Biotechnology Boom Reaches Agriculture

Major corporations and phalanx of new research firms bet bioengineering will make major impact down on the farm

The first wave of biotechnology companies aimed mainly at the medical and pharmaceutical market. Now, industry is moving to apply genetic engineering techniques to boost production and profits in agriculture.

The major initiatives have come from chemical, oil, and pharmaceutical companies that are expanding their own research capabilities or investing in the new "agrigenetics" companies that are proliferating. One result is stiff competition for the relatively small number of academic researchers with the requisite skills.

For university faculty with the right credentials, the boom in biotechnology has opened new opportunities for consulting assignments or careers in industry and also scope to become entrepreneurs themselves. A familiar plaint in universities has been that plant science research has long been underfunded by federal agencies and underappreciated by the agricultural research establishment. The new demand for research manpower in agricultural bioengineering creates problems for the universities in keeping faculty and maintaining graduate programs in the field. The increasing numbers of academics straddling the university and industry sectors are testing the ground rules governing such arrangements.

The science being counted on to justify industry investment stems chiefly from recombinant DNA technology and cell tissue culture work. Although some fundamental problems remain to be solved, the expectations are that biotechnology will ultimately make it possible to enhance crop yields, accelerate growth rates, and increase plant resistance to biological and environmental stresses.

Typical of the advances envisioned is improvement of biological nitrogen fixation in plants, which would reduce the need for fertilizer. The varied attack on the problem includes efforts to increase the nitrogen-fixing abilities of the bacteria which inhabit the nodules on the roots of legumes like soybeans and to use recombinant DNA techniques to introduce nitrogen-fixing capacities into plants such as cereals, which now require heavy applications of fertilizer.

The current state of the art in tissue culture makes rapid propagation of some plants and mass production of desirable types feasible. Cellular manipulation techniques appear to promise an ability in the future to produce mutants and hybrids in the laboratory, thus providing an advantageous alternative to conventional plant breeding.

The shadow on a generally optimistic picture is the fact that the genetic makeup of plants is far more complex than that of bacteria and fungi on which DNA research has been concentrated. And there is mixed opinion about how soon major returns on investment can be expected.

The current activity by industry actually represents a second stage. During the 1970's, a number of seed companies were purchased by chemical, oil, and pharmaceutical companies. Ciba-Geigy bought Funk, Sandoz took over Northrup King, and Occidental Oil bought Ring Around Products. Pfizer, Stauffer, Shell, Upjohn, and Atlantic-Richfield all purchased seed companies.

In recent years, investment by large corporations has focused more narrowly on research. On 1 August Monsanto opened a molecular biology laboratory for agricultural research as part of its central laboratories in St. Louis. A dozen Ph.D.'s were hired, and there is talk of expansion. Monsanto has also invested in first-wave biotechnology companies such as Biogen, Genex, and Genentech. Atlantic-Richfield is establishing a plant cell research institute in Dublin, California. Ciba-Geigy is watching work in biotechnology done by its pharmaceutical research group for applications in agriculture and is supporting plant cell tissue work in a company-supported research foundation in Basel. Companies with existing major agricultural research programs like DuPont are putting increased emphasis on biotechnology. Occidental Oil now owns Zoecon, a company in Palo Alto, California, formed to develop biological controls for insects, which is expanding its plant research capabilities.

The number of new companies concentrating on applications of bioengineering to agriculture is put at more than 50. Among those usually cited in discussions of the new industry are Agrigenetics Corporation based in Denver, International Plant Research Institute in San Carlos, California, and Advanced Genetics Science Ltd. of Bermuda and Greenwich, Connecticut.

First-wave biotechnology companies like Biogen, Cetus, Genentech, and Genex, which have worked mostly on medical applications, are expected to be increasingly interested in agriculture. Cetus is establishing a research labora-

0036-8075/81/0918-1339$01.00/0

tory in Madison, Wisconsin, that will focus on bioengineering in agriculture.

For corporations, the logic of owning a seed company as a condition of moving seriously into bioengineering research is compelling. Seed company expertise is in plant breeding, production, and marketing. Without such expertise, triumphs in the laboratory cannot be easily translated into the most likely product—seed.

Significantly, the major independent seed companies, notably Pioneer and DeKalb, and many food companies in the agribusiness galaxy are going slow on bioengineering research. This caution seems based on doubts about an early payoff. Pioneer Hi-Bred International, the dominant seller of hybrid corn seed with a third of the market, is establishing a microbiology department near its plant breeding center outside Des Moines, Iowa. And Pioneer chairman William L. Brown, who came up through the plant breeding and research side of the company, has no question that the genetic engineering will have a major effect on applications but says, "I think it will be some time before we'll be able to move genes around in higher organisms." Pioneer is establishing the new microbiology department, Brown says, because the company feels it is "good to get our feet wet" and be prepared to take advantage of opportunities in the future. The emphasis at Pioneer, he says, "will continue to be on classical plant breeding."

Successful plant breeding is an exercise in practical genetics. As background, the successful plant breeder needs a knowledge of plant physiology and pathology, entomology, statistics, and more than a dash of intuition and luck. It is a vocation that requires long hours of painstaking work in the field. Over the last generation, plant breeders who point out that they have been doing genetic engineering all along, have improved their effectiveness through the use of computers and new monitoring technology.

Industry plant breeders have their counterparts in the public sector, primarily in the land-grant universities and U.S. Department of Agriculture (USDA) experiment stations. A division of labor developed, with the public sector doing the basic research, providing graduate education, and developing breeding methodologies. Industry concentrated on applied research, breeding new plant lines and producing seed.

The recession in federal support of research hit plant science research hard at a time when it seemed to be on the threshold of new life promised by the postwar revolution in biochemistry. And as interest in biotechnology in agriculture warmed, industry found it had to take up the slack left by government. Now expenditures on biotechnology by government have been outpaced by industry spending.

The sudden growth in demand for research manpower in the field has created shortage conditions. In plant physiology, a discipline central to bioengineering in agriculture, for example, low levels of research funding have limited graduate education. According to G. Ray Noggle, a plant physiologist at North Carolina State who doubles as an official of the American Society of Plant Physiologists, about 50 institutions, most of them land-grant universities, have doctoral programs in plant physiology. The current yearly output of Ph.D.'s in the field is roughly 100, although some of these are interested in a more traditional brand of plant physiology and are not candidates for the biotechnology cadre.

An indication of a sellers' market in plant physiology is a number of postdoctoral positions currently unfilled. The society's August newsletter carries four pages of "positions available" notices. Top pay noted for postdoctoral positions in universities is $16,000 a year, with the average considerably lower. The Atlantic-Richfield Plant Cell Research Institute announces in the same issue that fifteen 2-year postdoctoral positions paying $20,000 a year are available in "molecular biology, genetic engineering and genetics, tissue culture, etc." Standard Oil Co. of Ohio is in the process of building a research group interested in increasing plant productivity, and Shell Development Company is also represented in the newsletter want ads.

The sudden growth in demand for research manpower in the field has created shortage conditions.

One established firm recently announced a major expansion in its program of plant research and advertised in the scientific press for recruits to both its molecular biology and plant breeding groups. A company executive describes the result—300 to 400 responses—as "overwhelming." Roughly 20 percent of the respondents proved to have the background and training sought, but the company official noted that those representing "the cream of the crop were entertaining several offers." He described the market as "competitive to highly competitive for the best talent."

The premium candidates divide into two main categories. The first is made up of scientists fresh from the universities with new Ph.D.'s or postdoctoral experience. In this category, says the company official, "there are more jobs than people." The competition is even greater for the category of "established scientists with national or international reputations. These are much fewer in number." They are counted on to become "the nucleus of a research group and provide scientific oversight" for a laboratory. "People like that are in very short supply."

No reliable surveys of pay in the field are available, but a safe generalization is that industry pays more than universities can. Industry salaries in the $30,000 range and up for researchers with recent Ph.D.'s in the hot specialties are apparently not unusual. For senior researchers, employment terms often include concessions of equity in a company or other elements not reflected immediately in income, but salaries of $75,000 and up are not unheard of for those who take full-time jobs.

In the universities, expansion of programs in high-demand fields will be difficult since research funding is almost static and few new faculty positions are available. At Iowa State University, for example, cytogeneticist Peter A. Petersen, who has made his mark with work on transposable elements in corn, has won recognition and encouragement from university administrators. Nevertheless, he has run up against shortages of research space and equipment. As a result he has turned to collaboration with a research group at a Max Planck Institute in Cologne, Germany, which is equipped for the genetic technology essential to his work.

More and more faculty members are dividing their time between university and industry on a formal basis. One of these is Winston Brill of the University of Wisconsin, noted for work on nitrogen fixation. Since 1 July, Brill has been scientific director of the Cetus Madison laboratory. He will spend half time at Cetus. Brill says that Cetus disarmed possible adverse reactions to the advent of what might seem to be an off-campus rival by consulting university officials and faculty throughout the process of planning and establishing the new lab.

How will Brill handle what appears to be two full-time jobs? He says he plans to spend half of every day at the university and half at Cetus. His university schedule will be revised to emphasize research. He will drop formal teaching responsibilities, but he says that he will give priority to keeping contact with students. Cetus is still seeking zoning changes for a laboratory site near the campus and will start in temporary quarters. The plan for the first phase of operations is to have a staff of 25 Ph.D.'s with double that number of master's and bachelor degree personnel in support. Agrigenetics Corporation will also operate a plant research lab in Madison.

A different formula has been worked out by Peter S. Carlson, a tissue culture expert at Michigan State University. Carlson is spending 3 months a year at Occidental Oil's Zoecon division. His title is chief scientist, and he is helping the firm to build a bioengineering capacity in agriculture equal to that in nonchemical measures of insect control.

Carlson says his dual role creates "no problem." He thinks that being "direct and up front" about negotiating such arrangements is important in avoiding difficulties. Carlson is candid in saying that the expertise he and his colleagues possess is in demand and provides "good leverage." In 10 years that may not be so.

Worries about conflict of interest are relatively new in the life sciences sector of agricultural research. Such concerns are much more familiar in engineering and other scientific disciplines with connections to industry, such as chemistry. In the universities, the 1980's are likely to be a sometimes uncomfortable period of adjustment for the biosciences. For industry, the decade will impose a test of patience on investors and company officials awaiting the dawn of the brave new world of biotechnology.—JOHN WALSH

Sir Isaac Newton: Mad as a Hatter

Historians spin complex theories to explain Newton's year of lunacy, but hairs from his head tell a simpler story: mercury poisoning

That Sir Isaac Newton went mad for a short period in the middle of a brilliant scientific career has never been the subject of debate among contemporary historians of science. The signs, especially from the dark year of 1693, are clear. Newton broke with associates, accused friends of plotting against him, slept little, and reported conversations that did not take place.

What puzzles historians are the reasons for this short-lived lunacy. Some scholars propose psychological factors and point to the death of Newton's mother. Others suggest more mundane causes, such as overwork, Newton's failure to get certain administrative posts, and the traumatic loss by fire of some valuable manuscripts.

Not about to settle for speculation on causes of the derangement, a chemist and a historian a few years ago wrote to Newton's descendants and other keepers of Newtonian relics and received four hairs from the head of the master, which they subjected to laboratory tests. The results of their detective work revealed elevated concentrations of mercury, leading P. E. Spargo and C. A. Pounds to conclude that the madness was "due principally to poisoning by the metals which he used so frequently and with such cavalier disregard for his own safety" (*1*). The explanation fits nicely, since before his bout with lunacy Newton was immersed in alchemical experiments on which he would toil late into the night. At times he would doze off next to a bubbling retort.

The signs of Newton's mental illness appeared sometime during 1692 and reached a peak during the following year. In September 1693, at the age of 50, he wrote to a colleague saying, "I am extremely troubled at the embroilment I am in, and have neither ate nor slept well this twelve month, nor have my former consistency of mind. . . . I must withdraw from your acquaintance, and see neither you nor the rest of my friends any more."

Newton wrote many odd letters during this period. One of the strangest was to his friend philosopher John Locke, whom he accused of "endeavoring to embroil me with women." One month later, on 15 October 1693, Newton tried to apologize, saying in a letter, "The last winter by sleeping too often by my fire I

Madness by mercury?

Pictured in this mezzotint by Johan Faber is Sir Isaac Newton as he appeared in 1725, some 2 years before his death.

0036-8075/81/0918-1341$01.00/0