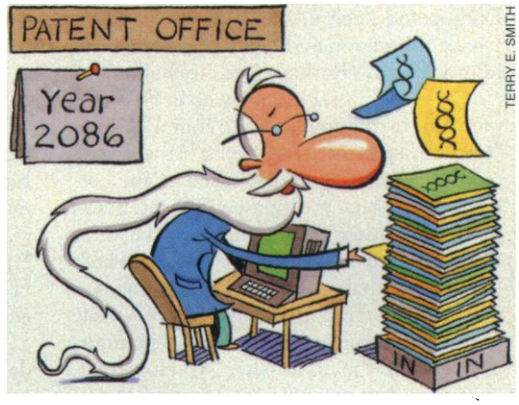
DNA PATENTS

Patent Office Faces 90-Year Backlog



Not so long ago, recalls author Robert Cook-Deegan, a grant reviewer at the National Institutes of Health (NIH) dismissed the automated DNA sequencer as "a $100,000 paperweight." That attitude is now dead and buried: Automated sequencers have not only gained respect, they've taken over like the sorcerer's apprentice, churning out a flood of high-quality genetic data. They have also caused a revolution in biology, and, it seems, a crisis at the U.S. Patent and Trademark Office (PTO).

Last month, PTO Commissioner Bruce Lehman called for help, inviting outside experts to suggest ways of managing the flood of DNA sequences in new patent applications. While some academic researchers have been signing a pledge not to patent raw DNA sequences (*Science*, 26 April, p. 477), companies that specialize in sequencing DNA—chiefly Incyte Pharmaceuticals of Palo Alto, California, and Human Genome Sciences (HGS) of Rockville, Maryland—have been channeling data from their mechanized processes into the PTO at a torrential rate. Unless changes are made, PTO official John Doll projects it could take a single senior staffer more than 90 years to examine the DNA sequences already in the queue. At Lehman's request, the PTO gave a public briefing on 3 April to outline the scope of the problem, then held public hearings—one in San Diego on 16 April and one in Washington, D.C., on 24 April—to elicit ideas from genome researchers, computer wizards, and attorneys on how to streamline a painstaking and time-consuming process.

The PTO in 1992 rejected an application from NIH that included thousands of gene fragments on grounds that the function of the DNA was not known. NIH decided not to appeal. But this hasn't deterred private gene hunters. Their strategy is not to win patents on every DNA sequence they've identified, HGS's bioinformatics chief Michael Fanon concedes. Instead, their goal is to establish priority, to show "we were there first," Fanon says.

Even if PTO ends up rejecting an application, it must first check each sequence named in the patent claims against other sequences stored in five major databases to ensure uniqueness, explains examiner James Martinell of PTO's group 1800, which handles DNA patents. The PTO employs a rigorous scanning routine, called the Smith-Waterman algorithm, to identify all potentially related data. It is more sensitive to weak or distant matches (and thus more demanding of computer time) than the programs used by Incyte, HGS, or the government's genetic data repository, GenBank. To handle the task, the PTO employs two sophisticated MasPar computers, each running 16,000 processors in parallel. Once the data search is complete, a staffer examines the results to ensure that each claimed DNA sequence is "nonobvious"—not a minor modification of one that's already been claimed. This requires the judgment of a senior examiner. Today, that means each claim gets a final review by Martinell.

So far, says Doll, head of group 1800, PTO has received about 100 large DNA patent applications. That may not sound like much, but each application may contain multiple sequences. To maximize the $1000 filing fee, the high-volume sequencers jam clusters of DNA fragments into each application. For example, Incyte puts as many as 5000 DNA sequences into a single application, says Incyte's chief scientific officer, Randy Scott. He estimates the company has filed "over 400,000" sequences.

Doll took the calculations a step further. He says it takes about 60 to 65 hours to examine a batch of 100 sequences, for a cost of about $5000. This means that the sequences now awaiting review will take the PTO a century to complete, for more than $20 million. Yet the fees may come to $100,000. So far, Incyte has not received any gene patents; HGS announced in April that it has received three—for human genes encoding a bone degrading enzyme, a blood protein, and a superoxide dismutase.

Lehman said in a phone interview that the PTO is facing an "unacceptable" situation. The agency will either have to give up hope of acting soon on most DNA sequence claims, or grab staff from other parts of the agency to satisfy the genomics industry. Because the PTO now supports itself entirely with customer fees, this means that chemistry and electronics applicants would be "taxed" to pay for DNA patents. Lehman thinks that would be unfair.

Several possible changes could be made, Lehman says. The PTO could ask DNA sequence applicants to do more background research themselves. It could put new limits on the applications it accepts. It could create a two-step process to screen applications that lack a substantial description of the function and utility of sequences before committing resources to examining them. And it could contract out its research. But each choice has drawbacks, and new legislation would be needed to make these options possible.

Lehman is mulling over the ideas that witnesses submitted at the hearings. Meanwhile, Incyte and HGS are forging ahead. "We've got our sequencers running in three shifts, 24 hours a day, 7 days a week," Scott says. And, like his competitors at HGS, he's expanding his fleet of robots.

–Eliot Marshall

GERMANY

Staff, Students Protest University Cuts

BERLIN—Not since the heady days of anti–Vietnam War protests and student strikes had Berliners seen such a massive university demonstration. But this time the 30,000 students who took to the streets on 24 April were not railing against the academic establishment; they were marching in step with militant university presidents, deans, faculty, and many scientists who joined in protesting deep cuts in Berlin's subsidies for higher education and university research.

Berlin's government ordered the reductions this spring as part of an austerity program to solve a budget crisis, and city officials said last week that they will be implemented in spite of the protests. The city government plans to slash budgets for Berlin's universities and colleges by $130 million this year, followed by another $166 million in cutbacks over the next 6 years. Aside from shrinking Berlin's combined student body by 30,000 (to 85,000 students), the cutbacks require the Berlin Free University (FU) to close its dentistry school; Humboldt University to shutter its pharmacy school; and the three main universities to save another $9 million by better coordinating studies and research.

Scientists at Berlin's three major universities have warned that the cuts could have a long-term impact on the ability of the city's university-based researchers to obtain grants and carry out some research projects. "If such cutbacks continue, it could be a catastrophe for the international competitiveness of our scientific research," says Michael Müller-Preussker, a physicist who is Humboldt University's vice president for natural sciences. FU President Johann W. Gerlach denounces the reductions as "a disaster." He joined Humboldt President Marlis