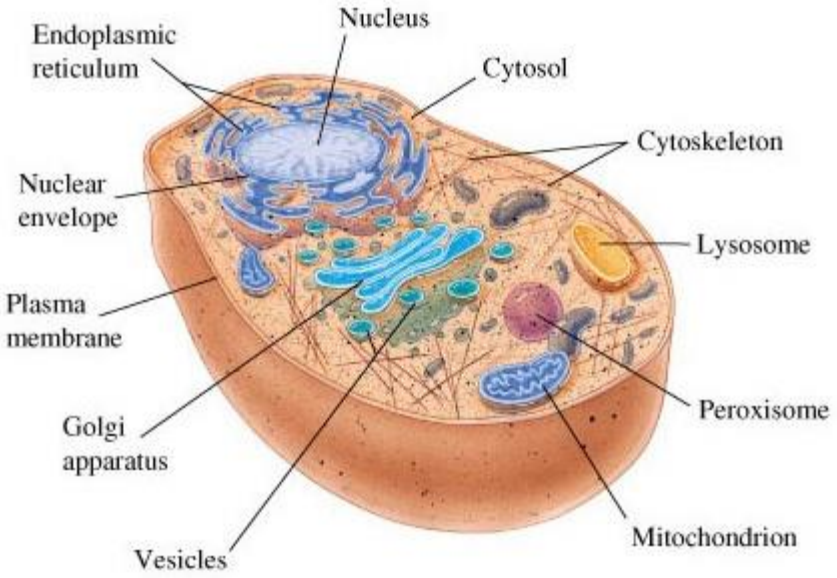
INTRODUCTION TO MEDICAL BIOLIGY
THE LIVING CELL



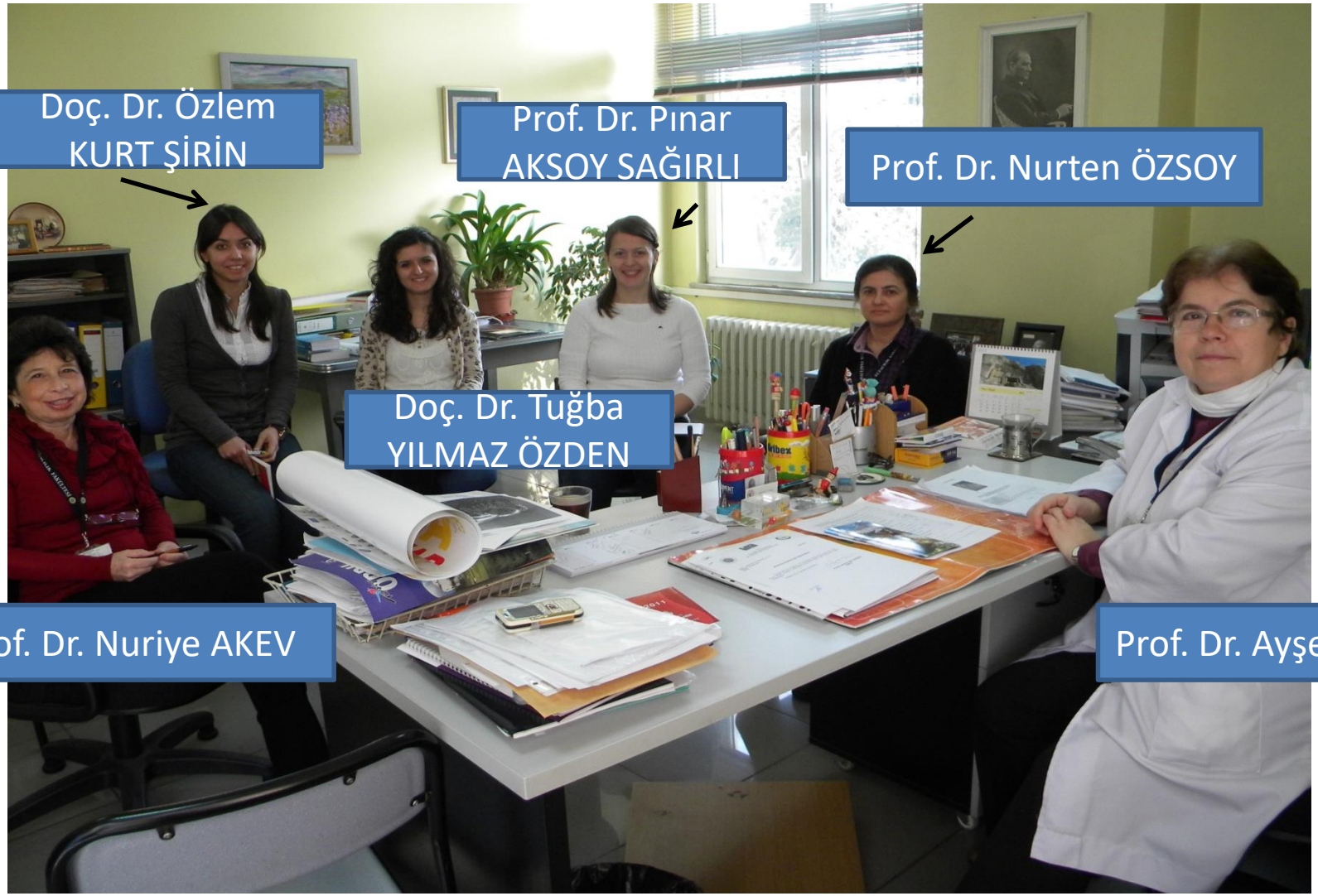
Prof. Dr. Nuriye AKEV

25 September 2018

Learning Outcomes

- The differences between living organisms and inanimate matter
- Evolution of life on earth
- Landmarks of science and important scientists for Biology and Medicine
- Discovery of DNA
- Discovery of the cell
- Differences between prokaryotic and eukaryotic cells

Teaching Stuff of the Biochemistry Department



LIVING ORGANISMS

Living organisms are made from lifeless molecules. What is the difference between living and inanimate organisms?

LIVING ORGANISMS

Inanimate molecules that constitute living organisms interact to maintain and perpetuate life. What are the extraordinary attributes that distinguish living matter?

LIVING ORGANISMS

- A high degree of chemical complexity
- Systems for extracting, transforming and using energy from the environment
- A capacity for precise self-replication
- Mechanisms for sensing and responding to alteration in their surroundings
- Defined functions for each of their components and regulated intreactions among them
- A history of evolutionary change

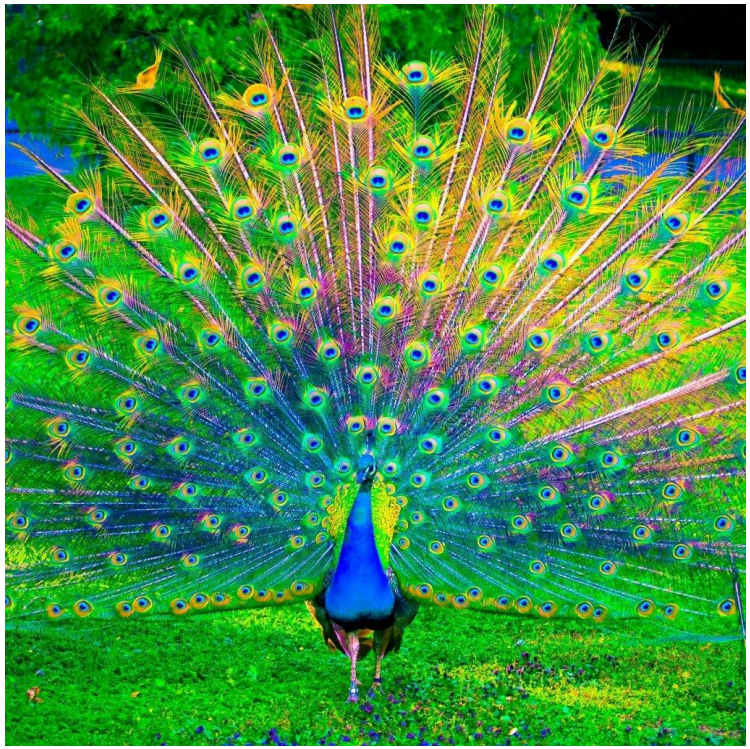
Evolution

Organisms change their inherited life strategies to survive in new circumstances resulting in the magnificient biodiversity of earth.

In summary what is the difference between living an lifeless?

- Reproduction
- Growth and development
- Response to stimuli
- Movement
- Nutrition
- Respiration
- Excretion
- Accommodation, adaptation
- Metabolism (Living organisms take substances from their environment, and employ them as an energy source, produce new elements and excrete waste matter.)

Albinism genetically transmitted form but it is not a disease



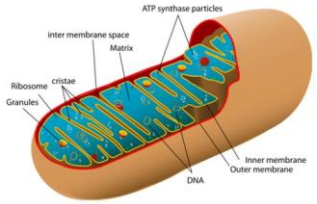
4.5 billion years ago
Earth was formed

3-3.5 billion years ago
Life started

2.3 billion years ago
The first prokaryotes in oceans (anaerobic life)

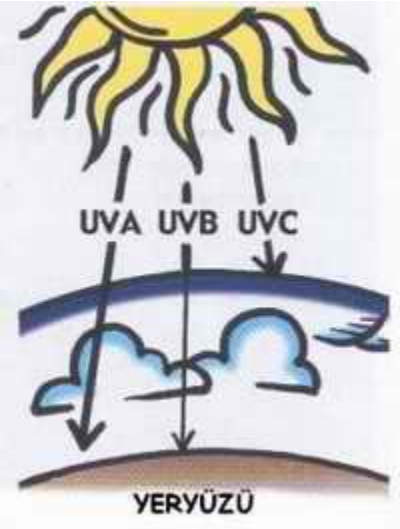
Stromatolites, cyanobacteria fossils found in Australia

2.3 billion years ago



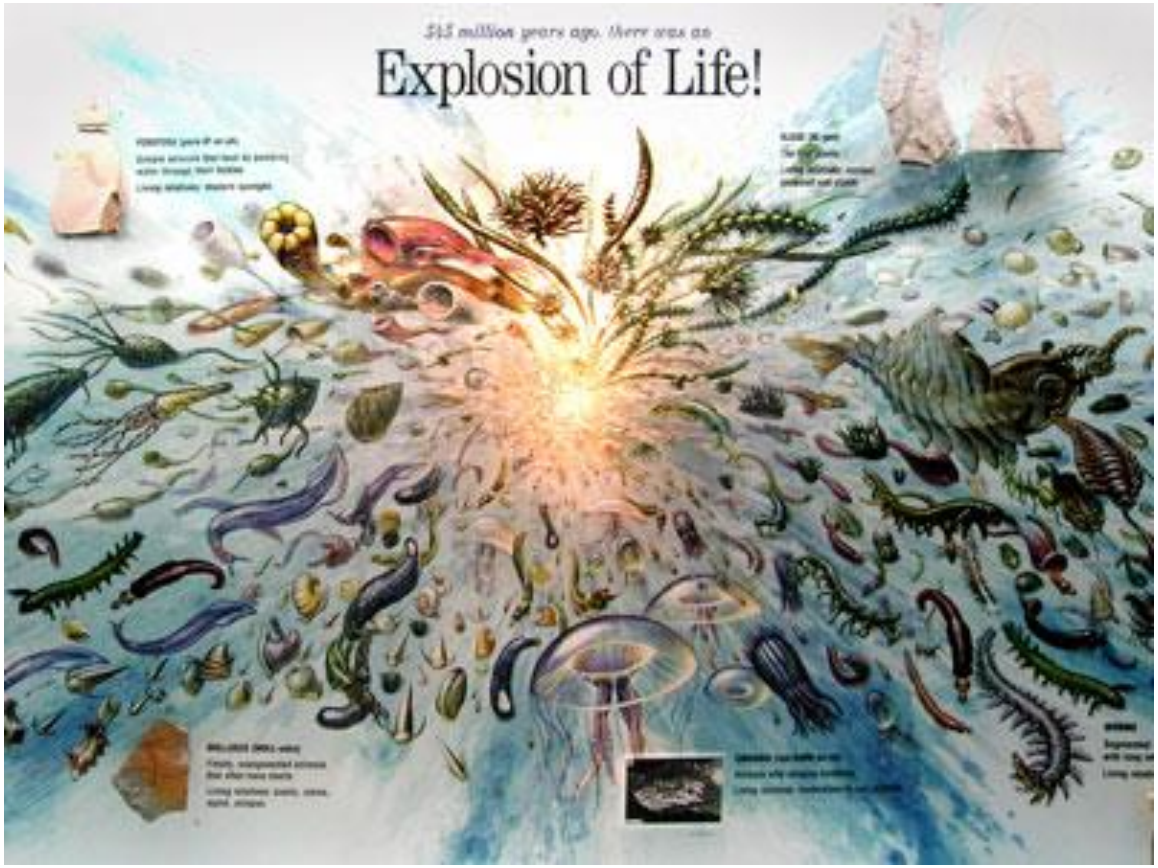
- The first prokaryotes (in the oceans)
- Oxygen starts to get released in the atmosphere (2.4 billion years ago) by the cyanobacteria
- Oxygen begins to accumulate in the atmosphere (2.3 billion years ago)
- This is the greatest extinction event in earth history and is called: "The Great Oxygenation Event" or "Oxygen Catastrophe".It is a catastrophe for anaerobic organisms
- The environment becomes suitable for eukaryotic organisms
- It is beleived that mitochondria are evolved from the symbiosis of two prokaryotic cells. A bacteria engulfed in a prokaryote

532 million years ago



- Ozone (O_3) starts to form and created a protective umbrella against the harmful effects of sun rays.
- Life could begin when the ozone layer attained a thickness that blocks UV radiation from coming to earth.
- In contrast to what was thought, animals colonized land before plants did.

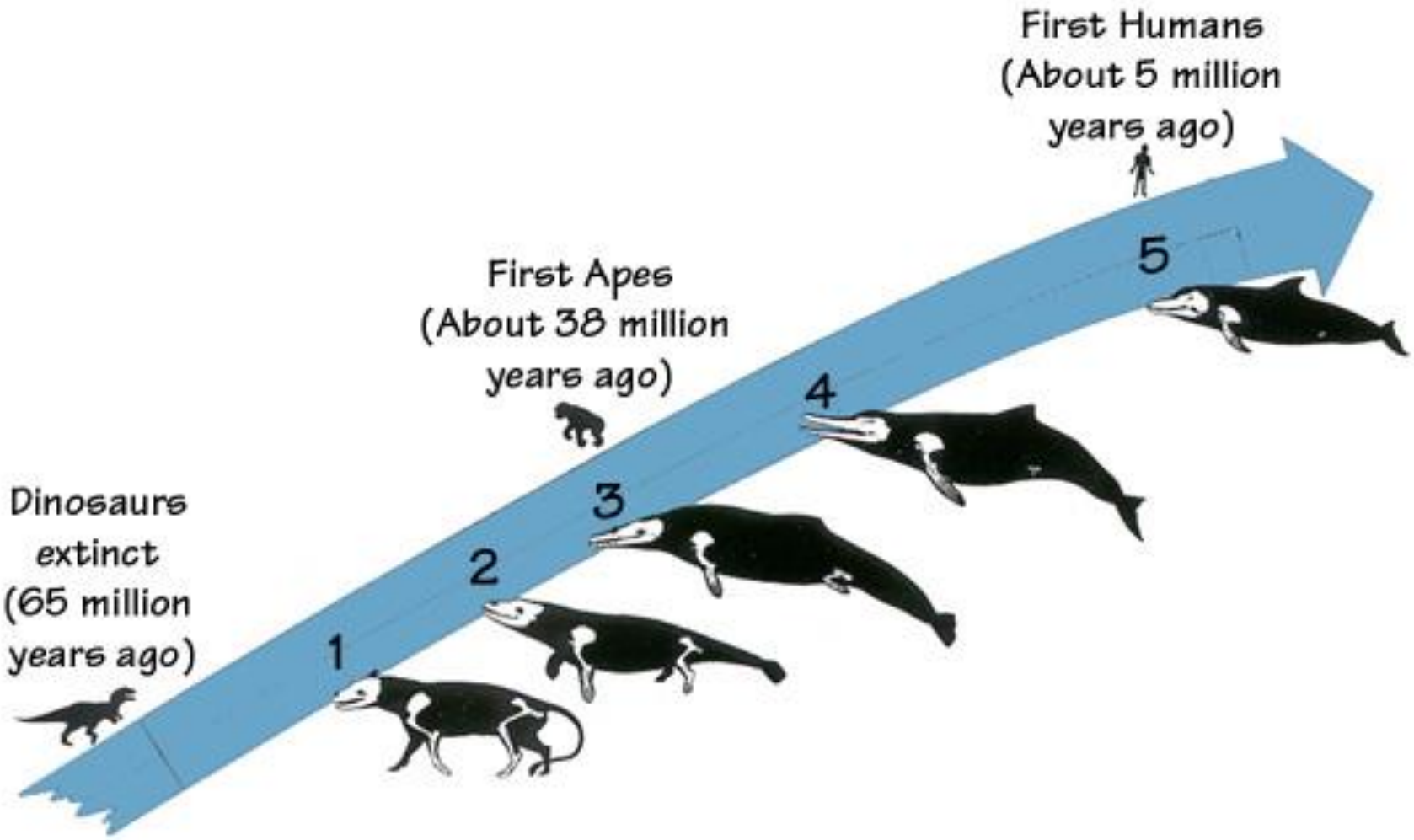
Cambrian Explosion: Explosion in the number of species and genera. Complex multicellular organisms. The first fish, the first preamphibians.



Dinosaurs

- They lived 230-65 million years ago.
- 65 million years ago a huge rock colliding what is now te Yucatan peninsula in Mexico, destroyed all of the large land and all the life forms especially the dinosaurs.
- Rodents, smaller animals, were able to survive by digging tunnels and are likely to be our ancestors.

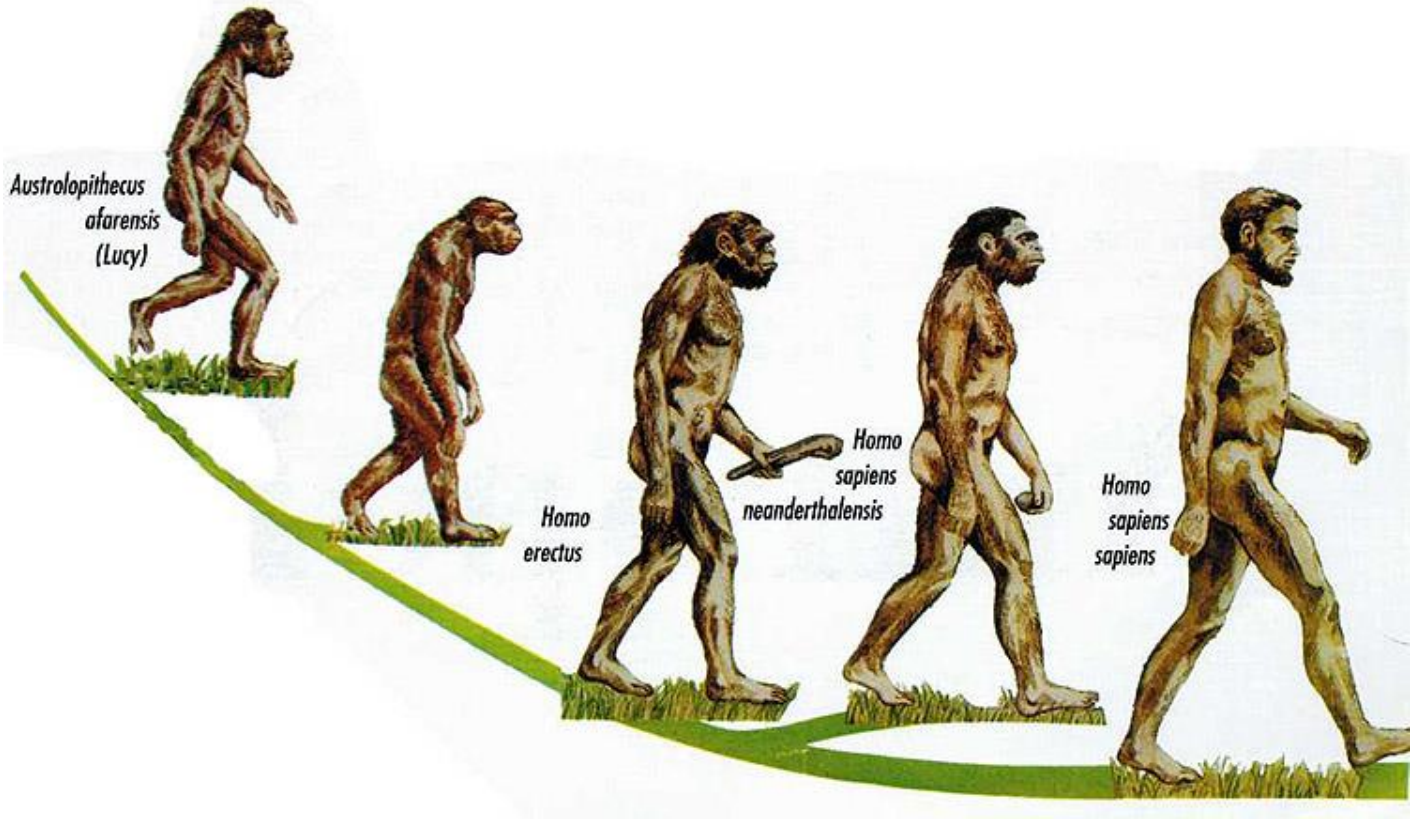
- To date it is scientifically beleived that life was formed by inanimate molecules through an evolution that runned for billion of years.

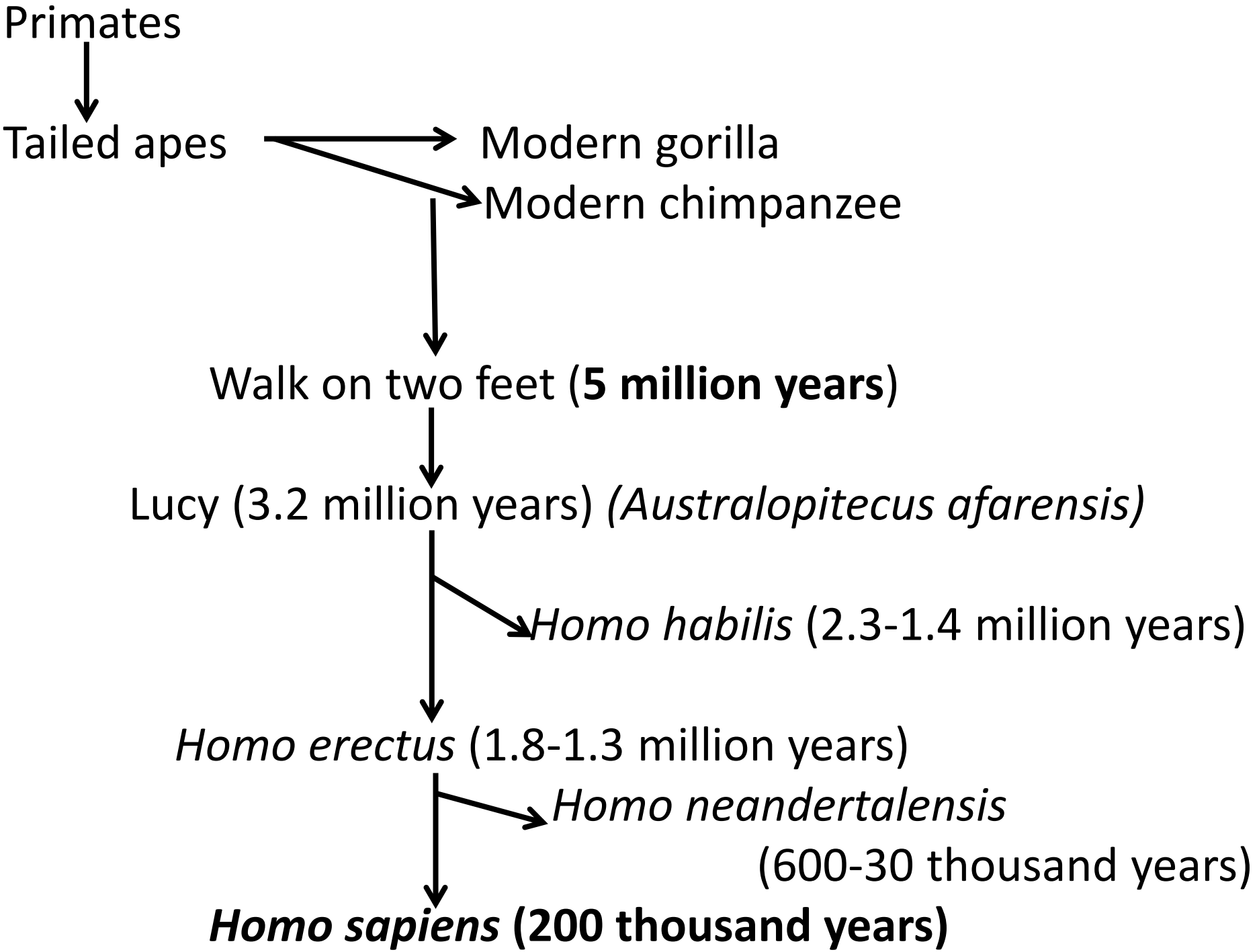


www.understanddolphins.tripod.com

5 million years ago:The first hominides walking on two feet appear

200 thousand years ago evolution to the «wise» man.



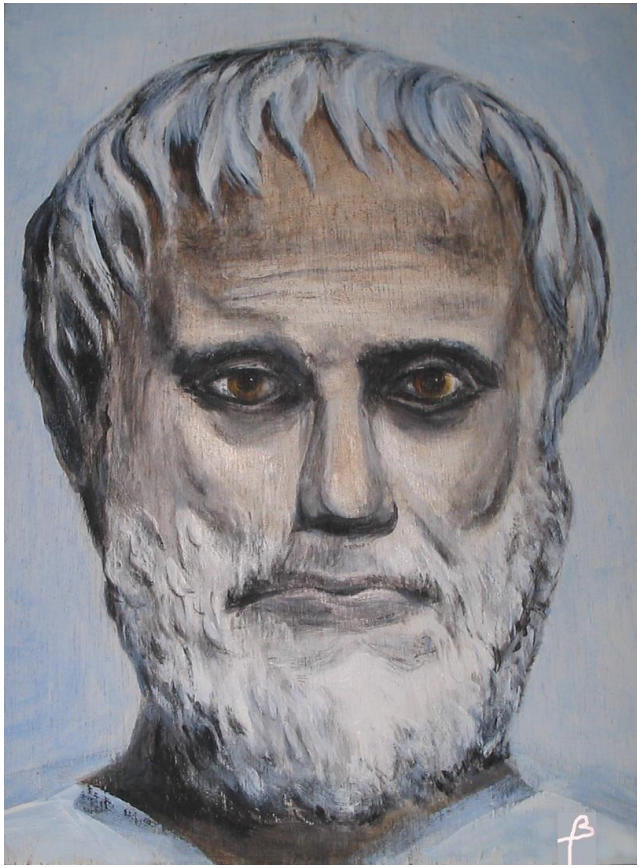

Primates
Tailed apes
Modern gorilla
Modern chimpanzee
Walk on two feet (**5 million years**)
Lucy (3.2 million years) *(Australopitecus afarensis)*
Homo habilis (2.3-1.4 million years)
Homo erectus (1.8-1.3 million years)
Homo neandertalensis
(600-30 thousand years)
***Homo sapiens* (200 thousand years)**

INTERNET VIDEOS

- https://www.khanacademy.org/science/cosmology-and-astronomy/life-earth-universe/history-life-earth-tutorial/v/first-living-things-on-land-clarification
- https://www.khanacademy.org/science/cosmology-and-astronomy/life-earth-universe/humanity-on-earth-tutorial/v/human-evolution-overview1995.
- https://www.youtube.com/watch?v=VTRIKgKLI_Y

HISTORY OF SCIENCE

- **Aristoteles** (384-322 B.C.)



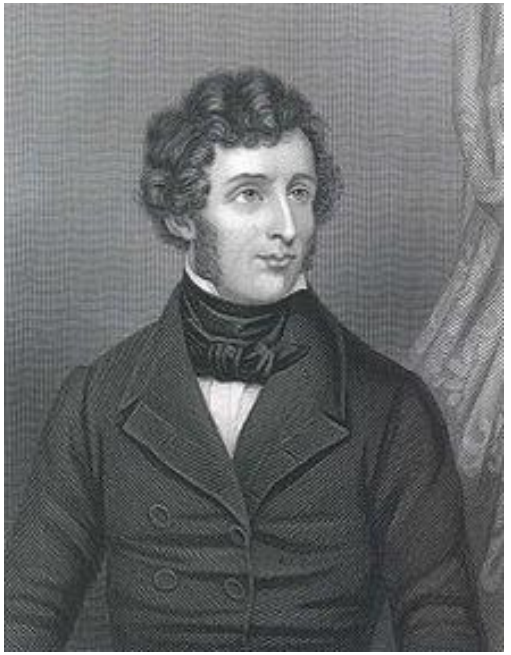
Vitalism philosophy

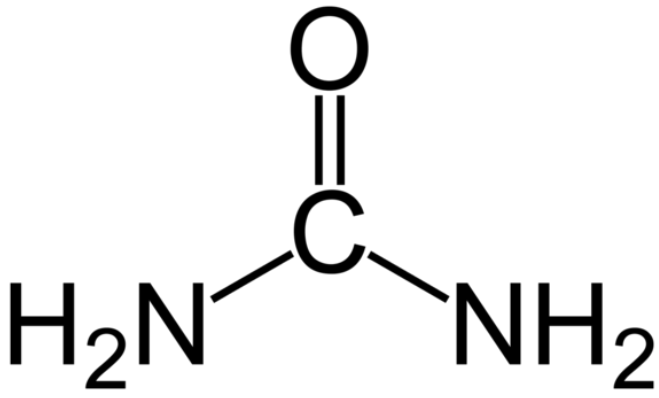
Living matter was different from inanimate matter and required a "vital force" for their secretions, and did not act according to physics and chemistry rules.

The synthesis of urea 1828

- **Wöhler** (1800-1882)

The synthesis of urea which was a living matter, from an inorganic substance ammonium cyanide, has shown that organic matter can be synthesized from inorganic substances and have completely destroyed the centuries-old vitalism theory.





Üre

The father of Modern Chemistry

The law of conservation of mass

- Nothing was said to exist from nothing, and in all experimental transformations, the substance remained the same in quantity, and the fact that the elements retained their quantitative and qualitative characteristics in all their compositions could be regarded as an indisputable axiom, and laid the foundation of modern chemistry.
- According to this law, during any physical or chemical change, the total mass of the products remains equal to the total mass of the reactants.

Antoine-Laurent **Lavoisier** (1743-1794)

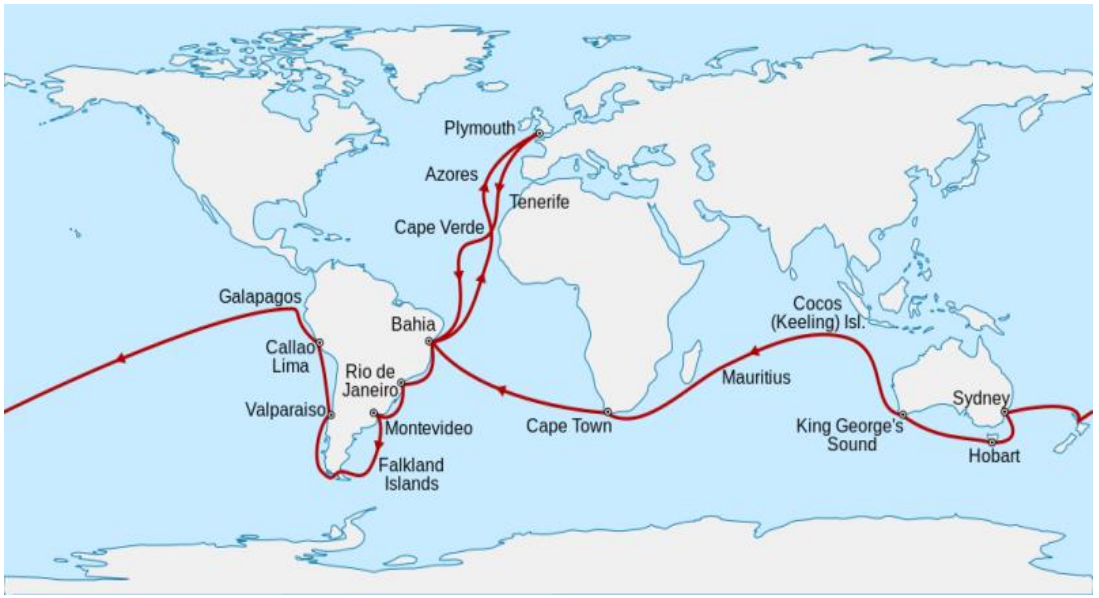
- At the time of his experiments on respiration in 1794, Lavoisier was summoned before the Revolutionary Court. Two charges have been targeted:
- The relationship with the aristocracy scoured as anti-revolution;
- Corruption in tax collection (Lavoisier spent a small part of the taxes he collected for his laboratory experiments).

His friends had rushed to the court to save Lavoisier, but the court found no need to listen to him even as a witness. The petition of the distinguished scientist of the day told:"*Citizen Lavoisier is a big scientist who honours France with his work,* we wish him to be forgiven ", the judge's response is precise and striking:"*The Republic does not need scientists!*"

Galileo spent the last ten years of his life in the custody of the Inquisition. The end of the Lavoisier is more tragic: when he was 51, his head was cut by a guillotine on behalf of the "revolution". Lavoisier, was reading a book while waiting for the execution. When the executioner came to him to bring him down to the guillotine, Lavoisier placed a bookmarker between the book in order not to forget where he was staying!

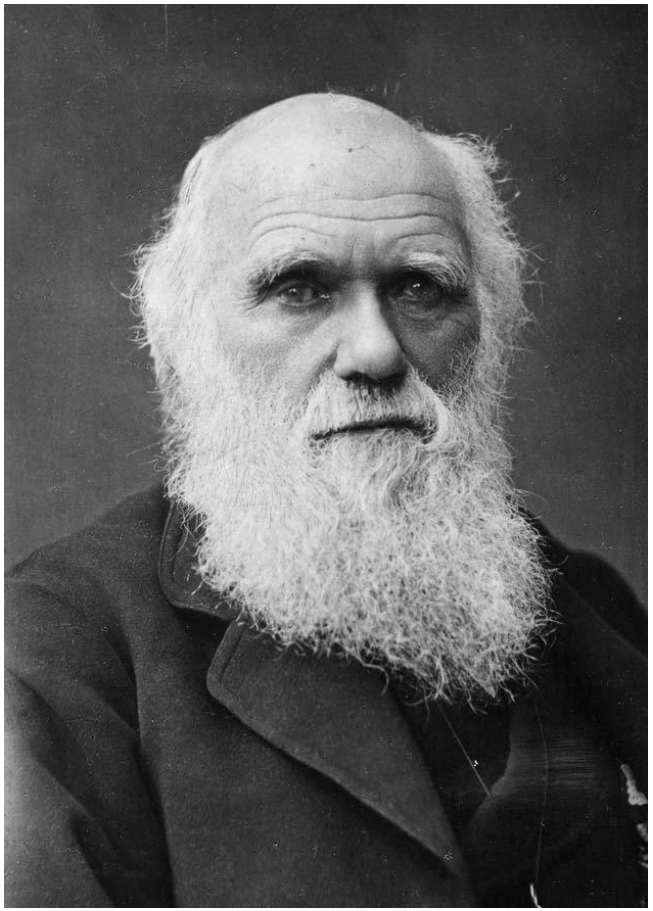
The father of Modern Biology

Charles Darwin
(1809-1882)



Darwin's paths through the HMS Beagle (1831-1836)

Darwin



- **With his theories of Natural Selection** and his book **The Origin of Species** published in 1859, **he is the founder of modern biology and in a time when DNA was not even known, by talking of evolution, he was also the messenger of genetics.**

The father of Modern Genetics

Austrian scientist and monk

Gregor Mendel
(1822-1884)

Pioneering research in the field of heredity: Mendel experiment 1865

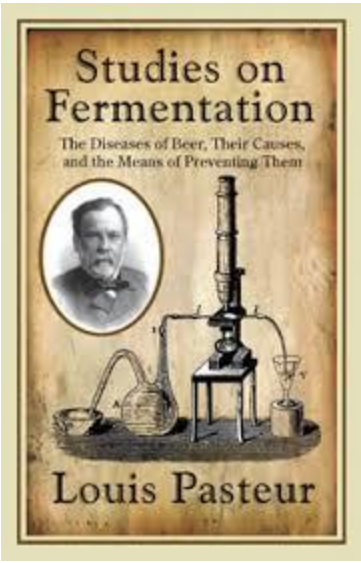
- Nevertheless, Mendel's first article did not attract much attention. By 1900, it was also in Amsterdam, Tübingen and Vienna, respectively that
- **Hugo de Vries,**
- **Carl Correns**
- **Erich von Tschermak**,

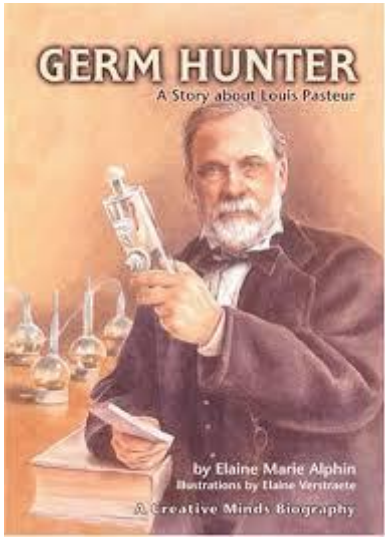
Did publish three articles on the same subject. All three honestly stated that this discovery was made by a person who lived in Brno (now Czech Republic) 30-40 years ago. Thus, 1900 was accepted as the starting date of genetic science.

The father of Microbiology

Louis Pasteur

(1822-1895)





When microbes were unknown and cannot be seen, he somewhat "feel" their existence. Father of microbiology, discoverer of rabies vaccination, pasteurization, stereoisomery.
"The savior of humanity"

The first discovery of DNA

Friedrich Miescher

(1844-1895)

His laboratory in Tübingen Castle (www.tau.ac.il) and the first DNA purified from salmon sperm.
(www.historiamaximus.blogspot.com Access 25.09.2015)

Tübingen Castle (Tübingen University)

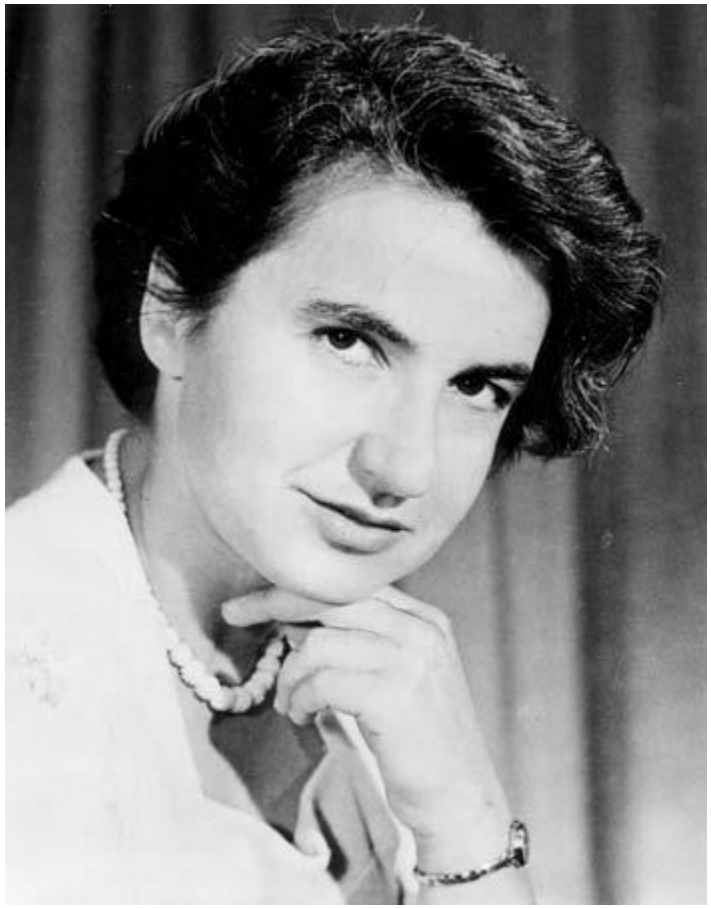
The labs of Felix Hoppe-Seyler and Friedrich Mischer were here. Hemoglobin and DNA were discovered here, 1860-70's.

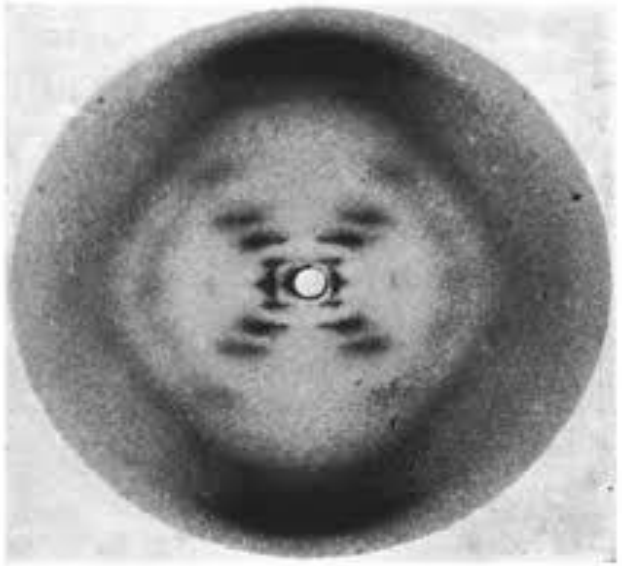
Friedrich Miescher

- The presence of DNA in the cell nucleus was discovered in 1869 and the first DNA material was isolated from lymphocytes isolated from the pus in the hospital dressings (bandage).
- Miescher purified DNA for the first time from salmon semen (Fig). Named as "Nuclein" the relation between this matter and heredity was still unknown.

1920-1953 the way to DNA double helix

- **Levene** determines the molecules that are part of the chemical structure of DNA.
- The relation between DNA and heredity was discovered after 1940 by, **Griffith, Avery, Mc Leod ve Mc Carty, Hershey and Chase**.
- Between 1949-1953, **Chargaff** found by chromatographic methods, that, among the 4 bases present in DNA, (the 4 nucleotides are shortly called bases) the number of A (adenine) equals the number of T (thymine) and, the number of G (guanine) equals the number of C (cytosine).
- **Franklin and Wilkins** elucidated the helical structure of DNA by X-ray diffraction method.



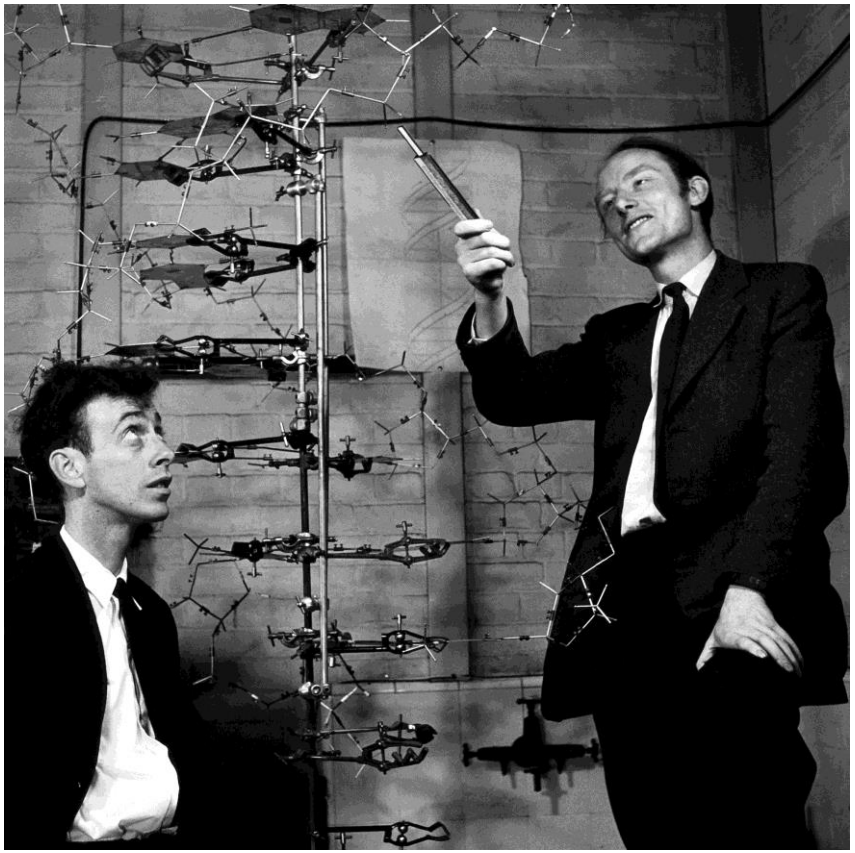


Rosalind Franklin (1920-1958)

And her famous X-ray crystallographic picture of DNA.

(www.en.wikipedia.org; www.brighthub.com Erişim: 25.09.2015)

DNA double helix elucidated 1953
Watson and Crick

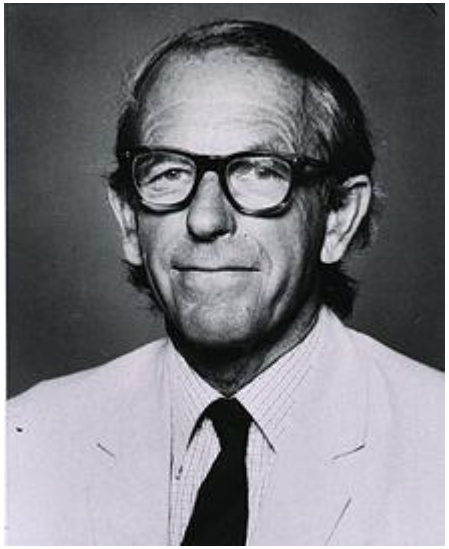


1962 Nobel Physiology
or Medicine award

James Dewey Watson (1928-) (88) and Francis Crick (1916-2004) in front of their DNA model (www.onedio.com) and in their older age (www.bbc.co.uk)

The DNA double helix, described as the invention of the era, lead to a legitimate Nobel Prize. In fact, the story of Watson and Crick is a story of great harmony. In 1953,35-year-old Crick had not yet given his doctorate, yet Watson, 12 years younger than him, had received his doctorate at the age of 22. In fact, the whole struggle was to win the Nobel Prize against Linus Pauling, who worked in the same laboratory. In 1962, the Nobel prize was given to **Watson, Crick and Wilkins**, but Rosalind Franklin, who has given the inspiration for the helical structure to Watson, with the best X-ray diffraction picture of DNA, was forgotten. The main reasons for this were Rosalind Franklin's being a woman and dying of cancer in 1953 (Nobel Prize is given to living persons only). In an age where men were mostly working and women were not even taken to the coffee room in the faculty, there was no one to whom Franklin could be close to.

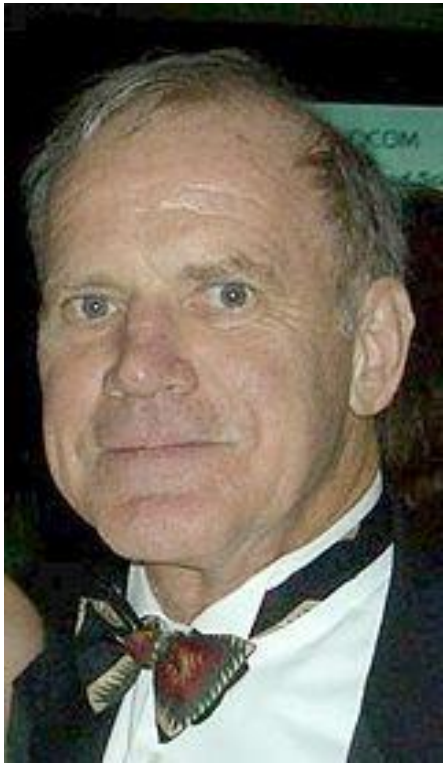
Paul Berg
(1926-) 92 years old
Rekombinant DNA



Frederick Sanger
(1918- 2013)
1952 Amino acid sequence of insulin (1958 Nobel Chemistry)
1977 DNA sequencing dideoxy method

Walter Gilbert
(1932-) 86 years old
1977 DNA sequencing method, introns and exons, RNA world hypothesis

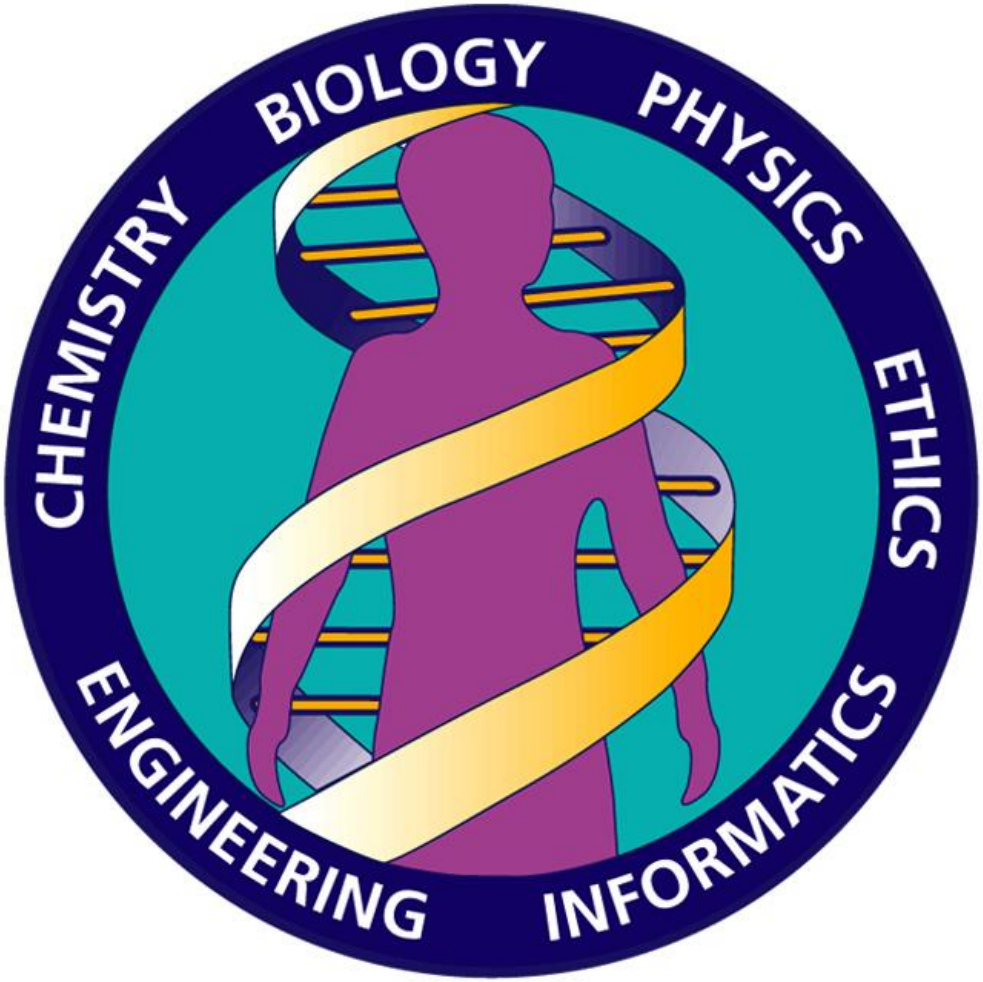
Share 1980 Nobel Chemistry Award



He surprised by the fact that he was opposed to AIDS and to the climate change, believed in astrology, and confessed that he has used LSD in his youth.

Kary Mullis
(1944-) 74 years old
1983 PCR DNA amplifying method
1993 Nobel Chemistry

Ian Wilmut and DOLLY
(1944-) 74 years old
1996 Rekombinant DNA and cloning



Human Genome Project (HGP) 1990-2003

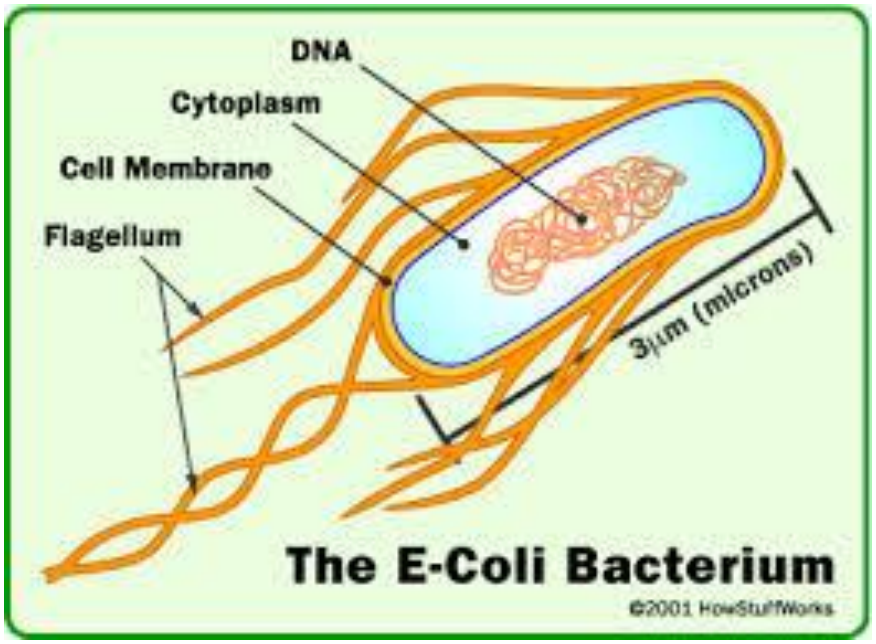
1998: It was declared that human genome contains 30.000 genes

"DO YOU, CYNTHIA, WHO IS COMPLETELY FREE OF ANY GENETIC ENGINEERING, TAKE RODNEY, WHO IS EQUALLY FREE..."

The molecular logic of life

- All living organisms come from a common ancestor
- All living organisms follow the basic laws of thermodynamics
- Living cells are a combination of organic molecules which have the capacity of self-replication and self-arrangement.
- Living cells use the energy for the synthesis of biomolecules necessary for them.

Biologic diversity rises with the development of organization level

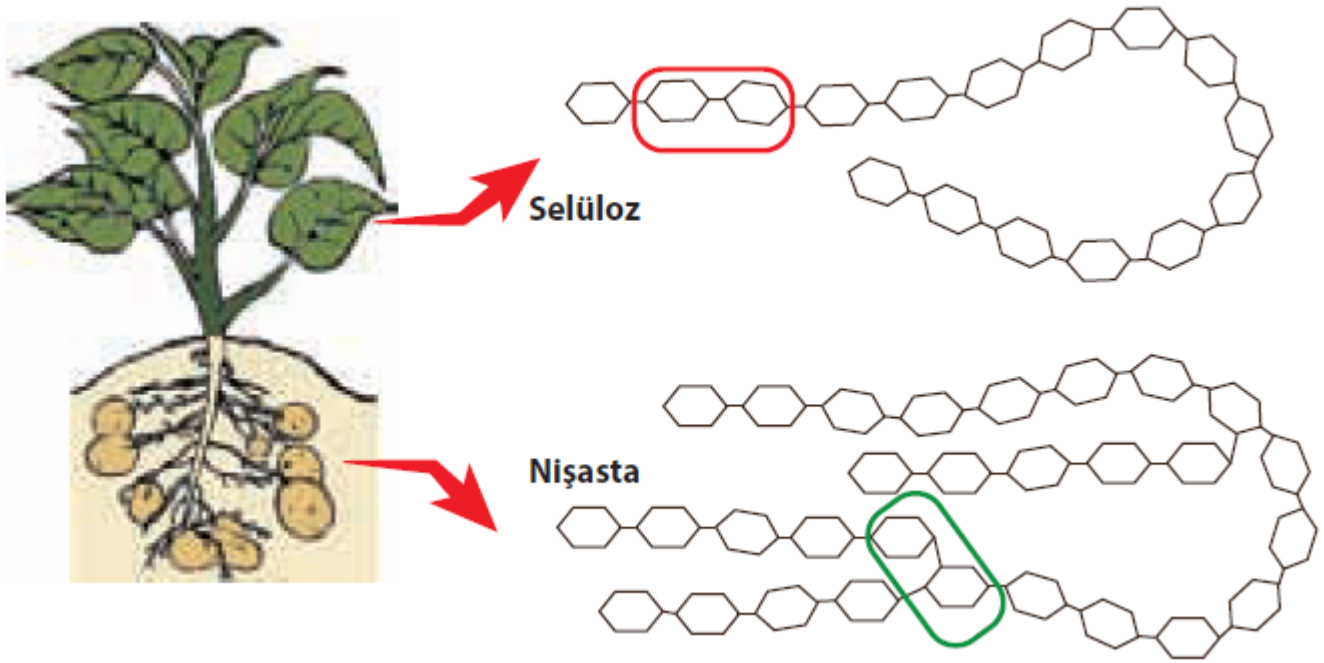


Escherichia coli :3.000 kinds of proteins

Human: 100.000 kinds of proteins

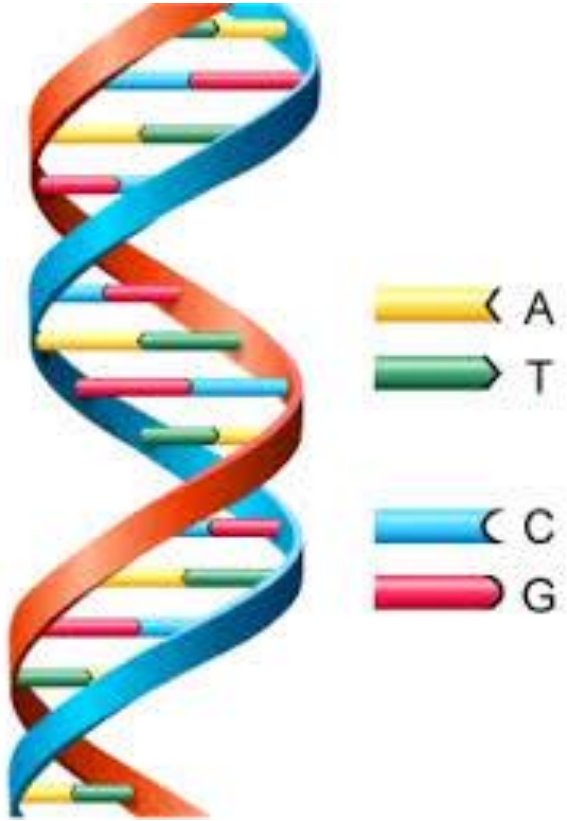
All proteins are made only from 20 different amino acids

Starch and cellulose are made from simple molecules



Glycosidic linkages link glucose molecules

DNA is made up from only 4 nucleotides



- These simple building blocks are the same in all living organisms
- Nucleotides play also different roles in the living organism like in coenzymes (NAD) and energy molecules (ATP)

- According to the first law of Thermodynamics, principle of conservation of energy. This means that heat energy cannot be created or destroyed.
- Living organisms transform the energy they receive from their environment into another energy suitable for them, which is called free energy - giving the amount of energy that is equal to the environment.

Living organisms

By converting energy into chemical bond energy , they use it,

- for the synthesis of the biomolecules needed
- for intercellular and intracellular transport mechanisms
- for muscle contraction

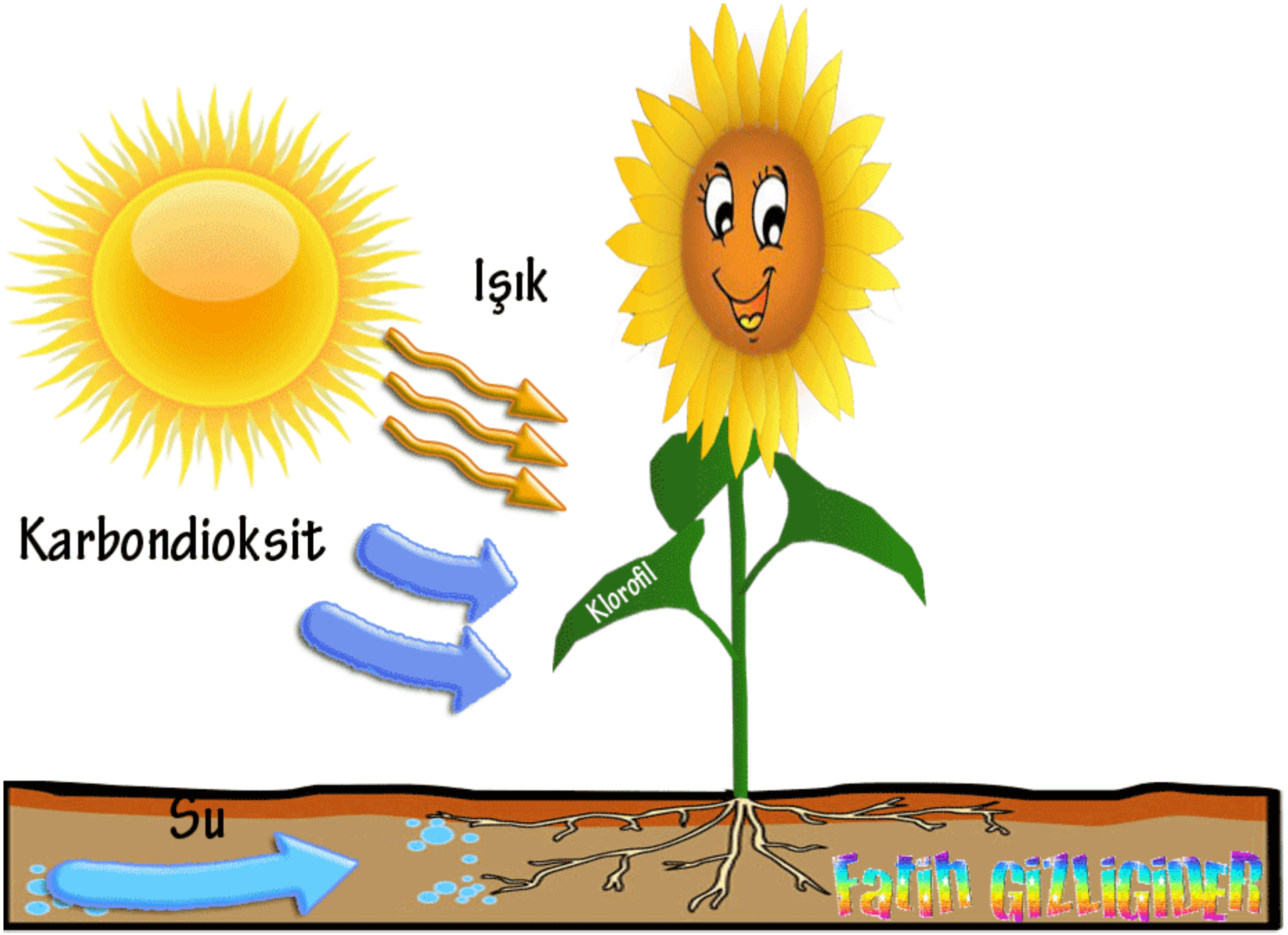
etc.

Homeostasis

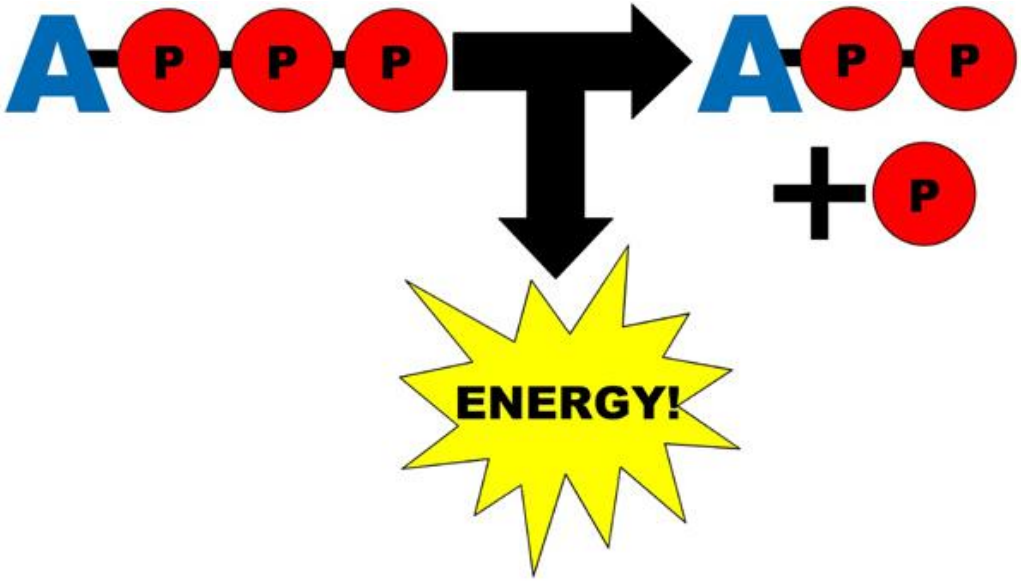
- homeo-:same; stasis: status, condition
- However, since the biomolecules forming the cells are rapidly deteriorating compounds, the cell must always remain at the same temperature and at the same osmotic pressure.
- **Enzymes** are biological catalysts that maintain homeostasis of the cells.

Living cells can be divided into two classes according to the energy they obtain from their environment:

- ***Photosynthetic cells***: They use sunlight as the main energy source. The sun's rays are absorbed by the chlorophyll pigment and converted into chemical bond energy. Cells in plants are included in this group.
- ***Heterotrophic cells***: They use the energy generated by the breakdown of high-energy organic molecules (biomolecules) to form the chemical bond energy. The cells in the animal world fall into this group.


Işık
Karbondioksit
Klorofil
Su
Fatih GİZLİGİDER

- Although they take energy from the environment in other forms, both cell types form the same high-energy compound that carries the chemical bond energy,
- This compound is **ATP**. ATP carries two high-energy bonds, each with a break of 7 kcal.



In summary

- ***The living cell is a combination of self-regulating, self-replicating, organic molecules at a given temperature.***
- ***These molecules use the energy they produce for the synthesis of the cell's own biomolecules, enzymes synthetised by the cell provides the fact that this synthesis in done at low temperature.***

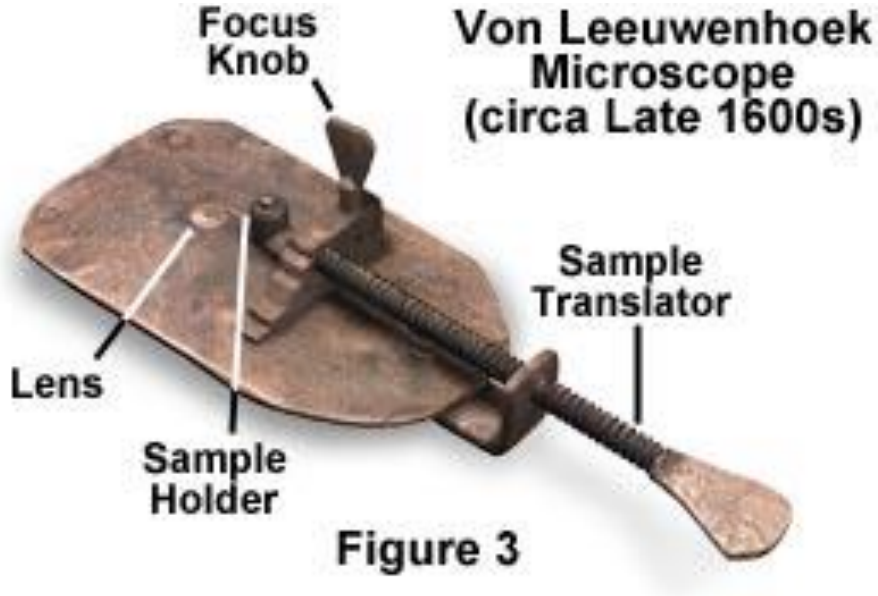
THE CELL

- The cell is the smallest structure where all the biological events necessary for life take place. All living organisms are made of cells. Every cell contains all the molecules necessary for life.

1674, Anton van Leeuwenhoeck

Created a simple microscope

21th century electron microscope



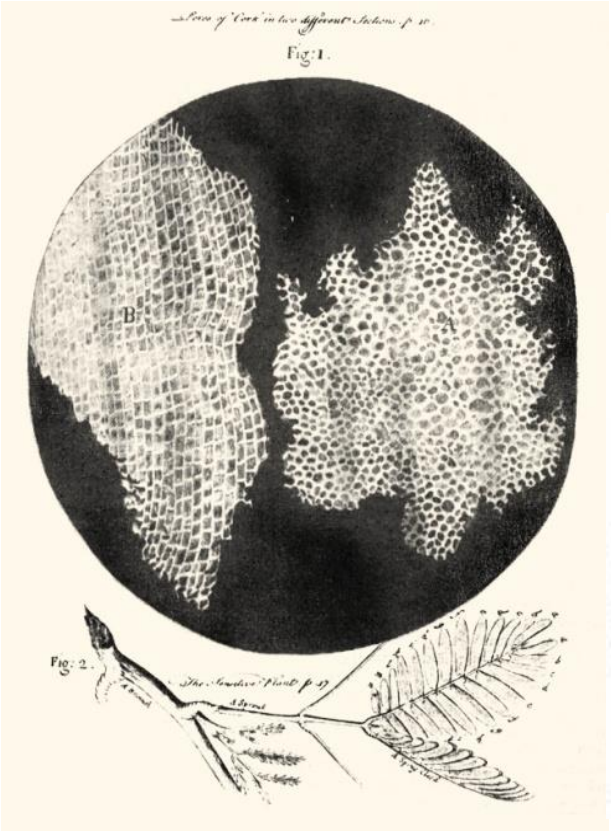
Light microscope's magnifying capacity 1500-2000, electron microscope's 10.000-100.000 times

First definition of the cell

- **1665, Robert Hooke,** an English physicist, observed a piece of cork through a magnifying lens and noticed many small pores, and called them "cells" from "**cella**" in Latin, meaning empty, cavity. Remind «cellar» and in Turkish «kiler»

Robert Hooke

(1635-1703)



Drawing of the cork tissue from the monograph Micrographia

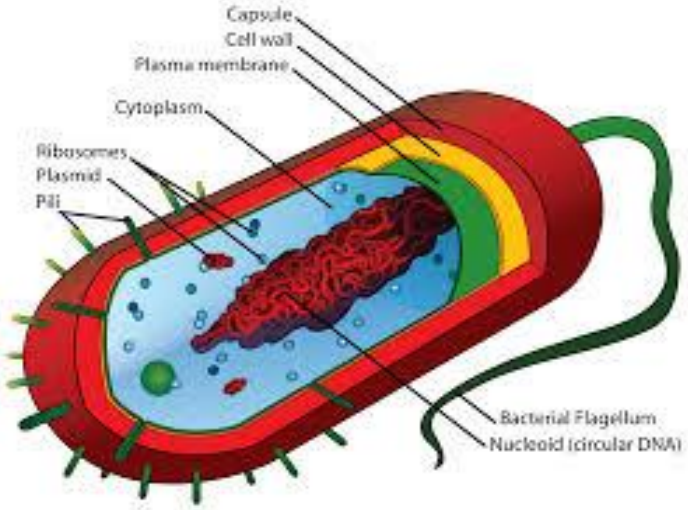
Robert Hooke's microscope

(https://upload.wikimedia.org/wikipedia/commons/f/fe/RobertHooke Micrographia1665.jpg),
(https://en.wikipedia.org/wiki/Robert_Hooke)

We can divide cells regarding their structural organization

- **Prokaryotic cells**. (In Greek, pro-: before and karyon: core, nucleus). Meaning that they existed before cells with nucleus
- **Eukaryotic cells**. (In Greek, eu-: true and karyon: core, nucleus)

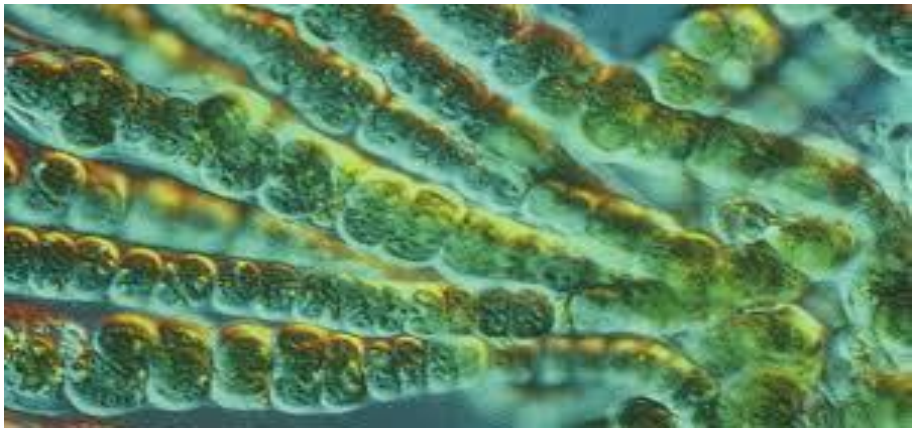
Prokaryotic cells



- Blue-green seaweeds (algae)
- Mycoplasms
- No nuclear membrane
- The genetic material DNA exists alone in the cytoplasm

Only three cell components:

- **Plasma membrane (plasmolemma)**
- **Ribosomes**
- **Nucleoid (DNA)**



Blue-green seaweeds

- Compact ribosomes smaller than eukaryotic cells.
- Different ribosomal proteins and RNA's.
- The nucleoid part holds the genetic material and is devoid of a membrane. This is the most important difference between eukaryotic and prokaryotic cells.

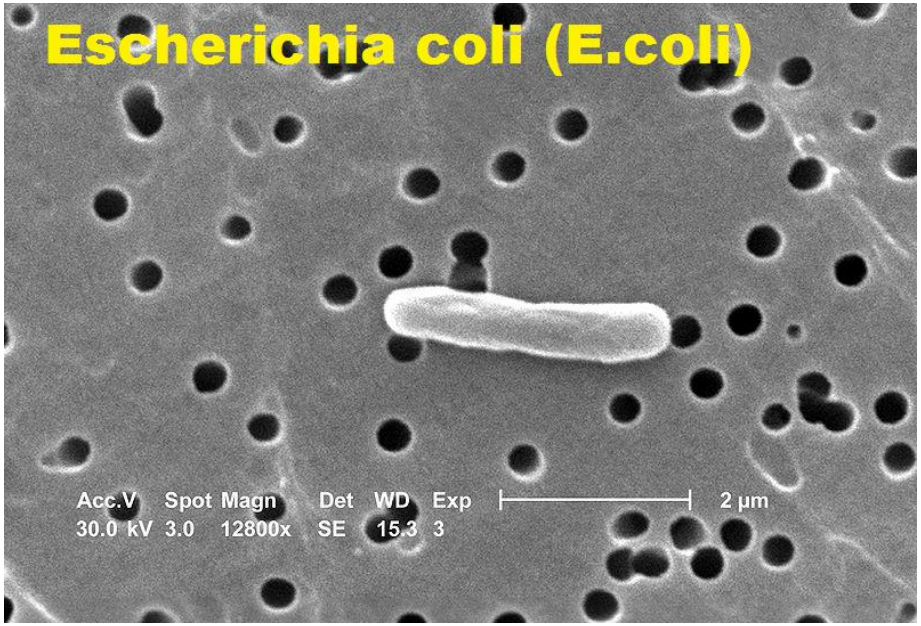
Prokaryotes could be divided in

- A-**Archebacteria** (anaerobic): They live in difficult environments such as swamps, ocean bottoms, salty waters and hot acid sources. They may even be present in thermal waters at temperatures up to 360°C.
- B-**Eubacteria**: It forms most of the bacteria. Aerobic green photosynthetic bacteria, purple photosynthetic bacteria, cyanobacteria formerly called blue-green algae, spirochetes, Gram positive and non-photosynthetic Gram-negative bacteria.

- Prokaryotes are the ancestors of life on earth.
- They were the first living organisms and lived for approximately 1 billion year alone and evoluted to new species.

Today prokaryotes are The sovereign of the earth!

Benefits of Prokaryotes



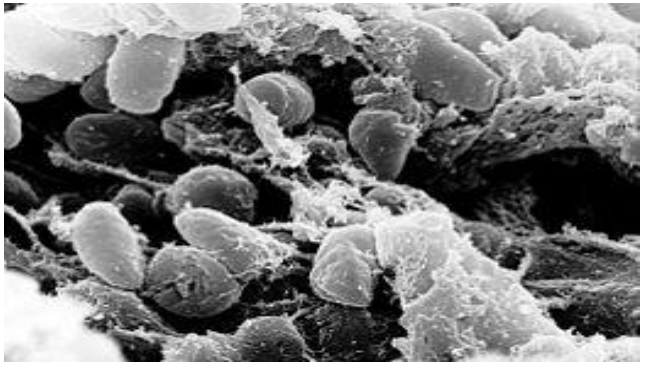
Bacteria living in intestines produce beneficial vitamins.

Damages of Prokaryotes

- In the 14th century (1347-1353) the **plague (the black death)** (*Pasteurella pestis* or *Yersinia pestis*) has wiped off 50% of European population. After pandemies in the 17th century columns were rised in memory in certain cities of Europe.

Vien

Budapest

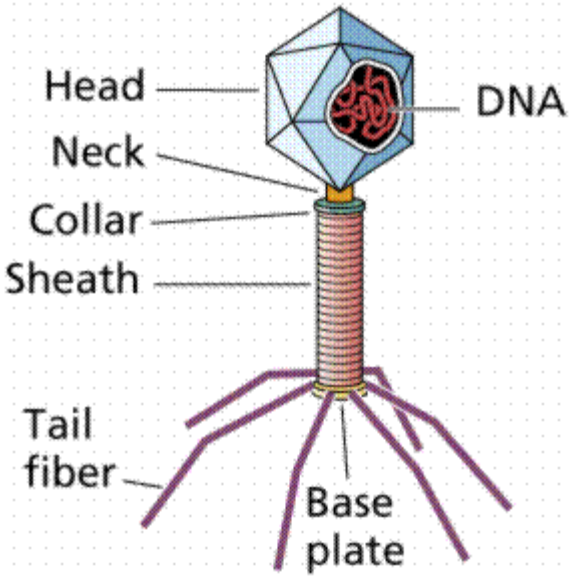


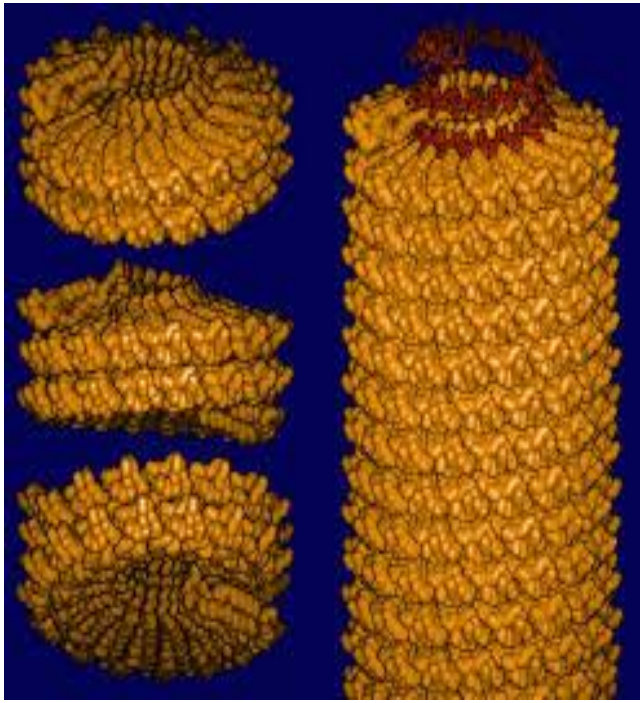
Yersinia pestis

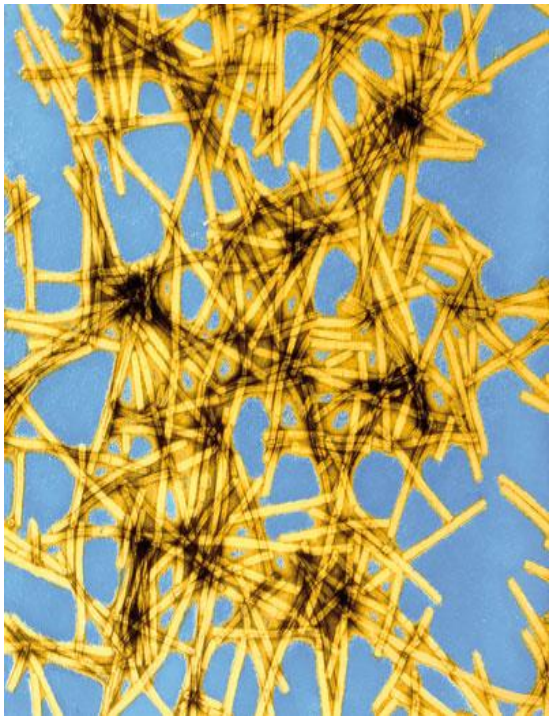
Viruses

- Viruses are the smallest living organisms known to date.
- A virus is 1000 times smaller than a common bacterium, 1000 000 times smaller than an eukaryotic cell.
- **Viruses have no cell structure, that is why they are not included in prokaryotes**.
- Viruses are not metobolically active out of host cells. Some viruses can be obtained in crystal form.
- Viruses are solely made out of RNA or DNA.

Viruses



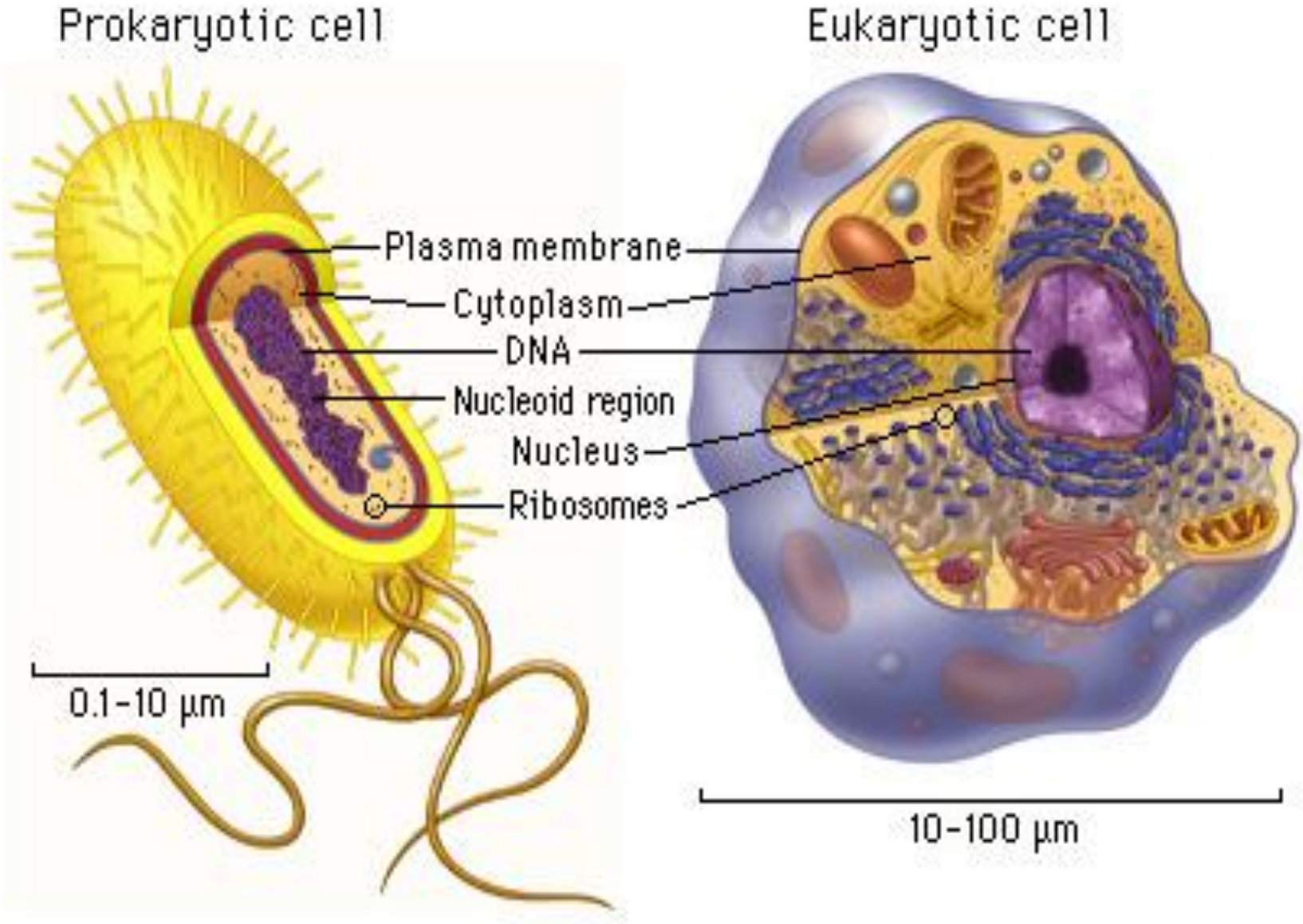




Tobacco mosaic virus (www.sb.fsu.edu) and its crystals (www.nature.com)

Eukaryotic cells

- Advanced structural organization
- **Eukaryotic cells have a nucleus and a nucleus membrane.**
- Cell membrane is semi-permeable.
- Cytoplasmic organelles such as mitochondria, ribosomes, Golgi apparatus, centrioles, lysozomes, peroxisomes, and in plant cells, plastides and vacuoles are present.



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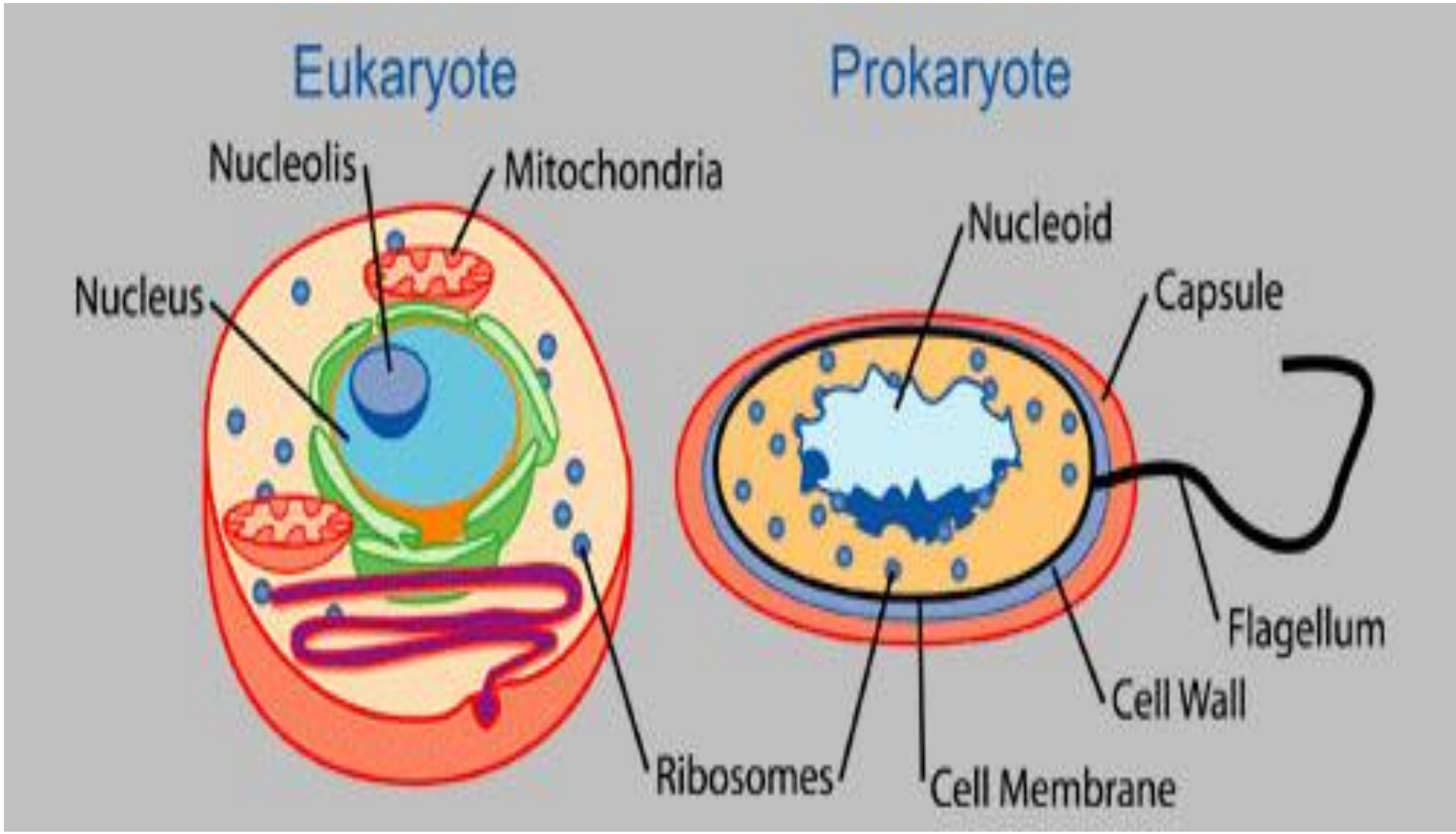
Differences Between Prokaryotes and Eukaryotes

	Prokaryote	Eukaryote
Genome	No nuclear membrane	Nuclear membrane
Membraned organel	No	E.R., Golgi, Mitochondria
Energy metabolism	Oxidative phosphorylation in the plasma membrane	Oxidative phosphorylation in the mitochondria
Cytoskeleton	No	Complex microtubules, intermediate filaments, actin filaments
Intercell mobility	No	Endocytosis, exocytosis, mitosis, vesicular transport
Cell division	Budding, division are observed but no mitosis	Mitosis and meiosis



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LEVELS OF BIOLOGICAL ORGANIZATION

- Atoms
- Molecules
- Cell organelles
- Cells
- Tissues*
- Organs*
- Organ systems*
- Organism (one cell or multicell complexes)

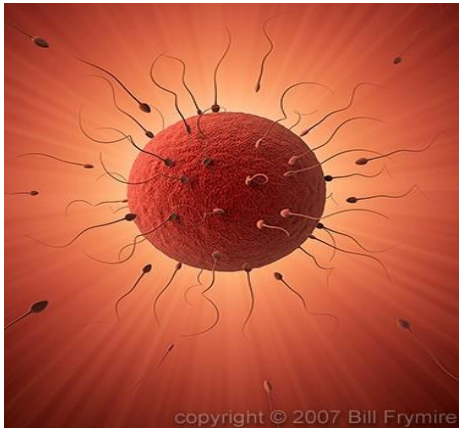
*This organization level does not exist in all organisms.

THE CELL

- It is the basic unit of life.
- It is the most basic structure that can realize all the activities of life.
- All organisms are composed of cells.

DIMENSIONS OF THE CELL

Smallest brain cells
4-5 mikrons



Human ovum 200
mikrons

Fish eggs 5 mm

Hen egg 30 mm

- The shape of the cells is very diverse according to their function, for example the sperm cell is small, oval and has a whip, while the inactive ovum is larger and round.
- Cells are usually colorless, pigment-bearing cells (e.g. erythrocytes) are colored.
- Under normal conditions, the size of cells in a human does not vary according to the size of the human, but the number of cells may vary. The number of cells in organ systems of adult individuals is within certain limits.
- The aging cell dies programmatically (apoptosis) and is replaced by new cells. Uncontrolled cell division may develop as a result of an irreparable change (mutation) in genes and leads to tumor formation (cancer)

Textbooks

- Tıbbi Biyoloji (Gözden Geçirilmiş 2. Baskı), Çarin, M.N., Aydın, F., Gürtekin, M., Nobel Tıp Kitabevleri (2013).
- Tıbbi Biyoloji Ders Kitabı, Ulutin T., Onaran, İ., Güven, M., İstanbul Üniv. Yayın No. 5206 İstanbul (2014)
- https://www.youtube.com/watch?v=URUJD5NEXC8
- https://www.youtube.com/watch?v=VgxIvBiUgiQ