



Interdisciplinary research and education at the biology–engineering–computer science interface: a perspective (reprinted article)

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Progress in the life sciences, including genome sequencing and high-throughput experimentation, offers an opportunity for understanding biology and medicine from a systems perspective. This ‘new view’, which complements the more traditional component-based approach, involves the integration of biological research with approaches from engineering disciplines and computer science. The result is more than a new set of technologies. Rather, it promises a fundamental reconceptualization of the life sciences based on the development of quantitative and predictive models to describe crucial processes. To achieve this change, learning communities are being formed at the interface of the life sciences, engineering and computer science. Through these communities, research and education will be integrated across disciplines and the challenges associated with multidisciplinary team-based science and engineering will be addressed.

► The emerging field of systems biology represents an integration of concepts and ideas from the life sciences, engineering disciplines and computer science. Recent advances in biology, including sequencing the human genome and massively parallel approaches to probing biological samples, have created new opportunities for understanding biological problems from a systems perspective. This new approach emphasizes the functional behavior of collections of components working together and builds upon the more traditional approach of studying the individual roles of single components. Systems modeling and design are well-established in engineering disciplines but, until recently, have been relatively rare in biology. To explore the application of complex systems analysis to biological problems, multidisciplinary teams of biologists, engineers and computer scientists are working together – applying principles and techniques from engineering with concepts and algorithms from computer science to solve problems

in biology and medicine. Likewise, through working on biological problems, engineers and computer scientists are creating new knowledge in their own disciplines. To be truly effective, community structures must be built to facilitate the interaction of researchers, educators and students from multiple disciplines. This effort is aimed at integrating multiple interests into one community, a community of practice. In addition, educational programs must be recast to produce a new breed of researcher prepared and suited to working at the interface of multiple disciplines, thereby creating a second type of integration, a new learning community. Several barriers must be overcome to achieve both forms of integration effectively. Progress has been made in building research communities at universities to approach problems in systems biology, and frequently these communities are built around graduate students and their education. Here we discuss challenges to and strategies for integrating students, staff and faculty

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from multiple disciplines to create new learning communities at the interface of biology, engineering and computer science.

A new approach to biology

Rapid progress in biological research now permits probing and perturbing living systems with exquisite control while monitoring their structural, dynamic and functional response through the measurement of up to tens of thousands of components simultaneously. Technological advances have made it clear to many biologists that progress in the life sciences can be accelerated by considering biological problems from the viewpoint of complex systems, where the focus moves to the holistic behavior of the system and the roles of the components are understood in the context of the larger system. Engineers, physicists, computer scientists and others trained in systems research also recognize that the fundamental technologies and emerging mechanistic understanding in biology make it feasible to study the life sciences, including medicine, from a systems perspective and to consider building a synthetic engineering field based on biological substrates ('synthetic biology').

This shift in focus from a component-based to a systems-based approach has important implications for medical research and the profile of diseases that have resisted effective treatment. For diseases where a single, non-essential factor, often a protein, is crucial to disease progression, modern medical research has generally been successful at designing therapeutic agents to interfere with

the target and ameliorate disease. In such cases, the focus on individual components in the absence of systems-level understanding is still sufficient to create an effective therapy. By contrast, there is a sense that many of the more complex but common diseases that have been more resistant to therapy, such as cancer, Alzheimer's disease and diabetes, require a systems understanding to combat them effectively. Thus, the paradigms developed through approaching biology from a systems perspective have the potential to revolutionize not only our knowledge of fundamental basic science but also applications to medicine and, additionally, biotechnology.

At MIT, research in systems biology includes levels of abstraction from molecules, cells and tissues through to organisms, populations and ecosystems (Figure 1). Questions being addressed include how cells make decisions based on environmental cues, how 3D architecture and spatial organization modulate the behavior of tissues, how genes are distributed amongst populations and how different species compete and co-exist in the same environment. One theme that unites these diverse questions is the method of addressing them, known as 'the four Ms' – measure, mine, model and manipulate (Figure 2) – which characterizes the body of MIT research in this field. Efforts in measurement emphasize the systematic collection of data and the development of new experimental methods and technologies (e.g. microfabrication). Mining large datasets identifies underlying relationships, which can be captured in predictive models. Finally, design is an important facet of systems biology where the goal is to make rational modifications to biological systems. This type of manipulation provides a forum for testing our understanding and models; moreover, it promises to lead to practical advances in biotechnology and medicine. A key paradigm in this research approach is the interplay between experiment and computation. The strong focus on building and testing detailed, quantitative and predictive computational models of biological systems is a defining feature of the MIT effort, which has been named the Computational and Systems Biology Initiative (CSBi) to indicate the interplay of computation and systems analysis with biology. Models can be built at multiple levels of abstraction, depending on the type of information available and the role of the model (Figure 1) [1]. Such models form the basis of understanding and the foundation for design.

It should be stressed that, in this view, systems biology is a way of thinking, an approach to formulating questions and knowledge and a framework for solving problems. Systems biology is not merely a collection of technologies whose routine application will by themselves be enabling. Likewise, the stress on computation should not be construed as advocating modeling as a replacement for experimentation. Rather, the introduction of a quantitative theoretical and computational component represents a fundamental departure from a more descriptive tradition that has dominated the life sciences.

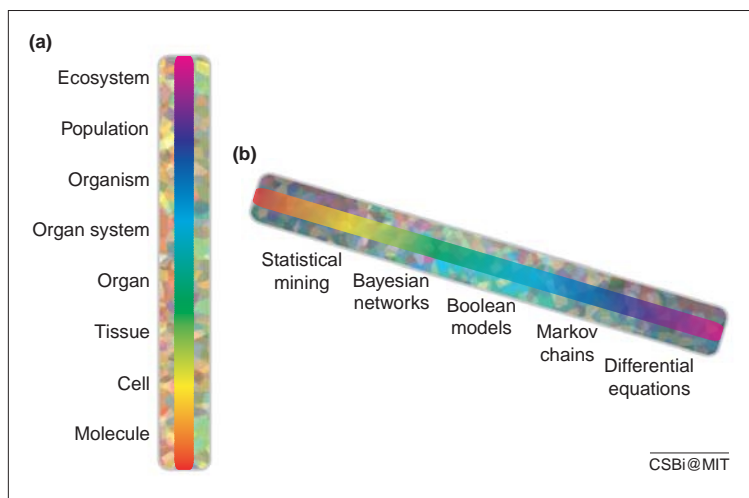


FIGURE 1

Systems biology involves the study at multiple layers of complexity. (a) Complex biological processes can be studied at all levels of abstraction, from molecules to ecosystems. A significant challenge involves bridging insights obtained from multiple levels and constructing models that effectively connect multi-level concepts and observations. For instance, therapeutic drug molecules exert their effect at the molecular level but are effective and safe only if they have the desired effect at the level of the whole individual (organism). (b) Modeling tools also span multiple levels of abstraction. Current research efforts span a progression of understanding from phenomenological, statistical relationships to more mechanistic understanding, exemplified by a model based in differential equations [1].

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