A History of Biotechnology

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Science, Technology and Society (LE202)

What is biotechnology?

Although the concept of biotechnology generally brings to mind genetic engineering, it can be conceived of very broadly.

Definition (Biotechnology)

Any use of biological organisms or processes in industrial, medical, agricultural and environmental engineering.

- In this way, we can trace the history of biotechnology from the beginning of scientific agriculture and fermentation at the end of the 19^{th} century.
- Throughout the 20^{th} century, there was both much hope for, and much disappointment in, the development of biotechnology.
- By the last decades of the 20^{th} century, biotech became a major component of the R&D of most developed nations.

Zymotechnology

- Zymotechnolgy is the old term for the study of the processes of fermentation in yeast and bacteria in the production of foods and beverages such as bread, cheese, tofu, beer, wine, sake, nato, etc.
- Of course, these practices go back to ancient times, however, in the 19^{th} century, with the rise of big industries, particularly in Britain and Germany, technoscientists began to isolate the microorganisms invovled and to study them.
- With the techniques of scientific biology of the 19^{th} century, it became possible to isolate pure strands of the various yeasts and molds involved in these processes, so as to standardize the mass production of these products.
- In this regard, at the end of the 19^{th} century, various industrial and governmental labs, and teaching institutions were established.

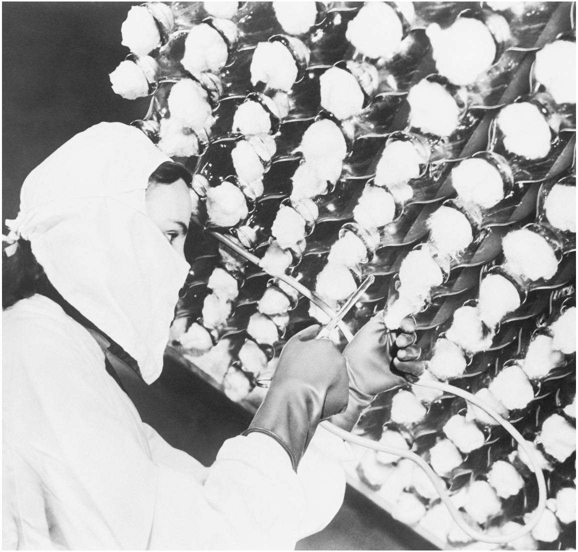
Early biotechnology

- In the early part of the 20th century, technoscientists began to see zymotechnolgy as included in the applied sciences, analogously to chemistry. They established institutions for collecting microorganisms.
- The concept of zymotechnolgy was broadened to a general concept of biological chemistry, involving the use of biological molecules such as amino-acids, proteins and enzymes in industrial production.
- The word 'biotechnology' was coined by Karl Ereky (1878–1952), in Hungary in 1919, to describe general processes of converting raw materials into useful products, such as on industrial farms.
- In Britain, Chaim Weizemann (1874–1952) developed bacterial fermentation processes for producing organic chemicals such as acetone and cordite propellants. During WWII, he worked on synthetic rubber and high-octane gas.

World War II: Penicillin production

- In 1928, Alexander Fleming (1881 –1955) accidentally discovered the properties of the penicillium fungus, but determined that it would not be possible to use it in medicine.
- In 1940, a team of researchers at Oxford University found a way to purify penicillin and keep it stable.
- Pfizer, which had made fortunes using fermenting processes to produce citric acid in the 1920s, turned its attention to penicillin.
  - The company developed a complicated production process and opened a new factory to implement it: Pure strains of the mold were first grown in small bottles, then seed tanks, then deep fermentation tanks. The mold was then purified using a crystallization process. Using this new method, they were able to produce as much in a day as they had in the previous year.
- The massive production of penicillin was another major factor in the Allied victory in WWII.

Penicillin production, 1944



Penicillin advertisement, WWII

Shell penicillin advertisement, WWII

Engineering nature: various visions

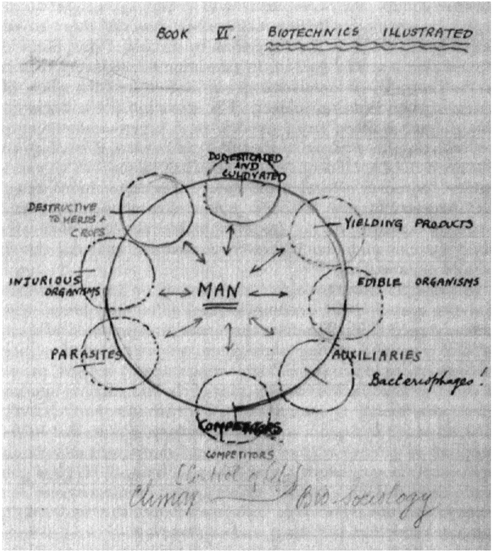
- During the interwar period, philosophers, sociologists and public intellectuals began to reflect on the growing link between biology and technology.
- They put forward the idea that biotechnology could be used to change human nature, and by changing human nature to change society.
- The Austrian Raoul Francé (1874–1943), for example, claimed that we could regard life as a series of technical problems, for which living organisms acted as optimal solutions.
- In Britain, biotechnology was conceived of as a possible solution to the damages of the industrial revolution.
- Patrick Geddes (1854–1932), the Scottish biologist, divided the history of technology into three stages: *paleotechnic* (1st industrial revolution), *neotechnic* (2nd industrial revolution) and *biotechnic* (future industrial revolution).

Raoul Francé's vision of a harmonious engineering

R. Francé, *Plants as Inventors*, 1920:

> *It was my thesis that we can conquer not only by the destruction of disturbing influences, but by compensation in harmony with the world. Only compensation and harmony can be the optimal solutions; for that end the wheels of the world turn.*
>
> *To attain its aim, life: to overcome obstacles, the organism — plant, animal, man, or unicellular body — shifts and changes. It swims, flies, defends itself and invents a thousand new forms and apparatuses.*
>
> *If you follow my thought, you will see where I am leading, what is the deepest meaning of the biotechnical tokens. It portends a deliverance from many obstacles, a redemption, a straining for the solution of many problems in harmony with the forces of the world.*

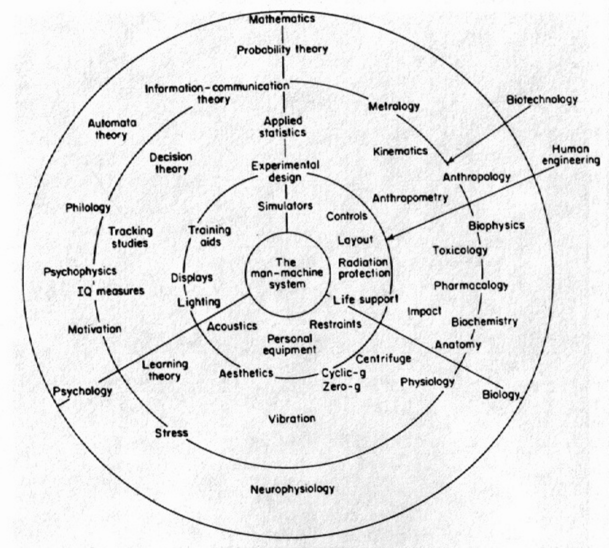
Patric Gedde's construction of biotechnics, notes



Institutionalizing the engineering of nature

- After WWII, technoscientists began to institutionalize biology and biotechnology in various ways; that is, to establish departments, institutes and ministries.
- During the war, a number of countries had used biotechnological means to supplement their shortages. These labs were now institutionalized.
- Cybernetics and general systems theory began to explore the parallel structures of machines and biological systems. That is, they began to explore the general theoretical similarities between biological and technological systems.
- At MIT there was already a department of biological engineering (1936). The first department of biotechnology was founded at UCLA in 1944, and, in the 1950s-60s, became widely respected for its work on man-machine interfaces.

U.S. engineering concept of biotechnology, 1963



SCIENCE

AS THE TEMPERATURE IN HIS HOTBOX RISES ABOVE 220°, DR. TAYLOR SQUIRMS IN HIS SEAT WHILE BEFORE HIM AN EGG ON A METAL PAN FRIES IN THE HEAT

HOW HOT CAN A MAN GET?

Tests show humans can stand heat 50° above boiling point of water

What happens to a human placed in an oven hot enough to cook an egg? The oddly equipped man above, Dr. Craig Taylor of the University of California at Los Angeles, is finding out in an experiment extremely important to modern aviation. In the present 600-mph jet-propelled planes, air compression and friction make the cabin almost unbearably hot when the refrigeration system fails. In even faster planes, the heat increase might be great enough to turn the pilot's cabin into a furnace. Because men are needed to fly these fast planes, the Air Force therefore must know just how much heat a pilot can stand and for how long without suffering either skin burns or internal injury.

Dr. Taylor has exposed himself to temperatures as high as 262°F. He once endured a 220°F temperature for 25 minutes. Except for a temporarily increased pulse rate, the tests produced no serious effects. The heat-recording thermocouples connected to his head and body show why (*drawing at right*). Because the body has its own cooling system (perspiration and mucous secretion), it lowers almost to body temperature all air coming into the lungs. And even when exposed to extreme heat the body does not let its own temperature rise more than one or two degrees above normal.

TEMPERATURE DROPS rapidly before air enters the lungs, as shown in drawing of the nose and throat above.

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Craig Taylor, prof. of biotechnology, University of California Los Angeles, at work

Time magazine article

The promise of a green technology

In the early Cold War period, biotechnology was considered as an alternative to a list of earth-destroying technologies developed by the "military-industrial complex." It was hoped that it might solve major social problems, such as energy and food shortages.

- **Imitation rhizobia:** There were projects to try to develop bacterial fertilizers that could convert nitrogen to ammonia like the rhizobia bacteria in beans.
- **Biogas and gasohol:** In rural countries like China and India, there were projects to convert biomass into fuel. In 1974, Brazil began a massive project to convert sugar cane to gas.
- **Single-cell protein:** During WWII, the Germans grew single-cell (fungal) protein for animal fodder. In the 1950s, the oil companies developed processes for growing bacteria on oil. In 1968, the Japanese produced 110 tones of single-cell protein bacteria.

Quorn, a food product made with mycoprotein

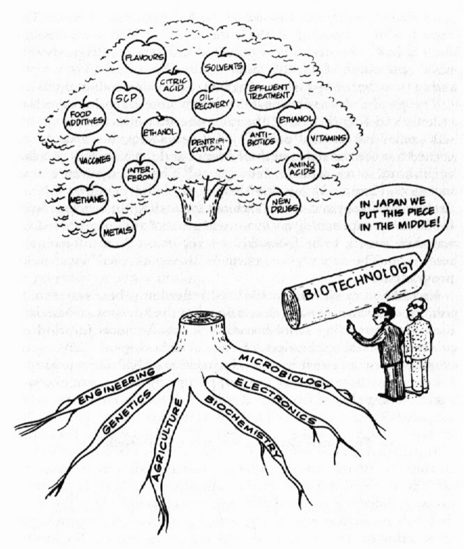
Early biotech policy: Japan

- Japan's long history of the use of fermentation processes (発酵, 醗酵) gave Japanese technoscientists a broad conception of biotechnology.
- In the 1970s, Japan became a world leader in biotech policy.
  - By the end of the 1960s there were serious pollution problems (公害問題), and this lead to the idea that biotechnology could be used to make environmentally sound technologies.
- In the 1970s, the Ministry of International Trade and Industry (MITI, 通商産業省) put special emphasis on life sciences and biotechnology.
  - *White Paper on S&T*, 1977: "Life Science, in particular, is for the study of phenomena of life and biological functions that will be made useful; for industrial, medical, agricultural and environmental purposes, and so this area of science is expected to set the pace for the next round of technical progress."

Early biotech policy: Germany and Britain

- In the 1960s the Germans also became concerned with environmental protection (*Umweltschutz*) and began to put emphasis on a new mode of development.
  - Symposium of Industrial Microbiology, 1969: "A future aim should therefore be to close the gaps by suitable training, to rise above classical fermentation technology, and to build up a modern science of biochemical-microbiological engineering."
- In Britain, chemical engineering, the antibiotics industry and applied microbiology developed as rapidly as in the U.S.
- In 1979, a government report outlined the country's policy on biotechnology, which it defined as "the application of biological organisms, systems of processes to manufacturing and service industries."
  - The British generally followed the Japanese and German policies, however, they put more emphasis on genetic engineering.

Cartoon from the *New Scientist*, 1979



The new genetics: Tatum and Lederberg

In the 1970s-80s, the path of biotechnology became intertwined with that of genetics.

- Edward Tatum (1909–1975) and Joshua Lederberg (1925–2008) shared the 1958 Nobel Prize for showing that genes regulate the metabolism by producing specific enzymes. They both did a great deal to advocate the use of genetics to biological engineering.
- At a conference in 1964, Tatum laid out the vision of the new biotechnology:
  - "Biological engineering seems to fall naturally into three primary categories of means to modify organisms. These are:
    1. The recombination of existing genes, or eugenics.
    2. The production of new genes by a process of directed mutation, or genetic engineering.
    3. Modification or control of gene expression, or to adopt Lederberg's suggested terminology, euphenic engineering."

Recombinant DNA technology and monoclonal antibodies

- In 1974, Stanley Cohen (1922–) and Herbert Boyer (1936–) developed a technique for splicing together strands of DNA from more than one organism. The product of this transformation is called *recombinant DNA* (rDNA).
- This technique, for the fist time, allowed the genetic engineering of new organisms.
- *Monoclonal antibodies* are antibodies that are clones made from a single immune cell. Antibodies are specific to a given antigen (a disease causing agent), so monoclonal antibodies could be used to engineer targeted medicines.
- Techniques for producing monoclonal antibodies were developed in 1975.

Public concern

- The technical progress of genetics, in the 1960s, lead to an increasing public concern about the ethics of biotechnology and the possibility of blurring the definition of ‘human.’
- In 1975, there was a conference at Asilomar, attended by scientists, lawyers and physicians, to set out guidelines for experiment design and safety, in order to reduce biohazards.
- In 1976, a moratorium on genetic research expired and the U.S. National Institutes of Health (NIH) published guidelines on good practice.
- Amid growing concerns from the general public, in the late 1970s, industrial research in genetically based biotechnology began to expand rapidly with the establishment of many new companies and the development of new techniques.

The 1980s: Technological developments

- In 1980, The U.S. Supreme Court (SCOTUS), in Diamond v. Chakrabarty, approves the principle of patenting genetically engineered life forms. In the same year, a U.S. patent for gene cloning is awarded to Cohen and Boyer.
- In 1982, Humulin, Genentech's human insulin drug produced by genetically engineered bacteria for the treatment of diabetes, is approved by the Food and Drug Administration (FDA). This is followed by many new drugs based on biotechnologies.
- In 1983, Kary Mullis develops polymerase chain reaction (PCR), which allows a piece of DNA to be replicated over and over again.
    - In 1984, the DNA fingerprinting technique was developed.
- In 1989, microorganisms were used to clean up the Exxon Valdez oil spill.

The 1980s: Policy in Japan, the U.S. and Europe

In the mid-1980s, the developed nations each spent around $100m a year on biotech R&D.

- In 1981, MITI (通商産業省) identified biotech as a key industry of the future. Policies for rDNA technology were developed and by the late 1980s corporate biotech R&D was more than doubling every year.
- The U.S., envious of the growth in Japan, was forced by local customs to focus more on basic research than industrial applications.
- In Europe, international agencies were established to promote and regulate biotech R&D, and to try to bring the agricultural and industrial sectors closer.

The 1990s: Technological developments

- In the 1990s, a growing number of drugs, produced using modern biotechnological techniques, were brought to market.
- In 1993, The U.S. Food and Drug Administration (FDA) declares that genetically modified (GM) foods are "not inherently dangerous" and do not require special regulation. GMOs are now widely available, but there is still a debate about labeling.
  - Calgene's Flavr Savr tomato, engineered to resist rotting, was approved for sale by the FDA.
- In 1997, Scottish scientists report cloning a sheep, Dolly, using DNA from adult sheep cells. (Dolly was euthanized in 2003.)
- In 1998, human skin was produced in vitro.

Patenting life

- As mentioned, in 1980, the U.S. Supreme Court approved the principle of patenting genetically engineered life forms. There was resistance in Europe and Japan, but this was later broken down. In the same year, U.S. patent for gene cloning is awarded to Cohen and Boyer.
- This has lead to the ability of technoscientists to patent the genes that they construct using rDNA techniques. This gave them legal ownership of these genes and allowed them to extract fees for use and distribution.
    - In 1992, James Watson stepped down as head the Human Genome Project over conflicts with Bernadine Healy (head of the NIH) over patenting gene sequences, when the NIH announced that they would seek to patent certain human genes.
    - The right to patent genes was struck down by SCOTUS in 2013.

Confusion and alarm

- The new technologies are rarely understood by journalists or the public at large, but there was, and remains, a vague feeling that something is not right.
- As an example, we can consider the milk-producing hormone, recombinant bovine growth hormone, or somatotropin (rBGH, rBST).
    - rBST is a chemical hormone that is produced using rDNA manipulated bacteria and then fed to normal cows.
    - One article read, "In other words, do you want your milk to come from Daisy or a genetically engineered and manipulated machine?"
    - The U.S. is the only developed nation that allows the use of rBST in milk production. It was banned in most other countries around 2000.

Opposition and resistance: Japan, the U.S. and Germany

- The technical successes of the 1980s–90s, lead to even greater concerns about the long term repercussions of biotech.
  - *Bio/technology*, 1989: In Japan, "77% of the readership of the science magazine *Newton* predicted that biotechnology will develop into the same sort of social problem as atomic energy."
- In the U.S., people who were uncertain about the long term repercussions of biotech sought to stop the release of genetically modified organisms through the court systems.
  - In 1982, two professors a U.C. Berkeley sought permission to test a bacterium called "Ice Minus," which would inhibit the frost on strawberry plants. This was contested in the courts.
- In Germany, a very strong environmental movement sought to address the new biotech on a number of fronts.
  - Gen-ethic Netwerk: "We must develop a new ethic for dealing with our knowledge and cannot entrust this task only to scientists, politicians and so-called experts, nor can we leave it to the mechanisms of the free market."

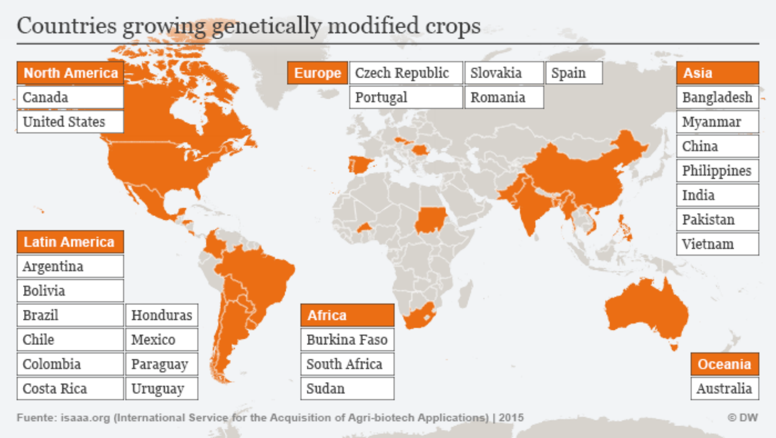
Corporate interests and control

- The debate about biotechnology and genetically modified products, however, have been strongly influenced by corporations that profit from this research.
- The framework of the debate has largely been set by *scientism* and *technological determinism*, with relatively little attention paid to social, political and economic factors.
- The patenting of genetic products have given the corporate holders of these patents considerable strength, especially in the agricultural sector.
- Japan, Europe and Africa have been much more successful than the U.S. at implementing a more complete dialog on these issues that is not completely dominated by corporate interest.

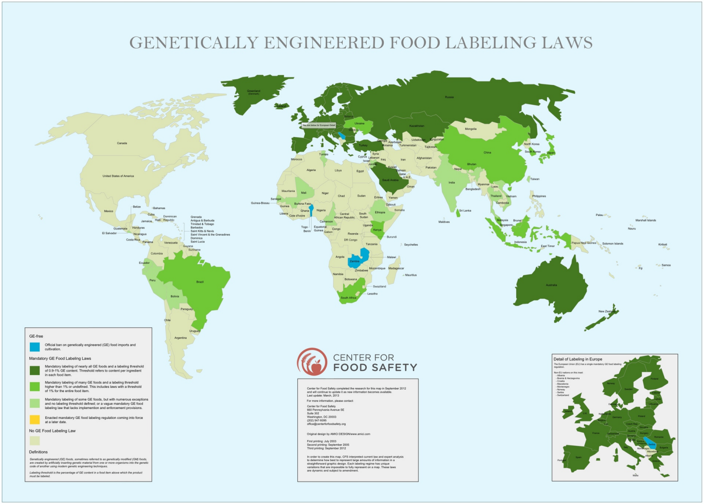
Genetically modified organisms (GMO) and foods

- Using rDNA techniques in GMOs produce can various effects:
  - Resistance to herbicides, resistance to pests and deseases, higher nutrient loads, etc.
- In 1993, the FDA declared that GM food was safe. The rest of the world also appears to be moving towards this position.
  - The production of genetically modified crops is a sector that has generally been expanding in the last 10 years.
- The use of genetically modified crops is protected by license (similar to software), which makes these crops prohibitively expensive for many farmers.
  - Recently, Monsanto charged Argentinian farmers license fees when they tried to sell their GM crops in Europe.
- One major concern with GM crops is "genetic drift," in which GM crops begin to "contaminate" the nearby crops or the wild populations.
  - There have been cases of organic crops becoming "contaminated" with GM organisms.

GM crop production worldwide, 2015



Countries that label GM foods, 2012



Some recent developments

- In 2003, TK-1 (GloFish) went on sale in Taiwan, as the first genetically modified pet.
- In 2006, the artist Stelarc had an ear grown in a vat and grafted onto his arm.
- In 2009, Sasaki and Okana produced transgenic marmosets that glow green in ultraviolet light — and pass the trait to their offspring.
- In 2010, scientists created malaria-resistant mosquitoes.
- In 2010, the Craig Venter Institute produced an “artificial” microorganism.

GloFish, 2003

Stelarc, grafted ear, 2003

Transgenic marmosets, 2009

Final Remarks

- We have looked at the historical development of the concept of using biological processes in engineering and manufacture.
- We have seen the rise of the pharmaceutical and agricultural use of biotechnology, based on genetic engineering.
- We have seen that biotechnology and genetic engineering has has come to be seen as a major key to economic development.
- We have seen that are a number of dangers and concerns with these new technologies.
- In the story of biotechnology, we see the boundary between science and technology, knowledge and power, becoming blurred.
- We see that in this field the Mertonian norms, which had been seen as a standard of scientific practice, are consistently and intentionally breached.
    - The recent SCOTUS decision is contrary to this general trend.