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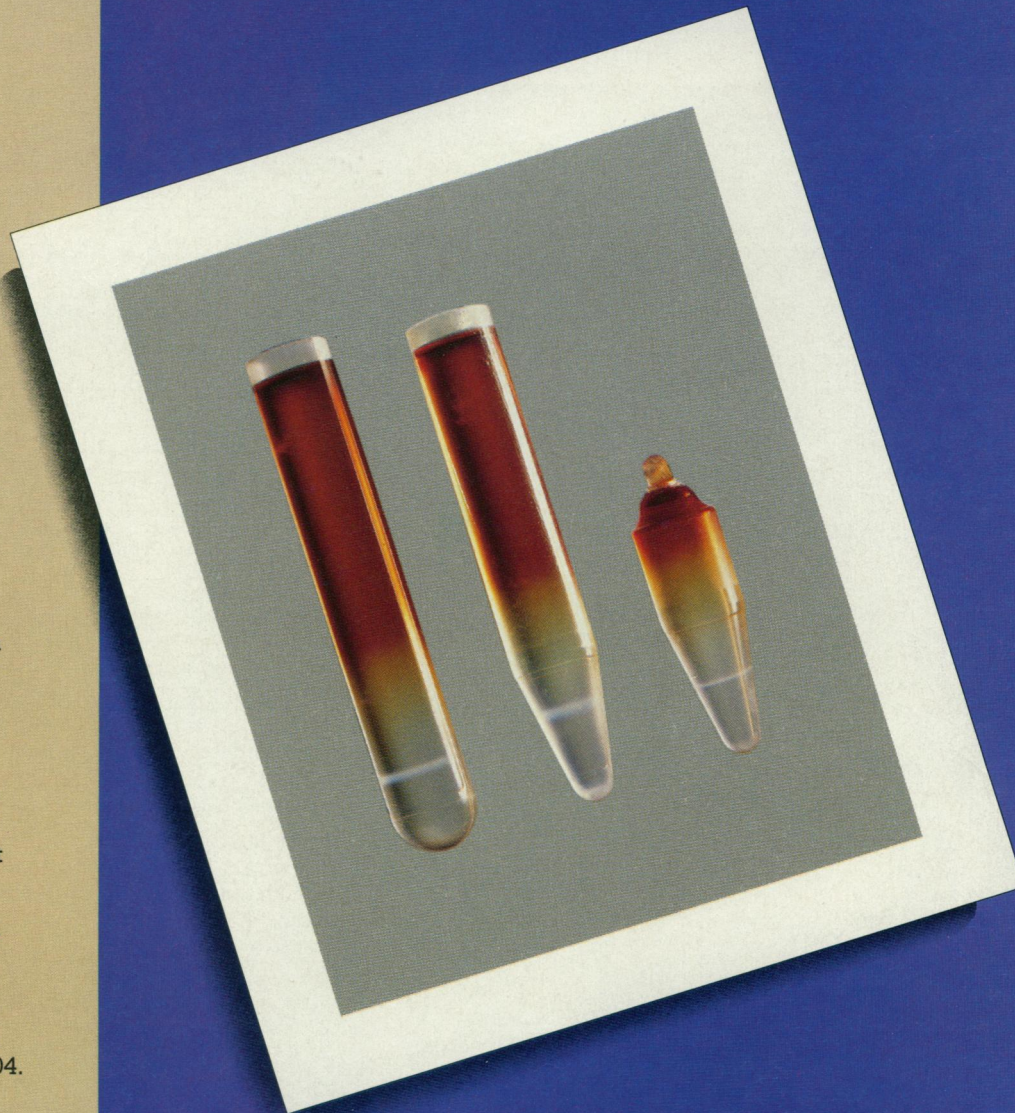


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HUMAN GENOME I

An International Conference On The Human Genome

1st Annual Meeting – October 2-4, 1989

Town & Country Hotel

San Diego, CA

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Daniel E. Koshland, Jr., Ph.D.
Editor of Science

Co-Chairman:

Charles R. Cantor, Ph.D.
Director of Human Genome Center
Lawrence Berkeley Laboratory

PROGRAM

KEYNOTE ADDRESSES

Opening Welcome:

Richard Atkinson, President, American Association for the Advancement of Science.

Role of the Meeting:

Charles Cantor, Director, Human Genome Center, Lawrence Berkeley Laboratory.

CURRENT STATUS OF THE GENOME PROJECT

THE GENETIC MAP: Raymond White, Howard Hughes Medical Institute, University of Utah.

RESTRICTION MAPS: Cassandra Smith, University of California, Berkeley.

CLONING: Ronald Davis, Stanford University School of Medicine.

ORDERED LIBRARIES: Sydney Brenner, MRC Molecular Genetics Unit, Cambridge, England.

APPLICATIONS: Thomas Caskey, Howard Hughes Medical Institute, Baylor College of Medicine.

SOCIETAL IMPLICATIONS: Daniel Koshland, University of California, Berkeley.

TECHNIQUE INNOVATIONS

PCR OF SINGLE SPERM: Norman Arnheim, Ahmanson Center for Biological Research, University of Southern California.

SEQUENCING METHODS: George Church, Harvard Medical School.

DNA CLEAVAGE: Peter Dervan, California Institute of Technology.

RADIATION HYBRIDS: David Cox, University of California, San Francisco.

IN SITU HYBRIDIZATION: Jeanne Lawrence, University of Massachusetts Medical Center.

RAPID MAPPING: Glen Evans, Salk Institute.

INTERESTING REGIONS

CYSTIC FIBROSIS: Francis Collins, Howard Hughes Medical Institute, University of Michigan Medical Center.

TELOMERES: Robert Moyzis, Los Alamos National Laboratory.

IMMUNOGLOBULINS: Tasuku Honjo, Kyoto University Faculty of Medicine.

IMMUNOGLOBULINS: Hans Zachau, Institute for Physiological Chemistry, University of Munich.

T-CELL RECEPTORS: Leroy Hood, NSF Science and Technology Center for Biotechnology, California Institute of Technology.

FRAGILE X: Jean-Louis Mandel, Institut de Chimie Biologique, Strasbourg.

APPLICATIONS

HUMAN EVOLUTION: Allen Wilson, University of California, Berkeley.

MULTIGENE DISEASES: Eric Lander, Whitehead Institute for Biomedical Research, Cambridge, Massachusetts.

HUMAN DIVERSITY: Jean Dausset, Human Polymorphism Study Center (CEPH).

SEX DETERMINATION: David Page, Whitehead Institute for Biomedical Research.

UNSTABLE SEQUENCES: Michio Oishi, University of Tokyo.

INTERPRETING SEQUENCE: Russell Doolittle, University of California, San Diego.

ORGANIZATION – DIFFERENT VIEWS OF CURRENT AND FUTURE SCIENCE AND PROCEDURES

HUGO: Victor McKusick, Johns Hopkins University School of Medicine; President, The Human Genome Organisation (HUGO).

NIH: James Watson, Cold Spring Harbor Laboratory; NIH Human Genome Project.

DOE: Charles Cantor, Human Genome Center, Lawrence Berkeley Laboratory.

EEC: Peter Pearson, Johns Hopkins University School of Medicine.

JAPAN: Nobuyoshi Shimizu, Keio University School of Medicine.

INFOMATICS: David Lipman, National Library of Medicine.

OVERVIEW: Renato Dulbecco, Salk Institute.

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COVER Computer simulation of the vortical flow over a delta wing at a high angle of attack. The wing shape is similar to that of the Lockheed SR-71 reconnaissance aircraft. See page 361. [Calculation made with the FL067 computer program by A. Jameson, Princeton University, Princeton, NJ 08540. Graphic visualization by G. Volpe and M. Siclari, Grumman Corporate Research Center, Bethpage, NY 11714]

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Specific binding to receptors has been shown in chick cardiac muscle⁽¹⁾.

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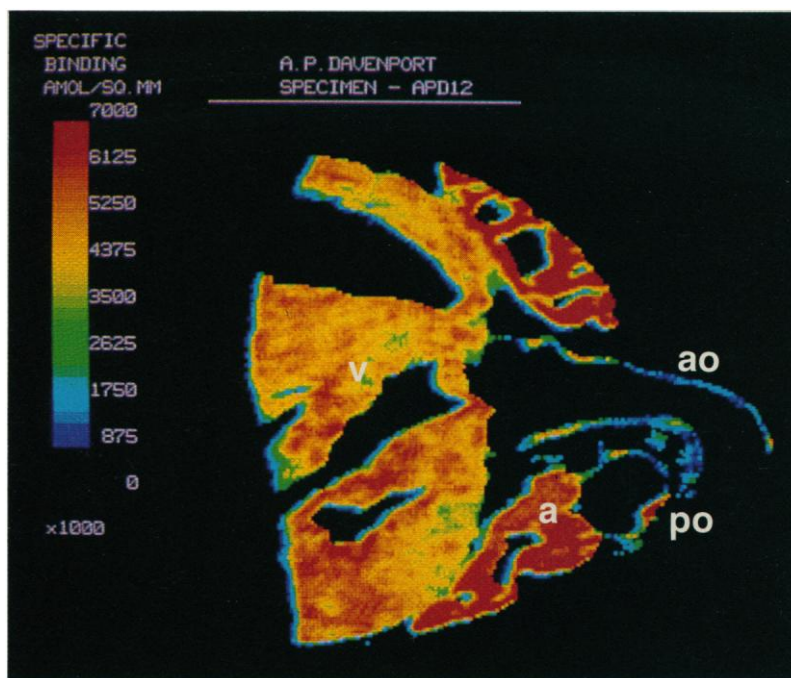
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⁽¹⁾ Yanagisawa Miyazaki. Personal communication.

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Coronal section of rat heart:

a — Atria ao — Aorta

v — Ventricles po — Pulmonary artery

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This Week in SCIENCE

Computational aerodynamics

A pitcher sending a knuckle ball toward the plate may not know exactly where the baseball will go; but then again, neither will the batter. In fact, designers of supersonic aircraft have it easier than these athletes: predicting the airflow past an intricate machine like the Boeing 747 at speeds beyond Mach 1 is in some ways simpler than predicting the airflow past a nonspinning baseball. Jameson takes advantage of the efficiency of high-speed computers in proposing a mathematical model (page 361) that describes aerodynamic properties in the transonic regime (from about Mach 0.8 to Mach 1.2, an efficient cruising speed for an aircraft). Computational aerodynamics must be able to predict the airflow past an airplane during all of the types of flying it might do, from takeoff to cruising and at various angles of attack (cover). An ideal set of computer programs would not only test the aerodynamic properties of existing shapes—it would aid engineers in designing shapes with optimal aerodynamic properties.

Cancer-cholesterol connection

KEY genes regulating normal cell growth can mutate to oncogenically active forms that encode altered proteins. Some of these unusual oncoprotein modifications need the assistance of the body's metabolic intermediates; for instance, modification of yeast α -factor and Ras protein needs a precursor formed during cholesterol biosynthesis. A well-placed interruption in the pathway can inhibit the modification. In studies based upon yeast mutants, Schafer *et al.* identify mevalonate (a precursor of sterols and other isoprenes such as farnesyl pyrophosphate) as one of the elements in this pathway needed for biological activation of the yeast and human Ras2 protein (page 379). In *Xenopus* oocytes, a class of drugs that inhibits the synthesis of me-

valonate also blocks the action of oncogenic derivatives of human Ras protein. This pharmacological approach opens the door on a new way of investigating and possibly controlling the transformation of normal cells to tumor cells, and also affords potentially novel targets for cancer chemotherapy.

Quantum GaAs clusters

IN the development of new types of electronic devices from semiconductor materials, small is beautiful. Smaller devices perform faster, and interesting quantum-mechanical effects can arise by fashioning particular shapes into a device, the so-called quantum wires, dots, and boxes. However, such effects are very sensitive to defects in the material and to deviations from ideal shapes, and thus the production of high-quality structures is an important goal. Sandroff *et al.* have grown GaAs microcrystalline clusters on high surface area SiO_2 supports (page 391). They attribute the high degree of crystallinity in the clusters to the high temperature used in their molecular beam epitaxy process and to the large surface-to-volume ratio generated by the shape of the supports. The size and quality of the microcrystalline GaAs surface allow for close study of its composition.

Around the DNA bend

INTRINSICALLY straight DNA chains migrate predictably enough to be sorted by mass through gel electrophoresis; chains that have natural bends due to structural polymorphism, or that are induced by the binding of certain proteins, move in a less regular fashion. The path of a DNA chain has been described as determined entirely by the random fluctuations of the leading segment of the chain as it passes through a fixed matrix or set of tubes used as a model for the gel. In this case a bend somewhere in the middle would not affect the chain's mobility, which is contrary to the observed anomalous mobilities of bent DNAs. Using models

of two different gels, Levene and Zimm find that the reduction of a DNA chain's mobility through a gel is larger for an intrinsically bent chain in a concentrated gel than for the same chain in a more dilute gel, regardless of the position of the bend (page 396). Terms representing the elastic free energy of the DNA chain and the elastic properties of the gel matrix account for the different dynamics. This result corresponds to previous observations that bent DNA molecules migrate anomalously in concentrated gels, such as polyacrylamide, but have essentially normal mobilities in dilute gels, such as agarose.

Plant evolution: water to land

NO one is exactly sure when plants migrated from water to land, but it may have been between the Late Ordovician and the Early Silurian, or about 400 million years ago. Green algae, the most likely ancestors of embryophytes (land plants), probably made the trip many times before gaining a permanent roothold. Fossils of the ancestors of land plants are hard to interpret: even as they adapted to life on the land, these pioneers lacked the hard parts characteristic of later land plants. The living alga with the greatest cytological and chemical similarity to embryophytes, the genus *Coleochaete*, is a tiny (1 millimeter in diameter) alga that lives in shallow, freshwater habitats, which may be similar to those occupied by the algal ancestors of land plants. Delwiche *et al.* (page 399) find compounds in *Coleochaete* that are similar to lignin (the substance that, together with cellulose, forms the woody cell walls of plants). The compounds allow the alga to withstand reducing treatments, which suggests that the living alga may have left traces in the fossil record. The presence of these compounds in the water-dwelling plant also supports the hypothesis that lignin's first role was as an antimicrobial (as opposed to a structural) agent.

■ PAT JANOWSKI

American Association for the Advancement of Science

Science serves its readers as a forum for the presentation and discussion of important issues related to the advancement of science, including the presentation of minority or conflicting points of view, rather than by publishing only material on which a consensus has been reached. Accordingly, all articles published in *Science*—including editorials, news and comment, and book reviews—are signed and reflect the individual views of the authors and not official points of view adopted by the AAAS or the institutions with which the authors are affiliated.

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The Underrepresentation Syndrome

“Birds of a feather flock together” is a truism that applies to scientific publishing. Authors like to see articles in their field in a journal to which they are considering sending the products of their research. In a magazine like *Science* that can create a problem. Our interest is to publish the cutting edge of research in every branch of science as well as to present research that will interest readers ranging from physicists to social scientists.

Because of that range of disciplines, a phenomenon, which we call the “underrepresentation syndrome,” arises. If an article in a well-represented field is turned down, the author may feel aggrieved but there is no generalization to his field, whereas the author of a paper in a less represented area frequently concludes that the subject area was the reason for the rejection and decides not to submit any more papers to *Science*. That perception can create a vicious cycle in which represented areas become more and more dominant and underrepresented areas less and less so. The problem is compounded because readers also tend to discount as representative of their own fields papers that are in different subspecialties of that field.

The chance of being published in *Science* is approximately the same for all fields of research, and the composition of the magazine reflects the percentage of articles received in each field, rather than a selection of certain favored areas. Articles at the frontier of any discipline are desirable but the journal recognizes that it is more unusual to report breakthroughs in mature fields than ones in which new technologies, such as computers, molecular techniques, and tunneling microscopes, are used. The advent of space travel and satellites has dramatically changed the contents of reports in astronomy and earth and planetary sciences, but the percentage of articles in these areas has not changed much over the years. We expect to be increasing pages to get more representation. But *Science*, because it is a weekly with large circulation, must limit its total pages to approximately 5000 per year in order to remain readable and portable. One of our goals is to maintain subject balance, and, all other things being equal, we tend to favor a paper in physical or social science over one in biology. After initial screening, articles with extremely favorable ratings go to a space meeting in which the best are selected. This means not only that they are highly regarded within their specialty, but that they also fulfill balance criteria and are of interdisciplinary interest. Thus it is possible for a paper to receive two excellent reviews and still be rejected. It may be competing for space with another excellent article that is either in an underrepresented field or of greater interdisciplinary interest.

Science serves a function by providing specialized scientists with developments in neighboring areas. The volume of the modern literature makes it ever more difficult to keep up in one's own specialty, but the impact of one discipline on another is also increasing. Scientists, therefore, will need to know what is happening in other fields. DNA sequencing is no longer of interest just to molecular biologists; it expands into forensic medicine, evolution, and disease diagnosis. Tunneling microscopes are not just interesting to physicists, but to chemists, students of ceramic and solid-state surfaces, and biologists as well. No scientist can be an island, and therefore *Science* performs a service by presenting in one place major advances on all frontiers.

Science also tries to serve the scientific community by hastening the recognition of areas that have not yet gained a great deal of exposure. For example, ecology played a very distinguished role in biology for a period of time, then seemed to diminish in interest because many of the studies were repetitive or inconclusive. But now, grave threats to the environment make that science ever more important. Low-energy physics, in the limelight because of superconductivity, continues to make advances which have practical application, not only commercially, but also to other scientists. These are only a few of the many areas that are particularly appropriate for a magazine like *Science*.

We receive many more manuscripts than we can possibly publish. But we wish to improve the fare for our readers and help the advancing frontiers of all science. Winston Churchill said, “Remember the turtle, he only makes progress when his neck is out.” There is credit for being a lonely pioneer as well as for being a participant in the gold rush.

—DANIEL E. KOSHLAND, JR.

Variability and Management of Large Marine Ecosystems

Edited by Dr. Kenneth Sherman, *Director, Narragansett Laboratory, National Oceanic and Atmospheric Administration*, and Dr. Lewis M. Alexander, *Director, Center for Ocean Management Studies, University of Rhode Island*

Large marine ecosystems (LMEs) are being subjected to increasing stress from industrial and urban wastes, aerosol contaminants, and heavy exploitation of renewable resources. This book is a state-of-the-art review of effective means for measuring changes in populations and productivity, physical-chemical environments, and management options for LMEs. For the first time, this volume treats LMEs holistically as regional management units by bringing together the all too often fragmented efforts to optimize ocean resources. 319 pp., 1986.

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Rifted Margins

Early Tertiary Volcanism and the Opening of the NE Atlantic. A. C. MORTON and L. M. PARSON, Eds. Published for the Geological Society by Blackwell Scientific, Palo Alto, CA, 1988. xii, 47 pp., illus. \$85. Geological Society Special Publications, vol. 39. Based on a conference, London, U.K., March 1987.

The geological expressions of continental rifting and separation prior to sea floor spreading are highly variable, ranging from extensive stretching and necking of continental lithosphere with almost no magmatism to less dramatic extension with voluminous magmatism. The opening of the northeastern Atlantic between Europe and East Greenland is one of the best documented cases of the latter type of rifting, and yet the roles of magmatism and other major geological processes remain controversial. This takes on special importance because similar geochemical and structural expressions occur in rifts and rifted margins worldwide.

This well-edited collection of short papers provides a case study of the magmatic activity that attended the rifting of the northeastern Atlantic. Thirty-three papers and four extended abstracts cover the seismic charac-

ter, petrology, geochemistry, and geochronology of the rifted margins of the northeastern Atlantic and of the classic East Greenland and British Tertiary Igneous Provinces and the voluminous related offshore lithologies. Most of the offshore data are presented for the first time outside of the *Initial Reports of the Deep Sea Drilling Project* or the Ocean Drilling Program or reports from private industry. The book also includes up-to-date reviews of the major igneous terranes on shore.

Most of the papers are rather limited in scope and emphasize objective reporting of data and straightforward interpretations. Only the first three papers provide much discussion of models involving the causative agents for the rifting. This is a welcome departure from volumes on rifting in which models heavily outweigh supporting data. Regrettably, the book has no summary chapter synthesizing the new data.

One of the important themes with which nearly all of the papers in this volume are explicitly or implicitly concerned is the cause of the magmatism. It has long been suspected that heating and uplift of the lithosphere caused by a mantle hot spot or plume can make overlying continents split and sepa-

rate. Such localized mantle heating is thought to produce the voluminous magmatic intrusions and volcanic eruptions that occur in some rifts. (The best modern example is Eastern Branch of the East African Rift.) In the case of the northeastern Atlantic, the evidence of such a process, presented by White, appears strong. Iceland lies like a smoking gun at the scene of the crime, and bathymetric ridges of thick crust leave trails back to the matching margins.

Hot-spot models require broad regional uplift and magmatism associated with the earliest rift faulting. Geological evidence of these relations has proven difficult to detect in the northeastern Atlantic because most of the area that would have been affected has subsided below sea level and been covered with thick basaltic lava flows that inhibit reflection seismic studies. The volcanic and plutonic rocks exposed on both shores of the northeastern Atlantic are only the outermost portions of a much larger igneous province and may not accurately reflect the initial magmatic events.

Papers in this volume show that indeed very early magmatism occurred during rifting in the northeastern Atlantic. However, the most spectacular igneous activity took