7 Interdisciplinarities in Action

> The moment you cease observing, pack your bags, and leave the field, you will get a remarkably clear insight about the one critical activity you should have observed—but didn't.
>
> The moment you turn off the tape recorder, say goodbye, and leave the interview, it will become immediately clear to you what perfect question you should have asked to tie the whole thing together—but didn't.
>
> The moment you begin analysis it will become perfectly clear to you that you're missing the most important pieces of information and without those pieces of information there is absolutely no hope of making sense of what you have.
>
> Know, then, this: The complete analysis isn't . . .
>
> Analysis brings moments of terror that nothing sensible will emerge and times of exhilaration from the certainty of having discovered the absolute truth. In between there are long periods of hard work, deep thinking, and weight-lifting volumes of material.
>
> —From Halcom's[1] Iron Laws of Evaluation Research
>
> (Patton 2002, 431)

The ethnographic research and analysis presented in this book makes no claims to being exhaustive. No less a master of ethnography then Clifford Geertz acknowledged, "I have never gotten anywhere near to the bottom of anything I have written about. . . . The more deeply one goes, the less complete it is" (Geertz 1983, 58). After twenty years of wrestling with ethnographic data as I have tried to fathom what there is to be learned about the epistemic practices of the bioengineering sciences and the nature of interdisciplinary research, I concur with the sentiment, but also with his claim to have made progress at least by "a refinement of debate" (1983, 58). I do claim to have made progress—and furthered debate—on the question I posed at the outset:

"How can we understand and account for the epistemic accomplishments of science given that scientists are limited beings and the natural world is vastly complex?" I framed one, significant, approach to answering that question this way: to seek to understand how cognition and culture are integrated in the modeling practices scientists create to investigate the world. That framing stemmed from years of investigating scientific epistemic practices as evidenced in historical and contemporary scientific research and from engaging with literatures that take science as their object of study, namely, philosophy, history, sociology, anthropology, and cognitive science. Once we began our preliminary investigations, the centrality of a specific kind of model-building in the research of each lab immediately became evident, and as we further investigated, its role as an integrative practice became evident as well. We focused our research, then, on how researchers create and use this kind of material culture through which they think and reason about complex biological systems that are otherwise inaccessible to them. Our research has taken an in-depth look at problem-solving practices in two different fields of bioengineering sciences, as well as two different subspecialties in each. The detailed case studies and analyses presented here provide important insights into the epistemic project of twenty-first-century biological engineering, which aims to get a grip on complex biological systems by making use of material, conceptual, methodological, and technological resources of engineering to both formulate and work toward the solution of biological problems of significant human consequence. Strikingly, across all labs, our interviewees stated that "helping people" was the primary reason for their choice of bioengineering, which offered them an exciting opportunity to be pioneers in developing approaches to doing so. Keeping that reason in mind also motivated them to persist through times when nothing seemed to be working out in their research.

At the end of each chapter, I have provided a high-level summary of its major points, which, now that you have reached this point, it might be good to review. In section 7.1 I follow these up with a summary of summaries. There I briefly remind the reader of three highlights in particular: distributed cognition as an analytical framework for investigating cognitive-cultural integration, the integrative epistemic practice of distributed model-based reasoning, and how we have seen epistemic warrant for specific models, as well as the modeling practices in general, is developed by the pioneering students and their visionary directors who have served as our protagonists throughout.

In section 7.2 I take a look at interdisciplinarities in action, more broadly considered. I like to conclude my books with a forward look to ongoing research and further implications—yet to be fully worked out—of the research I have discussed. In the case at hand, I look at the current epistemic situation of interdisciplinary practice, and then go on to point out what insights our own ethnographic investigations have thus far yielded, with a view to how such practice might be facilitated. Despite the fact that there have been major successes, clearly there is more research to be done to devise means to facilitate more effective ways to conduct twenty-first-century interdisciplinary research than is widely acknowledged to be the current state of affairs across the sciences, humanities, and arts. Thus, there are important insights to be gleaned from the in situ study we conducted of different kinds of interdisciplinary practices.

A major implication of those insights is how to foster learning in interdisciplinary research communities. What philosophers of science need to realize is that education is part of the *epistemic infrastructure* of scientific research. This issue comes to the fore in emerging fields, which lack established curricula or texts. Although scientists, administrators, and grant agencies recognize the need to build such infrastructure, scientists often cannot step back and see the learning requirements of their emerging practices on their own. This is where philosophers and cognitive scientists can help, and this is why we have been investing a great deal of time and energy to do so. I have given some indication of our educational research in BME in chapter 4. Here I focus in particular on five specific "interdisciplinary epistemic virtues" that we ended up distinguishing, and discuss some of the ways we have cultivated these through targeted educational experiences in BME and ISB. The chapter ends with a look at the responses from some of the ISB researchers who took part in brief experiences we devised to improve their abilities to collaborate, which show that even small, targeted interventions based on studying a kind of interdisciplinarity-in-action can have significant payoffs. These researchers told us with a lively sense of joyful amazement how these experiences had helped them gain new, realistic insights into what moved and occupied their counterparts from the other side of the disciplinary divide.

7.1 Highlights

7.1.1 Distributed Cognition as an Analytical Framework for Cognitive-Cultural Integration

In chapter 1, I argued that the D-cog framework, with suitable extension, provides both a method—cognitive ethnography—and a conceptual and analytical framework to investigate cognitive-cultural integration in scientific practice. In particular, it provides a means to analyze problem-solving in science as a *system phenomenon* in which scientists, as embodied agents, extend and enhance their natural cognitive capacities by building material, social, and cultural environments for problem-solving. A major scientific environment is the research lab, which I cast as a distributed cognitive-cultural system with epistemic goals. The extensions needed to accommodate science are, first, to include in the analysis an account of pertinent cognitive contributions of the individual, embodied mind/brain and, second, to include in the analysis an account of the epistemic aspect of scientific practice. There are multiple dimensions to each, and I chose to focus, respectively, on the role of mental modeling in reasoning processes and on the issues of how bioengineering scientists build models and develop warrant for their models, as well as for their innovative modeling practices.

In each lab we determined the most important cognitive-cultural resources for problem-solving, which include concepts, methods, materials, and epistemic norms and values. These resources are put to use in building models, which serve a dual function as cognitive artifacts needed for problem-solving and as material culture of the specific kind of epistemic community. As we have seen in this analysis, models are the loci of cognitive-cultural integration in the research of these labs. In the various bioengineering sciences labs we investigated, the researchers overwhelmingly came from engineering or applied mathematics backgrounds, and in their research they transferred and adapted engineering resources and epistemic norms and values to formulate and address problems that would enable them to get a grip on complex biological systems. We called the labs *adaptive problem spaces* in which researchers learn to adapt problems, concepts, and methods to manage the complexity of the biological systems of interest. In such adaptive processes, researchers learn the affordances and limitations of these resources for addressing their problems.

The multidimensional notion of interlocking models emerged from our coding process as an important cross-cutting thematic category, specific to cognitive-cultural integration. Interlocking models is a system-level interpretative notion that, in the first instance, captures dimensions of modeling practices that cut across many of our coding categories. In particular, it provides a means to specify in what ways the simulation models in each lab serve as hubs in which various dimensions of the cognitive-cultural system are fitted together as the models are developed and used. As with transportation systems, where many service lines interlock at central stations, models serve to interlock many dimensions of practice. Among the ways in which models serve as hubs, considered in this book, are how they provide the locus for interlocking problem-solving, learning, lab history, and mentoring; for interlocking facets of interdisciplinarity, including concepts, methods, materials, and epistemic norms and values; for interlocking configurations of devices in experimental situations (model-systems); and for interlocking researcher mental models and artifact models in simulative model-based reasoning (dynamic representational coupling).

In each chapter I present a detailed analysis of the epistemic practices of the research lab and specific cases of problem-solving. These analyses are based on many iterations of our research group's rigorous coding, thematic analyses, detailed case analyses, and triangulation of information from a range of data we collected to arrive at our interpretations. Following these thick descriptions, I go on to analyze the theoretical implications of our findings about the practices with attention to specific philosophical notions and theories and show how the concrete details are indispensable for developing the abstract accounts ("productive interplay"). Each chapter provides a different, though in some instances overlapping, focus on the concrete and the abstract based on data from a specific lab, but in many cases, it would have been possible to address similar issues or themes with a different lab. Section 7.2 will look at some important commonalities with respect to interdisciplinary research. In general, the overall analysis presented in this book provides, I believe, a demonstration of the fruitfulness of the cognitive ethnographic approach for the descriptive and normative projects of philosophy of science and for the advancement of the interdisciplinary project to establish a cognitive science of science.

7.1.2 Distributed Model-Based Reasoning

A major epistemic practice of biological engineering fields is to build models as the means to understand or control complex dynamic biological systems. These are systems for which there are no general theories of the biological phenomena under investigation, and so models are built from the ground up with the aid of engineering concepts and methods. Modeling the dynamics of such systems, whether in vitro or in silico, comprises cycles of design, construction, evaluation, experimentation, and redesign, that is, cycles of *building* to discover. In building models, researchers have to manage the complexity of not only the biological phenomena, but also of a variety of conditions pertaining to the kind of interdisciplinary practice, for instance, the lack of time-series data or effective collaboration for ISB or the need to fuse biological and engineered materials while maintaining biological functionality for BME. As we have seen, the course of interdisciplinary model-building is never smooth. Impasses, obstacles, and failures are ubiquitous. Cell cultures die in the midst of an experiment, in vitro model-systems fail to behave as anticipated, in silico models prove difficult to fit, borrowed concepts or methods fail to provide insights or even prove to be obstacles, and so forth. What we witnessed was the remarkable resilience and creativity with which the researchers addressed these challenges, largely through looking at them as opportunities to learn—an attitude that is inculcated into student researchers from their very first days in their lab. What is also remarkable is that, although it often took a few years for a student's research project to solidify, once determined, no one needed to abandon their model in the face of setbacks. Rather they found productive ways to modify it or their interpretation of its behavior.

Model-building not only addresses the research problem, but is also what drives the creation and evolution of the distributed cognitive-cultural systems of each lab. To understand how, in each case, requires numerous dimensions of the dynamics of processes through which models are built to be examined. Importantly, in collecting field observations and interviews around these processes, we were able to log the various methods, steps, and iterations of building; probe the decisions and judgments behind developing and altering that specific model; examine how and what kind of inferences experimental simulations with them enable; track the formation and changes in problems and goals; and note interactions among researchers relevant to the process. Our data provided a wealth of insights about the nature of the epistemic practices that would never have made it into the historical records—not even those of the likes of a Michael Faraday, who kept extensive, elaborate, and annotated records of his research practices.

In both fields, their research problems and goals require researchers to build models as epistemic tools through which to probe and learn about the behaviors of selected system components (endothelial cells of the cardiovascular system) or of the system as a whole (lignin production system in plants). In both instances, the models provide dynamic simulations of biological phenomena under experimental conditions that can be manipulated and controlled by the researcher. In the BME case, these hybrid in vitro simulation models comprise biological and engineered materials that enable researchers to isolate and experimentally control entities and processes of interest. In the ISB case, the models synthesize as much of the available data as possible to provide computational (in silico) simulations of system-level behaviors, such as intracellular signaling and metabolic processes, that enable researchers to perform experimental manipulations under real-world and myriad counterfactual conditions the researcher might consider relevant to the problem.

A central epistemic aim in both cases is to build a model that will provide the basis for inference about the target system, that is, to *build an analogical source*. Noting that these models are to function as analogical sources brings to the fore an overlooked aspect of analogical reasoning that is central to its use in creative scientific problem-solving. Often there is no ready-to-hand analogy to retrieve and map to the target problem. Instead, the analogical source needs to be created specifically to be mapped to the target. Such built analogies—at least of the sort I have examined thus far in bioengineering and, earlier, in physics (Nersessian 1992a,b, 2008)—are hybrid constructions that merge selected features and constraints from both source(s) (often multiple) and target domains. Building is a bootstrapping process in which a model is developed toward becoming a viable analogical source (think of the computational dish model) or refined in the direction of providing a better one (think of the construct–flow-loop model-system). In some instances, such as with the BME in vitro models, analogies need to be built in a nested manner; for example, the flow loop provides an analogy with blood flow shear forces; the construct, with the blood vessel wall; the animal cells and tissues, with human cells and tissues; and the flow-loop–construct model-system, with shear forces in the arteries. Once developed, models provide structural, functional, or behavioral analogue systems through which researchers can reason, about both the model and, potentially, the real-world system. In these pioneering labs, most of the reasoning we observed focuses on the model, especially its current capabilities and limitations and how to make it a better analogical source, which of course requires the researcher to think not only about the biological target but also about a range of resources available for building, including the constraints of the materials and methods. Only near the end of a building project—when the model is deemed satisfactory to the purposes at hand—is it possible to transfer inferences as hypotheses about the target system or claim to have provided scientific understanding about that system.

Our analyses show that model-based reasoning is, itself, a system phenomenon. Put in another way, in building models, researchers *distribute cognitive processes* across material artifacts, a process we cast as building distributed model-based reasoning systems. Typically, distributing cognition to artifacts has been cast as *off-loading* certain cognitive functions or processes to the artifact, such as memory. However, our metaphors of interlocking and coupling suggest a different relation between mental and material resources—that of *incorporation* into a D-cog system. We have argued, in particular, that the repeated back-and-forth information exchange between mental and real-world models during the building processes gradually incorporates them into an inferential system that enhances or expands the capacity of the researcher for simulative model-based reasoning. Two of the instances considered in this book are how the simulation capabilities of in vitro and in silico models enhance the reasoners' ability to imagine and probe counterfactual scenarios (thought experimenting) and how the dynamic visualization capabilities of the in silico models can drastically alter the problem-space. Of course, some processes are off-loaded within the system in that certain cognitive functions are performed by the researchers and others by the artifact, so the metaphors are not incompatible, but our emphasis on incorporation captures the system nature better. Finally, in the case of in silico models, we also considered the affordances and limitations of a D-cog system that incorporates wet-lab experimentation into the model-building process, with the bimodal strategy.

7.1.3 Building Epistemic Warrant

Science is an epistemic practice. As such, its methods and claims need justification, including a specification of their scope and limitations. As we saw, the bioengineering labs are by and large methodological pioneers in the application of engineering, mathematical, and computational concepts and methods to the investigation of complex biological systems. What this means is that they need to provide evidence and arguments for the credibility of both their models and their modeling practices. Our examinations of issues around credibility with each kind of modeling practice again demonstrate the value of an ethnographic approach for traditional philosophical concerns. In most cases, we were able to collect data on the assessments and decisions researchers were making about the makeup and performance of their models while they were in the process of building them and assessing their credibility. We were also able to probe them further about these in interviews. With respect to potential epistemic claims, researchers in all the labs evaluate models in relation to their function as analogical sources, which our analyses show requires an assessment as to whether the model *exemplifies the relevant features* of the biological system with respect to the problem and that nothing germane has been left out, or, if something has, a determination has been made as to ways the inferences from the model are limited. That a model exemplifies the relevant features of the target system provides assurance that the model has the potential to produce candidate inferences to transfer to the target system as hypotheses. Thus, analogy and exemplification are bound together in model-based reasoning. Although I have not demonstrated this here, I contend this relationship is important not only for the cases I examine, but with respect to modeling more widely.

With respect to the BME case, in designing an in vitro model, researchers aim to exemplify relevant biological entities and processes, subject to the constraints both of biology and of the engineering methods and materials used to construct it. They begin research by focusing on what they expect to be salient features of the phenomena, while bracketing potentially irrelevant features or those deemed too complex or not feasible to address at the outset. For instance, the tissue engineering lab deemed the endothelial cells that line the artery to be the relevant entities to study with respect to the problem of determining the effects of mechanical forces on the cardiovascular system on the basis that they are in closest contact as the blood flows through the lumen. The lab built the flow loop to exemplify laminar shear stress forces to a first-order approximation at normal blood flow rates, but also included the capacity to produce abnormal rates and turbulent forces that could be used should higher-order effects be determined to be relevant as their investigations moved along. The latter point underscores that part of a research project with in vitro models is to determine more specifically what are the relevant features. As we saw in the chapter 2 analysis of the design and evolution of the in vitro model-systems in both labs, the researchers are able to articulate the ways in which their model systems do or do not exemplify specific features of the in vitro phenomena that are considered relevant at that time, as well as to provide assessments of why specific features had been selected and in what way their simulation outcomes are delimited by those choices. But we also saw that even when the researchers deemed features relevant to their problems, building a model with those features might have to await developments in engineering methods and materials. Envisioning such further developments is also part of their research agenda. For instance, although the model-system made up of the flow loop and endothelial cells on slides could provide valuable information about morphology and proliferation, the researchers recognized it does not exemplify the functional behavior of the cells in the blood vessel wall because, at the very least, in vivo they interact with smooth muscle cells embedded in the wall tissue. But to build a blood vessel wall model—the construct—to exemplify that interaction and other features of the blood vessel wall required developments in tissue engineering capabilities. However, the negative analogy between the cells and the blood vessel wall opened a research opportunity to develop a better model-system that would exemplify more relevant features. Thus, in vitro models are built toward exemplifying relevant features, which themselves are further specified in the course of the research. A better, potentially more productive, analogy improves or enhances the relevant features the model exemplifies. Because experiments cannot be performed directly on human targets, the inferences drawn from the models are evaluated with respect to whatever data on the target systems are available. For instance, the response of the endothelial cells in the constructs to mechanical stimulation can be compared with genetic markers of the cells in the in vivo system, and so provide confirmation of stimulation effects. Additionally, the construct-baboon model-system marks progress in the direction of specifying the requirements for an arterial tissue graft for humans by experimental evaluation of the behavior of the construct seeded with EPCs in an animal model-system.

With respect to the ISB case, researchers aim to build robust and stable in silico models that exemplify the behaviors of complex biological systems. Here, too, model-building is an iterative and incremental process in which, at each phase, researchers assess how well the model data exemplify (replicate) the available data in the experimental literature, usually by means of comparing output graphs. As the model gains complexity, it develops the capacity to enact known and potential system behaviors. Once a stable and robust model, or convergent ensemble of models, is produced, it has the potential to provide an analogical source from which the researcher can derive experimentally verifiable hypotheses. For instance, we saw that in modeling the lignin system, G10 was able to make inferences about how to modify lignin production to create a better biofuel by knocking out specific genes and even to infer a missing element in the established lignin pathway. His experimental collaborators were able not only to verify these modification hypotheses, but also to determine, in a highly significant collaborative discovery, that missing element. Such discoveries establish that an in silico model not only exemplifies known features but also has the capacity to predict, and so exemplify, heretofore unknown features. In vivo experimental verifications of hypotheses that derive from a model confer credibility on it as an analogical source, as well as on the methods that produced it.

As to the methods, the researchers in all labs transfer and adapt engineering, mathematical, or computational methods largely developed in the context of building or modeling human-made systems to investigate biological systems. Unlike with established methods in a discipline, bioengineering researchers in emerging fields need to build credibility for this transfer and adaptation. As the methods gain credibility and develop an interdisciplinary history in biosystems modeling, they become projectible for future research. As we have seen, the main criteria are pragmatic, centered on success. Do the models built with them provide significant (or at least useful), verifiable information that enables the researchers to make progress on the research agenda to understand or control the behavior of the biological systems? Verification, to the extent and means possible, reflects back on the credibility of both the model and the methods.

In lab A, for instance, the in vitro flow-loop–cells-on-slides model-system provided useful information about the changes in cell morphology for a population because of controlled experimentation with shear forces, which can be compared against various in vivo changes detected in normal and diseased arteries. The success of this method in providing support for the hypothesis that pathological forces cause disease provides epistemic warrant for the continued use of the method of flow-loop studies. Limitations on the kind of information the method can provide can open new avenues of research. For example, limitations of flow-loop simulations with only cells led to the development of the construct, with which diverse cells and tissues could be subjected to flow-loop studies. Experimental outcomes on the functional behaviors of the cells—for example, that A7's preconditioned EPCs produce thrombomodulin in the construct-baboon model-system simulation—can be compared to in vivo cell behaviors. Verification of the outcome, in this case, establishes that the in vitro simulation methods both provide new understanding of the ways in which EPCs can become mature endothelial cells (by stimulation with mechanical forces) and make progress in controlling the EPCs behaviors toward the vascular graft application goal.

The success criterion also is central with respect to the methods used to build computational simulation models of biological systems. Some methods used in modeling biosystems are, of course, long-established computational methods, tested in a range of fields, such as Monte Carlo sampling. But many are being imported for the first time to use with biological systems; these are usually drawn from systems and control engineering, but can also be related to the specific engineering background of the researcher, for instance, the lab G researcher using wave-smoothing techniques from telecommunications engineering. We also saw that the lab G researchers continually innovate in algorithm development to build and fit models, such as the two-step procedure developed by G10 to build models of lignin production. All these methods gain credibility as they produce stable and robust models that are informative about the behavior of biological systems, which means that they replicate known data, as well as predict new, experimentally verifiable behaviors. These behaviors range from useful new information, such as what genes to target in the lignin system to produce a better biofuel, to highly novel and significant discoveries, for which G10's prediction of a missing element in the long-established lignin pathway provides an exemplar. Methodological innovation, as with model-building, is a bootstrapping process.

7.2 The Epistemic Situation of Interdisciplinary Practice

Interdisciplinarity is widely cast as a hallmark of frontier twenty-first-century research in the sciences and engineering. Interdisciplinary research is customarily characterized as "integrative" and "innovative," yet difficult to achieve. The obstacles lie in the complexity of the problems posed, the need to develop novel investigative practices, and the fact that interdisciplinary collaboration is fraught with difficulties that increase with the distances between the collaborating disciplines. Although a broad range of empirical methods is used to investigate these dimensions, studies of the dynamic processes of interdisciplinarity practices—that is, how interdisciplinarity is enacted in situations of scientific research and the challenges posed for researchers—are scant.[2] Further, although detailed taxonomies of different kinds of interdisciplinarity have been elaborated in the abstract since at least 1972 (see, e.g., Klein 2010), richly nuanced accounts of interdisciplinary practices, too, are needed when it comes to thinking about how to promote learning or how to facilitate a specific kind of research. Ethnography has long been a method used by anthropologists to study and interpret cultural practices situated in naturalistic settings. Most importantly for understanding challenges of interdisciplinary practice, ethnographic research enables one to examine both the insider ("emic") perspective of the participants and to develop the ethnographer outsider ("etic") interpretation of practices of interest. As the research presented in this book demonstrates, cognitive ethnography is particularly well-suited to examining the conceptual, reasoning, and learning dimensions of interdisciplinary problem-solving, where differing and often incompatible epistemic practices, values, and norms are in play. The method is perhaps uniquely suited to investigating the processes of integration in epistemic practices because it enables collecting fine-grained data as researchers attempt to solve interdisciplinary problems within a complex context of cognitive, social, material, and cultural resources and constraints. Cognitive ethnography provides nuanced findings about specific interdisciplinary practices—how they come to be as well as how they are used—that not only enhance our understanding of interdisciplinarity but also can help faculty and policy makers figure out how best to facilitate research, especially as they develop programs to educate the twenty-first-century scientist. Although valuable in themselves, findings from cognitive ethnography can also be used to enrich or validate findings from more theoretical or global methods of studying interdisciplinarity, such as bibliometric analyses of patterns of interaction and influence (see, e.g., Roessner et al. 2013).

It is widely agreed that the chief characteristic of interdisciplinary research is *integration*.[3] Integration is held to be what promotes creativity and innovation. What is needed, though, is both a more nuanced understanding of what "integration" means in the problem-solving practices of quite different interdisciplinary epistemic communities and of the specific challenges encountered in trying to achieve it. Cognitive ethnography has enabled us to examine in fine detail how the researchers determined how to reconceive a complex biological system with the engineering and computational resources at hand so as to be able to solve—or at least make progress on—the target problem. In both fields, problem-solving requires adapting concepts, methods, or materials from engineering to manage the complexity of the biological problem. We, thus, characterized these labs as *adaptive problem spaces*, in which different forms of adaptation emerge specific to the nature of the problems and goals and the requisite resources for problem-solving in the field or subdiscipline (Nersessian 2006; Nersessian and Newstetter 2013). In general, adaptation of the complex interdisciplinary systems within these spaces is a process of continually reconfiguring the components from which these are built, as the system gains experience (see, e.g., chapter 4). Research in these adaptive problem spaces requires that the individuals themselves achieve a measure of interdisciplinary integration—in how they think and how they act. The nature of the integration depends on the requirements of the kind of interdisciplinary problem-solving, which, as we will see, differs for BME and ISB.

As one can imagine, long-term investigations provide a wealth of data to mine, and our findings are rich and varied. We do not claim to have captured all the nuances of the range of interdisciplinary practices in either BME or ISB, but we have been able to formulate some significant insights. An important goal of ethnographic research of multiple sites is to assess *transferability*: to ascertain what abstracted insights might be in common across sites and possibly extended to the broader field, and which ones are unique to a site. Many of our findings of the challenges of integrating engineering and biology in BME transferred robustly across the two labs. The ISB labs differed in various aspects of the in silico model-building process. However, our major insights about the methods for and challenges of integrating biology, engineering, and computation in ISB problem-solving practices do transfer. We have presented our findings to audiences of researchers outside of our studies in each field and have done sufficient broad sampling of each of the fields to feel confident that our research provides significant insights relevant to the practices and challenges of interdisciplinary research and training across the fields.

I begin with a discussion of what I have been calling “interdisciplinary epistemic virtues” that facilitate interdisciplinary problem-solving. We derived these virtues from our assessments of the challenges and requirements for successful problem-solving faced by the researchers in the different kinds of interdisciplinarity I have discussed in the preceding chapters. We first determined and described the challenges and requirements as they arose in our coding process, and then considered them in light of analyses of pertinent notions in the literature on interdisciplinarity, where possible. I put this section first, even though the analysis of epistemic virtues came near the end of our investigation, so that I can use the notions in the subsequent discussion of interdisciplinarity in each field.[4] Sections 7.2.2 and 7.2.3 provide a brief overview, focused on the kind of interdisciplinarity, of actual epistemic practices and challenges in BME problem-solving and in ISB, respectively. Section 7.2.4 focuses on some of the challenges of collaboration in ISB, strategies we proposed to help mitigate them, and the enthusiastic insights of the students we tried them out on.

7.2.1 Five Interdisciplinary Virtues Distinguished

As part of the educational contribution of our research, we have sought to distill from our findings some overarching learning requirements for effective interdisciplinary research. We focused, in particular, on determining characteristics that could usefully be cultivated in the course of graduate education. To that end, we first determined the characteristics from our intensive coding of the in situ studies of interdisciplinary practices on the basis of what we found either to be present and effective in the practices of the labs, or to be lacking, and so posing an impediment. We then, where possible, related our codes to concepts in the theoretical literature on interdisciplinarity, while further elaborating both these preexisting concepts and the new notions uncovered in the course of our own research. Overall, we determined five highly significant characteristics that lead to effective interdisciplinary problem-solving:

1. Cognitive flexibility
2. Methodological versatility
3. Resilience in the face of impasse
4. Interactional expertise
5. Epistemic awareness

The case studies in this book provide numerous examples of these characteristics in problem-solving or, in some cases, the consequences of their absence. It is important to understand at the outset that although these characteristics are attributed, customarily, to individuals, on my analysis, they can be features of distributed problem-solving systems as well.

By *cognitive flexibility* I mean the ability to see or understand a problem from different perspectives, which facilitates the kind of adaptation needed to transform a complex problem into one that can be solved. It also promotes collaboration. Strictly speaking, developmental psychologists mean by cognitive flexibility an executive function that develops as the prefrontal cortex matures, not therefore through learning. However, in educational fields, the term is being used broadly in relation to learning, and that is how we use it as well (see, e.g., Spiro et al. 1994; Spiro et al. 1992). We have seen instances of cognitive flexibility in each lab. For instance, in the tissue engineering lab we saw researchers framing the interactions between cells and blood flow from the perspectives of mechanics and of biological properties and functions. In the combined computational/wet lab we saw researchers looking at interactions between cells and a therapeutic cancer drug using the perspectives of systems engineering and of ROS biology to build out and model pathways. We also saw how introduction of the in silico dish model into the D-cog system of lab D provided a different perspective on bursting phenomena in the in vitro dish.[5]

Methodological versatility is having multiple methods in the tool kit with which researchers can tackle a problem. Instances of such versatility we have seen include the ability to draw from computational model-building methods in several engineering fields (labs C and G); or to have facility with mechanical engineering design methods and wet-lab methods for culturing cells and engineering tissues (lab A); or to use both computational simulation and wet-lab experimental methods (lab C). We have also seen the advantage of having multiple methods in collaborative D-cog systems, such as the capacity to use neural engineering signal processing methods, software development, and computational modeling (lab D).

In pioneering interdisciplinary science research, failure, obstacles, and impasses are ever-present, as we have had ample opportunity to observe, so *resilience* is needed to find a way through them and even to see failure as an opportunity for learning. As we saw, cell cultures die, parameter fittings do not work out, collaborators do not respond, and so forth. In the lab D case, in particular, we saw their repeated failure to stop the dish from bursting for over a year, and then, after quieting it, they were unable to sustain a stimulus pattern from which it could learn ("drift" problem). Each researcher demonstrated resilience in trying different approaches to get around the problem. In particular, one member introduced a method novel to the lab (computational modeling of an in vitro model), which not only provided insights to move the research forward, but also created a more cohesive and resilient collaborative research system able to overcome significant obstacles, and, ultimately, jointly solve the problem.

Further, interdisciplinary researchers need to develop interactional skills for collaboration. *Interactional expertise* is a notion introduced first by Harry Collins and Robert Evans (Collins and Evans 2002) to characterize the nature of the expertise required of sociologists doing fieldwork. It marks a distinction between the development of conceptual understanding of the practices of collaborators, which enables each to engage linguistically with the practices, and the ability to perform the practice (contributory expertise). Collins, Evans, and Michael Gorman (2007) extended the notion to interdisciplinary collaboration more widely and stressed that, beyond language, interactional expertise is "tacit knowledge-laden and context specific" (661).[6] Again, our research shows that all researchers coming from either the engineering side or the biosciences/medicine side of biological engineering start with little understanding of the other side, and, where collaboration is required, research is slowed down, if not impeded. But we also saw in the BME case that such expertise can be cultivated when it is attended to explicitly in the systematic development of a curriculum. But, as I show in the ISB case (section 7.2.3), it can also be cultivated through limited informal, targeted interventions. Both kinds of approaches seek to promote individual learning, but aim, also, to create more cohesive and effective problem-solving systems.

We introduced the notion of *epistemic awareness* to call out epistemic norms and values in problem-solving (Nersessian 2017; Osbeck and Nersessian 2017). The notion comprises a metacognitive awareness that one's epistemic identity and epistemic norms and values play an important role in research, and that what constitutes good scientific research can be different from one discipline to another. Epistemic awareness, then, is the ability to reflect on the epistemic dimensions of one's own discipline and research practices as well as on those of the collaborators in the problem-solving system. We introduced this notion, in particular, because we witnessed in all the labs, including the ones requiring hybridization, that researchers coming from engineering and computational sciences had little awareness of the epistemic norms and values of biological research. The bioscience collaborators of the computational labs we interviewed also demonstrated a lack of awareness of those at work in modeling. Finding remedies for these problems remains a major challenge in the developing fields of biological engineering, but the first step is for researchers to become conscious of the need for such awareness. Again, our research has shown such awareness can be cultivated with explicit attention.

From an epistemological perspective, these five characteristics can be cast as epistemic virtues for the conduct of good interdisciplinary research, that is, as *interdisciplinary virtues*. According to Linda Zagzebski, an *epistemic virtue* is "a deep and enduring acquired excellence" motivated by and reliably successful at achieving intellectual ends (Zagzebski 1996, 137). Aristotle first introduced the notion that there are intellectual as well as moral virtues, and Zagzebski asserts along with him that virtues are acquired by practicing them. Interdisciplinary epistemic virtues, too, have sociocultural dimensions that can enhance the possibility of achieving intellectual ends. For instance, cultivating them can promote the development of effective collaborative communities of researchers.

The set we determined is doubtless incomplete, but we found these specific ones to be both central for creative and effective interdisciplinary problem-solving and open to being acquired in principle in both BME and ISB, when appropriate means are devised to cultivate them. We also found that when characteristics (3) and (4) are lacking, this significantly increases the complexity of problem-solving in ISB. In particular, both are interrelated with cognitive flexibility in interdisciplinary research. Generally, the skills associated with these characteristics are not easily acquired on one's own. Further, the challenges of cultivating these characteristics differ with respect to the context, in particular, the current state and aims of the field. As I discuss in the following sections, as part of our educational research, we investigated ways to cultivate such characteristics by means of experiences targeted to the research requirements for BME and ISB, respectively. A brief discussion of our efforts provides an opportunity to highlight, in a different way, the differences between these fields in the kind of interdisciplinarity practiced—and desired.

7.2.2 BME Problem-Solving: Hybridization

The overarching problems BME poses are directed toward how to use engineering design methods and principles to understand basic biological phenomena in order to control disease processes or create interventions for specific medical disorders. The problems investigated in the tissue engineering lab aimed at understanding the biological influences of the mechanical forces of blood flow in arteries, with an eye to determining the requirements to construct living implants that can perform normal functions of arteries. In the neural engineering lab, the problems focused on understanding the network behavior of neurons, in particular by teaching a cultured neuronal network to learn from feedback from its "body." A potential application would be to develop brain-controlled prosthetic devices that neurons can learn to use. In the years of our investigation, both labs were focused on the basic research, especially on how to develop in vitro simulation models as epistemic tools to investigate complex biological processes. In chapters 2 through 4, we examined in depth the epistemic practices of in vitro research in each lab. Here I focus on salient interdisciplinary features labs of these kinds have in common.

BME researchers develop programs of in vitro research that build physical simulation models to investigate selected aspects of complex biological systems because the problems the field poses require a level of control that either is impossible to achieve in animal research or would be unethical to conduct. These simulation devices are hybrid artifacts in which cells or cellular systems interface with nonliving materials in model-based simulations that are run under various experimental conditions. In each BME lab, more than one device was central to the research program. Because the devices are created to address the specific research problems of a lab, they are usually built in-house through several iterations. The devices participate in experimental research in various configurations of hybrid model-systems. The daily challenges of building devices and model-systems require the researchers to determine the relevant, selective interlocking of biological and engineering concepts, methods, and materials for the problem at hand. The ongoing processes of building simulation models create emergent hybrid problem-solving systems—with artifactual *and* mental components—within the adaptive problem spaces of BME. We, thus, coded the chief characteristic of interdisciplinary integration as we saw it enacted in the BME labs as *hybridization* to capture the processes of combining distinct elements into an inseparable whole.

One way in which problem-solving with in vitro simulation model-systems in BME requires cognitive flexibility is that researchers need to be able to transform a complex biological problem, such as neuronal network learning or pathologies in the cardiovascular system, into one that can potentially be addressed with conceptual and methodological resources from engineering. To build in vitro model-systems, work with them, and interpret and evaluate experimental outcomes requires the availability of a range of methods within the lab, not only from engineering, but also from biology—for instance, cell culturing or gene profiling—as well as the ability to use biological instrumentation, such as the confocal or two-photon microscope. The iterative and incremental processes of building a model to exemplify the relevant features of the biological system entails trial and error. The death or contamination of a cell culture can result in months of work being wasted. Impasses or failures of various sorts are a frequent occurrence in a context where "*no one has done this before*" is an oft-repeated sentiment, so researchers need to develop resilience to step back and evaluate the situation to figure out whether to persist in a direction or how to start in a new one. Although the research projects we saw in the labs were not collaborative, researchers still needed to develop interactive skills to take advantage of the expertise of others in the group and to participate in problem-solving sessions with researchers with different kinds of engineering backgrounds in the lab. Further, even hybrid biomedical engineers need to develop the skills to interact productively with people trained in medical and biosciences fields as they venture into careers in academia, industry, or policy. We called individuals with the ability to interact productively within interdisciplinary contexts *boundary agents*.

The BME labs we investigated were located in an adaptive problem space in which interdisciplinarity is explicit, reflective, and intentional. Their kind of in vitro research program was initiated by engineers who either could not recruit bioscience collaborators or who found such collaborations inherently difficult because bioscientists lack the requisite quantitative and engineering knowledge to facilitate collaboration. These researchers aimed to create a model of interdisciplinary research different from the standard, "team science" model of two or more researchers from different disciplines in collaboration. Thus, their learning aim is to create interdisciplinary integration not only with respect to concepts, methods, and objects of research, but also at the level of the individual researchers.[7] The educational program in which the BME researchers are embedded aims to design a kind of researcher who might, themselves, be considered emergent hybrid systems—bio-medical-engineering researchers who are not only self-sufficient in problem-solving with hybrid in vitro models, but are also able to collaborate fluidly with disciplinary colleagues in any of the three fields. The direction of emergence would depend on the subfield, such as tissue engineering or neural engineering. In developing the problem-driven learning environments I discussed in chapter 4, we aimed to begin to cultivate all of the interdisciplinary virtues we had identified students would need to be effective biomedical engineers and equip them to develop these further in the context of their subfields as they advanced in their research projects and chosen fields of employment. We aimed to equip them to become both an integrative biomedical engineer and a potential boundary agent.

7.2.3 ISB Problem-Solving: Synthesis

ISB is a young field, though it shares objectives with an older systems biology philosophy. The overarching goal of the field is to develop analyses of complex nonlinear biological phenomena at the system level. The traditional biological approach of well-controlled experimentation focused on characterizing select components or processes is seen as necessary, but not sufficient, to investigate how higher-level functionality emerges from myriad interactions at lower levels. The confluence of new kinds of data production and collection (high-throughput) technologies, computational resources (e.g., high-performance computing and novel parameterization algorithms), and the development of curated biological databases and Internet search engines for seeking biological literature has made it possible to bring quantitative and computational methods to bear on the problem of developing an integrative analysis of the behavior of complex biological systems at all levels, from intracellular interactions to ecosystem processes.

Finding solutions to the problems posed by the field creates an essential *epistemic interdependence* (MacLeod and Nersessian 2016; Andersen and Wagenknecht 2013) among the participating fields, which is likely to remain, given the complexity and sophistication of the research required from each field. These fields comprise various engineering fields, computational sciences (including applied mathematics), and biological sciences. ISB at present does not have a unified vision of what a researcher needs to learn/know to be an effective problem-solver. In a general sense, the adaptive problem space of ISB is integrative in that, to formulate and solve problems, researchers draw from engineering and mathematical concepts, engineering modeling methods, computational algorithms and methods from applied mathematics and computer science, engineering technologies, and knowledge, concepts, and data, and, in some instances, experimental methods (bimodal strategy), from molecular biology. What is striking is that the various possible configurations for research in this adaptive problem space are numerous and continue to emerge. Our labs provide a subset of possibilities. Still, we have gained important insights about interdisciplinary engineering-oriented research in this field.

Building computational simulation models of complex biological systems is the main epistemic practice in ISB. A major issue we witnessed in both our labs is that without effective collaborations, lack of biological knowledge and insufficient or inadequate data increase the complexity of the modeling work. Every problem requires modelers to adapt or tailor methodological strategies to transform it into one they have the potential to solve. Modelers are required, themselves, to search through the available biological literature and databases to build out the metabolic and signaling pathway diagrams of the system under investigation sufficiently to inform the modeling process. Usually, modelers start from a small piece of a pathway provided by a collaborator or found in the literature and then fill it out by making "*guesses*" about "*what is reasonable*" to add/alter in conjunction with running simulations, with and without pieces, as they build the model. They need to predict what effects a modification of the biological pathway representation will have and locate where a modification is needed to solve the problem. They try to check their guesses with their collaborators, but often find them unresponsive. Further, what resources are to be used to build the model are largely at the discretion of the modeler. Systems biology lacks the established domain theories that, in physics-based sciences, provide representational resources and methods to build reliable in silico simulation models. As we illustrated in the G10 and C9 case studies, every model is a strategic adaptation to a set of constraints, ranging from those of the complexity of the biological problem to the fact that simulation experiments and real-world experiments take place on vastly different time scales and, further, to the human cognitive constraints and to the challenges of collaboration. Most of these constraints cannot be eliminated, but our interviews with modelers and experimentalists did lead us to insights into limited learning interventions that might prove useful for enhancing collaboration, as I discuss in section 7.2.4.

Interdisciplinary "integration," then, in the ISB context largely means infusing experimental data gathered from a range of disparate sources into the in silico simulation models as they are built with systems engineering concepts and methods that combine these elements into a *dynamic synthesis*. Ideally, the output of a stable and robust model or small ensemble provides understanding into the system-level phenomena, or at least insight with respect to control of selected features, as well as novel hypotheses to guide biological experimentation. "Integration" at the conceptual level also means a kind of dynamic synthesis, as one researcher noted: "*The tasks of this new frontier require thinking beyond linear chains of causes and effects—thinking in terms of integrated functional entities; thinking in systems, networks, and models*."

We have sometimes characterized this kind of interdisciplinary field loosely as a "transdiscipline," but definitions of "transdisciplinary" in taxonomies are vague and often contradictory and do not quite capture the nuances of ISB practices. The kind of interdisciplinary integration we witnessed at the level of participating fields has features of what Peter Galison (1997) calls "intercalation," where fields keep separate identities and practices, though it is possible for practices within one field or the other to be transformed in significant ways in their interactions. But the need to work partly in the field of the other is not captured well by his analysis, and the kinds of adaptive processes we found did not fit well into his, now customary, characterization of interdisciplinary spaces as "trading zones." "Symbiosis" is perhaps a better characterization than "trade" of the relationship among engineers, computational scientists, and bioscientists in the adaptive problem spaces of ISB research.

As we have seen, problem-solving in ISB requires the cognitive flexibility to manage the complexity of a wide range of constraints that influence the model-building process for a specific problem. In addition, the same modeler needs to be able to function in a highly adaptive manner to work on a wide range of biological systems. The lab G director maintains that modelers have the ability to tackle a range of biological problems because they have the "*flexibility to recognize shared features of control/regulation across disparate domains*," which comes from experience with engineering systems. But that engineering understanding of control/regulation needs to be adapted to biological systems in order to transform intractable problems into potentially solvable ones. Problem adaptation is an iterative and incremental process in which researchers search through and adapt strategies for representing the problem and avenues for solving it given the governing constraints. The researchers we investigated do not generally follow specific methodological norms but pursue whatever strategy looks like it will enable them to get a handle on the specific problem they have, usually tailored to the kind or quality of data for the system. The situation puts a premium on having on hand a range of methods and strategies, as well as innovation and creativity in methodological approaches. Modelers need to be able to use a range of heuristics and to experiment with multiple methods drawn from their backgrounds or the experience of the lab director. In pursuing diverse methodological options, individual modelers can contribute understanding about the value of different methods to the wider field. Because of the wide range of options to build and to fit models and their attitude of "seeing what works," modelers need to anticipate failure and impasses and to look at these as resources for developing insight into the problem or direction of solution.

In ISB, methodological choices extend from specific low-level decisions by individual researchers about how to represent a reaction mathematically to much higher-level decisions by lab directors, such as how to organize their labs, whether to collaborate externally or integrate internally the various requirements for model-building, and even to the manner in which they choose to conceptualize the goals and aims of systems biology. As we saw with lab C, for instance, a possible adaptation is to develop hybrid modeler-experimentalists, that is, bimodal modelers. However, in the present situation, wherein specialized modelers (mainly engineers, applied mathematicians, and physicists) and specialized experimentalists (mainly molecular biologists and biochemists) are the dominant participants, the standard methodological choice is collaboration among specialists. As we have seen in chapter 5 and as I discuss further in section 7.2.4, with little knowledge of one another's fields, collaboration is fraught with difficulties. In the present state of the field, our research indicates the onus is on the modeler to be the boundary agent, who is required to step into the biological arena to build her models. Because the domain is continually shifting, however, our modelers all maintain that deep knowledge of a specific biological field would not be helpful. Thus, collaboration with experimentalists with deep knowledge of the biology of the problem at hand is critical to the objective of system-level analysis. From the situations we investigated, and from reports from the wider field about its current state, it is clear that most researchers on either the modeler or experimentalist sides of the "collaboration" lack the interactional expertise and epistemic awareness needed for collaboration to be effective, and feel frustrated by this.

In the next section I look at specific challenges that arose with respect to collaboration for researchers in lab G (the "unimodal modeling" approach), and strategies we used to start to mitigate them. I focus on this first, because collaboration, and not the bimodal strategy, is the dominant approach to model-building in the present state of ISB. This situation creates an interdependence that was expressed perceptively by a senior bioscientist who was just in the process of establishing a collaboration with lab G: "*Team science is the only way it's gonna work these days. Its gonna get hard to write a single investigator R01 [NIH grant] these days and expect to get it funded because everyone is now realizing the interconnectedness of everything. And for me to sit here and think that I can have all the expertise in my tiny little brain to do everything with all these approaches that I don't understand at all is ridiculous. So, we really are trying hard to put together a research team. . . . So, you know, we gather data, we talk with [lab G director] about how these data need to be put together, and what kind of inferences can he help us generate out of them. . . . You really need to have an interaction with people. . . . You're gonna be much more on one side or the other. So, you need the other half of your brain [bioscientist] to be in another person [modeler]*"

The push for the "*team science*" collaborative approach is the major direction in interdisciplinary science more broadly, especially as promoted by funding agencies (e.g., NRC 2015). However, productive "*interaction with* *people*" in the other field is difficult to achieve. It proved to be the case even with this researcher who expressed the need so clearly. Thus, it is possible that the kinds of strategies we developed can be applied more widely in team science. Collaboration needs to be attended to explicitly, which leads to the second reason I focus on it, which is that the vivid responses of the student researchers to the experiences we devised show how even just a little attention to building interactional expertise contributes to cultivating the other epistemic virtues.

7.2.4 Challenges and Strategies for Collaboration in ISB

Across interdisciplinary fields generally, the dilemma is couched as whether to educate researchers as specialists or polymaths to meet their problem-solving demands. Our investigations have led us to see the response to the "specialists or polymaths dilemma" as lying in compromises that are adapted to the specific situation of a research approach. Cognitive ethnography provides a unique means to investigate the details of these compromises and adaptations as they are made during the problem-solving process or diagnosed in response to problem-solving difficulties. In ISB problem-solving, modelers and experimental collaborators both have the objective to produce a computational simulation model that should be biologically informative, especially with respect to providing experimental guidance. Our focus has been on modelers, but our analyses also have been directed toward their interdependence with experimentalists. Although the requirements for effective model-building in these contexts lie more toward the specialist end of the spectrum for both, we found that effective collaboration requires more than cursory acquaintance with the collaborating field. Yet what we witnessed in the labs we investigated (and have been told by numerous other researchers is the current state of the field more globally) is that modelers have little understanding of the possibilities and constraints of experimental practices, and experimentalists have little understanding of the nature and requirements of model-building—and, I would add, neither has an understanding of the epistemic norms and values of the other.

Our strategy was to determine from the nature and challenges of the model-building practices we witnessed, and they discussed in interviews, what are some learning requirements, at a metalevel, for effective research. In analyzing the challenges of collaboration, we found it useful to form an understanding not only of needs, but also of what each side of the collaboration viewed as the deficiencies of the other with respect to collaboration.[8] Here I present a sampling of how some of the researchers, from each side, expressed their needs and perceptions of collaborators that were important for our choices about how to facilitate collaboration.

Our studies have identified several principal reasons for collaborative difficulties that result in significant challenges for the modeler. The modeler's primary need is for sufficient, high-quality data appropriate for the problem at hand. The collaboration usually starts with the experimentalist, who has become aware that modeling might help them get useful information out of the data they collected. As one modeler cast the interaction, the experimentalist approaches the modeler with "*You're a modeler and I do 'systems biology.' So, model these data for me*." The quotes around the term systems biology indicate the modeler recognizes there is a possible difference in understanding of just what that means or entails. But, from the modeler's perspective, "*the biologists produce the data they want. But those data are not actually what we want when we do parameter estimation—so there might be some gap between these two, between us. But even so, they don't produce enough data—they don't measure the concentration for example. And they have few kinetic data*." Models usually have specific parameter requirements, such as kinetic concentration and rate data for ODE models. However, modelers are usually not aware that to measure these kinds of data can be difficult, expensive, and time-consuming. As the experimental collaborator with the modeler just quoted told us, "*The data they want from us is something that is not simple to generate. So, if they want kinetic rate for an enzyme, we have to purify that enzyme. Then we have to create all the conditions to measure it in vitro. That's not a simple undertaking. That's probably six months of work. . . . The second problem is, yeah, if we are going to . . . spend six months generating what they want, then we would like—we would need—to have something that's going to come out of it*." As she viewed the situation, modelers, in general, are "*not taking it to the step where it's useful for the biologist*." Further complicating the situation, the modeler in this instance did not realize that, for her collaborator, as a vascular biologist, to produce the kind of data she needed was not something she ordinarily did since it was not of value for her own research project. And, further, sometimes, as another experimentalist noted, "*they ask things that are not biologically possible*."

The difference in the time scales of modeling and experimentation also creates an issue. On the one hand, as we saw with G10, the modeler can wait around months for data. But, on the other hand, it often takes several years to build a productive model, and by the time the modeler comes with hypotheses for which they want the collaborator to conduct experiments, their experimental research program has moved on. As another experimentalist told us, such new experiments, "*would be time consuming, and [cost] money and effort. Sometimes we already passed that point*."

On the other hand, modelers often expressed the view that experimentalists mainly do not understand the capabilities of models and the power of mathematical techniques to derive network structure and derive valuable predictions even from limited data through approximation. Further, they claim experimentalists fail to see the value and inferential power of the literature synthesis the model builds from years of data that experimentalists are no longer interested in looking at. Modelers contend that experimentalists often see them as just reproducing "*old*" data—or producing models that are "*tautologies*" that can offer no insight. Indeed, as an experimentalist told us, the modelers she was interacting with are "*trying to model something published fifteen years ago—well what are you going to do with that?*" and modelers are modeling "*for the sake of the model*," not of the experimentalist. Further, modelers often note how experimentalists are skeptical about models: "*They think of it [model] as something that's—just hooked up to—to, you know, match figures, . . . So, for them, it's like you're using your data and then plugging in some numbers to fit the output of your model to that, and then they would not possess a lot of faith in those models or what they predict*." One reason for lack of trust on the side of the experimentalists is that they view modelers as not understanding the complexities of biological research and its impact on the data they are using: "*We know how complicated the system is . . . one change in experimental condition can totally change the result*." The modelers did often present a naive view of experimental research, for instance, "*biology is memory*" or "*it's not that difficult—like a recipe, when you cook*." Experimentalists also cast modelers as not valuing accuracy: "*They are not really interested in actual numbers . . . it's more like getting a sense than accurate*." At the same time modelers cast experimentalists as not understanding the importance of system dynamics and the reasons for why they model trends rather than exact numbers: "*All they care is up/down—they don't care dynamics*," as well as not understanding the model and its capabilities in general: "*They treat it as a black box. . . . They will not get deep into the model's detail because that's maybe too complicated for them*." When there is significant misunderstanding and productive interactions are lacking, each side ends up with a caricature of the other. In general, the lack of understanding and the frustration on both sides can lead to each positioning the other in unflattering and unproductive ways, which in turn impedes collaboration and building trust (see, also, Andersen, 2010, 2016; Andersen and Wagenknecht 2013). Further, we found that often each side positions the other as a service provider rather than a collaborator. The experimentalist requests the modeler to "*model my data*," and in turn the modeler, as we frequently heard, "*order[s] my experiments*" from them.

It is clear that experimentalists do not understand much about how models are built and are not comfortable with what they do know of modeler practices, such as using data gleaned from a variety of experimental conditions, modeling trends in the data rather than exact data points, and making other abstractions. This lack of understanding often results in a lack of interest, not responding to queries in a timely manner even when they have requested the model-building, or, even, as we saw, being unwilling to part with unpublished data that the modeler needs in order to proceed with their request. On the other hand, modelers usually have no understanding of the experimental practices that have led to the data. We found that none of the modelers in lab G had even taken a biology class with a lab (except, of course, the bimodal postdoc)—and few in lab C. Their general attitude was that they could easily pick up any part of the biological knowledge they would need because it was "*horizontally organized*," unlike mathematics and engineering, which are "*vertical*" in structure and require progressive learning. Whether this might be the case with biological subject matter or not, it is not the case for sophisticated experimental practices, which require coordinating multiple kinds of biological, skilled-based, and technological knowledge that takes years of experience to acquire.

As I noted earlier, there is not an agreed-upon approach for how researchers in ISB should be educated, as there was in the BME program. There are institutions, for instance, that are working to develop full modeling curricula for biologists, on top of their biological education, in response to the widely recognized collaboration problem. The educational context of the modeling labs we investigated required the ISB graduate students to earn their degrees in an engineering major, bioinformatics, or BME (only C9 in our study) since there is no ISB degree. This meant they needed to cover a range of required courses in those fields. Neither students nor faculty seemed interested in extending the time to graduation. We decided that the most effective thing we could do in the learning dimension of our research on graduate education would be to propose or develop minimalist learning interventions that would facilitate smoother collaboration. Our strategy was to determine from the nature and challenges of the problem-solving practices we witnessed, and they discussed in interviews, what the important learning requirements for collaborative research in ISB are, as currently practiced. Then, because each side stressed the limited time available to spend on work that was not strictly modeling or experimenting, we needed to determine how such learning might be achieved using a "small interventions, big payoff" approach. In general, the issues for ISB epistemic practices around the theme of managing complexity that I identified in chapter 5, create significant demands for all participants in the cognitive-cultural systems of ISB research. Our analyses identified three of the interrelated characteristics discussed in section 7.2.1—cognitive flexibility, interactional expertise, and epistemic awareness—as most important to focus on for effective collaboration in this context..

At least in the current state of ISB (and quite possibly a necessary feature of this kind of research), the full "hybrid" curriculum is not desired as modelers and experimentalists need deep training in one discipline, sufficient to be solely a computational scientist (engineer, applied mathematician) or an experimentalist (bioscientist, medical researcher). But to realize the full potential of ISB requires some degree of penetration of each kind of researcher into the field of the other. At a minimum this means that modelers need to learn to adapt what they know to complex biological problems across a range of areas, as well as learn to know what biological information they need and how to seek and evaluate it, and that experimentalists need to learn enough about the nature and potential of modeling biological systems to produce the kind of data needed, and both sides need to know, as one experimentalist put it, "*the right kinds of questions*" to ask about how each can contribute to the model-building process in order to further a collaboration. Within our project we experimented with two learning interventions that aimed to develop, especially, the three interrelated characteristics early in the student's research career in order to mitigate some of the struggle of collaboration.

Because the model is central in ISB problem-solving, the engineers/modelers are taking the lead in moving the field forward. As we saw, modelers do more than just feed biological data into a model and provide predictive outcomes to experimentalists. They have to understand how to search the literature to find relevant data and build out the biological pathway, both of which require discernment and judgment about biological phenomena, about what it is feasible to do in experimentation, and about the reliability and relevance of the data, as well as the ability to discuss problems with experimentalists as they build the models. On the other side, sophisticated biological experimentation requires equally specialized training, but to be able to collaborate effectively with modelers, experimentalists need to understand the basics about how a model is built so as to, at the very least, devise experiments to produce the kind of data modelers need to construct and to test, experimentally, informative models.

We undertook two interventions with the newer researchers in our labs that proved quite successful, which I will discuss briefly. On the modeling side, as we saw, modelers develop cognitive flexibility in dealing with biological systems not through taking numerous biology classes, but through efforts to recast phenomena from disparate biological domains in terms of features of engineering systems, especially control and regulation. What biology classes they do take are usually theoretical or bioinformatics classes, without labs, so they have little understanding of how biological data are produced, which creates a major impediment to collaboration. We were told that our initial proposal—a full semester rotation in a biology research lab, which we still think a good strategy—would take too much time away from modeling work. We proposed, instead, an intensive "experimental summer camp" experience for beginning modelers, in which they spend a month in an experimental lab engaged in a real piece of research to learn hands-on what it takes to design and execute experiments, as well as something of the way experimentalists think about biological phenomena. The lab G director chose two modelers to spend the month at a laboratory working on yeasts with which he had a long collaboration. The modelers were not absolute novices to biology since they had been conducting the literature searches and building the pathways for about a year, as I discussed in chapter 5. However, they had no idea of the complex environment of a biosciences lab or sense of the nature and costs (time and money) of the experimental practices through which data are collected and analyzed. One was a telecommunications engineer (G16), the other a mechanical engineer (G5). G16 had no relation to the lab, but G5 had been collaborating with them for over a year. Both students came back excited about their experiences, each with a collaborative experimental paper under way from the research they had undertaken. It is instructive to quote highlights from our follow-up interviews from each about what they felt they had learned. Both were surprisingly reflective and articulate about this.

G16 contrasted her before and after understanding of the experimental procedures she had previously viewed as "*like recipes*": "*You are looking from far away. You just see this person is just going into the lab and pipetting, and that's not interesting and why would you do that? But then when you get it, you see there are a lot of reasonings going on and they are involved in their own sort of culture.*" She also expressed that her hands-on experiences, for instance, "*the stuff I saw—I actually pipetted a little bit,*" made her "*feel more self-confident in talking to biologists.*" In addition, she learned important things about her own practices. For instance, she had not understood why the lab director kept telling her to model trends in the data, not data points. She now understood why: "*Right now I would say there's a lot of human error in there. . . . It's both about the reliability of the data and the types of errors.*" Further, she was able to leverage her brief experiences to develop a more complex metalevel awareness of what she would need to know to collaborate better. As she told us in an extended reflection in which she appeared to talk to a potential experimental collaborator, "*We need to be able to communicate—we need to have an idea of what kind of experiments are done. . . . Their area of research is very limited. They just know some sorts of experiments they have in their labs with the equipment they have. And then you sometimes need to include someone else in the project, to do some other part for us to build a dynamic network of this pathway, this specific organism, we need this kind of data. If we don't have it, we can't. And then, 'I'm a modeler, you're a biologist, you don't do that type of experiment. Who do you think could do that?' And then 'how much do you think it will cost?' I can ask a question from you, but I need to have an idea that such a thing exists to be able to think about or suggest it at all.*" Perhaps most importantly, she had come to realize, "*So sometimes, like in a month, you just change inside. It's not about the exact things you learn—it's just knowing how to learn stuff.*"

G5 had already been collaborating with that experimental lab but found himself quite surprised by what he encountered when actually working in the lab. A major revelation for him was to understand that it is "*pretty hard to get time series data. Why they so focused on one pathway, one gene, one* *mutant—it's hard to imagine how hard it is to pull out.*" He recounted: "*And it's like—oh yeah and I think that the techniques we have now are still very limited. So, I spent two years to realize that the gene has strong thermal tolerance phenotype, but it's like I know the gene is in the very bottom of the cells and when we knock it down the cell can't grow well under heat stress. I spent almost three weeks [of the four at the lab]—and what happened between the phenotype and the thermal tolerance behavior and the gene, I have totally no idea. And thousands or more than thousands of pathways or relationships between them—I spent three weeks to realize these things. That there are many, many things that are still unknown. And each step takes time.*" He, too, discovered why the lab director had told him to model trends: "*They generate data so I can use it right. After this month, I need to reconsider the data I have because there are a lot of steps that might cause the inaccuracy of the data. I need to focus on the trend on the data rather than the exact value. The exact value is not that reliable, I think.*" He also learned he needed to approach the experimental literature differently, using his new skills: "*[Before]I just find a paper and read it and usually believe the results—used to skip over the methods section—now I look at experimental design as part of evaluation.*" Further, he felt he had a significant change in perspective on his own project—and possibly on what systems biology is about: "*So, before I, before this trip I totally focused on the mathematical problem—so how to make the model, how to process the data, all mathematical things. But now I can start to think about the links between my model and real world—it's not a quantitative behavior. It's like a property of the cell.*" When we asked whether he thought the experience would make him a better modeler, he said there had not been enough time since returning to say, but, importantly, he now felt confident he could alter the way the collaboration had been going. Before, there was "*zero interaction—I only got the dataset they published in 2004 and that's it.*" Now, he envisioned, "*Yes, it really changes things because, now if I have any problem about the data, I can just ask. Before I feel like I work alone.*"

In sum, the modelers described the following gains: increased self-confidence, comfort with experiments, and some understanding of experimental procedure; enhanced ability to anticipate the needs and questions of experimentalists, to understand experimentalist reasoning processes, and to evaluate experimental literature; and new appreciation for the difficulties/constraints of experimentation and the possibilities of errors in the data. The latter helped them to relax their engineering values, which favor precision, and to understand why their adviser kept telling them to model trends, not every data point. The outcomes suggest it would be even more valuable to build the full semester experimental rotation into the curriculum.

On the experimentalist side, learning about model-building cannot be achieved by visiting a modeling lab. Hands-on experience requires a more structured approach. Fortunately, the department was interested in developing a new introductory graduate course in biosystems modeling. As envisioned, students from the biological sciences would develop conceptual understanding of modeling and basic modeling skills while working on systems biology problems with engineering or applied math students, who would be learning to adapt their engineering knowledge and skills to model biological systems. Wendy Newstetter worked with both lab directors through several iterations of the course. It took a while for a significant number of biology students to take the course, and during our study the only one was from lab C. It was C11, the biologist lab manager and research technologist, who was just transitioning to a PhD student. At this point she anticipated conducting only experimental research for her project. Given that all the other members of her lab were only modelers or bimodal, she said she took the course in order to get a better sense of what modeling was about. She cast this move as "*going over to the dark side*," since her role as the sole biologist within the lab had positioned her as the staunch defender of biological practices when they were treated dismissively by the modelers. In an early interview as she was taking the course, she volunteered that she was beginning to rethink her PhD project in terms of adding a modeling component: "*I'm trying to stop myself from going to [lab director] and suggesting it actually (laughing). Every time I come out of the class and I'm like 'oh, this is fun, I learned something.' I want to go to her and go 'I want to do modeling,' but then I think I might regret it later, so I'm giving it some thought (chuckles).*" In the end (after our study concluded), she did develop a modeling dimension, becoming a bimodal researcher from the opposite direction from C9.

We interviewed her weekly as she was taking the course. It was interesting to see how, throughout the course, she experienced it through the lens of her earlier, unsuccessful research collaboration with a modeler in lab C. Even early in the course, she stated, "*You know I wish I had taken this class two years ago. I wish he and I had taken it together. Because we would have looked at each other and gone 'oh, I get it, I know what you're doing now.' And it would have been helpful for me to understand what kind of data he needed,* ***to understand what kind***

of questions he should have been asking of me*. . . . [I] didn't have insight into know exactly what kind of data would be useful to him. . . . And I think it is hard for him to explain it to me because he didn't know what I had to like go through to get the data. . . . It's funny because he's starting to do experiments now too, so I think he figured out the same thing from his end. It's easier if you have more knowledge on the other side*." The text I put in boldface is interesting from the perspective of interactional expertise because she now felt she understood what a modeler needs to elicit from an experimentalist with respect to the data requirements for a model. She continued to think about the requirements for collaboration throughout the course. Toward that end, she stressed the importance of having done coding herself now: "*I wasn't sure how he like converted what I gave him into something that could be put into code. . . . Now I'm going 'Oh, that's what he wanted. That's what he needed. Oh, OK, I wish I had known that. . . . I would have had better data for him'*."

She had coded only a little in MATLAB before, and had also taken math as an undergraduate, including calculus, and so had some experience with differential equations, but "*didn't realize what they were used for*" until she built ODE models. In her biological training, with a MS in ecology, she had thought of math not "*in terms of computers and math*" but in terms of what she called "*counting*" for instance, "*like how many birds do I have, how many bunnies, how many wolves. . . . We think of it as boring stuff you have to get through to get to the interesting, exciting bunnies and wolves*." Now, she described a new awareness of the affordances of models and a new understanding of math for biological analysis—as a flexible "*tool*" for "*actual real-world application*." She also reflected on the different epistemic norms and values of biology and modeling, and how it was a struggle to negotiate between them in her thinking: "*Biologists tend to think in a lot of details and it just seems there's no way you can build a model with all these details in it . . . it's hard for me. I have to like try and cut out a lot of things in my head when I think about how I would go about modeling something . . . because what I've been trying to do before is get all the details and not make any assumptions. It's like my whole training was like 'don't make any assumptions about what this will be.' And if you're modeling you have to start by making an assumption, 'cause otherwise you don't know where you're going to start. It's like 'I'm gonna assume this system is going to behave similar to this'*." She also noted that coming from biology to modeling might be the reason she was thinking of her models in terms of their biological subjects, for instance, the model she was building of cystic fibrosis for the class: "*I think of the model as a patient. . . . I don't think of it as trying to get the model to work as much as, 'but this would kill the patient, so I can't do that.' I think of [former collaborator's] things in the same way. I think of his model as a little bit of a cell.*" So, now, with her intimate experience of model-building (cognitive partnership), she was anthropomorphizing not only the cells, but also the models. In an interview after the course, she reported having a split-brain experience with respect to her attitudes: "*I'm a changed woman. Now most of my brain is going 'what? Why are you getting rid of a data point?' and the other part's going 'look a smooth curve!'*" Finally, she felt it had been "*beneficial*" to have "*people from different points of view take the same class, because we get the other side and hopefully get some intuition about both. I had no intuition about what a mathematical function could be used for. And then there are some people who have no idea about what might possibly be going on in a biological system. You need both if you're going to model. You need to know both.*" In sum, it was clear that by the end of the course she had developed sufficient familiarity with concepts, methods, and techniques for building systems biology models, even though the models were simple in comparison to what we saw in actual practice, to have a much more successful collaboration than prior to taking the course—and felt confident she could do so.

Admittedly, our samples are small, but at the very least they provide a "proof of concept" for the "small interventions, big payoffs" approach through which to help each side penetrate, however slightly, into the domain of the other. Although only a start, our findings suggest that specific, time-limited learning experiences are productive for cultivating characteristics needed for more effective collaborations, better reasoning, greater awareness of the affordances of the other's methods, and enhanced ability to reflect on both one's own perspective and that of the other. These researchers now had the capabilities to be effective boundary agents without needing the deep hybridization of the bimodal approach or that BME aspired to. In sum, even small, targeted learning interventions can have big payoffs to benefit collaboration, and thus effective problem-solving potential, in the ISB research space. It's conceivable that this approach would work in other interdisciplinary spaces as well.

7.3 Summary: "I Get It Now—I Know What You're Doing"

The goals of our project were multifaceted, but a major one was to investigate emerging interdisciplinary epistemic practices around problem-solving in frontier research laboratories in the bioengineering sciences, with an eye toward facilitating such research with situation-appropriate learning experiences. Cognitive ethnography provided the means to fathom both the nature of interdisciplinary problem-solving practices and how these are enacted in situ, in our cases, with respect to innovative model-building environments. Importantly, it provided the means to fathom ways in which the cognitive, social, material, and cultural dimensions of epistemic practices are integrated in model-building. We had no hypothesis about the nature of the interdisciplinarity we would encounter when we entered the BME labs. What we learned from our initial interviews, observations, and discussions with faculty constructing the fledgling BME program was both that in these labs engineers were tasked with conducting basic biological research through building living in vitro simulation models, composed partly of cells and cellular materials and partly of engineered materials, and that the faculty wanted to build an educational program that would require students to "integrate" all three dimensions of BME from the outset. In the chapters on the BME labs, we saw how hybridization is achieved for researchers and devices through processes of interlocking engineering and biological concepts, methods, and materials in order to build in vitro model-systems and conduct experiments that simulate selected biological processes. We participated in developing learning environments—classroom and instructional lab—for a novel curriculum that aimed to foster this kind of hybridization in BME problem-solving.

The preliminary research for preparing the grant proposal for our investigation of the ISB labs led to our hypothesis that "integration" in these labs would need a different characterization from the sort we had encountered in BME. Building systems-level computational models requires modelers to have both a sophisticated understanding of systems engineering concepts and the ability to adapt high-level computational and mathematical methods that have been developed for other purposes, as well biological collaborators who can conduct sophisticated, highly skilled wet-lab biological research to produce the requisite data. We found that the nature of the systems-level problems formulated in the emerging ISB field not only requires collaboration, but also that, at least to some extent, participants engage with the practices of the other fields, with little training to do either in the present state. The problem-solving situation in ISB creates an essential epistemic interdependence among the collaborating fields. The chapters on the ISB labs showed how it falls on the modeler to manage the complexity of the problem-solving process, which includes that the modeler determine how to adapt engineering concepts and methods to biological problems and how to find the biological data necessary to build, simulate, and test their models. Successful collaboration requires, at the very least, that experimentalists understand the data needs for building and testing systems models and that modelers understand the conditions and constraints under which data are collected. We developed minimalist strategies that would cultivate at least the chief interdisciplinary virtues we had determined to be required for effective collaboration in ISB.

Overall, the cognitive ethnographic research discussed in this book establishes that a method that was pioneered to examine cognitive practices in areas where problem-solving tasks and goals are largely well-defined can be extended fruitfully to investigate the open-ended problem-solving environments of emerging interdisciplinary sciences and engineering. Indeed, cognitive ethnography turns out to provide the primary means to develop nuanced, fine-structured analyses of the epistemic practices of varieties of interdisciplinarity as they are created and enacted in real-world, real-time situations. It provides a unique granularity for fathoming the nature and challenges of these exploratory, incremental, and nonlinear problem-solving practices, their development, and the epistemic principles guiding them. It can yield insight into how methods, norms, and standards come to be justified, and, thus, into why and to what extent it is reasonable to consider the fruits of such research to be trustworthy. And, as we have demonstrated, insights gleaned from intensive case studies can be used to develop strategies for facilitating specific varieties of interdisciplinary learning, integration, and collaboration. The research that has led to conclusions such as these started in a conversation with three visionary engineers who approached me with a wish for support to develop an educational program. Years after that conversation, this research has, in many respects, made me a “changed woman” as well.

Interdisciplinarity in the Making

Models and Methods in Frontier Science

By: Nancy J. Nersessian

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