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SOUTHWESTERN AND I	ROCKY M	OUNTAIN DIVISION			viding abundant sites for uptake and
Donald J. Nash President	M. Exe	Michelle Balcomb ecutive Director			transport of contaminants. Recent data support a decrease in the lead burden

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of the river. See page 439. [Nenad Iricanin, Department of Oceanography and Ocean Engineering, Florida Insti-tute of Technology, Melbourne 32901]

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Structure of cancer drug bound to DNA

An x-ray crystallographic study shows how cisplatin, one of the most widely used anticancer drugs, binds to bases in DNA (page 412). When cisplatin is bound to a synthetic dinucleotide that is similar to its most common target in DNA, adjacent bases are cross-linked and their normal stacking is disrupted. Sherman et al. theorize that the normal DNA repair mechanisms may not operate on cisplatin-disrupted DNA because the disruptions are highly localized; in addition, in cancer cells the repair enzymes may be repressed. Without repair, DNA replication will be inhibited, and the cells will die, thus accounting for the drug's lethal effect. The "trans" analog of cisplatin cross-links in a different way, connecting bases that are not adjacent. Although it also disrupts DNA, it is not an effective anticancer agent. perhaps because the disruptions are more obvious and can, more effectively, attract available repair enzymes.

Canadian astrobleme

New geochemical evidence supports the interpretation that the Sudbury Igneous Complex in Ontario, Canada, may be an astrobleme, a structure formed by the impact of a meteorite (page 436). The complex is the source of about one fifth of the world's nickel supply, large amounts of copper, and many other metals. Faggart, Basu, and Tatsumoto analyzed isotopes of neodymium (Nd) and concentrations of samarium (Sm) and Nd, both rare earth elements, in rock samples from the Sudbury basin. Rocks from the earth's crust can be distinguished from those in the underlying mantle by the ratio of Nd isotopes; the amounts of Nd and Sm also differ in these layers. Only patterns representative of crustal material were found in Sudbury igneous rocks, indicating that these rocks did not originate in the mantle (the usual source of crustal rocks). The presence of shatter cones in surrounding rocks and other structures that form only from strong impacts also support the meteorite theory. The impact of a meteorite 1840 million years ago would have caused extensive melting of rock in the crust and the formation of magma. The magma would have been emplaced in the crust where, today, the signature of crustal materials is found in the ores.

Lead load lowered

Regulations that were instituted 10 years ago to limit the amount of lead added to gasoline and in that way to diminish environmental lead pollution seem to be paying off (page 439). The amount of pollutant lead transported to the Gulf of Mexico by the Mississippi River in 1982 and 1983 was less than the amount transported a decade earlier, with an overall reduction of 40 percent. The river carries at least half the total sediment load and water transported by U.S. rivers and deposits much of that sediment and associated contaminants in the delta.

25 OCTOBER 1985

Trefry *et al.* analyzed the metal in water, suspended matter, and sediment from the river and its delta. The lead record showed that lead deposition was stable until the later 1800's, when, as a result of lead mining and the industrial revolution, it began to rise. In the 1920's, even more lead was introduced into the environment as lead was added to gasoline. The lead record in the river, together with studies showing decreased amounts of lead in the atmosphere, in soil, and in blood, indicates that environmental lead pollution is decreasing.

Hydrotropism studies take root

Roots of a mutant pea plant can grow straight up into the air for several centimeters in their quest for water as long as the plants are in a chamber with high relative humidity (page 445). This attraction to water, hydrotropism, has now been documented in the laboratory after a century of inconclusive analyses complicated by the powerful and often conflicting force of gravity. In a study of the mutant pea plant 'Ageotropum,' which does not respond to gravity when grown in the dark, Jaffe et al. found that roots will grow up, down, or sideways as long as they sense a gradient of water. The sensor was localized to the root cap, the cover at the tip of the root that protects fragile root cells from mechanical injury inflicted by objects in the soil. Roots could continue to elongate without their caps, but, capless, the direction in which they grew was not dependent on a water gradient. This tropism can now be studied further, isolated from other tropisms (touch, light, gravity) to which plant roots are known to respond.

Synthetic immunosuppressor

Immunosuppressive effects can be produced in culture by a small synthetic peptide fashioned after a membrane component that is common to a number of mammalian retroviruses (page 453). The peptide synthesized by Cianciolo et al. is identical in amino acid composition to a portion of the p15E protein found on the surface of the mouse leukemia virus; homologous proteins are also part of the surfaces of human, cat, and cattle retroviruses. In two separate assays, the synthetic peptide was shown to produce immunosuppressive effects similar to effects produced by natural p15E molecules. During retroviral infections, the immunosuppressive component might suppress the host's immune system, allowing tumor cells to grow in the host unchecked by antibodies or immune cells. Whether the gene for the suppressive substance is introduced into the cell during viral infection or is a host component that is activated by the virus is not known. In either case, its activation at the time of infection or neoplastic transformation could account for the immune suppression that is known to accompany retroviral infections, including the one associated with AIDS.

S

Sample

Let each drop absorb before proceeding

1 drop on S

1

each drop absorb before proceeding Place 1 drop of green (control) on C. Place 2 drops of sample on S. Place 1 drops of sample on S.

Place 2 drops of sample on S on C and Place 1 drop of red lenzyme) on C and

orop on S. Stuid around each hole. Nipe off excess third around each strain. Disce 2 or 2 drose of hire canadrates Wipe off excess fluid around each hole Place 2 of 3 drops of blue (substrate) on both C and on S.

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C

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LETTERS

Biotechnology Issues

I would like to clarify some points in relation to the U.S. Department of Agriculture's handling of biotechnology issues as related to Agracetus's efforts to field test tobacco plants made diseaseresistant by genetic engineering (News and Comment, 16 Aug. p. 634).

The federal government is involved in a very positive manner in an almost singularly unique situation of combining all agency guidelines and regulations in biotechnology in one document. This was done by the Cabinet Council on Biotechnology through the President's Office of Science and Technology Policy (OSTP) and published as a comprehensive statement in the Federal Register of 31 December 1984. Comments have been received from the public on both regulation and research in biotechnology for the entire federal government. As a result, a totally coordinated effort in the review process of biotechnology is evolving that should be to the benefit of all research scientists, industry, and the users of the products of biotechnology.

The Department of Agriculture has a logical distribution of responsibilities. All regulatory aspects of biotechnology are under the purview of the Animal and Plant Health Inspection Service (APHIS). For research issues, I chair the Department of Agriculture's Agriculture Recombinant DNA Research Committee, which reviews recombinant DNA research proposals in agriculture. This committee is department-wide and located in Science and Education under assistant secretary Orville G. Bentley; it is not a part of the Agricultural Research Service. The committee has representatives from all appropriate agencies in the Department of Agriculture, including the Agricultural Research Service, the Cooperative State Research Service, the Office of Grants and Program Systems, and APHIS, as well as representatives from the National Institutes of Health and the National Science Foundation. The entire federal structure for regulation and assessment of biotechnology of which this committee is a part is evolving through the leadership of Bernadine Healy of OSTP and now David T. Kingsbury of NSF, and it promises to function well. During the early evolutionary phases of the expanded recombinant DNA responsibilities, there may be some delays; but in the end it is anticipated that there will be a well-coordinated total federal system in place to the benefit of all parties concerned. A considerable amount of time and consideration has been given to bringing this program to fruition.

JOHN PATRICK JORDAN Office of the Administrator, Cooperative State Research Service, U.S. Department of Agriculture, Washington, D.C. 20250

Crystals in Space

Having many years of experience growing crystals of biological macromolecules, I would like to express my skepticism about growing crystals in space (Research News, 26 July, p. 370).

The problems associated with growing crystals of biological macromolecules for diffraction studies are finding solvent conditions for the production of wellordered single crystals of a suitable habit and a certain minimum size.

If we look at these problems in relation to the (rather meager) data (1) so far presented by the proponents of the space program, we might be able to decide whether it makes "scientific sense."

Each biological macromolecule is unique and, although we have certain general principles (2), the conditions for crystal-growing for each new system must be determined ab initio. Needleshaped or thin-plate crystals present problems to the crystallographer who prefers "chunky" crystals. Given an undesirable habit, it is necessary to search for other conditions to produce other crystal forms, as Blundell indicates. This may require many experiments changing a number of solution variables. Since the β-galactosidase crystals shown by Littke and John (1) are long thin needles, one would think the first priority would be to try to obtain different crystal forms rather than larger ones of the same form.

Most of the emphasis of the space program seems to be on the size of crystals, and Bugg might be correct in that convective currents prevent the growth of large crystals; but how large should they be? More than 30 years ago Low and Richards (3) described the growth in gelatin gels of β-lactalbumin crystals weighing up to 50 milligrams (about 30 cubic millimeters), and Lewin (4) grew crystals of mercury mercaptalbumin derivatives 7 mm long. A requirement for high resolution neutron diffraction is large crystals, and for this purpose lysozyme crystals up to 20 mm³ have been obtained (5). On the other hand, the advent of synchrotron x-ray sources has







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meant that the x-ray crystallographer can use much smaller crystals, say 0.01 to 0.1 mm^3 .

There are various problems associated with disorder in crystals of macromolecules, and what probably concerns us here are lattice defects, which have been attributed to rapid growth. So although Bugg is encouraged by the growth of large lysozyme crystals in only 5 days in space, neither he nor Littke and John (1) provide diffraction evidence that their crystals are better ordered.

It is clear that we need to know how to crystallize and grow diffraction-quality crystals of biological macromolecules. The amount of data now available provides no justification for the enormous costs of a space program to acquire this knowledge. The funds (or a fraction thereof) would be better invested in supporting programs aimed at the determination of the mechanics of crystal growth of biological macromolecules on Earth.

R. Leberman

Grenoble Outstation, European Molecular Biology Laboratory, c/o I.L.L., 156X, 38042 Grenoble, Cedex, France

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 G. A. Bentley, E. D. Duee, S. A. Mason, A. C. Nunes, J. Chim. Phys. 76, 817 (1979).

We would like to put the protein crystal growth experiment described in Kolata's article "The great crystal caper" in perspective. We agree with Blundell that 'there have been very, very few advancements (in the art of making crystals) over the past 20 years. We need a concerted approach." This is precisely why this project was undertaken. A team including fluid physicists, physical chemists, and protein chemists from the Marshall Space Flight Center and the University of Alabama in Huntsville with considerable experience in growing small molecule crystals, both on Earth and in space, has been combined with protein crystallographers from the University of Alabama at Birmingham and other leading institutions in this field to mount an interdisciplinary attack on this important problem.

At present, there are fewer than a dozen papers in the literature that deal with the processes involved in the growth of macromolecular crystals. Our ground-based research and the few papers in the literature strongly suggest

that the growth of most macromolecular systems is controlled by surface kinetics. Calculations indicate that transport of solute to the growth interface of a typical protein crystal in Earth's gravity is dominated by solutal convection after the crystal becomes larger than a few tens of microns. It can also be shown that such transport is sufficient to maintain an excess of solute at the growth interface so that growth is limited by the rate at which the solute can be incorporated into the lattice. By taking away gravity this convective transport can be eliminated, and the growth rate will eventually be controlled by diffusive transport instead of surface kinetics. We conjecture that this should result in a slower growth rate for a given solute concentration, which usually improves the degree of perfection, and a more compact growth habit because of the spherical symmetry of the diffusion field. There are also other advantages of growth in a microgravity environment. The growing crystal can remain suspended in a liquid droplet, which provides a more uniform growth environment that should improve its quality. Also, fewer nucleation events seem to occur in a quiescent supersaturated fluid than in one that is stirred by convection. The larger crystals grown in space by Littke and John (1) at least partially resulted from the fact that fewer crystals nucleated in the flight samples, which meant less competition for solute among the growing crystals.

The description of the experiment in Kolata's article leaves the impression that liquid diffusion is the only growth technique being considered. Our primary emphasis is on the vapor diffusion method, which is a space version of the widely used hanging drop technique. However, we are also exploring the dialysis method along with liquid diffusion.

The experiment performed on shuttle flight 51-D was a simple test of the concept of growing crystals in droplets suspended from syringes under microgravity conditions. One of the major issues was the proper design of the syringe tips to maintain such droplets under the combined effects of interfacial forces and low-level transient accelerations. The unscheduled pursuit of the errant Syncom satellite involved firing of the primary thrusters, which resulted in far greater accelerations than were anticipated. We believe most of the droplets were lost during these maneuvers. We have used what was learned in this flight to redesign the syringe tips to provide for a more stable droplet configuration. Small, inexpensive experiments such as

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Scientific Literacy

It is time to consider the problem of biconceptual education. The world today is divided into two conceptual groups, the scientist and the nonscientist, and the communication gap between them is wide and serious. It is not a problem of respect for scientists. We scientists get all the respect we need-any more is likely to make us candidates for television commercials. I am not saying that lawyers should start reading the Physical Review Letters or mayors the Journal of the American Chemical Society. What concerns me is that some of the fundamental concepts and methodologies of science are outside the understanding of the vast majority of the population, including its opinion-makers.

SCIENCE

For example, scientists in every discipline understand that certain decisions that must be made are associated with some level of risk, but we watch with consternation as society acts as if zero risk could be achieved. The same parents, for instance, who drive their children to school without seat belts demand a flat statement of certainty about the risk posed to their children by being in school with a child with AIDS. The ever-rising levels of malpractice awards are based on the premise that if doctors are punished enough they will become perfect, but ignore the possible outcome that the consequent fee increases will inhibit those with marginal incomes from going to the doctor. Living near a nuclear power plant may be safer than attending a rock concert, but what television viewer would believe that?

A second example is the methodology of "the control." When Pasteur was ready to test his anthrax vaccine he infected both the previously immunized sheep and some nonimmunized controls. The fact that the former lived and the latter died showed that he had made an effective vaccine. Political and civic decisions are frequently made, however, with no attempt to obtain a control sample, which would help determine the efficacy of a course of action. I attended a school board meeting at which a new math program was proposed. A board member suggested that students be divided by lot into two groups, one group to be taught by the new math and one by the old math, with some evaluation at the end of the year. He was denounced by almost everyone at the meeting because one should not conduct "a lottery with students' lives." Prison programs on rehabilitation, medicare programs to balance costs, bilingual education programs, and many other worthy enterprises might be better handled, and more readily improved, if the initial experiments had appropriate controls.

These two examples of scientific concepts are directly transferable to public policy and should be taught to students at the elementary, high school, and college levels. They should be part of a screening test for television anchors, judges, and gubernatorial candidates. Instead, most schools today are diminishing science requirements. Even at the college level, the few universities that have general education requirements allow them to be satisfied by tourist-bus surveys of the wonders of astronomy or the marvels of the body, rather than by a more demanding course in the simple logic of science. Judges and legislators with little or no scientific training are making sweeping decisions on risks to the environment and from nuclear war and industrial accidents. Common sense would argue that an organization such as the Environmental Protection Agency should list the major hazards to health and evaluate them systematically, taking the most important first instead of the most recent headline case.

Scientists will be denounced for trying to introduce cold-blooded reason into an area in which warm-blooded humanity is supposed to reign supreme. But warm emotion frequently gives way to hot-headed anger and even bigotry. The scientific method has been the most effective means of overcoming poverty, starvation, and disease. Even those who are not professional scientists can understand its fundamental concepts, which will aid their decision-making in an increasingly difficult and technological world. It is time to bridge the "concept gap" by improving scientific literacy.-DANIEL E. KOSHLAND, JR.

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No longer need you resort to multiple loading with its increased time and greater required sample volumes. Whether for nucleotide separations in agarose gels or sequencing in acrylamide gels, the technique of wedge-shaped field strength gradients lets you get linearly spaced bands for maximum resolution and ease of reading. Two new instrument systems from LKB render the technique rapid, reliable and above all, reproducible.

In the Maxiphor[™] horizontal electrophoresis unit (A), it is the simplest thing in the world to pour wedge-shaped agarose bridge gels directly on the central platform when adjustable legs beneath the cathode dam are extended. Gels can be run rapidly at high power even without external buffer circulation, the half-litre reservoir providing enough internal cooling capacity even at 500 volts. Want to use the Maxiphor for constant thickness bridge or submarine gels? Just as easily done. And you can run up to 40 samples every time.

For greatest economy and speed in fragment separations, the sibling Miniphor[™] unit (B) with its integral cooling jacket lets you run submarine gels at very high power. Companion to both units is the LKB constant power supply (C) that permits regulation to 1 volt or 1 milliamp with 1 minute precision for automated runs. And completing the system is the MacroVue[™] transilluminator (D) whose optical design permits you to detect as little as 1 ng DNA in a single band. This instrument makes publication grade photography easy.



cing in DNA/RNA electrophoresis <u>d gradient gels</u>

In the Macromould¹⁵ unit (E), you can cast wedge-shaped acrylamide gels that are covalently bonded to a glass plate for maximum support. (If you are interested in constant thickness gels, you can cast them as thin as 0.1 m, allowing much greater use of ³⁵S labeling with its attendant virtues of lower scattering and better resolution – without wrapping or refrigeration – as well as longer half-life and improved safety.)

When gels are run in the Macrophor[™] vertical electrophoresis unit (F), the unique thermostatic plate ensures constant high temperature, letting you use every millimeter of width to run a full 36 samples – without smiling. Consorts to the Macromould and Macrophor are the compact MultiTemp[™] II thermostatic circulator (G) and the Macrodrive[™] 5 high capacity power supply (H) with its digital display. And just as with the horizontal electrophoresis units, you can get here a full complement of chemicals, accessories and technical literature.

Two informative illustrated bulletins are waiting for you. Request them today.











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