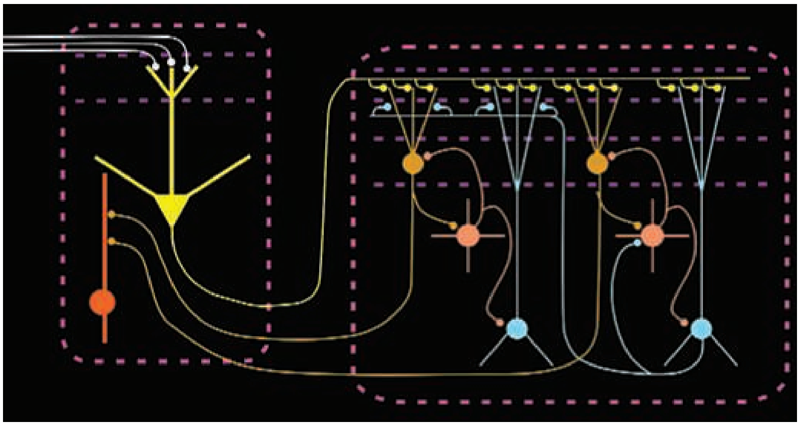
How Will Big Pictures Emerge From a Sea of Biological Data

Biology is rich in descriptive data—and getting richer all the time. Large-scale methods of probing samples, such as DNA sequencing, microarrays, and automated gene-function studies, are filling new databases to the brim. Many subfields from biomechanics to ecology have gone digital, and as a result, observations are more precise and more plentiful. A central question now confronting virtually all fields of biology is whether scientists can deduce from this torrent of molecular data how systems and whole organisms work. All this information needs to be sifted, organized, compiled, and—most importantly—connected in a way that enables researchers to make predictions based on general principles.

Enter systems biology. Loosely defined and still struggling to find its way, this newly emerging approach aims to connect the dots that have emerged from decades of molecular, cellular, organismal, and even environmental observations. Its proponents seek to make biology more quantitative by relying on mathematics, engineering, and computer science to build a more rigid framework for linking disparate findings. They argue that it is the only way the field can move forward. And they suggest that biomedicine, particularly deciphering risk factors for disease, will benefit greatly.

The field got a big boost from the completion of the human genome sequence. The product of a massive, trip-to-the-moon logistical effort, the sequence is now a hard and fast fact. The biochemistry of human inheritance has been defined and measured. And that has inspired researchers to try to make other aspects of life equally knowable.

Molecular geneticists dream of having a similarly comprehensive view of networks that control genes: For example, they would like to identify rules explaining how a single DNA sequence can express different proteins, or varying amounts of protein, in different circumstances (see p. 80). Cell biologists would like to reduce the complex communication patterns traced by molecules that regulate the health of the cell to a set of signaling rules. Developmental biologists would like a comprehensive picture of how the embryo manages to direct a handful of cells into a myriad of specialized functions in bone, blood, and skin tissue. These hard puzzles can only be solved by systems biology, proponents say.



Systems approach. Circuit diagrams help clarify nerve cell functions.

The same can be said for neuroscientists trying to work out the emergent properties—higher thought, for example—hidden in complex brain circuits. To understand ecosystem changes, including global warming, ecologists need ways to incorporate physical as well as biological data into their thinking.

Today, systems biologists have only begun to tackle relatively simple networks. They have worked out the metabolic pathway in yeast for breaking down galactose, a carbohydrate. Others have tracked the first few hours of the embryonic development of sea urchins and other organisms with the goal of seeing how various transcription factors alter gene expression over time. Researchers are also developing rudimentary models of signaling networks in cells and simple brain circuits.

Progress is limited by the difficulty of translating biological patterns into computer models. Network computer programs themselves are relatively simple, and the methods of portraying the results in ways that researchers can understand and interpret need improving. New institutions around the world are gathering interdisciplinary teams of biologists, mathematicians, and computer specialists to help promote systems biology approaches. But it is still in its early days.

No one yet knows whether intensive interdisciplinary work and improved computational power will enable researchers to create a comprehensive, highly structured picture of how life works.

–ELIZABETH PENNISI

CREDIT: MICHAEL T. SHIPLEY

What causes schizophrenia?
Researchers are trying to track down genes involved in this disorder. Clues may also come from research on traits schizophrenics share with normal people.

What causes autism?
Many genes probably contribute to this baffling disorder, as well as unknown environmental factors. A biomarker for early diagnosis would help improve existing therapy, but a cure is a distant hope.

To what extent can we stave off Alzheimer's?
A 5- to 10-year delay in this late-onset disease would improve old age for millions. Researchers are determining whether treatments with hormones or antioxidants, or mental and physical exercise, will help.

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What is the biological basis of addiction?
Addiction involves the disruption of the brain's reward circuitry. But personality traits such as impulsivity and sensation-seeking also play a part in this complex behavior.

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