The field of systems biology is capturing the attention of scientists, funding agencies, and private industry. This postgenomic approach appears to diverge from earlier genetic approaches in its attempt to grapple with complex systems in biology. Systems biology aims to analyze the vast amount of information produced by the genome sequencing projects and other collections of data to better represent biological complexity that could not be understood through a focus on genes. This chapter analyzes systems biology approaches that develop and use computational tools to map, navigate, and attempt to materially replicate this complexity. It explores how scientists’ engagement with complex systems can often lead to blurring, discursively and materially, of distinctions between mechanical and biological systems. It ends with a discussion of the implications and potential consequences of this approach.

By now, systems biology incorporates a range of different approaches. This chapter focuses on the role of mechanistic models and principles in modeling living organisms. It examines the use of metaphors and languages taken from engineering models of the complex systems of automobiles, airplanes, and robots to study complex living systems. The chapter concludes that systems biology represents the outcome of a series of movements back and forth across the machine–living organism border. Analogous movements can be seen in various “systems approaches” across the environmental sciences, including climatology, soil science, and ecology. I call these “technobiological imaginaries,” and this chapter argues for a careful analysis of their historical production, specifically around the question of what is lost in translation at these border crossings.

Each version of machine and living organism contributes to the final vision of what constitutes “mind,” “body,” and “nature” in systems biology. As social and historical studies of science have shown, particular versions of social arrangements often become embedded in conceptions and technologies of nature and machine. Individuals or groups author each concept and technology in particular contexts. This chapter contributes to an examination of authorship and the ways such authorship becomes embedded in technologies as regulatory practices that in turn produce particular kinds of minds, bodies, and nature. In order to do so, we have to understand which versions of machines and which versions of nature move back and forth, and when, across the machine-nature border in the
production of systems biological knowledge. By examining these multiple border crossings, we may learn about how what we know to be nature and machine is constituted.\(^5\) I refer here not just to representations, but also to material natures and machines. The promises of systems biology—that is, fabricated organs, drug treatment regimes, and the “healthy” body—are material productions and interventions.\(^6\) Or as my sociological forebears noted, representations are real in their consequences.\(^7\)

This chapter also discusses to what extent the machine–living organism border is itself a production of biological investigations throughout the twentieth century. In the past, biologists defined what is living in opposition to their understandings of what is human-made. What consequences will research and applications in synthetic biology and stem-cell biology have for this opposition?

This chapter is based on ethnographic research in scientific laboratories and at scientific meetings, interviews with researchers, and documentary analyses of published literature over a period of nine years.

**SYSTEMS BIOLOGY: ADDRESSING THE PROBLEM OF BIOCOMPLEXITY**

In May 2000 the National Science Foundation issued its call for research proposals on the theme of “biocomplexity” that emphasized “the interplay between life and its environment, i.e., from the behavioral, biological, social, chemical and physical interactions that affect, sustain, or are modified by living organisms, including humans.” Like ecological and environmental sciences, systems biology is a field of research that attempts to address biocomplexity in biological systems.

Systems biology research began in the late 1990s and has taken different forms. Some focus on multiple causality and interdependencies. Others use the language of flows, inputs, and outputs. Systems biologists generally want to connect networks, pathways, parts, and environments into descriptions of functional processes and systems. Although many systems biologists have focused on functioning organisms more than on environments, some systems biologists have incorporated environments into their models.

Systems biology approaches also differ by their theories and methods, including those borrowed from systems theory, mathematics, statistics, computer science, artificial intelligence, physics, engineering, robotics (which includes computer science and engineering), and social science (network theory). Understandably, there are disciplinary contests about both epistemic aims and methodological approaches among those researchers who call their work “systems biology” (Fujimura 2003; Calvert and Fujimura 2009). Despite these disciplinary contests, systems biology appears to be gaining influence in the production of
our present and future biological and medical research. It has attracted attention from scientific journals, academic institutions, and private industry in the United States, Japan, and the United Kingdom. At my home institution, the new Wisconsin Institute for Discovery has selected systems biology research from a host of applicants as one of its five key research themes.

Systems biology models biological complexities as organized systems in order to understand them. It seeks to explain how organisms function by using information on DNA, RNA, proteins, and other agents to develop systematic models of biological activities. A major methodological emphasis is the modeling and simulation of biological systems according to particular principles or rules. There are differences in terms of which rules are dominant in any system, which system is in focus, and which elements are included in a particular system. Computational experimentation is a major emphasis of systems biology. Experiments include introducing perturbations into simulated systems to see what happens under different conditions. The information used in the simulations is often taken from databases.

Systems biologists aim to help make sense of the bits and bytes of information produced by the transnational genome projects, but they also claim that their field is not reductionist and is instead a reaction to the failure of molecular biological approaches to provide a satisfactory understanding of the operation of biological systems. Some systems biologists argue that systems biology attempts a more holistic approach toward explanation. Like systems, reductionism and holism are “fighting words” in the history of biology. Philosophers of science and biologists have been engaged in debates about reductionism and holism for at least the last hundred years. I acknowledge these debates and the multiple meanings of these terms, and I use the terms here as the actors I interviewed used them. Generally, the debate is between parts and wholes. Some systems biologists use the term reductionism to refer molecular biologists’ attention to the parts of the organism, including DNA, RNA, and proteins, and their functions, as contrasted with their interest in understanding how parts are organized into systems because systems explain more than individual parts. Others argue that systems biology approaches can now experimentally as well as conceptually explore phenomena such as emergent properties in developmental biology, in contrast to the late twentieth century when wet-lab molecular biological reductionist methodologies were required because one could not vary more than one component at a time and keep track of the results. New computational and biological technologies have produced a multivariable developmental biology, which may allow developmental biologists to experimentally explore the holistic theories of Bertalanffy and Weiss (Gilbert and Sarkar 2000, 7–8).
One question I examine in this chapter is whether some systems biology approaches deploy another form of reductionism.

**SYSTEMS BIOLOGY MODELING: ANALOGIES TO MACHINES, CYBERNETIC SYSTEMS, AND ARTIFICIAL INTELLIGENCE**

A systems biology approach considered here attempts to meld ideas and methods from control engineering, mathematics, artificial intelligence, and robotics to model biological systems. This approach uses detailed molecular pathways as well as systems rules to frame an organism’s functions and organism-environment interactions. The new systems biology speaks of a holistic or organismic materialism that researchers consider to be holist as opposed to reductionist.

In this fashion, systems biology models of the functioning and development of organisms engages older discourses of “wholism” (e.g., Bertalanffy 1933, 1952; Weiss 1955) and organicism, as demonstrated by the journal *Science*’s March 1, 2002, special section on systems biology. The introduction to the section was entitled “Whole-istic Biology” and referenced, as the source of this word, Ludwig von Bertalanffy’s 1967 introduction to his book *General System Theory*, which included his writings that dated back to the 1930s. Like Bertalanffy, these approaches focus on regulation, on interactions among parts, on properties as emerging from these interactions, and on laws that govern organization of parts and processes.9

However, this citation process may be more rhetorically strategic than an actual description of the research approach (Fujimura 1996, 2003). My investigation of systems biology reveals a host of approaches that bring different traditions of research, different epistemologies, and different ontologies to the exploration of organic systems. Some systems biology approaches argue that physics has the right tools; others frame their studies in terms of the mechanistic ontologies of cybernetic systems, others in terms of biological “wholisms.” Some still argue that reductionist methodology is the correct approach, while many argue that reductionist genetics cannot answer questions of organismal functioning.

Despite these differences, mechanical analogies and cybernetic systems dominated the principles guiding systems biology modeling and simulation, especially in the period 2000–2007. For example, the language of circuitry is prominent in systems. Gene regulatory networks, metabolic networks, and signal transduction networks are also part of systems biology discourse and work with mechanical systems analogies.

This mechanistic analogy is further combined with control theory in this form of systems biology. Control theory is “the mathematical study of how to manipulate the parameters affecting the behavior of a system to produce the desired or
optimal outcome” (see http://mathworld.wolfram.com/ControlTheory.html). In engineering, control theorists work on problems such as traffic flow and traffic control. For example, Hiroaki Kitano (2002b, 1662), director of the Institution of Systems Biology in Tokyo, Japan, describes the knowledge objects of systems biology as “seek[ing] to know [. . .] traffic patterns, why such traffic patterns emerge, and how we can control them.” Leroy Hood, director of the Systems Biology Institute in Seattle, Washington, similarly likens his systems biology to solving problems in mechanical systems where “the behaviors of the different kinds of elements involved in automotive mechanics—mechanical, electrical, and control—would be integrated and compared to the model prediction” (Hood 2002, 24–26, see also Ideker, Gaitski, and Hood 2001). Kitano explains control and robustness using a Boeing 747 as his model. The 747 has an automatic flight control system that maintains a robust flight path (direction, altitude, and velocity of flight) against perturbations in atmospheric conditions. Kitano (2004a, 829) goes on to say that “although there are differences between man-made systems and biological systems, the similarities are overwhelming. Fundamentally, robustness is the basic organizational principle of evolving dynamic systems, be it through evolution, competition, a market niche or society.”

**CYBERNETIC THEORY AND BIOLOGICAL SYSTEMS**

Control theory is a close relative of cybernetic theory. Their view of the human-machine relationship is more dominant in some versions of systems biology than is Bertalanffy’s version of systems theory. Developed by scientists (e.g., Norbert Wiener, John von Neumann, Claude Shannon) working during World War II in operations research to develop war-related technologies, cybernetics was framed as a command-and-control communication system. It incorporates information theory and systems analysis. In information theory, “communication and control were two faces of the same coin,” and “control is nothing but the sending of messages which effectively change [control] the behavior of the recipient” (Mindell, Segal, and Gerovitch 2003). Biologists who also worked in operations research used some of this language to rethink problems in biology. Indeed, some of them used cybernetic theoretical and technological framework to rework biological representations of life itself.

According to Donna Haraway (1981–82), Lily Kay (2000), Evelyn Fox Keller (2000, 2002), and N. Katherine Hayles (1999), the application of cybernetic theory to biological problems led to the formulation of molecular biology’s view of the bodies of humans and other animals as information systems, as networks of communication and control. They further argue that cybernetic technologies
alone were not capable of transforming biology; that language, metaphors, and analogies were critical for this reshaping of biology.

Most significant in this reshaping was cybernetic science’s framing of problems of complexity as a way to think about how to control complex systems. For example, Keller (2002) argues that molecular biology began to seriously engage cybernetic theory because researchers believed that traditional embryology could not adequately explain the development of whole complex organisms. However, the molecular genetics of that era also was thought incapable of explaining the complexities of development in part because of the limitations of Crick’s dogma (DNA makes RNA makes protein). Keller argues that the problem of complexity led to the use of cybernetic theory to produce a view of the organism as a machine or a set of regulatory networks.

**CONTROL AND DESIGN**

In 2000 cybernetic theory reappeared as control and design in some versions of systems biology. Kitano’s institute’s approach aims at what they call the control-and-design method, a version of cybernetic theory’s command-and-control. Control-and-design methods are especially aimed at producing designed biotechnologies, including promises of more effective cancer treatments and reverse-engineered organs. For example, by modeling biological systems as mechanical systems, Kitano (2002b, 1662) hopes to delineate how the “mechanisms that systematically control the state of the cell can be modulated to minimize malfunctions and provide potential therapeutic targets for treatment of disease.”

Kitano also argues that biological systems models will be used to simulate potential effects and inefficiencies of drug therapies.

[Biological systems] models may help to identify feedback mechanisms that offset the effects of drugs and predict systemic side effects. It may even be possible to use a multiple drug system to guide the state of malfunctioning cells to the desired state with minimal side effects. Such a systemic response cannot be rationally predicted without a model of intracellular biochemical and genetic interactions. It is not inconceivable that the U.S. Food and Drug Administration may one day mandate simulation-based screening of therapeutic agents, just as plans for all high-rise building are required to undergo structural dynamics analysis to confirm earthquake resistance. (Kitano 2002b, 1664)

Working with California Institute of Technology control engineer John Doyle, Kitano uses control-and-design methods to represent and then biologically reverse-
engineer architectures of an organism. The idea is to use reverse engineering to eventually produce organs for transplantation and other applications (Kitano 2002b; Csete and Doyle 2002; see also Noble 2002). Doyle begins his reverse engineering by analogizing complex technologies, like the Boeing 747, to biological organisms, based on the assumption that they are alike in systems-level organization.

**ROBUSTNESS**

Complex mechanical systems such as those in 747s are engineered for robustness to allow them to adapt to and cope with environmental changes for optimal functioning. In order to promote robustness, control engineers try to build systems using four key parameters: feedback systems; redundancy for multiple backup components and functions; structural stability, where intrinsic mechanisms are built to promote stability; and modularity, where subsystems are physically or functionally insulated so that failure in one module does not spread to other parts and lead to systemwide catastrophe. Csete and Doyle (2002, 1664) applied this concept of robustness to biological complexity: “Convergent evolution in both domains produces modular architectures that are composed of elaborate hierarchies of robustness to uncertain environments, and use often imprecise components. . . . These puzzling and paradoxical features are neither accidental nor artificial, but derive from a deep and necessary interplay between complexity and robustness, modularity, feedback, and fragility. This review describes insights from engineering theory and practice that can shed some light on biological complexity.” Kitano (2003, 125; 2004b) has similarly proposed a model of cancer as a robust system that resists traditional drug therapy. “At the cellular level, feedback control enhances robustness against possible therapeutic efforts.” This control protects normal cells, but cancer cells—once they have been transformed from normal cells—may also have a similar robustness. In control-engineering language, “Computer simulations have shown that a cell cycle that is robust against certain perturbations can be made extremely fragile when specific feedback loops are removed or attenuated, meaning that the cell cycle can be arrested with minimum perturbation” (Kitano 2003, 125). Kitano argues for a “‘systems drug-discovery’ approach that aims to control the cell’s dynamics, rather than its components” (125). He calls for a “unified theory of biological robustness that might serve as a basic organizational principle of biological system,” a unified theory that would be “a bridge between the fundamental principles of life, medical practice, engineering, physics and chemistry” (Kitano 2004a, 834).
LIMITATIONS ON ANALOGIES BETWEEN CONTROL ENGINEERING AND BIOLOGICAL SYSTEMS

The control-engineering approach appears to be a top-down, engineered systems approach to biological organisms that begins with particular design requirements and principles. In contrast, biologists argue that biological organisms are ostensibly the results of evolution and that organisms, species, and evolving environments are historically contingent products. Molecular biologists have preferred bottom-up approaches because they argue that they better capture the complexities and idiosyncrasies that are the results of locally contingent evolution (Fujimura 2005; Calvert and Fujimura 2009).

Systems biologists acknowledge the historical contingency of biology systems by incorporating evolutionary theory in models of complex, robust biological systems. For example, Kitano (2004a, 829) connects robustness to changes in the environment and in genes. “My theory is that robustness is an inherent property of evolving, complex dynamic systems—various mechanisms incurring robustness of organisms actually facilitate evolution, and evolution favours robust traits.” Systems biologists further recognize that biological regulatory systems cannot be fully analogized to mechanical systems. “For example, current control theory assumes that target values or statuses are provided initially for the systems designer, whereas in biology such targets are created and revised continuously by the system itself” (Kitano 2002a, 208). When discussing the development of anticancer drugs, Kitano theorizes the robustness of cancer disease states where cancer cells can alter themselves and their surroundings to promote their survival. The system he theorizes is a very complex one, far from car mechanics.

REPRESENTATIONS OF THE COMPLEX HUMAN BRAIN:
FROM MACHINES TO BIOLOGICAL SYSTEMS TO MACHINES

Kitano was originally trained in physics and computer science. At one point in his career, he helped develop Sony’s AIBO, a robotic pet dog with humanlike neuronal control systems that would enable the robot to learn and develop. Aibo is a Japanese word that means pal or friend and an English acronym for artificially intelligent robot. Kitano’s Symbiotic Systems Laboratory (1999–2004) also developed PINO, a pint-sized walking humanoid robot, and an artificial voice-recognition system. For Kitano, robots were laboratories for his efforts to improve artificial intelligence software. They were “symbiotic systems” to aid the development of artificial intelligence. “Current research is aimed at the development of novel methods for building intelligent robotics systems, inspired by the results of molecular developmental biology and molecular neuroscience research.” For Ki-
tano, “symbiotic intelligence” was a complex biological system analogized as a cybernetic system.

The underlying idea is that the richness of inputs and outputs to the system, along with co-evolving complexity of the environment, is the key to the emergence of intelligence. As many sensory inputs as possible as well as many actuators are being combined to allow smooth motion, and then integrated into a functional system. The brain is an immense system with heterogeneous elements that interact specifically with other elements. It is surprising how such a system can create coherent and simple behaviors which can be building blocks for complex behavior sequences, and actually assemble such behaviors to exhibit complex but consistent behavior. (Kitano, http://www.symbio.jst.go.jp, 2001)

Rodney Brooks, MIT computer scientist and the director of MIT’s Artificial Intelligence Laboratory, is credited with convincing the computer science world of the benefits of studying biological systems such as the human brain for developing robots and other intelligent machines. Brooks said that an understanding of the complex organization of biological systems could be used as the groundwork for establishing complex robotic systems.

How is it that biological systems are able to self organize and self adapt at all levels of their organization—from the molecular, through the genomic, through the proteomic, through the metabolic, through the neural, through the developmental, through the physiological, through the behavioral level. What are the keys to such robustness and adaptability at each of these levels, and is it the same self-similar set of principles at all levels? If we could understand these systems in this way it would no doubt shed fantastic new light on better ways to organize computational and post-computational systems across almost all subdisciplines of computer science and computer engineering. Thus our grand challenge is to find a new “calculus” for computational systems that let us begin to control the complexities of these large systems that we are today building on an ad hoc basis, and holding together with string and baling wire, instead of with genuine understanding. (Brooks 2004)

In contrast to Brooks, Kitano became steadily less interested in robots and more interested in using computational tools to do systems biology. Kitano is now using control engineering and robotics to model living systems. He has moved from producing robotics that emulate biological systems to simulating biological systems using robotic systems.
Beyond the Seamless Border Between Humans and Machines

The fascinating conclusion to the human-machine analogy is that systems biology appears to be that representations of biological systems and of engineered systems are converging in some kind of symbiotic interaction. This convergence makes sense when we remind ourselves that human scientists have been building what we know of both biological systems and engineered systems, and the analogies between the two, since at least the seventeenth century (e.g., Hammond 1997; Otis 2002; Morus 2002; Westfall 1978). John von Neumann used a formulation of how the human brain worked as his model for the first digital computer. It appears that systems biology, the most recent biological approach to understanding biocomplexity, is the outcome of movements of representations back and forth across a machine-living organism border.11

Why should we care about this human-machine interaction? I argue that we need to examine closely what happens at this human-machine border for what is lost in translation in the production of particular systems biology models. Although many scientists argue that science produces only approximations of nature anyway, some philosophers of science argue that knowledges are not only partial, but also particular (e.g., Barad, Haraway). All approximations are not equal. Thus, representation may produce different consequences depending on what is gained and what is lost in this border-crossing production process.

This idea is perhaps easier to grasp when we consider the production of technologies, as contrasted with biological models. For example, the idea of AIBO as friend and robot epitomizes the emotions and thoughts that preceded the production of this robot. AIBO designers were optimistic about the potential for AIBO to help them learn how to design intelligent systems and its potential for producing robots that could be friends to humans—the ultimate in human-machine interaction. One idea guiding this development was that robots could provide friendship and care to both children and older people in Japan, where the birthrate has fallen to produce mostly one-child families and little family support for older adults. Although the view of AIBO as a tool for designing intelligent systems or as a design for human companionship seems innocuous or even positive, some technology researchers have argued that AI and robotics researchers endow their designs with specific characteristics and definitions that they define as “human” (Suchman 2001). That is, AI designers design systems to embody their own particular ideas about emotionality, embodiment, sociability, the body, subjectivity, and personhood. Suchman (2001, 7) is especially vigilant about “the ways in which autonomous machine agency might be consistent with regulatory practices aimed at producing certain kinds of humans and excluding others.” That is, we have to consider what kinds of humanities technologies provide and what kinds they exclude.
In the case of systems biology, particular forms of cybernetic and information theoretic models are incorporated into some systems biology models. Historians of cybernetics have argued that cybernetics was designed as a system meant to control and dominate, to achieve and affect power. Donna Haraway, for example, views cybernetics as “command-control systems” “ordered by the probabilistic rules of efficient language, work, information and energy” (Haraway 1981–82, 246). She reads capitalist mentalities and theories of male dominance into cybernetic systems’ exchange, and use of information for a particular end is an example of capitalist mentalities and theories of male dominance. Cybernetics contributed to this capitalist view of animal behavior the idea that information was the key commodity of exchange. Thus, human and animal behaviors are read in terms of engineering, labor sociology (the organization of labor of Frederick Winslow Taylor), linguistics (semiotics, to understand how systems of signs affect behavior patterns), philosophy, and operations research.

My point is that biological theories and representations of nature are human productions and often contain particular ideas taken from human understandings and goals. Many social studies of science have pointed to other examples where particular forms of social organization have been used to construct biological representations (see, e.g., Strathern’s After Nature [1992]). The mappings of social onto biological are never one-to-one but instead heterogeneous in their outcomes. Cybernetic theories used to develop systems biology models are one set of technobiological imaginaries used to produce renderings of nature.

So what is lost—and what is retained—in translation when cybernetic and systems theories are used to produce systems biology models? What kinds of ideas and representations do not become part of the production of systems biology models? For example, what representations of nature would be crafted if modelers used ideas of symbiosis or coexistence in place of ideas of dominance and hierarchy?

Symbiosis is the coexistence of organisms of different species in interdependent relationships where each benefits the other. For example, human bodies have multiple species of microorganisms living within them in relatively harmonious and mutually beneficial relationships. Indeed, microbiologists tell us that human functioning requires many of the microbes in our intestinal systems. Thus, the human body may be viewed as a composite of multiple organisms living together in an ecological community. While some biologists and ecologists argued for this view of biological functioning in early and mid-1900s, symbiosis was ignored by the waves of enthusiastic efforts to understand how genes work, using molecular-biological research, which flourished from the late twentieth
century until very recently. Molecular biologists used cybernetics ideas to study the human body as a conglomeration of molecules hierarchically controlled by what Keller called the “master molecule,” DNA, whose directions are translated by RNA to produce particular proteins, which constitutes a cell’s body and parts, and onward to ultimately produce a human body. That human bodies begin from cells seems to have disappeared from this master-molecule origin story. This is, in part, because the discovery of the structure of DNA led to a massive effort to study how it worked, leading to the technocratic big science project to map and sequence “the” entire human genome, which has in turn yielded more complexities. As noted above, the first official systems biologists were physicists who designed their ideas of systems biology to work from and with the massive collection of information produced by the various genome projects. This information was primarily in the form of DNA, RNA, and some proteins, so their systems biology focused on designing networks of molecules, beginning with genes.

More recently, however, systems biology models that view bodies as ecologies of multiple organisms are gaining attention and credibility as researchers have begun to say that genes cannot answer the complex questions of human biologies. These ecological models view human systems as constituted of many different organisms and environments interacting within and beyond the human skin—environments within and beyond. They add to early top-down approaches (discussed above) a diversity of biological entities and a specificity of biological processes. Thus, for example, complex systems models are now considering the roles of diet, nutrition, and microbial factors in the development of complex diseases and in the efficacy, metabolism, and toxicity of drugs in human populations (e.g., Nicholson and Wilson 2003, 669). Nutrition has been considered to be a significant factor in disease susceptibility, progression, and recovery, but often was not taken seriously because direct causal links were difficult to investigate in humans. Some systems biology models now propose to accomplish such modeling in mammalian—for example human—physiological systems.

Much of what I described as “systems biology” at the beginning of this chapter appears to be a genetic-reductionist approach. It wants to be the “middle ground,” connecting genetics and biochemistry with development and organismal physiology by using computer simulations and engineering expertise. Nevertheless, it maintains the epistemological primacy of the gene, in part because it applies systemic approaches to genomic information in databases. In this section, I have described attempts by other systems biologists to challenge earlier versions of systems biology.
CONCLUSION
This chapter examines some technobiological imaginaries used by systems biologists as they grapple with complexities in biology. Systems biology aims to represent gene networks, cells, organs, and organisms as systems interacting with each other and with their environments. It employs representations of complex biological networks to abstractly model these interactions. Molecular networks include protein-protein interactions, enzymatic pathways, signaling pathways, and gene regulatory pathways. Cells are envisioned as elements in a cell-signaling pathway and in a cellular computing system. Epigenetic explanations are framed as elements in the organism’s environment that turn on or off networks of genetic signals. Development is often discussed in terms of reverse engineering. Biological systems then are viewed as engineered systems, which have traditionally been described by networks such as flow charts and blueprints. According to Alon (2003, 1866), “remarkably, when such a comparison is made, biological networks are seen to share structural principles with engineered networks.” For example, three of the most important principles shared between biological networks and engineered networks are “modularity, robustness to component tolerances, and use of recurring circuit elements.”

In place of Alon’s amazement, I argue that it is not at all remarkable that biological networks and engineered systems share these principles. Mechanical systems have been analogized to model biological systems and vice versa since at least the seventeenth century in Euro-American biology. Most recently, molecular biology—which itself owes much to the cybernetic model—has produced the information in genomic databases that systems biology uses as the material it molds and simulates. More significantly, the border between representations of organism and machine has been crossed multiple times in both directions, and systems biology is only the latest new field or “discipline” that authorizes and promotes such border crossing. In place of amazement, we need to examine the production of these similarities.

Like nature, biology is a historical object and subject. It has been constructed of bits of things piling up, the accumulation of information, the sedimentation of ideas and objects. The human genome projects of the end of the twentieth century enabled the collection of masses of information through mechanization, lots of labor and love, private and public funds, and competition. To make knowledge of the collected information, however, researchers are searching for other tools, a change in methodology and epistemology. Some systems biologists are attempting to provide rules and principles to organize these bits of information into systems that help to explain the function and dysfunction of organisms. Some of these rules, concepts, and principles are borrowed from artificial intel-
intelligence, robotics, computer science, mathematics, control theory, and chemical engineering. The borrowed principles and rules provide the means to organize and explore information, to create models that can be used to test different values of parameters. However, these imported rules, concepts, and principles are not simply mechanical terms. They also are epistemologies that create new ontologies, that is, new realities. They can be used to manipulate systems to produce different natures, new biologies. These new biologies are and will be produced through human and material agencies.

Systems biology increases both the quantity and kinds of exchanges among expertises that move across the border between human bodies and machines. For example, robotic-engineered systems have taken much of their form from representations of biological systems, and now robotic engineering concepts are being used to model living organisms. This further supports the conclusion that the historical production of knowledge and technologies of living organisms and engineered systems, and the rules used to analyze and manipulate them, are co-produced forms.

The multiple border crossings make it difficult to tease out the translations between forms of representation. Yet examining these crossings is necessary to the study of systems biology. This is where the social study of biology can contribute to the analysis of the process as well as to the production of biological knowledge.

Disentangling the materialities of engineered and biological systems helps delineate the various border crossings in order to understand which representations and realities are lost in the translation. By “lost,” I mean more than “loss.” Translations can distort, transform, delete, and add. I do not refer to a loss of an “original” form of reality and a gain of a “false” form. I refer instead to the multiple realities, the multiple biological forms, which could possibly be created through the work of systems biologists. We know from recent bioengineering feats that biotechnologies are able to create different potential forms of reality. Bioengineers cannot always control their engineering as well as they would like; nevertheless they can produce new forms of life. Thus, understanding what happens at the border crossing between engineered and biological systems is crucial for understanding technobiological imaginaries and their potential consequences. Although Kitano, Doyle, and Hood understand that the Boeing 747 and the automobile are too simple to emulate existing biological systems, they nevertheless use principles from mechanical systems to model biological systems. In the process, their models may excise whatever cannot be translated into the instrumental and technical terms of control engineering as they calibrate between existing biological organisms and virtual, artificially created advanced technologies. This excision
does not make their productions any less material or real. But it may make them different.

The principles used by systems biologists frame which biological realities are created. If engineering and command-control principles continue to dominate systems biology models of living organisms, what will they produce? What will their sociomaterial consequences be (Fujimura 2005)? The control-engineering approach appears to be a top-down, engineered systems approach to biological organisms that begins with particular design requirements and principles. In contrast, biologists argue that organisms are ostensibly the results of evolution, which means that the organism and the species as well as the evolving environments are historically contingent products. Such historical contingencies mean that multiple biological forms are possible. Despite the dominant hierarchical master molecular theory behind much of molecular biology, molecular biologists have used bottom-up approaches because they believe that they better capture the complexities that are the results of historical evolution. Can scientists use mechanistic models to think about nature and simultaneously keep in mind that these mechanistic models are only one slice into understanding complexity? Or does mechanism limit our abilities to see and account for complexities? The very real practices of producing new biomaterialities through stem-cell engineering and synthetic biology often use systems biology models as their guides.

NOTES
1. Alternative approaches to those discussed in this chapter include developmental systems theory (e.g., Oyama 2000a, 2000b) and Kauffman’s complexity theory.
2. Synthetic biology is an example of current efforts to materially replicate biological complexity (Calvert and Fujimura 2009).
3. New developments include two other versions of systems biology, one that is steeped in specific biological systems or topics (e.g., the biology of aging) and another that is framed along the lines of the ecological sciences.
4. This term is taken from my earlier article on scientists’ “future imaginaries” (Fujimura 2003) and has synergy with Shelia Jasanoff’s concept “sociotechnical imaginaries,” which was the basis for a conference on “Sociotechnical Imaginaries” held at Harvard University, November 14–15, 2008.
5. See Traweek (1992) for border crossings in physics.
6. To acknowledge the agency of the material or biophysical does not mean that one accepts the readings of biologists, for example, as perfect understandings of those materialities. As the literature in science and technology studies has shown, the practices that produce biological knowledge are formulated and performed by humans acting within cultures, social institutions, professions, career strategies, technical styles of practice, and novel protocols. Beyond the poststructuralist assumption that biology frames nature through particular lenses,
Science studies has demonstrated empirically how those frames and the particular readings have been produced in many different cases.

7. W. I. Thomas’s words were, “If men define situations as real, they are real in their consequences” (Thomas and Thomas 1929, 572).

8. Systems, holism, and reductionism have also been politically charged terms in biology in terms of politics writ large. For instance, Richard Lewontin, Richard Levins (Lewontin and Levins 1985), and Susan Oyama (2000a, 2000b; Oyama, Griffiths, and Gray 2001) brought a Marxist perspective to their articulation of developmental systems theory in which genetic reductionism was morally suspect (i.e., it could lead to racism and sexism) and false because it was undialectical. They argued that it is impossible to “bridge” genetics and development because they are complementary. The general systems movement—led by Boulding (1956) and Rapoport (1986)—was fundamentally a New Left critique of 1950s science, which was perceived to be blinded by overspecialization and therefore not socially conscious. The antidote was interdisciplinarity and a more holistic perspective (Hammond 1997). For yet another example, ecology was considered “a subversive science” in the 1960s not because of the environmental movement per se (which had relatively tenuous links to academic ecologists), but because it worked outside of established disciplinary niches and insisted on surveying a broad swath of disciplinary territory.


10. See Mindell, Segal, and Gerovitch (2003) for a discussion of the relationship between cybernetics and control theory.

11. Similarly, social theories and biological theories have been analogized in previous centuries. Symbolic interactionism learned much from animal and plant ecology. Functionalism took as its model the biological functioning of organisms.

12. There is no “the” human genome, but many different genomes, both among humans and among other animals and plants.


15. E.g., the belted pig was an early bioengineering experiment that produced a “monster.” Monsters are always a possibility with such experiments. It is also important to remember that researchers at the Roslin Institute researchers made 277 attempts before successfully producing to Dolly, the cloned lamb, who then lived only six years before being euthanized for severe health problems.