INTRODUCTION

The cartoon shown in figure 1.1 features two male scientists in a genetics research laboratory. One is seated at the lab bench busy at work with his instruments and test tubes. The other scientist is twisting his body into the shape of a double helix. The seated scientist looks over his shoulder, chiding the contorted one: "Very good, Michaels—you're a DNA molecule. Now, get back to work.[1]

It would be easy to laugh with the scientist at the bench who derides his colleague's playful contortions as distractions from more important work. But what if the joke were on him? He thinks that he is getting his work done hunched over at the bench. This book argues that it is perhaps the helically wound-up scientist who is doing the important experiment. He uses his body to reason through the molecular structure of a complex biological molecule. It is by conducting a *body experiment*, an embodied twist on the well-known thought experiment, that he *figures out* the specificity of molecular form.

Those resembling the curmudgeonly scientist sitting at the bench are scarce among practitioners in the diverse disciplinary fields that converge around the task of protein modeling. Protein modelers engage their bodies actively in their work. They learn how to feel through molecular structures by experimenting with the forces and tensions in their own bodies. They get entangled—*kinesthetically and affectively*—in their modeling efforts. The term "kinesthetics" as I use it here describes the visceral sensibilities, movements, and muscular knowledge that modelers bring to their body experiments.[2] The term "affect," on the other hand, indexes the energetics, intensities, and emotions that propagate through modelers' efforts.[3] Both the kinesthetic and the affective dimensions of modelers' practices converge in the familiar realm of what we tend to call "feeling."[4]

Rendering Life Molecular documents the multifarious modes of body-work and play that are integral to protein modelers' research and teaching practices.

1.1. A body experiment. © 1992 by Nick Downes; from *Big Science*. Courtesy of the artist.

These modalities are striking in that they challenge assumptions about the kinds of labor required to do scientific research, and the ways that scientists are supposed to stand in relation to their objects of inquiry. Scientific objectivity is conventionally understood as a neutral, rational, and so disembodied practice. Scientists are expected to dissociate their cognitive activities from their bodies' complicating passions and proclivities. Michaels's body experiment, however, challenges these assumptions as it makes explicit the ways that seeing, feeling, and knowing are entangled in laboratory research. Michaels demonstrates well the dense thicket of kinesthetic and affective entanglements involved in model building. Like Michaels, the practitioners documented in this book reveal that life science research is a full-bodied practice.

An example from my ethnographic fieldwork in a protein crystallography laboratory at a research university on the East Coast of the United States is instructive. I spent several days alongside Edward, a postdoctoral researcher from the UK, as he conducted routine work in the lab.[5] On one of these days we were sitting in the computer room looking at his data and at the computer graphic models he had been working with on screen. He walked me through the steps he had taken in order to build an atomic resolution model of a protein structure (for an example of a crystallographic structure of a pro-

tein molecule, see plate 1; readers not yet familiar with the basics of protein science or protein crystallography may want to consult the appendix to this book for a brief introduction). He showed me a computer program he had been using to help solve a recalcitrant problem with his model. This was software developed to facilitate pharmaceutical research. Programs like this can be useful for researchers who try to design drugs to perform specific functions in cells and tissues. Their designs build on a mechanistic model of biochemical interactions first proposed by German chemist Emil Fischer in 1885. Fischer suggested that proteins and their substrates, the molecules they interact with, "fit together like a lock and key."[6] Once researchers know the structure of a protein they want to target, they can design molecules that fit into the "active site" of a protein. By "docking" or binding to a chemically reactive crevice in the protein, a drug can disrupt or amplify the protein's biochemical activity.

In the course of our conversation, Edward became frustrated. "I used the automated docking programs, but they were giving me garbage." This was, it seemed, one more in a long series of challenges he faced trying to coax workable data out of his computer. There were so many ways, it seemed, that his computer programs failed him. He explained where the snag was. He gestured at the screen to show me how to see what he was saying:[7] "They were putting the [molecule] there, which is just not right. I thought screw it. I'll just *look at it* because often common sense is just as good as a software program." I was struck by his use of the term "common sense." What I had been learning from him and his colleagues was how much their work relies on carefully honed expert judgment to evaluate the volumes of data that are generated by their computer programs.[8] When automated software fails him, Edward builds his computer graphic models and interprets molecular interactions by eye and by hand. To do this he draws on a kind of molecular intuition he has built up over the long process of his training. The "common sense" that he invoked was perhaps common only among his teachers and colleagues. This was an expertise and a sensibility that he had cultivated over time through intensive training.

Why is it is so difficult to use off-the-shelf software to predict how proteins might bind, or dock with one another? Edward explained that these tools don't work well for large molecules like proteins because "proteins are breathing entities." I interrupted him. I didn't think I had heard him right. "Did you say proteins are . . . breathing?" "Yes. Breathing entities," he responded, adding, "I don't know. Sounds a bit romantic, doesn't it." Where the model on-screen remained static, he relayed the qualities of his breathing molecule by wrapping his hands around an invisible, pulsing sphere. According to all

measures, Edward is a well-trained crystallographer. He tells me that he takes a "mechanistic approach" to protein function. He is clearly wary of enchantments that animate matter with mysterious forces. He certainly doesn't want to be seen anthropomorphizing molecules. Yet, the breath-like quality of proteins that he demonstrated for me was distinct from the kinds of random, Brownian motions that molecules are subject to inside cells. His animated gestures performed his conviction that molecules actively move and change in their watery, subcellular milieu.

His close study of chemical laws and the physical properties of proteins have certainly honed his "common sense." And yet, this sense of things has also been contoured by a kinesthetic and affective sensibility that he did not learn from books. He is particularly critical of the static data forms that are published in scientific papers. Two-dimensional images depict molecules as rigid bodies. He told me that these static images pose serious problems for those without the expertise to interpret the data. Sound interpretation of protein structures is an acquired skill, and according to him, many practitioners in the life sciences don't have the know-how to make sense of the data. In the space of our conversation he made some clear distinctions between different kinds of life scientists. Crystallographers are, for him, distinct from those practitioners who analyze cellular processes by manipulating genetic codes. He referred to them as "molecular biologists," and admonished them for being "notorious" for misinterpreting structures: "The main criticism crystallographers have about molecular biologists is that they don't think about the structure as a *breathing entity*. [For them] it's just a rigid body."

I understood well what he meant by this. I was trained as a molecular biologist and had started a PhD in 1997 to study the molecular genetic processes involved in plant and flower development. Over the course of my undergraduate and graduate training, I had never been introduced to protein structures. This was an era when genetic sequence data held sway and captivated researchers' attentions. At that time the precise atomic structures of the proteins encoded by the genetic sequences I worked with in the lab were unknown, and I had no way of making the leap between the one-dimensional genetic codes I was manipulating and the complex three-dimensional cellular structures and tissues that took shape over the course of development. Edward was right: just looking at the structure on the screen, I had no idea how proteins moved or how they participated in cellular activities. I did not yet have a feel for the dynamic physical and chemical properties of these biological molecules. With all my training in the life sciences, I was still a novice in this field. The static two-

dimensional images and three-dimensional models of proteins he showed me just did not convey the kinetic dimensions of molecular form.

This encounter with Edward crystallizes the central themes in this book. What kind of model is Edward building on his computer screen? How did he learn how to make proteins visible, tangible, and workable in this way? What are the skills and dexterities that distinguish protein crystallographers from other life scientists? Why can't he rely on computer programs to automate his modeling efforts? Moreover, what is significant about the tension between his mechanistic approach to protein modeling and his intuitions about molecules as breathing entities? And why is it that he is moved to articulate the forces and movements of this breathing molecule with his own body?

Part I of this book shows how practitioners like Edward cultivate intuitions about how proteins move and breathe through the time-consuming and laborious process of building models in the laboratory. Part II takes a close look at just what these molecular models stand for, and how members of this research community adjudicate the truth status of these models. Just as Edward leaned into the space between us to *effect* the *affects* of a lively body, part III of this book documents the analogies and anthropomorphisms that modelers use to animate their protein models. It examines how both lively and mechanistic articulations shape modelers' molecular imaginaries and their renderings of life. Throughout, this book asks: What is life becoming in protein modelers' hands?

This anthropological study pays close attention to scientists' modes of embodiment in the construction and propagation of visual facts.[9] It argues that the visual cultures of science must be understood simultaneously as performance cultures. Throughout, it shows how protein modelers' moving bodies and their moving stories are integral to scientific inquiry. As a sensory ethnography of scientific pedagogy and training it pays close attention to how protein modelers hone their intuitions and cultivate the kinesthetic and affective dexterities to construct and adjudicate crystallographic models and data. It observes how practitioners get entangled with their molecules, models, and machines in the course of their experiments. By homing in on the *affective entanglements of inquiry*, this ethnography challenges conventional assumptions about the practice of objectivity.[10] What is more, this book explores how protein modelers *do mechanism* in what at first might seem surprising ways.[11] This study reveals moments when these practitioners do not abide by the deanimated, mechanistic theories of life they are supposed to avow. By opening up gaps and fissures in mechanistic reasoning, this book documents practitioners' failure to mobilize mechanism in a way that would fully disenchant the life sciences. In the fields I

document here, mechanism does not acquire the hegemonic status many would assume it has achieved by the twenty-first century. Indeed, it is by paying attention to the affective entanglements of scientific inquiry that this book is able to amplify protein modelers' otherwise muted views about the *affectivity of matter*.[12] In their hands, protein molecules "breathe." Expert practitioners can tell when proteins are happy, stressed, in pain, under strain, or relaxed; when they are behaving and when they are misbehaving. If living substance is for them at least partially reducible to mechanical principles, it is also simultaneously lively, wily, and unruly. It is by observing how modelers perform their molecular knowledge through gestures, stories, and animate renderings that the mechanistic theories of matter they adhere to in their scientific texts can be seen to give way to livelier ontologies. This book thus reveals forms of animacy immanent to mechanistic logics. Modelers' invocations of the excitable life of matter offer up novel views of the sciences of life, with the promise that the biosciences today are more and other than what we may have long anticipated.

AN ANTHROPOLOGIST AMONG PROTEIN MODELERS

This study builds on a relatively recent tradition of ethnographic research in and around scientific laboratories. Anthropologists and their allies in science studies and history of science have, since the 1980s, turned their attentions to science as a culture and a practice. By extending the ethnographic methods of long-term fieldwork and participant-observation, these researchers have studied an array of sites inside and outside laboratories that allow them to examine how scientific facts are made, how they are made to circulate, and how these facts participate in larger economies of power and knowledge.[13] Anthropologists ask not only how facts are made, but also how these facts are "lived" and what these lived facts come to mean for scientists and their broader publics.[14] Moreover, a wide array of studies have shown that what counts as knowledge and as scientific method can vary widely between communities.[15] This book builds on insights from studies that have examined scientists' forms of life and their livelihoods, their practices of objectivity, and their status as brokers of knowledge and arbiters of truth. It is concerned with core anthropological issues such as the material, visual, and performance cultures of science, and human relations with nonhuman realms. It examines how transformations in techniques, technologies, and scientific "thought styles" participate in the formation of new ways of knowing and forms of expertise.[16]

This account of protein modeling is based on five years of anthropological fieldwork, between the years 2003 and 2008. I conducted this study among

several communities of structural biologists and biological engineers working in academic laboratories in the United States. My primary field site was a private research university on the East Coast. There, and at nearby institutions, I observed laboratory practice and conducted multiple in-depth interviews with protein crystallographers and other protein modelers working on projects in the varied fields of biology, chemistry, physics, synthetic biology, biological engineering, computer science, mathematics, and mechanical engineering. Some of these practitioners focused on protein folding and molecular dynamics, and some used different techniques such as electron microscopy to model their molecules. The participants in this study were at various stages in their careers, and they included principal investigators, research coordinators, course directors, postdoctoral researchers, graduate students, teaching assistants, and undergraduate students. My training in the biological sciences gave me the opportunity to engage my interlocutors in conversations on matters they cared deeply about, and at the same time our conversations gave them space to think through issues and express ideas they did not otherwise have the opportunity to voice. And while I was fluent in the language and laboratory techniques of molecular genetics, the practices of protein crystallographers and biological engineers were strange to me. Little was self-evident to me about their practices and ways of knowing.

In order to understand how protein modelers acquire their skills and intuitions, I observed semester-long graduate and undergraduate courses, including courses on macromolecular crystallography, biomolecular kinetics and cellular dynamics, protein folding, basic biology, and biological engineering, as well as a hands-on laboratory course for biological engineering majors. To document how experts in this field communicate their knowledge of protein structure, I observed numerous public lectures on structural biology, protein crystallography, and other modalities of biological visualization and interviewed a number of protein crystallographers and structural biologists working at other institutions on the East and West Coasts of the United States. I learned about the ways visual facts in this field circulate by attending several professional conferences and meetings, including a weeklong interdisciplinary workshop on protein folding dynamics attended by mathematicians, protein crystallographers, biophysicists, mechanical engineers, and computer scientists in 2008. That year I also tracked the history of protein models in the Archives of the Laboratory of Molecular Biology in Cambridge, UK, and conducted interviews with long-term members of that institution.

In addition to reading scientific papers, I searched the Internet for news

sources, blogs, and videos that would help me stay abreast of ongoing events in the field. I spent considerable time exploring the online archive of protein structures, downloading data sets and manipulating molecular models on-screen. I also tuned in to the public life of protein science by examining a range of pedagogical materials, videos, and films that were circulating widely on YouTube and other web-based media platforms. As a life-long dancer, my attentions were especially attuned to the relationship between movement and forms of knowing in science. And so I watched with delight when beginning in 2008 a science journalist teamed up with the American Academy for the Advancement of Science (AAAS) and *Science Magazine* to mount what has become an annual dance competition that invites scientists to stage their findings in choreographic form. These sites generated significant ethnographic insight into the modes of embodiment and performance cultures of science.

It is crucial that I situate myself in this ethnography. As will become clear in this book, I am no neutral observer of science. I care a great deal about the life sciences and what life is becoming in laboratories today.[17] The account I offer here feeds on all sorts of concerns and anxieties about what the life sciences are up to and desires for how they could be otherwise. This is an aspirational account: in response to descriptions that tend to flatten both scientists' practices and the stuff of life, this ethnography attempts to render life and science in ways that might change what we think science is and what it could become. My intervention works by amplifying a range of practices that are otherwise muted, overlooked or even disavowed. These are practices that remain tacit among scientists, or are otherwise not readily perceptible to observers of science. In this sense, my account remains partial, and necessarily occludes as much as it reveals. Its findings are not meant to be decisive or complete. Rather, the aim is to supplement current work in the anthropology of science and science and technology studies by shifting perceptions of scientific practice in a way that may change the questions we ask about life, matter, and forms of knowing.

TANGIBLE BIOLOGY

> Today the world is messages, codes, and information. Tomorrow what analysis will break down our objects to reconstitute them in a new space? What new Russian doll will emerge?
>
> —François Jacob, *The Logic of Life*, 1973

The distinction Edward made between protein crystallographers and molecular biologists—those who work with protein structures and those who work

with genetic codes—raises important questions about the status of protein crystallography in the life sciences today. This is especially so in light of the prominence of molecular genetics and genomic approaches, and at a moment when biology is being lauded as an information science.[18] How are the three-dimensional data forms generated by protein modelers reconfiguring biological explanations and imaginaries? Are informatic models of life giving way to a new kind of tangible biology?

Proteins had a particularly rich history in the life sciences during the late nineteenth and early twentieth centuries. In the 1860s, for example, British scientist Thomas Henry Huxley popularized a "protoplasmic theory of life." He proposed that the unifying basis of all life—the material that united the plant and animal kingdoms—was the proteinaceous substance of the cell that he named the "protoplasm."[19] It was the irritable and contractile capacity of the protoplasm that demonstrated for him the vital powers of the cell. Protoplasm was a veritably "excitable" substance.[20] Yet, Huxley was no vitalist: his theory proposed a mechanistic view of life in which the "vital forces" of the cell could be reduced to mechanical, "molecular forces."[21] By the late nineteenth century, the protoplasm was already figured as a molecular substance that adhered to mechanical laws. As historian Lily Kay has shown, by the 1930s Huxley's protoplasmic theory had given way to a widespread view that proteins were the "principal substances" of life. Indeed, through the 1930s and 1940s, and up until the determination of the structure of DNA in 1953, proteins were thought to be the material basis of heredity, and intensive effort was invested in determining their elemental composition, chemical specificities, and cellular activity.[22]

Efforts to visualize protein structures were first initiated in the UK in the 1930s. In contrast to Edward's twenty-first century nomenclature that distinguished molecular biologists from protein crystallographers, "molecular biology" was the term mathematical physicist Warren Weaver coined in 1938 to circumscribe research into the structural properties of biological molecules. Molecular biology promised to bring physics to the study of life at the molecular scale.[23] W. T. Astbury, a biophysicist and member of the growing "protein community" in the UK, was among the first to popularize the field.[24] In 1951, Astbury insisted that "molecular biology" was to be understood as the "predominantly three-dimensional and structural" study of the biophysical and chemical properties of molecules.[25] By 1967, however, the definition of molecular biology was already changing. In his widely cited lecture "That Was the Molecular Biology That Was," biologist Gunther Stent forecasted the decline

of the structural school of molecular biology. Stent defended the structural school's "down-to-earth," "physical" approach, which promoted the "idea that the physiological function of the cell" could be understood "only in terms of the three-dimensional configuration of its elements." And yet, at that time Stent did not see how these contributions could be "revolutionary to general biology."[26] After all, by that time, it had taken over twenty years to determine the structures of just two proteins: hemoglobin and myoglobin.[27] The revolution was, according to Stent, going to be led by the "one-dimensional" or "informational school," whose "intellectual origin" in the emerging computational cultures of cybernetics and cryptography in the 1950s and 1960s was "diametrically opposite" to the physical understandings of molecules championed by the structural school.[28]

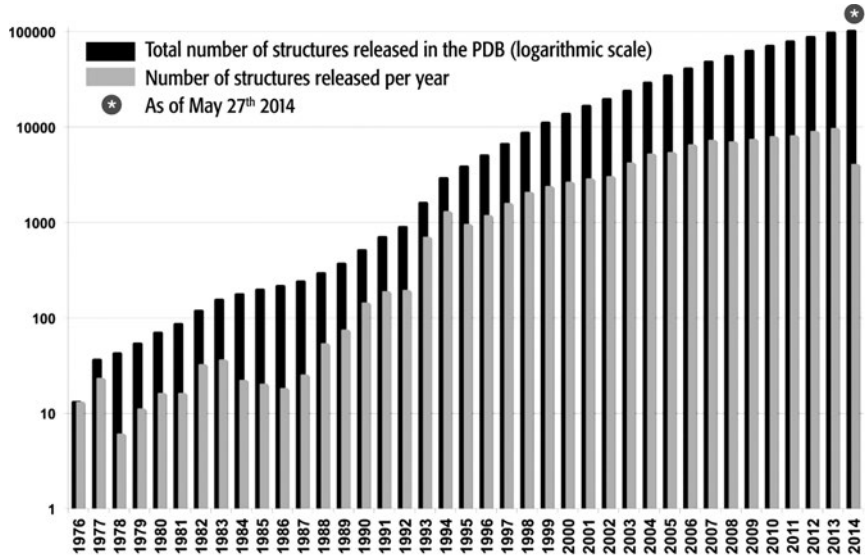
While "structural biology" did not disappear, the contributions of this field did lose traction during the sequencing craze of the molecular genetics and genomics revolutions.[29] During the 1980s and 1990s, in particular, a kind of "genetic fetishism" swept over the life sciences.[30] This new "molecular vision of life" that took root in the wake of the determination of the genetic code was a vision that flattened life into thin threads of genetic "information." However, since the late 1990s, with the completion of the genomes of humans and other organisms, and the ramping up of postgenomic investigations, the terrain is shifting again. Researchers, funding bodies, and venture capitalists are launching a range of "omic" initiatives, such as proteomics and metabolomics, which aim to document and analyze all the molecular species or metabolic processes in a given organism at a particular stage of development or over the course of its lifetime. In the process, these projects are revealing the limitations of genetic sequence data for accessing the multidimensional problems that biology poses.[31] Today, as major journals such as *Science* and *Nature* are publishing newly determined protein structures almost weekly, life scientists can be seen turning from matters of code to matters of substance—that is, from spelling out linear gene sequences to inquiring after the multidimensional materiality of the protein molecules that give body to cells.

This recent and dramatic rise of structural biology can be mapped through the history of its primary data archive, the Protein Data Bank (PDB). This essential research tool enables practitioners to share their data and to access the atomic coordinates of molecules determined by X-ray crystallography and other structure determination techniques.[32] A data archive was first conceived in the year 1970 when crystallographic techniques were just beginning to be refined. By that time, practitioners were already facing challenges archiving

and sharing their data. The issue was that protein structures generated massive data sets. Some proteins are made up of several thousands of atoms, and crystallographic data sets describe the three-dimensional coordinates of each atom in the molecule. The computational capacity available in the 1960s and 1970s was limited to punch card computers. In order to share data, stacks of punched cards would have to be sent through the mail. Given that "each atom was represented by a single card," the exchange of data for a crystallographic structure of a molecule like myoglobin "required more than 1000 cards."[33] Transferring the data set for hemoglobin, a molecule that is four times larger than myoglobin, would have required over four thousand cards. Data sharing was severely hindered by the labor required to prepare data sets for transfer, and so at that time the "coordinates for individual entries had only been exchanged among a few research laboratories."[34]

American crystallographer Helen Berman, the director of the archive in its current form, recounts that she and her colleagues first came up with the concept of a "central repository for coordinate data" at a 1970 meeting of the American Crystallographic Association in Ottawa, Canada.[35] The following year, Cold Spring Harbor Laboratories hosted "Structure and Function of Proteins at the Three Dimensional Level," a symposium that was described as "a coming of age" for structural biology.[36] At that meeting, British crystallographer Max Perutz, who would go on to win a Nobel Prize for solving the structure of hemoglobin, convened an "informal" gathering of protein crystallographers to explore "how best to collect and distribute data." By October 1971, crystallographers at the Brookhaven National Laboratories on Long Island in New York, and the Cambridge Crystallographic Data Centre in the UK had come together to establish the Protein Data Bank to facilitate the electronic exchange of data. According to Berman, when the first newsletter for the PDB was issued in 1974, "thirteen structures were ready for distribution and four were pending." Just two years later the PDB had archived a total of twenty-three structures, and in 1976 alone, "375 data sets had been distributed to 31 laboratories."[37] Ten years later, the PDB issued a press release announcing that fifty thousand data sets had been uploaded (see figure 1.2).[38]

As of December 2014 the coordinates of 105,839 protein structures have been deposited online in the RCSB PDB,[39] and contributions continue to grow exponentially from laboratories around the world. In 2013 alone, the PDB logged a total of 3,850,473 unique visitors from about 190 countries worldwide. These queries accessed approximately 19,479 GB of data.[40] The RCSB considers itself a "global" resource.[41] It now hosts the wwPDB, a "worldwide"



1.2. "Yearly Growth of Structures Released in the PDB Archive," visualized on a logarithmic scale. RCSB Protein Data Bank, 2013 Annual Report.

data bank that integrates the RCSB's PDB with the Macromolecular Structure Database at the European Bioinformatics Institute (MSD) and PDB Japan (PDBj) at the Institute for Protein Research at Osaka University, Japan.[42]

As the data bank extends its geographic reach, it is also expanding the diversity of its collection of proteinaceous forms.[43] The archive includes data on protein structures derived from a vast menagerie of organisms, including species of microbes, viruses, animals, and plants. *Escherichia coli* and *Saccharomyces cerevisiae*, two of the most common microorganisms in biology labs, account for 18.4 percent and 9.1 percent of all the proteins in the database, respectively. Proteins sourced from humans (7.06 percent), mice (3.68 percent), chickens (2.23 percent), wild boar (1.47 percent), wheat (0.40 percent), and fruit flies (0.34 percent) are among the best represented in the database.[44] The largest proportion, a remarkable 27 percent of all proteins archived, are derived from one relatively rare microorganism, *Thermus thermophilus*, a thermophilic, or heat-loving, extremophile. Since the publication of its genome in 2004 this microbe has become a major model organism for researchers in the growing field known alternately as structural genomics or proteomics. Researchers in these fields are developing high-throughput technologies for protein structure determination.[45] As they make rapid contributions to

the PDB, they are reconfiguring the distribution of data on model organisms, and with this, which bodies are coming to matter in biomedical research.

For centuries scientists have relied on illustrated atlases to document the remarkable diversity of natural phenomena. These "atlases of observables" enabled experts and novices to train their visual sensibilities and hone their expert judgments on a panoply of natural forms.[46] The Protein Data Bank can be thought of as an extension of this tradition of the scientific atlas. It offers a collection of data sets that can be visualized on a platform that allows modelers to compare and contrast protein structures derived from distinct species and distinct experimental contexts, as well as structures that have been synthesized *de novo*. And yet this atlas does not just train researchers' eyes: the protein structure data contained in the PDB is made tangible in the form of three-dimensional computer graphic models that allow users to manipulate the structures on screen. As an "atlas of manipulables" it offers an interactive medium through which structural biologists can entrain their sensibilities to a wide range of protein folds and forms. The PDB is thus making visible and tangible the structural properties of a vast array of life's molecular possibilities.

EMBODIED VISION

The trials and tribulations Edward encountered working with automated software offer a glimpse into the challenges crystallographers face confronting the indirect nature of molecular vision. He draws attention to the fact that there is no automated computer program or assay that can detect the chemical structures of a protein and provide a readout of the coordinates of its atoms. Crystallographic modeling techniques require the active participation of the modeler at every stage of the process. This makes model building painstakingly slow and laborious. One of the most remarkable and time-consuming features of this technique is that modelers must turn protein molecules, the very objects of their inquiry, into devices that are integral to the apparatus used to make them visible. Chapter 1 of this book documents closely how crystallographers transform proteins into visualization technologies by working with these molecules in crystalline form. Protein crystals are different from the sometimes-colorful mineral crystals that are familiar from museum collections and shops that sell New Age paraphernalia. While those often grow under pressure in the dark recesses of the earth, proteins can be coaxed to grow into microscopically sized crystals in vitro in the laboratory. Well-formed crystals are highly organized materials: their growing forms incorporate thousands of

molecules into regular, repeating arrays. Crystals have fascinating properties, and one is their ability to scatter high-energy radiation, like X-rays. Modelers use protein crystals as the inverse of a microscope lens: rather than focusing light into an image, as a lens does, their crystals diffract X-ray radiation into irregular patterns that show up as spots on a detector. They expend great effort trying to decipher these patterns of scattered spots. With the help of computer power and carefully honed intuitions, they render their data into maps and models that indicate the probable three-dimensional configuration of hopefully most of the atoms in a given molecule.

To appreciate the peculiarities of protein crystallography, this technique must be understood in the context of other modalities of scientific visualization.[47] Microscopy offers a generative counterpose. In the seventeenth century, British scientist Robert Hooke recognized the prosthetic nature of his microscope as a tool that could "enlarge" his senses, drawing "the hitherto inaccessible, impenetrable, and imperceptible" into view.[48] Hooke sought a means to bolster what he perceived to be the "inherent fallibilities" of perception and so used his "Instruments" as "artificial Organs" in an attempt to remedy "the 'infirmities' of the 'human senses.'"[49] Like microscopists, protein crystallographers must get themselves fully entangled with their instruments to facilitate a prosthetic extension of their senses into the molecular realm.[50] The diffractive optics they engage in their work certainly reconfigure their senses and sensibilities. Historians of science Steven Shapin and Simon Schaffer astutely observe that scientific instruments like microscopes "imposed both a correction and a discipline upon the senses."[51] In the context of protein crystallography it is, however, necessary to understand the terms "discipline" and "correction" in the most generative sense; that is, in a way that appreciates how modelers' senses are enlisted, honed, cultivated, and trained, rather than merely controlled or constrained. Indeed, what were once considered the "fallibilities" and "infirmities" of the senses are now, in the context of protein crystallography, deemed essential resources. The indirect vision generated through diffractive optics and the hands-on labor involved in building models require that practitioners get actively involved in the work of making molecules visible. In addition to their well-trained intuitions and dexterities, modelers must engage their entire sensorium in the work of building models. Modelers' subjective perceptions are not so much a corruptive force to be disciplined; rather, in this context the "capacities" and "productivity of the observer" are celebrated.[52]

The phenomenological tradition in philosophy offers a generative response

to the long-standing illegitimacy and suspect status of the human senses. Maurice Merleau-Ponty's phenomenology challenges the disembodied claims of Cartesian objectivity.[53] His approach emphasizes a body's full participation in acts of perception. Whereas eyes have long been conceived as disembodied instruments of vision, for Merleau-Ponty sight and seeing become the capacities of a lively sensorium tethered to a lively world. He proposes a "crossing over" between the "visible" and the "tangible," such that our visual exchanges with other bodies and objects engage us viscerally in physical encounters with the world.[54] From this vantage point, our eyes and hands become extensions of one another, such that looking becomes a way of feeling out the world, and seeing, a way of being touched by others.[55] Phenomenological studies of scientific vision insist that rather than corrupting "objective" methods, bodily knowledge is integral to science, including practices such as theory making and reasoning, which are conventionally understood as the domain of the mind.[56]

Similarly, feminist science studies scholar Donna Haraway draws attention to the embodied nature of scientific vision to offer an antidote to the moralizing discourses of distance and neutrality that condition conventional accounts of objectivity.[57] Her insistence on embodied vision resists the alluring myth of objectivity conceived as a form of disembodied and omniscient vision. She outs this view as a "god trick" that pretends to see "everything from nowhere."[58] Her approach to vision challenges the "myth of body-lessness" that is perpetuated in standard accounts of scientific practice and objectivity.[59] By grounding vision in the peculiarities and specificities of technologically mediated bodies, she articulates a feminist epistemology that insists all claims to truth must be located. Where Cartesian approaches to objectivity hinge on a disavowal of one's complicity, feminist objectivity requires accounting for the limits, contingencies, and partiality of what we can and cannot see and know about the world.[60] It is by training ethnographic attention on the remarkably multisensory, affective dimensions of model building that this book makes palpable how corporeal knowledge shapes the facts of molecular life.[61] Protein modelers' practices offer a refreshing counterpose to conventional norms of objectivity. Theirs is a "situated knowledge practice" in Haraway's sense of the term. Indeed, these modelers are insistent about locating their contributions to the work of crafting molecular facts.

CRAFTING MODELS

If it is possible to make a generalization about scientific models, it is that they are indeterminate objects that are hard to pin down. Philosophers and

historians of science have made major contributions to the literature on a wide array of scientific models, including among others, two-dimensional diagrams, flow charts, and analogical models.[62] This work builds on movements in the history, philosophy, and sociology of science that aim to reorient long entrenched assumptions about science as a theory-driven activity.[63] Until recently, historians have largely regarded three-dimensional models as "mere" "memory tools" or "mneumotechnical devices" that aid in teaching and learning, with little to offer scientific research.[64] In an attempt to recuperate a lost history, numerous scholars have endeavored to bring attention to models as tools in research contexts.[65] Studies of the experimental lives of models have shown that modeling practices are intimately entangled in the tacit knowledges, social negotiations, moral economies, work cultures, and figural vocabularies that shape laboratory life.[66] Philosopher of science Ian Hacking suggests "models are doubly models": they are both representations of theories and of phenomena.[67] Philosophers Mary Morgan and Margaret Morrison describe this dual function of models as their capacity to set up a "relation" to their two referents, both theories and worldly phenomena.[68] A model can be a theoretical elaboration, an empirically informed abstraction, a figment of the imagination, or all of these at the same time. Science studies scholar Sergio Sismondo suggests that models occupy a "messy category," one that we should not try to clean up.[69] He insists that models spread out across a "continuum" of possible forms and functions and "cut across boundaries of pure categories": they are "monsters necessary to mediate between worlds that cannot stand on their own, or that are unmanageable."[70]

Three-dimensional models are a unique species along this continuum. Scientists who build and use three-dimensional models explicitly demonstrate the embodied, multisensory nature of scientific visualization.[71] Researchers rely on three-dimensional models as objects-to-think-with: they are recursively made and remade in attempts to conceptualize and actualize new hypotheses and new modes of inquiry. Chapter 2 of this book examines three-dimensional models as handcrafted objects that disrupt assumed binaries between the intellectual and physical labor of research.[72] More than visual traces, marks, or inscriptions, three-dimensional models explicitly blur the boundaries between automated machinic productions and the skilled work of scientists. In this sense, they do not conform to the "immutable mobiles" that Bruno Latour has described in his studies of molecular biology labs. Automated "inscription devices" are tools that are meant to ensure fidelity in recording the signatures of nature. One familiar example might be electropho-

resis gels so common in molecular genetics laboratories. By applying electrical current to a sample of a substance embedded in a thin rectangle of agar gel, these devices can separate substances by molecular weight and so be used to indicate the presence or absence of a particular molecule in a sample. Once stained or visualized under UV light, such gels can be "read" like a two dimensional graph or chart. For Latour, such flat inscriptions promise the efficient movement of facts through scientific networks, and deftness in mobilizing allies to resolve arguments over scientific claims.[73] Yet, historians have argued that the wide circulation of three-dimensional facts through models demonstrates that the "visual worlds of science" aren't so "flat."[74] In order to appreciate the import of three-dimensional models in research contexts it is necessary to understand that they are not legible in the same ways as flat inscriptions. Historians of the life sciences Nick Hopwood and Eric Francoeur insist that building and using three-dimensional models cannot be reduced to textual practices of reading and writing.[75] Rather, model building is a full-bodied practice: making three-dimensional facts visible and legible demands ongoing corporeal engagement with tangible media, whether these are physical materials or virtual tools.

ENACTING MODELS

This study brings attention to models as they are built and used. Reflecting on the nature and use of three-dimensional models in the history of the life sciences, philosopher and historian of biology James Griesemer insists that accounts of modeling practices must include a history of the "gestural knowledge" that shapes how models are made and how they are made to circulate. Studies must take into account the *enactment* of models, which includes "gestural as well as symbolic knowledge and the variety of means and modes of making, experiencing, and using models."[76] Where historians are often faced with the challenge of reconstructing this gestural knowledge from the wear and tear on objects and instruments, and textual documents and images stored in archives, ethnographers can observe this ongoing gestic choreography in practice.

Modelers get physically entangled in their modeling efforts. To do their work well they depend on a synesthetic tangle of sensory perceptions. Crystallographers do not just see with their eyes, they practice a kind of "haptic vision"; that is, their ability to perceive molecular worlds is intimately coupled with the visceral modalities that make up the sense we commonly call touch. Modelers' moving bodies and their curious hands are informed through the senses

of kinesthesia, a kind of muscular sensibility, and proprioception, an awareness of their bodies in space.[77] These synesthetic modalities do not just inform modelers' bodily tissues; they simultaneously inflect their ways of thinking. As such this form of "haptic vision" is coupled to a kind of "haptic creativity" that extends modelers' intuitions, memories, and imaginations as they engage their bodies and various forms of tangible media to play through hypothetical permutations in protein form.[78] Such forms of haptic creativity are vividly demonstrated in Michaels's body experiment and Edward's performance of his breathing molecule. Indeed, modelers engage their entire bodies, including their hands, arms, shoulders, heads, necks, torsos, and even legs in model building. Chapter 8 of this book shows how they practice a kind of "molecular calisthenics" as they figure out (for themselves) and relay (for others) their intimate knowledge of molecular forms and movements. While this is a practice that both enables and constrains how they imagine molecular worlds, their bodies provide a pliable, readily available medium for reasoning through the specificities of protein structure and sharing their insights with others. In this way, modelers not only "do things with words," in the sense that philosopher J. L. Austin defined "the performative," they craft expert modes of communication and reasoning by *folding semiosis into sensation* and propagating an affectively charged repertoire of gestures and movements.[79] These enactments can serve to enroll new generations of life scientists by tacitly and explicitly entraining them to these subtle ways of knowing. Protein crystallographers demonstrate well how the visual facts of science are both *performed* and *performative*.[80]

RENDERING LIFE MOLECULAR

This book develops the concept of rendering to account for both the performance of molecular models as they are made and used, and the performativity of molecular facts. In other words it pays close attention to how particular enactments *rend the world as molecular*, changing meanings and material realities for practitioners, their students, and wider publics. Consider the indirect nature of crystallographers' molecular vision. They do not "see" molecules or produce "images" of biological phenomenon; rather, they *make* models to *render* the molecular world visible, tangible, and workable.

Protein models are renderings in that they are representations of molecules.[81] Like a translation, a work of art, or a detailed architectural drawing, these models show their users and viewers what molecules "look like." However, the verb "to render"—which also means "to make"—draws our attention explicitly to the craft of model building. Models are things *made*. Ian Hacking

has suggested that scientific representation hinges on modes of intervention.[82] For example, one simply cannot just look through a microscope and see the details of a cellular world. Rather, in order to make a translucent smear on a microscope slide visible and legible as an aggregate of individual cells, a microscopist must intervene directly in the optical system by applying dyes that bind to specific regions of the cell or by modifying the light sources. In microscopy, such interventions assume some contiguity between the thing on the microscope slide and the image that is perceived through the objective lens: the image changes visibly as the microscopist manipulates the material on the microscope slide. Crystallographic vision is, however, much more indirect. There is no material or optical contiguity between the diffraction pattern generated by a protein crystal and the three-dimensional model that rotates on a modeler's computer screen. The resulting model is in this sense a fabrication.[83] Modelers make molecules visible and palpable by crafting proxies that can stand in as analogs for molecular configurations. The concept of rendering is particularly salient in contexts like this where the gap between the representation and its referent is so wide. For crystallographers this gap between model and molecule is traversed by an elaborate choreography involving living substance, instruments, X-ray sources, computers, and an array of modeling materials. Additionally, this experimental configuration must be supplemented by the modeler's creativity, intuitions, sensibilities, and kinesthetic dexterities. As things made, these models are also thus partly "made up";[84] this concatenation of fact and fabulation is a key feature of renderings.

The concept of rendering can account for the creative ways that practitioners confront the limits of molecular vision. Consider one meaning of the term, where a rendering is understood as an artistic performance, as in the rendering of a play or musical score. A rendering carries the mark of the artist: different singers, for example, will inflect the same musical score with unique tones, textures, and affects. Crystallographic renderings are more than empirical descriptions of molecular structures. They are simultaneously creative elaborations, shaped by modelers' intuitions and imaginations. Renderings are not just performances; they are also *performative*. What this means is that they not only represent the molecular realm, they also make the world molecular and so sediment particular ways of seeing and knowing. As parts II and III of this book show, renderings are simultaneously material and semiotic.[85] Both models and modelers act as proxies, speaking as and for molecules; in so doing, they participate in a kind of molecular storytelling that renders salient some aspects of molecular life, while obscuring other dimensions.

As a performative approach to representation, the idiom of rendering insists on paying attention to how models *rend* the world. What forms of life come to matter in the hands of protein modelers, and which do not?[86]

MODELING PROTEINS, MAKING SCIENTISTS

Edward demonstrates how crystallographers must grapple directly with their data in order to make protein structures visible. His reliance on what he calls "common sense" raises crucial questions about classroom pedagogy and laboratory training, and especially what counts as "proper" training in this field. How is it that Edward can tell the difference between correct structures and the "garbage" that his automated software was spewing out? How do scientists-in-training learn to discriminate between good and bad models? How do practitioners teach their students how to see, feel, and know the difference?

Laboratories are not just factories for the production of scientific facts: they are sites for the making of new scientists.[87] Laboratory life, especially in academic institutions, revolves around the training of novice scientists.[88] These are also sites where expert practitioners continually retrain as they experiment with new techniques to approach new research questions. Educators and researchers in this rapidly expanding field are struggling to find ways to introduce protein structures into classrooms and innovate molecular modeling techniques in the laboratory. They are charged with training a new generation of scientists whose forms of knowing must simultaneously be attuned to the subtlest chemical affinities, physical forces, and molecular movements, and keyed to the tangible logic and rhetoric of a mechanistic vision of life.

How do expert practitioners model proper scientific practice? Pedagogy can itself be approached as a modeling practice. Experts model techniques and practices through the face-to-face apprenticeships that take shape in laboratories. These include both formal mentorships between students and their professors, and the more informal, day-to-day peer mentorships through which students are continually called on to share their know-how with lab mates.[89] It is in the space of apprenticeship that an expert models their tacit knowledge for a novice. Tacit knowledges include the skills that cannot be read about in textbooks and the kind of know-how that one picks up through experiences of trial and error and observing others in practice.[90] In a field where experts must often rely on their well-trained intuitions to know the difference between a good and bad model, or between good and bad data, tacit knowledge is highly valued. As chapter 3 of this book shows, in protein crystallography the act of model building itself is a crucial pedagogical event. This book docu-

ments how, as students submit themselves to the challenges of model building, they learn the physical and chemical forms and affinities that hold a protein together. Edward's well-honed "common sense" is a reminder that, over time, model building refines a student's sensibilities, intuitions, and judgments. It turns out that making sense of these otherwise imperceptible phenomena demands intensive sensory engagement from modelers.

Art historian Caroline Jones defines the term "sensorium" as "the subject's way of coordinating all of the body's perceptual and proprioceptive signals as well as the changing sensory envelope of the self."[91] The sensorium is for her, "at any historical moment shifting, contingent, dynamic, and *alive*."[92] The senses, as I explore them here, are not innate, biological functions that can be divided up into the five familiar modalities of sight, touch, taste, hearing, and smell.[93] Sensing bodies are not separate from the worlds they reach toward in acts of sense making. Sensing takes shape between bodies and worlds. Moreover, broader social, cultural, and economic forces condition both the contours of a person's sensorium and what Jacques Rancière identifies as "distribution of the sensible." Such distributions are the effects of sensory regimes, themselves shaped by processes such as capitalism, colonialism, and biopower.[94] These regimes of the sensible powerfully shape what we can and cannot see, say, feel, or know, and often remain so self-evident that they are as imperceptible as the air we breathe.

This book focuses on the distribution of the sensible and the making of expert sensoria in the context of protein modelers' efforts to make sense of life at the molecular level. Bruno Latour's marvelous account of how perfumiers train their noses to distinguish the finest notes in a fragrance offers a generative approach to the aliveness and plasticity of a sensorium-in-training. He proposes the concept of "articulation" to account for the ways that practitioners train their senses to distinguish—and so articulate—finer and finer differences in a phenomenon. Perfumiers train their noses through "odor kits" that present smells in a particular sequence. Before training, students are "inarticulate": odors would waft over them "without making them act, without making them speak, without rendering them attentive, without arousing them in precise ways: any group of odors would have produced the same general undifferentiated effect or affect on the pupil. After the session, it is not in vain that odors are different, and every atomic interpolation generates differences in the pupil who is slowly becoming a 'nose.'"[95]

For Latour, a "nose" describes a practitioner who has become sensitive to the finest "atomic" propositions of matter. For him, "it is not by accident that

the person is called 'a nose' as if, through practice, she had acquired an organ that defined her ability to detect chemical and other differences."[96] A nose is someone who has become articulate, who has learned how "to be affected" by the subtlest of differences in odors.[97] Becoming articulate demands "passionate" interest in the phenomenon, and a willingness to be "put into motion by new entities" and so "register" their differences "in new and unexpected ways."[98] In this formulation, Latour produces a performative, nonrepresentationalist theory of the senses. That is, rather than assuming that there is a preexisting world "out there" that impinges on the mechanics of an observer's sensory physiology, he insists that sensing is an active process that relies on the passionate involvement of the observer in an ever more interesting world. It is a practitioner's willingness to expand sensory dexterities that allows them to begin to learn how to articulate the world's remarkable multiplicity of propositions. In this view, both subject and world become increasingly interesting and articulate, in the fullest senses of these terms.

In the context of protein modeling, novices must subject themselves to training in order to articulate their entire sensorium. Only this will allow them to articulate the remarkable diversity of protein forms. Here the dual meaning of Latour's concept becomes clear: articulation is both the discrimination of difference and the naming of that difference. In the place of an odor kit, it is in the very process of building their first models that students learn to resolve and report finer and finer differences in a molecule's chemical configuration. The concept of articulation propagates throughout this book to describe the myriad of ways that practitioners acquire the kinesthetic and affective dexterities that allow them to distinguish not only where each amino acid is located in the molecule, but also between good and bad models, skills they need in order to learn how to adjudicate these complex visual facts. It is thus in the process of articulating protein models that articulate modelers are made.

To conduct this research I too have had to articulate my sensorium. Passionately interested in the relation between movement and knowing, I have learned how to entrain my ethnographic attention to modelers' movements, gestures, and affects. In order to "tune in" and parse their nuanced gestural vocabularies, I have relied on an affinity for movement built up over twenty-five years of training, first in classical ballet, and later in contemporary dance. As an ethnographer, I have had to experiment with ways to detect, recall, and relay modelers' subtle bodily affects.[99] In the process I have learned how to remember and document the nuanced cadences, tempos, rhythms, and tones that inflect their models, animations, and animated forms of body-work.

NATURALLY OBSESSED

In 2009 a documentary film about graduate student life in a protein crystallography laboratory was released. This film challenged me to think carefully about how scientists and observers of science tell stories about laboratory life. *Naturally Obsessed: The Making of a Scientist* is set in Larry Shapiro's laboratory at Columbia University. It documents the harsh realities of graduate student life in this challenging field. The filmmakers, Richard Rifkind, professor emeritus and former chair of the Sloan-Kettering Institute for Cancer Research, and his wife, Carole Rifkind, a filmmaker and educator, spent three years filming in the lab and a full year in the editing studio. They are frank about their struggle to stitch together a good story from the hundreds of hours of footage they generated in their extensive study.[100] The final cut is moving. It is tuned to a musical score that lifts emotions to a fever pitch. Their edit dramatizes recurring scenes of dismal failure and desperation; and then, finally, when one of the students publishes his crystal structure, triumph. Stylistically it wavers ambiguously between the genres of documentary and competitive reality TV shows. It has received widespread attention, critique, and commentary and has been viewed in laboratories, university lecture theaters, and high schools across North America and Europe.[101] This rendering of laboratory lives tells some salient stories, if it also simultaneously occludes others. Given its widespread distribution and the wide-ranging responses of its audiences, this documentary provides an exceptional archive of ethnographic material to consider in this book.

The filmmakers track the lives of a few select members of Larry Shapiro's protein crystallography laboratory. In addition to Larry, the documentary features three graduate students at various stages of their training. Kil, Gabe, and Rob are in the thick of things. Stitched-together scenes document the students' mundane, daily activities in the lab and show them fumbling with machines, instruments, and recalcitrant materials. Viewers listen in as the students reflect on their sometimes-wavering goals, desires, and drives. The cameras follow the lead characters out of the lab and into the streets of New York City. The audience is invited into their cramped apartments, where we meet their partners and their pets, and observe how their training interferes with their relationships, tests their resolve, and forces each of them to second-guess their dreams of becoming a scientist. The documentary makes palpable how graduate students must contort and reorient their lives around the task of crafting molecular facts. The film documents how they submit themselves

to training in order to fashion themselves into scientists who can persevere under the most challenging circumstances.

As students in the film struggle to master the experimental techniques proper to protein crystallographers, they not only learn how to calibrate their instruments, they also learn how to adjust their attitudes, postures, and sensibilities to a research culture contoured by intense competition. The film makes palpable the kinds of "institutional gazes, bodies, gestures, architectures, routines, incitements, examinations, and punishments" that condition the bodies and minds of scientists-in-training.[102] We get to see close up what Michel Foucault has called the productivity of power and the "positive economy" of training and discipline—that is, how regimes of "institutionalized training" shape students' modes of embodiment, norms, mores, and values, as well as the very grounds of knowledge.[103]

Larry Shapiro sets ambitious goals. His students work on high-impact molecules whose mechanisms are thought to have major biomedical significance. These are the kinds of protein structures that will get graduate students a publication in a top-tier journal like *Science* or *Nature*. One of the proteins that students in his lab work on is AMP protein kinase, an enzyme involved in regulating the metabolism of fat. This protein structure promises to be a "goldmine" for drug development. Figured as a mechanical "metabolic switch," it is identified as a prime target for therapeutic drug design in obesity and diabetes research. Already figured as a form of "promissory capital," this protein structure anticipates serious returns for pharmaceutical companies seeking to develop drugs that can control metabolism at the molecular scale.[104]

Getting a grip on the molecular mechanisms that "drive" vital processes is depicted as a high-stakes game in *Naturally Obsessed*.[105] Tensions run high as the students in this film compete with one another and with other laboratories to be the first to solve the structure of this valuable molecule. The rivalry becomes intense when the students recognize that their futures hang in the balance. At one point in the film Rob turns to his lab mate Kil, who has just made headway on his project, and says, "The race is on, and I'm behind." In the style of a competitive game show, this documentary's scenes are charged with frustration, jealousy, and despair, glimmers of hope and moments of sheer elation.

Observers of the life sciences attuned to the coproduction of power and knowledge, and wary of the ways that scientific knowledge about life can so readily be used to control and govern life, will see *Naturally Obsessed* as a vindication of their critiques of biocapital and the biopolitical economy of science. If a biopolitical economy is one geared toward bringing "life and its mechanisms"

into the realm of "explicit calculation," then *Naturally Obsessed* offers a perfect portrait of one that is doubly fecund.[106] Larry's laboratory is not only home to competitive, entrepreneurial scientists who gear their labors toward the capture and control of life's vital mechanisms; it is also a site for the production of new scientists whose technical and affective dexterities are in the process of being finely tuned to this task. Able critics will find in *Naturally Obsessed* all the elements of a smoothly functioning biopolitical machine: compulsively laboring scientists, fetishized facts, life mechanized and captured, capital incentives, and exploitative values. And if the documentary continues to circulate widely and does its work as a pedagogical device, it will serve to recruit would-be scientists to commit their lives to the labor of extracting even more capital from life.

LIFE ITSELF, CAPTURED?

Larry Shapiro's efforts to model proteins whose structures may contribute valuable data to the development of drugs that can treat obesity and diabetes is one example of the broader practical horizon of protein crystallographers' labors. As these practitioners transform the forms of data that circulate through life science laboratories, they are also shifting research agendas. Protein structures are becoming objects of multidisciplinary interest and investment. With the promise of novel insights into basic biological processes, biomedical research, drug development, biofuel engineering, and environmental remediation, biologists, chemists, physicists, engineers, mathematicians, and computer scientists are accessing the coordinates of the vast array of structures housed in the Protein Data Bank. Value can be extracted from this data in the form of patentable designs and innovations.[107] Protein structures are especially valuable to practitioners working in the fields of biological engineering. Once frustrated by the opacity and recalcitrance of the gooey, proteinaceous substances that constitute living systems, biological engineers can now engage proteins as concrete, physical objects that they can measure, manipulate, and redesign. As I show in chapter 6 of this book, in their hands proteins are rendered as the "machinery of life," and this machinery can be reengineered, repurposed, and "enterprised up."[108] "Life itself," it seems, has been captured and put to work in the form of a streamlined assemblage of molecular machines that hum productively on the factory floor of our cells.[109]

Protein structures also have military applications, such as in the design of biological weapons and molecular defenses that can "preempt" enemy attacks.[110] A sobering reminder of such applications of protein structure research came in 2007, when I received an invitation from DARPA (Defense Ad-

vanced Research Projects Agency), a research unit funded by the U.S. military. I was asked to participate in a biological weapons design workshop at their headquarters in Arlington, Virginia. Their invitation suggested they had "tantalizing evidence" of the "role of shape, rather than chemical composition, in biological systems." They were hosting a one-day event "to explore innovative methods to produce synthetic macromolecular assemblies for applications in biological control." Their research team was working with the hypothesis "that analogues" that "mimic the shape—but not the composition—of their natural counterparts, may be fabricated and used for exquisite control of biological processes in a number of denied physiological applications." I found the invitation chilling—I could not comprehend how I got on this list of invitees, which included a large group of leading practitioners in biological engineering and protein modeling. I never did get the chance to attend the meeting. As soon as the organizers discovered that I was not the artist they had hoped would inspire them to think in new ways, but an anthropologist, and, what was even worse, a Canadian, I was promptly uninvited.[111] Apparently there was no way I could get security clearance in time to attend the meeting.

The militarization of protein structures is just one reminder of how inquiry in the life sciences is never innocent;[112] knowledge of the structure of biological molecules can always be applied to bring "life and its mechanisms" into the realm of "explicit calculation." In this sense, protein crystallographers and their collaborators participate in a kind of *molecular biopolitics*,[113] where knowledge of the stuff of life is intimately entangled in efforts to govern human and nonhuman lives and worlds.[114] Scholars in science studies and anthropology of science have generated crucial critiques of the recent ramping up of efforts to capture life in commodity form. They have closely examined the ways that scientists and their knowledge projects are complicit in global regimes of capitalism, war, racism, colonialism, and neoliberalism.[115] These critiques offer essential tools for grappling with the complex formations of power and knowledge in the life sciences.

At the same time, some of these critiques also participate in sedimenting stereotypes about science and scientists, as if all participants in technoscience were bent on the capture of "life itself" for capital gain. One effect is that these critiques can further constrain assumptions about the ways that scientists relate to the living phenomena they study in laboratories. While I am convinced these analyses are necessary and generative, I can't help but wonder whether there are other analytic frames and other ways of telling stories about the sciences and lives in science.[116]

Take the example of *Naturally Obsessed*. When viewed through the lens of these critiques it becomes clear that the documentary propagates the very caricatures and stereotypes about science and scientists that give critical analyses of biocapital and biopolitics their traction. This book seeks to disrupt the temptation to read this documentary, or interpret my field notes, through a frame that can see only the negative, controlling dimensions of biopower and biocapital. While this study builds on insights from the film, it does not take this documentary as a complete description of life science practice. Its story line is too constrained by what have become all-too-convenient scripts and conventions. Rather than taking these scripts and norms literally, it is necessary to make their self-evidence strange. To follow the scripts, without recognizing the specificities and constraints of their form, would be to generate an impoverished rendering of laboratory life. This book asserts that there are other ways to observe and tell stories about the life sciences, ways that don't foreclose what this practice is and what these practitioners are up to in their laboratories. Throughout I examine a number of the scenes in the film, as well as outtakes that are posted online, to explore contexts where slippages and deviations from such constraining scripts and "thought styles" begin to surface. I show that close ethnographic attention to the entanglements among modelers, their molecules, models, and machines can amplify the subtle ambivalences, contradictions, and diverse subjectivities that are integral to laboratory life.

This book thus offers a supplement to critical accounts of biocapital and biopolitics by bringing ethnographic attention back to the laboratory to trouble pervasive assumptions about the life sciences today. This study renders lives in science in ways that aim to keep open what it is possible to see, say, feel, and know about both scientific practice and the stuff of life. It offers what Beatriz da Costa and Kavita Philip have called a "tactical biopolitics," an approach that recognizes that the productivity of biopower can generate unexpected forms of life, and that power can move in unpredictable ways.[117] In so doing, this account gestures toward the possibility of an "affirmative" or "life affirming" biopolitics that holds out hope that there are forms of life and subjectivities taking shape in these laboratories, ones that are perhaps not so readily captured.[118]

EXCITABLE ONTOLOGIES

Fernando is a fifth-year PhD student working in the same lab as Edward. In the course of one of our many conversations, we talked about the nature of molecular life. He insisted that proteins are not alive and tried hard to stick

to mechanical analogies to describe living processes. He likened the cell to the factory floor of a Ford car plant (see chapter 6). And yet, his mechanistic description of living substance wavered and in several instances veered toward livelier articulations. For him, the stuff of life is not inert. "We have," he explained, "a physical, very *motional* relationship to the world": "Things are always in change. Okay. When things reach stasis, equilibrium, they die. That's basically death. You have reached equilibrium. Nothing comes in nothing comes out. So how can you not describe molecules and life as a set of motions, as tensions? Okay. Someone described this to me once as: 'Life is a constant struggle between the hydrophobic and the hydrophilic.'"

"Hydrophobic" and "hydrophilic" describe two of many possible affective states of matter. It is the water-loving and water-hating properties of the different amino acids that make up protein molecules that shape how a protein folds and unfolds in its watery milieu. Fernando's insistence that it is a love/hate (-philic and -phobic) relationship that sets life in motion caught my attention. Everything, he assured me, including our relationships to the world, is "motional." It is kept in motion through the chemical affinities and repulsions of molecules that either "love" or "hate" water. For Fernando, when this "tension" is lost, "things reach stasis," and they die. In his essay, "How to Talk about the Body?," Bruno Latour recalls his response to the provocative question, "What is the opposite of a body?" Channeling Spinoza and Deleuze, he suggests that, if "a body" is defined by its capacity to affect and be affected, then the opposite of "a body" is the loss of this capacity to be moved by another. The opposite of a body for Latour amounts to death.[119] Fernando's definition concurs. *Affectivity* in Fernando's formulation is a life-giving property of matter. The liveliness of matter is its capacity to affect and be affected by other bodies. Matter, in other words, is *excitable*.

Fernando demonstrates how, in spite of his efforts to deanimate matter and provide mechanistic explanations, the stuff of life keeps coming alive his hands. Like Fernando, Edward's breathing molecule is not just a "romantic" holdover from some more enchanted moment in the history of the life sciences. His enactment is hooked into a widespread phenomenon among protein modelers, who are continually confronted by living phenomena that evade capture in their experimental apparatuses. Protein modelers render their objects in *ambi-valent* registers: in their hands proteins waver continuously between deterministic machines and lively, wily bodies. These simultaneously machinic and lively renderings come alive in modelers' conversations with one another at the laboratory bench, in group meetings, in conference

talks, and during classroom lectures. These phenomena would be imperceptible if one's attention were solely focused on the texts that scientists write and disseminate. While scientific publications offer excellent resources for examining the prominence of mechanism in conventions of scientific writing, ethnographic observation of modelers in their laboratories and classrooms makes palpable the slippages and deviations from this script. Part III of this book tunes in to ask how these practitioners "do mechanism," amplifying the otherwise muted registers in which modelers articulate their molecular knowledge. What it finds is that in practice, mechanism fails to cohere as a singular, hegemonic discourse. Rather, it is always contaminated by livelier stories. This study shows that forms of animism are immanent to mechanistic logics.[120] The ongoing oscillation between lively and mechanistic renderings produces a new discourse and way of knowing among protein modelers. Theirs is a *lively mechanism* that conjures an *excitable* world of wily molecules. This is a significant shift given the foundational logics of neo-Darwinism that undergird most concepts in the life sciences today. Neo-Darwinism relies on a firmly mechanistic approach to biological processes. Part III and the conclusion to this book explore the implications of protein modelers' *excitable ontologies* for the evolutionary stories we tell ourselves about the origins of life and the adaptations of organisms.[121]

To be clear, the account I offer here is not an enchantment or reenchantment of the life sciences. It is an account of practitioners' failure to comply with a mechanism that would fully disenchant their practice or deanimate their objects.[122] It is by hitching a ride on the stories these modelers tell through their animated renderings that I have learned that proteins are "up to stuff" in cells. Indeed, these modelers generate a lively account of what might best be called the *molecular practices of cells*. These are stories that work athwart the deterministic logics of mechanistic descriptions of molecular and cellular life, those renderings that can so easily get swept up by the pharmaceutical industries and military interests. The practitioners documented in this book thus model forms of life that may as yet escape complete capture.

RENDERING LABORATORY LIFE

> render, v. . . . to give in exchange, to give back, to produce, to yield . . . to let go, give up, to surrender . . . to pay (service) to . . . to bring or put (someone) into a particular state or condition, to make . . . to emit, give out, give off . . . to bring up, to deliver, take, lead, . . . to repeat, report, to deliver or give up (a person) to a religious life . . . to surrender, transfer, to pronounce (sentence, judgment, etc.) . . . to translate word

> for word, to represent, to reproduce, to portray . . . to restore . . . to cause to reappear, to expel, throw up, to throw back (an image), reflect, to echo, to reproduce in speech, repeat, to utter in reply . . . to ascribe, attribute, to hand over . . . to give an account of, to set forth, to give (judgments) . . . to bring forth, to bring about, to cause to be or become . . . to perform . . . to fulfill, to carry out.
>
> —Oxford English Dictionary

The verb "to render" is multivalent, and its many meanings propagate throughout this book. The concept itself serves as a guide to the chapters that follow. In order to introduce the techniques involved in protein modeling, part I of the book is situated in protein crystallography laboratories. The first chapter, "Crystallographic Renderings," provides a guide to these techniques with a focus on the effort and skill that are required to purify proteins and coax them to form crystals. These practices make palpable other meanings of the term "rendering," which includes "to separate," as in the rendering of fat from bone when making chicken soup. This sense of the term is a reminder that "to rend" is also to tear or rip things apart, an especially salient connotation in light of the visceral and sometimes violent work involved in extracting, separating, and purifying proteins from once-living bodies.[123] Another dimension of the concept comes to the fore in chapter 1, which documents how students submit themselves to training. In this sense they "render themselves up," giving themselves over to the labor of model making in ways that evoke early uses of the term to mean "to surrender (one's life, soul)."[124] Indeed, these efforts to render life molecular get modelers entangled with their molecules, models, and machines.

Chapter 2, "Tangible Media," examines the materials and media crystallographers use to build physical and computer graphic maps and models. It pays close attention to the material cultures of modeling and the improvisational, experimental forms of haptic creativity that are integral to crafting tangible maps and models.[125] In the field of computer modeling, a rendering is "the processing of an outline image using color and shading to make it appear solid and three-dimensional."[126] Where in the past, models were built with ready-to-hand physical materials, protein modelers now make extensive use of computer graphic processing to elaborate, add to, and augment their data to render it in three-dimensional form.

To render also means "to decipher." This is an apt description for the work involved in rendering crystallographic data into the form of maps and models. This labor is frequently likened to "puzzle solving." Chapter 3, "Molecular Embodiments," examines how crystallographers must grapple directly with their

data in order make it legible and workable. That chapter also explores other nuances of the verb "to render," including its meaning "to give over to" and "to give birth to." It documents how modelers give their bodies over to the work of model making in a practice that articulates their senses and sensibilities. This chapter attends to the intimacies that take shape among modelers and their models, relationships that shift conventional assumptions about the imagination, scientific reasoning, and even intellectual property.

Part II of the book raises epistemological and ontological questions by exploring how modelers know what they know, and examining closely how their models stand in relation to molecular phenomena. Chapter 4, "Rending Representation," documents protein crystallographers grappling with the limits of their vision and their ability to represent otherwise imperceptible phenomena. It examines experts' anxieties about the ways that static models can misrepresent dynamic molecular phenomena. To render means to represent in the sense of "to recite," "to echo," and "reflect," but it also means "to create." This chapter draws attention to the performative dimensions of rendering. It explores how protein models do not just represent the molecular world; they also materialize a world that is constituted by molecules.

Another meaning of the verb "to render" is "to give" or pay "homage," or "allegiance." This meaning is salient in the ways that crystallographers' models must stay true to molecular form; in this sense their models must maintain an "allegiance" to actual chemical configurations. Only robust facts should stand up for review and evaluation. To render is also "to put forward for consideration, scrutiny, or approval," and "to hand over or submit" (as in "to render up" a verdict or a document). Crystallographers must upload their structures to the Protein Data Bank in order to make them available to their colleagues for evaluation and further investigation. This raises the question of how practitioners adjudicate crystallographic models. Chapter 5, "Remodeling Objectivity," documents responses to three recent events that spurred serious controversies in the protein structure community. These events included the high-profile retractions of numerous protein structures published by two different laboratories, and the simultaneous publication of two different models of the same molecular assemblage. These events shed light on the peculiar culture objectivity that has taken shape among these practitioners. Eschewing myths of objectivity as a neutral, disembodied practice, modelers appear to advocate a modest, situated objectivity grounded in partial truths.

Part III of the book picks up on rendering as a practice that "inflects" representations. It draws attention to rendering as the action of "infusing a quality

into a thing," "describing as being of a certain character," and "portraying, or depicting artistically." This part of the book considers the forms of molecular life that are coming to matter in the hands of protein modelers. Chapter 6, "Machinic Life," homes in on biological engineers' renderings of proteins as molecular machines, while chapter 7, "Lively Machines," examines how these machinic renderings are inflected with a new range of affects when they are animated in time-based media. Chapter 8, "Molecular Calisthenics," turns attention to the ways modelers use their own bodies as animating media to communicate the fine details of protein models in their laboratories, in classrooms, and at conferences. Drawing ethnographic attention to these ephemeral practices, modelers can be seen *moving with and being moved by* molecular phenomena. Indeed, another meaning of the verb to render is "to surrender," "to give in exchange," "to yield to," and "to utter in reply." This chapter explores how modelers give their bodies over to a practice of *mimetic emulation*. In the process, it shows how modelers *transduce* and so propagate a range of molecular affects.

Ethnography is also a rendering practice. The concept of rendering is especially salient to the methods I engage here to document forms of life in structural biology. Modelers work to *amplify* otherwise imperceptible phenomena and *animate* the peculiar qualities of their proteins. In turn, my rendering amplifies and animates modelers' practices. In so doing, I render up a range of practices that are otherwise hard to see. I tune in to amplify the otherwise muted registers in which scientists articulate their intimate knowledge of protein molecules, and I animate a host of subjectivities, sentiments, and values that are not otherwise readily visible in twenty-first-century laboratories. Rendering is an inherently performative practice: in other words, a rendering not only depicts a phenomenon; it conjures and so materializes some aspects of that phenomenon, to the exclusion of others. This ethnography animates some forms of life in the laboratory and not others. My aim here is to keep open rather than foreclose what it is possible to see, say, feel, and know about scientific practice and the living world. And as supplement to other accounts of science, this ethnography aims to render life science *otherwise*.