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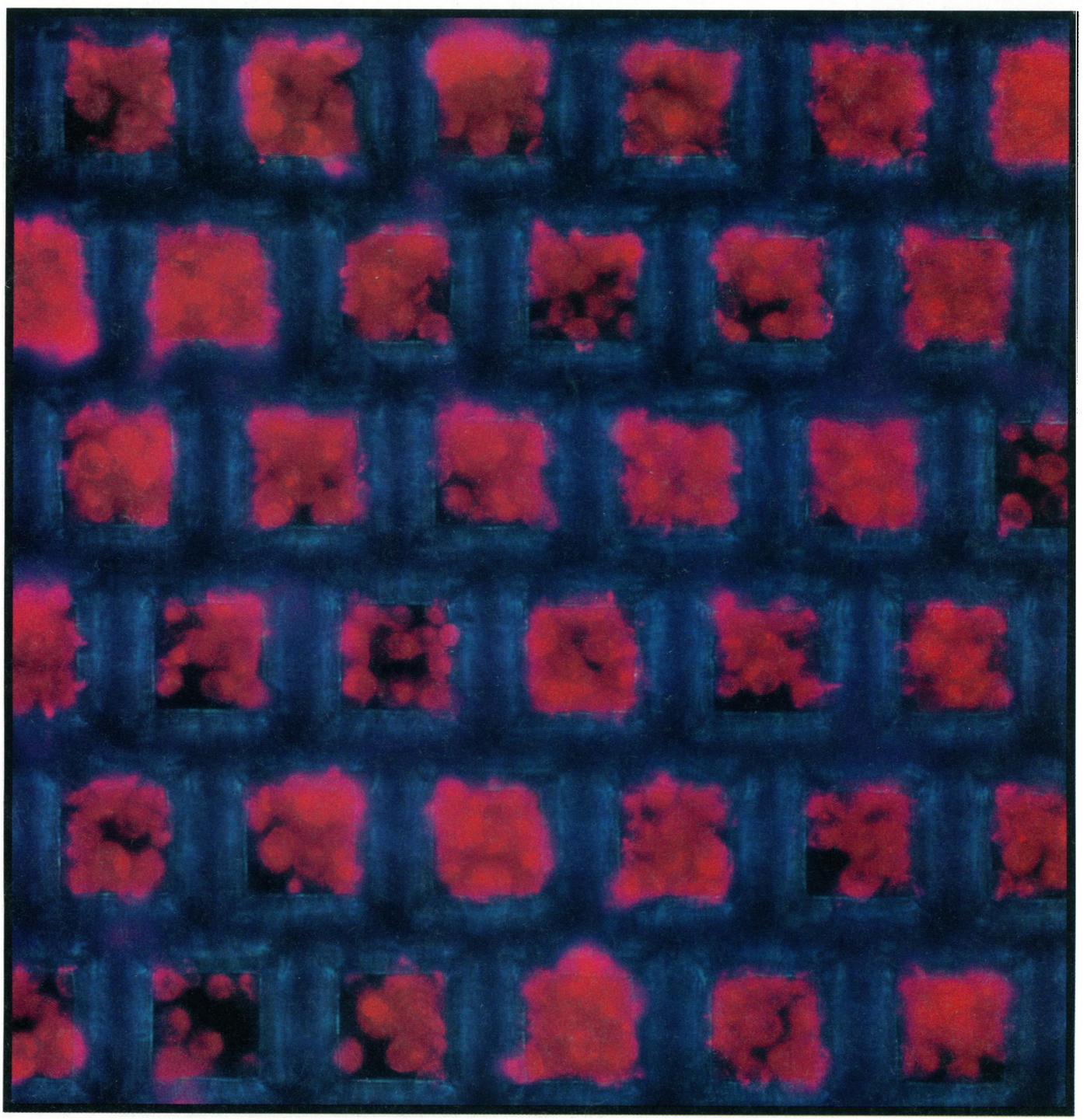

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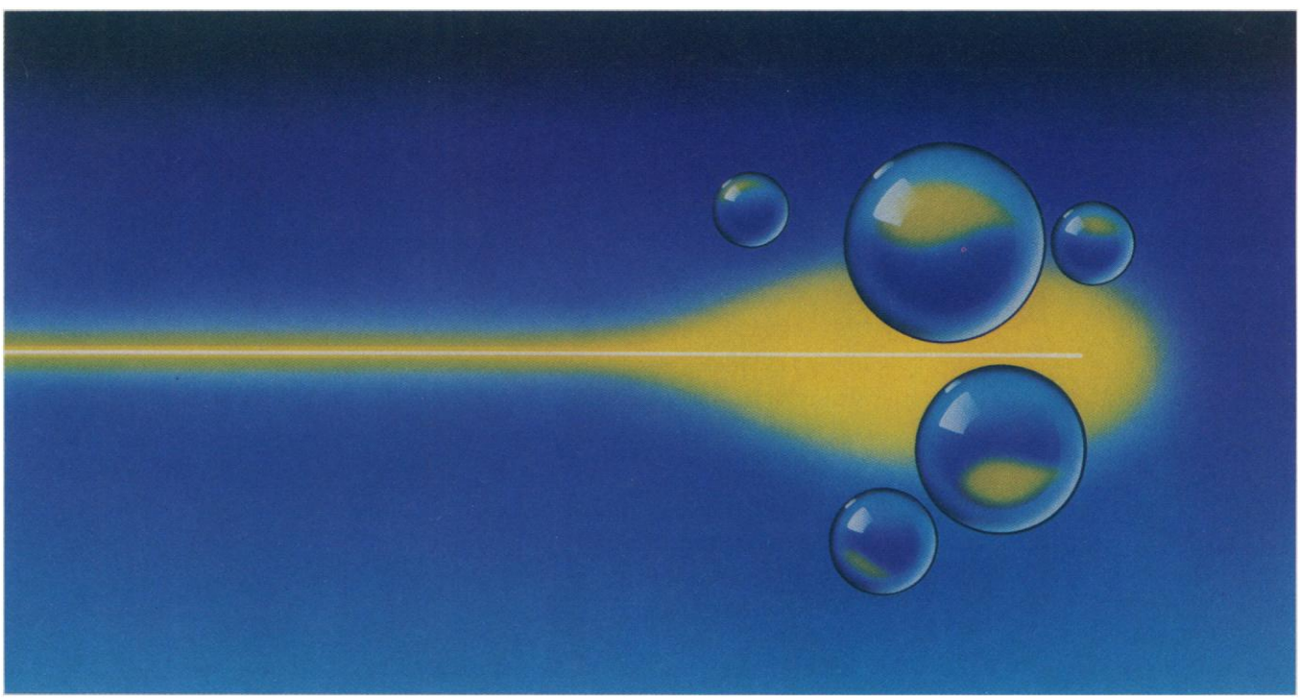

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COVER Living nonadherent P388D1 cells (from murine lymphoid neoplasm), stained here with a red fluorescent dye, are retained in wells (50 μm square and 50 μm deep) etched into the surface of a potentiometric silicon biosensor. The sensor measures metabolic rates, which are affected by a variety of biological and chemical agents. See page 243. [Photograph by J. C. Owicki and K. M. Kercso, Molecular Devices Corporation, Menlo Park, CA 94025]

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Lectin-sugar interactions

LECTINS are proteins that bind noncovalently but specifically to carbohydrates. The name lectin comes from the Latin word legere, which means to choose: different lectins "choose" to bind to different carbohydrates. Studies of lectins have been carried out in numerous systems—viruses, bacteria, protozoa, slime molds, plants, and higher animals. They were first identified in plants but are now thought to be ubiquitous in living organisms; mounting evidence suggests that they are crucial to cell-cell recognition. Sharon and Lis review lectin research and discuss insights that have been gained regarding cell-cell recognition in various normal and aberrant states, including normal organ and tissue differentiation and growth, normal migration of cells throughout the body, pathogen and host interactions, and metastatic growth of malignant tumors (page 227). Lectins may work alone or in concert with other recognition molecules to bring about recognition, but, in either case, interventions in lectin-carbohydrate interactions could be effective in blocking infections and other pathologic processes.

Silicon microphysiometer

A tiny biosensor can detect biochemical changes taking place in as few as 1000 cells in 100 nanoliters of fluid (page 243). As the sensitivity of this microtechnology grows, fewer and fewer cells will be needed; eventually it may even be possible to measure biochemical changes in single cells. Cells are placed in a flow chamber and bathed in a physiologic solution; the silicon biosensor measures how the acidity of the solution changes (cover). The solution becomes more acid when two breakdown products, lactic acid and carbon dioxide, are generated inside cells, and acidity thus provides a measure of the cell's catabolic rate. Parce *et al.* illustrate the use of the device on a variety of coupled stimuli and cells—a metabolic inhibitor acting on a macrophage cell line, epidermal growth factor acting on normal epidermal cells, chemotherapeutic drugs acting on tumor cells, irritants acting on cells of the eye, and antiviral agents acting on viruses that are infecting host cells. It is clear that this biosensor will be an important adjunct to standard in vitro and in vivo assays for the rapid screening of drugs and toxic substances that may, in subtle or dramatic ways, alter cellular biochemistry.

Fungal pathogenicity

PLANTS produce toxic compounds called phytoalexins that help to protect them from dangerous pathogens. For example, pea plants make a phytoalexin called pisatin that counters some of the effects of infecting fungi. However, some infectious fungi fight back with a protein—pisatin demethylase—that degrades pisatin to a less toxic substance. Schäfer *et al.* investigated what happens when pisatin demethylase is produced by fungi that normally are not pathogenic for peas (page 247). The gene for pisatin demethylase was transferred into and expressed in a fungal pathogen of maize and into another fungus that normally lives on decaying organic matter. The first became pathogenic for the pea plants; the second did not. The pathogenicity of the first fungus for its normal maize host was not enhanced by the introduction of the pisatin demethylase. The pisatin demethylase gene appears therefore to be a necessary but not a sufficient gene for making a fungus pathogenic for peas.

Interleukin-1 action

INTERLEUKIN-2 is secreted by T lymphoid cells; its production precedes the proliferation of T cells, a crucial step in effective immune responses. Two known separate external signals are required for the induction of interleukin-2: one is the binding of an antigen or a lectin to the T cell receptor on the cell surface and the other is the binding of interleukin-1 to a high affinity interleukin-1 receptor. Muegge *et al.* have studied what happens in the nucleus after these inducers have acted at the surface (page 249). Lectin binding induces production of messenger RNA for the c-*fos* protein; interleukin-1 induces messenger RNA for c-*jun*; when the c-*fos* and c-*jun* proteins combine they form the AP-1 factor. This factor attaches to the AP-1 site in the promoter region of the interleukin-2 gene, contributing to the production of interleukin-2. There are many cell types that respond to interleukin-1, and it may be through AP-1 that interleukin-1 induces the pleiotropic effects in inflammation and immunity for which it is known.

Hazard for fumigators

GRAIN supplies, which can be destroyed by insects and microorganisms, are routinely and repeatedly fumigated. Otherwise, crop deterioration and destruction may occur not only while the grains are still in the field but also while they are being transported from field to storage bins, while they are being held in storage bins, and while they are later transported out of storage and processed. Among the most commonly used fumigants are phosphines, which are poisonous flammable gases that smell like garlic. Aluminum phosphide and magnesium phosphide are applied to the grains in pellets; phosphine gas is generated in a timed-release fashion (and as quickly as within 5 minutes) that is dependent on temperature and humidity. Garry *et al.* report that exposure to phosphines alters the chromosomes of workers who apply them (page 251). Workers in Minnesota were studied both at the time of phosphine exposure and some months later, when the fumigation "season" had ended. Sizable numbers of lasting chromosome rearrangements were detected in circulating lymphoid cells. Whether these changes presage development of specific malignancies or deficiency diseases in these individuals remains to be seen.

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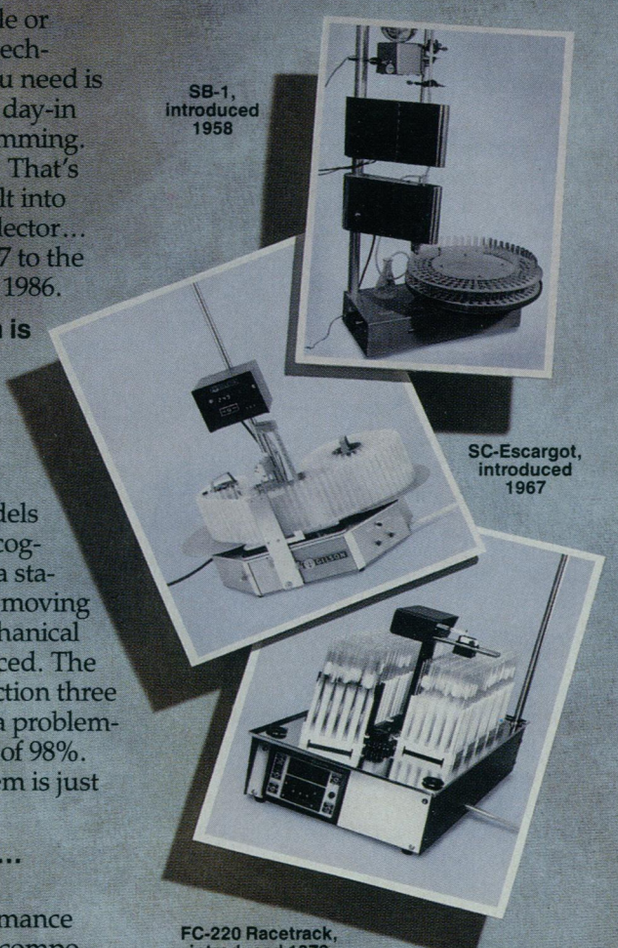

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SC-Escargot, introduced 1967

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SCIENCE

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Sequences and Consequences of the Human Genome

The sequencing of the human genome involves big money, big consequences, and big controversies. Within the scientific community there is the question of money because of the "big science" image. The cost of the genome project ($3 billion in 15 years) is much smaller than the cost of a supercollider or of a space station, and it is more of a mom-and-pop store enterprise than the mass production assembly line of real big science. The Cystic Fibrosis Foundation has spent $120 million in the past 4 years on one illness, to say nothing of the other foundation and federal money spent on the same project. In that context a price of $200 million per year, the figure for the human genome project, for work that applies to many diseases and untold discoveries in biology sounds cost-effective.

The benefits to science of the genome project are clear. Illnesses such as manic depression, Alzheimer's, schizophrenia, and heart disease are probably all multigenic and even more difficult to unravel than cystic fibrosis. Yet these diseases are at the root of many current societal problems. The costs of mental illness, the difficult civil liberties problems they cause, the pain to the individual, all cry out for an early solution that involves prevention, not caretaking. To continue the current warehousing or neglect of these people, many of whom are in the ranks of the homeless, is the equivalent of providing iron lungs to polio victims at the expense of working on a vaccine.

Other medical applications of a genome sequence include an early warning system that may help individuals predisposed to diseases such as alcoholism, colon cancer, and depression. The early warning may allow them to avoid the problems by behavior or diet modification or frequent medical checkups. Family planning also will be made more accurate. No individual should be forced to obtain genetic information but none should be denied information either.

The "sky is falling" group, who denounce the genome project, sound like they are paraphrasing a Woody Allen admonition by saying, "We stand at the crossroads. One road leads to hopelessness, the other to utter despair. We must have the courage to make the right decision." The potential risks from the new knowledge gained by sequencing the human genome appear, on close examination, to be old problems revisited. Genetic counseling already exists for Down syndrome, Tay Sachs, and sickle cell anemia. Personal insurance policies already ask for lung x-rays, heart condition tests, and information on such behaviors as smoking. Group insurance is available without test. Fingerprints are not required of the general population but are kept on file for those who commit a crime. The information in the genome adds accuracy and scope to many of these applications but no new or threatening principles. If the higher visibility of the genome project causes a qualitative change, then, of course, new procedures may be needed.

A genome sequence should not be a precondition of employment, and legislation might be needed if that problem were to arise. However, less accurate data of the same type would be available today from family histories, and that does not seem to be part of current employment forms. If more accurate information provides temptation for abuse, action will be needed.

The argument that dictators would alter genes to convert their enemies is farfetched. The idea that a Hitler or a Stalin would prefer the engineering of Jews into Aryans or capitalists into communists as cheaper or more satisfying than killing them (as they did) is absurd. We must be vigilant about ethical concerns but not paralyzed by outlandish scenarios.

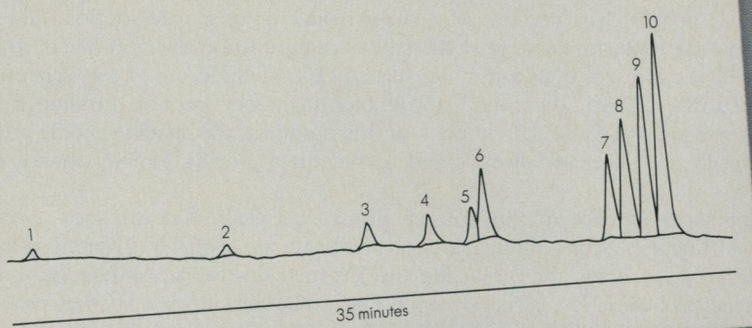
The belief of biologists that studying simple organisms such as *Escherichia coli*, flies, and rats is relevant to human physiology and behavior has been brilliantly confirmed. But there are differences. One cannot extrapolate carcinogenic potency from the mouse to the rat with precision, and even less to the human. Some diseases involve speech and mental states unique to man. Sequencing the human genome puts us on the threshold of great new benefits and some real but avoidable risks. There are immoralities of commission that we must avoid. But there is also the immorality of omission—the failure to apply a great new technology to aid the poor, the infirm, and the underprivileged. We must step boldly and confidently across the threshold.—DANIEL E. KOSHLAND, JR.

Nucleic acid analysis

Sample: Hae III Digest of φX
Column: Gen-Pak™ FAX (4.6mm x 100mm)
Detection: UV at 260nm
Eluent A: 100mM Tris/Cl, pH8.0, 1mM EDTA
Eluent B: 100mM Tris/Cl, pH8.0, 1mM EDTA, 1M NaCl

Fragment size

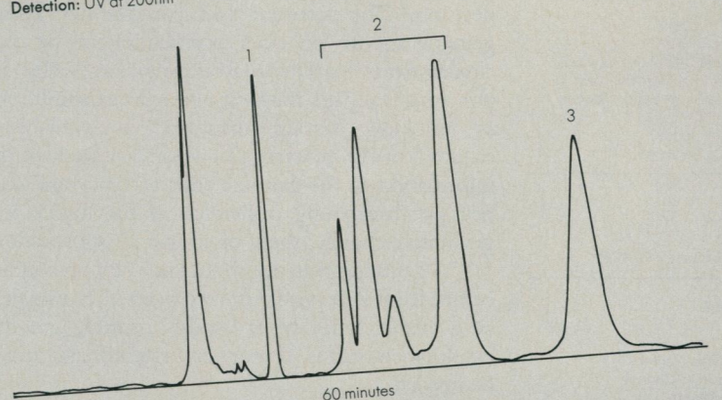
1) 72	6) 281,310
2) 118	7) 603
3) 194	8) 872
4) 234	9) 1078
5) 271	10) 1353



Carbohydrate characterization

Sample: Mixed neutral oligosaccharide standards
Column: Glyco-Pak™ N (7.8mm x 300mm)
Eluent: CH_3CN/H_2O (68:32) (v/v)
Detection: UV at 200nm

1. N-acetylglucosamine
2. biantennary complex
3. high mannose (MAN9)



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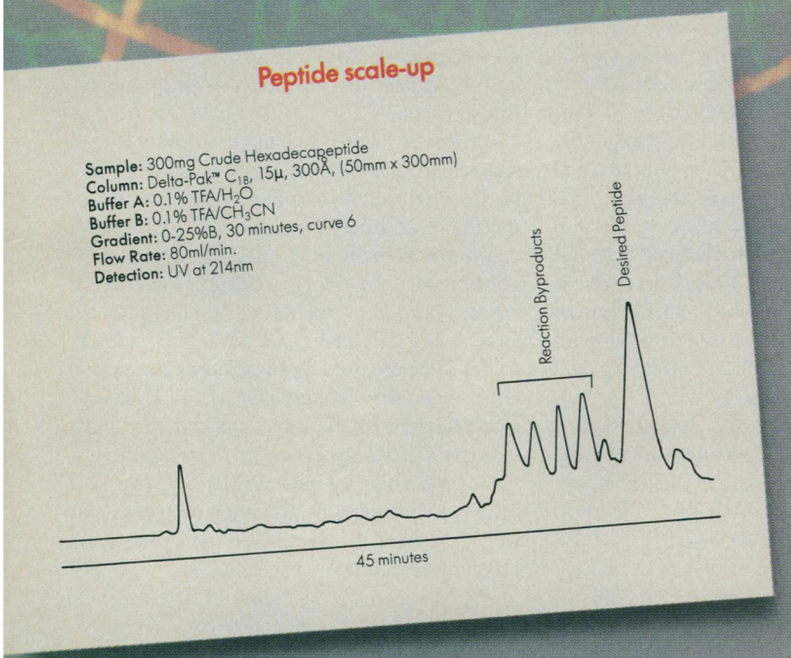

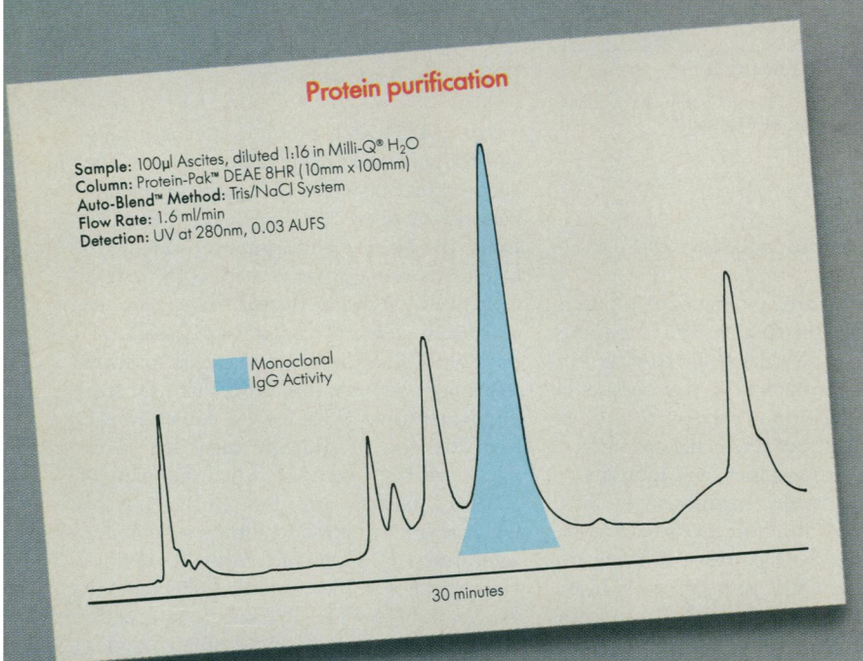

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sage as is the ICBM force, should one be issued, and may even receive it before the ICBM force does. It is true that, in order to enhance survivability, communication to the SSBN force is not two-way. However, as long as one-way communication is reliable, which can be demonstrated, the need to spend the money that would be necessary to obtain secure two-way communication is not obvious today. Finally, while Deutch asserts that there are "doctrinal" reasons for not relying on Trident, he does not tell us what these might be.

Third, there is citation of the dreaded "ASW [antisubmarine warfare] breakthrough." No one can prove that such a breakthrough will not occur. The Navy does, however, maintain an extensive program designed to ensure the security of its SSBNs. This program is subject to comprehensive, national-level oversight. The oversight groups agree that there is no danger of such a breakthrough in the foreseeable future. Furthermore, even if there were to be a breakthrough in detection, the problems inherent in turning detection into kill would remain nontrivial. In this context, it might be pointed out that, while the air is certainly at least as transparent as the ocean, few people have cited this transparency as a bar to the survivability of mobile ICBMs.

In the end, the real role of ICBMs would appear to be, in the words of Brent Scowcroft and R. James Woolsey (*1*), to "augment" the Trident force. The most important question about ICBM modernization, then, and one that Deutch does not ask, let alone answer, is just how large and powerful such an augmentation needs to be and just how much survivability is affordable for it given this role?

MICHAEL F. ALTFELD
Strategic and Theater Nuclear Warfare Division, Department of the Navy, Washington, DC 20350–2000

REFERENCES

1. B. Scowcroft and R. J. Woolsey, in *American Agenda: Report to the Forty-First President of the United States of America* (Washington, DC, 1988).

Deutch argues that land-based missiles need to be modernized for three reasons: (i) as a hedge against a possible Soviet antisubmarine warfare (ASW) breakthrough, (ii) because ICBMs remain the most controllable part of the triad for prompt and selective nuclear response, and (iii) to show "our allies and adversaries that the United States still possesses the political resolve to field a weapons system that . . . is considered a principal measure of deterrence and political military might." Having looked at the ASW problem in some detail, we remain unconvinced of the likelihood of a breakthrough by the mere statement of the possibility. The difference in promptness between submarine-launched ballistic missiles (SLBMs) and ICBMs is not significant. The "selective nuclear response" argument has some validity, not because of "a host of technical and doctrinal reasons," but simply because it would require launching individual missiles, which could potentially compromise a ballistic missile submarine's location. While this is indeed a problem, it is not insoluble. If land-based ICBMs are to have a role in the future, it will likely be related to this suggestion of selective nuclear response. The demonstration argument is unconscionable given the high cost of the suggested Midgetman system and current fiscal constraints.

In general, we found the article a valuable contribution, particularly for its discussion

University of Delft in The Netherlands.

In the insert "Can Europe survive on chips?" Dickson calls the "mega-project" of Philips and the German companies a "mega-flop" because, soon after it started, "Siemens decided it would be cheaper to buy the chips off the shelf from Japan." The aim of the "mega-project," which began in 1984, was to develop submicron technology. A 4-megabit DRAM (Siemens) and a 1-megabit SRAM (Philips) were used as "vehicles"—the first commercial targets—to be on the market by 1989. It was anticipated that by that time the main competitors would have reached that stage. Philips and Siemens were minor producers of MOS VLSI memories (Philips being an important supplier of bipolar memories), but they both had to take a large leap forward in a comparatively short time.

From a technological standpoint, the "mega-project" is already a success. Of course there is still the problem of building up a strong market position. Siemens, therefore, bought Japanese technology—not chips—in order to produce 1-megabit DRAMS without overloading its own development program. [Philips chose to develop additional products like 64K and 256K SRAMS, as well as a version of the latter using submicron ("mega-project") technology.] As a result, a good quantity of German-made 1-megabit DRAMs are now being sold. These are being followed by 4 megabits made with "mega-project" technology, so Holland will soon be known as a producer of chips 'n cheese as well as of bulbs.

C. LE PAIR
Secretary, JESSI-Planning Council, Post Office Box 3021, 3502 GA, Utrecht, The Netherlands

Early Hominid Mating Systems

In Table 1 of their article "Finite social space, evolutionary pathways, and reconstructing hominid behavior" (17 Feb., p. 901), Robert A. Foley and Phyllis C. Lee incorrectly characterize my model of early hominid social systems both in relation to its "key behavioral features" and to its "social structure," listing the former as "female mate choice and sexual selection" and the latter as "pairbonds (monogamy)." The key mechanism I proposed is what Darwin called "double selection," that is, both male competition and female choice *and* female competition and male choice. Likewise although I discussed various hominid mating systems, my key argument was that ape-hominid speciation (and bipedalism) occurred through intense male competition by means of nuptial food gifts to females of scavenged brains and bone marrow. I argued that, while males tried to mate with and control several females (resulting in polygyny), females tried to increase their access to food gifts through multiple matings (resulting in polyandry), and hence that the earliest hominids were to some degree promiscuous.

SUE TAYLOR PARKER
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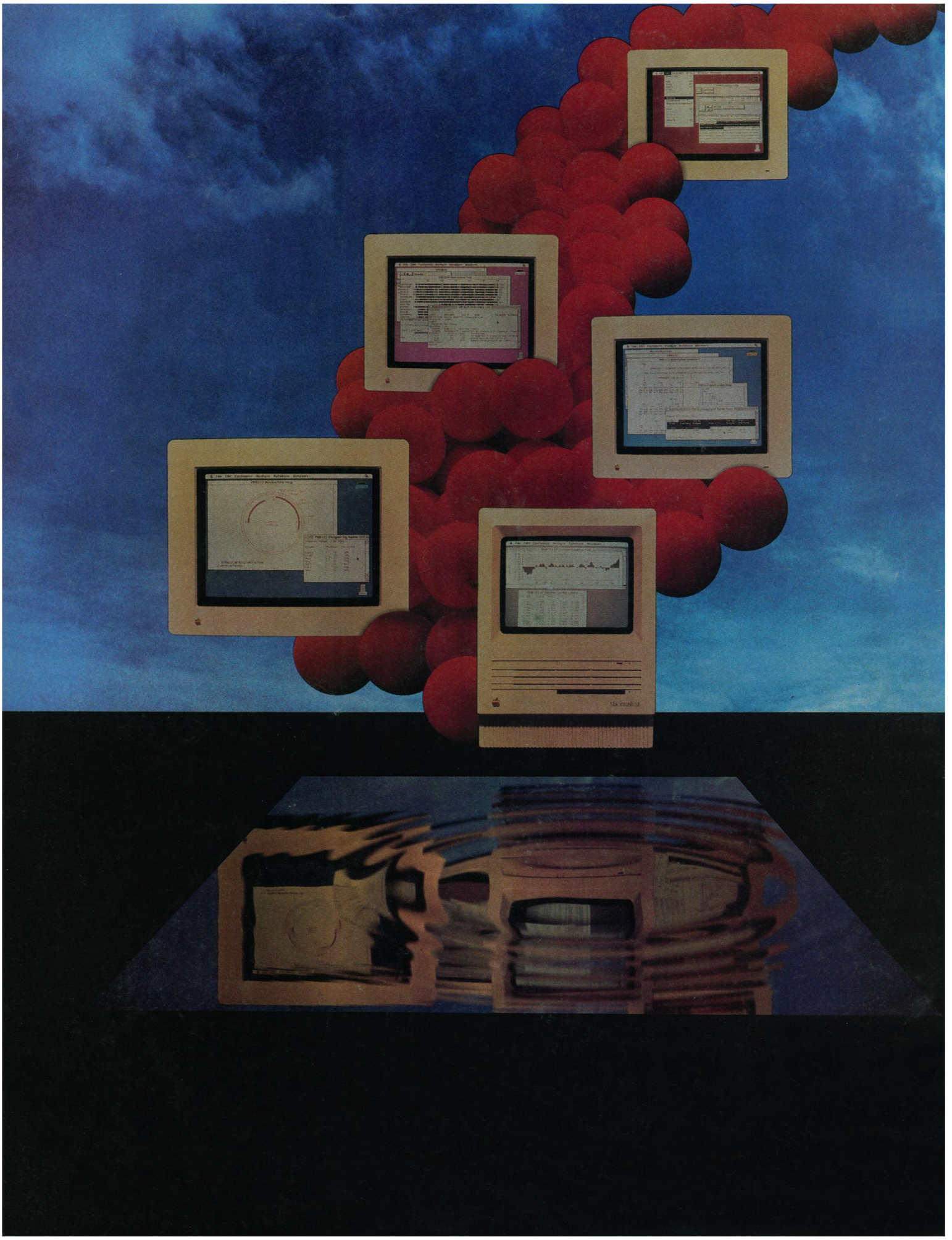
Erratum: The Author Index to volume 244 that appeared between pages 1480 and 1481 of the issue of 29 September 1989 covered the months July–September 1989, not "April–June 1989," as printed.

Erratum: The credit line for the photograph of the U.S. Capitol building accompanying Joseph Palca's article "The pill of choice?" (News & Comment, 22 Sept., p. 1319) should have read, "John Ficara/Newsweek."



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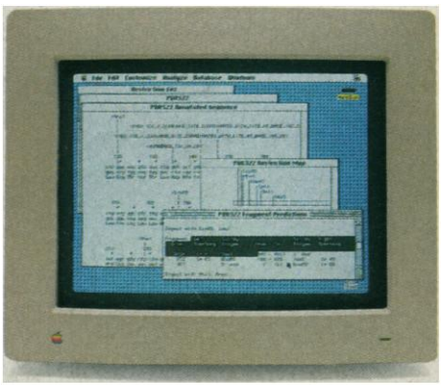

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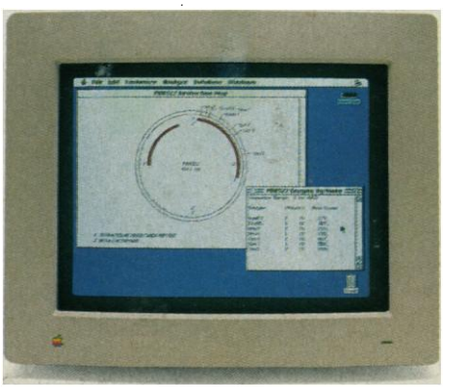

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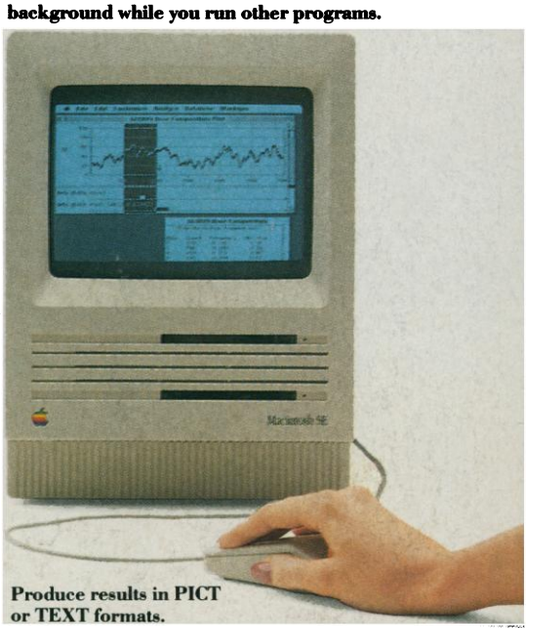

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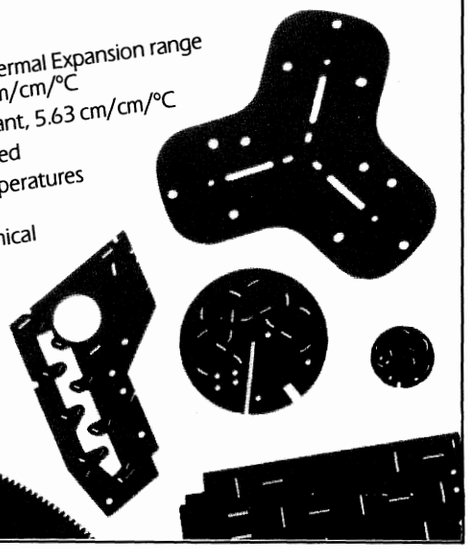

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and streaming birefringence, which characterize chain conformation. These measurements are already well known for flexible chains, following the work of Flory and many others, but they have been less successful in the case of more rigid polymers (aromatic polyamides, cellulose and cellulose derivatives, polypeptides, polymeric liquid crystals), in part owing to experimental difficulties.

Tsvetkov has devoted much of his life to exploring such solutions, primarily using optical and hydrodynamic techniques. He belongs to the "Leningrad school," which has pioneered studies of polymer chain conformation. This book is a valuable collection of contributions from Tsvetkov and his associates, many of which have not been readily available to non–Russian-speaking readers.

Tsvetkov provides an excellent review of experiments and theory on this topic. He emphasizes the so-called "free-draining" state (as opposed to the non-draining case, where hydrodynamic interaction is important). This approximation, which is not good for coil-like molecules, becomes better with increasing molecular rigidity. In such cases, the Kuhn segment length may exceed that for flexible-coil molecules by an order of magnitude or more, leading to their unique hydrodynamic, electrical, and optical properties. This arises in part from the effects of their rigidity on their equilibrium properties and thermodynamics, but largely from the effects of their dynamics on their motion in solution. The author extensively employs the worm-like–chain model introduced by Kratky, which gives rise to the concept of the persistence length as a measure of rigidity. A strong point of the book is the comparison of the behavior of rigid and flexible molecules.

The book presents a good discussion of translational and rotational motions of molecules and their effects on viscosity, streaming, and electric-field–induced birefringence. The presentation is "classical" and is, for the most part, readily understandable by physical chemists and engineers as well as by physicists. There are extensive references, many from the Russian literature. Relatively few references, however, date from after 1983, and the book misses important recent work in areas like liquid crystal polymers, the non-linear optical properties of such systems, and their employment in devices dependent upon their high molecular anisotropy. It also would have been desirable to include something about the commercial use of rigid-chain polymers in preparing high-performance fibers like Kevlar® and blends with flexible molecules to make "molecular composites."

Overall the presentation is clear, and the translation is good. There is a good mix of theory and experiment accompanied by extensive experimental details, and the book will prove a useful reference. It provides an excellent perspective for more recent developments.

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