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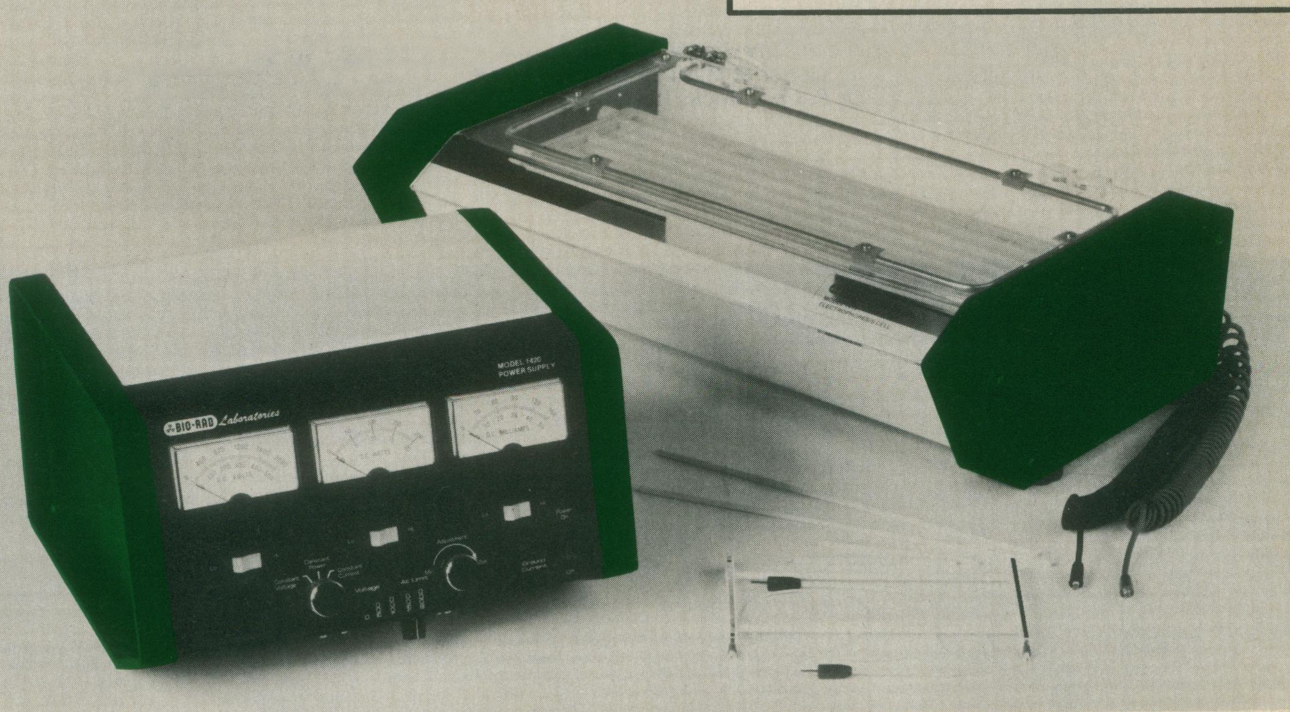

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18 April 1980

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SCIENCE

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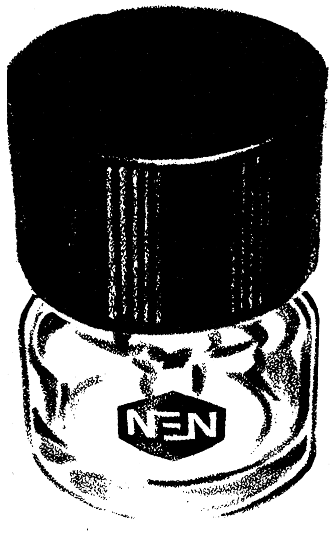
COVER

Cape Lookout Bight, North Carolina (southward), located behind a barrier island cuspate foreland. The bight is a quiet water lagoon enclosed by an active, northerly migrating recurved spit. The spit's morphology is partially controlled by a large rock jetty (far right). The lagoon is a sedimentation trap for fine-grained, organic-rich, suspended particles exiting to the ocean via nearby Barden Inlet. The inlet's ebb tidal shoals appear in the lower left. Note the inactive recurved spit within the bight. See page 285 for chart of the area. [A. C. Hine, University of South Florida, Tampa, and C. S. Martens, University of North Carolina, Chapel Hill]

74 Research Assistants for Receptor Site Studies



α-Adrenergic
Clonidine hydrochloride, [4-^{3}H]-
Desmethylimipramine hydrochloride, [2,4,6,8-^{3}H]-
Dihydro-α-ergocryptine, 9,10-[9,10-^{3}H(N)]-
WB-4101 (2,6-Dimethoxyphenoxyethyl) aminomethyl-1, 4-benzodioxane, 2-[*phenoxy*-3-^{3}H(N)]-
Epinephrine, *levo*-[*methyl*-^{3}H]-
Norepinephrine, *levo*-[7,8-^{3}H(N)]-

β-Adrenergic
Carazolol, DL-[3,6-^{3}H(N)]-
Dihydroalprenolol hydrochloride, *levo*-[*propyl*-2,3-^{3}H]-
Epinephrine, *levo*-[*N-methyl*-^{3}H]-
Hydroxybenzylisoproterenol, *p*-[7-^{3}H]-
Iodohydroxybenzylpindolol, [^{125}I]-
Isoproterenol, DL-[7-^{3}H(N)]-
Norepinephrine, *levo*-[7,8-^{3}H(N)]-
Propranolol, L-[4-^{3}H]-

Aspartate
Aspartic acid, D-[2,3-^{3}H]-
Aspartic acid, L-[2,3-^{3}H]-
Methyl-D-aspartic acid, *N*-[*methyl*-^{3}H]-

Benzodiazepine
Diazepam, [*methyl*-^{3}H]-
Flunitrazepam, [*methyl*-^{3}H]-

Cholinergic
Muscarinic
Acetylcholine chloride, [*N-methyl*-^{3}H]-
Choline chloride, [*methyl*-^{3}H]-
Pilocarpine, [^{3}H(G)]-
Quinuclidinyl benzilate, DL-[*benzilic*-4,4′-^{3}H(N)]-
Scopolamine methyl chloride, [*N-methyl*-^{3}H]-

Nicotinic
Acetylcholine chloride, [*N-methyl*-^{3}H]-
α-Bungarotoxin, [^{125}I]-
Choline chloride, [*methyl*-^{3}H]-
Tubocurarine chloride, *dextro*-[13′-^{3}H(N)]-

Dopaminergic
ADTN Amino-6,7-dihydroxy-1,2,3,4-tetrahydronaphthalene, 2-[5,8-^{3}H]-
Amphetamine sulfate, D-[^{3}H(G)]-
Apomorphine, [8,9-^{3}H]-
Chlorpromazine, [^{3}H]-
Dihydroxyphenylethylamine, 3,4-[*ethyl*-1-^{3}H(N)]- or [*ethyl*-2-^{3}H(N)]-
Haloperidol, [^{3}H(G)]-
Propylnorapomorphine, *N*-[*propyl*-^{3}H(N)]-
Spiroperidol, [1-*phenyl*-4-^{3}H]-

GABA
Alanine, β-[3-^{3}H(N)]-
Aminobutyric acid, γ-[2,3-^{3}H(N)]-
Dihydropicrotoxinin, α-[8,10-^{3}H]-
Isoguvacine hydrochloride, [^{3}H]-
Muscimol, [*methylene*-^{3}H(N)]- or [4-^{3}H]-
Nipecotic acid, [*ring*-^{3}H]-

Glutamate
Glutamic acid, L-[3,4-^{3}H]-

Glycine
Glycine, [2-^{3}H]-

Histamine
H_1
Histamine, [^{3}H(G)]-
Pyrilamine, [*pyridinyl*-5-^{3}H]- (Mepyramine)

H_2
Histamine, [^{3}H(G)]-

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Ethylketocyclazocine, [9-^{3}H]-
Morphine, [6-^{3}H(N)]-

Serotonin
Hydroxytryptamine binoxalate, 5-[1,2-^{3}H(N)]-
Hydroxytryptamine creatinine sulfate, 5-[1,2-^{3}H(N)]-

Steroid
Androgen
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Moxestrol, [11β-*methoxy*-^{3}H]- (R2858)*

Glucocorticoid
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Prednisolone, [6,7-^{3}H(N)]-
Triamcinolone acetonide, [6,7-^{3}H(N)]-

Mineralocorticoid
Aldosterone, D-[1,2,6,7-^{3}H(N)]-

Progesterone
Dihydroprogesterone, [1,2-^{3}H(N)]-
Nor-17α-ethynyltestosterone, 19-[6,7-^{3}H(N)]-
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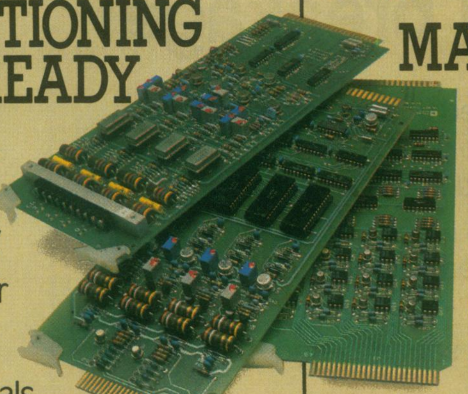

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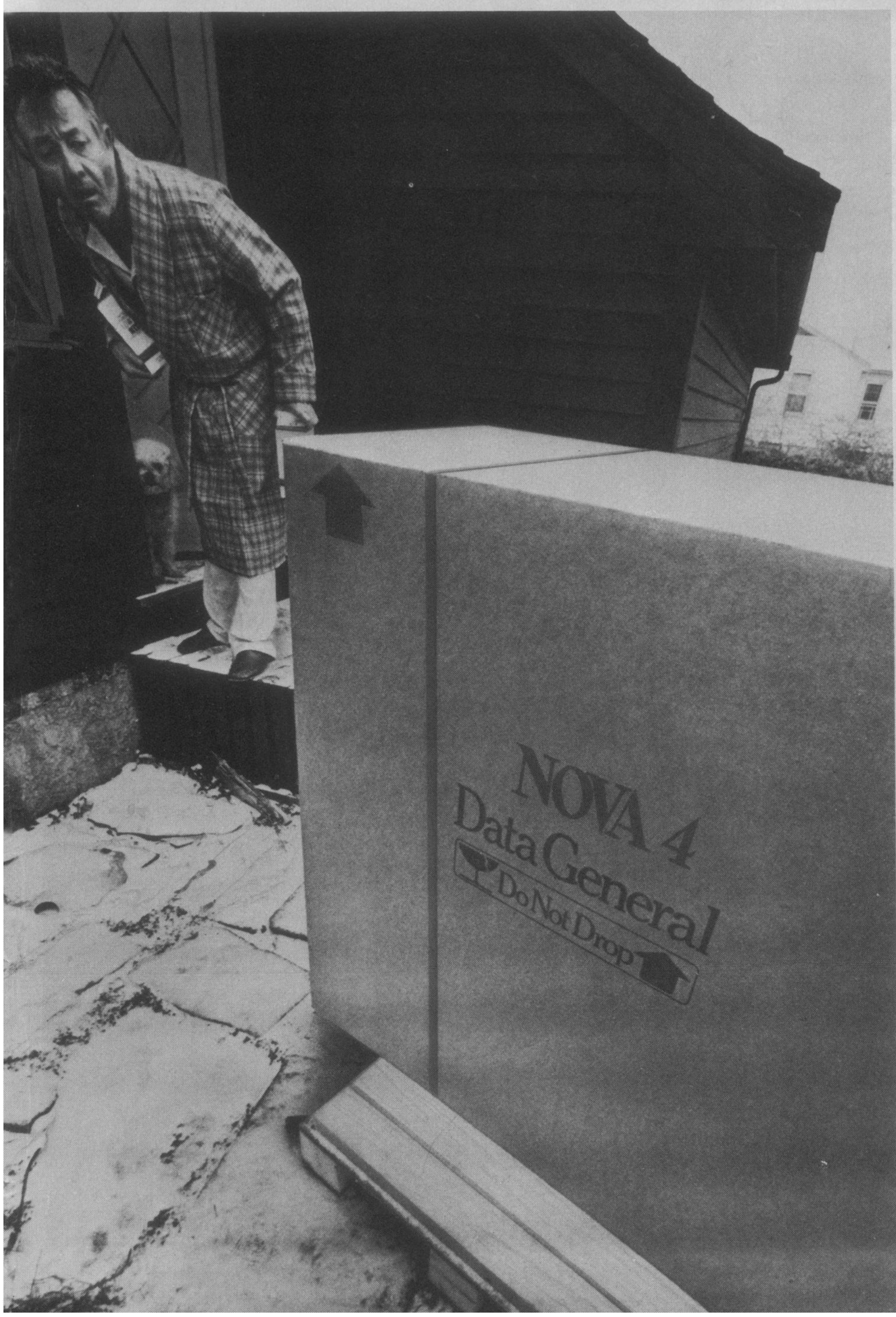

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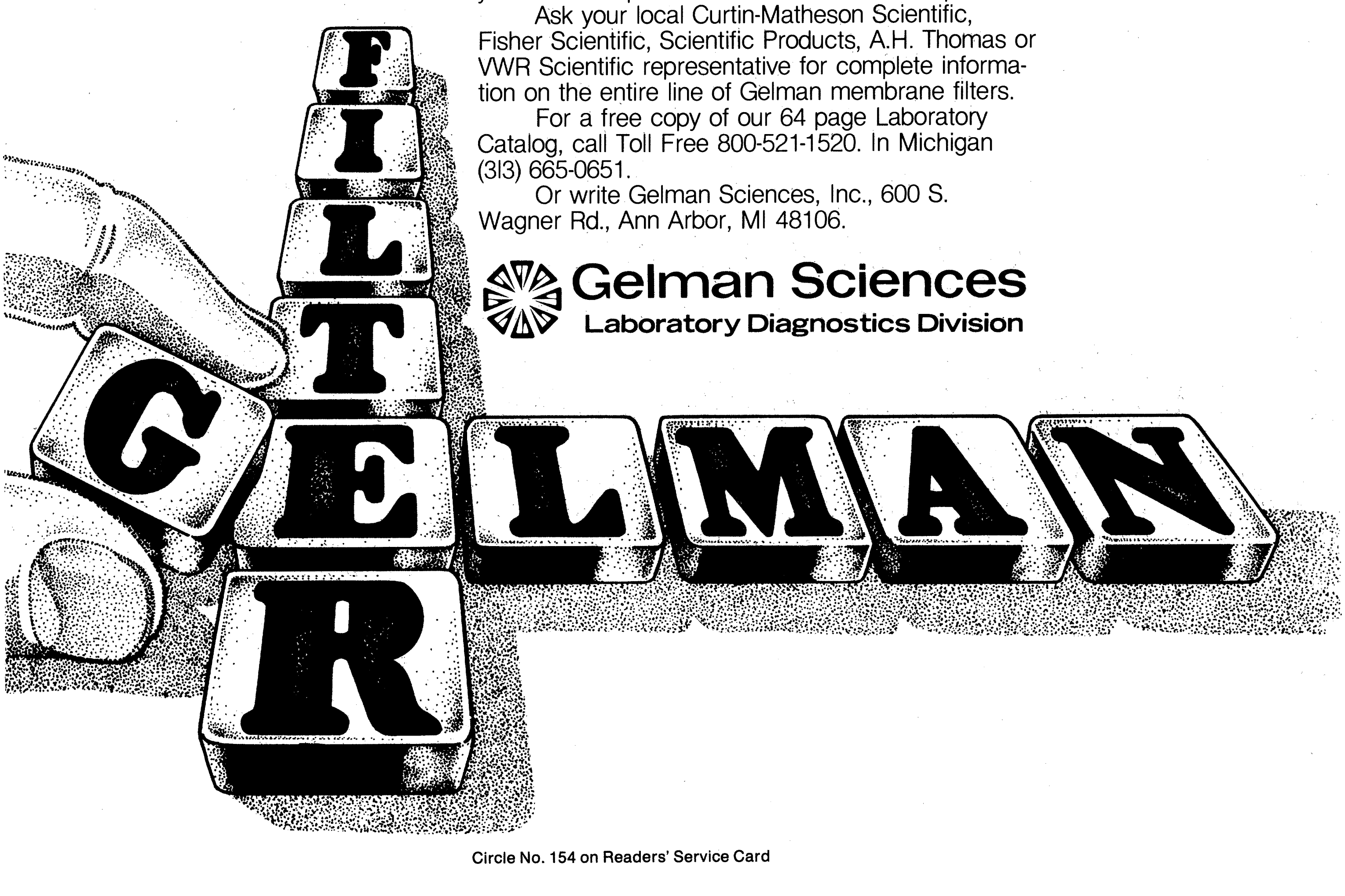

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LETTERS

Osteoporosis: A Cautionary Note

Jean L. Marx, in her excellent article about osteoporosis (Research News, 8 Feb., p. 628), suggests that imbalance between two competing processes—resorption, in the form of dissolution of the calcium-containing mineral, and bone formation—could be at the heart of the osteoporotic puzzle. We would like to comment on some aspects of this pattern.

Morphological data characteristically show osteoporotic bone trabeculae to be less numerous and thinner than normal ones (*1*). However, this phenomenon is not the net result of a bare loss of mineral combined with a loss of organic matrix, it is accompanied by physical and chemical modifications of the mineral and organic phases of the bone.

Osteoporotic bone trabeculae (the inner part of bone, as opposed to cortical bone, the outer weight-bearing structure) have a higher specific gravity and a higher calcium content per unit weight (*2*) or volume (*3, 4*) correlating with higher calcium and phosphorous-to-hydroxyproline ratios (*5*). Thus, osteoporotic bone is more porous and more mineralized; this if anything, could account for its being more brittle.

In addition, components are more homogeneous in osteoporotic bone than in normal bone: magnesium content (*4*) and noncollagenous proteins (*4, 6*) both decrease with age and, in osteoporosis, show a negative correlation with specific gravity and calcium content (*4*); furthermore, the collagen molecules of the matrix become less extractable with age (*3*), suggesting stronger cross-links; hence a greater degree of homogeneity and a higher order of organization are achieved in osteoporotic trabecular bone, while the crystallinity of cortical bone has been shown to remain unaltered with age (*7*).

We can speculate therefore that, in order to reverse osteoporosis, any agent influencing the balance between bone deposition and resorption should also be able to reverse the time-dependent evolution of extracellular trabecular bone components toward a more compact and orderly structure.

Basic knowledge of the physics and chemistry of extracellular bone components in humans is still scanty with respect to age groups and in view of the vast problems arising from the mere effects of time [and weightlessness (*8*)] on bone components; more extensive studies of the latter are particularly indicated and caution is justified when optimistic statements are made claiming reversal of osteoporosis on the basis of an exclusively biological approach, no matter how well substantiated experimental results might be.

People in affluent societies expect to lead an active life beyond menopause or andropause. How much such expectations justify the needed heavy investments in view of the population explosion and the ever-widening gap between developing and affluent societies is a matter where self-interest, scientific interest, and worldwide policy are difficult to disentangle.

S. ORLOFF
D. MANICOURT
Department of Rheumatology and Internal Medicine, Brugmann Hospital, B-1020 Brussels, Belgium

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The "Ellipsoid Algorithm"

Gina Bari Kolata's article (Research News, 2 Nov. 1979, p. 545) on the algorithm for linear programming (LP) published by L. G. Khachian was the first report on it to the general scientific community. Since then, amid a flurry of comment in the press, many applied mathematicians (and others) have studied it, tried it out, and proposed improvements. The Mathematical Programming Society (MPS) has received 42 technical papers written about the algorithm since Gács and Lovász presented their version at the Tenth International Symposium of the MPS in Montreal last August. These papers are listed in a bibliography (*1*), along with relevant previous work and some of the subsequent press coverage.

Eighty researchers attended the MPS "Workshop on polynomial-time algorithms for linear programming" held in New York on 8 February. The 17 reports presented and lively discussions added much to our knowledge of the subject. There are no written proceedings,

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Scientists and Engineers Pledge Moratorium on Behalf of Colleagues

On 22 January 1980, our colleague Andrei Sakharov, an outstanding scientist and world-renowned leader of human rights, was arrested and exiled to Gorki by the Soviet authorities, for the "crime" of expressing his personal opinions. Since then he has been repeatedly harassed and even physically assaulted by the police. His wife reports he is in poor health. We must help!

To protest the Soviet government's savage treatment of their colleagues Orlov and Shcharansky, more than 2,400 American scientists pledged last year to restrict their scientific cooperation with the Soviet Union. This action was strongly applauded by Sakharov and other Soviet dissidents (and was widely denounced in the Soviet media). Nearly 1,000 French and Australian scientists have also adopted similar pledges. Because of Sakharov's exile and the deteriorating plight of other dissident scientists, we must act now and in much greater numbers than ever before.

We appeal to you, our fellow scientists and engineers the world over, to join together in a strong and significant protest of the Soviet Union's blatant violation of the human rights provisions of the Helsinki Accords to which it is a signatory. We propose a moratorium on scientific cooperation with the Soviet Union for a limited duration linked to Helsinki Accords actions.

To commemorate the founding of the Moscow Helsinki Watch Group by Orlov, Shcharansky and others, the Moratorium shall begin on the fourth anniversary of that date, 12 May 1980. Six months later, on 11 November 1980, there will commence a major conference in Madrid to monitor compliance with the Helsinki Accords, with representation from all 35 countries which signed the treaty. We propose to maintain the Moratorium until the end of the Madrid conference. Evidence from that meeting can then help determine the need for, and the course of, future action.

Scientists everywhere, acting independently of their governments, must express their deep concern now! We urge you to sign the pledge coupon below and to solicit additional signatures from your professional colleagues. The pledge does not preclude personal communication with Soviet scientists in the interests of promoting human rights and world peace.

We will publicize the pledge, along with the names of signers, and send the list to Soviet President and Secretary Leonid Brezhnev and to the President of the Soviet Academy of Sciences, A. P. Aleksandrov.

Moratorium Pledge

To protest the human rights violations by the Soviet Union in the cases of Sakharov, Orlov and Shcharansky, we, the undersigned scientists and engineers, pledge a moratorium on professional cooperation with the Soviet scientific community for a period beginning 12 May 1980, the anniversary of the founding of the Moscow Helsinki Watch Group, and ending at the completion of the November 1980 Madrid Conference to monitor the Helsinki Accords. During this period we will not visit the Soviet Union or welcome Soviet scientists and engineers to our laboratories.

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but most of the short presentations were extracted from authors' longer written papers reviewed in (*1*).

We learned that most of the algorithm Khachian used is the work of other Soviet mathematicians: D. B. Yudin and A. S. Nemirovsky of Moscow, and N. Z. Shor of Kiev, whose article (*2*) states the algorithm in its clearest form and also its best form for practical computation—not only for LP, but for the much more general "convex programming" problem. Because of the multiple authorship and the basic idea—the generation of numbers which, geometrically, describe a sequence of ellipsoids which must all contain a solution and which shrink, so that it is eventually identified—we agreed to refer to it and its near relatives as the "ellipsoid algorithm" (EA). (Khachian showed that, for one EA variant, each step, and thus the whole algorithm, could in principle be executed in "polynomial time" on a suitable computer. That was the finding which excited theoretical computer scientists, since the simpler versions of the generally used method for solving LP problems, Dantzig's "simplex method," have been shown not to run in polynomial, but in exponential time, in the worst case. "Worst case" behavior is always the easiest to study; a theory of "average" behavior, which would explain the fact that, in practice, the simplex method acts like a highly efficient polynomial-time algorithm, does not exist. Misconceived as applying to the traveling salesman and other "NP-complete" problems, Khachian's result overexcited some journalists.)

There is agreement that Khachian's variant will not be used. In both theory and practice it can take thousands of steps to solve trivial problems. A typical real problem of good size might require, say, 1 hour of high-speed computer time to be solved by the simplex method. The computer time for Khachian's variant would be about 50,000,000 years (it is an algorithm for which the "worst case" and "average" behavior are not far apart).

The idea of the EA, though, is intriguing and admits a large number of possible improvements, to which most of the papers at our workshop were directed: the starting ellipsoid chosen can be much smaller than early work indicated; the sequence can often be made to shrink much more rapidly (the way of doing that was discovered independently by 16 of the 42 authors); there are better ways of formulating the LP problem for solution, ways to reduce its size as the EA progresses, improved "stop rules," and proposals for hybrid methods that would use the EA to locate a rough solution which could then be polished off by the simplex method.

Perhaps in combination these ideas will improve the computing speed by several orders of magnitude, and a few hope that, after enough development, the EA will overtake the simplex method for LP. Since the simplex method was invented in 1947, improvements in the algorithm itself are thought to have speeded it up by no more than a factor of 10; the more important development has been the exploitation of "sparseness," the fact that almost all the data in the large matrices used are zeroes and need not enter into the arithmetic. This could account for a factor of 100 in the problem mentioned above, which thus might require 1000 hours, or 0.1 years, using the original version of the simplex method (and 10,000 years on a 1947 model computer). It seems the EA would not have competed with the simplex method had it been available in 1947; what's worse, no one has yet seen how to use the valuable "sparseness" devices in the EA.

One can, however, say this for the EA: it solved a significant theoretical problem and can be used to solve others; it may still be practically useful for the difficult nonlinear problems that Shor deals with; and it certainly brought a new kind of excitement to one area of applied mathematics.

PHILIP WOLFE
Office of the Chairman, Mathematical Programming Society, IBM Research Center 33-2, Post Office Box 218, Yorktown Heights, New York 10598

References

1. "A bibliography for the ellipsoid algorithm," March 1980. Available on request from P. Wolfe, IBM Research Center, P.O. Box 218, Yorktown Heights, N.Y. 10598.
2. N. Z. Shor, *Kibernetika* **13**, 94 (January–February 1977); translated in *Cybernetics* **13**, 94 (September 1977).

A Second "Random Walk"

For a second edition of *A Random Walk in Science* (Crane-Russak, New York, 1974), I should welcome contributions of humor in science, historic and contemporary: anecdotes, witty accounts, cartoons, self-deceptions, and hoaxes. Especially sought are items which, while humorous, also have value for history and insight—in all fields of science. Please identify fully the sources of contributions.

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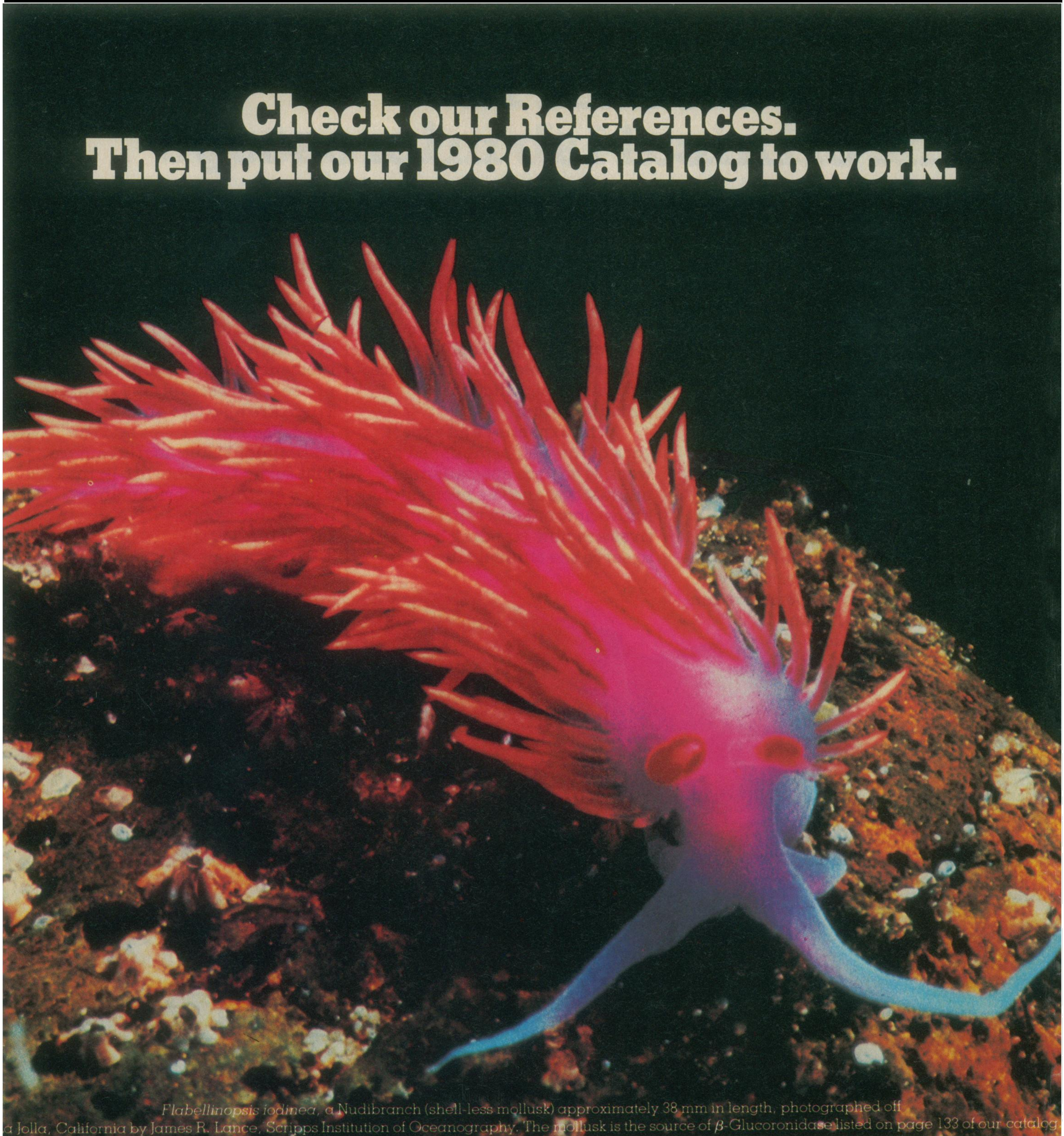

Flabellinopsis iodinea, a Nudibranch (shell-less mollusk) approximately 38 mm in length, photographed off [L]a Jolla, California by James R. Lance, Scripps Institution of Oceanography. The mollusk is the source of β-Glucoronidase listed on page 133 of our catalog.

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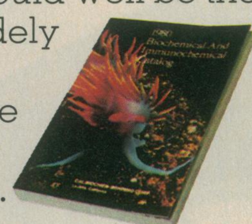

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SCIENCE

U.S. and Soviet Agricultural Research Agendas

Disparities between the United States and the Soviet Union in investments in research and development have been detailed in recent reports.* The Soviets edged out the United States in percentage of gross national product (GNP) committed to total R & D in 1968. They have since increased that lead to 3.4 percent of their GNP compared to 2.2 percent for the United States. By any criterion—percentage of GNP, number of scientists per 10,000 in the labor force population, or absolute numbers—the Soviet Union leads the world in R & D investment.

Nowhere is the gap widening more rapidly than in the area of investments in agricultural research. Reports in the mid-1970's suggested that one-third of the world's agricultural research was conducted in the United States. This is not true in 1980. There are now more than 60,000 agricultural scientists in the Soviet Union and more than 150,000 supporting personnel. They man 48 agricultural experiment stations and 175 research institutes. By comparison, there are around 12,000 agricultural scientists in the United States receiving public support—the combined total in the U.S. Department of Agriculture's Federal Research and State Agricultural Experiment Stations—and a nearly equal number from the industrial sector and others outside the land grant system: a total of 25,000 for the nation.

The number one agricultural research priority in the Soviet Union is stability of production. Seventy percent of the land is not favorable for agriculture, being marginally cold or marginally dry, or both. A related priority is breeding of plants for higher yields and better adaptation to climate variations, mechanization, and resistance to pests. Increasing production of animal products is high on the list. There is a problem in producing sufficient grain and fodder to feed the increasing numbers of livestock. Seed production of forage crops is difficult because of the short growing season.

Soviet scientists are world leaders in wheat genetics (they have moved winter wheat production 200 miles farther north), the development of high-yielding hybrid dwarf sunflowers, and research to reduce environmental stresses on crops and livestock. Expenditures beyond those in the United States are being made for research on photosynthesis, genetic improvements in crops and livestock, forage production, water management, and the soil sciences. There are 21 centers for animal breeding, and institutes in every republic for mechanization, soils and fertilizers, and pest control.

Agricultural academicians hold eminent positions in the Soviet academies—in medicine, engineering, and their National Academy of Sciences. Thirty-four have been designated as heroes. One single advantage of the U.S. agricultural system over the Soviet system is a climate that dependably produces an abundance of crops and livestock. That advantage can be overcome in time by the significantly greater technological inputs now directed by the Soviets into the management of resources, their genetic improvement programs, and their research emphasis on control of the basic biological processes that limit the magnitude and stability of crop production.

The Soviet Union, with its resources of climate, land, and water, its technological inputs, and economic incentives, cannot consistently meet its food needs. The resource base can, however, change with time and technology. The recent imposition of a grain embargo for strategic purposes will accelerate the change. Meanwhile, the share of total R & D expended for agricultural research in the United States has fallen from 39 percent of the total in 1940 to 2 percent in 1980. All this should stimulate debate in Congress, the White House, the federal agencies, and the National Research Council about corrective measures for the low level of support for agricultural research, the kinds of research to be done, and how such research should be managed.—SYLVAN WITTWER, *Director, Michigan State University Agricultural Experiment Station, East Lansing 48824*

*L. E. Nolting and M. Feshbach, *Science*, 1 February 1980, pp. 493-503; National Science Board, *Science Indicators—1978* (National Science Foundation, Washington, D.C., 1979); J. Rhea, *High Technology*, February 1980, pp. 54-61.