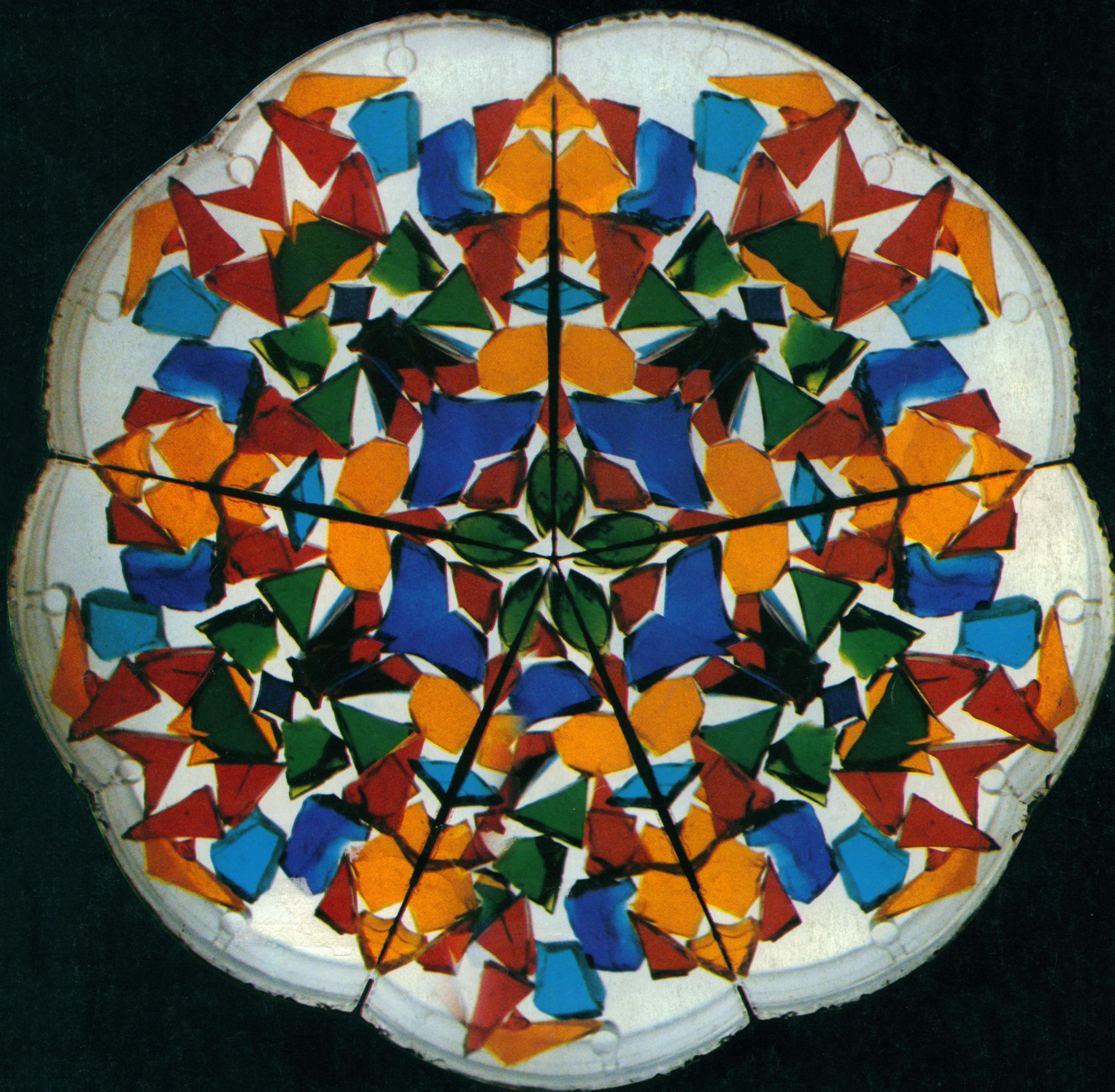


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SCIENCE

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DNA Synthesis Made Easy

The System 1 Plus DNA Synthesizer is the latest advancement in DNA synthesis. It uses the popular IBM-PC as its interactive graphic controller, and makes the synthesis of single-stranded DNA easier than ever before. Even operators unfamiliar with DNA synthesis can move smoothly through the program.

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Once synthesis has begun, you can use the IBM-PC for

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Simple to Buy

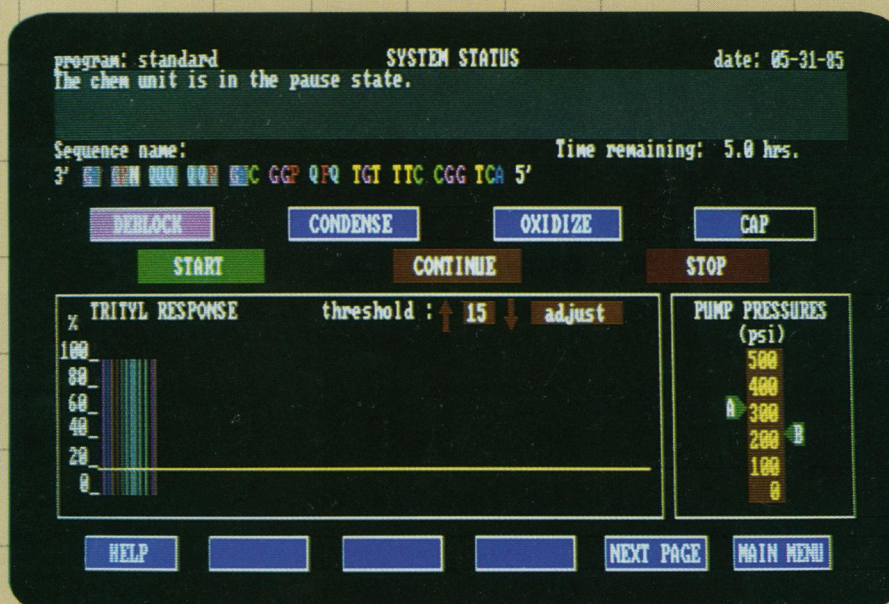
System 1 Plus makes DNA synthesis easy, with repetitive yields greater than 98%, less than 15-minute cycles, and low operating costs. Beckman makes it easy to purchase with an introductory package that will surprise you. Ask your Beckman representative for details, or write: Beckman Instruments, Inc., 1050 Page Mill Road, Palo Alto, CA 94304.

The system status screen is used to start a synthesis, and can be easily accessed at any time.

It displays the sequence entered, with the current base position highlighted.

Color-coded lines give an immediate graphic display of coupling efficiency and selected threshold level is indicated.

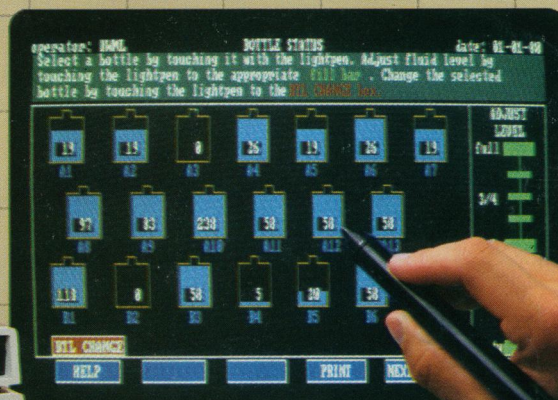
Help is always available simply by touching this box.



Time remaining in the synthesis is indicated to the minute.

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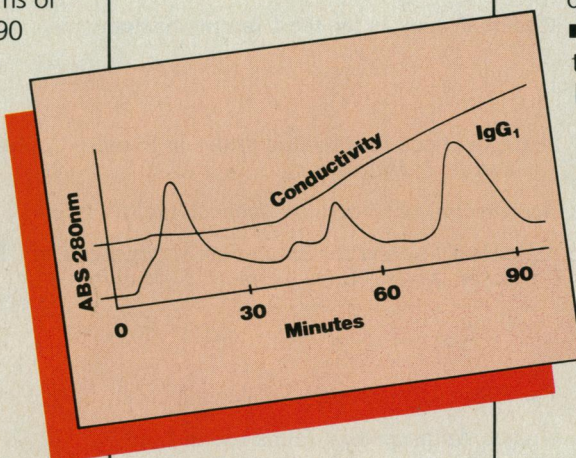
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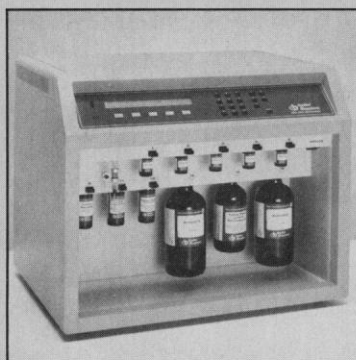
COVER

Kaleidoscope pattern used in testing human memory. Lists composed of kaleidoscope patterns were about as difficult for humans to recognize as were lists of travel pictures for pigeons and monkeys. They allowed for direct comparisons among species, and some striking similarities in list memory processing were revealed. See page 287. [Anthony A. Wright, University of Texas Health Science Center, Houston, Texas 77030]

BIOSYSTEMS UPDATE

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Soot in the troposphere

Particles in the troposphere (the atmospheric region extending upward from the ground for 10 to 20 kilometers) absorb four times as much light as expected; Clarke and Charlson suggest that the primary absorber is soot (page 263). At the Mauna Loa Observatory in Hawaii, where the background aerosol was expected to be relatively free of pollution, particles from the troposphere were collected and their light-absorbing and -scattering properties measured. Coarse particles consisted of Asian dust and other materials from the earth's crust. Fine particles included the light-absorbing species and the dominant (by mass) nonabsorbing sulfur-containing components. Hemispheric rather than local transport of combustion-derived particles into the troposphere may be occurring; the persistence of the particles must be taken into consideration in climate models.

Enhancer of bacterial virulence

Staphylococcus aureus—a bacterium that can cause severe infections, endocarditis, osteomyelitis, pneumonia, and arthritis—may share with metastasizing cancer cells and circulating cells of the immune system a mechanism for moving into and out of the bloodstream (page 275). Lopes *et al.* found that *S. aureus*, like those cells, has surface receptors for laminin, about 100 binding sites per organism. Laminin is an important protein of the membrane layer lining blood vessels and other epithelial tissues. If attachment to laminin helps cells move through the body to establish new sites for infection, disease, or immune responsiveness, the presence of laminin receptors on the *S. aureus* surface may contribute to this organism's extreme virulence. *Staphylococcus epidermidis*, a close relative of *S. aureus*, lacks laminin receptors and is not virulent.

Suppressed receptors in the pituitary

Steroid hormone receptors are found on cells of the pituitary gland's intermediate lobe only when normal suppressive factors are removed (page 277). The pituitary gland, situated at the base of the brain, is attached by a stalk to the hypothalamus from which it receives signals. The pituitary or "governing" endocrine gland of the body secretes hormones that regulate other endocrine organs; it is thus vital to growth, maturation, and reproduction. Antakly *et al.* showed that receptor expression on intermediate lobe cells developed only when cells were isolated from the influences of the hypothalamus. In contrast, cells of the anterior lobe have active surface receptors and are responsive even when in the pituitary. Studies of suppressed receptors in the pituitary may help explain mechanisms of hormone resistance in other normal and cancerous tissues that also have the required receptors.

Similarities of myelin and viral proteins

Neurologic complications that sometimes follow vaccinations against viral diseases (such as Guillain-Barré syndrome that paralyzed some people who had received swine flu shots) or viral infections (such as measles encephalitis) may occur because antibodies or immune cells made in response to the virus react with and damage proteins of the host's nervous system (page 282). Such immunologic cross-reactivities could occur if viral proteins and proteins of the nervous system have structural similarities. Jahnke, Fischer, and Alvord did a computer search of primary structures (amino acid sequences) to compare sequences in a library of almost 3000 proteins with those of the human myelin proteins that form part of the protective sheath around the nerves. Sequences of ten amino acids in length were studied since they are not too small to induce encephalitis experimentally and a number of immunologically important regions of myelin are contained in regions roughly this length. Measles, Epstein-Barr, influenza, and other viruses were found to have proteins with sequences homologous to portions of myelin.

Brain cells and nerve growth factor

Alzheimer's disease and Huntington's chorea, two degenerative diseases of the nervous system, are characterized by death or dysfunction of brain cells (page 284). Among the affected cells are cholinergic neurons that contain an enzyme, choline acetyltransferase (ChAT). A decrease in ChAT activity in the corpus striatum region of the brain has been a consistent marker of Huntington's chorea. Mobley *et al.* found that injection of nerve growth factor (NGF) led to increased ChAT activity in corpus striatum cholinergic neurons of rats. NGF, which also increases ChAT activity in brain regions altered in Alzheimer's disease, may be implicated in the functioning of cholinergic neurons as well as in degenerative disorders of these cells.

Memory

The easiest item to remember in a series is either the first or the last (page 287). The length of the interval between exposure to the series and the cue given to remember an item determines which will be the easiest to remember: if the interval is short, it is the last item (recency effect); if long, it is the first item (primacy effect); and for intermediate length intervals, both the primacy and recency effects operate. Wright *et al.* found that the memory process was the same in humans shown kaleidoscope patterns (cover) and monkeys and pigeons shown travel slides. The major difference among the species was the length of time—shortest for pigeons and longest for humans—required for the primacy effect to appear and the recency effect to disappear.

SCIENCE / SCOPE

A new technique may expand the use of lasers in commercial and military applications. The approach, called optical phase conjugation, is considered a major advance in optics because it offers a solution to distortion problems that have limited the use of lasers. When a laser beam passes through a turbulent atmosphere or a severely strained optical component, the beam is distorted and the information it carries is degraded. Hughes Aircraft Company's technique, however, forces the laser to retrace its path through the distorting medium so the beam emerges free of distortion. The method eliminates the need for complex electro-optical and mechanical components to correct the distortions.

A future generation of infrared "eyes" for space surveillance systems will be far more capable as the result of technology advances at Hughes. These systems will be able to see distant targets in space, in the air, or on the ground—and relay data instantly to ground stations. Advances are being made in focal plane design, signal processing architecture, and in the design of a unique sensor with very steady telescoping optics. By building modularity and programmability into the new technologies, researchers are making it possible for systems to use tailored combinations from a single family of hardware and software. For its advances, Hughes received an Award for Technical Achievement from the Strategic Technology Office of the Defense Advanced Research Projects Agency. This effort was sponsored by DARPA and monitored by the U.S. Air Force Space Technology Center.

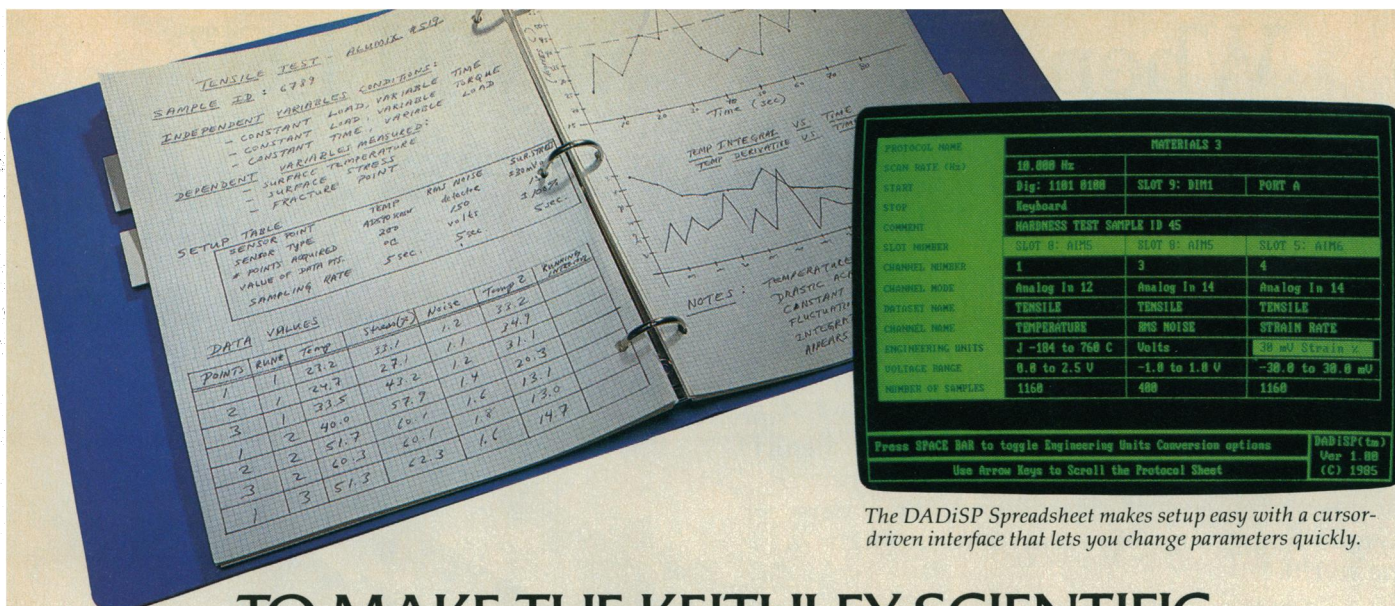
A laser that won't cause blindness or other eye injuries will be used in a rangefinder now under development by Hughes for the U.S. Army. The lightweight device, designated the AN/PVS-6 Mini Eyesafe Laser Infrared Observation Set (MELIOS), resembles a binocular case. Its neodymium yttrium aluminum garnet laser beam is sent through a chamber, or cell, filled with high-pressure methane gas. There the 1.06-micron wavelength is transformed into a wavelength of 1.54 microns. The new signal is safe because it never reaches the retina, but instead is absorbed in the vitreous humor, the white area of the eye between the retina and the lens. MELIOS is being developed under a competitive contract from the U.S. Army Night Vision and Electro-Optics Laboratory.

Large ceramic circuit boards will be built into the Amraam missile to help keep the missile reliable, lightweight, and low in cost. These boards, measuring 5x7 inches, are used instead of standard printed wiring boards where many components must be crammed into a small space and where a lot of heat must be dissipated. The cost of these circuit boards has been lowered significantly by replacing gold circuits with copper. The boards are manufactured by a thick film process in which layers of copper and glass dielectric are alternately applied to provide a multilayer circuit board. Hughes designed and developed the advanced medium-range air-to-air missile for the U.S. Air Force and Navy. The manufacturing facility is located in Tucson, Arizona.

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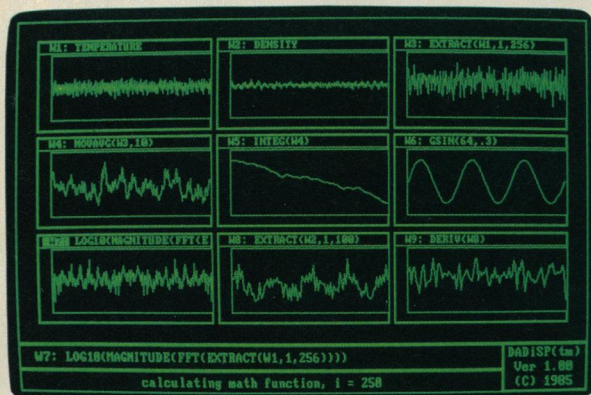
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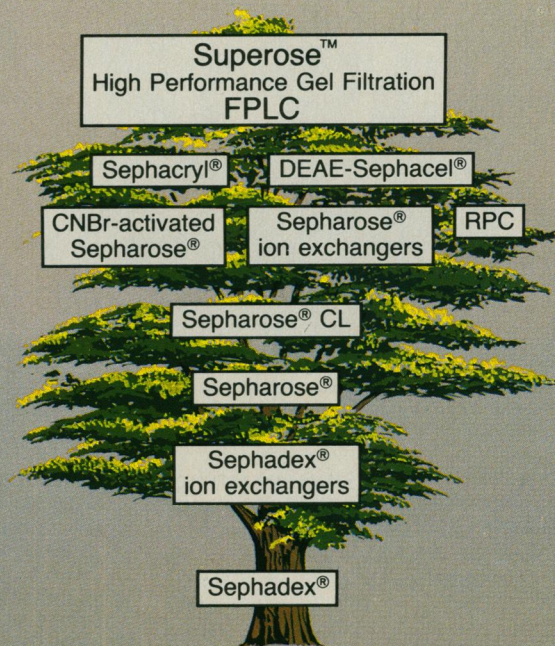
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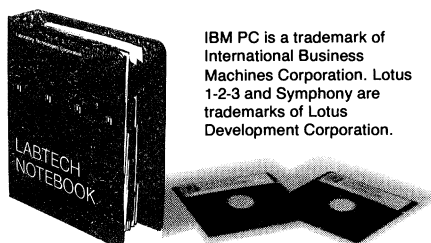
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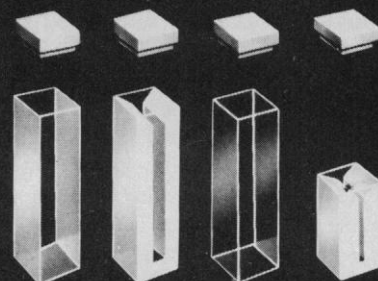


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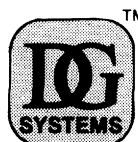
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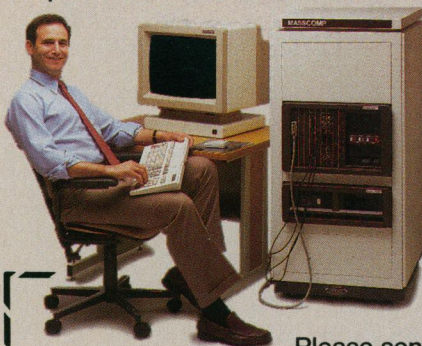
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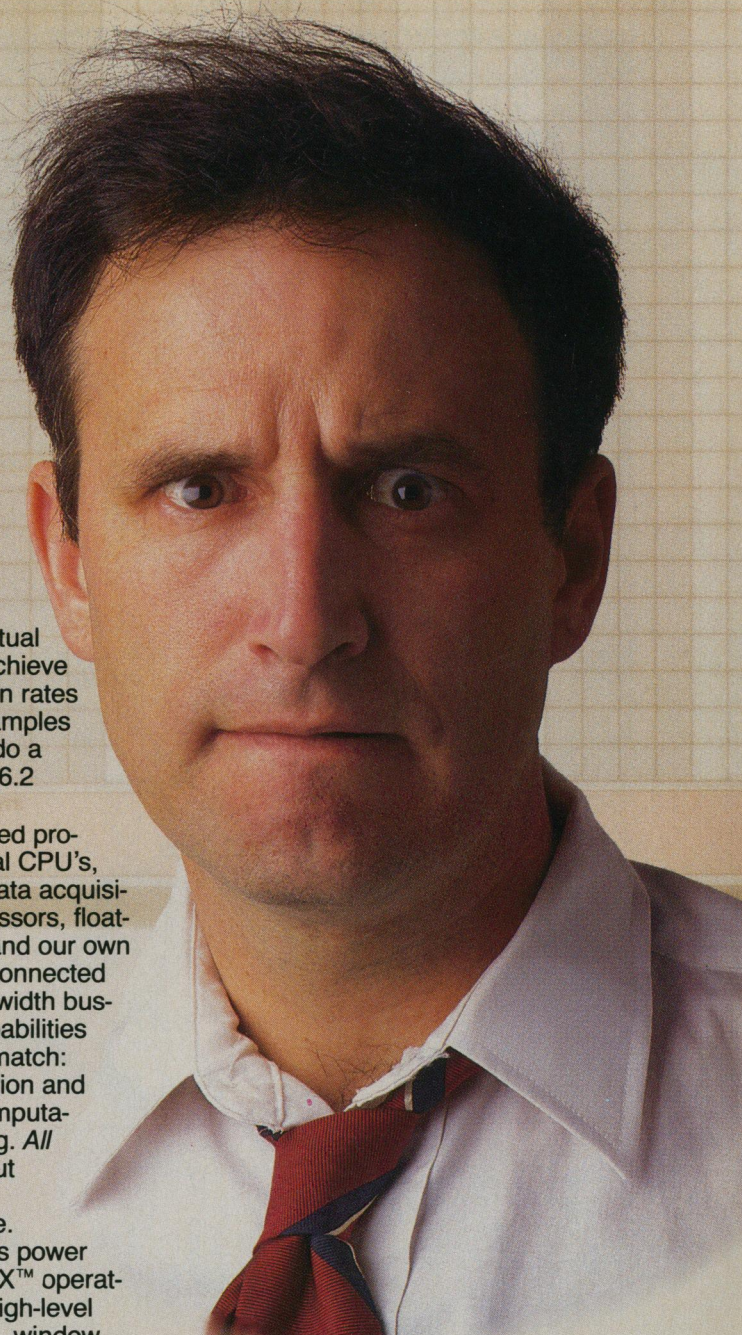
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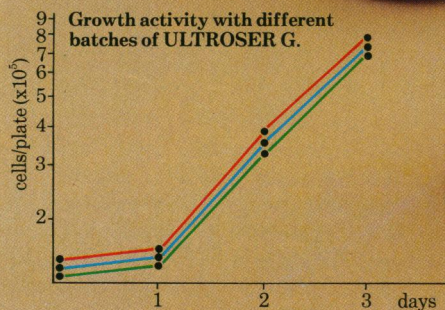
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Modest Proposals for the Granting System

I have already commented on the importance of peer review and the fact that reviewers are, in some cases, blamed for problems that are outside their control. Now I want to suggest some ways in which the granting system might be improved. I will focus on the National Institutes of Health and examine other agencies at a later time.

One problem at NIH which has raised alarm is the high priority rating that is required for funding. Increased competition for funding is a fact, but priority scores are not always a true indicator of the level of competition because there is "priority score inflation," an infectious disease akin to grade inflation. Between 1975 and 1985, for example, the average percentage of grants funded (per total grant applications) has dropped from 46 to 35 percent. Yet, during that same period, the priority score required for funding has changed even more abruptly in some reviewing panels. This apparently has been caused by members of these panels who attempt to outguess the system and help their fellow scientists. In the long run such efforts are counter-productive because administrators are forced to normalize priority scores to obtain correct readings. The sooner the peer panels return to realistic evaluations, the better. A backup system in which administrators or councils can decide to fund a grant that receives a score just below the cut-off line—because it is the sole support of an investigator—and deny the *n*th grant of a more distinguished individual, with a score just above the cut-off line, has been used in some institutes and should be extended, with caution.

The fraction of the total research funding that is assigned to overhead costs deserves a systematic study. The increase in overhead is not alarming per se because the average figure for overhead is 31 percent of direct costs, but it has been increasing at a rate of 0.5 percent per year. One of the built-in dangers here is the competition among university administrators to indulge in "creative financing" for their own institutions. Busy scientists, not wanting to get involved in such arrangements, frequently go along, assuming that since "University X is getting 90 percent overhead—why shouldn't we?" Moreover, some outside agency that has little knowledge of the specific research or the appropriate charges is involved in negotiating with campus administrators. (The Defense Department evaluates overhead for NIH in certain areas of the country, for example.) An examination of this system by an independent team of accountants might reveal that a national average overhead cost would be fair, with some allowances made for special circumstances.

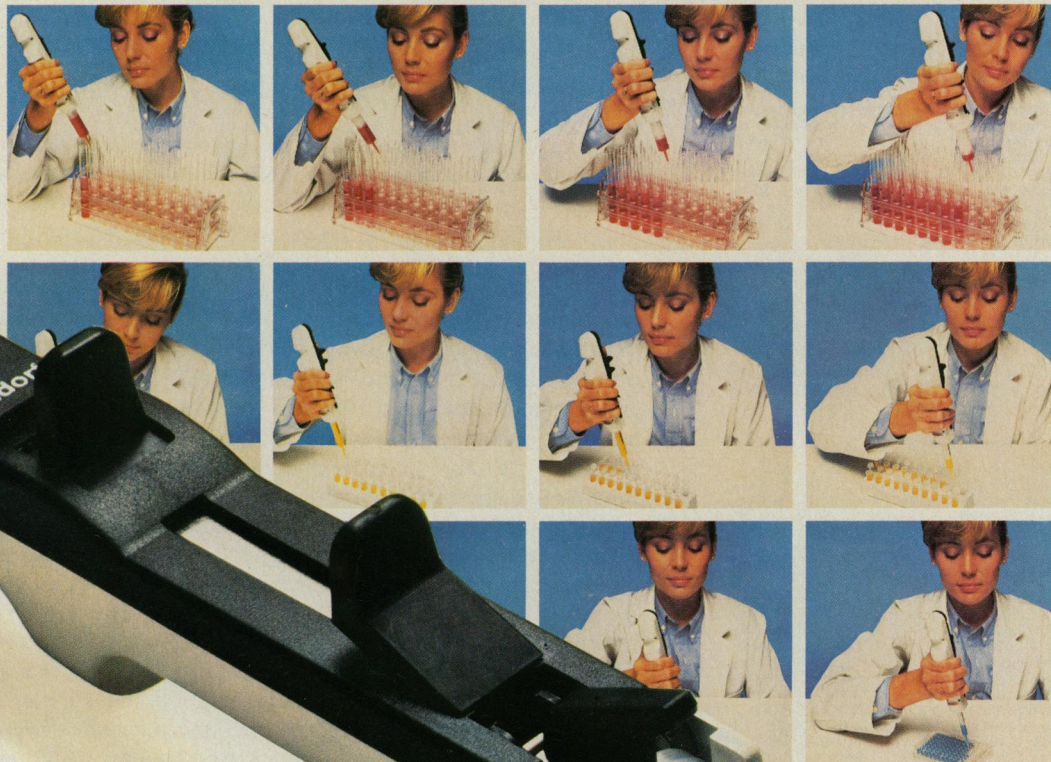
Another possible improvement would be to emphasize the track record of a seasoned investigator in preference to the evaluation of the specific proposal. The chance that an investigator will lose grant support during the first three renewal periods is 50 percent. The chance of losing support after the third renewal is less than 10 percent. Focusing on track records and using a short grant form might reduce paperwork and be a more humane and efficient system for peer evaluation of proven investigators.

Finally, there is the difficult question of salary. It is the most vexing single item to NIH officials. Any drastic reduction in salaries would threaten the viability of the smaller institutions, yet salaries of principal investigators are increasingly eroding research dollars. Peer reviewers are told that they have no jurisdiction over salaries, but inflated salaries should be their concern. Should we not establish more rational guidelines and apply them gradually over the years to lessen withdrawal pains?

Only with constant vigilance will our granting system maintain the respect that it has earned and deserves from the recipients of its decisions and the outsiders who ask that scientists run their affairs well.

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