Research News

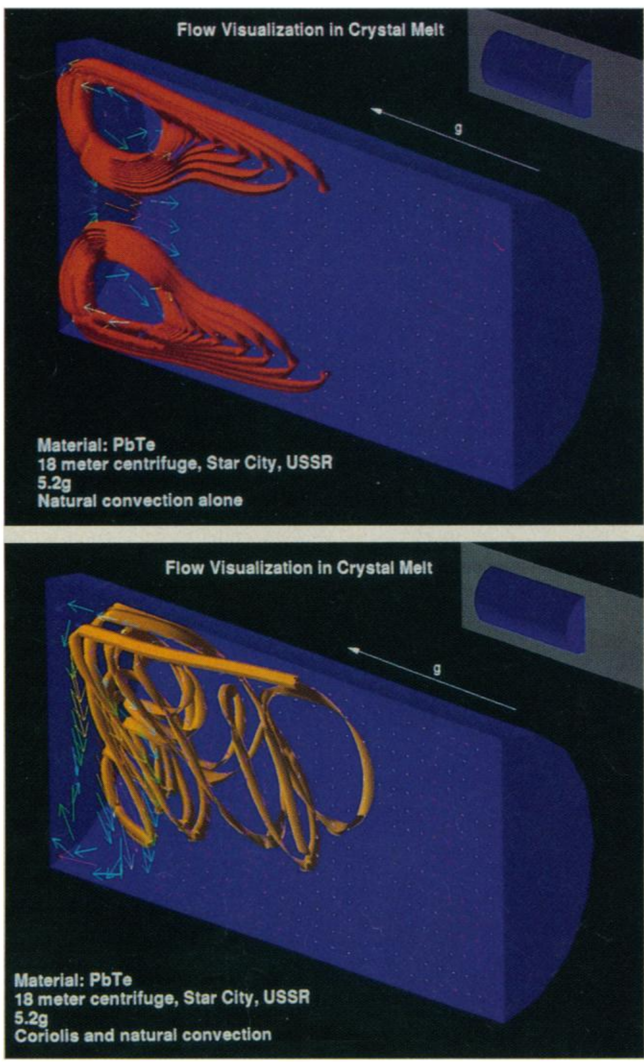
The High Side of Gravity

When g's go up, crystals can grow bigger and better. Materials scientists are wondering how it could have taken them so long to notice

IN THE FALL OF 1965, CHEMIST PAUL Shlichta stood watching as a friend of his, biochemist Makio Murayama of the National Institutes of Health, removed a glass tube from a centrifuge. The tube had gone into the centrifuge holding a uniform red solution of the blood protein hemoglobin, but now a beautiful red layer of the protein molecules had collected at the bottom of the tube, while the overlying solution had emerged clear and colorless. As Shlichta noticed how the high-gravity ride in the centrifuge had concentrated the hemoglobin, he suddenly saw a link between centrifuges and his own interest in crystals. By concentrating solute molecules at the bottom of a solution, he realized, a centrifuge could hasten crystal growth. "The next week," Shlichta says, "I was growing crystals in a centrifuge in my lab," then at the McDonnell Douglas Corp. in Huntington Beach, California. By 1968 he and a colleague had published a paper called "Growth of Crystals by Centrifugation" in the *Journal of Crystal Growth*. Trouble was, no one paid much attention.

That was then. Now, 20 years later, Shlichta finds himself part of an international alliance of researchers who have discovered that cranking up the force of gravity can do more than speed crystal growth. While NASA struggles to sell its multibillion-dollar space station, in part by touting its potential for processing high quality materials in low gravity, Shlichta and colleagues are achieving something similar in centrifuges that hike the g's. There, crystals and alloys can be formed more uniformly and freer of defects than under normal gravity. As these researchers see it, they have experienced gravitational consciousness-raising.

In their experiments, these innovators have passed beyond the conventional view of gravity as an inviolable condition, not to be tinkered with. Instead, they see gravity as a tweakable variable like temperature, pressure, and chemical composition. But that doesn't mean that the members of this fledgling high-gravity club can yet control the effects of their newest variable. While they envision applications for their improved materials ranging from novel microelectronics and sensors to chemical catalysts, high-strength ceramics, and thermal insulation, they are working by trial and error—only sometimes do higher g forces yield better materials, and when they do nobody knows just why. So there is a second motivation for work in the field. As materials theorist Arnon Chait of NASA's Lewis Research Center explains it, researchers are enticed by the scientific mystery of how the forces generated by centrifuges affect fluid flow and solidification in melts and solutions.



Chait and Arnold

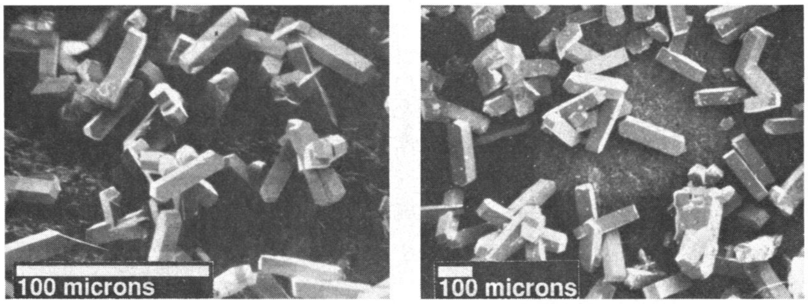
Going for a spin. *A Cray-3 simulates fluid motions in a lead telluride melt at 5.2 g. Laminar flow gives way to thorough mixing when the Coriolis effect is included in the model.*

The puzzle of high gravity's favorable effects is underscored by ordinary gravity's propensity for mischief—its relentless capacity for eliciting defect-producing motions in crystallizing liquids. For example, gravity pulls colder, denser regions of a liquid downward, forcing warmer, less dense regions upward. This process of convection, together with other gravitational effects like sedimentation, leads to uneven crystal growth. As a result, crystal growers have long been eager to escape gravity altogether and carry out crystal growth in space.

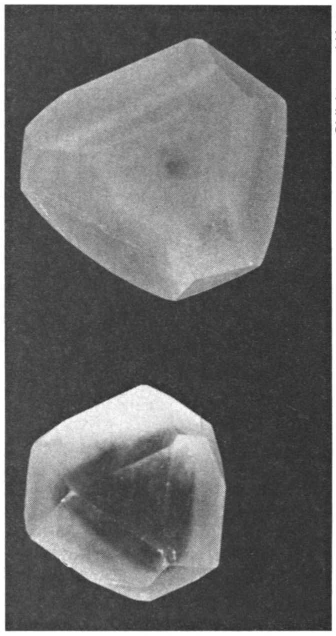
Indeed, many of the researchers now studying high gravity first explored it only because they were searching for a counterpoint to their microgravity studies. But in doing so they stumbled across evidence that escaping normal gravity can be worthwhile no matter which direction you go in.

Whether they reached the high-gravity realm by chance, as Shlichta did, or by way of low gravity, high-gravity researchers have tended to work in obscurity, isolated from each other and from the wider scientific community. Many of their publications have appeared in non-English journals, effectively keeping much of the world in the dark. Also, the field is so new that it doesn't yet have clear academic niches or its own journal.

But a sense of community has begun to well up. These globally distributed centrifuge twirlers are discovering one another, starting collaborations, giving talks at prestigious forums such as the Gordon Conferences, and trying to establish national and international high-gravity research centers—one in Boulder, Colorado, and another near Moscow. Some of the first graduate students in high-gravity



Hayhurst *et al.*


Shlichta and Knox

Crystal power. *Zeolite crystals grown at 50 g* (above right) *dwarf ones grown in normal gravity* (above left)*, as revealed by the scale bars. Lead nitrate crystals come out cloudy at 121 g, but 41,300 g yields unexpected clarity* (below).

materials science are spreading enthusiasm about the field to their post-graduate destinations. And at the end of May, dozens of members in this new research specialty gathered for the "First International Workshop on Materials Processing in High Gravity," held by the banks of the Volga River in Dubna, USSR. There they discussed topics ranging from centrifuge growth of high-quality protein crystals to high-gravity superconductor processing—an effort that has yielded intriguing hints of materials that become superconductors at record high temperatures.

As much as anyone, Liya Regel, the workshop's primary organizer and head of materials processing in space at the Space Research Institute in Moscow, deserves credit for getting the new research agenda under way. In 1987, she dubbed the field "gravitational materials science." And with her long-time research collaborator, Huguette Rodot of the National Center for Scientific Research (CNRS) in Meudon, France, she provided some of the most dramatic demonstrations of high gravity's potential for spawning pristine crystals.

Like many others in the field, Regel and Rodot first discovered the attraction of high gravity while exploring low gravity; indeed, they first met 11 years ago at a conference on low-gravity crystal growth. Regel's position in the Soviet Space Research Institute gave her access to an enormous centrifuge at the Gagarin Cosmonaut Training Center in Star City, near Moscow. The centrifuge's principal use was to twirl cosmonauts sitting in a cabin at the end of the 18-meter arm into a high-g state, but Regel and Rodot decided to replace the human cargo with crystal-growing apparatus. They hoped to accentuate convection, sedimentation, and other unruly crystal-tainting motions due to gravity; data from the centrifuge, they thought, would complement results from low-gravity experiments.

Equipped with a crystal-growing furnace designed specifically for the centrifuge experiments, the researchers studied the crystallization of semiconductors such as lead telluride at gravitational values up to 8 g. Rodot and her husband, Michel, replicated those semiconductor experiments in a smaller French centrifuge in Nantes. In other studies, Regel and Rodot studied the solidification of metal alloys, including tellurium-selenium and aluminum-copper.

To their amazement, the researchers did not get the exaggerated imperfections—bubbles, dislocations, and boundaries between crystal phases—that they anticipated. Instead, "these experiments unexpectedly revealed the possibility of suppressing impurity striations in semiconductor crystals," Regel noted in a recent unpublished review making the rounds of the high-gravity club. As for the alloys, they often sported fewer imperfections than those prepared under normal gravity, and quite different microstructures. "It appears possible to obtain materials that are better than those grown with only Earth's gravity imposed," Regel said in an interview.

Stranger still, these beneficial effects were most pronounced at certain "magic" g values—5.2 for the Soviet centrifuge and about 2 for the smaller French machine in Nantes. At g's above and below these figures, the quality of the product declined. What is special about these g values, and why they vary in different machines, remains mysterious. "The very terminology 'magic g' enunciates our ignorance" of the mechanisms underlying solidification at high gravity, says William R. Wilcox, director of the Center for Crystal Growth in Space at Clarkson University in Potsdam, New York, a co-organizer of the Dubna meeting.

But theorists are beginning to make some headway. One researcher who thinks he has some insight into what is happening at high-g is Georg Müller of the Friedrich Alexander University in Erlangen-Nürnberg, Germany. In his own experiments, Müller studied how high gravity could prevent defect striations from forming in crystals of impure indium antimonide. After doing numerical simulations of the fluid flows that might be wiping out the striations, Müller arrived at a theoretical explanation, which he published last year and presented at the Dubna workshop.

Müller's theory, which researchers consider to be the most complete so far, relies not so much on the high gravity generated by the centrifuge as on a byproduct of the centrifuge's whirling motion: the Coriolis effect, which acts to deflect the flow of fluids in rotating systems. Flows twisted by the Coriolis effect, Müller proposed, swirl through the solidifying sample, giving it a much more thorough and steady stirring than it would get if it were stationary. The defect striations that ordinarily would form are effectively homogenized. Following Müller's lead, theorist Chait and Clarkson University graduate student William Arnold have done computer simulations of Regel's and Rodot's studies with lead telluride to help visualize some of the complex fluid mechanics—governed partly by the Coriolis effect—that might be occurring in centrifuge-spun crystal melts.

But Chait thinks that though the Coriolis effect may indeed play a part in the favorable influence of a centrifuge ride, it surely isn't the only factor. "Whenever you have motion in a centrifuge, life gets messy," concurs civil engineer Robert Schmidt of Boeing Aerospace Company, an expert in the physics of centrifuges. Other factors that might affect solidification in still unknown ways include slight variations in the gravitational force in different parts of the sample, depending on their exact position in the centrifuge, and Earth's ever-present 1 g, pulling downward on samples as they whirl around in their "swinging-bucket" containers like children swung by their parents. Temperature fluctuations within the samples and variations in sample density are also likely to leave their mark.

But had Edison waited until he completely understood what he was doing, the light bulb might have had a much later debut. So some high-gravity explorers have already begun looking toward potential commercial spinoffs from their high-gravity work. David Hayhurst of Cleveland State University and his colleagues at Battelle

Memorial Institute in Columbus began pondering alternatives to microgravity after the space shuttle Challenger exploded in 1986. By 1988, the team was looking under the microscope at excitingly large zeolite (silicalite) crystals—labyrinthine catalyst crystals used in such key industrial processes as cracking big oil molecules into the smaller components making up gasoline—grown in a centrifuge at 20 to 50 times Earth's gravity.

Without the centrifuge, the team had been able to convert roughly 10% of their starting materials into silicalite crystals with diameters in the 200 micron range, already big compared to the 1 micron of standard industrial zeolites. In the centrifuge, "we went to the 500 micron range, and we could make almost all of our starting material usable," Hayhurst says. The team has applied for a patent on high-gravity zeolite making, and Battelle is now investigating ways of transferring the technology to industry.

Shlichta also hopes to make high-gravity processing a commercial reality; he now heads his own company, Crystal Research, in San Pedro, California. Right now he's taking aim at scintillation crystals, which are central to medical imaging technologies such as positron emission tomography (PET) scanners. Growth in a centrifuge, he thinks, should yield higher quality scintillation crystals, less riddled with sensitivity-limiting defects.

Shlichta sees no end to the possibilities of gravitational materials science, which he thinks will be played out all across the gravitational spectrum. He divides that spectrum into several regions—low gravity in space, normal gravity on Earth, a range of about 1 g to about 20 g in large centrifuges like Regel's, and a range of hundreds to many thousands of times normal gravity in ultracentrifuges. Wilcox adds another exotic gravity region—between 1 g and the micro-g of space—that could be produced in a centrifuge spinning on a spacecraft. Each region of the spectrum, Shlichta suspects, will turn out to be best for processing specific kinds of materials. For example, microgravity in space might be best for making most protein crystals and the 1-50 g range for growing more perfect semiconductors.

For Shlichta and his cohorts, the lack of theoretical guidance about what they will find as they explore the gravitational spectrum only adds to the excitement: "We have a brand new baby here and we don't yet know what it will grow into," he says. But then Shlichta's tone turns grave as he reflects on how long it has taken for scientists to realize that the value of g is an experimental condition—something to fool around with. "We should have just had our fiftieth [high-gravity] conference, not the first one," he laments. ■ IVAN AMATO

Three Li'l Pigs and the Hunt for Blood Substitutes

Human hemoglobin can now be made in pigs. But will it provide an easy path to a human blood substitute?

LAST MONTH WHEN DNX, INC., A BIOtechnology company in Princeton, New Jersey, reported that its scientists had created genetically engineered pigs that produce human hemoglobin, the achievement was widely hailed—most notably in a front page story in *The New York Times*—as a milestone in the effort to develop a human blood substitute. Medical researchers have been trying to produce such a substitute for about 50 years. Ideally, it would have several major advantages over the fresh human blood now used for transfusions. It would have a long shelf life and not require refrigeration. And it would be unlikely to trigger possibly lethal immunological reactions or to transmit AIDS, hepatitis, and other viral diseases.


Mark Lyons

Down on the gene farm. *One of DNX's pigs, genetically engineered to make human hemoglobin, takes it easy.*

But little heralded in the news accounts about the transgenic pigs were a number of significant obstacles that DNX will still have to overcome before the medical community gets its long-sought blood substitute. "The production of transgenic pigs represents a genetic feat," says hematologist Joseph Baron of the University of Chicago's Pritzker School of Medicine, "but it does not address the key issues in medical therapy."

The transgenic pigs produced by DNX make normal human hemoglobin—and so far efforts to adapt normal human hemoglobin for use as a blood substitute have not panned out for several reasons (also see *Science*, 21 December 1990, p. 1655).

A blood substitute has to perform one critical function: It must pick up life-supporting oxygen in the lungs and deliver it to the tissues of the body. In the bloodstream, of course, that's done by the hemoglobin carried within the red blood cells. But researchers learned early on that hemoglobin alone doesn't work. The free hemoglobin protein binds oxygen all right—but with such high affinity that it can't release enough to the tissues.

And there's another serious problem that also prevents use of plain, purified hemoglobin as a blood substitute. When hemoglobin is removed from the confines of the red blood cell, the molecule, which is composed of four protein chains, breaks into two halves. These dimers are rapidly filtered out of the blood by the kidneys, which may become irreparably damaged for reasons that aren't fully understood.

In recent years, a number of companies, including Northfield Laboratories, located north of Chicago, and Biopure Corp., an Upjohn subsidiary in Boston, have tried to surmount these problems by chemically modifying hemoglobin so that the protein chains are crosslinked or polymerized. That produces a molecule that is both stable and capable of releasing the oxygen that tissues need. But while animal studies of the modified hemoglobins have been encouraging, human trials haven't fared well.

Last year, for example, Biopure conducted a successful trial of its modified bovine hemoglobin in Guatemala, but this spring the company's parent, Upjohn, abruptly halted a similar trial it was conducting in Kalamazoo, Michigan, for reasons that company officials haven't explained. Similarly, Northfield successfully administered its polymerized human hemoglobin to healthy