



# INTRODUCTION TO BIOTECHNOLOGY

FSAQ-3210

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# WHAT IS BIOTECHNOLOGY?

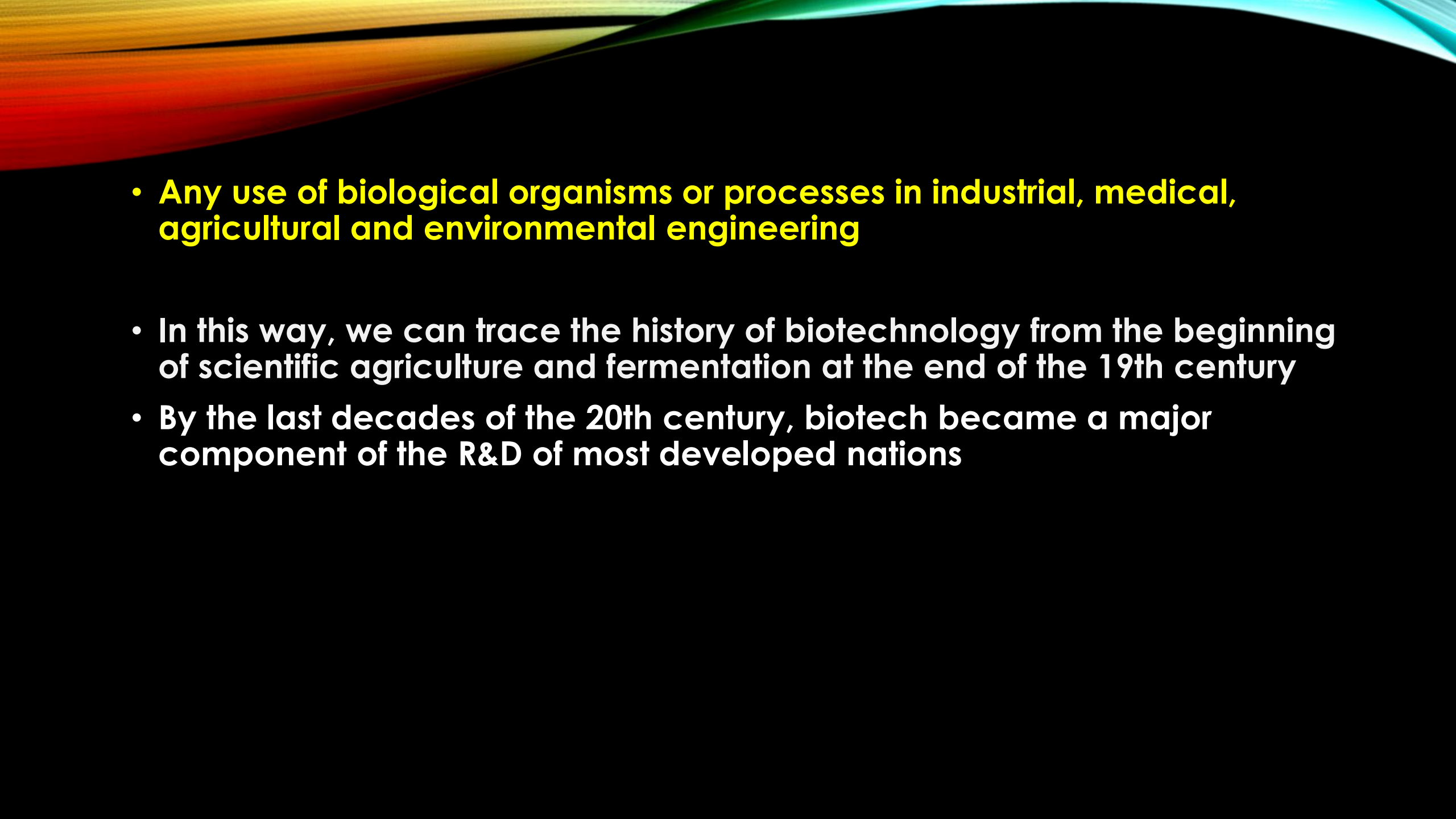
- **Biotechnology**, the term, is a combination of two words '**bio**' and '**technology**', — '**bio**' means **biological systems or processes**, and '**technology**' refers to methods, **systems, and devices** used to make useful products from these biological systems.
- Thus, biotechnology refers to the different technologies that make use of living cells and/ or biological molecules to generate useful products for the benefit of mankind

# DEFINITIONS

- Any technique that uses living organisms or substances from those organisms to make or modify a product, to improve plants or animals or to develop microorganisms for specific uses
- The integration of natural science and organisms, cells, parts thereof, and molecular analogues for products and services (European Federation of Biotechnology)
- Use of living organisms in systems and processes for the manufacture of useful products; it may involve algae, bacteria, fungi, yeast, cells of higher plants and animals or subsystems of any of these or isolated components from living matter (Gibbs and Greenhalgh, 1983)

# HISTORICAL PERSPECTIVES

- **Ancient biotechnology** had taken root as early as in the Paleolithic era, around 10,000 years ago, when early farmers began to cultivate crops such as wheat and barley
- However, the most classical example of biotechnology in the medieval times is the use of fermentation technology for production of bread, cheese, wine and beer.

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- **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 19th century
  - By the last decades of the 20th century, biotech became a major component of the R&D of most developed nations

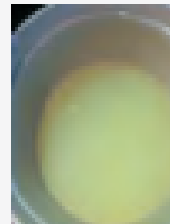
Fresh Milk  
boiled to  
100°C and  
cooled to  
37°C



Add a teaspoonful  
of one-day-old curd  
and leave  
undisturbed for  
4-5 hours




Two phase  
separation of  
curd and whey



Observation: The raw material, milk, has been  
converted completely into a semisolid sour tasting  
product.

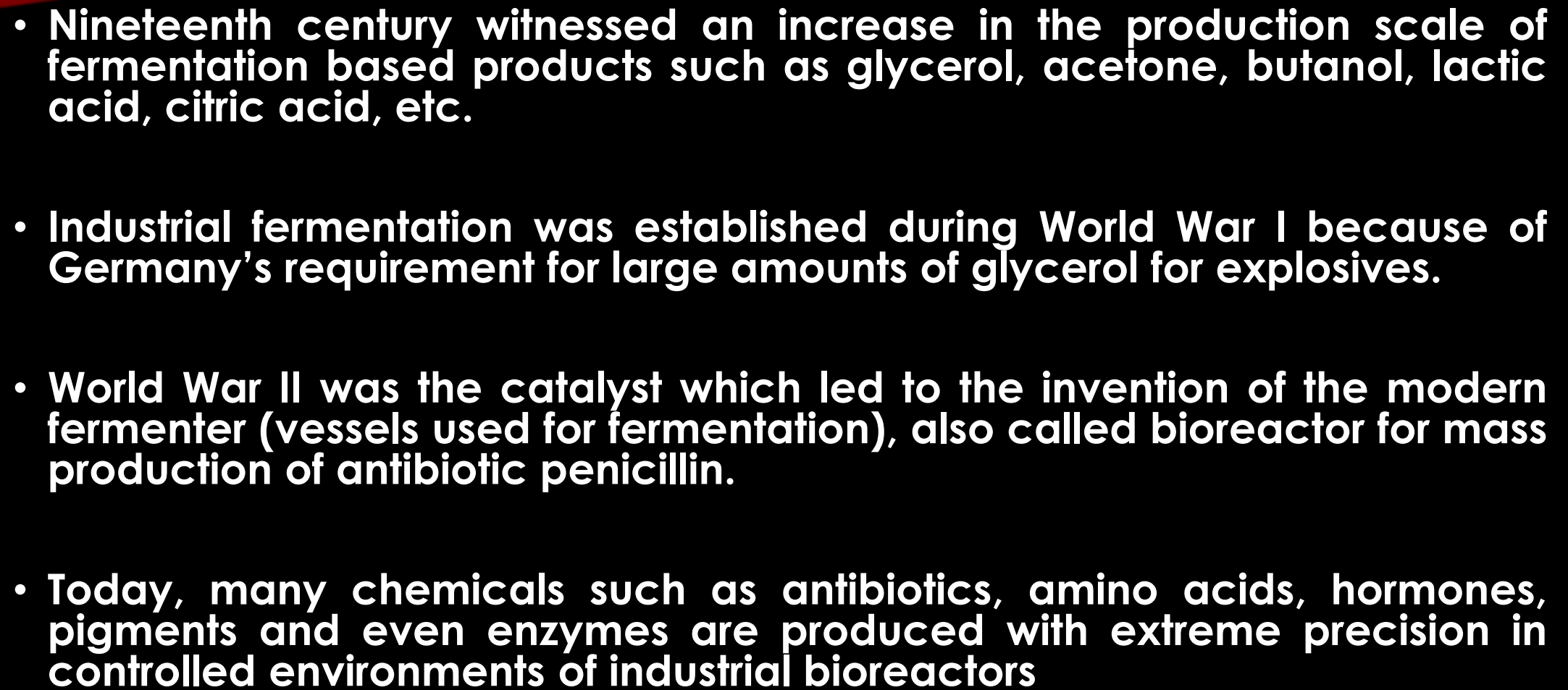
### WHAT HAS ACTUALLY HAPPENED?

Lactobacillus bacteria from  
the curd react with the milk  
protein casein. Lactic acid  
formed as a by-product,  
denatures the globular  
proteins and coagulates to  
produce the solid curds and  
separates the watery whey  
protein layer

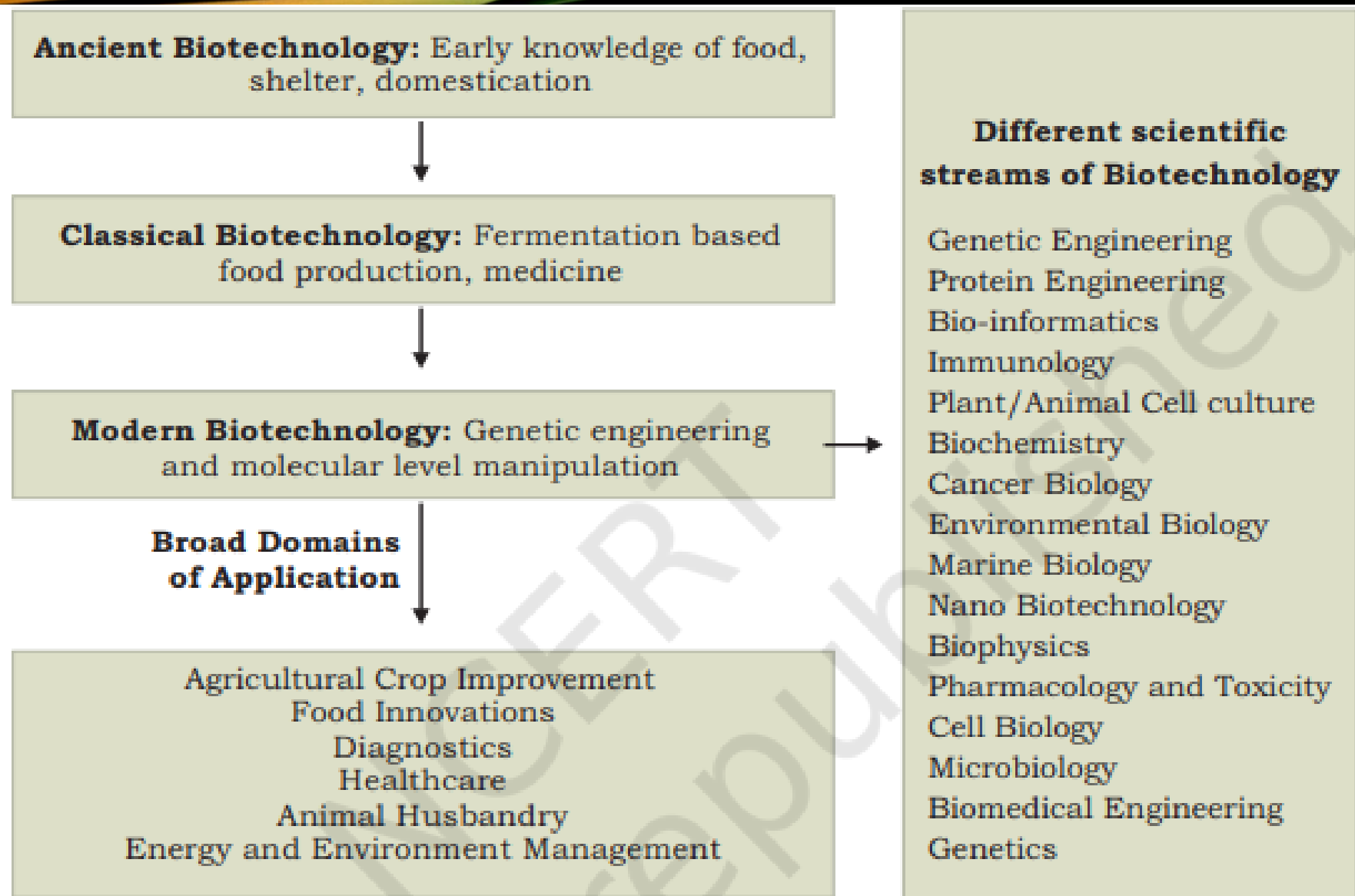
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- The Chinese were also using fermentation technology by 4000 B.C., for production of their traditional food items, such as soy sauces and fermented vegetables
  - Vinegar production was known to the Egyptians by 2000 B.C., by preserving crushed dates for a longer time
  - Beer making may have begun as early as between 6000 and 5000 B.C. using cereal grains such as sorghum, corn, rice, millet, and wheat
  - Wine was probably made by accident, when grape juice was contaminated with yeast and other microbes. Between 1850s and 1860s, Louis Pasteur established that yeast and other microbes were responsible for fermentation

# EARLY BIOTECHNOLOGY

- 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 Weizmann (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.

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- Nineteenth century witnessed an increase in the production scale of fermentation based products such as glycerol, acetone, butanol, lactic acid, citric acid, etc.
  - Industrial fermentation was established during World War I because of Germany's requirement for large amounts of glycerol for explosives.
  - World War II was the catalyst which led to the invention of the modern fermenter (vessels used for fermentation), also called bioreactor for mass production of antibiotic penicillin.
  - Today, many chemicals such as antibiotics, amino acids, hormones, pigments and even enzymes are produced with extreme precision in controlled environments of industrial bioreactors

- The foundation of modern biotechnology were laid down with the advancements in science and technology during the eighteenth and nineteenth centuries.
- Thus with the advent of the first compound microscope, made by Dutch spectacle-maker **Zacharias Janssen** in 1590, which could magnify about 3×-9×, enabled humans to 'see' things that were not perceived by naked eye
- Modern biotechnology is based on the rDNA technology that has revolutionized biotechnology by allowing scientists to cut and join different pieces of DNA, and place the new recombinant (Chimeric/hybrid)
- Since the advent of **rDNA technology**, biotechnology has become more advanced and led to advancements in medicine, agriculture, animal science and environmental science



*Fig. 1.2: Multi disciplinary nature of modern biotechnology and the areas of its application*

Periods of biotechnology history	Events
<b>Pre-1800</b> (Early applications and speculation)	<p><b>6000 BC</b> Yeast was utilized to prepare beer (Sumerians and Babylonians).</p> <p><b>4000 BC</b> In Egypt, a process was discovered to prepare leavened bread by means of yeast.</p> <p><b>420 BC</b> Greek philosopher Socrates (470–399 BC) hypothesized on the similar characteristics between parents and their offspring.</p> <p><b>320 BC</b> Greek philosopher Aristotle (384–322 BC) theorized that all inheritance originates from the father.</p> <p><b>1000 AD</b> Hindus recognized that some illnesses may 'run in the family'. At the same time, the theory of abiogenesis, or spontaneous generation based on the idea that organisms arise from non-living matter, developed. According to this theory maggots could develop from horse hair.</p> <p><b>1630</b> William Harvey explained that plants and animals are similar in their reproduction, i.e. they reproduce sexually.</p> <p><b>1660–1675</b> Marcello Malpighi (1628–1694) investigated blood circulation in capillaries using a microscope and found that the brain is connected to the spinal cord by bundles of fibers which form the nervous system [20, 21].</p> <p><b>1673</b> Antonie van Leeuwenhoek (1632–1723) was the first researcher to explain micro-organisms such as protozoa and bacteria, and also identify that these micro-organisms play an active role in fermentation.</p> <p><b>1701</b> Giacomo Pylarini found that the deliberate administration of smallpox could prevent its occurrence later in life, especially in children. Later, this procedure was termed 'vaccination' and a process that uses cowpox instead of smallpox was established as the most reliable treatment [22, 23].</p>
<b>1800–1900</b> (Significant advances in basic understanding)	<p><b>1809</b> Nicolas Appert invent a technique using heat to can and sterilize food.</p>

<b>1868</b> Casimir Joseph Davaine cured plants suffering from bacterial infection by a novel heat treatment. While working in a hospital, Johannes Friedrich Miescher separated nuclein (a compound made of nucleic acid) from pus cells. These pus cells were derived from waste bandages [24].
<b>1870</b> Walther Flemming discovered mitosis [25].
<b>1871</b> During the period 1873–76 interest in DNA research began. DNA was initially derived from the sperm of trout (found in the river Rhine). During this period Koch investigated anthrax and explored certain techniques to identify, culture and stain micro-organisms. He also took images of them which were later supported by Gram, Cohn and Weigart [26].
<b>1880</b> While working on fowl cholera, Louis Pasteur explored weakened (attenuated) strains of micro-organisms that might not be virulent but could nevertheless potentially prevent healthy individuals against severe forms of a similar disease [26].
<b>1881</b> Koch explained techniques for harvesting bacterial colonies on potato slices, gelatin and agar medium [26]. For the isolation of pure culture and for distinguishing the nutrients needed for genetic mutations, the agar technique was one of the most common methods. Thomas D Brock considered this breakthrough as the single most important discovery in the development of microbiology.
<b>During the same period Pasteur explored the application of the attenuation process in the production of vaccines against certain bacterial pathogens, e.g. fowl cholera and anthrax; this was an early stage in immunology which led to the exploration of areas such as preventive medicine [26].</b>
<b>1884</b> Koch established his 'claims' for assessing whether a microbe or another agent is responsible for disease. During the same period Pasteur established a rabies vaccine [26]. Gram described the differential staining technique for cellular peptidoglycan-containing bacteria now known as Gram staining [27]. Mendel passed away after 41 years of predominantly investigating the heredity 'factors' of pea plants. He did not receive any technical support during his lifetime, but said before his death, 'My time will come' [28].

**1827**  
In the field of heredity, there had long been a hunt for the so-called mammalian egg. It had proved elusive, however, in 1827 the first report of canine eggs offered a basic clue to major breakthroughs in reproduction, at first in lower animals

**1850**  
Ignaz Semmelweis utilized epidemiological examinations to suggest the theory that puerperal fever could be transmitted from mother to mother by physicians. He also suggested that all physicians should wash their hands after investigating each patient. For this suggestion he was criticized by medical professionals and ultimately lost his employment.

**1856**  
Carl Ludwig discovered a procedure for keeping animal organs alive under *in vitro* conditions. This was done by supplying blood to them. In contrast to the concepts of Justus von Liebig, Pasteur (1822–1895) suggested that microbes are responsible for fermentation.

**1859**  
Charles Darwin (1809–1882) speculated that animal populations adapt their forms to eventually best utilize the surroundings, a process he described as 'natural selection'. During his stay in the Galapagos Islands, he saw how the finches' beaks on each island were adapted for the environment, especially regarding food sources.

**1863**  
Pasteur discovered the method of pasteurization. In this method he heated wine enough to inactivate microbes (that would otherwise convert the 'vin' to 'vin aigre' or 'sour wine') and realized that this procedure did not affect the flavor of the wine [26].

Heinrich Anton de Bary established that a fungus was responsible for potato blight. A major challenge for researchers during this period was to differentiate whether a microbe was responsible for this or whether it was the outcome of a disease.

1900–1953

(Genetics:converging on DNA)

#### 1900: Mendel's work finally took on importance

Mendel's work had given birth to genetic science. It was revived again by three researchers, de Vries, von Tschermak and Correns, who were working on the application of original work done by Mendel [29].

#### 1902: Human genetics is born

Sutton found that chromosomes (paired) contain certain elements which are transferred from one generation to another. During this transfer, traits are transported through carriers called chromosomes. He also advised that Mendel's 'factors' are sited on chromosomes [30].

#### 1905: X and Y chromosomes related to gender

Edmund Beecher Wilson and Nettie Stevens shared the same idea of separating X and Y chromosomes for the determination of sex. They also demonstrated that a single Y chromosome determines maleness, while two copies of the X chromosome decide femaleness [31].

#### 1905–1908

William Bateson and R C Punnett, along with other researchers, found that several genes alter or modify the action of other genes [32].

#### 1906

Paul Erlich also investigated atoxyl compounds and discovered the important features of Salvarsan (the first chemotherapeutic agent) [33].

#### 1907

Thomas Hunt Morgan started his investigation into fruit flies that would reveal that chromosomes have a defined role in heredity; additionally, he discovered mutation theory. This resulted in an understanding of the basic concepts and mechanisms of heredity [34].

#### 1909: Mendel's laws to animals

Wilhelm Johannsen used the word 'gene' to mean the carrier/transporter of heredity. He also coined the terms 'genotype' and 'phenotype'; the genotype is the genetic composition/establishment of an organism, whereas the phenotype describes the actual organism or its morphological characteristics, resulting from a blend of the genotype and a range of external/environmental factors [35].

#### 1910: Basis of modern genetics

Morgan also demonstrated that carriers of genetic information, called asor genes, are present on chromosomes, creating the basis for modern genetics. This work later assisted him in utilizing *Drosophila* fruit flies to examine heredity [36].

#### 1912

Crystallography era: William Lawrence Bragg discovered the application of x-rays in the determination of the molecular structure of crystalline substances [37].

#### 1918

Herbert M Evans stated (mistakenly) that human genetic material is made up of 48 chromosomes [38].

#### 1924: Eugenics in the United States

Several US diplomats, encouraged by the eugenics movement, accepted the US Immigration Act (1924), limiting the admission of illiterate refugees from Southern and Eastern Europe on the basis of their alleged genetic inferiority.

#### 1926

Morgan published *The Theory of the Gene*. This was based on Mendelian genetics (breeding investigations and optical microscopy) [36].

Hermann Joseph Muller discovered that x-rays are responsible for genetic mutations in fruit flies taking place 1500 times faster than under normal conditions. This innovation offered researchers and scientists a procedure to induce mutations. Later, various mutagens were explored to understand the complexity behind different genotypes [39].

#### 1928

Frederick Griffiths observed the 'transforming principle' in which a rough type of bacterium is transformed to a smooth type when a mysterious 'transforming element' from the smooth type is present. After 16 years, Oswald Theodore Avery discovered that 'transforming element' to be DNA [40].

Alexander Fleming studied an old culture of bacteria infected with fungal growth and found that it did not show any bacterial growth in a radius surrounding a piece of mold (fungi) in a petri dish. This breakthrough gave birth to the antibiotics era or penicillin age, and penicillin was accessible to patients 15 years later for therapeutic use [41].

#### 1938

Proteins and DNA were studied by means of x-rays. This was the dawn of a new age of crystallography in which large molecular weight complex proteins can be studied by x-rays. The term 'molecular biology' was coined.

#### 1941: One gene, one enzyme

George Wells Beadle and Edward L Tatum examined *Neurospora crassa*, a mold that usually invades and grows on bread, and proposed 'one gene, one enzyme' theory: each gene encodes for or is translated into an enzyme to accomplish tasks within an organism [40].

#### 1943

The Rockefeller Foundation (New York) collaborated with the Mexican government to start the Mexican Agricultural Program [42]. This was the first step toward plant breeding at a global level.

#### 1943–1953

Cortisone (17 $\alpha$ ,21-dihydroxypregn-4-ene-3,11,20-trione), a pregnane (21-carbon) steroid hormone, was first produced in great amounts. Cortisone is considered as the first biotech product.

#### 1944

Selman Abraham Waksman (a Ukrainian-American researcher) explored streptomycin, an active antibiotic against TB.

#### 1945

The United Nations Food and Agriculture Organization was established in Quebec, Canada, with the objective of encouraging agricultural practices.

#### 1945–1950

For the first time, animal cell cultures were harvested in laboratories, giving birth to the field of animal tissue culture.

#### 1947

Barbara McClintock first demonstrated 'transposable elements' known as 'jumping genes' with the capability to move (or jump) from one site on the genome to another site. Scientific society did not welcome the implications of her discovery at the time [44].

#### 1950

Erwin Chargaff discovered that the same levels of adenine and thymine are present in DNA, as are the same levels of guanine and cytosine [45]. These associations were later named 'Chargaff's rules'. Later, Chargaff's rules functioned as an important principle for James Watson and Francis Crick in measuring different models for the structure of DNA.

#### 1953–1976: Expanding the boundaries of DNA research

The discovery of the structure of DNA finally resulted in an explosion of research into molecular biology and genetics, providing the resources for biotechnology development.

#### 1953

The journal *Nature* published Watson and Crick's article based on unfolding the double-helix structure of DNA.

#### 1953

Based on his technical exposure George Otto Gey developed the HeLa human cell line. Cells taken from cancer patient Henrietta Lacks (who died in 1951) became the first immortal human cells and were cultured to develop a polio vaccine.

DNA research, science explodes (1953–1976)

**1957: Central dogma of DNA—how DNA makes a protein**  
Crick and Gamov studied 'central dogma', demonstrating how DNA functions to construct protein [47].

#### 1959

François Jacob and Jacques Lucien Monod documented the veracity of gene-based regulation. They explained gene mapping with mappable control functions sited on the chromosome in the DNA sequence which they later named the 'repressor' and 'operon' [48].

#### 1962

Watson and Crick were awarded the Nobel Prize in Physiology or Medicine with Maurice Wilkins. Disappointingly, Rosalind Franklin, who actually contributed to the discovery of the double-helical structure of DNA, died before this date, and Nobel Prize conventions do not permit a prize to be awarded posthumously [49].

#### 1966: Genetic code cracked

The genetic code was explored by several researchers. Marshall Warren Nirenberg, J Heinrich Matthaei and S Ochoa reported that a genetic sequence of three nucleotide bases (called codons) decides each of 20 amino acids [50].

#### 1967

Arthur Kornberg reported a study using single-stranded natural viral DNA to assemble 5300 nucleotide building blocks, and at the same time his Stanford group synthesized viral DNA [50].

#### 1970: Oncogenes

Virologists Peter H Duesberg and Peter K Vogt identified the first oncogene in a virus. This gene can be utilized to study various human cancers [51].

#### 1972: First recombinant DNA molecule

Paul Berg, a biochemist, utilized a restriction enzyme to cut DNA into fragments. He employed a ligase enzyme to join two DNA strands concurrently to form a hybrid circular molecule. This was the first recombinant DNA (rDNA) molecule synthesized.

#### 1972: NIH guidelines for rDNA

Berg and other researchers at the National Institutes of Health (NIH) worked hard to establish guidelines to sanction the strategy for DNA splicing. Their concerns resulted in the Asilomar Conference (1975).

#### 1973: Ames test

Bruce Nathan Ames, a biochemist at UC Berkeley, developed an investigation to distinguish chemicals that damage DNA. Later, the Ames test became extensively used to identify cancer-causing substances [40].

#### 1975: rDNA moratorium

A global meeting was held in Asilomar, California, with the objective of approving guidelines regulating rDNA experimentation. All the scientists involved discussed the development of 'safe' bacteria and plasmids.

#### 1976: More about oncogenes

J Michael Bishop and Harold Varmus at the University of California, San Francisco (UCSF) established that cancer-causing genes called oncogenes become visible on animal chromosomes, and modifications in their structure or expression can result in metastatic growth [53].

#### 1976: Release of NIH guidelines

The NIH released the first set of guidelines for rDNA experimentation. Later, these guidelines restricted several types of trials.

#### 1977-present: The dawn of biotech

With the advent of genetic engineering it was possible to produce human protein in bacteria for the first time. Biotech-based organizations started focusing more on the applications of genetic engineering. In 1978, Herbert W Boyer at UCSF synthesized synthetic human insulin by introducing the insulin gene into the bacterium *Escherichia coli* [54]. This breakthrough opened the gateway for further developments in DNA sequencing and cloning techniques.

#### 1977

Genentech Inc. was the first organization to achieve the synthesis of a human protein (somatostatin) in a bacterium. Somatostatin is a human growth hormone (hGH)-releasing inhibitory factor. A synthetic, recombinant gene was for the first time employed to clone a protein. Several researchers believed that this was the beginning of the age of modern biotechnology [55].

#### 1978: Recombinant insulin

Genentech Inc. announced that its laboratory had achieved the synthesis of human insulin using rDNA technology [55].

#### 1980: Patents allowed

The US Supreme Court granted that genetically modified living organisms could be patented. According to a Supreme Court decision (1980) the Exxon oil company was allowed to patent an oil-eating micro-organism. Kary Mullis and other researchers at UC Berkeley, California, established a tool for multiplying DNA sequences *in vitro* using the polymerase chain reaction (PCR) [56].

#### 1982: Site-directed mutagenesis

Genentech Inc. signed an agreement from the US Food and Drug Administration (FDA) to further market genetically engineered

human insulin. In 1982 the FDA allowed the first genetically engineered drug in the form of human insulin produced by bacteria. Michael Smith at the University of British Columbia, Vancouver, established a procedure for producing precise amino acid changes anywhere in a protein.

#### 1983: Site-directed mutagenesis

Eli Lilly obtained a license to make and sell insulin.

#### 1985

During this period genetic fingerprinting stepped into the court room. Cal Bio produced a gene by a cloning method that encodes human lung surfactant protein, an important step toward reducing premature birth complications. For the first time, genetically modified plants that resistant to insects, viruses and bacteria were examined. The NIH published guidelines for performing experiments in gene therapy on humans.

#### 1986

Chiron Corp. obtained FDA approval for the production of the first recombinant vaccine for hepatitis. A genetically modified crop (the tobacco plant) was allowed by the Environmental Protection Agency (EPA).

#### 1987

Calgene Inc. obtained a patent for the tomato polygalacturonase DNA sequence, which was later used to synthesize an antisense RNA sequence that can further extend the shelf life of fruit.

#### 1988

Harvard molecular geneticists Philip Leder and Timothy A Stewart were granted the first patent based on a genetically modified animal (a mouse that is highly susceptible to breast cancer) [57].

#### 1990

UCSF and Stanford University achieved their 100th rDNA patent license. At the end of the 1991 financial year, both organizations had received \$40 million from the patent.

#### 1990: Patents and money

The first gene-based treatment was performed on a four-year-old girl suffering from an immunological disorder known as adenosine deaminase deficiency (ADA) deficiency. Gene therapy emerged, however ethical concerns surrounding gene therapy were highly debated.

Commencement of the Human Genome Project, with the global objective to plot all of the genes in the human body. The expected cost was \$13 billion.

1977-present (modern  
biotechnology)

Michael Crichton's novel *Jurassic Park* was released, in which bioengineered dinosaurs wander in a paleontological theme park; the project goes wrong, with deadly outcomes.

**1992**

The US Army started taking blood and tissue samples from all new employees as part of a 'genetic dog-tag'. This course of action was intended for better identification of soldiers killed in battle.

**1993**

Researcher Kary Mullis won the Nobel Prize in Chemistry for inventing the tool of PCR [58].

**1996**

A groundbreakingly efficient diagnostic biosensor test allowed for the first time the instant detection of the toxic strain of *E. coli* (strain 0157:H7), the bacteria responsible for several food poisoning outbreaks. The possibility of its use against anthrax and other bioterrorism agents was also assessed.

The discovery of a gene linked to Parkinson's disease offered researchers a significant new chance for the determination of the cause of, and potential treatments for, the incapacitating neurological disorder.

Reports showed that there were public concerns about research into the human genome and gene therapy, with a combination of fear and mistrust.

**1997**


Researchers at the Roslin Institute in Scotland announced that they had cloned a sheep called Dolly from the cell of an adult ewe. Dolly was the first mammal cloned by a technique called nuclear transfer technology. Nuclear transfer allows the introduction of complete genetic material from one cell into another enucleated unfertilized egg cell.

**1998**

A group of researchers succeeded in culturing embryonic stem cells. A number of researchers at Japan's Kinki University cloned eight identical calves by means of cells taken from a single adult cow. A rough draft of the human genome map was created, presenting the sites of more than 30 000 genes.

**1999**

A fatal neurological disease called bovine spongiform encephalopathy (BSE), also known as mad cow disease, that spread from cattle to humans, was diagnosed by a new medical diagnostic examination that facilitated the quick detection of BSE/Creutzfeldt-Jakob disease (CJD).

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- The development of biotechnology can be divided into broad stages or categories, including:
    - Ancient biotechnology (8000–4000 BC): Early history as related to food and shelter; includes domestication of animals.
    - Classical biotechnology (2000 BC; 1800–1900 AD): Built on ancient biotechnology; fermentation promotes food production and medicine.
    - 1900–1953: Genetics.
    - 1953–1976: DNA research, science explodes.
    - Modern biotechnology (1977): Manipulates genetic information in organisms; genetic engineering; various technologies enable us to improve crop yield and food quality in agriculture and to produce a broader array of products in industries.

**Table 1.2.** Biotechnological processes and products developed in the ancient period.

Process or product developed	Events that contributed to its development
Domestication	<ul style="list-style-type: none"><li>• Food supplies were often seasonal. In winter, food supplies could become quite low.</li><li>• People came up with ways of capturing fish and small animals.</li><li>• 15 000 years ago, large animals were difficult to catch.</li><li>• People may only have had meat when they found a dead animal.</li><li>• Domestication most likely began 11 000–12 000 years ago in the Middle East.</li><li>• It involved the adaptation of organisms so they could be cultured.</li><li>• Seen by scientists as the beginning of biotechnology.</li><li>• Cattle, goats and sheep were the earliest domesticated food animals.</li></ul>
Food preservation	<ul style="list-style-type: none"><li>• People knew that some foods rotted, while others changed form and continued to be good to eat.</li><li>• Foods stored in a cool cave did not spoil as quickly.</li><li>• Foods heated by fire also did not spoil as quickly.</li><li>• Immersion in sour liquids prevented food decay.</li><li>• Food was stored in bags of leather or jars of clay.</li><li>• Fermentation occurs if certain micro-organisms are present, it creates an acid condition that slows or prevents spoilage.</li></ul>
Cheese	<ul style="list-style-type: none"><li>• One of the first food products made through biotechnology.</li><li>• Strains of bacteria were added to milk, resulting in sour milk.</li><li>• An enzyme called ‘rennet’ was added.</li><li>• Rennet comes from the lining of the stomachs of calves. It is genetically engineered today.</li><li>• Not all cheese is made from rennet.</li><li>• It may have been first developed by nomadic tribes in Asia some 4000 years ago.</li></ul>

## Yeast

- Long used in food preparation and preservation.
- Used in bread baking.
- Produces a gas in the dough causing the dough to rise.
- Used in fermented products such as vinegar.
- Ethanol production require the use of yeast in at least one stage of production.

## Vinegar

- Used in pickling.
- Keeps foods from spoiling.
- Juices and extracts from fruits and grains can be fermented.
- Biblical references to wine indicate the use of fermentation some 3000 years ago.
- Ancient product used to preserve food.

## Fermentation

- Process in which yeast enzymes chemically change compounds into alcohol.
- In making vinegar the first product of fermentation is alcohol.
- In ancient times, this likely happened by accident.
- Advancements occurred in the 1800s and early 1900s.

## Fermenters

- Allowed better control, especially with vinegar.
- New products such as glycerol, acetone and citric acid resulted.

## Antibiotics

- First drug produced by microbes.
- Used in both human and veterinary medicine.
- Use of fermentation hastened the development of antibiotics.
- Penicillin was developed in the late 1920s.
- Introduced in the 1940s as a drug used to combat bacterial infections.
- Many kinds are available today.
- Limitations in their use keep disease-producing organisms from developing immunity to antibiotics.
- Some disease organisms are now resistant to certain antibiotics.

**Table 1.3.** Historical and current events that form the basis of modern biotechnology.

Year	Discoveries
	The 1950s
1952	<ul style="list-style-type: none"><li>• George Otto Gey created a continuous cell line taken from a human cervical carcinoma. This cell line, known as HeLa, is still used in therapeutic research.</li></ul>
1953	<ul style="list-style-type: none"><li>• Watson and Crick explored DNA as a genetic material, and discovered its structure, called the double-helix.</li></ul>
1954	<ul style="list-style-type: none"><li>• Joseph Murray carried out the first kidney transplant between identical twins.</li></ul>
1957	<ul style="list-style-type: none"><li>• Scientists revealed that sickle-cell anemia occurs due to an alteration in a single amino acid in hemoglobin cells.</li></ul>
1958	<ul style="list-style-type: none"><li>• Arthur Kornberg created DNA in a test tube for the first time. The first mechanical protein sequencer, the Moore–Stein amino acid analyzer, is developed.</li></ul>

### The 1960s

- 1960 • A French researcher discovered messenger RNA (mRNA).
- 1961 • François Jacob and Jacques Monod demonstrated the concept of Operon.
- 1962 • Osamu Shimomura explored the green fluorescent protein in the jellyfish *Aequorea victoria*. He afterward developed it into a technique for examining formerly invisible cellular processes [60].
- 1963 • Samuel Katz and John F Enders developed the first vaccine for measles [61].
- 1963 • Autonomous groups in the USA, Germany and China produced insulin, a pancreatic hormone.
- 1964 • The existence of reverse transcriptase was predicted.
- 1967–71 • Maurice Hilleman made the first American vaccine for mumps [62].
  - The first vaccine for rubella was developed.
  - Rubella was combined with the measles and mumps vaccines to yield the measles/mumps/rubella (MMR) vaccine.
- 1968 • How the arrangement of nucleotides in nucleic acids regulates the cell's synthesis of proteins was discovered.

# BRANCHES OF BIOTECHNOLOGY

- • **Red biotechnology:** This area includes medical procedures such as utilizing organisms for the production of novel drugs or employing stem cells to replace/regenerate injured tissues and possibly regenerate whole organs. It could simply be called medical biotechnology
- • **Green biotechnology:** Green biotechnology applies to agriculture and involves such processes as the development of pest-resistant grains and the accelerated evolution of disease-resistant animals.
- • **Blue biotechnology:** Blue biotechnology, rarely mentioned, encompasses processes in the marine and aquatic environments, such as controlling the proliferation of noxious water-borne organisms.
- • **White biotechnology:** White (also called gray) biotechnology involves industrial processes such as the production of new chemicals or the development of new fuels for vehicles

## Some Global Revolutionary Success Stories of Biotechnology



### **Dolly Sheep** (5 Jul 1996-14 Feb 2003)

First mammal cloned from adult somatic cell using nuclear transfer. Died due to progressive lung disease.



### **Bt Cotton**

Genetically Modified Organism (GMO) with a foreign gene From *Bacillus thuringiensis* (*Bt*) expressing protein conferring resistance to Bollworm



### **Human Growth Hormone**

Human GH gene isolated from pituitary gland cell and inserted in *E.coli* expressing recombinant Human GH, cultured in fermenters



Lepidopteran resistant  
Bt Brinjal (Right)



### **Humulin**

Human insulin gene isolated from pancreatic cells and inserted into a bacterium expressing insulin cultured in large scale fermenters

# SCOPE/APPLICATIONS OF MODERN BIOTECHNOLOGY

- Modern biotechnology, which is based on rDNA technology, exhibits a wide range of applications
- The broad application areas of biotechnology include pharmaceutical and therapeutic research, disease diagnostics, crop improvement, vegetable oil, biofuels, and development of environmental friendly products (for example biodegradable plastics).
- Thus, the applications of modern biotechnology mainly focus on the following major areas:
  - **1. Medicine and health care**
  - **2. Crop production and agriculture**
  - **3. Food processing**
  - **4. Environmental protection**

