An Omnifarious Data Bank for Biology?

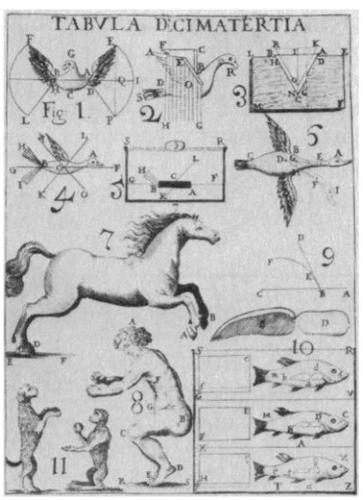
New theories could arise from restructuring of available knowledge, says NAS panel on biomedical models

"Unity in diversity" is a bedrock concept in biology, referring to the commonalities in structure and function throughout nature and among widely diverse organisms. A recent report from the National Academy of Sciences (NAS) suggests this concept as the basis for what could become a more explicit and comprehensive theoretical structure for biology.

The report, "Models for biomedical research: A new perspective,"* was produced in response to a request by the National Institutes of Health (NIH) to assess the relevance for biomedical research of various models, including mathematical ones. The committee concluded that because of the rapid accumulation of biological knowledge, much more sophisticated and extensive use can now be made of lower organisms. But the report went beyond that to assert that better organization of existing information may well yield new knowledge: "we seem to be at a point in the history of biology where new generalizations and higher order biological laws are being approached but may be obscured by the simple mass of data. . . . "

The committee, headed by Yale University biophysicist Harold J. Morowitz, found itself confronting "some issues usually considered by philosophers of science rather than by experimentalists," according to the report. While scientists are aware of the pervasiveness of many common strategies in the animal kingdom, the members often came upon unexpected examples of intertaxonomic relationships which "caused some of them to revise their view of the implications of biological relationships between and among diverse taxa, other model systems, and human beings." They were impressed that "in every hierarchical level from molecules to ecosystems, common hardware, common programs, and common strategies are used to achieve diverse ends."

For example, researchers have found similar molecules in protozoans, bacteria, and yeast. And a signaling molecule in yeast mating has also been found in the sex hormones of higher organisms—which belies the assumption that endocrine glands, a much later development than yeast, evolved their own signaling molecules. Another example involves research on myasthenia gravis, believed to be caused by an autoimmune response to acetylcholine receptors (AChR's). When the purified AChR from electric eels was injected into rabbits to make antibodies, it also produced myasthenic symptoms in the rabbits. This was an unexpected finding, providing evidence of "a sufficient conservation of protein structure between fish and rabbit to result in immunologic cross-reactivity . . . " Says Morowitz: "these cross-relations are intruding on us so we can't ignore them anymore."



De Motu Animalium *by Alphonsi Borelli. Ex Typographia Anglei Bernabo. Romae MDCLXXX. Courtesy, Dibner Room, Special Collections Branch, Smithsonian Libraries.*

The report notes that there are two ways to model something in biology: homology (referring to evolutionarily related structure and functions such as fins and arms) and analogy (isolated correspondences between organisms). Because of the pervasiveness of such correspondences, the latter approach offers fruitful possibilities which deserve more thorough exploration, says the report.

It also discusses the use of "one-to-one" versus "many-to-many" modeling, both in organisms and disease entities. A one-to-one model for AIDS, for example, would be simian AIDS; whereas a many-to-many model entails drawing on analogies from the fields of immunology, cancer, infectious diseases, and so forth. The report suggests that the latter approach can be used more extensively while still avoiding the perils of reductionism that arise when biologists attempt to borrow from the paradigms of physics.

Biology, unlike physics, lacks universal postulates. But it does contain "generalizations," the structure of the DNA molecule being perhaps the most fundamental. The committee adds, though, that many common features "exist at relatively high levels of organization," and "are much more extensive than was perceived at the outset" of the study. It therefore proposes that more refined organization of the data, in a form which makes recognition of the cross-connections more explicit, will turn up new generalizations.

To this end, the committee suggests that scientists start thinking about how to develop a biology-wide information system—a computerized "matrix data base"—structured so that it can be accessed from a multitude of dimensions. Categories would include, for example, level of organizational complexity (from atoms to populations); phylogenetic status; physiological responsiveness (behavior); metabolism, and biological regulation.

The committee observes that development of such a data base will require "a new kind of scientist," with dual expertise in biology and information science. The data base would vastly expand the array of possible models used by making available information on phenomena that are analagous to various aspects of the subject under study. Being designed to search for "general laws and structures . . . [it] will make general biology much more easily accessible to the biomedical scientist."

The committee is quite excited about its report and, says Morowitz, "we keep being surprised at the kind of responsive chord this is striking in the scientific community." In late May, after the report was issued, the last of the budget was spent on a workshop to talk about the matrix data base. According to embryologist Samuel Ward of the Carnegie Institution of Washington, there are various prototypes in existence, such as the DNA registry (Genbank) started by Los Alamos Laboratory. But the matrix would be more flexible and elaborate, containing an indefinite number of interrelated information banks. One possible category, says Ward, could be "mole-

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cules that affect cells." Encompassing all of pharmacology, it would erase artificial distinctions between natural and synthetic compounds. For example, Ward says, "we might discover that some toxic chemicals have the same effect as hormones."

Another way to cut across subject matter might be to structure the topic of energy utilization so that it can be compared between an ecosystem and an individual organism—or even with inanimate functions. The report observes, for example, that a goose and an airplane are analagous in that each optimizes its energy-to-weight ratio by carrying its fuel as saturated hydrocarbons. Another pivotal theme for the matrix might be feedback regulation, as it is expressed in everything from bacteria to ecosystems.

A knowledge system that strives to put "all of biological knowledge in relation to the rest of it" is "somewhat premature," comments Lindley Darden of the University of Maryland's philosophy of science department. Rather, at this point, it is the "Platonic ideal." Indeed, as the committee notes, a more urgent need right now is for a "data base of data bases."

For the moment, the NIH is advised to think more according to the concepts embraced by the report. Investigators should be encouraged to think of models along "many-to-many" lines. More research on nonmammalian species should be promoted, and good research should be supported "without taxonomic or phylogenetic bias."

NIH likes the report. James D. Willett, head of its new section on Biological Models and Materials, says it has "all the earmarks of being on the doorstep of a new theoretical biology." The National Science Foundation, which discussed some of the concepts at a December workshop on advanced computing in the life sciences, is also "very interested" in the data bank idea, according to Mary Clutter, director of the division of cellular bioscience. After sitting in on the final NAS panel meeting, says Clutter, "I had a feeling I had a glimpse into the future."—CONSTANCE HOLDEN

Host of Problems Threaten National Parks

Park officials, legislators, and environmentalists take stock and suggest solutions

During the past month, a rash of studies, meetings, and congressional hearings have suggested that America's national parks are in trouble and that the National Park Service is in need of serious reform before it can successfully tackle the problems. Encroaching development, pollution, and overcrowding by tourists has steadily intensified, making it even tougher for the park service to balance the goals of preserving the parks and providing a place for recreation.

The problems challenging the parks are legion. The haze over the Great Smokies is no longer blue, but gray from air pollution. The grizzly bear may be approaching the point of extinction in Yellowstone National Park. Last year, private owners of 160 acres within the Grand Teton Park boundaries sought to develop their property. Ozone is damaging the giant trees in California's Sequoia National Park. Cape Cod National Seashore is fighting a legal battle with people who want the right to drive dune buggies on the beach.

Conservation Foundation president William Reilly, recently announcing a new report on national parks, said that the park system "has entered an era for which its traditions and policies have not prepared it." Federal legislators at a House hearing 20 and 21 May called for better monitoring of air pollution in the parks. A panel of national park managers and scientists at the annual meeting of the American Association for the Advancement of Science stressed the need to beef up science and research to help management make better decisions. The Conservation Foundation study concluded that there is an "immediate need" for a comprehensive program that would address the many problems, from mending fences to changing management practices and recommended that the federal government undertake a new half-billion dollar initiative.

All this discussion comes at a significant time. Last month, William Penn Mott, Jr., was sworn in as the new National Park Service director and is highly regarded by environmental groups. Mott, 75, has spent 46 years in park work and was director of the California state park system between 1967 and 1975 while Ronald Reagan was governor. He is credited with doubling the state's park system and initiating new kinds of agreements to create parks in cities. Environmentalists are hopeful that Mott, with his past ties to President Reagan, will be able to spearhead reforms and secure the necessary money.

In addition, the legislation that has provided the principal source of money to buy more than 1.5 million acres for national and state parks will expire in 1989. The Conservation Foundation report says, "No other single decision will so fundamentally shape the National Park System of the future as the selection of the successor to [this legislation]."

The Reagan Administration has strongly supported the restoration of existing facilities but has actively campaigned against the addition of new park land. Under former Secretary James Watt, the Department of the Interior initiated a $1-billion, 4-year program to restore national park facilities that even environmental groups acknowledge needed repair. New sewer lines have been replaced, roads mended, and buildings renovated. But the Administration has discouraged the purchase of more park land and encouraged economic development on existing acreage. Nevertheless, Congress has been spending an average of $100 million annually since 1980.

The Conservation Foundation proposes that the federal government double its annual expenditures to buy park land and that it also spend an additional $50 million per year for the next 10 years on resource management, an increase of about 30 percent over the current budget. The report goes on to list many recommendations that emphasize preservation rather than recreation:

- The park service should create a new program to train specialists rather than generalists to help manage the parks. The complexity of the many problems confronting the parks needs to be addressed by experts in natural and cultural resources.
- Park management should look to new ways to establish new parks and protect present ones. Gone are the days