs, lab technicians, and staff scientists. Their training is inherently tied to lab labor; as one participant, Sonia, put it plainly, "we are essentially workers. After our first year, we don't even take any classes, we just work in the lab." Thus in what follows, I intentionally use the term *workers* to encompass trainees, to underscore the tensions they experience in these liminal positions, and to highlight the well-documented precarity of pursuing scientific careers under academic capitalism.[iii] In doing so, this article centers the experiences and voices of everyday laboratory workers as they navigate the pursuit of scientific careers in academic science.

Methods

Over an eight-month period, semi-structured, in-depth interviews were conducted with biomedical research laboratory workers at research intensive institutions who spent 70% or more of their weekly pre-pandemic work time at the lab bench. Eligible workers included advanced doctoral students, postdoctoral researchers, and lab staff at United States (US) institutions with

high research activity (R1s).[iv] Initial interviews (T1) were conducted in September-October 2020 (n=39), approximately six months into the pandemic. Follow up interviews (T2) were conducted in February-March 2021 (n=36)[v], approximately six months following each participant's first interview. This second time point was approximately one year after early cases of COVID-19 were reported in the United States, and eleven months following widespread shutdowns. Having spent much time in biomedical laboratory settings as an ethnographer, I was familiar with the hustle and bustle of laboratory spaces. When the pandemic hit, it was clear that the nature of work would need to change in order for workplaces to be safe. In the absence of observations, open-ended semi structured interviews provided the best way to collect data on the events unfolding during the pandemic, and are regarded as a method that yields rich qualitative data (Charmaz 2014; Weiss 1995).

Participants were recruited through academic institution listservs, website advertisements, and by word of mouth. Participants were offered a $25 gift card in appreciation for their time. Participants represented multiple disciplines within biomedical sciences, and were located at universities and research institutes .[vi] T1 interviews ranged from 45-90 minutes, and covered trainees' background and training, COVID-19 disruptions and consequences for research projects, experiences working during the pandemic, mental health and wellbeing, and reflections on trainees' roles in science, as well as future plans and career goals. T2 interviews ranged from 30-75 minutes and followed-up on each of the areas discussed in T1 interviews, gathering further data on how laboratory work progressed between T1 and T2, new challenges and experiences of participants, and reflections on work and future plans.

All interviews were audio recorded and transcribed for analysis. All data was imported into MAXQDA for analysis. Analysis procedures followed constructivist grounded theory

practices, including memoing and coding of data (Charmaz 2014). Interview memos were written following T1 and T2 interviews. In the spirit of iterative data collection and analysis, analytic memos and interview memos were used to develop T2 interview guide questions. A codebook was developed inductively from open coding initial interviews. The refined codebook, which included code clusters on COVID-19 disruptions, mental health, laboratory organization, scientific practice, career planning, and institutional structure, was then used to complete focused coding on all interviews (n=75). All names used in this manuscript are pseudonyms. Institutional review board approval was obtained from the University of California, San Francisco.

Laboratory Life in the Pandemic

Across the board, workers experienced the pandemic lab life—from shutting down to developing shiftwork models to going into work—as chaotic. This section explicates what working in a lab was like for laboratory workers during the pandemic, from the time of shutting down to about one year later. Importantly, the new mode of lab life was marked by scarcity: not only of time in lab, but also in terms of leadership from their PIs. As I show in this section, the lack of leadership emblematic of laboratory groups during the pandemic months, led to a new normal that exacerbated and extended inequities in lab groups.

Lab Maintenance & Division of Labor

In the weeks leading up to their institutions' shutdowns, most participants reported that they, and their PIs, did not expect lab work to be disrupted or at least for not such an extended time. In lab meetings, many did not even talk about the possibility of shutting down. When some academic science institutions began shutting down, or at a minimum, instructing employees to

work from home when possible, some participants at other institutions brought this up with their PIs. For instance, Isabel recounted, "I remember having an exchange with my PI that really bothered me in which he wrote, 'well, your work is hands on.'" Even once institutional closures were announced, some lab PIs appealed to their institutions to permit their labs to remain open, on grounds that they were conducting essential research, resulting in lab workers continuing work as normal in the early days of the pandemic.

The shutdown ended up having very little lead time, in part because of this resistance, which meant that lab workers found themselves traveling into the lab at a moment's notice or working longer hours to finish experiments and get their materials in order, freeze cell lines and worms, or prepare flies for safe storage for an indefinite time. Biomedical research heavily relies on the use of model organisms such as *Drosophila melanogaster* (flies), *C. elegans* (worms), zebrafish, and rodent models (e.g., mice, rats) that are specifically bred for studying certain biological processes, disease conditions, and potential therapeutics (Creager et al. 2007; Rader 2004; Nelson 2018). These models, or "tools," are both bought commercially as well as developed in labs. For many labs, building these model organisms is an important aspect of the research itself and they are costly both in terms of financial resources and time.

Model organisms are highly specific to experimental work: they must be at particular developmental stages, exhibit specific genotypes, and be maintained at specific conditions in order to be used in a given experiment. Critically, these model organisms are often not ready made, but instead the process of building the transgenic models for cells, flies, mice, worms, and other model organisms can often take many weeks if not months or years.[vii] Most biomedical research institutions have dedicated animal facilities where organisms are housed (though some, particularly worm and fly models typically have their own rooms within a given lab).

Institutional animal facilities have their own technicians and veterinarians for animal care and veterinary needs, but during the pandemic, animal maintenance was a particularly challenging obstacle as it requires extensive labor on highly regimented schedules.

During the period where operations were fully shut down, it was common practice for labs to designate "skeleton crews" that were responsible for going in a few times a week to maintain animals and cells. Across the board, participants noted that these responsibilities fell to postdocs, graduate students, and animal technicians—those lower in the lab hierarchy—and not PIs. While some PIs asked for volunteers to do this work, many workers found themselves assigned to this role. As Maia explained:

> I wasn't asked whether I wanted to be, I was sort of voluntold that I was going to be this "essential" person. And through all of that, there's been no acknowledgement really that those things have fallen to the people who earn the least.

Similarly, Nisha acknowledged that "someone needs to take care of the mice and the cells but that didn't feel comfortable about it: "I would go super early in the morning so that I wouldn't see anybody else. Honestly, in the beginning of this, I was a little—I didn't want to [go in] basically. I was a little worried."

Implementing Shift Labor Models

As institutions allowed research operations to resume in the late spring and early summer, many labs returned at 12.5% capacity, ramping to 25%, and eventually 50%.[viii] To navigate these capacity restrictions, most labs adopted shift schedules. By and large, PIs tasked lab groups to "come up with a plan that worked for [them]." Participants attributed this tactic to the "democratic" and "hands off" style their PIs often exhibited. Yet without clear leadership over how resources would be allocated during the pandemic, such hands-off approaches led to

inequitable distribution. Participants described idiosyncratic approaches to shift models: some adopted a group model where the lab was divided into two or three groups depending on size. Each group could sign up for times, and the order would then rotate (to create equity in preferred shifts and total amount of time per week). Others opted for "pod" models to keep the same people working together to limit necessary contact tracing in the event of someone becoming ill. Still others, especially smaller labs, opted for a free-for-all signup sheet. If there were "priority" projects happening in lab (e.g., papers in revision experiments) PIs did step in. If working on these projects, workers were able to get first dibs on hours. For instance, Jasmine's PI emailed her lab saying, "let Jasmine choose the hours because we are trying to do this [project] as fast as possible."

If the idea of shifts seemed reasonable on paper, implementing them in practice was far more complicated—and the burden of these adjustments were not distributed evenly across lab workers. Many discussed an assumption that because many postdocs and doctoral students were in their late twenties and thirties, often without children, that they should be more accommodating and flexible. Maia described her frustrations:

> It seems people have pitted against one another parents and non-parents. I've seen so many articles and commentaries on Twitter about how hard it is for parents right now and how non-parents need to understand that burden. I would rather if the dialogue was more like, "this hurts everybody, because when we don't have good support for parents, then they're not able to contribute as much as they want to, to the team." The responsibilities get shifted around in strange ways. And so I don't feel at all that the lack of childcare only affects the parents. Then [the institution] gets to kind of take a backseat and people aren't talking about the right things. People are instead talking about how we should work. We should be ready to meet at weird times 'cause parents might need that. And instead, we should be discussing how our society doesn't support science *and* working parents.

Maia and many others in the study felt unable to voice these frustrations in their labs and institutions. They felt that the pivot to lab work as shift work pitted individuals against one

another, obscuring the institution's responsibility to support its workers and failing to create the space for conversations about equity.

Accompanying the shiftwork models that labs adopted, logistics such as commuting and planning lab time became substantial obstacles. While this added layer of planning was merely a nuisance for some workers, it was overwhelming for many—especially those with long commutes and those who relied on public transportation to get to work. Participants explained how they often needed to go in earlier or stay longer in order to accomplish necessary lab work. Labs that implemented morning and afternoon shifts left "non-business hours," typically before 7am and after 6pm and weekends, up for grabs. Those working the morning shift, typically 7am-1pm, often felt they needed to come into lab earlier in order to have enough time to complete experimental work before the afternoon shift workers arrived. For workers with a 45-60-minute commute, which was quite common for participants in this study, this meant waking up around 4am in the morning, in order to arrive in lab by 6am. This was complicated by the realities of transportation: public transit often didn't start running until 5am or 6am, particularly on limited operation schedules during the pandemic. Moreover, in the early days of the pandemic, few participants felt comfortable taking public transit altogether due to the unknown risks of infection.

One participant said her PI's expectation for workers to show up for their assigned shifts regardless of transit challenges sent a message: "It feels like, 'Hey, you go risk your life. And I'll be at my house because I own a house in [expensive west coast city].'" Initially, some PIs offered to pay for car services (e.g., Lyft, Uber) or reimburse parking expenses. Other participants explained that they felt the offers to pay for individual cars only served to underscore that their PIs still expected them to come into lab, even if they did not feel safe going

in. Moreover, as Luis explained, the reimbursement offers often did not last long: "initially our boss said, 'I can pay, I can reimburse you for parking.' After a month or two, he was like, 'actually I don't think I can do it anymore.'" This left intact the expectation to continue lab work, while shifting the costs of commuting—in both safety and financial terms—back to the workers. Consequently, some participants scraped together funds to purchase cars or bicycles.

While participants expressed excitement when they were finally able to return to lab, this shared enthusiasm obscured the new asks being made of lab workers. Ronnie explained how her PI anticipated everyone was excited to be going back to work after a few months of shutdown. She explained that during a virtual lab meeting:

> My PI said, 'You guys must be so happy to get back in the lab. I bet you're all willing to work 24 hours.' He was a proponent of the 24-hour schedule and people in my lab were getting that. He offered to pay for our Lyfts, and with that felt like a desire or expectation that we can work weird hours.

For Ronnie, her PI's anticipation around a 24-hour lab schedule and expectations for productivity highlighted the very different playing fields of lab workers and their PI. Though she did not feel comfortable going into lab, especially when research operations resumed initially, she also felt unable to voice her discomfort. Her new schedule consisted of working from home during the morning and early afternoon, then going into lab in the late afternoon and staying until eleven o'clock or so in the evening. Not only did she have to buy a bicycle to avoid public transit for her commute, but now her workdays stretched to 12 hours and often more. Like many other workers who transitioned to working from home during the pandemic, most participants in this study reported increased number of hours per week spent working (Maurer 2020). Indeed, typically regarded as highly technical, expert knowledge work, laboratory work began to bear new resemblance to shiftwork labor.

Adjusting to New Working Realities

At the time of initial interviews, in September and October 2020, many participants reported they felt these adjustments were somewhat feasible and were willing to work unconventional shifts and navigate cumbersome work protocols because they didn't anticipate it lasting long. But at the time of the follow up interview, a year into these shift schedules and a "new normal," those working early morning and late-night shifts were utterly exhausted and felt unable to voice their complaints to their PIs. As one participant put it, "Doing it for a couple months is okay. Doing it for six months plus, a year… it's just not sustainable." Aimee explained feeling "exasperated," saying:

> The earliest train I can take to work gets me there at like six. I have to leave my house a little bit before five, which means I'm waking up around four and then of course my body has gotten adjusted to that. It starts waking up before my alarms and I wake up at 3:30am. I'm going to bed around 8pm, and it just disrupts your whole life. I've kind of just started getting really resentful about it, I guess. There's research about how shift work leads to poorer quality of life. I feel that. I'm unhappy. I'm certainly not as healthy. I know I've gained weight, I'm not exercising as much. I get home and I'm exhausted.

For Aimee, it was the little things that symbolized her daily experiences of alienation and powerlessness. She relayed a recent experience seeing her PI when she was leaving the lab for the day around lunchtime, having been there since 6am that day. "I happened to notice him in his running clothes, leaving the building for a run and it made me so angry. Cause it's just, sure you can get exercise when you're coming into work at nine o'clock. That must be great."

Though it was common for many workers to go in semi-regularly on weekends as needed in pre-pandemic times, the adoption of shift schedules and reduced time made working on weekends an expectation. Many participants required the use of core facilities to conduct particular aspects of their experimental work, which was extremely challenging especially for those working on weekends when core facilities were closed.[ix] Many reported feeling slighted

when others in their lab got advantageous hours, especially over the long term. Mina described how competitiveness in her lab increased because of inequity in scheduling, where people working on the weekdays had access to equipment and core facilities that were closed on the weekends:

> Competitiveness in lab got worse because people during the week were able to get more done. Some people got almost normal hour shifts and they were able to keep producing data. And here I am trying to mish-mash my shifts and trying to work on a Saturday and Sunday when the equipment isn't available to me.

This had implications for people stuck with shifts where these facilities were unavailable, or when the only hours not booked were in the midnight hours—again leading to implicit expectations that they would make these schedules work.

Finally, the act of going into lab during this time also looked very different both in terms of COVID-19 protocols, as well as in terms of how people organized their working time. Once in lab, only one lab member could be in a bay, the U-shaped workbenches characteristic of laboratories, at a time. Yet the nature of life in the lab is constant movement: from tissue culture hoods and centrifuges, to microscopes, to imaging machines, to computers and desk areas. Put simply, staying six feet apart from one another was impossible to accomplish in reality. Moreover, many participants talked about the space in which they work: old buildings with poor ventilation, some windowless, and many in open shared spaces with other labs. The design of these spaces, particularly in the early months of the pandemic when uncertainty loomed about how COVID-19 was spreading, added to concerns about working in this environment. One worker, Isabel, was so concerned and fed up that she bought her lab fans and an air purifier. While she did bill these expenses to the lab, it took her initiative to get them purchased.

Participants often contextualized their experiences, knowing that the negative impacts of the pandemic were widespread—for scientists and otherwise—and unevenly distributed in

society. The world was in chaos, and after detailing their struggles in interviews, participants often felt the need to acknowledge their social positioning. Many echoed the sentiments of Elise, who said, "I know it is worse for others. I'm fortunate to still be getting a paycheck." Nevertheless, the working conditions during the pandemic made lab life extremely stressful for the participants in this study. Going into work itself was a "logistical nightmare," as Olga described it, and became taxing in ways that participants felt were not recognized by lab leadership nor by their institutions. As time went on, participants were quite frustrated that explicit conversations about the "new normal" were not happening. As I elucidate in the coming sections, these frustrations were compounded by changes to the nature of scientific work during the pandemic.

Losing the Sociality of Science

The advent of shelter-in-place and requisite pandemic work practices demonstrated just how social the practice of laboratory work is; sociality not only made work enjoyable for laboratory workers, it was also essential to doing good science and making structural inequities more bearable. As STS scholars have shown, science is a social practice. Scientific work is carried out through interactions (e.g., conversations, negotiations, debates), and it is often through these interactions that researchers come to understand and create meaning from data (Knorr-Cetina 1999). For participants in this study, the *absence* of this sociality during the pandemic made visible and crystallized just how important social aspects were to their scientific work and to their experience in the workplace.[x]

When asked what they missed most about pre-COVID lab life, across the board participants reported missing social interactions with lab members and the social aspects of

science more broadly. Being in community with other lab members made lab work enjoyable for many—and without it, they began to wonder what it was about science that drew them in the first place. Not only did the sociality of the lab make the mundane aspects of science more pleasurable, but it was also critical to troubleshooting, moving work forward, and feeling creative and energized in their science. Many participants remarked that they hadn't previously realized or appreciated how important the social life of the lab had been. The loss of this was profound for participants and they felt its impacts on their mental health and wellbeing as well as on their work's progress.

Helen explained how social interaction was fundamental to creating "the lab experience" and in fact, "the whole science experience." She explained, with the physical distancing and density restrictions:

> You have to be so isolated, even if there are other people in the lab. There are times where I've felt I'm almost reconsidering whether I really enjoy doing science. Because I just realized how social interaction is so important. It's so fundamental to create the lab experience, and going into lab where it's quiet, not talking to anyone, doing experiments for six hours straight…and it feels like it's been twice as long because there are no breaks. You're just doing the experiments consistently, not chatting to anyone. It definitely has changed the whole science experience. I personally don't consider myself a very extroverted person. I enjoy going into a dark microscope room and imaging for many hours. But I really also enjoy those discussions after a talk, the random bumping into people, and it's become so apparent how important those interactions have been.

Bumping into lab mates and colleagues from other labs spurred conversations about current experiments, and inevitably, struggles with those experiments. Researchers shared pointers or referred to others who they knew were experts in an area, creating connections in their scientific communities. These conversations were important, yet were challenging to recreate virtually. Rachel explained:

> The hardest part about not being there together is just the lack of knowledge. It's like in the air, maybe the best thing to say about it. One thing that I miss a lot is that the lab would have lunch together. Half the time we'd talk about movies or whatnot, but things

> come up. It's like, 'Hey, I have this cloning problem.' 'This isn't working and I don't understand it.' Or, 'I read this thing in a paper. What do you all think?'

Similarly, Heidi explained how her lab's break room, where people were allowed to eat and drink and "do fun things" that were prohibited in the laboratory space, was an important site of community building and collective troubleshooting:

> The break room was where you went with your cup of coffee to just think it through or to talk to someone… *[shaking her head]* The amount of problems that got fixed in that room. I'm convinced that if we still had that level of conversation and just casual interaction about science, I could probably have saved myself quite a few weeks in shelter in place when it's just been me thinking to myself.

Activities like causally sharing data were made more difficult during the pandemic. Ronnie explained how when she saw something interesting in her data, she would normally just turn to someone nearby and say, "Hey check this out. What are your thoughts?" Sharing data was hard over Slack, the online platform her lab had adopted for work management, and the impromptu nature of the conversation was lost.

Participants talked about how in pre-pandemic times, their time in lab was less efficient—due to social interaction—but that its benefits far exceeded this . Lane, for instance, talked about coffee and lunch breaks that extended their workdays. Nisha talked about the nagging feeling, in normal times, while attending talks or social events of "I know I should be working right now." Yet for both, this was a part of the lab experience and made their work enjoyable. In the absence of these interactions, they questioned whether they wanted to pursue careers in science. Even further, participants noticed that the absence of socialization negatively impacted their work and energy. For instance, Elise highlighted the exhaustion after 12-hour shifts in lab:

> Before we would just be chatting, or at lunch for an hour and time was eaten up. Now when I come into work my time is not chewed up by that kind of stuff. It's literally

> chewed up by just work. It's a lot to go 12 hours non-stop. It's hard to want to do things when you get home. I'm spending more time actually working, and I'm also trying to get everything you can done because you don't know when the next chance might be.

This time crunch also led to dwindling camaraderie, and a mentality of getting in and getting out, just to get one's own work done. Marsha noted that it felt like, amidst the scarce resource of time, that it was "everyone person for themselves." Others noted that it seemed colleagues just had less energy to give. Rita reflected that there was "less camaraderie now. And, of course, we're only doing virtual lab meetings and people are not paying attention as much. So, you're not getting as much feedback or suggestions for your work from people. I notice this for myself, too." Similarly, Olga described:

> There is a marked decrease in interaction from people, nobody wants to interact during lab meetings on zoom. Nobody wants to interact during subgroup or department seminars. It was definitely bad at the beginning, but I think people were trying and then now it's just abysmal."

She explained that she had recently given a talk to her department, virtually, and felt like she was "speaking into a vacuum."

Many labs tried to recreate a sense of community, but it was challenging during the pandemic, when many were feeling overwhelmed by the ever-changing pandemic environment, compounding current affairs, and juggling shifts. In normal times, Melissa's lab had an ad hoc journal club where someone would come across a paper of interest to the lab and they would then meet in a week's time to discuss; she relayed that "We tried once during COVID to do that virtually and it was okay, but no one's tried it since." Heidi explained how her lab's attempts at recreating community ended up becoming another stressor. Her lab started a "casual" zoom lunchtime and research chat. She explained:

> No one ever showed up, so then they became mandatory. Then they were definitely not casual because it suddenly involved a sign-up sheet. And you're wondering, how is this a

> casual science? People started preparing slides and it became like a tiny little group meeting instead of anything else and it's stressed all of us out."

Spontaneous activities that once sparked rich conversation now had to be required, leading to more work and stress for lab workers. The loss of social interaction in the lab environment negatively impacted lab workers' experiences working, as well as their ability to move projects forward. Workers felt alone, physically and mentally, in their science. Though the conditions of their working environment had greatly changed—highly regimented shifts, severely restricted time in lab, and no social interaction—the pressure to produce persisted. Weekly lab meetings, one-on-one meetings with PIs, and other accountability mechanisms kept on throughout the pandemic. As I demonstrate in the following section, this unrelenting pressure seemed to make the failures land harder.

No Time to Fail

Failure is a normal part of doing science; a successful experiment and eventual publication represent many failures along the path of finding what works. It was common for participants to talk about how normal failure is in science. Jasmine said bluntly, "When you're doing original research, only 5% of what you do is ever going to work." While many acknowledged that this can be demoralizing in normal times, failure was readily accepted as par for the course. As I show in this section, the restricted lab time combined with the loss of socialization in scientific settings during pandemic lab life intensified participants' experience of failure leading to further estrangement from their work.

No matter what shiftwork model a lab adopted, across the board, time in lab was substantially reduced from pre-pandemic times, where participants in this study reported

spending a minimum of 30 hours in lab per week (and for many, well above 40). In the first few months of reopening, participants averaged around 10-15 hours back in lab and many were going in far less.[xi] Indeed, routine lab failures that would otherwise have been normal parts of science now felt insurmountable because they led to delays of days and weeks. Many described that normally when a given assay or experiment failed, they would often get ready to restart a protocol the same day. With shifts, there was no longer the time to do this in lab, and when coordination with other labs or core facilities were needed, this was even more challenging. Luis put it simply, "You fail and it sets you back a week basically, whereas before maybe it set you back a day." On top of this was a fear of not knowing when things might need to shut down again, and whether it was worth starting long and/or expensive experiments. Carmen felt as if time was slipping away:

> Just knowing that you're on like a finite time limit, you know? It's kind of like an hourglass, you can see the time slipping away, but you can't do anything to get back that time that's been lost. So if you're doing an experiment that fails, previously it was, "oh, I have time to do this again." But now there's so much unknown. […] Constantly I'm worrying about if I do get sick, I would have to quarantine many days. Having that at the back of my mind makes me think like I'm not doing everything fast enough.

These failures, and the resulting extensions to time horizons for degree completion or applying for postdoc and faculty positions, coupled with the looming economic uncertainties that the pandemic imposed on academic science, impacted participants' longer-term goals. Longer experiment timelines delayed papers and subsequent goals of graduation and future jobs. Those at critical junctures of their PhD and postdoc training, nearing the "transition stage," as Ines called it, felt this pressure particularly acutely. Some participants, for example, found themselves trying to negotiate with their PIs how many more experiments were needed before they could submit a paper, a critical step in most biomedical science doctoral programs. Others, like Ines, felt they needed to move on but found it hard to do so. She had been looking for postdocs, but

was finding that many labs (her own lab included) were not currently taking on new postdocs. This worried her, saying "the context of a pandemic makes it even stranger because it restricts people's perception of funding. I don't know that funding has actually changed." Though others assured her things would work out, the looming uncertainty brought on by university hiring freezes in response to the pandemic worried Ines and others about their own future prospects. These uncertainties contributed to workers' experience of failure, and questioning of their place in their fields.

In normal times, participants felt they had outlets to help process and contextualize their failures, typically with their peers over lunch or on breaks. With the loss of sociality discussed in the previous section, these failures seemed more demoralizing. As Heidi reflected:

> I have some stuff that hasn't been working and it feels so much bigger than it used to. I don't think I have more lab failure now than I did before, but emotionally it feels way worse than before, it feels like I'm like getting off course way faster. Whether it's like a real project plan, one that I've made myself, or some like unspoken expectations I have of progress, it just feels like it deviates from that much, much faster in a way where it rarely feels in my control. And there's much less room for it—we have some things as I'm sure most like wet labs do, where you just gotta do it for two weeks and figure out what is happening. And that feels totally unreasonable. And I don't know if that's the pressure of you gotta be productive when you're in lab because you know, it's precious time, or if it's because everything is really hard right now.

Across the board, participants felt like their current failures were tangibly more difficult than they normally were both in terms of delaying lab work, as well as mentally overcoming them. Some attributed the latter to not having other things in their lives to take their minds off lab work. Lena explained it this way:

> Seeing friends super regularly on the weekends, even though it's not every day… there's this continuity of other activities [in normal times]. When that's happening, then I do love science. But it's hard when it's the only thing going on. It's the *only* thing and it's just hard when it feels like a constant failure. When you're only focused on your little experiment that just hasn't worked for a month, it really spirals you down.

For Lena and many other participants, social activities outside of lab were important to taking her mind off lab failures, and to feeling like a *whole* person. During the pandemic, Lena said that failures sent her "spiraling." Similarly, Olga said, "the work itself is hard and the failure is hard. When you don't have the social aspect or even just the opportunity to talk about your project… it just feels like, what am I doing?" Several participants experienced depression during the pandemic, and many described an utter loss of joy and estrangement from in their scientific work.

While participants routinely told me how normal failure was, they also explained that failure is rarely talked about by their PIs or in settings where science is "on display." Participants often talked with their peers—grad student to grad student or postdoc to postdoc— about their failures, struggles, and anxieties. But beyond that, these experiences of failure were not often publicly discussed. Helen explained:

> The lab environment doesn't set the tone that it's okay to talk about failures and like talk about things that aren't working. Every lab meeting has a certain way of presenting things. And so it's weird or different to talk about it, or it might seem like it isn't as productive or successful to talk about the failures and things that aren't working. I think talking about the slog is useful to have the people who are higher up, the PI, set the tone to talk about it. So if he's talking about it, for instance, then it feels like it's okay as a student or postdoc to do that. But, of course, the PI doesn't present at lab meetings ever or really have any informal conversation.

Similarly, Isabel recalled a recent experience where she was pleasantly surprised a PI shared his own struggles with her in passing. For her, this spoke to bigger issues in leadership among PIs. She explained:

> There have been a lot of times when I've wanted a real strong leader and to feel like I'm part of a real team and maybe that would have helped. I've been thinking about the leadership of a PI and how COVID has exposed vulnerabilities in that sense or existing problems around leadership. I ran into a very senior PI on my floor recently. He asked 'How's it going?' And I said, 'Oh, it's actually, it's okay. But pretty slow.' And he was like, 'Everyone's having that.' I was shocked because my boss has never acknowledged that. He says things like, 'I've written so much. It's so productive.' Just the acknowledgement

that things are difficult right now helped me.

For Isabel and others, not seeing their PIs discuss their own struggles and failures in their work, reinforced the notion that these conversations were taboo.

Though failure was largely understood as a normal part of scientific work, the loss of socialization in scientific settings coupled with unrelenting pressures to produce, failure became particularly taxing. Participants experience of failure during the pandemic was intensified by reduced time in lab, alongside continued expectations of productivity emanating from lab leadership and cultural norms of academic science. In other words, the very sense of having *no time to fail* is the product of a particular environment produced by the trends of academic capitalism and bureaucratization. The productivity-at-all-costs culture of many high research activity institutions in the US intensified for lab workers during the pandemic. As I show in the next section, participants readily acknowledged this in interviews and among peers, yet they felt bound by the cultural norms in academic science to that all too often serve to minimize and silence critique.

"The World is a dumpster fire" yet "data comes first over everything": Workers' critique of 'science as usual'

Without the space to process what was going on in the world, or the toll lab work was taking on their lives, the distance between "science" and "society" became jarring for participants, and their experiences throughout the pandemic sparked poignant critiques about science as usual. Overwhelmingly, participants felt like they were expected to continue producing data at pre-pandemic levels, despite having less time in lab and reduced mental capacity to do so.[xii] Many participants explained that they received no messaging from their PIs

about expectations. In the absence of acknowledgment and alongside the unaltered accountability mechanisms such as weekly lab meetings, many interpreted this as an expectation to continue as if the world was not, as both Callum and Beth put it, a "dumpster fire." In what follows, I explicate how workers' lived experiences during the pandemic led them to articulate their estrangement, and to launch critiques of academic science. And yet however emboldened workers were to raise these issues among their peers and in interviews with me, within the context of prevailing power dynamics in their labs, they felt unable to raise them with their PIs.

Heidi explained that her lab received institution-wide messages about COVID-19, as well as other crises co-occurring (e.g., racial injustice and multiple extrajudicial killings of people of color by the police, record wildfires on the west coast, the Capitol insurrection) from the university, but no communications from their PIs. She explained that this lack of communication was interpreted by those in the lab as if they should continue working as usual. "It's just kind of showing some of those like weaknesses in our community system," she said. Miriam also felt pressure to just keep working, despite what was happening in the world. She explained:

> It's coming mostly from my PI being like, 'you should have a paper together.' And then me getting mad at that and being like [to myself], 'what do you want from me? It's a global pandemic and none of my stuff is working.' I feel like he knows there's a global pandemic and so it's not useful to really say that. For my PI in particular, there's probably a couple of things going on. One is that he hasn't been into lab in almost a year to the day now. He doesn't understand what it's like to do work here.

She explained that because PIs rarely are in lab, and because "he doesn't see the parts that are actually bad" it felt challenging to bring up the issues she was facing in a constructive way with her PI. Many workers described how their PIs seemed to be frustrated by the lack of data being produced in their labs during the pandemic months. Luis said his boss was "fed up with the whole shut down… My PI told me, 'you need to be more greedy with your time. You need to

take more shifts.' And I'm like, okay, I'm not taking more shifts because I'm trying to allow everybody to have their full amount of time." He later learned that his PI had been giving this advice to multiple lab members. Routinely, workers explained that their PIs' expectations were unrealistic, but that they were unable—or did not see the point in trying—to push back against such demands for continued productivity.

Participants' frustrations built up over the course of the pandemic, leading to strong structural critiques of academic science and its culture. Just as the pandemic had crystallized the value of the social and interactional aspects of science, it also made visible longstanding issues that participants had previously just accepted as 'science as usual.' Nico explained:

> I still feel pretty frustrated at the environment of my lab, but not even just my lab. Kind of just all of academia and this institution. And the culture where data comes first over everything, literally everything, even the health of the people doing this work. So that's a bit frustrating. I feel like my PI tries her best in the way that she knows how to be understanding and to accommodate, but it only goes so far. I'm doing the best that I can, but I still feel like the expectations are unreasonable.

Like Nico, many participants pointed to the broader structure of academic science, in which papers and grants—and the data needed to achieve them—is paramount.[xiii] Data updates were a routine part of weekly group meetings pre-pandemic, and many participants described that these meetings and their normal structure continued throughout the pandemic, adding to the pressure they were feeling. Though workers' lab time was severely cut, the continuation of weekly lab meetings, alongside silences about expectations, implied that lab workers should still be as productive as in normal times. Callum explained how this contributed to the pressure he felt:

> I feel like my PI still has the same expectation of productivity as before the labs shut down. Especially because we're still having those weekly meetings and you're supposed to present data every week. Sometimes I just don't have data, like I can't go down [to lab]. I can't even do anything. But I feel like we're still expected to produce the same amount every single week.

Throughout the pandemic months, there were multiple compounding social crises that contributed to participants' experience of upheaval and uncertainty. This was particularly frustrating for participants in the wake of the killings of multiple people of color in the spring and summer of 2020, and the institutional responses that followed. #ShutdownSTEM, an event focused on acknowledging systemic racism in academic science and the cumulative disadvantage faced by Black academic researchers, occurred in the height of the pandemic, and many participants reported that their PIs did not publicize or actively encourage participation. As institutions started hosting events to talk about institutional racism, many lab groups did not take up these topics unless a lab member brought them forward. In these cases, participants reported that PIs were encouraging and often lead to dedicated discussions among the group. But largely, these ongoing events were siphoned off, in both explicit and subtle ways. For instance, Maia explained that her PI sent a subtle message when she asked to reschedule a lab presentation:

> Our institute started hosting a lot of Black lives matter related discussions and activities over zoom. And sometimes they conflicted with our lab meetings and my PI didn't reschedule. So even one time when I was scheduled to present, I said, "if possible, I'd like to like present and leave a little bit early, like present quickly and then leave because there's a person of color caucus meeting that I wanted to attend at our Institute at the same time." I was hoping they might say, let's just reschedule your presentation. But they didn't do that.

Like Maia, many participants discussed how their PIs failed to discuss life events that impact the wellbeing of lab workers. As these events seemed to pile on, PIs' insistence on continuing "science as usual" became untenable for workers. Participants expressed that they wished their PIs would acknowledge the state of affairs in a more meaningful way than a quick mention with no substantive discussion. For instance, Callum expressed disappointment that his lab carried on with meetings the day of the Capitol insurrection (January 6 2021). Reflecting on the culture of these meetings, he continued:

> We still have meetings. And then my PI is like 'You know, this is not the country we live in. It's hard for me to focus. Okay. Let's continue.' Maybe PIs feel that we can sit around and kind of mope about it, but we can't really do anything to fix the situation. Maybe that's how they felt. But I don't know, he literally just said like one sentence, like 'God, I'm having like a hard time focusing, but let's continue with the meeting.'

Similarly, Carmen described how her PI begins meetings with "lab business" and then immediately jumps into data talk, but never makes space to discuss all of the events that might be affecting people working in the lab. She explained:

> You know, there isn't really a time to give a state of the union address. We don't have that, which I think would be nice. Acknowledgment that, oh this week has been hard. This is what happened. It would be nice if we had something like that, but we don't. It's always been about the data and it really hasn't changed. Even when we had in-person meetings, it's always been that way. Just straight to the data.

Participants voiced concerns about working in the lab during the pandemic, productivity expectations, and research failures with lab mates or other small circles, but never "up the food chain" so to speak. When I asked trainees why these felt like hard conversations to have with their PIs, they often paused reflectively and found it challenging to answer. When they did respond, they were clear that it felt like an unimaginable encounter. Heidi pondered:

> I don't know. But it seems totally unimaginable…I think part of it is like not wanting to appear weak. Yeah. I mean, so many of us put on this front that like, everything is fine and we're doing fine. I kind of talk myself out of it with this like very stupid thing that I don't think she can change it. But then sometimes maybe just her knowing, like, I'm sure that that would be, make a difference.

At the time of our second interview, Heidi's lab had just had its "state of the lab" annual meeting. Some participants' labs held similar meetings at the beginning of each year to discuss priorities for the coming year, plans for funding, and to acknowledge the past year's progress and challenges. Heidi explained that at this meeting it would have been nice for the challenges of 2020 to be acknowledged. Instead, "as always, there was the 'we're not publishing enough'

which we get every year." With the unrelenting focus being on the data and scientific progress, participants internalized that social issues were not appropriate conversations to have in the space of the lab.

Critically, the ethos of "data comes first over everything," as Nico put it so plainly above, is not inevitable. Instead, as this analysis underscores, it is socially promoted and produced – not only through affirmation, but also through silences. In pandemic times, silences about expectations, social issues, and a lack of overt recognition about how challenging the times were important boundary management moments. Workers consistently explained how their PIs seemed to take these events in stride and often did not acknowledge them within the working environment in substantial ways, subtly but firmly reinforcing the boundary between private and professional life and between social issues and scientific work. This neglect shaped the culture of lab groups, reinforcing notions about what can be discussed in scientific settings and what is deemed inappropriate or unprofessional. During the pandemic, this boundary management exacerbated workers' frustrations and anxieties and it also led to their articulation of these issues as structural problems with academic science.

Conclusion

This study attends to critical questions that science studies scholars have raised about how academic capitalism and bureaucratization are reshaping scientific careers, the training of junior researchers, and about science as a *calling* (Hackett 1990; Lee & Walsh 2021). In their recent article, Lee and Walsh (2021) contend that in the age of bureaucratized academic science, marked by increased division of labor, hierarchy and standardization science is "at risk of losing its vocational character" (p. 14). Under these current institutional and organizational regime and

alongside pandemic realities, workers questioned their love of and calling to science. Conducting scientific work in the pandemic required a new mode of lab life that negatively impacted workers from their mental and physical health through to finding their fulfillment in their scientific work. Emergent working conditions, combined with the compressed time and loss of sociality in lab, led many participants to question whether they really felt called to the practice of science, a calling that many described as deeply connected to their identity and sense of self. Their enthusiasm and commitment had been exploited to work extended hours and onerous shifts. Their failures hit harder. The demands to produce data were endless. Moreover, the failure of lab leadership to investigate and acknowledge how ongoing events impacted workers, as whole people and not just workers, magnified the estrangement they experienced. Without the key elements that enabled workers to tolerate and navigate power dynamics and failures in normal times, the new realities of lab life not only resulted in a loss of creativity and problem-solving capacities, but also in their estrangement from science itself.

It would be a mistake to credit this estrangement to the pandemic, as time and again workers explained that the organizational inequities and their daily frustrations with the culture of academic science were long in the making; they were frustrations with key features of "science as usual" under academic capitalism. In this case, as with so many others, the pandemic may be best understood in this case as illuminating what had always been bubbling under the surface. Indeed, the pandemic and its disruptions made visible existing inequities in academic science as well as provided a lens through which laboratory workers could articulate their concerns—even if only in protected spaces. Though nearly all participants in this study were vexed by the lab environment during the pandemic, none felt comfortable bringing such issues up with lab or institutional leadership. The inability workers described to raise concerns—about

inequities in shift schedules, logistics of lab work, experiences of failures, and expectations of productivity—show how power operates in academic science. PIs active policing of the boundary between science and society, however artificial that boundary may be, served to silence dissent. Actively not making space to pivot and alter course as current events were impacting workers, and instead continuing as if the conditions of laboratory life had not changed, reinforced a culture of academic science in which there is not space for more than just "the science."

While much of the literature has pointed to macro-level trends that structure academic science, this study links these trends with interpersonal dynamics at the level of the lab group. These relations are essential for understanding the culture of laboratory work, as well as how norms, values, and hierarchies are reproduced. While academic capitalism and bureaucratization certainly structure how scientific work is carried out, they are not the only forces that shape scientific work. Put another way, the meso- and micro- dynamics, at the levels of the institution and lab group, also shape everyday laboratory life. Lab workers in this study articulated not only the structural causes of their estrangement, but also how critical interpersonal relations within laboratory groups—particularly laboratory leadership—are to creating an environment in which doing science is more than just labor.

CHAPTER 6: CONCLUSION

When biomedical technologies are developed, they often present as if their success is inevitable. Technologies seen as promising and promissory can attract followers and investors of all kinds, including private investors, but also government funders, industry stakeholders, researchers, and the public, who are willing to bet on the technologies' potential for disruption and transformation. Narratives of technological emergence and adoption obscure the social processes of construction, and the labor that is requisite for new technologies to emerge, be materialized, and get taken up. These processes involve working out, and then concealing, questions of whether novel technologies will work, if they will be transformative, and whether they are necessary and worthy of investment.

This dissertation attempts to make visible the construction of a set of emerging technologies called organ chips, excavating the social processes at play that enable these tools to not only become technically and scientifically doable, but also to be seen as valuable technologies worthy of sustained public and private investment. In this concluding chapter, I first summarize my key findings, and next attend to the theoretical contributions of this dissertation. I then discuss future directions for this work, and finally, offer some closing reflections.

Summary of Dissertation Findings

In Chapter 2, I traced the construction of the "translational crisis" in biomedicine. I argued that the particular discursive framing of the problem as an acute but endemic crisis enabled it to be seen as in need of deep and significant solutions. This framing included attributing the cause of the crisis to the infrastructure of academic research—its norms and incentive structure, publishing practices, and siloed organization—and proposing solutions that

serve to embed industry values and logic into the existing infrastructure. 'Science as usual' cannot solve the translational crisis; expertise and practices from outside the academy are necessary. I then analyzed activities that seek to change and rebuild the academic science infrastructure—including establishing national centers, funding streams, and publication outlets—to encourage translational research as well as leverage existing training programs and funding streams that encourage the commercialization of science. These changes served to instutionalize the commercial ethos of translation, to incentivize and prime academic researchers to always already be thinking about the commercial potential of their scientific work.

As industry has been positioned as a worthy, valuable, and necessary partner in the production of translational research, I show that commercialization has come to signal translational success. And as a result, what were once understood as financial versus scientific conflicts of interest, where the potential for privatized commercial gains is seen to be inherently at odds with scientific objectivity for the public good, have paradoxically become aligned, and are increasingly celebrated indicators of academic capital. I closed the chapter by attending to the implications of these findings for the governance of conflicts of interest, which have historically been considered problematic for the production of knowledge.

Chapter 3 examined the assemblage of material, social, and discursive elements that developers and stakeholders organize to construct the rightness of organ chips. Engaging Clarke and Fujimura's (1992) concept of "the right tool for the job" and Fujimura's (1987) concept of articulation, I offered an account of how organ chips are on their way to becoming the right tool for particular jobs. I identified and described four sociotechnical conditions of possibility, broad trends happening in biomedical science that, taken together, enabled organ chips to be both technologically possible and socially valuable: the translational crisis and growing discontent

with the inadequacy of non-human animal models (both of which were detailed in Chapter 2), the rise of cell culture technologies and *in vitro* experimentation, and the integration of engineering approaches in the life and biomedical sciences.

While these sociotechnical conditions enabled organ chips to be socially valuable and technically possible, they are insufficient in and of themselves to make organ chips the right tool for the job. Thus, I then turned to analyze the actors, networks, and power relations through which these conditions come to have social force. I demonstrated how state and industry actors play a central role in positioning organ chips as *doable* and *right*. Later in the chapter, I argued that 'hyping' is integral work for constructing rightness and excavated the types of hyping work that must be accomplished in different settings. Given the audience and goal, hyping entails generalized claims of the disruptive and performative potential of organ chips as well as claims of technical legitimation and superiority. Finally, I showed how standardization becomes a key component of rightness, given that organ chips intervene in a heavily regulated space.

Then, in Chapter 4, I attended to the construction of organ chips models, surfacing the social processes of scientific decision making. I began by showing generally how organ chips are produced, and how the human cells used in the models are sourced. I then showed that while organ chips are marketed as "human-based" models, this obscures that there are different kinds of human cells that are used. Researchers use induced pluripotent stem (IPS) cells, primary donor cells, and cell lines depending on their experimental questions. The choice of cell type has implications for physiological relevance, reproducibility, and scalability, and has led to state actors encouraging the use of IPS cells motivated by the goal of more easily integrating organ chips into the existing regulatory and market infrastructure for drug development. I then follow two cases, the lung chip and the female reproductive system, to trace how organ chips become

collectively understood as "human enough," and how market priorities explicitly shape the design of organ chips.

Finally, Chapter 5 examined laboratory life during the COVID-19 pandemic. I began Chapter 5 with reflections on the implications of the pandemic on conducting data collection for this dissertation and my decision to pivot and launch the Disruptions to Laboratory Life (DLL) Study. The remainder of the chapter was written as a standalone article. Drawing on interviews with biomedical research trainees over an eight-month period, the chapter offered an account of how the pandemic changed the nature of laboratory life. I showed how daily life in the lab during the pandemic was marked by emergent stratifications and inequities in access to sufficient lab time, increased stress around productivity, and frustrations with the culture of academic science. The loss of social interaction, and the ensuing lonely struggles that constituted much of scientific work during the pandemic, made visible the importance of sociality in science for laboratory workers. Finally, I argued that pandemic disruptions not only amplified and exacerbated existing social inequities in lab settings, but also resulted in workers' estrangement from science itself.

Theoretical Contributions

One key theoretical intervention this dissertation makes is simultaneously temporal and methodological: Rather than waiting until a technology has become normalized, accepted, and standardized, I contend that we must examine its in-progress social shap*ing* as it is under construction. This is a critical task for STS scholars, both for the purposes of more deeply analyzing the mak*ing* of the right tool for a job, but also to potentially and more effectively intervening in its unfolding development. My emphasis on shap*ing* and mak*ing*—the present participle and gerund forms of these verbs—is deliberate. While the future of organ chips and whether they become the right tool remain to be seen, and an ongoing empirical question, I argue

and demonstrate that this particular time in their development offers an analytically rich window in which the negotiations and construction of *rightness* are overtly worked on and therefore acutely visible. In doing so, I illuminate the social processes of scientific negotiation, and how particular tools become right for particular jobs, and excavate how power relations shape the construction of science and technology.

Second, while scholars who have attended to translational medicine and its allied fields have shown that industry risk is transferred to the public sector, effectively de-risking investment in research and development for pharmaceutical and biotechnology companies (Robinson 2019), they have not attended to the specific mechanisms through which the infrastructure of academic biomedical research is shifting. I add to this literature by demonstrating how industry interests and values are becoming more deeply enmeshed in the infrastructure of academic biomedical research. I argued that as translation has been taken up as a key priority in biomedicine, successful translation comes to mean commercialization, as manifested in the imbrication of academic with industry interests, knowledge generating with profit generating interests, and scientific innovation with economic production.

Third, scholars have not offered a critical analysis of the construction of the translational crisis and the discursive power of 'translation.' Translational medicine makes sweeping promises of offering a social good that is challenging to critique: it promises to get biomedical advances into the hands of the public, to have tangible benefits for society, faster and more efficiently. Yet by unpacking the framing of the translational crisis, I show how the crisis of translation and its proposed solutions encourage the strengthening of industry relations in academic research as well as accelerating socialization of academic researchers to always already think about the commercial potential of their research. The very notion that industry is necessary to solve and

save academic biomedical research is a particular framing. The logic of translation I examine shows how beliefs about the appropriate role of industry in biomedicine, the productive alignment of government, academia, and industry, and pathways to achieving broader impact, all prioritize private interests in the name of public health. Moreover, the alignment of interests that becomes co-constitutive of the pursuit of translation radically reframes relations that were once understood as conflicts and thus threats to the public trust in biomedical science. I therefore raise important questions about what types of research will be pursued in the name of translation, how conflicting interests will be managed, and how benefits of translational research may be equitably distributed.

Fourth, I add complexity to existing STS scholarship focused on scientists' agenda-setting activities and how they construct doable problems. Work in this area has often taken individual researchers as the main site of analysis, examining how they articulate their work to create sustainable research agendas, build fields, and manage controversies (Fujimura 1987; Frickel 2004; Hoffman 2021; Jeon 2019; Panofsky 2014). In my case, I show how state and industry priorities intersect to shape academic research agendas, and demonstrate how articulation work happens in both top-down and ground-up ways: while individual researchers do some of the work of articulating organ chips as doable and right, much of this work is initiated by state actors. The always-already presence of industry actors, biomedical engineers, and funding agencies is consequential for what organ chips have come to be, the kinds of tools they are, and the jobs for which they are 'right.'

Finally, I join scholars who have shown how biomedical models are used to create knowledge about the human body, and the series of social negotiations required to render a model "good enough" (Lewis et al. 2012). In this case, I showed how organ chips become

"human enough" through negotiations about the minimum units of organ function and cellular architecture, longevity, and cell source. I focused on the issue of cell sourcing in order to show how decisions about human cell type (IPS cells, primary donor cells, or cell lines) shapes the kinds of knowledge that can be generated using organ chips. Moreover, I add to this literature by showing how market forces shape the construction of models. While many have shown that academic capitalism shapes research project choice and the political economy of biomedical models shapes model selection and distribution, I show how considerations of the market impact the very design of scientific objects.

Future Directions

Like the organ chips themselves, my work following their development is also in progress. There are therefore multiple directions future work could take to add depth to the findings presented in this dissertation. I plan to continue to trace the trajectory of organ chips, investigating new efforts that I noted in Chapter 3 that are focused on creating disease models using organ chips, modeling human difference, and simulating clinical trials on chips. At the time of this writing, developments in each of these areas are underway, and there are critical sociological questions to be asked in each domain.

Second, future work will explicitly attend to how race, sex, and other forms of human difference are used in organ chip research. As discussed in Chapter 4, demographic data was often absent from modeling efforts, given that standardization efforts geared toward achieving regulatory approval and integration into pharmaceutical regulation infrastructure actively worked to erase human difference. Yet many presentations I observed were haunted by notions of human difference: while it was rare for researchers to explicitly address racial and other forms of difference, they often alluded to it through imagery or in passing mention. Moreover, organ chips

are actively being promoted for *precision* medicine efforts, which aim to develop targeted therapies and diagnostics for individuals and population groups. Therefore, in order for organ chips to become the right tool for precision medicine research, they will need to be able to model key human differences that researchers believe are critical. That is, rather than simply being "human enough," organ chips will have to be seen as, for example, female enough, raced enough, old enough, or diseased enough, for their utility in precision medicine research.[i]

Closing Reflections

When I present this work, audience members often ask me how I chose this topic. How and where did I come across organ chips? My interlocutors often wondered the same thing. Organ chips are, after all, technologies that rather invisible in the infrastructure of biomedical research. Situated in the earliest stages of preclinical research, they are not technologies that everyday people are bound to come across. Indeed, my own introduction to organ chips was marked by the hyping work of organ chips I discussed in Chapter 3: on a spring day in 2017, around the time I was determining what I might pursue for my dissertation research, I happened to catch a radio segment about organ chips on National Public Radio's (NPR) All Things Considered. Sitting in a Target parking lot, I too was captivated by these technologies—not because of how they might transform early-stage pharmaceutical testing—but because they appeared to be so ripe for STS questions, and connected with my deep interests in how we come to understand and represent the human condition, health, and illness through science and technology.

On this particular segment, a researcher from the Evatar team was being interviewed about recent advances. As it turned out, this was not the first time organ chips had been discussed on NPR. In fact, All Things Considered, as well as other NPR programs, had held

multiple shows in earlier years devoted to this topic with other prominent organ chip researchers (NPR 2010, 2012, 2015). But in the 2017 segment that first caught my attention, considerations of ethics came up. The host noted that "the researchers stress that they only want to use these models to study anatomy and come up with new treatments" (NPR 2017). The host then turned for input from a bioethicist, who suggested that while researchers creating organ chips may have good intentions, they were advancing at "such a rapid pace" that would not be able to control how others took up the technologies and toward what ends they used them for, and that it was at that juncture where ethical concerns arose. I was struck, if unsurprised, by how potential ethical conundrums were being circumscribed. It was not a question of how the developers of the technologies themselves could fall prey to ethical missteps, but rather how possible *others* might misuse these technologies. Moreover, it was presented in such a way that the very tasks at hand— creating these models to study anatomy and come up with new medical treatments— could not themselves be sites of ethical quandaries.

This segment started me on this project, as well as a broader questioning of why and how developers of emerging technologies continue to avoid, defer, truncate, and/or wall off considerations of downstream social and ethical consequences. Throughout this project I have often been asked about the social and ethical implications of organ chips. Given their status as novel technologies at the margins of biomedicine, it remains to be seen how these technologies will matter, and so in many ways the questions of what harms might be accrued, or avoided, or substituted, remain open questions. Yet such a large body of scholarship exists in STS and medical sociology that attunes us to issues to look for, and for places where we can learn from past empirical cases.

Over the course of conducting this project, I frequently worried I had made a risky choice to research something still so nascent. The state of organ chips means that the "so what?" of it all often felt less clear: there are not yet specific consequences or harms to point to, to say with conviction that *this* is why a sociological account of these technologies is crucial. Indeed, it remains to be seen if and how organ chips will change the landscape of pharmaceutical toxicity and efficacy testing, and how they will be used to understand diseases and model clinical trials. But over the course of conducting this research, I have come to understand this as a strength (on good days, anyway). Whether organ chips fail or succeed in their endeavors to become the right tool for multiple jobs is not necessarily the most important for a sociological study like this one: rather, the pursuit has been to excavate the sociality of science, including the social negotiations requisite for scientific work as well as the power relations at play in shaping the production of novel biomedical technologies.

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NOTES

Chapter 1 Notes

[i] The NCATS Tissue Chip Program includes "Tissue" instead of organ in the name. However, organ chips quickly seemed to take on life as "organ chips." Similarly, early publications always used the phrase "organ-on-a-chip" which in later publications was simplified to organ chips or microphysiological systems. I discuss the politics of naming further in Chapter 3.

[ii] Kleinman & Vallas are careful to note that it would be a "mistake to assert that the new university-industry relations constitute a novel thread to autonomous faculty control of research and agendas, and it is equally problematic to assert that these partnerships mark an exceptional incursion into the idyllic free exchange of ideas and research materials" (2001, 459). In their description of the *asymmetrical convergence* occurring between academic research and industry research, they note that particular fields lend themselves better to this vision of academic research. Those like the humanities and social sciences stand to "lose" in a university climate in which patents, commercialization, and industry partnership are desired.

[iii] This literature has also highlighted that shifting academic-industry relations not only implicate individual researchers, but increasingly institutions. As universities and other non-profit research institutes pursue intellectual property and industry partnerships, industry partners may be perceived as having inappropriate influence over the institution's decision making. As such, research institutions and universities have had to develop strategies to manage this, such as creating committees to independently evaluate decisions, as well as establish private institutions that operate independently in order to support and manage spin-outs and investments (Resnik 2015).

[iv] Namely, Clarke and colleagues asserted that medicalization theory was insufficient and too narrow to capture the social nature of medicine, particularly in the late twentieth century. Peter Conrad's later work on medicalization, on the other hand, argues that we have not moved beyond the process of medicalization, but that the "engines" that drive medicalization have shifted. He asserts that the new drivers—biotechnology, consumers, and managed care systems—need to be analyzed (Conrad 2005, 2007). In our recent update to biomedicalization, we note that biomedicalization does not replace medicalization, but rather that it describes broader shifts (Clarke, Jeske, Shim & Mamo 2021).

[v] One notable exception is Jill Fisher's work, which has elucidated the political economy of clinical trials(see, for example, Fisher 2007, 2020).

[vi] After much back and forth between me, my advisor, and the IRB representative, we learned that this designation was the result of the IRB trying to prevent "creep," in which the IRB spends resources reviewing studies that have very low risk of harm to participants. Because the study was about the "work of doing research", and about the development of science, they decided it was not of high enough risk to warrant review.

Chapter 2 Notes

[i] Investigators seemed to value transparency, and I do not mean to suggest that they did not take the disclosure of these conflicts seriously. At all conferences I observed, presenters (who were typically the principal investigators of their laboratories) routinely disclosed their conflicts of interest, sometimes in painstakingly detailed slides that disclosed years of collaboration,

including consulting positions with pharmaceutical and biotechnology companies and contract research organizations, and increasingly their own spinouts from technologies developed in their academic laboratories. Some conceded that these conflicts were indeed concerning (typically in interviews), and others seemed less reflect and were, at least publicly, more sarcastic. One researcher, for example, disclosed his conflicts and then candidly said, "so take what I say with a grain of salt!" His remark was met with chuckles from the audience.

[ii] Conversations concerning the translation of basic research findings into applications well predate the turn of the twenty-first century. Particularly concerns regarding the use of around non-human animals in biomedical research, the inefficiencies translating findings have been well documented since at least the 1960s. Aviles (2918) work has shown investment in translation at the National Cancer Institute began in the mid twentieth century. However, at the institute-wide level, the NIH (the federal agency funding biomedical research) began investing in translational efforts at the turn of the century. Scholars have debated, skeptically, if translational medicine represents a paradigm shift as actors in the empirical arena often declare it. I agree with other scholars who posit that translational medicine is perhaps best understood as a "reconfiguration of the structure of biomedical research" rather than a new paradigm (Robinson, 2019; Solomon, 2015).

[iii] In addition to this concern, translational medicine advocates also lament that because of high costs, there is a lost opportunity to test many more compounds that can currently be explored. In a sense this is the imagined failure of the all the *potentially* effective compounds that could be out there, but for which there are not resources to test. As I discuss in Chapter 3, organ chips promise a cheaper alternative, effectively enabling pharmaceutical companies to test more compounds than they might be willing to given current methods and their relative cost.

[iv] See, for example, Vagtborg, 1968. "Within the last decade, however, it has become increasingly evident that the data from small-animal experiments are ofttimes not applicable to man. For more sophisticated studies in pharmacology and toxicology, more than ever, other types of animals are needed."

[v] In creating the Roadmap concept, the NIH "consulted with more than 300 nationally recognized leaders in industry, government, academia and the public" (NIH 2014a, 2).

[vi] There were several other, earlier, efforts geared toward translational research. At NIH, the Roadmap laid the groundwork for the establishment of the "Common Fund." Other efforts included the expansion of the Bench-to-Bedside Awards program, the establishment of the Clinical and Translational Science Awards Program in 2006. Additionally, The Common Fund offered a novel way to fund biomedical research, pooled money from all the centers and institutes to move research forward in three ways: (1) foster high risk-high reward research, (2) enable the development of transformative tools and methodologies, and 3) foster collaboration and change academic culture to better fill fundamental knowledge gaps (NIH, 2014).

[vii] The US Congress created the SBIR program in 1982. The STTR program was created in 1992. Federal agencies with extramural budgets over $100 million are required to dedicate a certain percentage of their budget to SBIR. Federal agencies with extramural budgets over $1 billion are required to dedicate a certain percentage of their budget to STTR. (SBIR n.d.)

[viii] The I-Corps™ (Innovation Corps) was founded by the National Science Foundation (NSF) in 2011. NIH began its program in 2014.

[ix] Similarly, it has become increasingly common for universities to count patents toward tenure and promotion, a key characteristic of academic capitalism (Sanberg et al. 2014)..

[x] This estimate comes from a previously published piece examining the shifting meaning of "interest" in translational medicine (Jeske 2021a). At least 70% of research articles published in *Journal of the American Medical Association (JAMA*), *Nature Biotechnology*, and *Science Translational Medicine* in 2019 were authored by teams comprised of researchers with conflicts of interest. This estimate includes all articles where at least one member of the authorship team had one (or more) conflict of interest to disclose. For the purposes of this analysis, I defined "original research" articles based on type of content published in a given genre from each journal. This included more than just the full-length research articles; I included article types for which content offered empirical evidence in the form of analysis or development of a resource (e.g. database). In *JAMA*, I included both "original research" and "preliminary correspondence" categories. For *Nature Biotechnology* publications, I included research articles, research letters, analysis, and resources. For *Science Translational Medicine*, I included research articles and research resources. Descriptions of these genres can be found on the journal websites. *JAMA*, *STM*, and *NBT* were selected for this analysis as they are outlets where translational medicine researchers routinely publish. For more details, see Jeske 2021.

[xi] While outside the scope of this chapter, one might also interpret the journal's decision not to disclosure conflicts alongside the main text of its published material, as other journals continue to do, as a reflection of its stance regarding COIs. As the debate about the purpose of conflict of interest disclosure continues to play out, journals are adopting standardized forms of disclosure, and often removing disclosure statements from the main text of articles. A concerned reader then must download an additional file, which may be dozens of pages long or more in order to understand the nature of a given researcher's conflicts. Such distancing requires additional labor on the part of the reader to find and then interpret potential conflicts of interest.

Chapter 3 Notes

[i] Landecker writes, "while it was known that parts of the body could survive long after the death of the whole, cell culture enabled not only the survival of cells, but fostered movement, growth and differentiation" (2007, 32).

[ii] Both Yamanaka and Thomson widely recognized as the founders for this critical development in the biological sciences. Shinya Yamanaka was awarded the Nobel Prize for his developments with IPS cell reprogramming. James Thomson is also a famous cell biologist, who is best known for developing the first human embryonic cell line in 1998.

[iii] According to Engineers Australia, a professional engineering society, first engineer recorded in history, known by "name and achievement" was Imhotep, builder of the pharaoh Djsoer's step pyramid in Saqqara, Egypt in the 27th century BC. This was the earliest large-scale cut stone project. (Diemar, 2021).

[iv] Bioengineering has many sub-areas including biomaterials, cell & tissue engineering, biomechanics, and biomedical imaging, among others. Bioengineering draws engineers and approaches from a variety of specialties, including mechanical, electrical, and materials science engineering (Peppas and Langer 2004).

[v] Academic actors in this arena include both those who were funded by the NCATS Tissue Chip Program and DARPA, as well as those who have taken up this approach in the field more broadly. While the initial Tissue Chip Program created a consortium of organ chip researchers (all of whom were researchers at academic institutions) who met collectively each year, this technology was quickly taken up (and likely being developed simultaneously) by other academic biomedical engineers. The researchers I interviewed did not characterize the network of

researchers developing organ chips as a "community" per se. Some described it as a "loose network" in the sense that they were familiar with one another's work, particularly the more famous researchers in the arena. Researchers in this arena tended to share work at the same conferences, received funding from the same institutes, and some had trained at the graduate and postdoctoral level under other researchers in the field, but collaborations across groups creating chips of the same organ model were infrequent. Indeed, what started out as a small consortium of researchers has become a scientific bandwagon in biomedical engineering (Fujimura, 1988). Fujimura used the metaphor of bandwagon to describe the phenomenon in which large numbers of scientists, laboratories, and organizations commit resources to one particular approach to a problem.

[vi] NCATS, DARPA, and FDA also funded eight two-year projects that explored the use of stem and progenitor cells to differentiate into multiple cell types that represent the cellular architecture within the organ. These awards were not within the scope of this study.

[vii] The principal investigator of this project moved multiple times over the funding period, first to Washington University St. Louis and then to University of California, Davis.

[viii] The FDA defines medical countermeasures as "FDA-regulated products (biologics, drugs, devices) that may be used in the event of a potential public health emergency stemming from a terrorist attack with a biological, chemical, or radiological/nuclear material, or a naturally occurring emerging disease." (FDA, n.d.). Countermeasures include biological products (e.g., vaccines, blood products, antibodies), drugs, and devices (e.g., diagnostic tests, personal protective equipment).

[ix] Affiliates are mechanisms through which special initiatives are taken up in the broader Consortium. The Affiliates take up interests to the broader group, but "have their own budgets, steering committees, and priorities." They have a "cross-pharma governance structure" with established memberships and data-sharing agreements. There are currently two affiliates, one focuses on drug induced liver injury and another on microphysiological systems (MPS) (IQ Consortium, n.d.).

[x] Organ chips researchers came together in multiple physical and virtual spaces to promote organ chip work and to demonstrate its rightness for particular jobs. During the first phase of the NCATS program there were annual meetings where organ chip researchers in the consortium would come together to report progress and identify challenges they were facing. Critically, these were closed meetings, meaning that only those invited were in attendance. In a sense, these were closed door meetings that provided a place where researchers could discuss research progress, and setbacks, openly.

[xi] Of particular note, in the US context researchers rarely discussed or leveraged animal ethics arguments for organ chips. In the EU network, events I attended sporadically throughout fieldwork, researchers much more openly talked about the three Rs (replacement, reduction, refinement) that have been taken up in animal research protocols. While animal rights organizations often advocated for technologies like organ chips, and some organizations even funded this work, researchers themselves seemed to distanced themselves from this discourse.

[xii] Although the Kim & Takayama (2015) paper quoted suggests that "few cells" are required, during my lab observations when I was invited to look at cells under the microscope, I saw more on the order of hundreds. While I do not know the minimum number of cells organ chips require, it may be that the claim that "few cells" are needed is part of the hyping work that proponents perform.

[xiii] "Organ chip labs" was the lingo used to describe labs where the development of organ chips was their primary area of work. This would be contrasted with most labs where developing an organ chip might be part of their agenda, but the main agenda is broader. Organ chip labs often produced a wide range of different organ chips, versus the others in which they might have one or two organ chips because they are specializing in technologies and research related to that organ or disease.
[xiv] List adapted from Baran et al. 2022.
[xv] This search was performed using the explicit terminology of "organ-on-a-chip." Many other terms are now used for these technologies, and including them greatly increases the number of returns.
[xvi] See here for an overview of current organ chip initiatives funded by NCATS: https://ncats.nih.gov/tissuechip/projects

Chapter 4 Notes

[i] In their account of how animal models come to be "good enough," Jamie Lewis and colleagues argue that the purpose of models is to simplify the complexity of originals. If not, they "will expand to encompass the same degree of detail as the original. […] Models simplify, standardize, and stand proxy for other objects" (Lewis et al, 2012, 778).
[ii] Stanford Medicine offers the following estimates: 95% of animals used in US biomedical research are rodents, 1% are cats, dogs, and non-human primates, and the remaining 4% represent a wide range of species including (but not limited to) frogs, nematodes, zebrafish, eels, and armadillos.
[iii] Following Clarke and Fujimura's seminal work on the "right tools for the job," discussed in Chapter 3, historians launched their own conference on the "right *organisms* for the job" and a subsequent special issue in the *Journal of the History of Biology* in 1993. This has been taken up in a recent issue revisiting the topic, see Bolman 2022.
[iv] A second category of models are "exemplary" models, which serve as an exemplar of a larger group; for instance, the zebrafish is considered to be an exemplar of vertebrates. Exemplary models are often used in basic research to "elucidate fundamental or general biological patterns and mechanisms" (Bolker 2009:487) that are widely shared across species.
[v] While beyond the scope of this chapter, another point of tension that emerged in my data was around whether and when science needs the "best models." While researchers generally agreed that "better" models than existing ones were needed, others questioned the value of having the "best models" for every organ and whether it was a good use of federal research funds or if what currently existed could be good enough to predict what was necessary to move to the next stages of projects. One researcher put it simply, saying "I'm a bit critical of saying, you know we need the best tissue [model] for everything."
[vi] While throughout my ethnography, the predominant framing of this particularly issue was about making smarter decisions earlier on in order to save money—for both the public (via federal funding) as well as private companies—the "upshot" of potential gains was always present. On multiple occasions I heard organ chip researchers and stakeholders discuss the potential therapeutics that could be out there, that would be safe and efficacious in humans but were shown to be toxic in animal models. They typically pointed to cases like aspirin, which has been used in humans for over a century but would likely fail pre-clinical testing requirements today, given its toxicology profile in non-human animal models, to make it to human clinical trials (Hartung 2009, 2013; J. Bell 2019).

[vii] As discussed in Chapter 2, the 3D nature of organ chips was another area in which researchers felt there was a significant obstacle with regulators and the scientific community more generally. Researchers often explained why 3D was more compelling for creating models of the organs they study particularly because of its physiological relevance. We humans are 3D and so, they felt, models of the body should be too. For a researcher working on kidneys, he explained that the kidney has a very "complex architecture" and that the flows and shear stresses and forces that were relevant to kidney physiology really lent themselves well to microphysiological systems and organ chip platforms. Another researcher discussed his frustrations with 3D models being compared to 2D models, which are well characterized even if scientifically regarded as inadequate, or less "real."

[viii] Among others, Jenny Reardon has interrogated the ethics of broad consent donations. She challenges the notion that donations acquired through medical center are true 'donations.' Many medical centers now have patient intake and long consent forms that, buried in the many pages of dense text, patients being asked for blanket consent that whatever cells/tissues are sampled, biopsied, removed, etc., that you consent to 'donate.' Patients do not decide to donate specific cells, and because this consenting happens in the context of receiving healthcare services, it can be confusing for patients to know what they can and cannot opt out of, when, and how.

[ix] These centers were at Texas A&M, Massachusetts Institute of Technology (MIT), and University of Pittsburgh. The MIT Translational Center for Tissue Chip Technologies for Quantitative Characterization of Microphysiological System Technologies, offered computational biology and biostatistics testing to characterize tissue chips and to "translate experimental results to clinical outcomes." The MIT center was designed to become a "self-sustaining service provider for the pharmaceutical industry" (NCATS 2019). The PI of this award has since launched a biotechnology company, Javelin Biotechnology, that creates and validates organ chip technologies. The Database Center at Pittsburg University was responsible for supporting the informatics arm of the Tissue Chip Consortium, by storing data about the projects funded through the Tissue Chip Program for open access within the broader scientific community

[x] The principal investigator of the lung chip project is Emulate's founder, remains on Emulate's advisory board, and routinely gives scientific presentations at Emulate sponsored events. According to their website, Emulate's mission is to

> Share the success of these efforts with the broader life sciences community. Since our inception, we have been focused on delivering exceptional science across multiple organs and applications. In 2019, Emulate researchers published a pivotal paper in Science Translational Medicine demonstrating how the mechanisms of drug-induced liver injury can be dissected using the Emulate Liver-Chip. Today, Emulate counts eighteen of the top twenty pharmaceutical companies as customers, including leading academic and government entities around the globe. (Emulate n.d.)

[xi] The principal investigator who developed this technology has written defending the use of PDMS. His team's work has shown that when cured properly, PDMS does not have the problems reported elsewhere in the literature (Grant et al. 2021).

[xii] In this community, "widget" carries a derogatory connotation, usually used to refer to technologies created that were not particularly impactful, or technologies that society needed.

[xiii] The lab developing Evatar was a highly resourced, large lab focused on female reproductive health. The microphysiological systems research was one of many areas. This person was a

representative of the lab and worked to acquire samples for the various projects underway from the affiliated medical center.

[xiv] While beyond the scope of this chapter, the heteronormativity and conflation of sex and gender built into Evatar's marketing description and of the future "partner in crime" HEvatar is notable.

Chapter 5 Notes

[i] At most institutions, laboratories doing COVID-19 research, or intending to, were an exception to this rule. However, some labs not engaged in COVID-19 found loopholes to continue work, and others outright ignored instructions to shut down. Of the labs represented by participants in this study, about 90% shut down for at least some time.

[ii] Writing on alienation and estrangement, Marx (1844 [1959]) wrote the estranged worker "does not feel content but unhappy, does not develop freely his physical and mental energy but mortifies his body and ruins his mind. The worker therefore only feels himself outside his work, and in his work feels outside himself" (33-34). For Marx, estranged workers were not affirmed through their labor but rather denied.

[iii] While the literature has not traditionally included trainees as academic marginals (Hackett 1990, Lee & Walsh 2021), I make the case in this paper for their inclusion. Not only are trainees on the lower rungs of the status ladder, they are also in increasingly precarious economic situations. Funding that provides household income for trainees ranges widely, even within a given lab. While beyond the scope of this article, funding source has important ramifications for trainees, including establishing their pay range and access to benefits (e.g., healthcare, paid sick leave, maternity leave, and vacation), especially at institutions where research trainees are unable to unionize. It also plays a role in determining what projects they support while in the lab group. In this study alone, some trainees received salaries or stipends from their institution, others from federal funding agencies through grants of their PI, others had secured independent training fellowships through federal agencies, and still others were supported by industry funding acquired by PIs.

[iv] Advanced doctoral students included only those who had defended their dissertation proposals. In the biomedical sciences, doctoral students typically complete a rotation in laboratories during their first (and sometimes, second) year of their doctoral work. These trainees were not considered eligible, as they would not have spent enough time in a lab to understand the flow of the lab, organizational structure and power dynamics, and to be deeply embedded in scientific work of the lab. Data and sample reported on in this paper do not include lab staff, due to small numbers of participants in this category.

[v] Three participants were not available for follow up interviews. Data from initial interviews with these participants were used in analysis.

[vi] This study does not stratify by institution or discipline. Biomedical sciences represented in this neuroscience, microbiology, immunology, bioengineering, chemical biology, among other interdisciplinary biomedical sciences (in fact, one degree represented was called "biomedical sciences" in which students decide how to specialize). This heterogeneity was purposeful because it highlights the flows of laboratory life—and the pandemic disruptions—were happening across fields. The key unifier was that these are all laboratory-based biomedical sciences.

[vii] Participants in this study described the challenging decisions that needed to be made around which organisms to keep and which to sacrifice. Many needed to pare down stocks to colonies in

order to both decrease the overall number of animals to be maintained, and because the initial shutdown period would cause many organisms to pass the required ages for experimental work.
[viii] As local COVID-19 positivity rates dropped, institutions were able to increase capacity. When surges in cases occurred, capacity was reduced. At the time of T1 interviews, most participants' institutions were oscillating between 12.5% and 25%, given their local context. At T2, many were at 50%+, with some at full capacity. At T2, lab workers were still not working in their labs at pre-pandemic rates, continuing to do some work at home. Most lab group meetings continued to be held virtually.
[ix] Core facilities are a hallmark of big science and are central feature of most universities and institutions with high research activity. Core facilities are specialized labs that house equipment (and typically dedicated staff) and operate as fee-for-service labs, providing services (eg. training, instrument use, testing, etc.) to researchers. See (Hockberger et al. 2018)(Hockberger et al. 2018).
[x] One might argue that the sociality of science had a pacifying effect, in the sense that the social nature of the work, and friendships with labmates made the struggles of daily life in the lab more bearable. Participants often talked about complaining together over coffee, drinks, and/or shared meals. This often took the shape of "venting," as participants called it, rather than organizing to leverage their collective power. Some participants talked about trying to galvanize lab mates to write letters to PIs or arrange meetings, to no avail.
[xi] Though only going into lab 10-15 hours per week, participants reported working from home on average more than 30 hours per week. Especially in early stages of the shutdown, participants conducted data analysis at home, computational work, or wrote manuscripts on data that had been collected pre-pandemic. Some participants used this time to learn new skills, such as taking open coding courses.
[xii] While outside the scope of this article, nearly all participants talked at length about mental health and wellbeing during the pandemic.
[xiii] After discussing pressure to produce from their PI, many participants would explicitly note that this pressure to produce was not only driven by lab leadership but rather a structural feature of academic science. Many participants talked about this both being about external pressures from their PIs, but also an internalized pressure. Sonia put it simply, "it's an intrinsic thing for me." Similarly, Nina explained there's some pressure, "not just from my PI, but from myself. I want to get this paper out and I want it to be in a really good journal."

Chapter 6 Notes

[i] When reprogrammed, IPS cells are still sexed. There is a broad literature on how female and male IPS cells behavior differently.

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