

# 100 Years of Biotechnology

Events and publications that moulded the industry's place in society

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## 10 CELEBRATING A DECADE OF EXCELLENCE

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In the ten years of *Bio/Technology*, modern biotechnology has grown from new-born to youngster. In that time, the world around biotechnology has been transformed; commercial competition is replacing the threat of superpower conflict. Concerns over high technology, the environment, international competition, intellectual property, and biodiversity have sharpened public interest in biotechnology.

But biotechnology's line stretches back more than a decade; it has a recognized history of at least a century.<sup>1-4</sup> For a hundred years, scientists and industrialists have dreamed that by bringing engineering and biology closer together, they could control and

even harness the power of the living cell in the laboratory and factory. This year marks the twentieth birthday of recombinant DNA, the fortieth of the double helix, and mass-produced penicillin is fifty years old. There are other anniversaries in 1993, too, which I have tried to capture here as frames of film pulled from the reel of the past.

This approach has one huge advantage—brevity—but two inherent deficiencies: it cannot convey the continuity of the movie that is the development of biotechnology, and it will lose many important developments both to brevity and to the cracks between the anniversary years. What is left, however, encapsulates not merely the technical changes that shaped biotechnology but also the events and publications that moulded biotechnology's place in society.

### A century ago—1893

Back in the nineteenth century, the application of microbiology causes excitement. In Germany and Britain, the Koch Institute and the Lister Institute are following in the wake of the Pasteur Institute in developing excellence in the study and use of microorganisms. The manufacture of citric acid using microorganisms is patented by Carl Wehmer. The process proved hard to develop commercially but it marks the transition in fermentation from craft roots to modern industry. Diphtheria anti-toxin was first used just over a year before by Emil Behring. The first isolated enzyme, zymase, will be prepared from yeast four years later by Eduard Buchner.

### Seventy-five years ago—1918

The word "Biotechnologie" in German is coined around this time by Karl Ereky (1917) [*Mitteilungen der Deutschen Landwirtschafts-Gesellschaft* 34: 541-50]. World War I comes to an end and economic microbiology has come of age: four key processes have been developed within the previous four years of war. The

acetone-butanol process, introduced in 1915, uses aseptic fermentation techniques to produce large amounts of acetone to make explosives smokeless, and will produce the butanol solvents for paints in the car industry. Food yeast and glycerol have been produced in Germany, one to feed the animals and the other to feed the guns. And the activated sludge process is developed for sewage disposal.

### Sixty years ago—1933

Fact and fiction combine to plant and fertilize social and moral concerns about biotechnology. In Germany, the Nazis promote their own rendition of genetic engineering. The previous year Aldous Huxley's *Brave New World* was the first science fiction story to reflect on genetic engineering. It was, in part, a response to J.B.S. Haldane's *Daedalus* of 1923, which had prophesied an era of "Biological Inventions."

### Fifty-five years ago—1938

The beginnings of structural biology with the X-ray crystallography of two classes of biological macromolecules—proteins (he-

moglobin and chymotrypsin) by Bernal, Fankuchen, and Perutz [*Nature* 141: 523-24] and DNA by Astbury and Bell [*Nature* 141: 747-48]. The low-resolution determination reveals DNA as an organized structure, the "pile of pennies." The phrase "molecular biology" is coined by Warren Weaver [*Report of the Rockefeller Foundation* (1938)].

### Fifty years ago—1943

Mass production of penicillin by deep fermentation reduces its price to \$200 per million units. Here is not just a wonder drug—one of the first that can actually cure disease—but a means of production (aerobic fermentation) that can generate the vast quantities required by patients and the profits required to build a major industry. Meanwhile, and quite separately, Beadle and Tatum's "one gene-one enzyme" hypothesis, which will link biochemistry with genetics, is already two years old [*Proc. Natl Acad. Sci. USA* 27: 499-506]. A year later Schrödinger publishes *What is Life?* Luria and Delbrück's quantitative study of mutation in bacteria (1943) marks the beginning of bacterial genetics [*Genetics* 28: 491-511].

### Forty-five years ago—1948

The first genetic map of bacteriophage from Hershey and Rotman [*Proc. Natl Acad. Sci. USA* **34**:89-96 and, a year later, *Genetics* **34**:44-71]. The previous year, "biochemical engineering" had been baptized by the journal, *Chemical Engineering*. A year later Pauling would inspire the notion of "molecular medicine" with a paper describing sickle-cell anemia as a "molecular disease" [*Science* **110**:543-48].

### Forty years ago—1953

The double helix structure of DNA is elucidated and molecular biology becomes a superstar [*Nature* **171**:737-38]. What had been an esoteric specialty—molecular biology—becomes the basis for understanding all life. Peterson's 1950 fermentation route to cortisone is providing a new boost for industrial microbiology.

### Thirty-five years ago—1958

DNA polymerase discovered and its action demonstrated by Kornberg's group [*J. Biol. Chem* **231**:163-170]. Two years previously Sanger and his team had for the first time sequenced a protein, insulin. Early the following year, *The Journal of Biochemical and Microbiological Technology and Engineering*, which will be retitled *Biotechnology and Bioengineering* in 1961, is founded by Gaden, Donald, and Crook.

### Thirty years ago—1963

Social responsibility for biology as the age of biotechnology is forecast. Two conferences, one in London and the other at Ohio Wesleyan University, ponder the implications of the new molecular biology and warn the public that the age of genetic engineering is imminent. Joshua Lederberg advocates eugenics (phenotypic modification) rather than eugenics [*Nature* **198**:428-29]. Meanwhile the first meeting on the Global Impacts of Applied Microbiology (GIAM) foreshadows a world in which the imaginative use of microorganisms is going to be a crucial economic and social re-

source. On the technical front, Bruce Merrifield develops solid phase peptide synthesis [*J. Am. Chem. Soc.* **85**:2149-2154].

### Twenty-five years ago—1968

*The Biological Time Bomb* is published by British journalist Gordon Rattray Taylor. Warning the public of the potential impact of modern biology, he demonstrates the success of the scientists who had wanted to raise public consciousness. What had they started?

### Twenty years ago—1973

Cohen, Chang, Boyer, and Helling publish the process of recombining DNA *in vitro* and the age of the new biotechnology is born [*Proc. Natl Acad. Sci. USA* **70**:3240-44]. Its implications seem so awesome that, at Asilomar in 1975, biologists in the United States confirm a moratorium on further work that lasts until the National Institutes of Health forms its guidelines and its Recombinant DNA Advisory Committee in 1976. Elsewhere research on recombinant DNA is delayed still longer. The other arm of the new biotechnology, monoclonal antibodies, would be discovered by Köhler and Milstein in 1975 [*Nature* **256**:495-97]. The era of gasohol begins. British Petroleum awards a contract for detailed engineering design and construction of a 100,000 ton single-cell protein plant in Sardinia. The Oil Crisis caused by the Middle East War puts a premium on biological resources, but undermines the case for single-cell protein grown on petrocarbons. The British Petroleum plant was never commercially operated.

### Fifteen years ago—1978

Genentech announces production of human insulin in *E. coli* and demonstrates the commercial potential of the company based on recombinant DNA technology. Another prospect for the future had been published the previous year when two groups—Sanger, Nicklen, and Coulson in Cambridge, England, and Maxam and Gilbert in Cambridge, Massachu-

setts—both found ways to sequence DNA [*Proc. Natl Acad. Sci. USA* **74**:5463-67 and *Proc. Natl Acad. Sci. USA* **74**:560-64]. Big chemical companies look to biotechnology: Monsanto and Du Pont base future strategies upon it.

### Ten years ago—1983

*Bio/Technology* founded. The era of thinking and writing about practical commercial and regulatory issues in biotechnology has got into full swing. *Biotech '83* claims to be the first world conference and exhibition on the commercial applications and implications of biotechnology. New biotechnology firms have raised \$500 million in U.S. public markets. Genentech's recombinant human insulin, licensed to Eli Lilly, has been on the market for a year. The first successful transfers of foreign DNA into plants using the Ti plasmid are reported at the Miami Winter Symposium. *Bio/Technology* (April) reports "plant molecular genetics has finally come of age."

### Five years ago—1988

U.S. patent granted to Harvard University for the "onco-mouse," the first mammal to be patented, and the age of patenting animals begins. In Europe the implications still seem so worrying that it is another three years before it is decided that a patent could be granted there. The National Institutes of Health are awarded \$17 million by the U.S. Congress for work on the human genome. The Office of Human Genome Research founded, with James Watson as Director. The first commercial PCR had been introduced by Perkin-Elmer Cetus the previous year.

### Now—1993

Things are moving so fast in biotechnology that, between the writing and the reading, the world may have changed. Will the National Institutes of Health's appeal against patents on the human cDNAs be upheld? Will the GATT talks conclude with worldwide agreement on regulation of biotechnology products? Will the word "biotechnology" be permitted by most computer spell-checks?

### References

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