development," he says. Although there are some promising approaches, such as using mass spectrometry and a DNA "chip" (*Science*, 27 September 1991, p. 1489) to determine sequences, there have been no "breakthroughs" on the sequencing front that will speed things up (or lower the cost) in a way that would make starting a large-scale sequencing program practical.

But, Hood adds, even "if I gave you tomorrow a DNA sequencer that could do 50 times the throughput of sequencing, in many ways it wouldn't do you any good. The front end of producing the fragments for sequencing, and the back end of the computational tasks have to be matched," he says. "So there's this enormous task of systems integration which has largely been ignored."

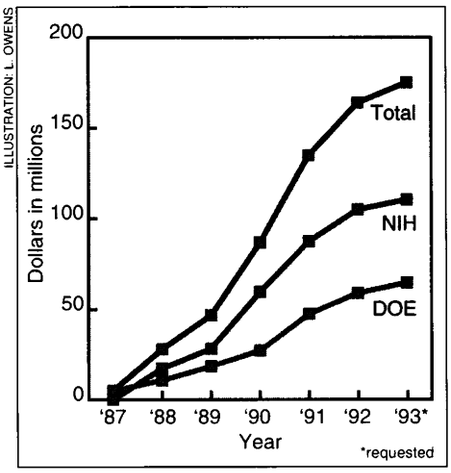
Big vs. small science

Hood's complaint lies at the core of the debate that the next director will have to resolve: how to balance small science that usually fosters innovation with the larger infrastructure needed to complete the genome project. The European Community has proceeded with a kind of "cottage industry" approach to the yeast genome (*Science*, 8 May, p. 730), but even proponents of that scheme admit it is not the most efficient way of getting the job done. So Watson, along with DOE, decided to establish larger centers.

There are now seven NIH-supported centers scattered around the country, and they account for about one-quarter of the NIH genome budget. Their share of the project is expected to grow, and that, says UCSF molecular biologist Bruce Alberts, is bound to cause political problems: "They are going to need more support than they have, and more support than the community would like, because it's the kind of support that most of us never get." Maynard Olson, a physical mapper at Washington University, agrees. Olson, who will leave St. Louis next fall to join a large genome effort being organized by Hood at the University of Washington in Seattle, says there is a reticence to move away from investigator-initiated projects: "There are many people in the American scientific community who will support small mediocrity before they will even consider the possibility that there can be some large excellence."

But in the minds of many, the move toward big genome centers is keeping people away from the genome project. Craig Venter, a sequencer at the National Institute of Neurological Disorders and Stroke, is a proponent of a distributed structure for the program. Venter, who caused a stir by applying for a patent on several thousand gene fragments without knowing the biological function of the proteins the genes coded for, says bigger isn't better: "People were told, 'If it isn't going to be large scale, don't apply here. If you're not going to sequence 2 million bases, don't send in an application because it will get turned down,'" says Venter. "As a result, nobody has sequenced 2 million of anything."

Stanford geneticist Paul Berg, who chairs the NIH Program Advisory Committee on the Human Genome, agrees that the next director should listen to what smaller labs say they can do for the genome project. Berg argues that more of the budget should be spent on pursuing the interesting biology that is discovered as scientists work on maps and sequences—a belief that put him at odds with Watson. "Clearly, Jim and I differ in that way. Jim says if you want to get the genome project done, you've got to keep people's nose to the grindstone, and not let them go off on tangents to satisfy their curiosity," he says. "I think that to maintain interest and excitement about the program, we have to link it to [gene] function in some way."



Reaching a plateau. Federal funding for the genome project, split between NIH and DOE, has begun to level off.

"Paul Berg has never really understood the point of the thing," says Watson, betraying the blunt style that some find off-putting. "He thinks we should be spending some of our money on gene function. I don't think so. We're there as a resource for other people. So if you want to study your gene, that part of the chromosome is already at hand, and you don't have to isolate it yourself."

Wanted: working scientist

What kind of leader would be able to satisfy all the constituencies that make up the ge-

A Standing Ovation From the Troops

James Watson may have rubbed some researchers the wrong way with his blunt, abrasive style during his 3-year reign as head of the Human Genome Project at the National Institutes of Health. But, to judge by the reception he received last week from more than 450 scientists gathered at the Cold Spring Harbor Laboratory for the annual genome mapping and sequencing meeting, his leadership will be fondly remembered. In what was clearly a bittersweet moment for all concerned, Watson made a brief appearance before the overflowing crowd, which gave him a standing ovation.

"I had wanted to quit—but not necessarily the way I did," said Watson, in an obvious dig at NIH Director Bernadine Healy, who Watson says forced him out—a charge Healy roundly denies (*Science*, 17 April, p. 301).

Then Watson had a few words of advice for his successor: Whoever takes the job must be willing to fight for more money amid a chorus of demands for more support from other areas of biology, he said, adding in vintage Watson style: "All science isn't equally interesting. Getting the human genes and the other genomes is the most important thing in biology."

That kind of passion is just what the project will need in its new leader, says Maynard Olson, a physical mapper who will join the University of Washington this summer—and Olson should know: just last week he was appointed by Healy along with 13 other top scientists to act as a search committee (see accompanying story).

Watson, in any case, is convinced that he's handing the project over in good shape, a conclusion he said is evident from last week's meeting—with its 350 talks and posters. Even though large-scale sequencing still lags behind expectations, mapping is clearly going full tilt, and some notable advances were reported, including an all-but-complete map of the Y chromosome, done by David Page's group at the Whitehead Institute; the mega-YACS, or yeast artificial chromosomes, developed at the Centre d'Etude du Polymorphisme Humaine in Paris (without NIH funding), which promise to speed genome mapping worldwide; and the extensive maps of the mouse genome developed by Eric Lander's genome center at the Massachusetts Institute of Technology. "It has been an American success and an international success, and I am very pleased," said Watson.

–Leslie Roberts