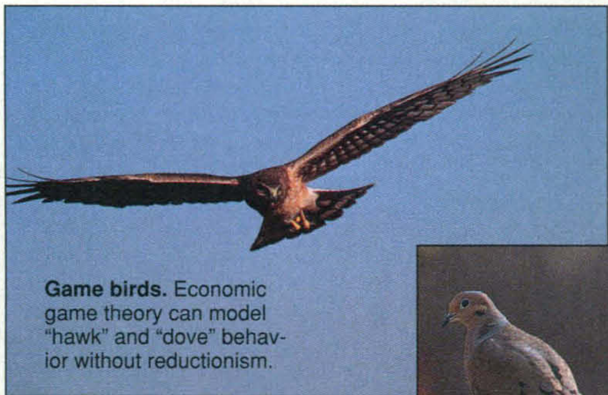
PHILOSOPHY OF SCIENCE

Biologists Cut Reductionist Approach Down to Size

LONDON—For the past 2 centuries, scientists have been animated by the belief that a complex system can be understood by seeking out its most fundamental constituents. This approach, known as reductionism, views nature as something of a Russian doll: Features at one layer are explained by the properties of the layer below. Hence, physicists search for the basic particles and forces; chemists seek to understand chemical bonds; and biologists scrutinize DNA sequences and molecular structures in their efforts to understand organisms.



R. DAY/ANIMALS ANIMALS

Game birds. Economic game theory can model "hawk" and "dove" behavior without reductionism.

J. HEIDECKER/VIREO

Among biologists, however, resistance is growing to what physicist Steven Weinberg of the University of Texas, Austin, has called "grand reductionism": the idea that the most fundamental layer of nature holds an explanation for all the features of the outer, higher layers. A group of 30 distinguished biologists and other researchers met here recently at the Ciba Foundation to discuss the future of the reductionist approach. The meeting saw some spirited attacks, as biologists discussed cases where reductionism falters, drawn from fields ranging from cell biology to behavioral strategies. But other talks demonstrated how powerful the approach remains, epitomized by computer models of embryonic development that show how just a handful of molecular signals can give rise to complex patterns. Many participants came away concluding that reductionism is just one of many tools biologists will need to fathom the mysteries of nature.

Thomas Nagel of New York University, the only philosopher at the meeting, presented a two-part case against reductionism. First, he said, even though nature could, in principle, be explained in terms of universal basic laws, in practice our finite mental and computational capacities mean that we either cannot grasp the ultimate physical explanation of many complex phenomena—or we can't fruitfully link this basic level to higher order phenomena. The second, more controversial, part of Nagel's argument was that additional principles, not evident in the laws governing basic constituents, are needed to explain higher order phenomena.

Such additional principles might be required to explain what biologists refer to as "emergent properties"—properties that are found at higher levels of organization of an organism but are absent at lower levels, as if one layer of the Russian doll had features in its appearance totally unrelated to the doll below. Emergent properties are found in chemistry and physics: Temperature, for example, is a property of a collection of particles and is irrelevant to individual particles. But biologists can point to an extraordinary array of features, such as genes, eyes, and wings, that are meaningless on the level of atoms and molecules.

Cell biologist Paul Nurse of the Imperial Cancer Research Fund in London says that even a biological system as small as a single cell exhibits a wealth of features that are absent at the molecular level: positional information, compartmentalization, kinetics of signaling, oscillations, and rhythms, to name a few. By focusing on molecules, he believes cell biologists may be missing out. "Cell biologists haven't yet thought much about this," he says.

Many features, however, are not obviously emergent; only a detailed analysis of complex interactions at the organism level shows that they are genuinely new features that only appear at higher levels. For example, physiologist Denis Noble of Oxford University has been studying a key ion-transporter molecule found in heart muscle that is involved both in maintaining normal rhythm and also in some life-threatening abnormal rhythms. Attempts to treat the abnormal rhythms by chemically blocking this transporter had been unsuccessful, so Noble set about producing a computer model of its activity. To create an effective model, he found he had to consider not only how the molecule behaves throughout a key population of cells responsible for generating cardiac rhythm, but also how those cells are linked to other regions of the heart. These sophisticated interactions showed why simple blocking drugs had been "spectacularly disappointing," says Noble.

Other computer models seemed to even the score for reductionism. Biologist Michel Kerszberg of the Pasteur Institute in Paris has developed computer models of signal-transduction pathways in early embryos created by gradients of chemical signals called morphogens, produced by the embryonic cells. "I can show from the complexity of morphogen concentration gradients in the embryo surprising precision and reliability in signal delivery to the appropriate cells," he says. "The number of variables needed to create complex states is sometimes very small, often three or fewer," says biophysicist Benno Hess of the Max Planck Institute for Medical Research in Heidelberg, Germany.

Another analysis, however, showed that biological complexity can be modeled without any regard to its molecular constituents, presenting a challenge to reductionism. Economic game theory, which was developed to study how humans respond to various economic situations, can often predict complex behavior of organisms without analysis at the molecular level. Computer models in which individuals behave as "hawks" and take an aggressive stance in interactions while others, called "doves," take a passive stance have helped reveal strategies that bear a stunning similarity to some real situations. "Game theoretical models move up rather than down the reductionist scale," says biologist John Maynard Smith of the University of Sussex in the United Kingdom, a pioneer in applying game theory to biology.

But perhaps the biggest challenge to reductionism comes from the concept of information. In biology, information is carried and received by molecules, which is fully consistent with reductionist principles of physics and chemistry. Yet natural selection has often produced multiple chemical and physical ways of conveying the same message, so that by looking only at the molecules, researchers may be missing the message. "Information is not reducible," says psychologist Jeffrey Gray of the Institute of Psychiatry in London. About 50% of the genome of a multicellular organism may code for proteins involved in cell signaling, says biologist Dennis Bray of Cambridge University; hence, organisms can be viewed as complex information-processing systems, where molecular analysis alone may not be sufficient. "There's a need to realize that information may be transmitted in ways that may be lost by studying molecules alone," says

Nurse. "It may not be possible or even necessary to explain all cellular phenomena in terms of precise molecular interactions."

Participants argued that genetic redundancy poses a similar challenge to reductionism. Researchers who have created genetically modified organisms in which a single gene has been deleted or blocked, known as "knockouts," have often been surprised to find that some other gene can take over at least part of its function. "Some mouse knockouts have turned out to be messy," says Nurse. These lessons have forced researchers to look harder at how genes map onto the form, or phenotype, of developing organisms, particularly their behavior. Biologist Sydney Brenner, of the Molecular Sciences Research Institute in La Jolla, California, argues that studying genes can help researchers understand how organisms are put together, but may not be helpful in describing some of the ways they function. "You can map genes onto behavior, but [the map] doesn't give you a causal explanation," he says.

Participants in the conference agreed that reductionism has a future in biology—but only as one approach among many. A growing number of questions will require other approaches. Some delegates felt that a deeper understanding of the role of information may yet throw a spanner in the grand reductionist scheme and that Nagel may be right in his suggestion that additional principles are needed. Asks biochemist Max Perutz of Cambridge's Laboratory of Molecular Biology: "Will there be new laws of biology?"

–Nigel Williams

COMPUTER SCIENCE

Model Explains Internet 'Storms'

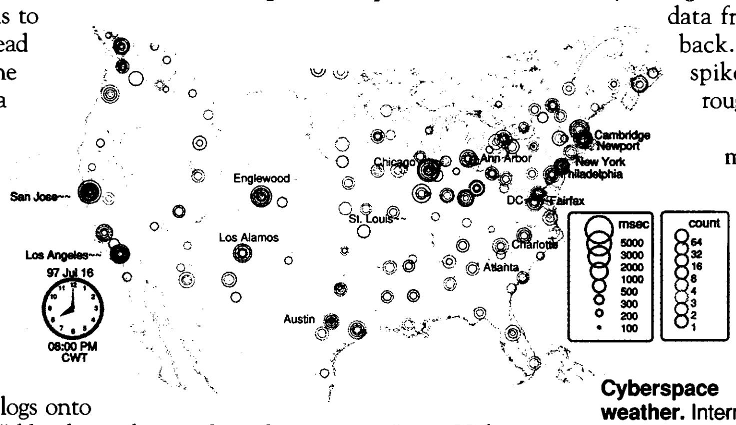
Every cyber-junkie knows that the Internet is a crowded place. As computers send volumes of data from server to server, phone lines fill up, causing Internet traffic jams—and making Web browsers chug away in fruitless attempts to retrieve information. Then, moments later, the congestion abates. On page 535, two physicists present mathematical and computer models that point to the causes of these Internet "storms." The explanation, say the researchers, lies not in technology but in social behavior: Millions of users who have no incentive to economize flood the Internet with data, clogging it, and then get discouraged, relieving the congestion—all at roughly the same time.

The researchers, Bernardo Huberman and Rajan Lukose of the Xerox Palo Alto Research Center in California, aren't the first to recognize that the Internet tends to be overused because most users pay a flat rate for unlimited access. Instead, their achievement is to show exactly how these incentives lead to the spates of congestion seen on the Internet, says Kenneth Steiglitz, a computer scientist at Princeton University. "You look at the Internet and say, 'My god, it's a mess; nobody's going to understand it,' but Huberman gets qualitative insights into very complicated problems," says Steiglitz. Huberman himself thinks these insights might eventually point to ways to unclog the Internet.

He explains that everyone who logs onto the Internet faces a "social dilemma" like the one posed by a group dinner in which the bill will be split evenly. If you are in a selfish mood, you might order a lobster, hoping that your friends will economize and choose the salad. Because the price of the lobster gets split among the whole group, you would pay little for a sumptuous meal. But your friends see no reason why they should settle for salad while you order shellfish. They order the pricey lobster as well, placing a heavy demand on the lobster chef and leaving the whole group with a hefty bill.

The Internet is like one big, expensive dinner where no one expects to pay his share, says Huberman. Because of flat-rate pricing, people have no incentive to limit the size of their downloads, their Web meanderings, their e-mail, or their Internet chatting. As everyone consumes bandwidth—just as when everyone consumes lobsters—there is a price to pay: in this case, congestion. "Individually, their actions are rational, but collectively they're suboptimal," says John Bendor, a political scientist at Stanford University. The result of this collective display of self-interest, adds Lukose, is "overusing and degrading the value of resources. That's the tragedy of the commons."

But unlike the gradual deterioration of other common resources—for example, the atmosphere, where countries see no incentive to reduce greenhouse-gas emissions if other countries don't cut back as well—the Internet's congestion is sporadic. "There are short spikes of congestion," says Huberman, "on the order of seconds or tens of seconds." To explain this behavior, he and Lukose created a mathematical model of Internet use in which each user behaves rationally, overusing the Internet most of the time but logging off when congestion becomes too great.



SOURCE: MIDS

Cyberspace weather. Internet delays, as measured round trip between Austin, Texas, and hosts around the United States.

The model borrows from statistical mechanics, a branch of physics that deals with the collective effects of many simple objects, such as molecules or magnetic spins. It predicted the statistical properties of the network delays as many agents—each representing an Internet user—logged on and off. The result was a so-called lognormal distribution, which resembles a skewed bell curve, indicating "latency"—the extra time it takes to send a packet back and forth—on the horizontal axis and how often a user would encounter each latency on the vertical axis. Most of the time, the latency fell on the hump of the distribution, and the delays were small. But every so often—on the tail of the distribution—the delays spiked in an Internet storm as a large number of users put a load on the system at the same time.

To see what this statistical behavior would mean in the real world, Huberman and Lukose wrote a computer model based on the equations. By plugging in values for such things as the network bandwidth, the number of users, and how much congestion it takes to discourage a user, they were able to simulate congestion on an actual network. They also tested the mathematical model's predictions by timing how long it took to send packets of data from Stanford to England and back. Sure enough, they measured spikes of congestion distributed roughly in a lognormal curve.

Explaining Internet storms may prove easier than controlling them, because doing so will entail changing the behavior of vast numbers of users. "As the size of the group grows, it gets tougher to produce collective levels of common good," says Bendor. The answer, Huberman thinks, will lie in new pricing schemes, such as a pay-per-packet scheme or a priority-pricing method (the Internet equivalent of Federal Express). Huberman hopes to put his model to work studying the effects of various changes in incentives on Internet congestion. But one thing is already clear, he says. "I don't think the idea of a [flat-rate] Internet will go on forever."

–Charles Seife

Charles Seife is a writer in Riverdale, New York.