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SCIENCE • VOL. 272 • 31 MAY 1996
Three-dimensional power spectrum of solar oscillations from observations by the Global Oscillation Network Group (GONG). These data are for sound waves with 30 to 150 wavelengths around the sun of varying latitudinal extent and periods of 4 to 12 minutes. Greater power is denoted by blue-green tones. The curved sheets represent distinct radial overtones of the oscillations. See the special section on helioseismology (pages 1281–1309) and a News story (page 1264). (GONG is an international project supported by the National Science Foundation.) [Image: N. Brummell and D. Haber]
NEW TETRAD™ CYCLER OFFERS HUGE CAPACITY

FOUR INDEPENDENT BLOCKS

Fully Compatible With Earlier DNA Engine; Uses Same Interchangeable Alpha™ Blocks

WATERTOWN, Mass. – MJ RESEARCH proudly announces the introduction of an ultra-high-capacity model in its DNA Engine™ line of thermal cyclers. Called the PTC-225 DNA Engine Tetrad™, this speedy cycler has four fully-independent blocks, accurate and reliable Peltier-Joule heat pumps, and networking capabilities that make the cycler fully compatible with earlier PTC-200 DNA Engines—as well as with new automated systems.

In fact, the Tetrad cycler uses the same Alpha™ sample-block/heat-pump assemblies that fit the earlier DNA Engine. These interchangeable blocks deliver the same thermal precision and NIST-traceable accuracy no matter what machine they are plugged into—and swapping an Alpha takes just ten seconds. Eight different Alphas are currently available, and they fit 0.5ml or 0.2ml tubes, 96-well or 192-well plates—or even combinations of vessels in dual blocks. Two newer blocks fit 384-well plates (see below) and microscope slides for in situ reactions. These different Alphas can be mixed or matched in a single Tetrad, for a total capacity of up to 1536 simultaneous reactions. No cycler made by any other manufacturer offers such versatility or throughput.

This instrument is the latest in the long line of Peltier thermal cyclers offered by MJ RESEARCH. Since 1988, this innovative manufacturer has pioneered development of Peltier-effect instrumentation for laboratories, having introduced the PTC-100 cycler that year and the portable PTC-150 MiniCycler™ in 1991. MJ RESEARCH is also the company that blazed the trail to in situ amplification, and its line of PTC-200 DNA Engines sets a standard against which all other cyclers are now judged.

The PTC-225 Tetrad™ with four independent blocks, each with its own Hot Bonnet™ heated lid.

Automated Systems

Slim Cycler Works Well With Robots

The Tetrad was designed to integrate easily with robotic or automated systems, and its hardware and software were carefully crafted to make integrations straightforward and reliable.

For example, an important consideration is geometry. The Tetrad has a compact footprint (37x55cm), low height (25cm), and front-back airflow—features that facilitate easy fit into a robot without excessive occupation of the work envelope. Further, motorized Power Bonnet™ heated lids are available, and these open a full 115° to allow easy access to the block. They operate automatically and use variable-ratio cams to seat the heated lid firmly and evenly.

NETWORKING SOFTWARE

Control Can be Effected Through Keypad or Computer

Perhaps the most advanced feature of the DNA Engine line (i.e. the PTC-200 & 225) is the sophisticated networking software that is exclusive to MJ RESEARCH. Not only does the software offer three methods of thermal control, improved editing and filing features, and multi-tasking capability—it also allows up to 15 cyclers to operate on a single, computerized network. Full control can be effected by a computer through either a RS-232 or an IEEE-488 port, or the individual blocks can be programmed or controlled through use of a keypad and the LCD/LED displays on the cycler itself.

“What About the 384-Well Format?” Ask Scientists in the Human Genome Community

The Quest for Colossal Capacity

Now that thermal-cycle sequencing of M13 templates seems to have become the sequencing method of choice for the Human Genome Project (Science 267, 783-4; Nature 375, 93-4), investigators are faced with the engineering chore of scaling up equipment. Three billion bases in human DNA need decoding, and the older standard format of disposable vessel—96-well plates—is generally too small for this sort of large-scale investigation.

Thus, a new 384-well format is in development. It shares the same basic V-well shape as the 0.2ml 96-well format, but density has been multiplied 4X by decreasing well-to-well distance from 9 to 4.5mm. This allows the use of the same multi-channel pipettors and automated dispensers as with the 96-well format; alternate wells are accessed in a back-and-forth fashion. MJ RESEARCH is working with others to develop disposables, and although vessels are not yet available, 384-well Alphas for PTC-200 & 225 cyclers can be ordered. Reactions must now be conducted in 96-well plates; these vessels fit the 384 block adequately, but useful reaction volume is decreased to 20μl per well.

PCR is covered by patents owned by Hoffmann-La Roche, Inc. and F. Hoffmann-La Roche Ltd. Users should obtain license to perform the reaction.

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The MJ RESEARCH NoteBook

Volume VI...No. 16 A Bulletin of Technological Advance in Molecular Biology

Spring 1996
Against the grains
Carbonaceous chondrites contain refractory aggregates of calcium-aluminum–rich inclusions that are thought to represent some of the earliest condensation products from the solar nebula. Greshake (p. 1316) found nanometer-sized oxide phases of MgO, TiO2, CaO, and Al2O3 within and between grains of these refractory aggregates. These oxides may represent primary condensates, an origin that seems to require a more complicated early evolution for these inclusions.

Coulomb steps
Nanometer-sized metal particles can have electronic energy levels that more resemble the discrete states of atoms than the bands of bulk crystals. Devices in principle be constructed that use these levels to control electron tunneling currents through barriers, thus providing a scheme for switching. In a step toward such a goal, Andres et al. (p. 1323) have built a nanoscale structure that exhibits “Coulomb staircase” behavior at room temperature. Gold nanoparticles are held on a gold surface by a self-assembled monolayer of alkane dithiols, which form a tunneling barrier. A scanning tunneling microscope tip provides the current source and the other tunneling barrier.

A welcome decline
The production of halocarbons, the main culprits in stratospheric ozone destruction, has been restricted by the Montreal Protocol and its adjustments and amendments, but much uncertainty surrounds their effectiveness. Montzka et al. (p. 1318) present evidence for an overall decline in the tropospheric abundance of halogen attributable to anthropogenic halocarbons by mid-1995, with chlorine declining since 1994 but bromine still increasing. These data suggest that if current trends continue, the abundance of reactive halogen in the stratosphere will peak between 1997 and 1999 and decline thereafter, and the ozone layer may begin to recover by the turn of the century.

More potent pollen
Cytoplasmic male sterility in plants results from mutation of a widely expressed gene encoded by the mitochondrion. The pollen is particularly affected. Fertility can be restored by the combination of two nuclear-encoded genes. In cloning one of these genes from maize, r2, Cui et al. (p. 1334; see the Perspective by Levings, p. 1279) show that it resembles an aldehyde dehydrogenase. The proposed function suggests certain insights into the metabolism of developing pollen.

Abundant ethane in comet Hyakutake
As comet C/1996 B2 Hyakutake made its closest approach to Earth, Mumma et al. (p. 1310; see the news story by Peterson, p. 1263) used the NASA Infrared Telescope to measure the volatiles sublimating from the cometary nucleus. High-resolution infrared spectroscopy focused on the water, carbon monoxide, and methane bands, but surprisingly ethane was also detected with an abundance just over half that of methane. The rare detection of relatively abundant ethane suggests that Hyakutake may have evolved through more complex interstellar ice processes.

Ties that unbind
Multiple families of transcription factors, such as the helix-loop-helix (HLH) proteins and the nuclear hormone receptor superfamily, function as homodimer or heterodimers. The Id proteins, members of the HLH family, inhibit the function of a subset of HLH proteins when they heterodimerize with them because they lack a region necessary for DNA binding. Seol et al. (p. 1336) found a somewhat analogous inhibitor for some members of the nuclear hormone receptor superfamily. SHP (small heterodimer partner) lacks a DNA binding domain and inhibits the activity of retinoid receptors and thyroid hormone receptor when it heterodimerizes with them.

Kidney disease genes
Autosomal dominant polycystic kidney disease (ADPKD) affects 1 in 1000 individuals. Renal cysts develop that can lead to chronic renal failure. The PKD1 gene, which accounts for about 85% of ADPKD cases, codes for a 4304-residue protein with a large extracellular domain and other motifs that suggest a role in cell-cell signaling. Mochizuki et al. (p. 1339) identified a second gene, PKD2, that accounts for the remaining cases of ADPKD. PKD2 is an integral membrane protein with sequence similarity to PKD1, but is significantly smaller (968 amino acids), lacks cell-cell signaling domains, and has similarity to voltage-activated calcium and sodium channels. PKD1 and PKD2 may function in the same signaling pathway.

All wrapped up
In vitro selection methods have been used to obtain RNA molecules, or aptamers, that can recognize small molecules such as amino acids. Yang et al. (p. 1343) used nuclear magnetic resonance to determine the three-dimensional structure of two RNA aptamers that differ at only 3 out of 44 positions but that can differentiate between two similar amino acids, citrulline and arginine. The amino acids are an integral part of the structure and are held in a deep binding pocket through hydrogen bonds and nonpolar interactions, rather than by binding at the surface of the RNA.

Stress stimulation
Many metabolic stresses on cells induce the activation of a signaling pathway that results in activation of the mitogen-activated protein (MAP) kinase family member called p38. Wang and Ron (p. 1347) describe a mechanism by which stress-induced activation of p38 MAP Kinase may influence cellular growth and differentiation. The p38 MAP kinase phosphorylates and increases the activity of the transcription factor CHOP. CHOP, in turn, influences the activity of members of the C/EBP family of transcription factors, which regulate expression of genes that influence growth and differentiation of some cell types.
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Tobacco Council and Research

In contrast to the statement by Brown University's Paul Calabresi (26 Apr., p. 493) in the special news report by Jon Cohen "Tobacco money lights up a debate" (26 Apr., p. 498) about research funding by the Council for Tobacco Research (CTR), this funding agency provides a "no strings attached" source of peer-reviewed funding in amounts often not obtainable from nonprofit private funding agencies. This source of funding is crucial to furthering biomedical research by allowing young investigators to start a research program and enable established investigators to begin new projects. Thus, the money is used to expand basic disease-related research, which is not different from the government using tobacco tax revenues to support socially significant programs.

To question the morality of using money from tobacco products to further disease-related research is to beg the larger question, What is the responsibility of private industry to contribute to funding basic research in an era of ever-contracting federal support? Why is there no "Council for Pharmaceutical Research" to support basic biomedical studies that are the foundation of the pharmaceutical and biotechnology industries? Although large technology-based corporations claim to have bottom-line considerations that do not allow them to invest in risky long-term basic research endeavors, it is clear from the CTR example that, when corporations see an advantage to supporting such research, funds can and will be made available. Perhaps it is time for the biomedical research community to make clear to others of the private sector that there are broad advantages to contributing greater financial support to the basic research that provides the technologies and insights from which the profits of their industries derive.

Finally, it is noteworthy that several research institutions refuse to allow their investigators to apply for CTR funding. In contrast to their high moral position, one wonders if a low indirect cost rate (15%) plays a role in their eschewing these awards.

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Mercury Stockpile

With great environmental and economic naïveté, the U.S. Department of Defense (DOD) is considering selling its mercury stockpile—60% of the world's supply. The sales would thwart scientific, regulatory, and industrial efforts to protect human and ecological health by limiting mercury release to the environment.

Individual states have long worked with industries, utilities, and the U.S. Environmental Protection Agency (EPA) to reduce, collect, and recycle mercury in industrial products and processes. European nations have taken similar actions. Sweden will phase out most mercury uses by the year 2000 and is considering permanent storage to remove mercury from global commerce (1).

The actions are in response to rising environmental mercury contamination, notably in lake fish from remote regions of

Letters
Scandinavia, Canada, and the United States. The principal source is long-distance atmospheric transport of mercury, most from anthropogenic uses (2, 3). In aquatic systems, mercury can be converted to methylmercury, a neurotoxic compound that bioaccumulates. Game fish may contain 225,000 times the mercury levels found in water (3, 4), and state health departments advise anglers to limit consumption of fish from most Upper Midwestern lakes.

Since 1970, market demand for mercury has dropped steeply, and DOD sales are likely to reduce mercury prices. This could depress the market for recycled mercury but stimulate mercury mining. Mercury mines today are subsidized by foreign governments. Typically run to maximize revenues for workers, such mines usually raise production when prices drop.

Eventually, DOD's mercury could end up in such applications as gold mining. In 1989 alone, gold mining in Brazil released 168 metric tons of mercury into the environment, most of it imported from nations that restrict mercury within their own borders (5). Because volatile mercury is likely to enter the atmosphere, DOD's stockpile will come back to haunt us. DOD's plans are not consistent with national policy to curtail environmental mercury releases.

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References

Bioethical Issues

Eliot Marshall's News & Comment article "Policy on DNA research troubles tissue bankers" (26 Jan., p. 440) and Lori B. Andrews's Letter "Genetics and informed consent" (8 Mar., p. 1346) address very important, but difficult and emotion-laden issues that lie at the intersection of patient privacy and confidentiality and the substantial public benefit that for generations has been derived from research on human tissue specimens. Such research—applying novel molecular biological approaches to tissue samples removed for medical reasons and archived in our nation's academic medical centers—provides often unique access to fundamental questions of human disease pathogenesis and generates insights that can have a powerful impact on diagnosis, treatment, prognosis, and even strategies for prevention of some of the major afflications of mankind.

The meeting described by Marshall was organized in response to concerns within a broad cross-section of the leadership of American pathology that the processes under way to examine these issues and recommend policy guidance did not have adequate representation or input from the pathology community or, for that matter, from the many other scientists engaged in such research. Accordingly, the several draft proposals that have emerged from those processes were perceived to reflect an abundance of bioethical sensitivity and perspective but a deficit of informed medical and scientific insight. In contrast to the opinion of Andrews, the proposals also were thought in some instances to impose unreasonable, impractical, and costly requirements that

Even Carl von Linné would have difficulty classifying us
were incompatible with standards of sound patient management and could well impede, or even stifle, a line of contemporary scientific inquiry of extraordinary promise.

The meeting did not lead to resolution of any of these difficult matters, but it was successful in affording some of the major stakeholders the opportunity to exchange views and share concerns. I am confident that, with further cooperative effort involving all of the parties, guidelines and regulations can be crafted that will better balance the legitimate private interests of patient confidentiality and informed consent with the compelling public interest in continuing to foster research on human tissue samples.

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Hippocampal Cell Death

In the Research News article "Is hippocampal cell death a myth?" by Ingrid Wickelgren (1 Mar., p. 1229), the relationship between neuronal number and memory decline in normal human aging is questioned on the basis of evidence from a new method of cell counting (stereology) and its application to research on rats. With that counting method, neuronal number did not distinguish between old rats with poor versus very good memory. Traditional hippocampal neuronal counts (density measures) in humans, on the other hand, have repeatedly shown a correlation with level of verbal memory.

The source of the traditional evidence is temporal lobe epilepsy patients who have undergone unilateral resection of the anterior temporal lobe and hippocampus (often ages 8 to 40 years) for the relief of drug-resistant epilepsy; hippocampal neurons are assumed to be lost because of detrimental consequences of the epilepsy. The effects on memory are asymmetrical; verbal memory level is associated with neuronal counts in the left hippocampus, the side of language lateralization in the human brain. Magnetic resonance imaging (MRI) studies have confirmed the association between laterality of hippocampal neuronal loss and memory. There is no convergent evidence yet for the stereology method, and the conclusion that there is no association between neuronal counts and memory in aging is premature.

The discrepancy between the human findings and the new counting method reported in Wickelgren's article could stem from several factors: counting methodology (1), kind of experimental subject (2), sensitivity of memory test (3), age (4), or all these factors and others (5). We must await the application of the new method to human subjects who undergo sensitive memory tests before generalizing the findings on rats to the relationship between memory and neuronal cells in the human hippocampus.

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References

Wickelgren's article was balanced and well written, and raised some highly important questions. Certainly, the work of Mark West...
Peter Rapp, Michela Gallagher, and their colleagues (1) cited in the article is of high quality and has a sound theoretical basis. Nevertheless, there are a number of unresolved experimental issues which suggest that caution is warranted before one reaches the conclusion too quickly that age-related cell death in the hippocampus is a myth.

The negative findings about cell death described in the article were based either on autopsy material or on a different strain of rat from that (F344) usually studied in aging research. In addition, the results are based on quite small samples of subjects (for example, n = five per group) and limited amounts of tissue. The general theory underlying the "new stereology" of the disector and fractionator methods has been clearly validated, but it should be emphasized that, in these specific studies, the analysis relies on a random sampling method that counts very few neurons per subject (100 to 200) within a structure that is not uniform throughout in cell density. Also, the optical fractionator method samples small fractions and relies a great deal on experimental skill, because the investigator or technician who performs the counts must distinguish neurons from glia and keep careful track of which cells have been counted. With this disector method, no photographic records are available to double-check the counts. The quality of tissue preservation of autopsy material varies enormously, which could influence, among other factors, the ability to evaluate cell type and, consequently, the accuracy of counts. The normal aging changes in hippocampal density previously reported were subtle, being on the order of 20 to 30%. Therefore, tissue variability or small samples, or both, could substantially affect detection of these differences. Rat strains also differ considerably in their rates and patterns of aging; moreover, behavioral performance in a maze, which was used to separate the groups in the study by Rasmussen et al. (2), may be influenced by several factors other than cell loss, including dendritic atrophy, synaptic loss, or excitability changes. These are all important technical issues that should be evaluated systematically before the initial results are generalized too widely.

Numerous studies, including several by some authors of this letter, have found aging-related reductions in hippocampal neuronal packing density [see, for example (3)], but studies of hippocampal volume in aging rats (4) have found little evidence of the substantial increases in hippocampal volume that would be needed to account for such density changes if cell loss had not occurred. It should also be noted that reactive glia and other signs of neuronal damage consistent with cell loss are found in normal hippocampal aging in humans and rats, and West did observe loss of cells in human subiculum, which is closely related to the CA1 field. In addition, one of the primary effects of brain aging appears to be to enhance the vulnerability of neurons to other neurotoxic conditions. Thus, aging-related cell loss may not be apparent in all species, strains, or individuals, depending on the other influences present. For example, aging is the major risk factor for the extensive hippocampal neuron loss seen in Alzheimer's disease, suggesting an interaction of aging changes with the neurodegenerative-disease process.

Few in our field think that age-related memory loss depends solely on cell death. Although memory loss is presumably worse after cell death, the death of the cell is generally seen as the final "denouement" of a long phase of declining function (accompanied by memory impairment) during which it is possible that neurons could be "rescued."

Philip W. Landfield
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References

Recent research suggests that loss of hippocampal pyramidal cells may not occur in normal aging, forcing the question as to what does change in the aging hippocampus that may underlie age-related memory loss. In this context, it is important to note that strong evidence for an alternative to the cell-death explanation has been known for some time. Studies involving iontophoretic application of neurotransmitters to hippocampal pyramidal cells in aging rats clearly demonstrate reduced responsiveness of these cells to two neurotransmitter agents heavily implicated in memory processes: acetylcholine (1) and met-enkephalin (2). These changes in neural responsiveness with age may be the mechanism behind the “disruption of cells’ ability to communicate chemically” that “could underlie a fading memory.” The death of the “cell death” hypothesis may give birth to a renewed interest in neural changes such as those that occur in the normal aging hippocampus.

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2. H. J. Haigler, L. F. Cahill, M. R. Crager, E. Charles,  

Corrections and Clarifications
The caption for the illustration accompanying the 17 May Perspective “Stratospheric control of climate” by Alan Roback (p. 972) should have begun, “Surface air temperature anomalies over North America for December 1982 through February 1983.”

The ScienceScope section of the issue of 26 April (p. 473) was edited by Jocelyn Kaiser, not Richard Stone, as stated.

In the affiliation given for R. M. Zinkernagel (Letters, 3 May, p. 635), “Universität Zürich” was inadvertently omitted.

Letters to the Editor
Letters may be submitted by e-mail (at science_letters@aaas.org), fax (202-789-4669), or regular mail (Science, 1200 New York Avenue, NW, Washington, DC 20005, USA). Letters are not routinely acknowledged. Full addresses, signatures, and daytime phone numbers should be included. Letters should be brief (300 words or less) and may be edited for reasons of clarity or space. They may appear in print and/or on the World Wide Web. Letter writers are not consulted before publication.
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Getting old. NSF needs advice on upgrading solar telescopes such as this one in New Mexico.

Taking Stock in Solar Astronomy
A host of new international solar projects in space and on Earth has made the sun a hot research topic (p. 1264; Articles). But the ground-based telescopes needed to support this work are becoming obsolete, and in U.S. universities, the outlook for solar physics is hazy. So the National Science Foundation (NSF) is hoping the National Academy of Sciences (NAS) will conduct a study on what's needed to keep the field strong.

For most ground-based observations, the country's several hundred solar physicists and astronomers rely on a half-dozen solar telescopes run by the National Solar Observatories (NSO), which gets about $3.4 million for the instruments from NSF and $700,000 from NASA and the Air Force. But NSO's telescopes haven't been upgraded since 1972, and the few run by universities are closing or barely staying afloat. Supporters say the field has lost out to nighttime astronomy, whose results are more likely to catch the public's eye.

The NAS study would be intended to tell NSF how to make the most of its ground-based solar physics budget, perhaps by consolidating facilities. A second issue, says NSF astronomy division director Hugh Van Horn, is whether the scientific community should be concerned about the dwindling supply of U.S. solar physicists. The field is thriving in Europe and Japan, but traditional U.S. strongholds such as the University of Hawaii and the California Institute of Technology have cut positions. "Is it really just a matter of transferring expertise [to other universities], or are we seeing a downturn that's a serious thing for the nation?"

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Ocean Research Bill Steams Ahead
A plan to give at least $20 million to the Navy for oceanographic research involving partnerships with academia and industry is sailing through Congress and seems likely to become law this year.

This month the House voted to create the National Oceanographic Partnership Program as part of a bill to authorize 1997 spending levels for the Department of Defense (DOD). The bill is now pending before the Senate. Although President Clinton has threatened to veto the $267 billion defense bill because it would give DOD $12 billion more than he requested, the research partnership program enjoys bipartisan support and is expected to survive any legislative compromise. "Our goal is to sanction partnerships and set up a structure for them within the framework of meeting national security needs," says a congressional aide. "The oceanographic community will take it from there."

The program, backed by the university-based Consortium for Oceanographic Research and Education, drew favorable comments from several top Administration officials during a House hearing earlier this year (Science, 2 February, p. 591). The legislation would make the secretary of the Navy head of a policy-making council that includes top officials from the National Oceanic and Atmospheric Administration, the National Science Foundation, NASA, and the National Research Council. Although the bills differ in the level of proposed funding—$30 million in the House version and $20.5 million in the Senate—both include money for a peer-reviewed grants program, ship time on the U.S. academic fleet, and an ocean-sensing database.
Cutting Red Tape With Plastic

Give a government scientist a credit card and authorization for a shopping spree—and the government will save a huge amount of money. That’s the lesson from a pilot program at the U.S. National Institutes of Health (NIH) that allows scientists to sidestep some of the usual procedures. One researcher saved almost $245,000 on a single item.

Last year, Victoria Puck at NIH’s National Center for Human Genome Research (NCHGR) in Bethesda, Maryland, received a government-issued credit card that authorized her to buy any lab or office item costing $2500 or less. Puck, who is also a physician, took it to a discount pharmacy, where she was able to obtain a year’s supply of interleukin-2, an immune messenger used in research but also available commercially for boosting the immune systems of people undergoing certain types of chemotherapy. Normally, Puck would have had to fill out government requisition forms, get them approved, and then wait, perhaps weeks, for her order. But at the pharmacy, she simply bought an annual supply of interleukin-2 for $2500—about 1% of what the stuff would cost from a scientific supply house. The pharmacy sold her a bulk order while suppliers provide only single-unit packages, which add up to about $250,000 over a year, explains NCHGR geneticist Jeffrey Trent.

Puck is one of 30 NIH researchers who have spent some $1.23 million on 2500 purchases over the past 9 months by flashing their plastic. The experiment, part of the Administration’s attempt to “reinvent” government, is being conducted in many federal agencies, says Donald Kemp, who oversaw the NIH credit card program.

Savings have been phenomenal. Researchers are buying common items, such as plastic containers, at local stores for about a tenth their cost at these scientific suppliers. And some of those suppliers have dropped prices by 10% because they’re getting paid more promptly, says Trent.

The one snag comes at the end of the month, when the purchasers and then their supervisors have to verify the items on each credit card statement. But Kemp says there are plans to automate this—and then many others at NIH can have their own piece of plastic.

Lilliputian Topography

What does the world look like to the inhabitants of leaf surfaces? To a fungus the surface may seem like the American West, with microbial equivalents of the Rockies or California’s San Francisco Valley.

Ecologists may soon be gaining a fungus-level view of these microscopic landscapes with the aid of a tool developed primarily for materials science, the atomic force microscope (AFM). Biologist Wendy Mechaber of the University of Arizona, Tucson, and her colleagues have adapted the scope—whose tip rides over the surfaces of atoms like the needle on a phonograph record—to scan the undersides of cranberry leaves. In the 14 May Proceedings of the National Academy of Sciences, the scientists note that hilly leaf undersides erode with time, an environmental change never noticed before, and one that could explain why some leaves are more prone to microbial colonization than others.

Mechaber and her colleagues at Tufts University in Medford, Massachusetts, began atomic-scale examinations of leaves while she was a grad student there. She first used a scanning electron microscope (SEM), but it distorted the height dimension, so she decided to try AFM, which portrays depth well. She mapped the topography of five young and four old leaves. New leaves had broad plates along their surfaces, bounded by narrow, steep ravines at leaf cell boundaries. In older leaves, those ravines had broadened, leaving just peaks of the plateaus behind, Mechaber and her colleagues report. “You’re seeing what’s left after a lifetime of exposure to the environment,” she says.

“One small success is to look at the leaf on the scale that would matter to a bacteria or a fungus,” says theoretical ecologist Timothy Allen from the University of Wisconsin, Madison. In narrow grooves, for example, he says, moisture may build up, creating dampness encouraging to fungal infections. “There’s a real good chance we’ll get a whole new class of insights,” says Allen.

Eye on EPA Science

In the latest of a series of moves to bolster the science behind its rules, the U.S. Environmental Protection Agency (EPA) is setting up a new board of outside advisers to (continued on page 1271)
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take stock of its labs and research programs.

The EPA already has a science advisory board whose main purpose is to review big reports such as the agency's dioxin assessment. Now in-house research conducted by the Office of Research and Development (ORD) will also be subjected to outside scrutiny. The board will assess EPA internal research programs, visit labs, make recommendations, and help develop standards for evaluating scientists' performances. ORD officials are still finalizing the list of board members, but hope the group will hold its first meeting in July.

Gene Modulates Prostate Cancer Risk

Most of the known genetic defects that increase the risk of cancer are "digital"—one either carries the defect or one doesn't. Now, however, researchers at Boston's Dana-Farber Cancer Institute have discovered an "analog" risk factor for one kind of cancer. It's a genetic stutter of varying lengths that may raise or lower a man's chances of developing prostate tumors.

The stutter is in the gene encoding the androgen receptor molecule, according to Philip Kantoff, who presented his group's results at last week's meeting of the American Society of Clinical Oncologists in Philadelphia. Male hormones such as testosterone bind to the receptor, which leads to the activation of certain genes in prostate gland cells. Several years ago, researchers found that the androgen receptor gene contains a three-nucleotide sequence, CAG, that repeats between 11 and 33 times in different men. It acts like a volume control—the fewer repeats, the more effectively the receptor molecule transmits its "on" signal.

Kantoff and his colleagues have now found that the stronger this signal, the higher the risk of prostate cancer. Using blood samples collected as part of the 22,000-member Physicians' Health Study, they compared CAG repeats carried by 591 physicians with prostate cancer to those in an equal number of healthy controls. For every six fewer repeats, Kantoff found, a participant's risk of prostate cancer increased 30%. The effect was largest among the 269 physicians with the most aggressive tumors: a 70% increase in risk for each decrement of six repeats.

"This is not another BRCA1," says Kantoff, referring to a defective tumor-suppressor gene implicated in breast cancer. Rather, he says, it's a continuous variable, comparable to high cholesterol as a risk factor for heart disease. "It's a credible and fascinating observation," says William Catalona, a urologist and prostate cancer researcher at Washington University in St. Louis. "One of the things we really need is a marker for tumors that... need to be treated aggressively, and for other tumors that can be left alone. This does have that possibility."

Age of Asteroids?

Two years ago, after comet Shoemaker-Levy slammed into Jupiter, astronomers warned that the same thing could happen to Earth. It hasn't yet—but two asteroids swung by our home planet this very month, with one coming near enough to count as an astronomical close shave. On 19 May, the 150-meter-wide asteroid 1996 J1A1 passed within 453,000 kilometers of Earth, scarcely farther away than the moon and the sixth-closest asteroid approach on record. J1A1, discovered on 13 May by University of Florida astronomy graduate student Timothy Spahr, will return every 4 years, but won't come nearly as close again, scientists say.

Another asteroid, 1996 JC, was first sighted on 8 May by astronomer Robert H. McNaught of the Siding Spring Observatory in New South Wales, Australia. It passed within 3 million km of Earth on 24 May. Both asteroids could have made a considerable impact on Earth if their courses had been just a little bit different, says David Kring, an astronomer at the University of Arizona. "If they had hit Washington, D.C., or New York City, there wouldn't be anything left of those cities," he notes. The odds of a 1.4-km asteroid hitting Earth have been put at 1 in 3000 per 100 years. So "it is unusual to have within a single month two very close approaches," says Gareth Williams, associate director for the Minor Planet Center in Cambridge, Massachusetts. The asteroids triggered a buzz among Internet astrobuffs, with some wondering why they went unnoticed for so long. Williams explains that astronomers have spotted less than 10% of the 1-km objects that cross Earth's orbit; amateurs find the rest.

Ancient Ancestor—New Name

Another human ancestor has turned up in Africa—or at least an ancestor by another name. In January 1995 paleoanthropologist Michel Brunet of the University of Poitiers found a 3-million-plus-year-old partial lower jawbone in Chad. It was preliminarily named Australopithecus afarensis, the same species as the famous "Lucy" skeleton found in Ethiopia 2400 kilometers to the east (Nature, 16 November 1995). But Brunet and his colleagues suspected it to be a new species (Science, 17 November 1995, p. 1117).

It turns out Brunet was right. Last Monday, he told a group of scientists at the Musée de l'homme in Paris that it ranks as a new species: Australopithecus bahrelghazalia. His colleague David Pilbeam of Harvard University explains that analyses have demonstrated that "the combination of features in the Chad mandible differs from all known Plio-Pleistocene hominids."
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Vignettes: Career Economics

Is a Harvard education more valuable than an education from Clinch Valley Community College because of its professors' skills and efforts or because of the students' skills and efforts? There is little market at universities for so-called good teachers. That is, whatever investments a professor makes in being a good teacher is specific to the university and cannot be exported or capitalized in the market. Moreover, the professor is not able to capture any of the residual that accrues to the students in the form of increased earnings. There is an analogy with the theory of the firm in that the owners are the ones who monitor the inputs because they own the specific capital that is at risk if there is shirking or a diminished brand-name. A research professor, on the other hand, invests in capital that is more general and can be exported in the market. That is, if a university experiences a decline in its reputation and financial base, research professors can still maintain a return on their capital by moving to another university.


The aging scientist might decide to reallocate research and writing time to administration. . . . This tendency will be accelerated if his accumulated experience enables him to obtain a high salary in an administrative post. By raising his potential earnings in an alternative activity (administration), experience increases the opportunity cost of his remaining a researcher. Another thing that increases that cost is—success. Successful scientists and other successful creative people are invited, sometimes even badgered, to give prestigious lectures, accept honorary degrees, serve on boards and committees, consult, advise, write popular papers, give memorial addresses, appear on television, write letters of recommendation, and so forth, and to the extent that they yield to these importunities, as most of them do (because these activities produce psychic and sometimes pecuniary income), they have less time for research. A partially offsetting factor is that the successful, prominent person is in a better position to obtain criticisms from able people; indeed, his success, his prominence, may make him a target for criticism—which he can learn from, if he does not dismiss it as a product of envy. But that is what he is apt to do. I am led to predict that creative people who remain obscure throughout their lifetime will reach their creative peak later than those who are successful in their lifetime.

—Richard A. Posner, in Aging and Old Age (University of Chicago Press)
from early dispersed H. erectus, dated 1.6 to 1.8 Ma, to anatomically modern Homo sapiens. The mtDNA data embrace much more recent times, the last 200,000 years in the prevailing view.

In my article (1), I quoted the conclusion of Goldstein et al., derived from the analysis of 30 DNA polymorphisms, that the deepest split separating African from non-African populations occurred 156,000 years ago (2). But I also quoted estimates for the origin of anatomically modern humans, derived from mtDNA, of 200,000, 143,000, 298,000, and 622,000 to 889,000 years ago; and estimates derived from Y chromosome studies of 270,000, 168,000, and 37,000 to 49,000 years ago. I did not favor any particular date, but rather pointed out that the discrepancies underscore "the need for more extensive and accurate data" (1).

I do not find it surprising that disparate estimates exist for the origin of anatomically modern humans or for the split between African and non-African populations. The estimates depend on many uncertainties, including the assumption that rates of molecular evolution are constant and that we know precisely enough what rate to apply in each particular case. Rather, what I find surprising is the "assurance with which some molecular evolutionists assert the precise dates they infer from their analyses." (3).

Templeton states that he knows of "no evidence for a split" between African and non-African populations. But there is plenty of evidence. Cavalli-Sforza et al. (4), for example, have analyzed 120 genes in 42 populations broadly representative of the world, and shown a deep split between African and non-African populations. The split is statistically robust, present in about 83% of bootstrap replications. When the 42 populations are collapsed into nine compact clusters, the bootstrap value rises to 98%. Perhaps Templeton would argue that this split and other evidence is not conclusive of the African replacement hypothesis (because the split can also be explained by models that assume restricted gene flow between populations); this happens to be my view as well. The weight of evidence, I wrote, favors a recent African origin for modern humans, but the replacement may not have been complete everywhere. Many uncertainties remain, so that only the future will "provide more definitive and precise answers" (1).

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REFERENCES

15 February 1996; revised 23 February 1996; accepted 2 April 1996

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The AAAS–Newcomb Cleveland Prize is awarded to the author of an outstanding paper published in Science. The value of the prize is $5000; the winner also receives a bronze medal. The current competition period began with the 2 June 1995 issue and ends with the issue of 31 May 1996.

Reports, Research Articles, and Articles that include original research data, theories, or syntheses and are fundamental contributions to basic knowledge or technical achievements of far-reaching consequence are eligible for consideration for the prize. The paper must be a first-time publication of the author's own work. Reference to pertinent earlier work by the author may be included to give perspective.

Throughout the competition period, readers are invited to nominate papers appearing in the Reports, Research Articles, or Articles sections. Nominations must be typed, and the following information provided: the title of the paper, issue in which it was published, author's name, and a brief statement of justification for nomination. Nominations should be submitted to the AAAS–Newcomb Cleveland Prize, AAAS, Room 1044, 1200 New York Avenue, NW, Washington, DC 20005, and must be received on or before 30 June 1996. Final selection will rest with a panel of distinguished scientists appointed by the editor-in-chief of Science.

The award will be presented at the 1997 AAAS annual meeting. In cases of multiple authorship, the prize will be divided equally between or among the authors.
The following reports were presented at the AAAS Council meeting on 11 February in Baltimore:

**Report on Board Actions**

AAAS President Rita Colwell presented highlights of Board actions in the past year. She noted that the Board had selected Floyd Bloom as the new editor-in-chief of *Science* and that his vision for electronic enhancements would help to lead the journal into the future.

Colwell talked about AAAS concerns regarding decreased federal funding for science and technology and the Board-initiated resolution in support of continued strong funding for science and technology. She noted that the resolution was approved by AAAS affiliates and forwarded to the President and Congress. Colwell said that the Science and Policy Directorate was playing an important role in providing updated analyses of budget information and in hosting several briefings on the budget actions by Congress.

Colwell reported that the Board had approved an initiative for young scientists and that "Science's Next Wave," an online journal that addresses the career concerns of the next generation of scientists, had been launched.

Finally, she indicated that the Board had been very involved in decisions relating to building the new AAAS headquarters, scheduled for completion in spring 1996.

**Report of the Committee on Sections**

Jane Lubchenco, who chairs the Council's Committee on Sections, reported on the group's activities. She reminded the group that this was a new committee, formed at last year's meeting as a result of a recommendation by the Section Task Force. She said the group was focusing on issues related to section budgets, fellowships, procedures, and improved communications.

Lubchenco noted that the group was serving an important purpose as a forum for discussion of section-related matters, and said the committee welcomed input from Council members and section officers.

**Report on Science**

Ellis Rubinstein, editor of *Science*, reported on new initiatives. He spoke about efforts to increase the international dimensions of the journal, in both news coverage and solicitation of high-quality manuscripts. He noted the creation of a *Science* office in Cambridge, the hiring of more international correspondents, and the use of more international scientists as reviewers and members of the Board of Reviewing Editors.

Rubinstein introduced the recent AAAS experiments in electronic publishing. He noted that the electronic components of the magazine, called "Science Online," were being produced in cooperation with HighWire Press of Stanford University. Rubinstein reviewed the on-line features, which include "This Week in Science," the "Table of Contents," summaries of news stories, on-line forums, and "Beyond the Printed Page." He also discussed experimental plans for future special features, including an electronically enhanced "Perspectives" section with hyperlinks to research citations.

Rubinstein also described "Science's Next Wave," created to deal with career concerns of the next generation of scientists. Among the features he described were essays on alternate career options, on-line forums and discussion groups, and a global network of young scientist correspondents.

**Overview of AAAS Activities Related to Federal Budget**

Nan Broadbent, director of the AAAS News and Information Office, and Al Teich, director of the AAAS Science and Policy Directorate, spoke about AAAS's efforts to keep the science and engineering community informed about the impact of proposed federal budget reductions and outyear projections during protracted budget process.

**Resolution on Government Shutdown**

Whereas the strength of U.S. science and engineering contributes greatly to the nation's well-being and its international leadership; and

Whereas appropriations-related closures in the operation of federal agencies that support and conduct scientific and engineering research caused significant disruptions in programs for science and engineering research and education, including seasonal, longitudinal, and time-dependent studies;

Whereas such interruptions not only caused delays but risked permanent damage to the value to society of these research studies and loss of the taxpayers' investment in producing such knowledge;

Therefore be it resolved, that the American Association for the Advancement of Science deplores the interruption of normal government functions in support of science and engineering research and education and calls upon Congress to abjure any further use of tactics that interrupt them; and

Further be it resolved, that the Association calls upon the Congress and the President to complete promptly appropriations legislation that funds scientific and engineering research and education programs on their merits and without extraneous conditions.

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Gretchen Seiler
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**PRODUCTS & MATERIALS**

**Near-Field Optical Force Sensor**

A novel multifunctional probe uniquely resolves the problems of near-field super-resolution optical imaging while fully integrating such imaging into all conventional scanner probe microscopes. The aim of these near-field optical elements is to readily allow subwavelength points of light to be brought within the near-field of a surface that is to be interrogated in conventional scanned probe microscopes. The new design permits the capabilities of super-resolution near-field optical imaging to be extended to the growing community of scanned probed microscopists. In the past, if one wanted to obtain near-field optical images it was necessary to struggle with the limitations of simple tapered-glass optical elements. The new advance involves a cantilevered structure in which the fiber tip is bent and coated so that light can be transmitted to the tip with the same efficiencies as those of conventional, straight, tapered near-field optical elements. Nanomics. Circle 138.

**PCR Template Preparation Dipsticks**

IsoCode Stix are blood collection dipsticks for isolation of DNA prior to polymerase chain reaction (PCR). High quality DNA can be isolated in less than 35 min inexpensively and reproducibly, without the use of hazardous reagents and with consistent results from locus to locus. A matchbook-like configuration contains four dipsticks, each with a perforated triangle at the end that serves as the area for collection of 10 to 12 μl of blood. Upon elution, blood components that inhibit amplification, such as hemoglobin, remain on the matrix when the DNA is released. Eluted DNA is suitable for both standard and long-range PCR. IsoCode Stix can be used with heparin- and EDTA-treated blood. Schleicher & Schuell. Circle 139.

**Immunomagnetic Particles**

The MagNIM product line is a series of sub-micron-sized, coated immunomagnetic particles for the isolation and purification of rare cells, subcellular components, nucleic acids, and macromolecules, and for enzyme-linked immunosorbent assay applications. Antibodies coupled to these particles will bind to specific sites on cells. The targeted materials with the magnetic particles are separated out of solutions by way of an external magnetic field. The separated magnetic particles are captured in the flux lines of the magnetic field inside a vessel, test tube, or flow cell until the magnetic field is removed, when the particles lose their magnetic properties and resuspend with the purified targeted materials. Cardinal Associates. Circle 140.

**High-Speed Cell Sorting**

The Turbo Sort Option is a high-speed cell sorting module for the FACS Vantage flow cytometer system. The option provides researchers with the necessary speed, purity, and cellular viability to sort rare cell populations. The option is also available as an upgrade for the FACSStar-plus flow cytometer. Becton Dickinson Immunocytometry Systems. Circle 141.

**DNA Probe Assays**

PathoGene DNA Probe Assays detect and identify a wide range of infectious agents.

Newly offered instrumentation, apparatus, and laboratory materials of interest to researchers in all disciplines in academic, industrial, and government organizations are featured in this space. Emphasis is given to purpose, chief characteristics, and availability of products and materials. Endorsement by Science or AAAS is not implied. Additional information may be obtained by circling the appropriate number on the Readers’ Service Card and placing it in a mailbox. Postage is free.