commentary

Small Science and the Big Picture

By David Bochner

The cell is an amazingly complex thing, full of tiny, interconnected parts that all have to work together for everything from communication, to adaptation, to the survival of a whole organism. Historically, biologists have studied these interactions by reducing them to small, provable properties in order to understand the details of the individual cogs in the machine. But in the process of studying the elements of life, we are in danger of straying from biology's original goal of understanding these parts within the context of life as a whole. Hypothesis-driven science, as it exists now, is best equipped to study individual elements—one gene, one protein, one cell type, but not to answer all of the larger questions of how and why a cell or an organism functions in its environment.

It's not that in-depth, hypothesis-driven science is irrelevant—far from it. Rather, it's that we need better tools for making biology's discoveries relevant to both one another and the organism as a whole, in order to understand both how and why they work. A relatively recent integrative approach to the study of life, termed "systems biology," appears to be the toolbox that modern biology is looking for.

Systems biology is, according to the Institute for Systems Biology, "the study of an organism, viewed as an integrated and interacting network of genes, proteins and biochemical reactions which give rise to life" (1). It is an approach to studying biology, rather than a separate field, a set of methods and philosophies that can be applied to the study of just about any part of an organism. Dr. Pamela Silver of the Harvard Department of Systems Biology defines a systems-level question slightly differently, but at the same scale: "at any level, why does the organism work the way it does?" (2). One part of this approach is experimental, requiring the collection of large amounts of data in a relatively short time, in order to identify the elements of living systems and their properties (1). This drives technological expansion, encouraging innovation in order to create more accurate, more efficient means of measuring and understanding these biological processes (1).

Innovations in computational methods, driven by the needs of systems biology, are already helping us to discover vastly complicated connections between genes, proteins, and processes (1). However, bringing together data for analysis is not sufficient for such an integrated approach; systems biology must also bring together the people analyzing the data, in order to understand its true patterns. Thus, systems biology also aims to foster communication across labs, and even across different fields, since collaboration is essential for understanding connections between different researchers' work (1).

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Modern biology's need for a new approach lies in the way that hypothesis-driven science plays out in today's labs. Today, researchers spend much of their time trying to develop a small-scale model of how a single molecular or genetic component of an organism works. At the pinnacle of their research, they may know everything it binds to, every little reaction it catalyzes. But this approach, says Dr. Silver, "lacks the kind of quantitative detail that you need…to ask why the organism works the way it does"(2). In modern academic research, these scientists work in a comparative vacuum, separated by fields and lacking the input from and challenge of alternate viewpoints from other disciplines. Systems Biology aims to generate a complete picture that fundamentally requires describing a process from every angle.

The strongest evidence for the future success of systems biology comes from what it has already done. Systems biologists look past genes and proteins to genomics and proteomics, larger ways of keeping track of all the proteins and genes in a system and, in some cases, and entire organism (3). Advances in modern technology allow scientists to put thousands of molecules on a microchip, and use them to test which proteins might bind to treat a disease, or which groups of genes are turned on and off in a cancer cell (4). New fields such as degradomics and interactomics quickly arise as new types of biological processes are subjected to the processes of systems biology (3). All of these new fields allow for both quantitative and qualitative analysis of massive amounts of data.

This emphasis on generating and analyzing data has focused contemporary systems biology on what is called bioinformatics, the study of how to analyze data and use computing to bring its patterns to light (1). This approach has already found novel patterns in gene expression, and mapped new protein interactions, indicating possible targets for drug treatment (1). Systems biology has fostered technological progress, allowing researchers to get more accurate data, faster, and efficiently analyze it. Primarily, these larger scale results are broken down into smaller-scale questions, which are answered by hypothesis-driven research. Larger patterns of gene expression are broken back down into their individual genes and tested, and are often confirmed by smaller-scale science (5).

In neuroscience, according to Dr. Joshua Sanes of Harvard's Center for Brain Sciences, systems biology "is interested not just in the functions of individual molecules, synapses, or cells, but also in how they work together to account for behavior" (6). New advances in biological techniques have just begun to allow us to understand these relationships. New imaging technology allows us to view changes in entire circuits or individual neuronal connections. The same gene microchips used to study cancer cells can be used to look at the entire genome of an animal with a unique behavior, to try and find a genetic component to the neural activity underlying that behavior (6).

But what if, as we are deconstructing these larger patterns, we are missing the point? If there is a larger pattern of which genes are turned on and off in a certain situation, is it really right to say the next step is to figure out how only one of them works? A better question, perhaps, might be why they are all turned on at once, or how they fit together to govern a cellular process.

As it exists now, systems biology is primarily used to generate larger questions, to be broken down into smaller, hypothesis-driven segments. If the field of systems biology is to accomplish its own goals, it must try to construct the big pictures of the way life works, to understand interactions both within and between larger processes, and why they function as they do. For this to occur, systems biology must place a heavier emphasis on the interdisciplinary methods it has already started to implement. In some sense, more interactions between disparate disciplines allow scientists to see their work from new angles, to see bigger pictures. "It really forces people to talk in a different way," says Silver, "but at the same time it brings to the table people who…can have completely different ideas about how things might work" (2).

If systems biology continues in this manner to pursue its own goals, it could lead to great advances in our understanding of life. By understanding how genes and their products can organize cells into tissues, we can engineer new organs and tissues for patients in need of transplants (7). In neuroscience, systems biology may let us connect such disparate fields as molecular biology and human psychology. According to Dr. Sanes, "systems neuroscience has a huge role to play…in figuring out the wiring diagrams and relating them to the output, the behavior" (3).

The ultimate goal of all science is to understand how the world works. Biology, as a whole, has kept its heart in the right place, and has generated innumerable advances in how we understand life, and how we fix it when it goes wrong. While hypothesis driven biology is essential to obtaining provable knowledge about the components of life, the 21st century requires that we take this valuable knowledge to the next level. Armed with advances in technology and understanding, we must boldly enter a realm where innovation, theory, and practice unite biologists across disparate disciplines, and allow us to understand life as more than the sum of its parts.

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