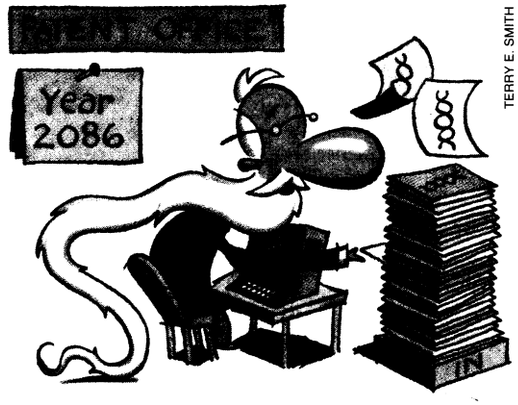
DNA PATENTS

Patent Office Faces 90-Year Backlog



TERRY E. SMITH

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

Dürkop and Technical University President Dieter Schumann in the protest march and a rally at Berlin's Rathaus, the city hall.

Physicist Günter Kaindl, who is FU's vice president for natural sciences, complains that "science departments are being hit very seriously—particularly by the speed of the cutbacks." He says the number of untenured teaching positions in the sciences will be "drastically reduced"—thereby weakening research efforts—and that as a result university scientists may have trouble competing for some outside grants that require major "matching" commitments from the university. At Humboldt, chemistry department chair Manfred Meisel agrees that "budget problems in research and teaching will become critical in coming years."

Other Humboldt scientists express concern that the cutbacks may delay the plan to move Humboldt's science departments to Berlin's new Adlershof research center and high-tech industrial park. While Berlin remains committed to Adlershof, the budget cuts will hit subsidies for the Institute for Applied Chemistry there, and will force Humboldt's science departments to shrink their faculties.

Some academics fear the reductions will damage Berlin's reputation as a scientific center—the city had already slashed subsidies to the FU's prestigious Dahlem Conferences (*Science*, 9 December 1994, p. 1636). But the Berlin official responsible for higher education, Peter Radunski, insists that Germany's capital will remain an important center for scientific research. He says the subsidy cutbacks will give Berlin's universities the opportunity to "break taboos and come up with new approaches." While city officials say the cuts are final, university students are planning other protests, perhaps culminating in a student strike later this spring.

–Robert Koenig

Robert Koenig is a writer in Berlin.

GENES AND BEHAVIOR

Wiley Drops IQ Book After Public Furor

Psychologist Christopher Brand of Edinburgh University got some extensive prepublication publicity for his new book on intelligence quotients (IQ) earlier this month when he made some provocative comments to reporters on race differences in IQ. But the publicity won't help sales: As a result of the furor his remarks touched off, the publisher, John Wiley & Sons, withdrew the book on the eve of publication. Edinburgh University, following student protests and calls for Brand's dismissal, has arranged for an inquiry into his teaching. Meanwhile, Brand's supporters are calling on academics to boycott Wiley.

Review copies of the book, a 247-page work called *The G Factor*, have been circulating in the United States and the United Kingdom since February. The work aroused no special attention, however, until the outspoken Brand began telling reporters that he believes genes play a role in average IQ differences between races. Asked if he were a racist, Brand told one weekly, *The Scotsman*, that he might be called a "scientific racist" because "I do think not only that there's a link between race and psychology, in particular between race and IQ, but of course I think and have the honesty to tell you—other people wouldn't—that the link is, shall I call it, deep-seated?"

Such statements evoked outraged headlines, protests from members of Parliament, student boycotts of his lectures, calls for his resignation—and a change of heart at Wiley. On 17 April, the day before the U.K. publication date, the New York office issued a statement: "After careful consideration of the statements made recently by author Christopher Brand (as reported in the British press), as well as some of the views presented in his work ... we have decided to withdraw the book from publication. [Wiley] does not want to support these views by disseminating them or be associated with a book that makes assertions that we find repellent."

The G Factor—"g" refers to "general intelligence," a factor derived by psychometricians from IQ tests—reviews current research on IQ, to which Brand's best-known contribution has been "inspection time" experiments that purportedly show that IQ is related to the brain's speed of information processing. Other researchers say the book contains little that's new. About 10% of it is about race, according to Brand. Among other things, it states that IQ tests are not racially biased, that there is a persistent 15-point IQ gap between blacks and whites, and that research has not yet identified environmental factors that could explain that difference.

LARA ELSWORTH-JONES

Author without a book. Psychologist Christopher Brand's comments gave Wiley cold feet.

Susan Spilka of the Wiley corporate communications department says that Wiley initially had no problems with the book, which she describes as "a scientific monograph intended for a very limited audience." But after Brand talked to the press, she says, management took a closer look. It decided that his public comments were "inconsistent with the general tone of the book." But not totally inconsistent—management also felt that "one could infer some of the same views" the author had conveyed to reporters. Spilka says "We have told Mr. Brand we will cooperate in any transition process to another publisher [including] supplying films or unjacketed copies."

Brand is not taking this about-face lying down. "I am fighting 100% on all fronts," he told *Science*. He's demanding $75,000 compensation from Wiley, has called for an academics' boycott of Wiley products, and is looking for "a no-win-no-fee American lawyer to smash U.S. Wiley."

Many of Brand's colleagues have expressed dismay over Wiley's action. "I thought we were moving away from this political correctness sort of thing. It just boggles the mind," says psychologist Thomas Bouchard of the University of Minnesota. Psychologist James Flynn of the University of New Zealand sent an e-mail to colleagues supporting Brand even though he disagrees with his views on race differences in IQ. Says Flynn: "The cowardice of publishers is a real problem that makes progress toward understanding the real world ... difficult."

Edinburgh University is busy trying to smooth the domestic waters. The principal, Sir Stewart Southerland, has assigned Neil MacCormick, dean of the faculty of social sciences, to "compile a report on the teaching relationship" between Brand (who has taught at Edinburgh since 1970) and his students, "particularly in the light of reports of dissatisfaction by students."

Brand is not the only author to run into problems publishing books that touch on race differences in IQ. Indeed, the patriarch of modern U.S. IQ research, Arthur Jensen, professor emeritus at the University of California, Berkeley, says he has had a hard time finding a publisher for his magnum opus on intelligence. The first 12 chapters of the 800-plus-page tome—also called *The G Factor*—are now sitting at a publisher's awaiting a final decision on a contract. The publisher he finally pinned his hopes on? John Wiley & Sons. A Wiley editor says there should be no problem with publishing the book "assuming the reviews [on the final two chapters] are as positive as they have been" for the rest of the book.

–Constance Holden