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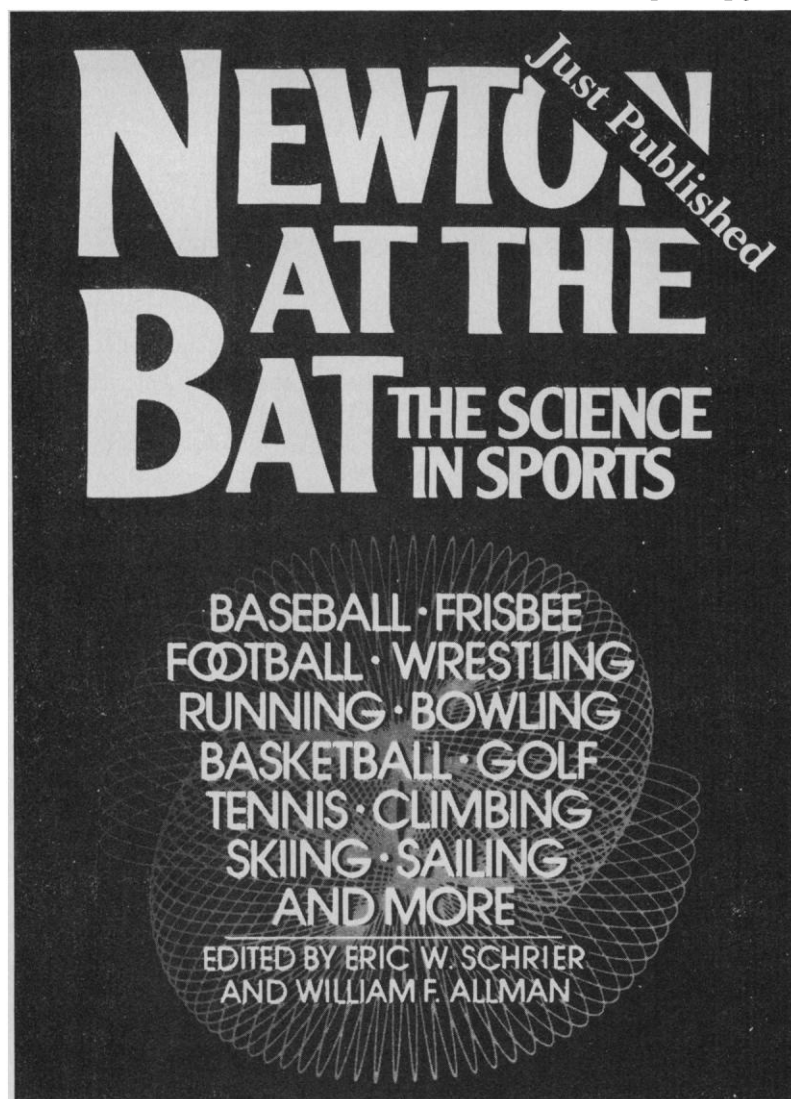
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## COVER

Masked booby (*Sula dactylatra*) adult on Christmas Island, Republic of Kiribati, central Pacific Ocean (12°N, 157°W). The booby was one of 18 species of tropical marine birds resident on the atoll whose breeding was temporarily terminated and whose populations disappeared during the 1982-83 El Niño Southern Oscillation. See page 713. [Ralph W. Schreiber and Elizabeth Anne Schreiber, Natural History Museum, Los Angeles County, Los Angeles, California 90007]

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## LETTERS

### Bacterial Contamination of Human Tumor Samples

Since the discovery that certain human tumors contain activated oncogenes, a great deal of effort has been dedicated to searching for genetic alterations that may explain their neoplastic properties. While screening human carcinomas for possible rearrangements within *ras* oncogenes, we have encountered an artifact that I would like to report to other investigators engaged in similar endeavors. We have detected significant amounts of pBR322-related sequences, presumably of bacterial origin, in DNA's isolated from about 20 percent of colonic tissues (both tumors and polyps) and occasionally in tumor material that was stored frozen in a repository. We suspect some of the latter material may have been suboptimally stored. These human tumor DNA's contain DNA fragments of a high molecular weight (8 to 30 kilobase pairs) that hybridized with certain oncogene probe preparations. This hybridization was due to a low percentage of pBR322 sequences which are invariably present in probes obtained from DNA fragments subcloned in pBR322, even after two cycles of electrophoretic purification. Because the relative contribution of these residual vector sequences varies tremendously with the size of the DNA fragments used as probes, the pBR322-related DNA fragments present in human tumor DNA were detected with probes of less than 300 base pairs but not with probes of 2 kilobase pairs or larger. In view of these observations, I strongly recommend the routine use of vector probes as controls in Southern blot analysis of human tumor DNA's.

MARIANO BARBACID  
*Developmental Oncology Program,  
National Cancer Institute-Frederick  
Cancer Research Facility,  
Frederick, Maryland 21701*

Recently in the study of hepatitis B virus (HBV) integration and hepatocarcinogenesis, there has been concern about getting false positive results due to bacterial contamination of autopsy materials.

Using both an HBV DNA probe and a pBR322 probe, we hybridized DNA from hepatocellular carcinomas (HCC) obtained at autopsy from 70 humans. The HBV DNA probe showed 1 to 6 bands per case in 32 HCC's, whereas the pBR322 probe revealed bands in 15 HCC's, including a hepatoblastoma,

with exactly the same pattern as that obtained with the HBV DNA probe. Histological study revealed bacterial colonies in some HCC tissues that had given rise to the bands with the pBR322 probe. This indicates that false positive bands may result from hybridization of the probe with bacterial plasmids in autopsy materials.

When these false positive cases were deleted, our corrected figures for the integration of HBV DNA were as follows: 15 out of 20 as opposed to 18 out of 20 HCC's from carrier patients; 0 out of 16 as opposed to 6 out of 16 HCC's from patients with HBV antibodies (noncarriers); and 1 out of 34 as opposed to 4 out of 34 HCC's from patients clinically negative for HBV.

OKIO HINO  
TOMOYUKI KITAGAWA  
HARUO SUGANO

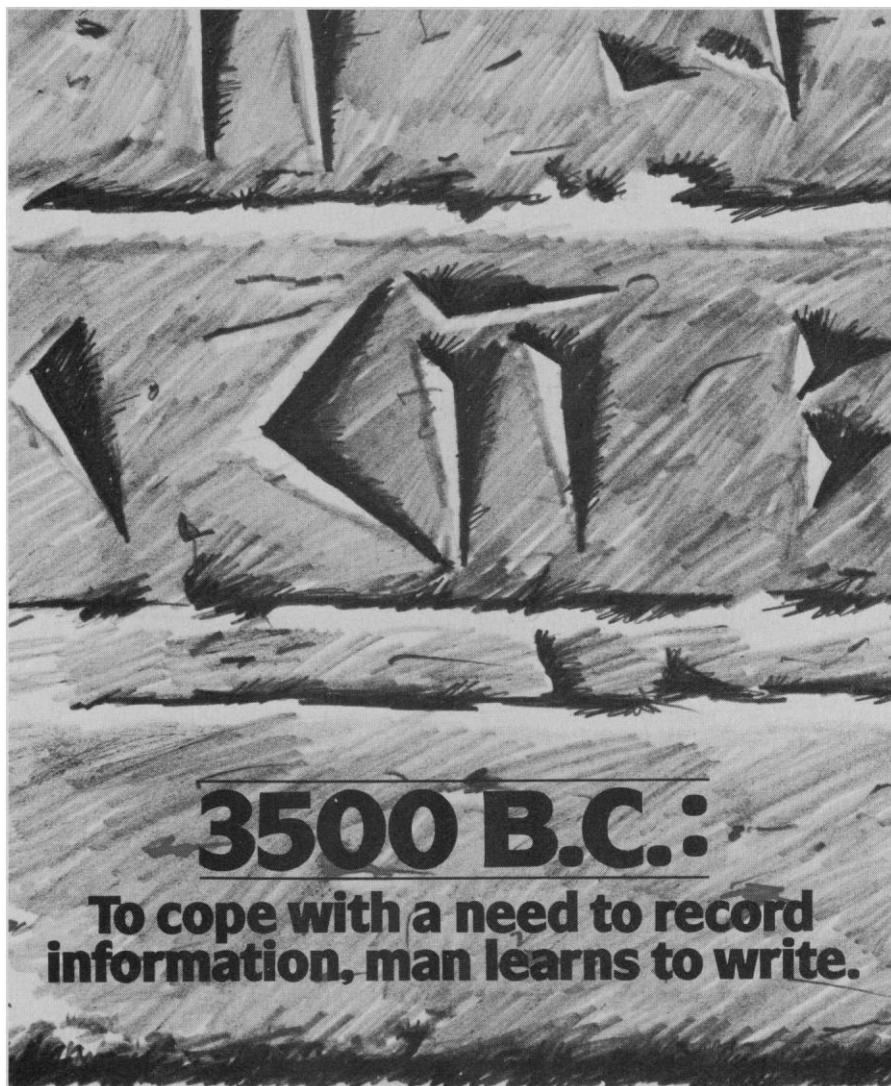
*Department of Pathology,  
Cancer Institute,  
Kami-Ikebukuro, Toshima-ku  
Tokyo 170, Japan*

### Seroepidemiology

Gina Kolata, in her commentary on "The new epidemiology" (News and Comment, 4 May, p. 481), discusses the use of serum collections that are taken for one purpose and used for another. She gives the examples of the serum collections of the Harvard Hypertension and Follow-up Program that are being used to determine the relation of levels of vitamin A, vitamin E, or carotenoids to cancer. The low cost of \$6000 for the study is emphasized. She also refers to the Comstock collection of serum from 25,000 healthy persons in follow-up studies of cancer.

I was pleased to see the usefulness of serum banks recognized; however, "the new epidemiology" is neither so new nor so inexpensive as indicated. The World Health Organization has promoted the multiple uses of serum collections since 1959 (1) and has established three serum banks (2). The applications of seroepidemiology have been presented over the past 20 years, and results from the use of the Comstock collection in the seroepidemiology of Hodgkin's disease were presented in 1981 (3).

Readers should also be aware of the continuing costs of maintaining the serum collection, continuing follow-up for diseases such as cancer in prospective studies, and carrying out tests on the serum. We are currently working with the Harvard School of Public Health on a large prospective study of Hodgkin's dis-



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## SCIENCE / SCOPE

Artificial intelligence is the focus of a new advanced technology center at Hughes Aircraft Company. The facility brings research and development efforts under one roof. Scientists and engineers will work closely with universities throughout the country to develop software and equipment to build the so-called expert systems. Studies will center on knowledge representation, symbolic reasoning and inference, natural language processing, and knowledge acquisition and learning. Technology will be developed for image understanding for missile targeting and geological surveys from space, smart avionics to reduce pilot workload, self-controlled systems, simulation and training, fault diagnosis and maintenance, and manufacturing resource allocation and planning.

The sights, sounds, motion, and urgency of combat await pilots who learn to fly the F/A-18 Hornet strike fighter in the first computerized simulators of their kind. A pilot wears full flying gear and sits in an exact replica of an F/A-18 cockpit located inside of a 40-foot-diameter sphere. High-resolution pictures of earth, sky, and targets are projected onto the inner surface of the sphere and matched with appropriate sounds and vibration. Pilots thus experience runway vibration, aircraft stalls, buffeting, missile launches, cannon fire, dazzling aerial maneuvers, and enemy aircraft and missiles approaching at supersonic speeds. The Hughes simulator will save the U.S. Navy and Marine Corps millions of dollars by providing combat training without costly flight operations.

Computers will be troubleshooting hybrid microcircuits used in new sophisticated missiles at Hughes. Computer-aided troubleshooting (CATS) will cut troubleshooting time, improve effectiveness by automatically locating faults, eliminate mistakes and wasted time, and simplify the technician's decision-making. CATS also will be able to use past repair records as a key to speed up troubleshooting. A typical case: An automatic bar-code reader identifies a failed part and data about the failed test is retrieved from a main computer. A probe then automatically takes measurements at key internal circuit nodes so the fault can be isolated. Next, the computer displays a schematic of the failed circuit area and compares actual and ideal signal values. The technician then determines which component has most likely failed and selects rework instructions accordingly.

Development times for semicustom very large-scale integrated (VLSI) circuits have been cut from greater than one year to 20 weeks at an ultramodern computer-aided training and design center at the Hughes facility in Newport Beach, California. Utilizing advanced design automation software, a comprehensive library of predesigned logic functions (called Macros), and preprocessed wafers, the new facility is helping engineers design chips with 2,000 to 8,000 gates and with as many as 180 pins. New 3-micron dual-layer metal HCMOS processes are applied to both standard cell products and state-of-the-art gate arrays. Skilled design engineers and education specialists at the Newport Design Center provide training and technical support for IC designers throughout the company.

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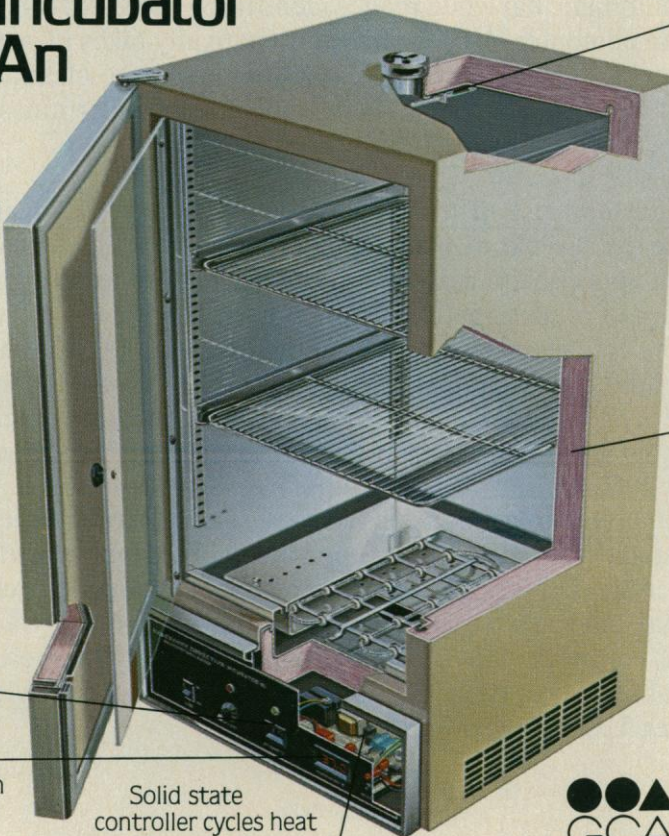
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## The Graduate Curriculum

In this country, the graduate curriculum is determined primarily by departmental and disciplinary requirements designed to produce the most advanced researcher, scholar, or practitioner in a given discipline. As a consequence, the graduate curriculum is viewed as a series of disparate programs held together by a minimum number of programwide requirements. Recent national reports on the status of graduate education suggest that the graduate curriculum today may need to address issues and problems that cut across disciplines and that are not usually embraced by primarily discipline-oriented programs.

The issue before us is what should the future doctoral recipient look like after 4 to 6 years of intensive graduate study. If we look at industrial research laboratories, we note that they are being staffed increasingly by multidisciplinary research teams. We have heard from many corporate executives that their research laboratories require creative and flexible researchers with training from several fields. The coupling of organic chemistry and computer science to model the geometry of molecules is but one of many examples. We observe also the increasing convergence of separate disciplines into multidisciplinary areas such as biotechnology, the cognitive and decision sciences, and the neurosciences, all of which cross traditional departmental boundaries.

The Northeastern Association of Graduate Schools, a group of 90 graduate institutions from Maryland to Maine, has made some suggestions for modifying the graduate curriculum to respond to these developments. They include four principal changes.

The adoption of a cohesive minor for doctoral students would stress linkages among disciplines and prepare students to embrace research challenges from converging branches of knowledge and technology. This requirement might be assessed by comprehensive examinations following completion of the minor.

A new seminar focusing on the process rather than the products of inquiry could be required for all doctoral students during the early stages of their programs. Researchers from different disciplines, describing how they frame and execute their research, might provide students with alternative perspectives for approaching specific disciplinary research projects and possibly break some of the paradigms perpetuated under a strictly discipline-oriented curriculum. The advancement of the arts, humanities, and sciences might take some new and perhaps more coordinated directions as a result of such an approach.

A didactic short course focusing on the ethical, governmental, and legal forces that shape and influence research and scholarship could also be included in doctoral programs. The current issues surrounding the conduct of human and animal experimentation, the management of hazardous research materials, intellectual property rights, technology transfer, and close examination of the specific ways in which research and scholarship contribute to society could be systematically presented and examined.

Finally, the doctoral dissertation defense could be expanded to test systematically a candidate's ability to communicate the specific research project to a broad scholarly audience to show the implications of the research for other disciplines. This requirement would stress the broadening of the conception and communication of a research project.

The discussion of programwide requirements for the graduate curriculum has not been focused since the debates many years ago over retaining language requirements or substituting more timely technological skills. Such a discussion is long overdue. It may also be of value to consider the different disciplines as a part of, rather than apart from, a more unified graduate curriculum while still promoting excellence in given areas of specialization.—ROBERT B. LAWSON, *Dean of the Graduate College, University of Vermont, Burlington 05405*





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