

need of improvement. It recommends that the traditionally independent Max Planck Society forge closer ties to universities and develop research groups that can respond more quickly to rapid new developments in science. In addition, it suggests that universities replace the post-Ph.D. "habilitation" qualification for aspiring professors with something like the U.S.-style "assistant professor" system, and that the DFG restructure its peer-review system and its strategy for promoting new disciplines. Overall, panelists found, the research system tends to be driven by middle managers, such as Max Planck institute directors. "There are great merits in a strong middle, but we'd also like to see a bit more life at the upper and lower levels," says Brook, who directed a Max Planck institute in Stuttgart from 1988 to 1991.

After its yearlong inquiry, the panel concluded that closer cooperation between Max Planck institutes and university researchers might help improve what Brook calls the "mixed reputation" of German universities. Some scientists criticize Germany's university system for being too rigid, especially during the habilitation years. German federal research minister Edelgard Bulmahn, deputy chair of the BLK, has pointed out similar shortcomings. In a recent interview with *Science*, she said she wants to phase out the habilitation—a lengthy process during which postdocs do major projects under the strict supervision of professors—and bolster ties between university and nonuniversity research. Last week, Bulmahn called for "an intensive discussion" of the report's findings.

Brook says the panel found the DFG granting agency to have "a conservative nature" that could be revitalized by revamping aspects of its structure and programs, and perhaps by more actively steering researchers toward areas of research that it deems important. The report suggests a "strategically oriented program" for research grants, as well as a more active approach to funding progressive university programs, such as those supporting the early independence of young scientists. It also recommends opening up the DFG's peer-review system—for example, by including more women and younger researchers as reviewers.

Both the DFG and Max Planck responded swiftly to the report. The DFG's president, biochemist Ernst-Ludwig Winnacker, calls it "a thorough analysis" and says the DFG has already set up new funding programs for independent young scientists and is expanding its roster of peer reviewers. But Winnacker questions the suggestion that the DFG cherry-pick areas of new high-priority research: "The DFG cannot, must not, and should not compete with the federal and state governments, which are extensively involved in research funding that is guided by

general political criteria."

In a statement, Max Planck said it was already "well prepared" to implement some of the commission's suggestions, in part because the society is in the midst of an internal reassessment, and also because it has already taken steps to strengthen its connections to universities and to bolster its programs for young researchers. The society plans to establish several "International Max Planck Research Schools" near universities, increasing the number of Ph.D. students who conduct research at its institutes.

Brook says he expects German research to continue to thrive, especially if reforms are embraced: "It's much more difficult to evaluate a high-quality research system, such as Germany's, than a low-quality one."

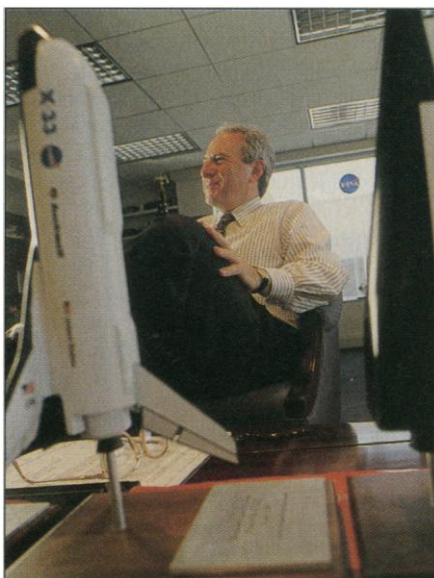
—ROBERT KOENIG

PHYSICS

Come Fly With Me, Goldin Tells Physicists

BATAVIA, ILLINOIS—Space is the final frontier for particle physics, NASA Administrator Daniel Goldin declared in a 28 May press conference here at the Fermi National Accelerator Laboratory (Fermilab). But Goldin's vision of joining forces with the Department of Energy (DOE) and other agencies in an all-out assault on the mysteries of gravity and high-energy physics failed to uplift some listeners when he labeled Earth-bound accelerators—the focus of DOE's high-energy physics program—a "smokestack approach" to research.

The message of the press conference, which also included representatives from DOE and the National Science Foundation

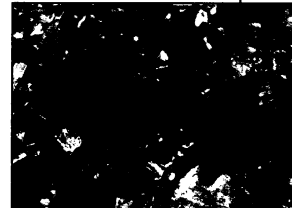


All aboard. Goldin wants high-energy physicists to propose space experiments.

ScienceScope

Experimental Shellfish Mussel Shoals—now known as Muscle Shoals—may once again live up to its name. The U.S. Fish and Wildlife Service (FWS) announced last week that it wants to re-introduce 16 species of endangered shellfish to the 20-kilometer stretch of Alabama's Tennessee River, once known for its dense populations of freshwater mussels.

In the 1930s, pollution and dam construction devastated the shelly shoals. But the river has bounced back, and biologists believe that they could soon begin to restore monkeyface, pigtoed (above), and other mussels. Before replanting can begin, however, the FWS has to reassure some local shellfish harvesters and governments that the protected species won't bring unwanted regulation. To jump that hurdle, the service has proposed calling the returnees "nonessential experimental" populations, a designation that "will avoid lawsuits," says one FWS official. Shellfish friends and foes have until 26 July to comment.



Making Amend(ment)s The battle over a law that requires federally funded scientists to hand over raw data to anyone who files a request has shifted back to Congress. This spring, the White House Office of Management and Budget (OMB) collected more than 8,000 comments on its proposal for implementing the 8-month-old measure, many from scientists worried that it would hinder research by threatening patient confidentiality and proprietary collaborations with companies. In response to that concern, House appropriations committee members James Walsh (R-NY) and David Price (D-NC) plan to offer an amendment to OMB's funding bill that would put a 1-year hold on the law pending a study on its effects.

Business groups are squaring off over the amendment. Supporting the delay are pharmaceutical, biotech, and other firms, including GM and IBM. They are opposed by a legion of oil companies, the U.S. Chamber of Commerce, and small business groups. No use handicapping this contest: "It could go either way," says a Walsh staffer.

If approved by the House and Senate, the amendment—which could be offered as early as next week—wouldn't go into effect until 1 October, after OMB is expected to have issued its final rule.

(NSF), was that the agencies are encouraging grant proposals submitted to them jointly. Goldin argued that because of the colossally high energies at play in the big bang, the neighborhood of black holes, and within neutron stars, these astrophysical phenomena should be regarded as physics experiments that dwarf anything that can be done on Earth. NASA satellites, he said, could exploit those natural experiments by collecting radiation or particles, insuring that physicists would no longer be "victims of the last [terrestrial] machine you built."

Goldin's reference to scientists who focus on "the next bigger machine based on yesterday's technology," however, ruffled some scientists at Fermilab, which was just four days away from dedicating its latest particle accelerator, the \$260 million Main Injector. Physicist and DOE Under Secretary Ernest Moniz, who was seated next to Goldin, interjected politely that physicists can look forward to "important advances, as well, in accelerator-based experiments."

A subsequent speech by Goldin during a conference here had been purged of disparaging references to standard particle accelerators that appeared in earlier drafts and received generally positive reviews. "Dan Goldin's inspiring set of things to do was really spectacular, I thought," said Leon Lederman, a Fermilab Nobel laureate in particle physics. "That's a grand vision," added Scott Burles, an astronomer at the University of Chicago, although "you're going to have to be very clever to come up with [actual] missions."

Goldin was short on specifics, and Moniz, at the press conference, stipulated that no new advisory body would be formed to guide the effort, whose direction would instead be determined by individual proposals that passed peer review. Nor was there any mention of new money to fund the initiative. In his speech, however, Goldin said that several years ago, when he first proposed NASA's "Origins" program to study the origins of life in the cosmos, "we didn't have a nickel in the budget" for it, but funding materialized as his vision got fleshed out.

In response to a question at the press conference, Goldin did show some interest in a concrete proposal by Saul Perlmutter of Lawrence Berkeley National Laboratory to build a telescopic satellite that would vastly expand both the quantity and precision of observations of distant supernovae, which have suggested that space is filled with a strange form of energy that counteracts gravity on large scales (see *Science*, 18 December 1998, p. 2156). The satellite would rely on new charge-coupled device light-sensing technology developed at the DOE lab. "I think it's very exciting," said David Spergel, a Princeton University cosmologist

who is familiar with Perlmutter's concept. If NASA and DOE can get in the same flight pattern, particle physics may yet go where it has never gone before.

—JAMES GLANZ

SYNTHETIC CHEMISTRY

40 Steps to a Chemical Synthesis Summit

Like mountaineers who set off to scale ever more challenging peaks, organic chemists over the past half-century have tested the limits of their skills by attempting to synthesize increasingly complicated natural molecules, such as antibiotics and steroid hormones. The most fiendishly complex tar-

particular finesse. "The functional groups bump into each other so that it's difficult to work on one portion of the molecule without affecting another part," he says.

The CP molecules originally attracted attention when researchers at the pharmaceutical giant Pfizer showed that they inhibited the work of a cancer-causing gene known as *Ras*, which is overactive in up to 80% of human cancers. CPs, it turns out, block the addition of a chemical group known as a farnesyl group onto the *Ras* gene, a key step in its activation. Other more potent farnesyl blockers have been discovered, says Takushi Kaneko, a medicinal chemist at Pfizer's research center in Groton, Connecticut, who helped nail down the CP molecules' struc-

ture. But the new synthesis work could still prove vital, he says, by allowing chemists to manufacture CP analogs that may prove even more potent and also easier to produce than the CPs themselves.

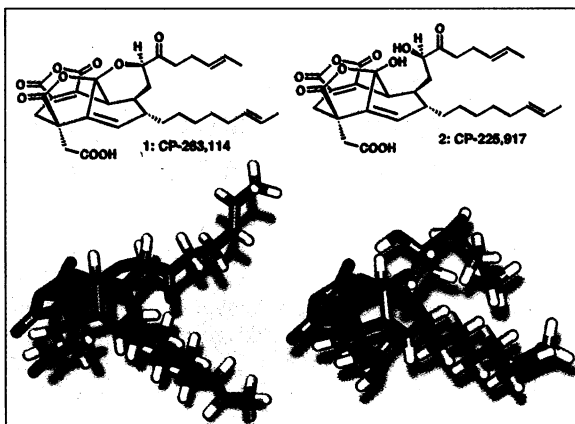
Getting this far was a nearly 2-year slog. In all, it took more than 40 chemical steps and many grams of starting materials to make milligrams of the molecules, which consist of a core ring of nine carbon atoms bearing three more carbon-oxygen rings. And twice the group had progressed to key intermediate compounds along the way,

only to find that although they were only a few bonds away from the complete structure, they could not forge the final links.

The final attempt that got them to the summit took three key steps. First, the researchers had to convert a linear hydrocarbon precursor molecule into the nine-membered ring at the core of each CP molecule. They turned to a well-known ring-forming process known as an intramolecular Diels-Alder reaction and tweaked the reaction conditions to coax the precursor to adopt the correct ring-shaped structure.

For the next step, the Scripps researchers developed a set of novel "cascade" reactions. Cascade reactions run through a staccato of intermediate steps—each one automatically producing the right materials and conditions for the next—before ending up at a final product. The researchers used two of their cascade reactions to fuse two additional five-membered carbon and oxygen rings to opposite sides of the core. A final summit push, consisting of a flurry of reactions, provided them with one of the CPs, called CP-263,114, the more stable of the pair.

But they also wanted to make its partner, CP-225,917, which differs only in that one of the three attached rings is broken, the



Molecular mountains. Two years of chemical finesse went into mimicking these natural molecules.

gets have taken synthesis labs a decade or more to conquer. With the completion of each new project, labs scan the horizon for even higher peaks. And in the past 2 years, few mountaintops were more tantalizing than a pair of jellyfish-shaped molecules found in 1997 in a fungus.

One enticement was the anticancer and cholesterol-lowering properties of the natural compounds, called CP molecules. The other was their complexity. The molecules' compact structure, crammed with chemical groups, made them "diabolical" targets, says K. C. Nicolaou, an organic chemist at The Scripps Research Institute in La Jolla and the University of California, San Diego. But in the 1 June issue of *Angewandte Chemie*, Nicolaou and his colleagues report having scaled that demonic peak: They have performed the first-ever complete synthesis of the CP molecules.

"It's an extremely impressive accomplishment," says Samuel Danishefsky, whose own group at Columbia University in New York City was closing in on the same goal. Other recently synthesized molecules have been more than four times the size of the CPs, which have 31 carbon atoms each. But Danishefsky says the CP molecules require