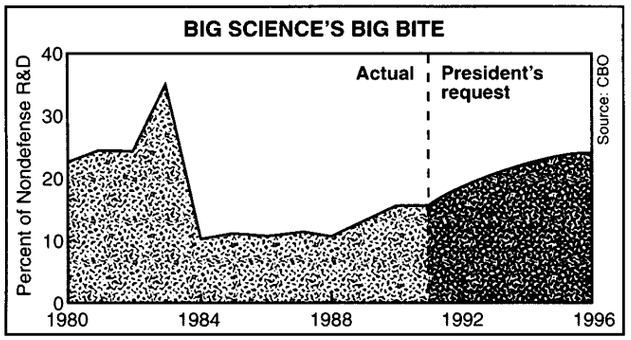
Tilting Toward Megaprojects

As you watch Congress approve billions of dollars for the space station, perhaps you get the impression that Big Science is taking a bigger and bigger bite out of the federal government's research budget. You're right. The 80 largest government science projects —those costing more than $25 million apiece—will consume 15% of nondefense R&D funds this year, up from 10% in the mid-1980s. And, if the Bush Administration's budget proposals were to be adopted, Big Science would eat up 22% of federal nondefense R&D by 1996 (see chart). But before you rail at the unprecedented gluttony of Big Science, look back to 1983. Big Science accounted for a whopping 35% of nondefense R&D spending, thanks in large part to the enormous appetite of the space shuttle in its final stages of development.



Back to the future. *The Big Science spike in the early 1980s was caused by the space shuttle; much of the rise in the 1990s reflects space station funding.*

The figures come from the Congressional Budget Office (CBO), which last week published perhaps the most comprehensive look yet at the balance between big and little science in the federal budget.* While not every trend line will confirm the worst fears of small science supporters, that group will see plenty in the report to worry about. For example, it won't take 80 projects to munch up 15% of all nondefense R&D by 1996. The three biggest projects—the space station, the Superconducting Super Collider, and the Earth Observing System—will manage that all by themselves.

Of course, the Bush Administration's budget projections assume that overall spending on nondefense R&D will climb fast enough over the decade to accommodate the growing cost of Big Science and still provide healthy increases for other R&D projects. Indeed, the CBO study points out that that has been the case for the past few years: Although Big Science has increased its share of the total, most other areas of science and technology have also experienced real growth.

The report warns, however, that overall growth in nondefense R&D cannot be counted on. One reason: Last year's budget agreement will hold down total domestic spending through 1995, so any expansion in total R&D budgets will be at the expense of other programs. Moreover, if the megaprojects experience cost overruns—a common feature of the genre—they will inevitably cut into some of the growth projected for little science. A combination of slow overall growth and cost overruns could be disastrous. In CBO's worst-case (though unlikely) scenario, the Administration's proposed funding for R&D other than big projects would be reduced by 45% by 1996.

CBO notes that some big projects—it cites the shuttle and the space station as examples—are not, strictly speaking, science projects, but they compete directly with other R&D projects. Says the report, the shuttle has been "the most dramatic instance of a large R&D project crowding out other R&D spending in the 1980s."

Would canceling one or more big projects help alleviate the pressure on other science budgets? Perhaps. The report notes that scrapping the space station would save $2 billion to $2.6 billion a year. But there's no guarantee that those savings would be applied to science rather than, say, housing, or a more costly bank bailout, or some yet undiscovered S&L-like scandal.

■ COLIN NORMAN

**Large Nondefense R&D Projects in the Budget: 1980-1996,* Congressional Budget Office, July 1991.

Communist Academics Refuse to Fade Away

Berlin—Communism may be dead and buried in eastern Germany but at least one of its legacies—the old boy network of communist-appointed university staff—appears to be alive and kicking. Earlier this month, the renowned Humboldt University in east Berlin succeeded in upsetting delicate arrangements made at the time of unification by winning an injunction against the Berlin government. The result: University staff appointed by the old regime can hold onto their tenured jobs, even if they had links to the STASI, the former regime's state security apparatus—indeed, even if they had helped dismiss free-thinking colleagues. A prolonged legal battle with widespread implications looks set to follow.

The case of *Humboldt* v. *Berlin* began when the new city-state government of Berlin inherited the university, which is public in the U.S. sense of the word and is situated on Unter den Linden right in the center of old Berlin. Closing it down altogether appeared out of the question, given that it was founded in 1810 by Wilhelm von Humboldt—the great statesman and philosopher to which Germany owes the idea of the university as an independent body combining research and teaching. But to the democrats running Berlin it seemed equally impossible to take over the university just as it was, with a large number of appointees adhering to the party line of the former communist government.


Bettman

Turning in his grave? *Wilhelm von Humboldt.*

Last December, the Berlin government opted for a middle way, closing all departments that appeared to be ideologically slanted and dismissing their staff. The Berlin government planned to reopen the departments and hire a new staff later. Some would be rehired from the previous staff—but only those proven to have no links to the STASI or to alleged human-rights cases involving abuse of subordinates.

The plan seemed perfect. By closing departments instead of dismissing individuals, strict West German laws that protect individual employment rights could be avoided. Without a way around these laws, some Germans joke that unification would have been canceled—each and every one of the 14,000 university research workers and 18,300 employees of the Academy of Science (to say nothing of 1.7 million civil

servants) whose workplaces are being reorganized would have had the right to sue the government. The judicial system would have crashed.

"Abwicklung," or winding up—popularly regarded as a way of removing the rights of people being made redundant—was agreed to by both East and West German governments before unification and, at first glance, appeared to have won the approval of the Supreme Court when it ruled on the practice in April. But it seems that the Berlin government did not read the fine print of that ruling as closely as did Humboldt University's endangered faculty.

University officials noticed that the court wrote: "The winding up of a facility implies its disintegration." In legal terms, that means that either the body disappears altogether or it is taken over by another body, neither of which has happened to the Humboldt University.

With that technicality behind them, 700 of 2522 tenured staff whose departments had officially been wound-up in December are now once more secure in their old jobs. This has infuriated longtime opponents of the old regime. At Berlin's Free University—founded in 1948 by professors and students forced out of the Humboldt by political pressure and now competing with the Humboldt for scarce research funds—there are calls for the "complete disintegration" of the Humboldt. That, of course, would be lawful.

It is not a suggestion that the Humboldt takes kindly. For Heinrich Fink, a theologian and freely elected president of the Humboldt, the issue is whether the Berlin government should have a say in the closure of university departments—whether they contain appointees of the old regime or not. He is sure to fight for the university's right to settle the matter in its own way.

The Berlin government is not simply going to leave the matter to the university. Aware that the Humboldt disagreement may prove a test case for other east German institutes where the policy of "fire-and-rehire" has been used, Berlin's senator for science and technology, Manfred Erhardt, is instead going to try to win the case in the courts. If necessary, he states, he is determined to take the case all the way up to the Federal Administrative Court, where issues of civil administration can be settled at the national level.

But this could prove a dangerous gamble—the case may take years to settle and if the government loses, Erhardt will have set a precedent with very costly repercussions.

■ RICHARD SIETMANN

Richard Sietmann is a free-lance science writer living in Berlin.

Promising AIDS Drug Looking for a Sponsor

Citing corporate strategy, Hoffmann-La Roche has decided not to pursue a compound that has excited AIDS researchers

AIDS RESEARCHERS ARE GENERALLY LEERY of expressing a lot of enthusiasm for new therapies, for fear of raising false hopes. But listen to their testimonials about a new compound that blocks the action of a viral protein called *tat*:

"From everything I know and have seen, and I have personally worked with the drug in vitro, it looks like a very promising and exciting compound," says virologist Douglas D. Richman of the University of California at San Diego.

"If it really is a relatively safe inhibitor of *tat* function or *tat* expression, it sounds like a fantastic way to approach the problem," says molecular biologist Robert C. Gallo of the National Cancer Institute.

"It's a very tantalizing approach," says Martin Hirsch of Harvard Medical School, chairman of the AIDS Program Advisory Committee to the National Institutes of Health.

So with this much enthusiasm for the drug, surely its developer, international pharmaceutical giant Hoffmann-La Roche, is pulling out all the stops to rush it into clinical development, right? Wrong. Apart from one small phase I toxicity trial at Johns Hopkins University Medical School in Baltimore, the new drug, code-named RO 24-7429, is going nowhere. The company has apparently decided that it would not make an adequate profit by developing and testing the drug itself and is trying to license it to another company. Roche spokesman Paul Oestreicher says several companies have expressed interest, but so far there have been no takers.

The story of RO 24-7429 illustrates the difficulty of setting public health policy when legitimate corporate interests are at odds with public health priorities. Roche scientists began looking at a *tat* inhibitor as a potential AIDS therapy in 1987. The federal government, through the AIDS program at the National Institutes of Allergy and Infectious Diseases (NIAID), agreed that the work was promising, and has been providing about $700,000 a year for basic research on the *tat* protein to a consortium of groups headed by Roche since September 1988. Two other companies are also working on anti-*tat* drugs, but they are said to be not nearly as far along as Roche.

The reason there is such interest in an anti-*tat* drug is that it represents a completely new approach for attacking the AIDS virus (see box). The tat protein binds to a specific site on the virus's own RNA and promotes the expression of other genes coding for functional proteins essential for the virus' survival. Mutant forms of HIV lacking the *tat* gene appear normal, but are incapable of infecting cells. Moreover, *tat* has been implicated in a variety of the clinical syndromes associated with HIV infection, including fostering the spread of Kaposi's sarcoma and damaging immune functioning. Blocking *tat*'s activity could have several therapeutic benefits.

Roche scientists developed an assay to screen compounds for their ability to prevent the *tat* protein from binding to the viral RNA. To their surprise, the most effective compound they tested was a benzodiazepine derivative, the class of drugs—including the Roche drug Valium—that are used for anti-anxiety therapy. Tests in rats showed that the first candidate drug had unacceptable kidney toxicity, but by the start of this year the company had found a close chemical relative that appeared safe enough to be tested in humans. Moreover, laboratory research showed that the anti-*tat* compound had the added advantage of acting synergistically with drugs like AZT to stop the spread of the viral infection.

News that a trial was imminent first appeared in *AIDS Treatment News*, a newsletter published in San Francisco. The toxicity trial, initially involving about 18 patients, began at Johns Hopkins University in May. But after a few weeks, it was stopped. The reason, according to Roche spokesman Oestreicher, was that the company decided to focus its efforts on two other compounds further along in the drug development pipeline—DDC, a cousin of AZT, and an anti-HIV-protease drug being tested in England. Oestreicher says the decision not to pursue RO 24-7429 does not represent a lack of commitment to AIDS therapies: To the contrary, Oestreicher points out that in addition to the antiviral compounds, Roche is marketing AIDS therapies such as interferon alpha for treating Kaposi's sarcoma