Introduction to Genetic Engineering

The term genetic engineering (**recombinant DNA technology** and **biotechnology)** was coined in 1919 by Karl Ereky, a Hungarian engineer. At that time, the term included all the processes by which products are obtained from raw materials with the aid of living organisms.

Nowadays, **genetic engineering** is defined as any technological application (a set of techniques) that uses biological systems, living organisms, or derivatives thereof, to make or modify products or processes for specific use.

Man has used artificial selection to exploit and manipulate organisms for thousands of years, between 8000 and 1000 b.c. horses, camels, oxen, and many other species were already domesticated; by 6000 b.c. yeast was used to make beer; by 5000 b.c. plants such as maize, wheat, and rice were bred.

In 420 b.c. Socrates speculated on why children do not necessarily resemble their parents; by 400 b.c. Hippocrates would propose that males contribute to a child's character through semen: the idea of **heredity** was thus established.

It was not just Greeks or Romans who were in a constant quest for an answer to how life originates. Between 100–300 a.d. Hindu philosophers were giving much thought to the same questions of reproduction and inheritance. By the first millennium, they had already established the foundations of **genetics**; they observed that certain diseases might run in the family. They also came to believe, almost correctly, that children inherit all the characteristics of their parents.

With the exponential increase in the number of biochemical studies during the 19th century, such as those on nucleic acids and amino acids, and the speeding up of the fermentation industry, biology took on a whole new direction. In 1864, Mendel presented his work on peas and published the results in 1865 in. The work was largely neglected for quite some time, and the term **gene** or **genetics** was not yet coined.

The next century saw a huge accumulation of data and know-how that would eventually lead to the first biotechnology products, including the use of agar described in 1882 by the Koch lab, the development of the autoclave in 1884 by a French company (Chamberland's Autoclaves), the discovery of X-rays by W. Roentgen in 1895, followed by the application of this information to X-ray crystallography by physicist Sir William Henry Bragg and his son William Lawrence Bragg and many others in 1913. However, most of the leap in tech-

nology in genetic engineering or recombinant DNA owes its progress to the physicists who became deeply interested in the biology of the cell after World War II.

> Biology is a very interesting field to enter for anyone, by the vastness of its structure and the extraordinary variety of strange facts it has collected. … In biology we are not yet at the point where we are presented with clear paradoxes and this will not happen until the analysis of the behavior of living cells has been carried into far greater detail. This analysis should be done on the living cell's own terms…

In 1951, Hershey performed his famous "blender experiment" with his assistant Martha Chase, showing that the hereditary material is DNA and not protein. Luria and Hershey also demonstrated that bacteriophages mutated, and introduced criteria for distinguishing mutations from other modifications.
In 1945, William Astbury, a leading biophysicist in the field of X-ray diffraction analysis of structures of biological macromolecules, devised the term **molecular biology**. In the early 1950s, Rosalind Franklin and Maurice Wilkins obtained the X-ray diffraction data for DNA, which would prove crucial for Watson and Crick to establish their model of two helically intertwined chains tied together by hydrogen bonds between the purines and pyrimidines in 1953.

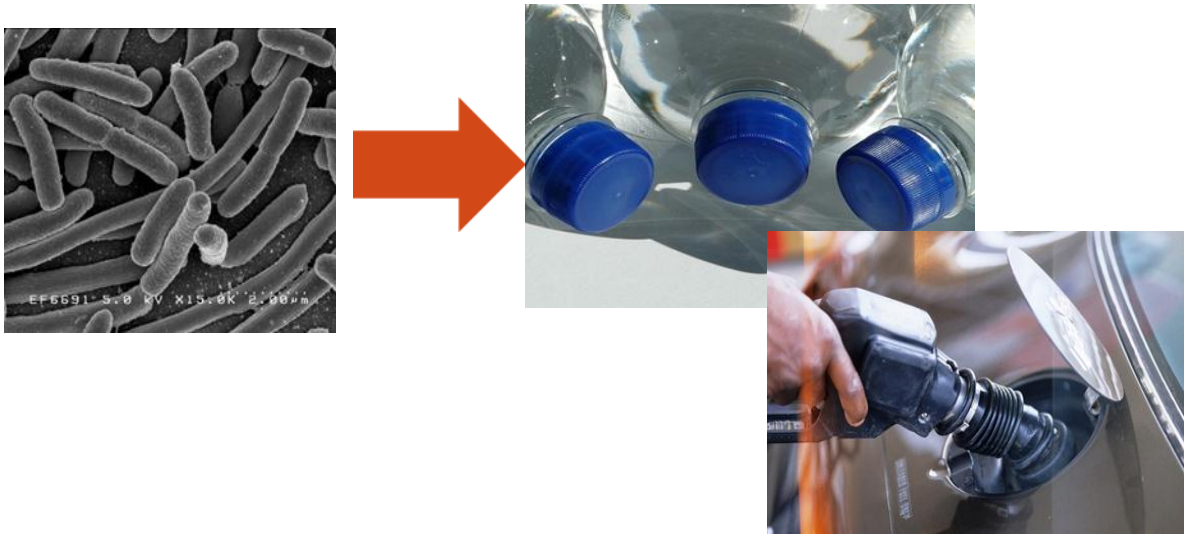
At around the same time, bacterial plasmids were defined as autonomously replicating material, and in the late 1960s, Werner Arber identified the **restriction enzymes** in bacteria that were designed to cleave DNA. And in 1970, Temin and Baltimore independently identified the viral enzyme **reverse transcriptase**, which would result in the birth of recombinant DNA technology—the first recombinant DNA was produced in Boyer Laboratory in 1972, and in 1976, the first biotechnology company **Genentech** was born.
The big biotech boom would be seen in the 1980s, especially after the invention of the **polymerase chain reaction (PCR)** by Karen Mullis in 1983. Genentech's recombinant interferon gamma and Eli Lilly's recombinant human insulin appeared on the market in 1982. The Human Genome Initiative, later to be renamed the **Human Genome Project**, was launched in 1986 and its completion was announced nearly two decades later. Another biotech company, GenPharm International, created the first transgenic dairy cow to produce human milk proteins for infant formula in the 1990s, and in the same period the first authorized **gene therapy** began on a four-year-old girl with an immune disorder known as ADA, or adenosine deaminase deficiency. This hype was perhaps at its peak in 1997, when flash news came from Scotland's Roslin Institute that the first mammalian clone, Dolly the sheep, was born, through a procedure known as somatic cell nuclear transfer.

Now we have the complete genomes of many species, from bacteria to men; we have techniques to screen for genetic polymorphisms in individuals (such as those done for James Watson and Craig Venter), we can manipulate stem cells and generate knockout animals, transgenic animals, or even clones. This course merely seeks to give some basic background on the recent techniques employed in genetic engineering.

Applications of genetic engineering

1- Industry

Bacteria are the most common GMOs because their simple structure permits easy manipulation of their DNA. One of the most interesting uses for genetically modified bacteria is the production of hydrocarbons (plastics and fuels) usually only found in fossil fuels. Cyanobacteria have been modified to produce plastic (polyethylene) and fuel (butanol) as byproducts of photosynthesis. *E. coli* bacteria have been modified to produce diesel fuel.



2. Health and medicine

In the area of health and medicine, genetic engineering has numerous and important functions. Genetic engineering is used to develop diagnostic tools for identifying diseases. It is also used to produce more effective and efficient vaccines, therapeutic antibodies, antibiotics, and other pharmaceuticals.

Figure 1: Modified virus injected in sapling tree causes the bananas to contain virus proteins

3. Environment

Development and usage of alternative fuels that burn cleaner and improve air quality through reduced pollution of the environment is possible by genetic engineering means. Micro-organisms are used to decompose wastes and clean up contaminated sites by the technology of bioremediation. The use of disease-resistant cultivars can make crop production less environmentally intrusive by reducing the use of agrochemicals.

4. Forensics

Since the DNA profile, i.e. the nucleotide sequence of the genome, is unique in every individual, it can be used as a powerful basis of identifying individuals in a population. DNA-based evidence is used in cases involving paternity disputes and family relationships. Forensic experts use DNA profiling to identify suspects in criminal cases, especially when body fluids and other particles like hair and skin samples can be retrieved.

5. Agriculture

Genetic engineering can complement conventional breeding for crop and animal improvement. Instead of extensive re-arrangement of genes, as occurs in conventional breeding, biotechnology enables targeted gene transfer to occur. The genome of the recipient individual remains intact, except for the introduced gene (or genes), thus accelerating breeding programs and the development of organisms with desirable characteristics. This biotechnological application is used to improve the yield of crop and animal species and their product quality such as nutritional value and shelf life.

Figure 2: Reasons to Genetically Modify Crops, Insect resistant, Herbicide resistant, Drought/freeze resistant, Disease resistant, Higher yield, Faster growth, Improved nutrition & Longer shelf life.

Figure 3: Fast-Growing Salmon, Genes from two other fish cause this salmon to continually produce growth hormones.

Abbreviations and Acronyms:

B.C.: Before Christ: years before the birth of Christ

A.D.: (1) Anno Domini: years after the birth of Christ

(2) Activation domain.

DNA: Acronym for deoxyribonucleic acid, which is a molecule that contains an organism's complete genetic information.

Definitions:

Nucleotide: The building block of DNA.

Gene: The molecular unit of an organism that contains information for a specific trait (specific DNA sequence).

Genome: An entire set of genes for an organism.

Plasmid: The circular DNA structure used by bacteria.

Protein: Large biomolecules used by an organism for a number of purposes; in this context, to express a desired trait.

Trait: A distinguishing characteristic.

Recombinant DNA: DNA to which a section has been removed and replaced (recombined) with a new sequence.

Restriction enzyme: An enzyme that "cuts" DNA when specific base pair sequences are present.

GMO: Acronym for genetically modified organism.

Gene cloning: the development of a line of genetically identical organisms which contain identical copies of the same gene or DNA fragments

Gene therapy: the insertion of a functional gene or genes into a cell/tissue/organ to correct a genetic abnormality.

PCR: abbreviated from polymerase chain reaction, an in vitro process by which specific parts of a DNA molecule or a gene can be rapidly made into millions or billions of copies within a short time.

Recombination DNA: a hybrid DNA molecule created in the test tube by joining a DNA fragment of interest with a carrier.

DNA Southern blot: a procedure that is used to transfer DNA from a gel to a nylon membrane, which in turn allows the finding of genes that are complementary to particular DNA sequences called probes.