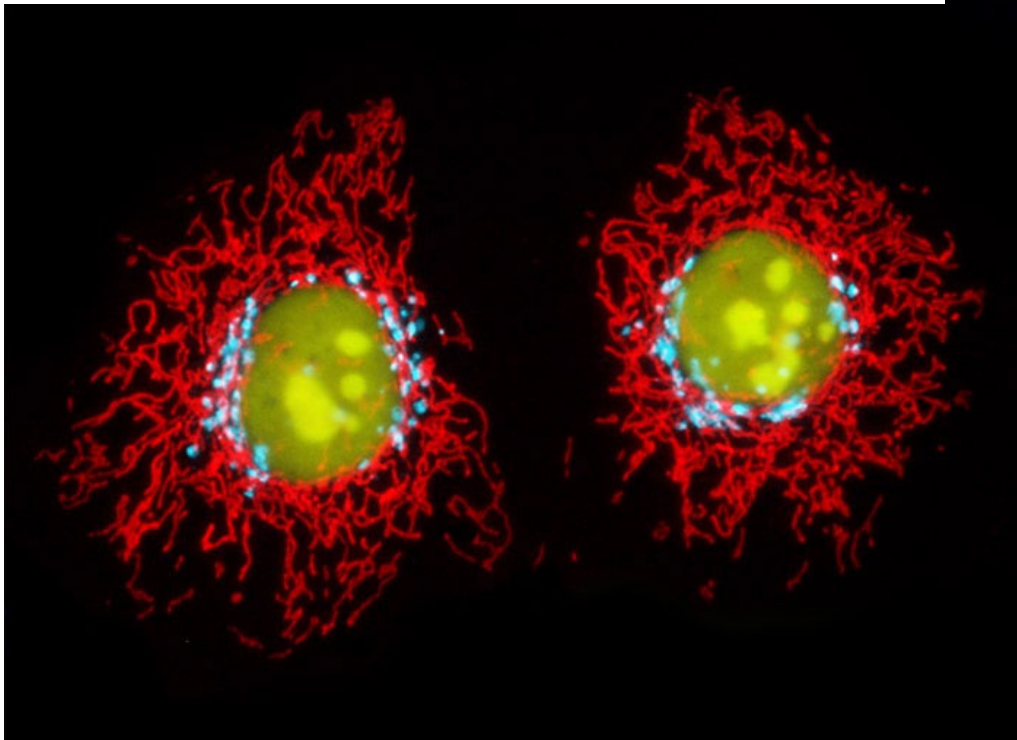
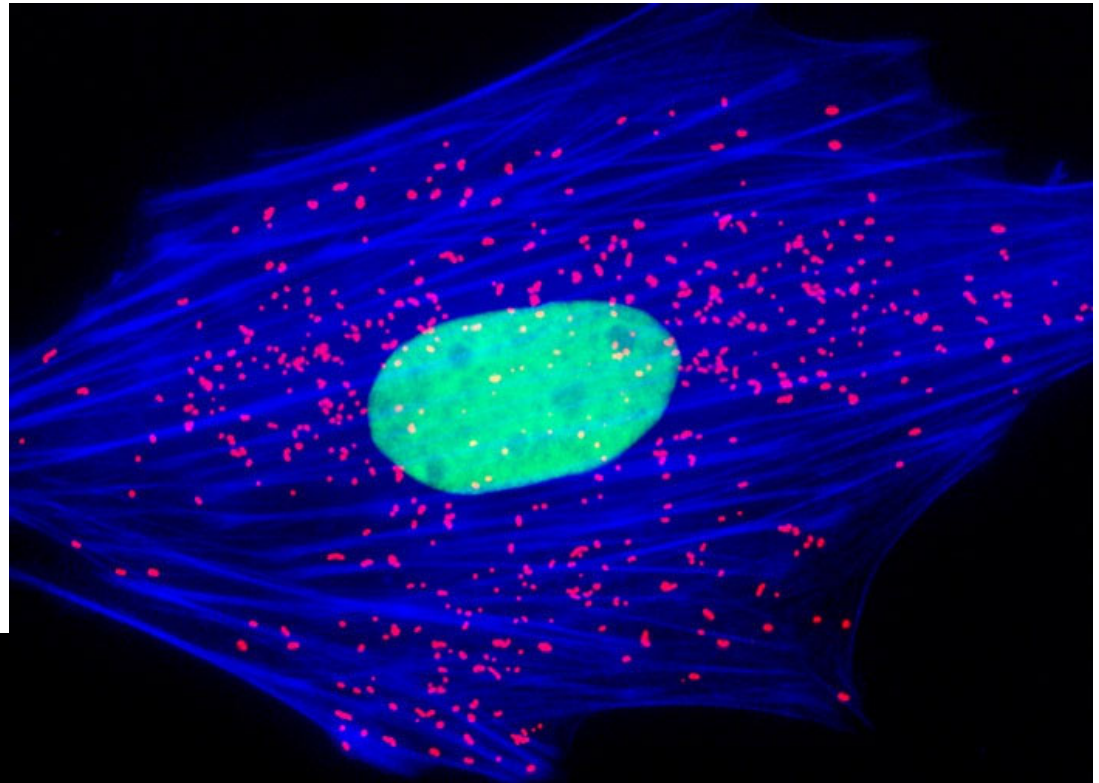
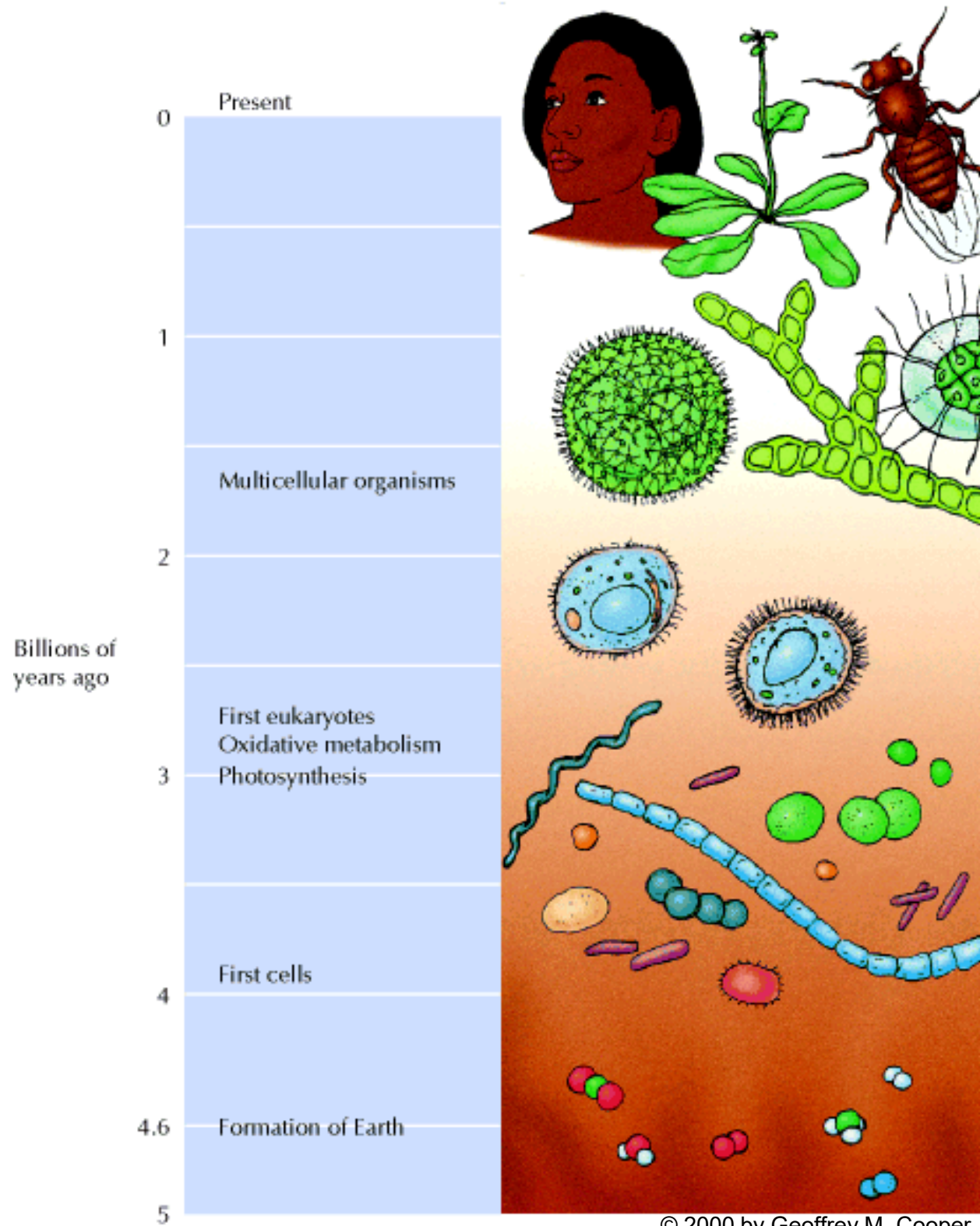


Introduction to Cells



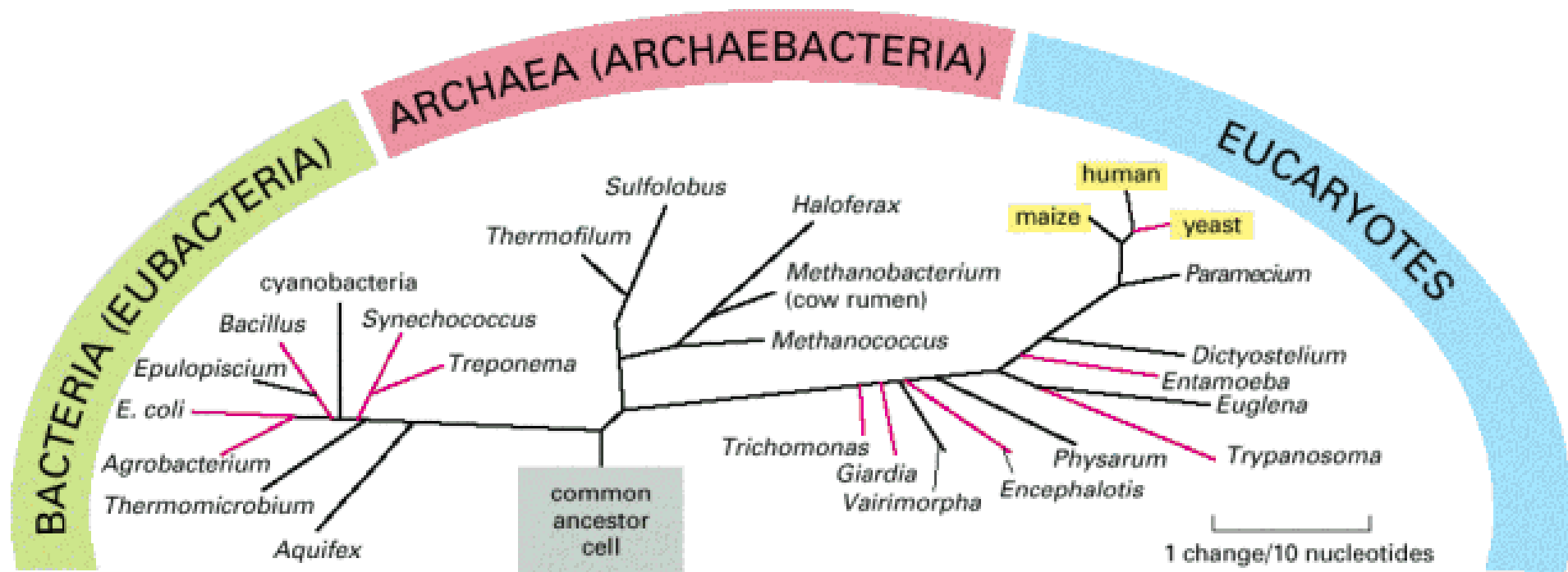
Z. Lygerou, University of Patras
School of Medicine



All living organisms descend from a first cell that appeared on Earth about 4 billion years ago

All living organisms share a common ancestor

The tree of life...



The three domains of life: Eukaryotes, Bacteria and Archaea

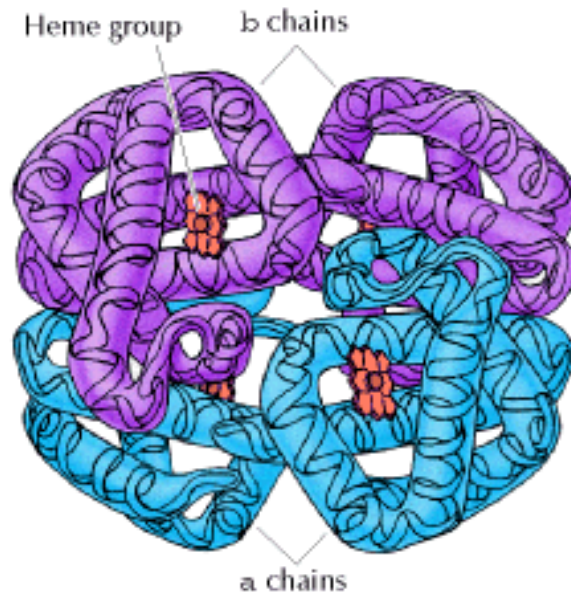
All cells are made from the same building blocks

What are the main biomolecules?

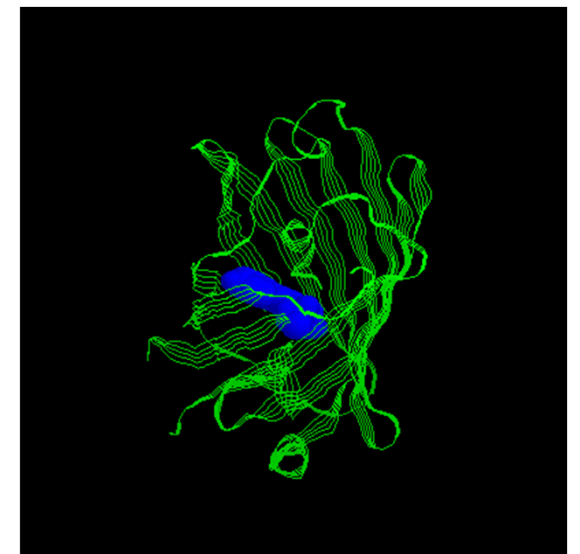
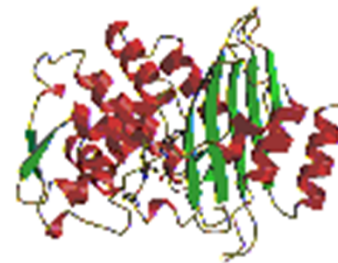
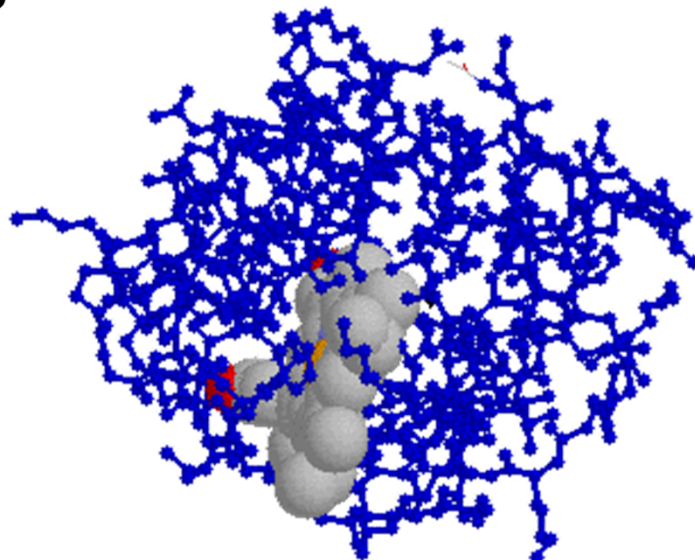
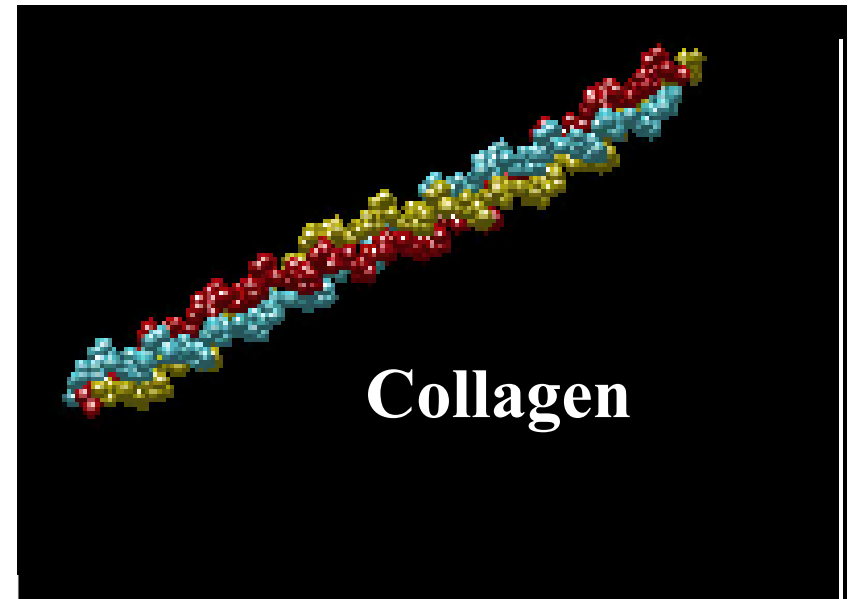
DNA, RNA, proteins, polysaccharides, lipids

Which biomolecule is the principal structural and functional component of cells?

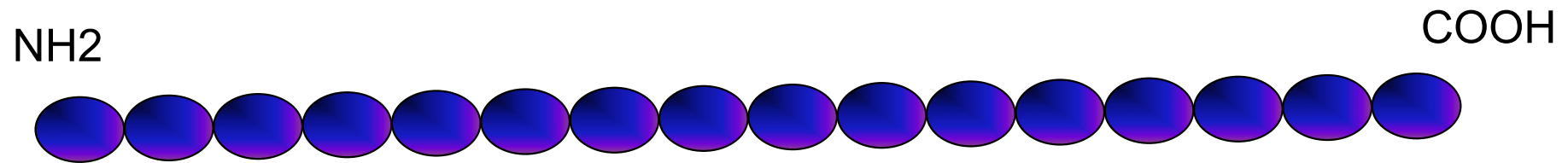
Proteins



Hemoglobin

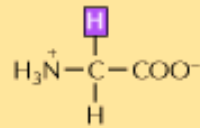


Proteins are chains of amino acids

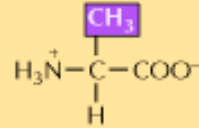


Proteins contain 20 different amino acids

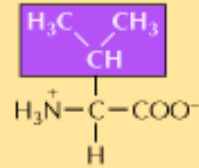
Nonpolar amino acids



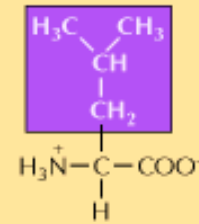
Glycine (Gly) G



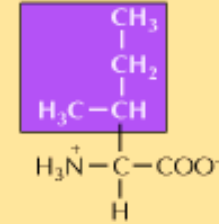
Alanine (Ala) A



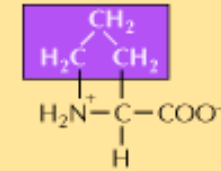
Valine (Val) V



Leucine (Leu) L



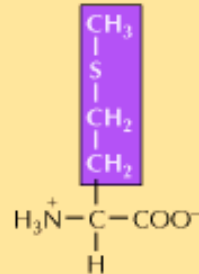
Isoleucine (Ile) I



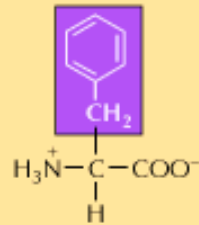
Proline (Pro) P



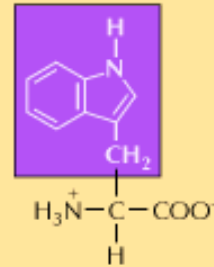
Cysteine (Cys) C



Methionine (Met) M

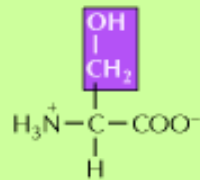


Phenylalanine (Phe) F

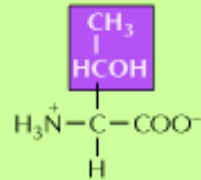


Tryptophan (Trp) W

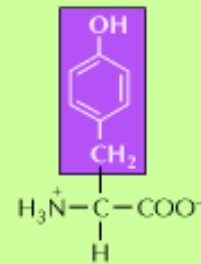
Polar amino acids



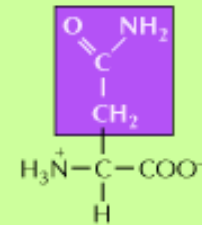
Serine (Ser) S



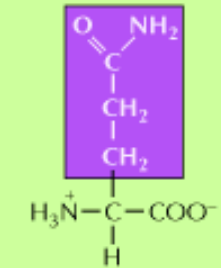
Threonine (Thr) T



Tyrosine (Tyr) Y

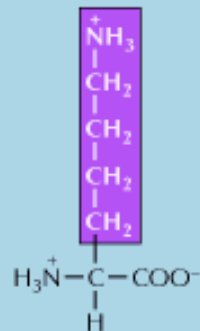


Asparagine (Asn) N

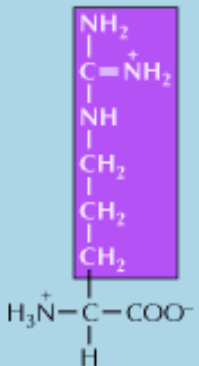


Glutamine (Gln) Q

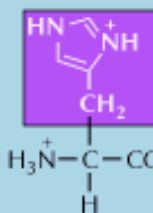
Basic amino acids



Lysine (Lys) K

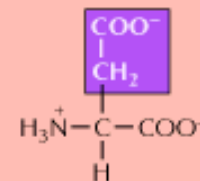


Arginine (Arg) R

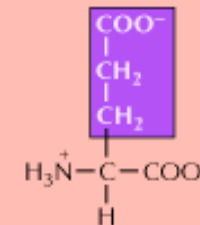


Histidine (His) H

Acidic amino acids

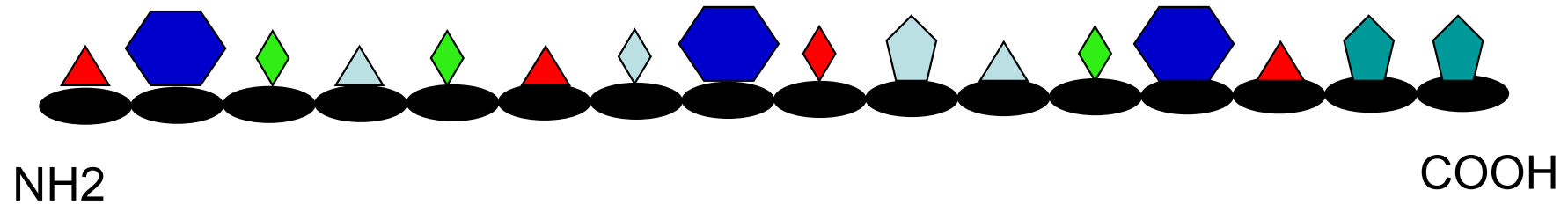


Aspartic acid (Asp) D

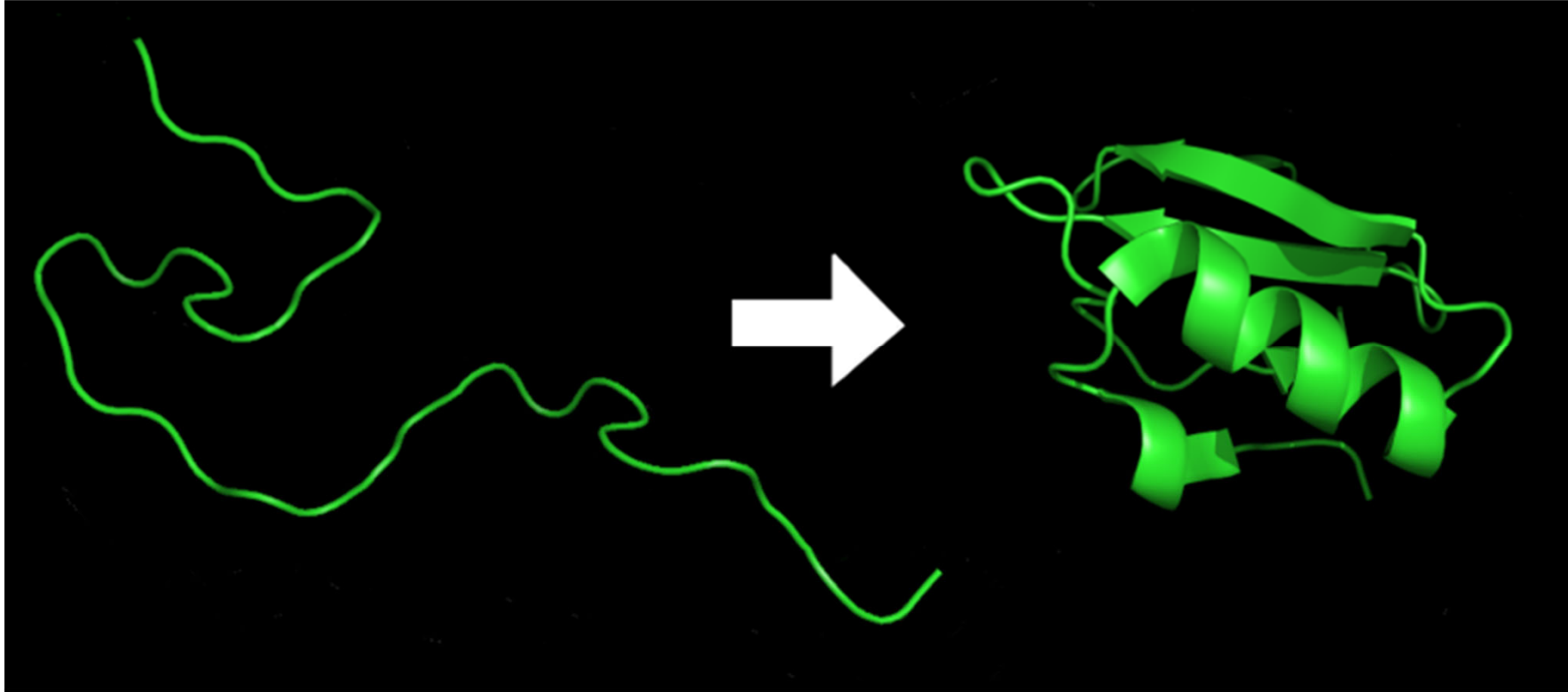


Glutamic acid (Glu) E

The properties of amino acid side chains determine protein structure and function



Proteins fold into stable three-dimensional conformations that enable specific functions



The amino acid sequence contains all the information for protein structure and function

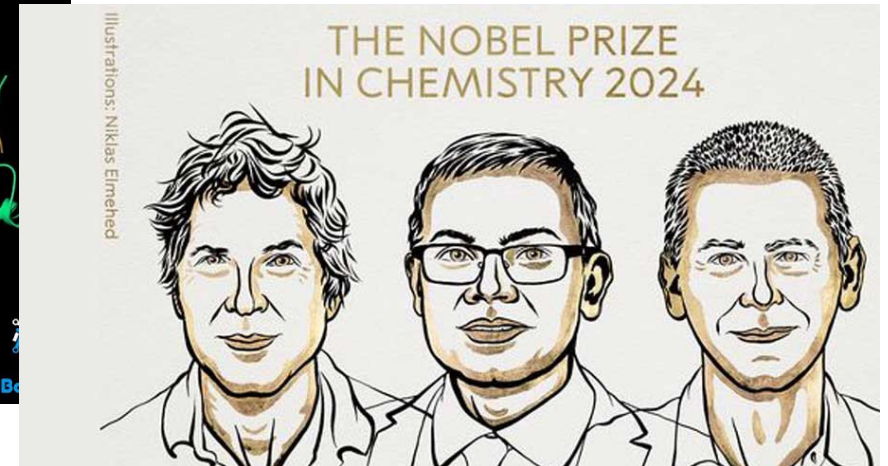
2020: prediction of 3D protein structure from amino acid sequence

Another achievement of artificial intelligence

DeepMind AlphaFold (look it up!)

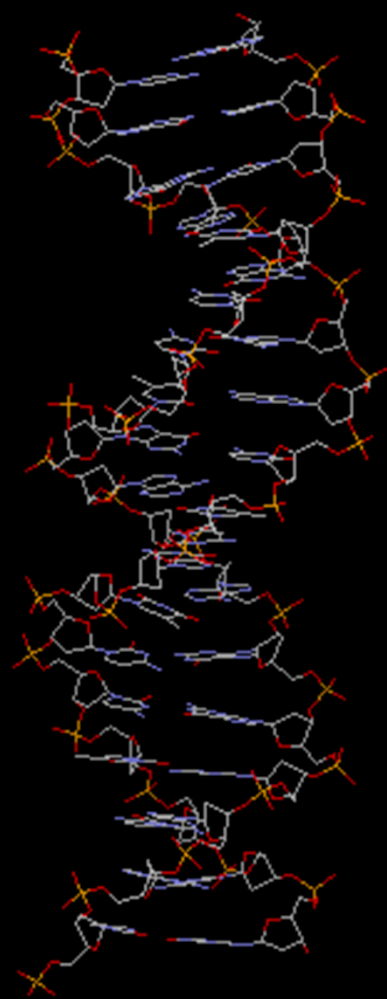
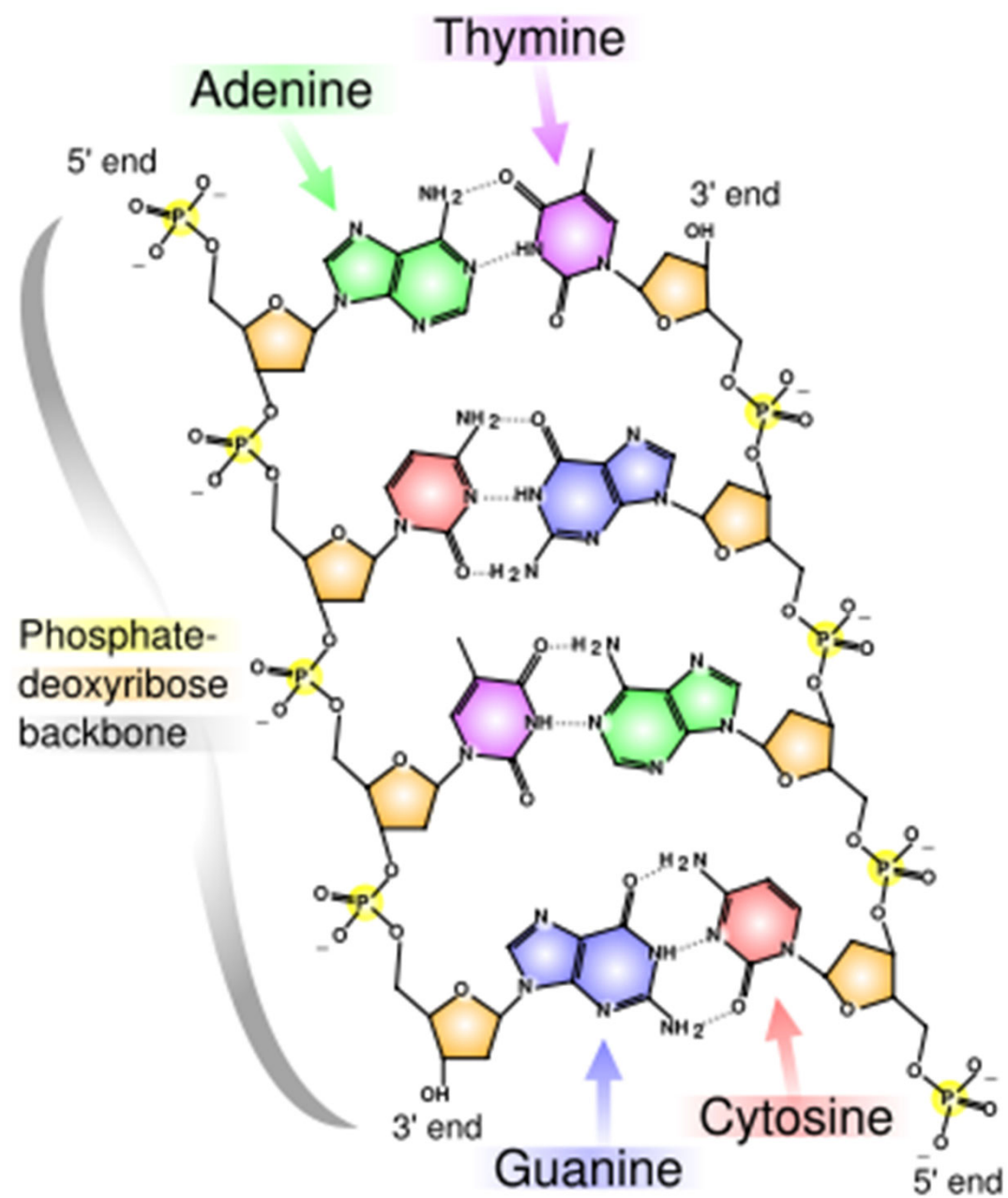


Demis Hassabis

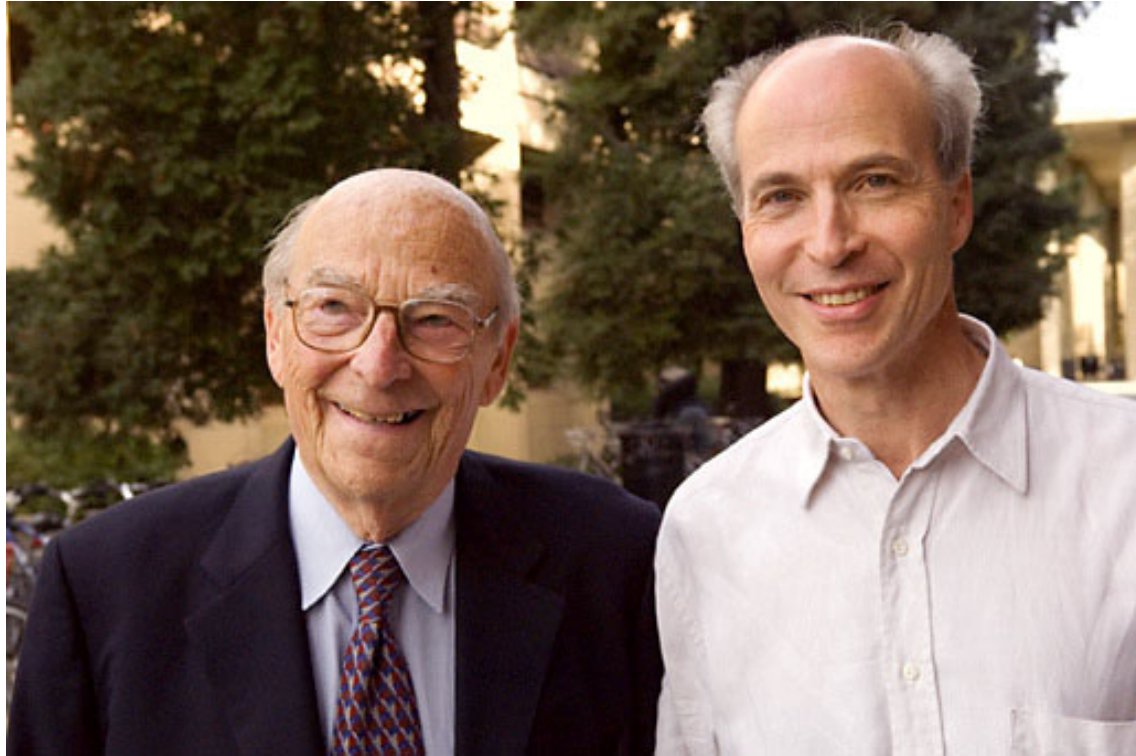


In July 2022, structures of 200 million proteins were announced
Almost all known proteins

How is the amino acid sequence of proteins determined?



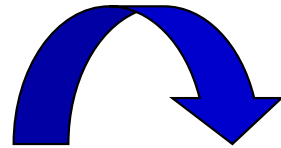
The central dogma: a family affair...



Arthur Kornberg
Nobel Prize 1959
Replication

Roger Kornberg
Nobel Prize 2006
Transcription

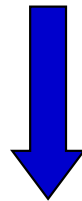
The central dogma of biology



Replication



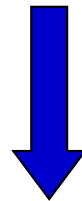
DNA



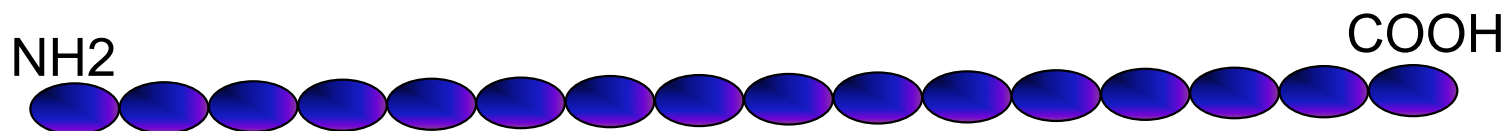
Transcription



RNA



Translation

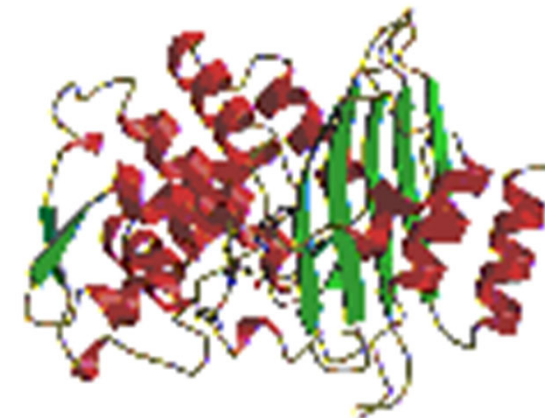
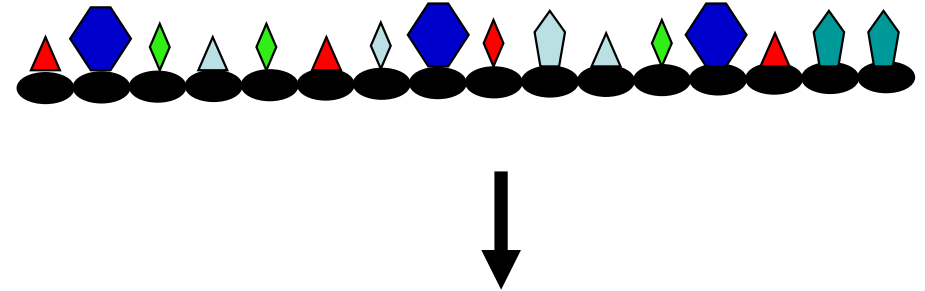


Protein

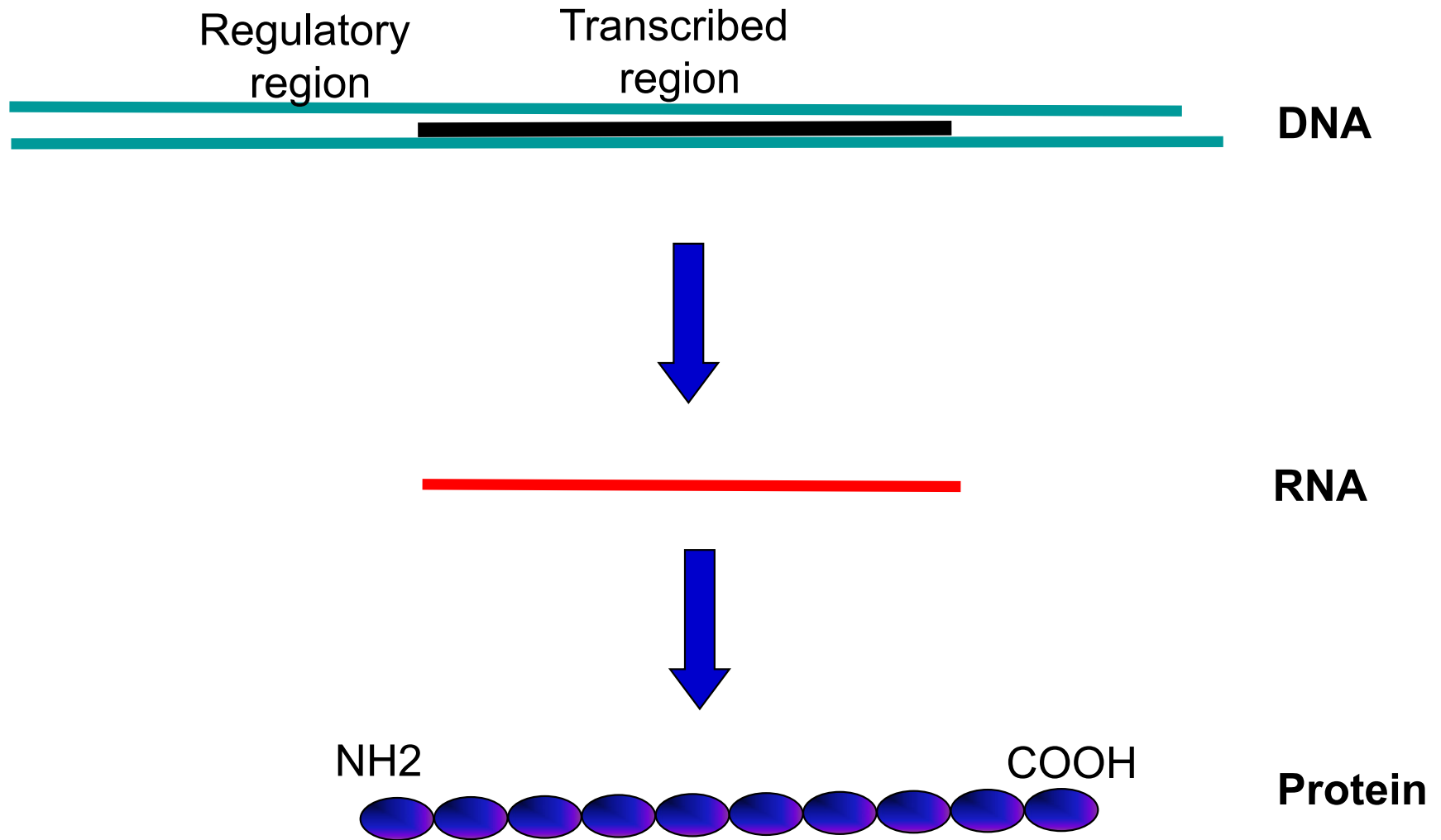
The DNA sequence dictates the sequence of amino-acids in each protein



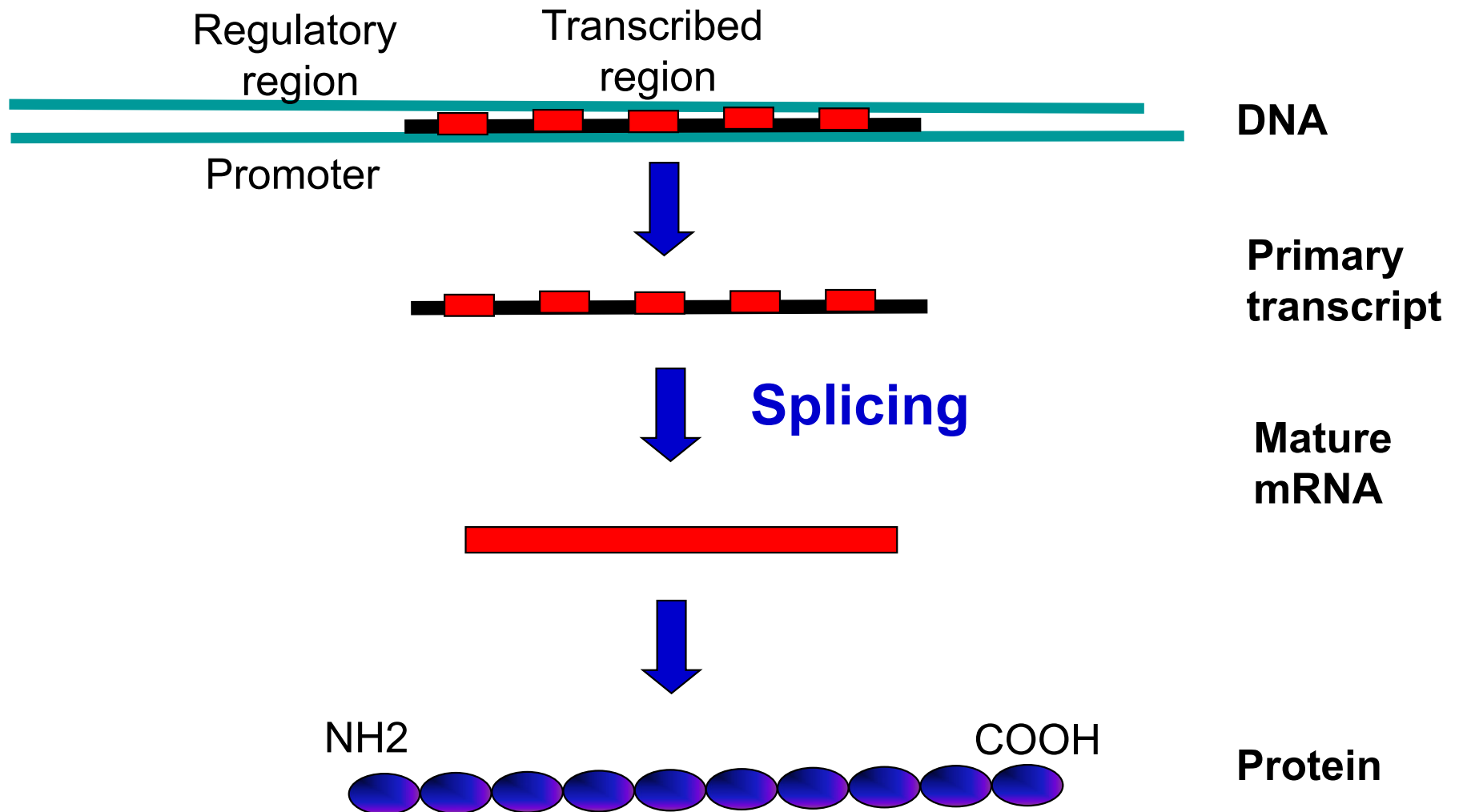
5'GATGTTTCATCGTA.....GTAGCTAACATATCA3'



Genes are the functional units of the genetic material: a part of the genome which codes for a product with a specific function



In eukaryotes, the genetic information is split...
Genes contain parts coding for function (exons) interrupted by non-coding parts (introns)

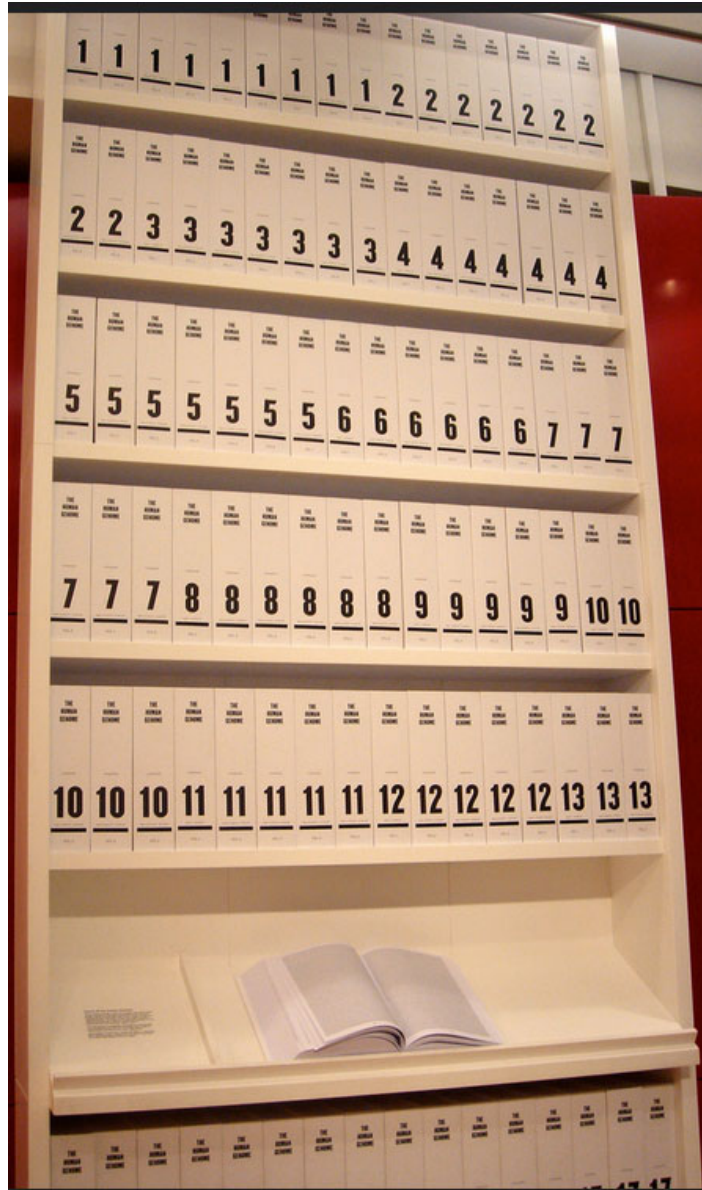


Genome:

all the genes in our DNA

all of the genetic material in the nucleus of each one of our cells

all of the 6×10^9 bp of DNA sequence



The human genome has
around 20.000 genes

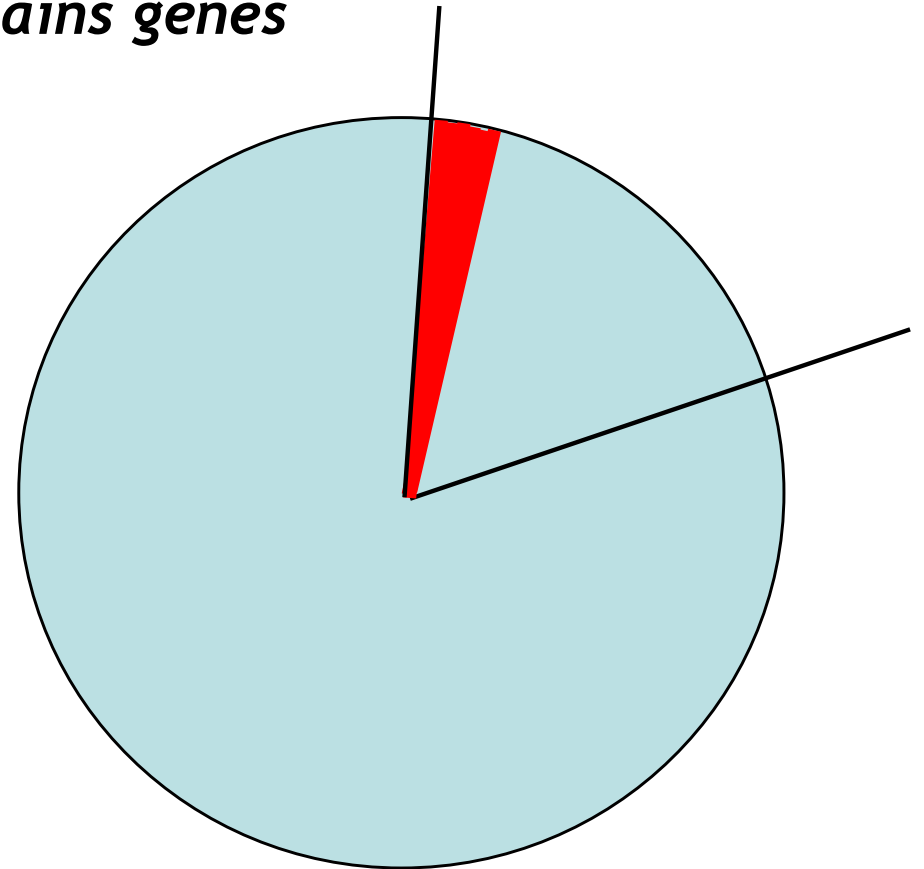
*In addition to genes, there is a lot more in a genome...
especially in the human genome...*

*Less than **30%** of our genome contains genes
(introns and exons)*

*Less than **2%** of our genome
codes for protein*

***50%** of our genome is repetitive
DNA*

***30%** of our genome are
transposable elements*



All living organisms are made of cells

Cells are the structural and functional units of all living organisms

Some organisms are unicellular (e.g. bacteria), whereas others **are multicellular (e.g. humans, with 10^{14} cells)**

All cells arise from pre-existing cells

The essential functions of organisms take place within their cells

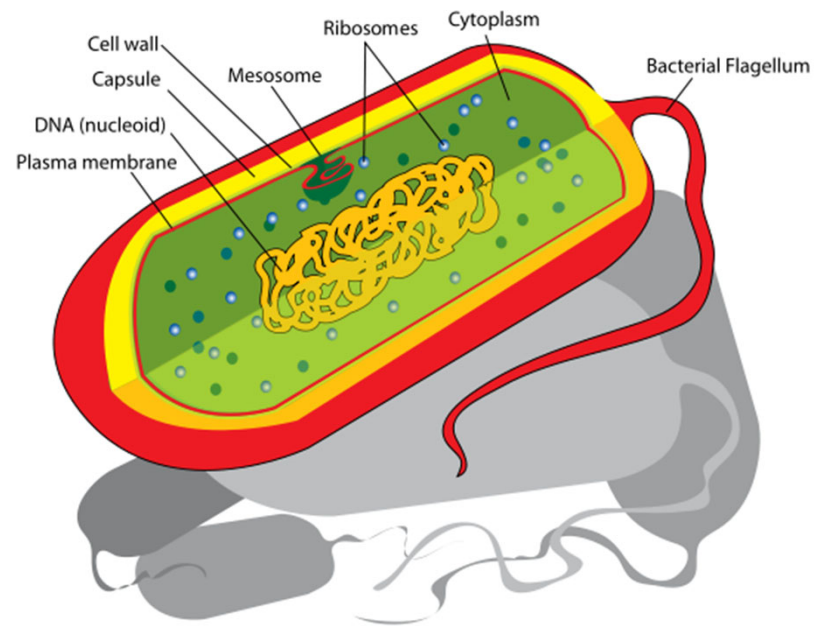
All cells contain the genetic information needed to regulate cell function and pass this information to the next generation

All cells have ribosomes to translate genetic information

Viruses? Prions?

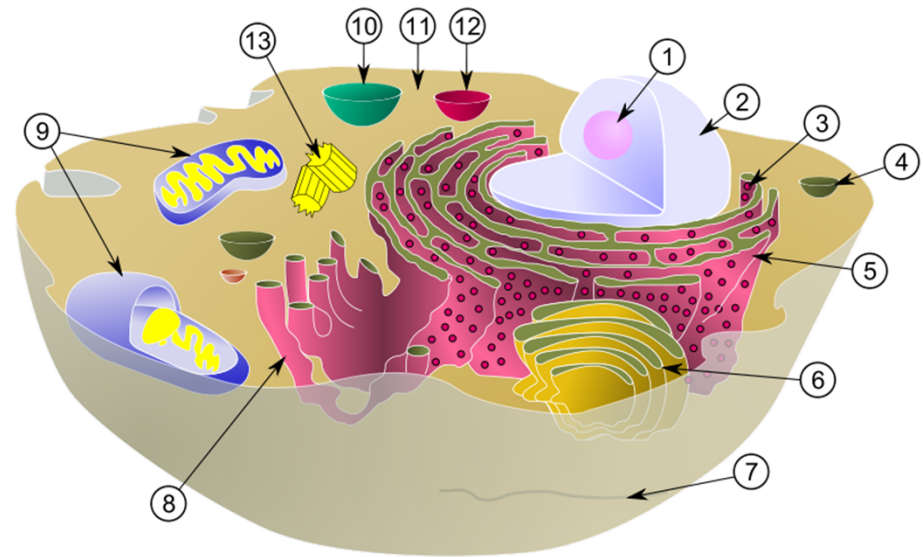
All living organisms are made of cells

Prokaryotic cell



1–10 μm

Eukaryotic cell



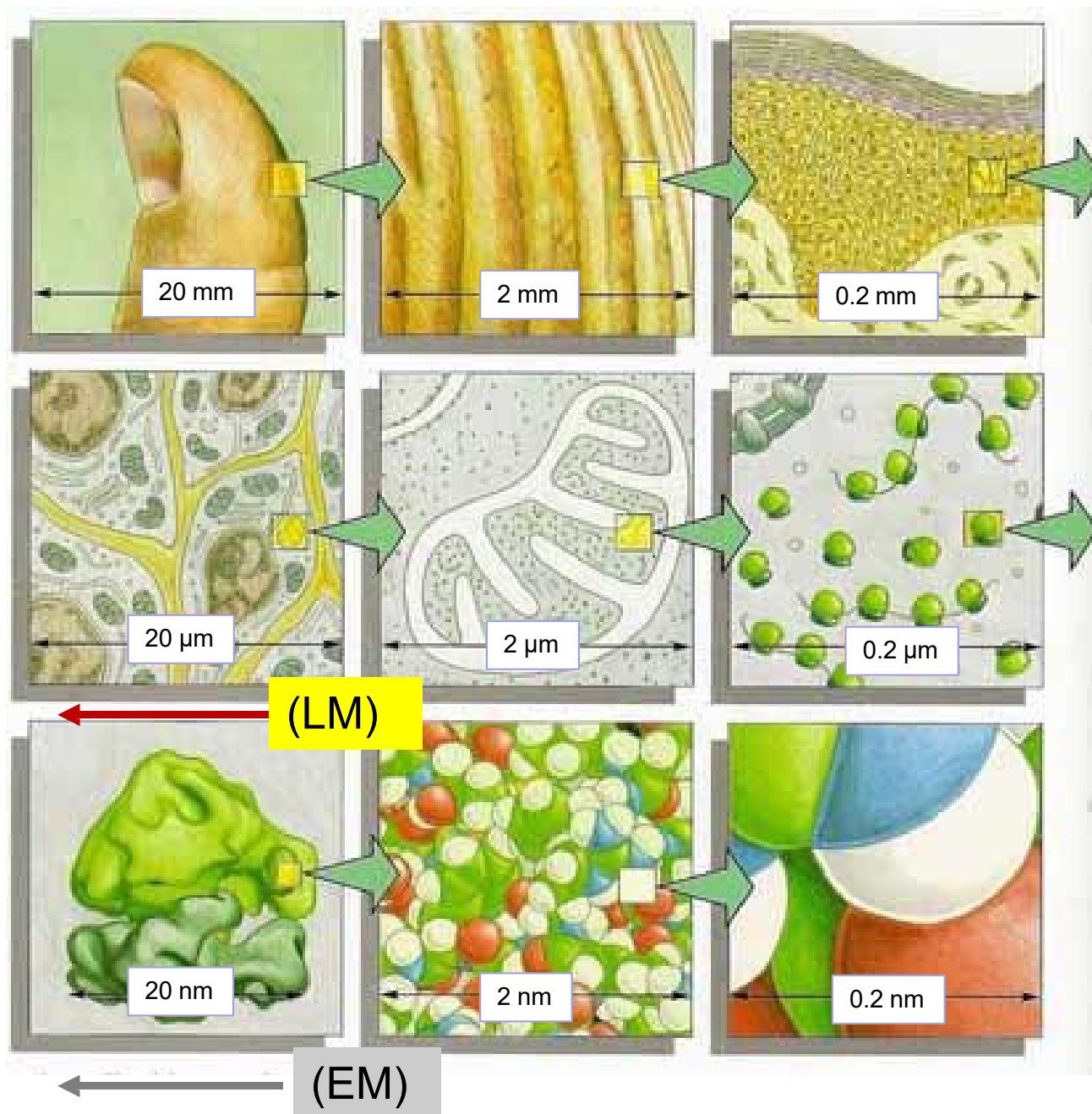
10–100 μm

Levels of biological organization

Molecules → Organelles → Cells → Tissues → Organs and organ systems → Organisms (individuals) → Populations → Communities → Ecosystems → Biosphere

Each higher level of biological organization has new properties (emerging properties)

At every level of biological organization,
structure is closely related to function



Nine orders of magnitude (10^9 -fold) separate our bodies from atoms
 We need specialized instruments to observe life at the cellular scale

How do we study cells?

Microscopic observation

Study of cell components in extracts (e.g. subcellular fractionation)



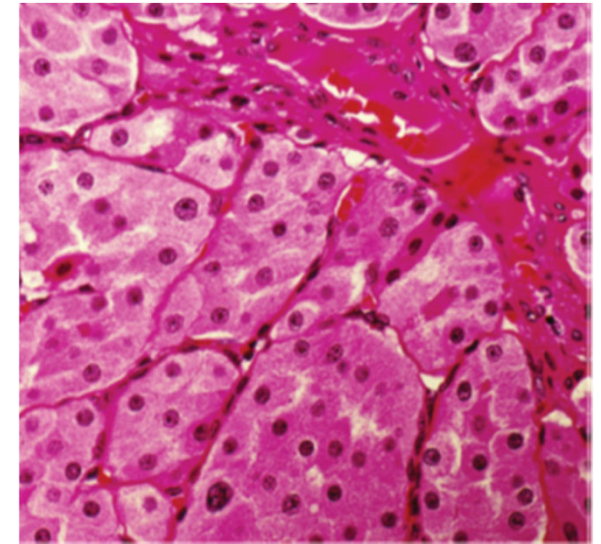
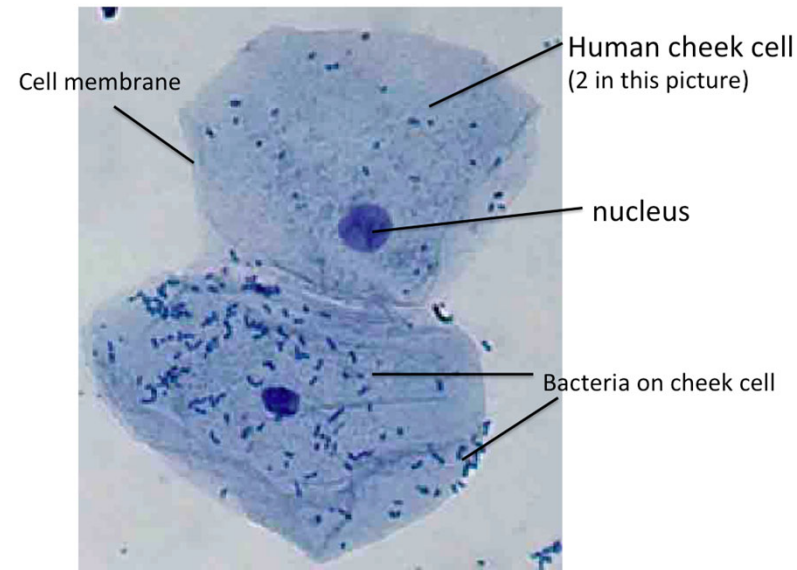
Light (Optical) microscope

Uses visible light (photons)

Bright-field

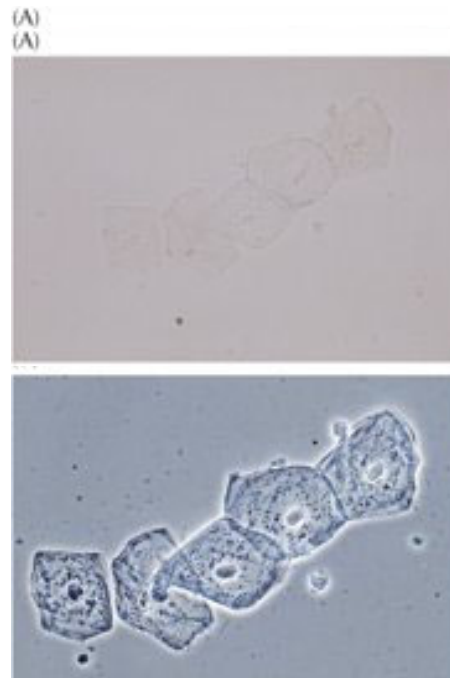
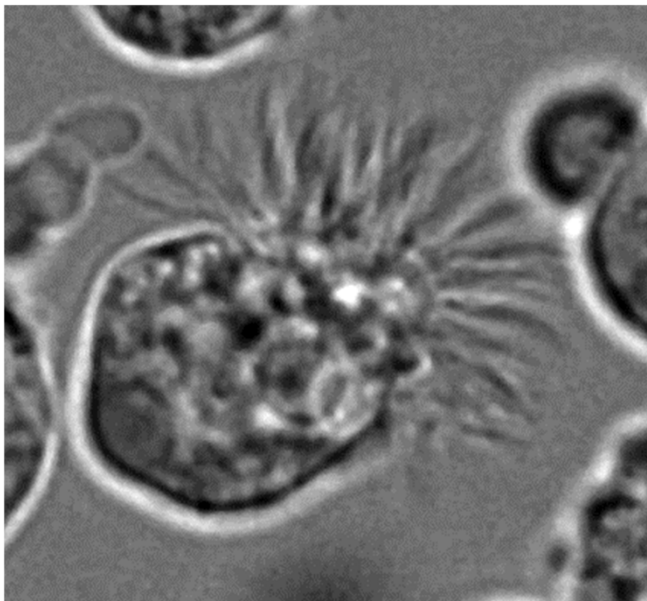
(stained specimen)

*Fixation and staining
laboratory*



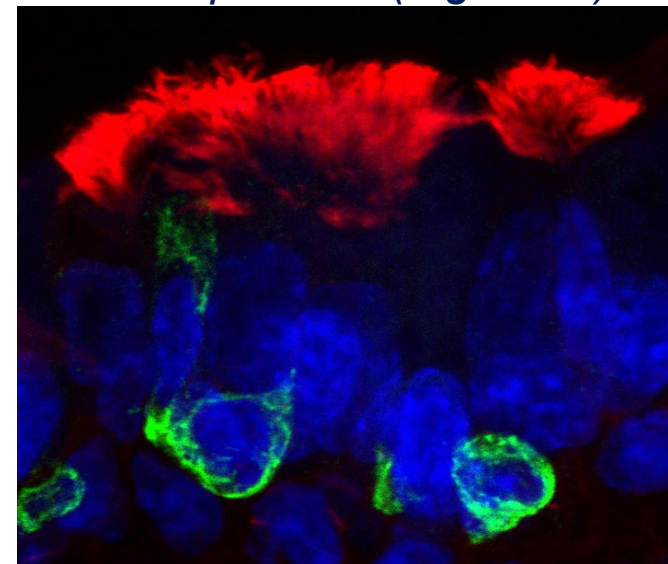
Phase-contrast

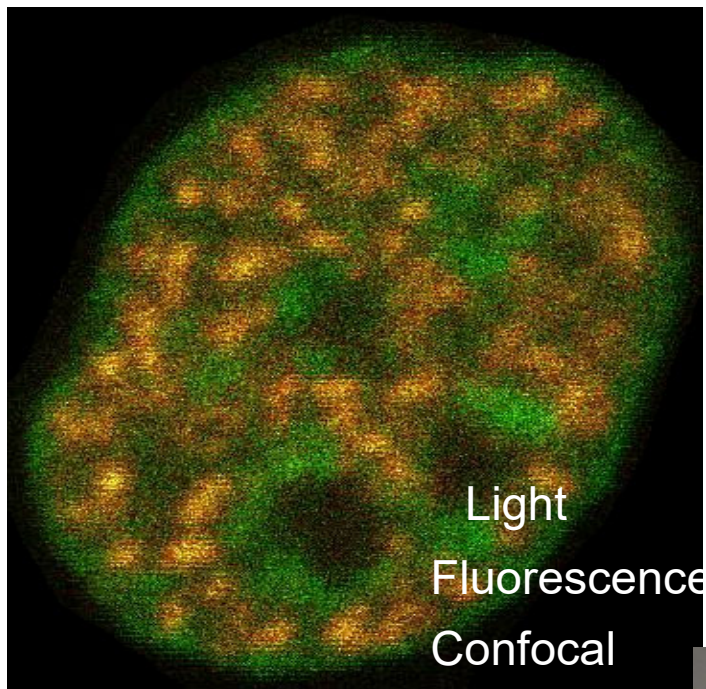
(living cells, time-lapse)



Fluorescence

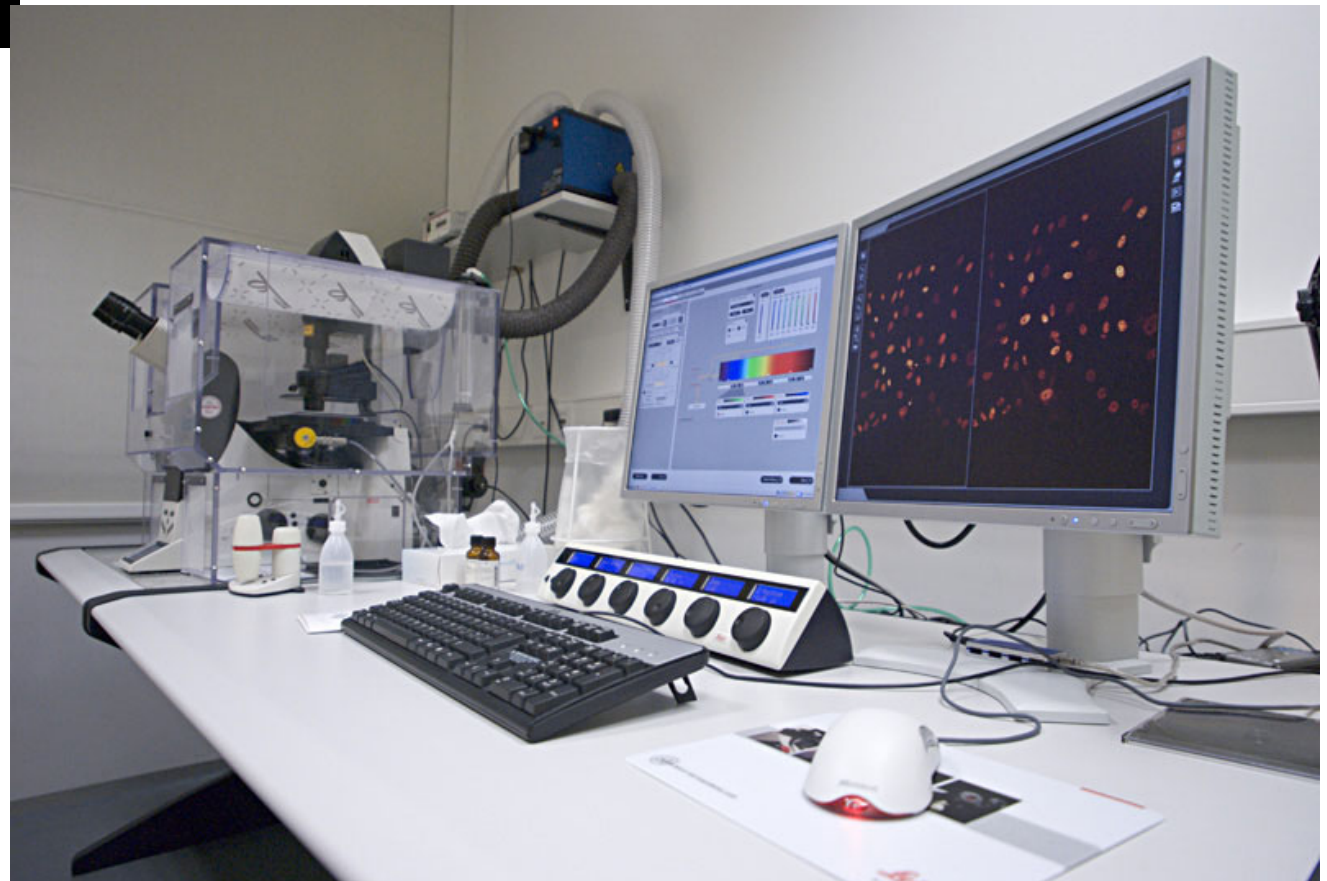
*fluorescent antibodies (immunofluorescence)
or fluorescent proteins (e.g. GFP)*

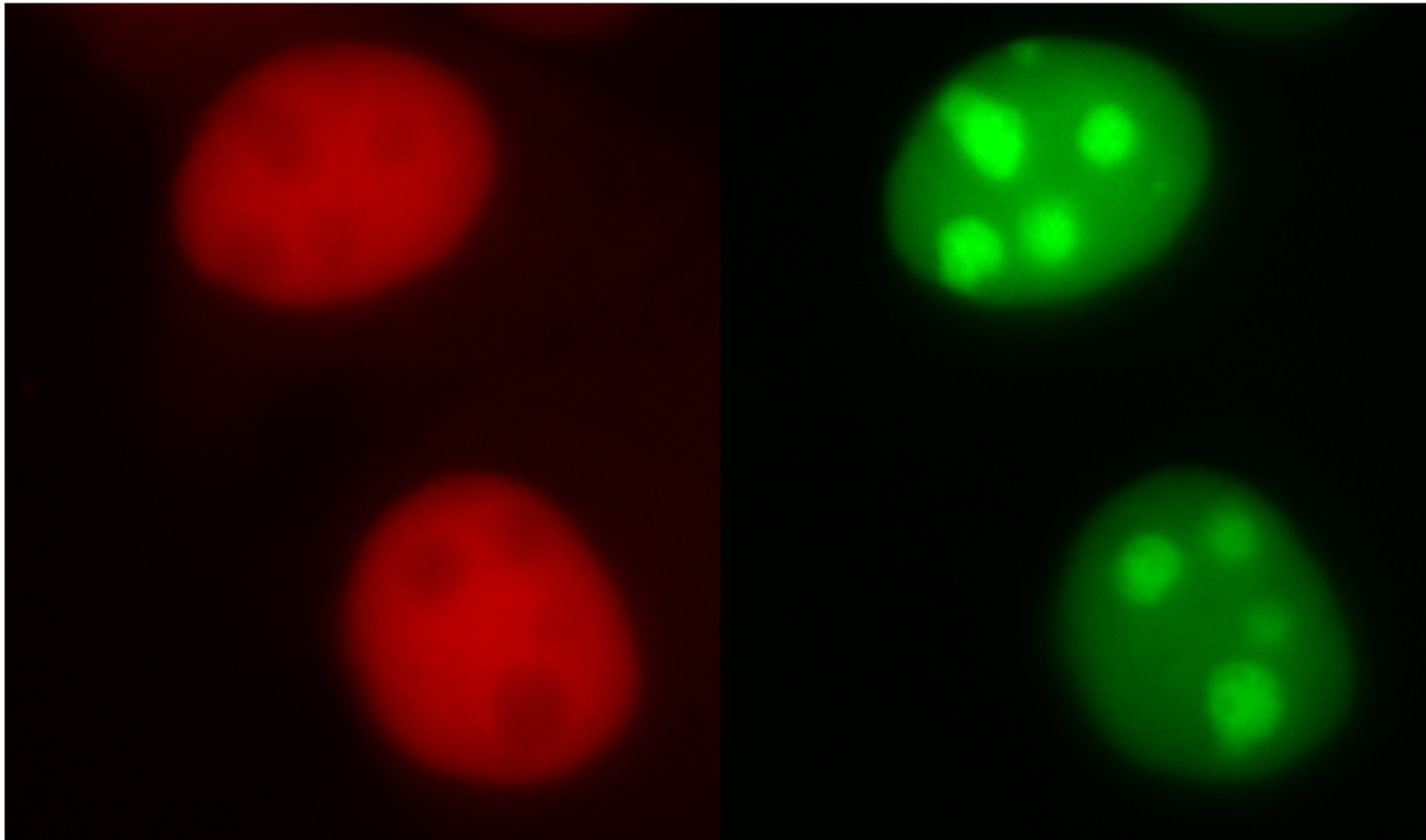




Fluorescence microscopy: a type of light (optical) microscopy

specific subcellular components (e.g. DNA or specific proteins) are labelled with fluorescent molecules (e.g. fluorescent antibodies) and located using a fluorescence microscope





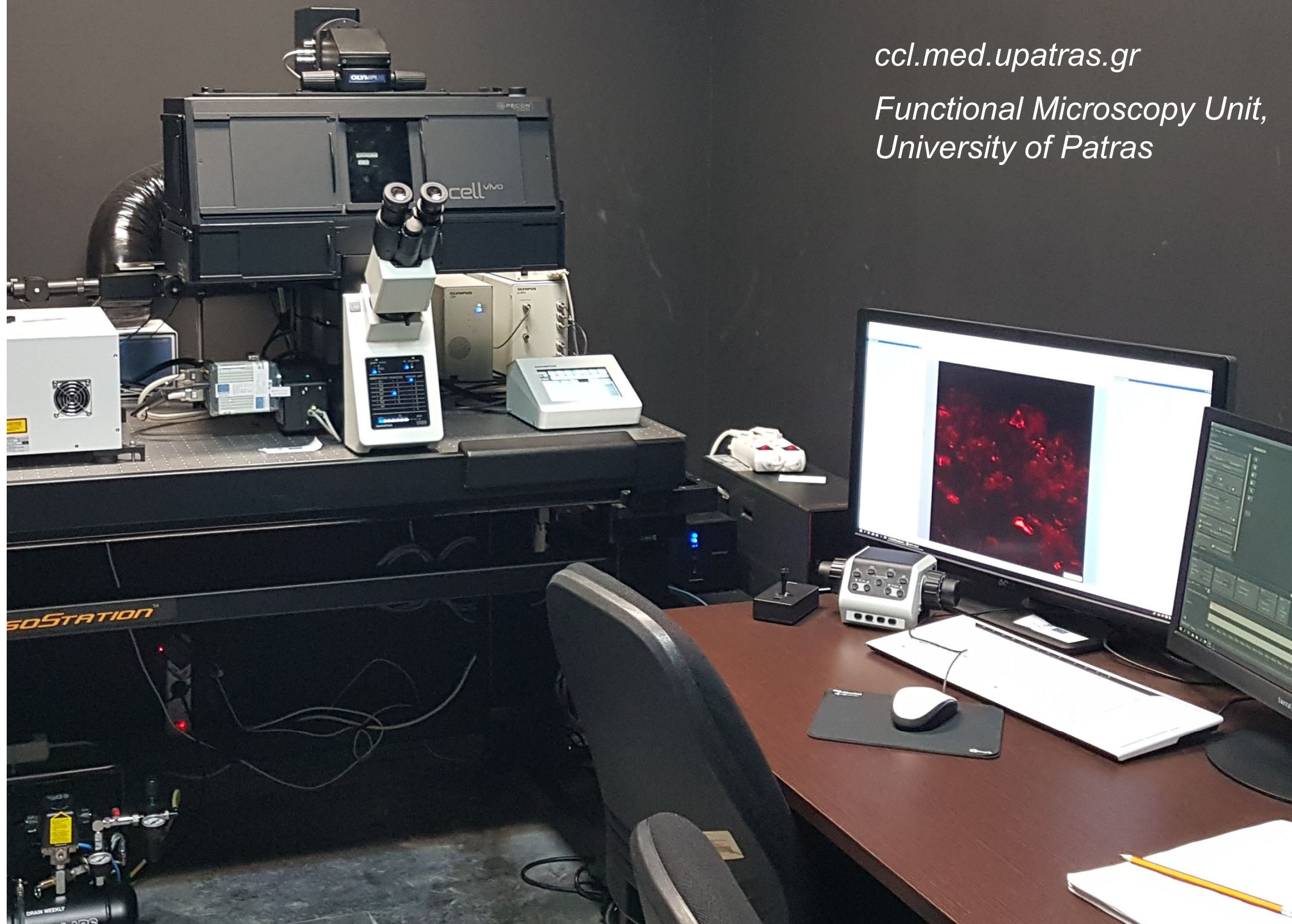
Light microscope

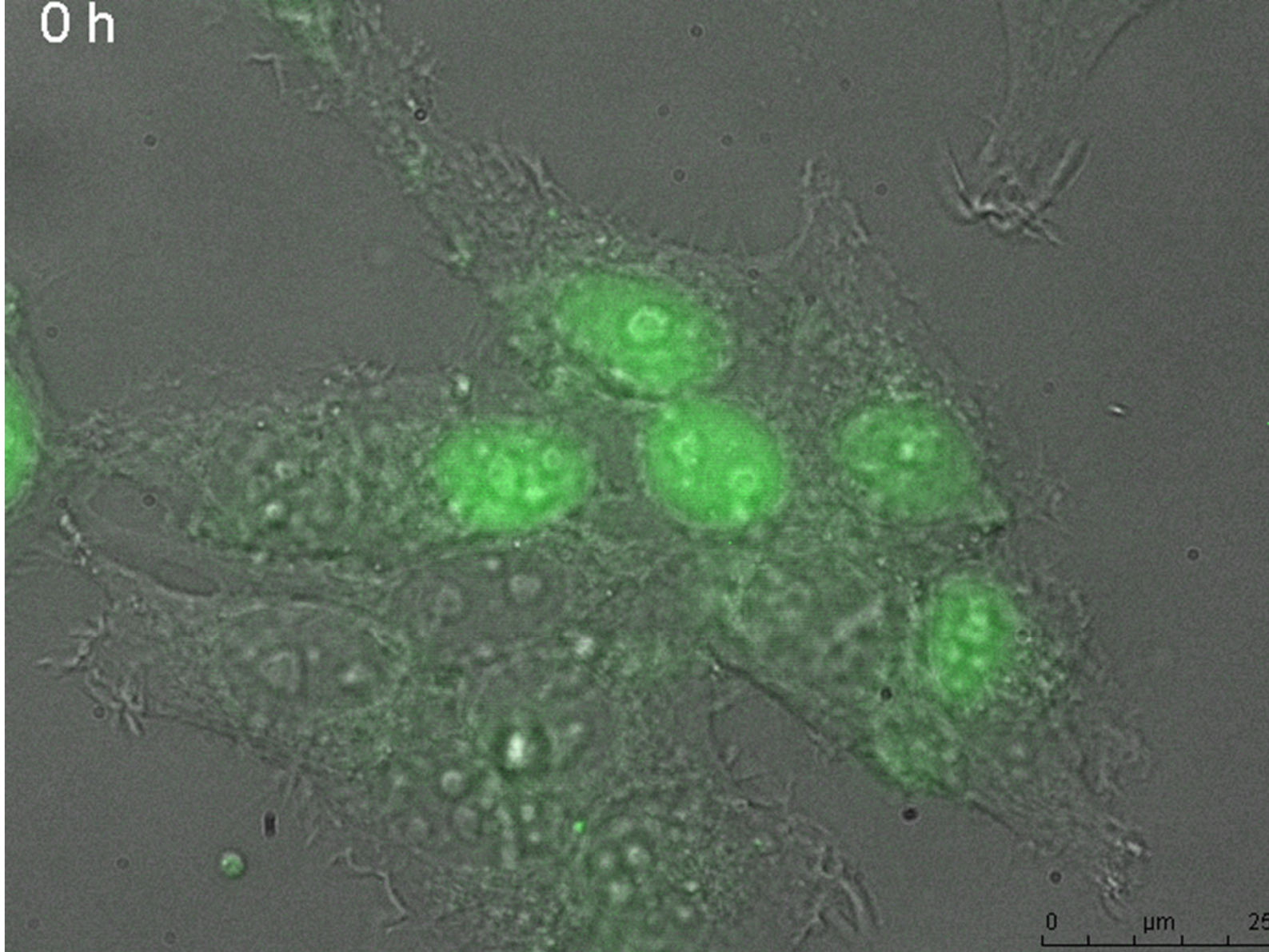
Fluorescence

Time-lapse

ccl.med.upatras.gr

*Functional Microscopy Unit,
University of Patras*

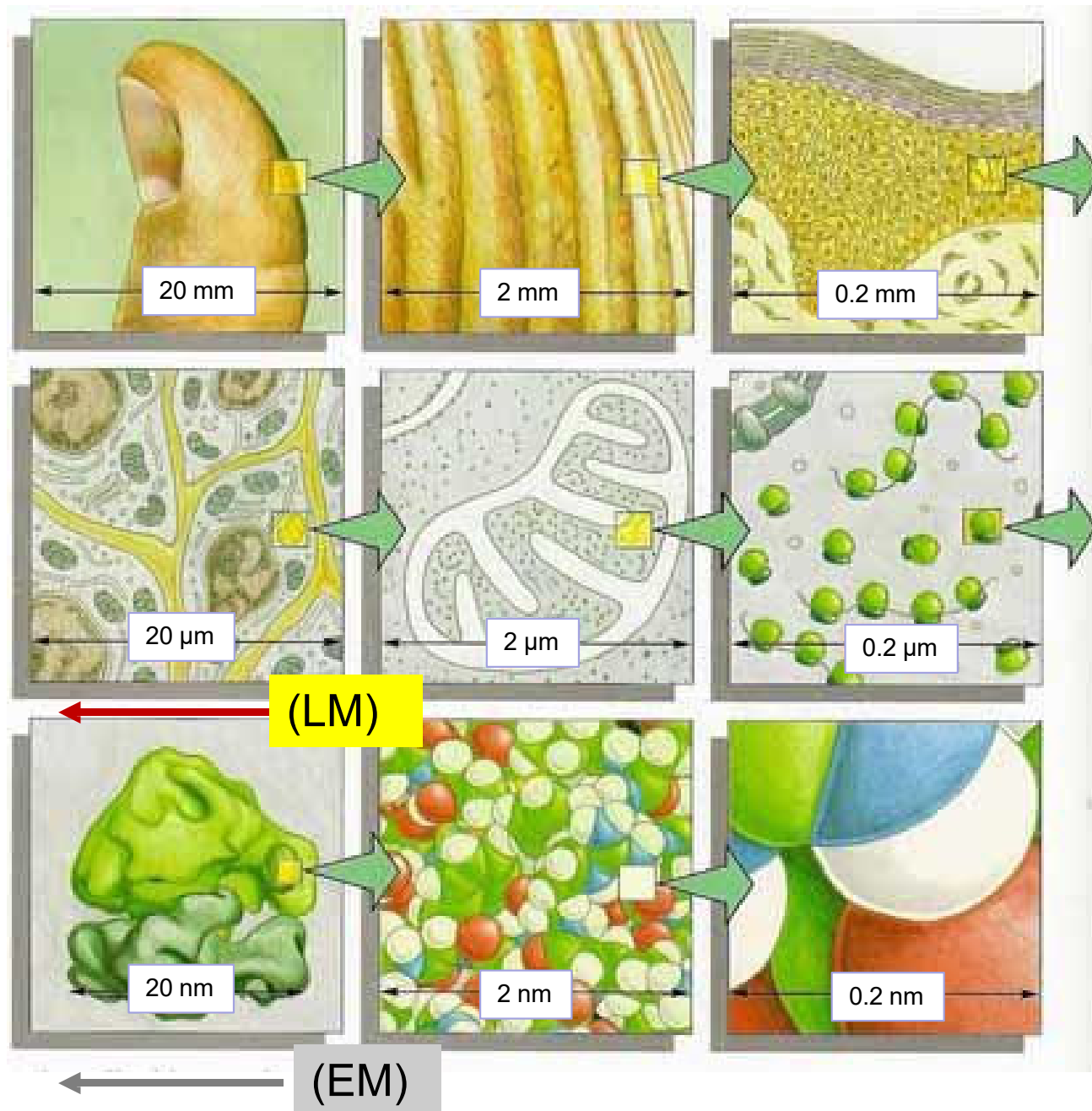


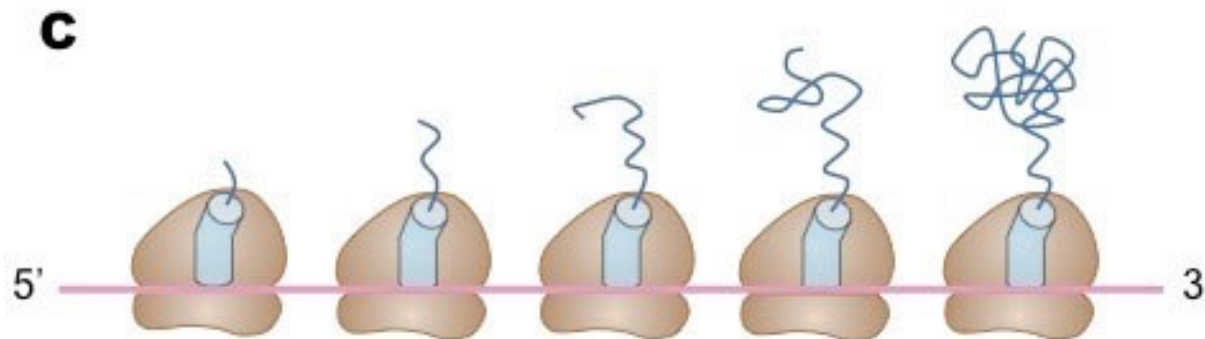
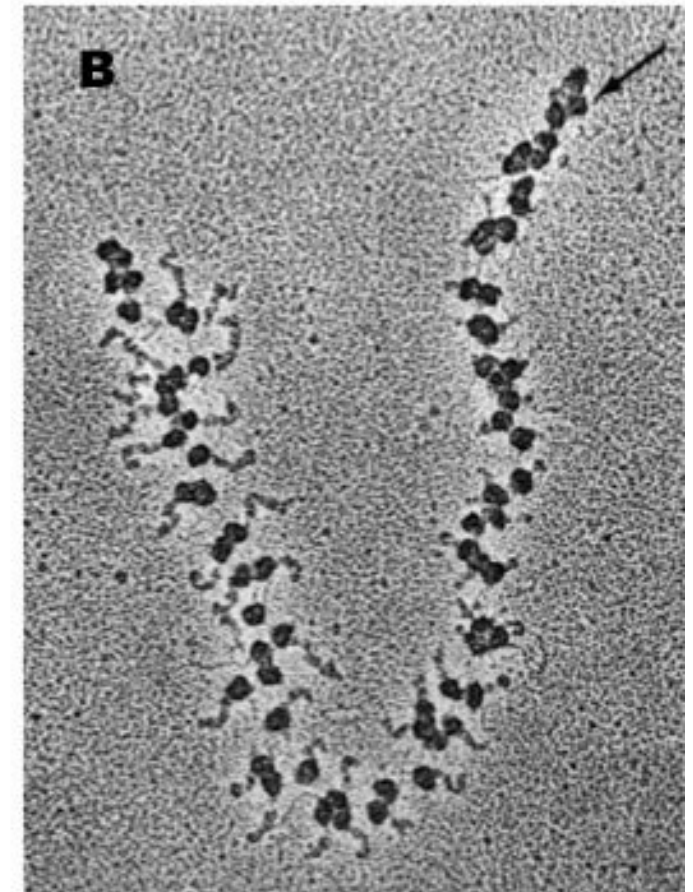
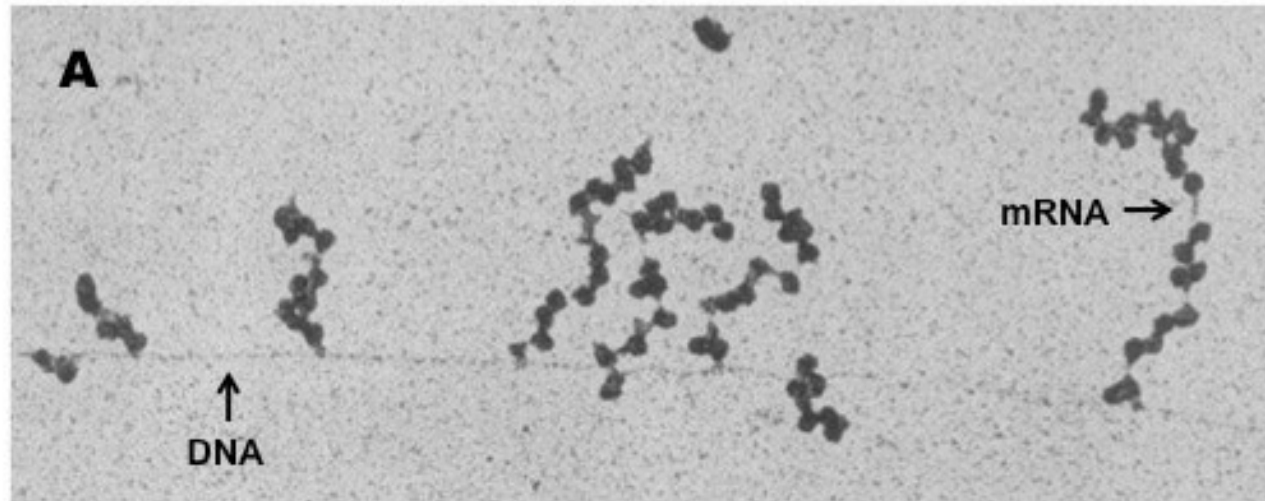


Light microscope

Combined phase-contrast and fluorescence

A light microscope cannot resolve objects separated by less than
~200 nm (resolution)

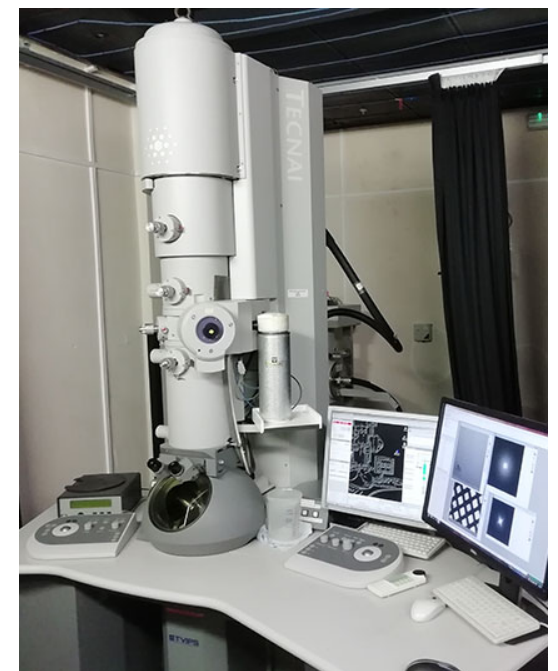
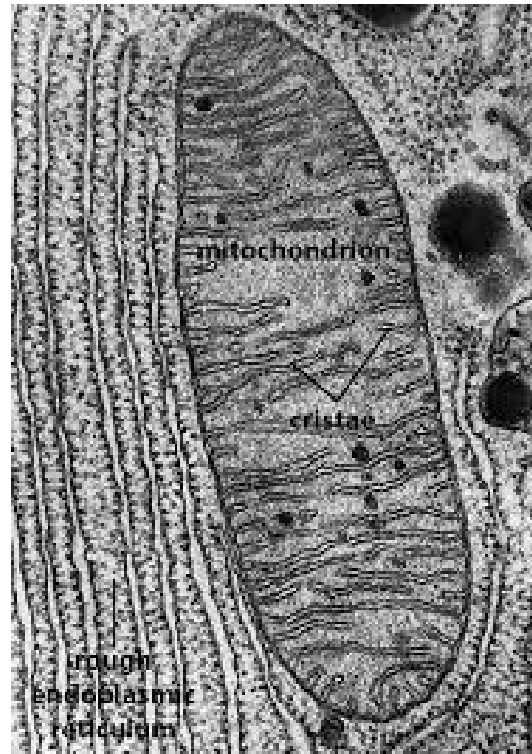
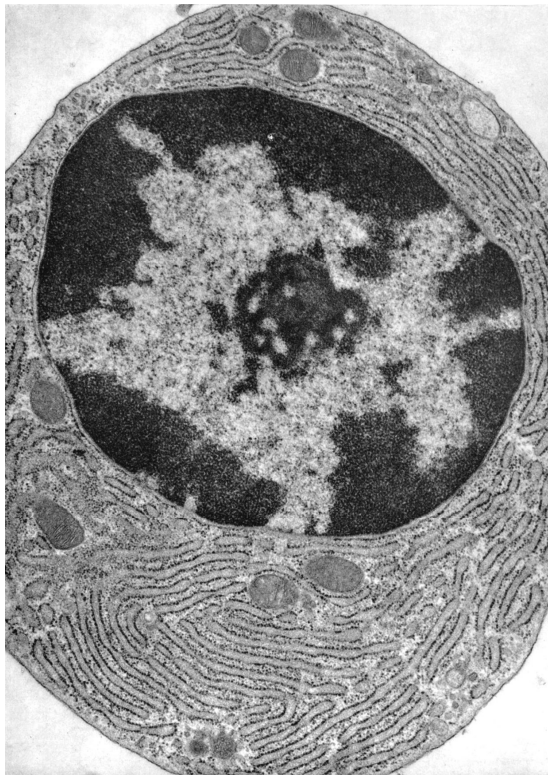




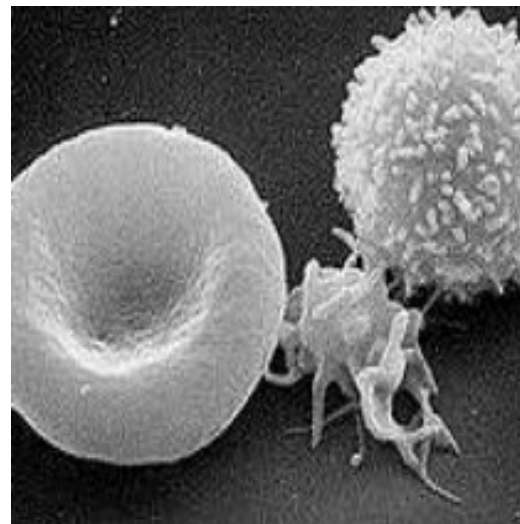
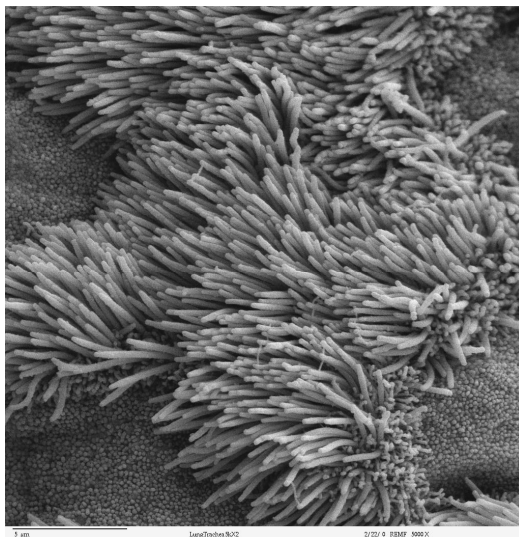
- A:** Polysome formation on RNA strands being transcribed from a DNA template (prokaryote)
- B:** Polysome formation on a eukaryotic mRNA transcript (arrow indicates 5'-end of transcript)
- C:** Diagrammatic representation of polysomes (polypeptide chain gets longer as ribosome moves 5' → 3')

Electron microscope

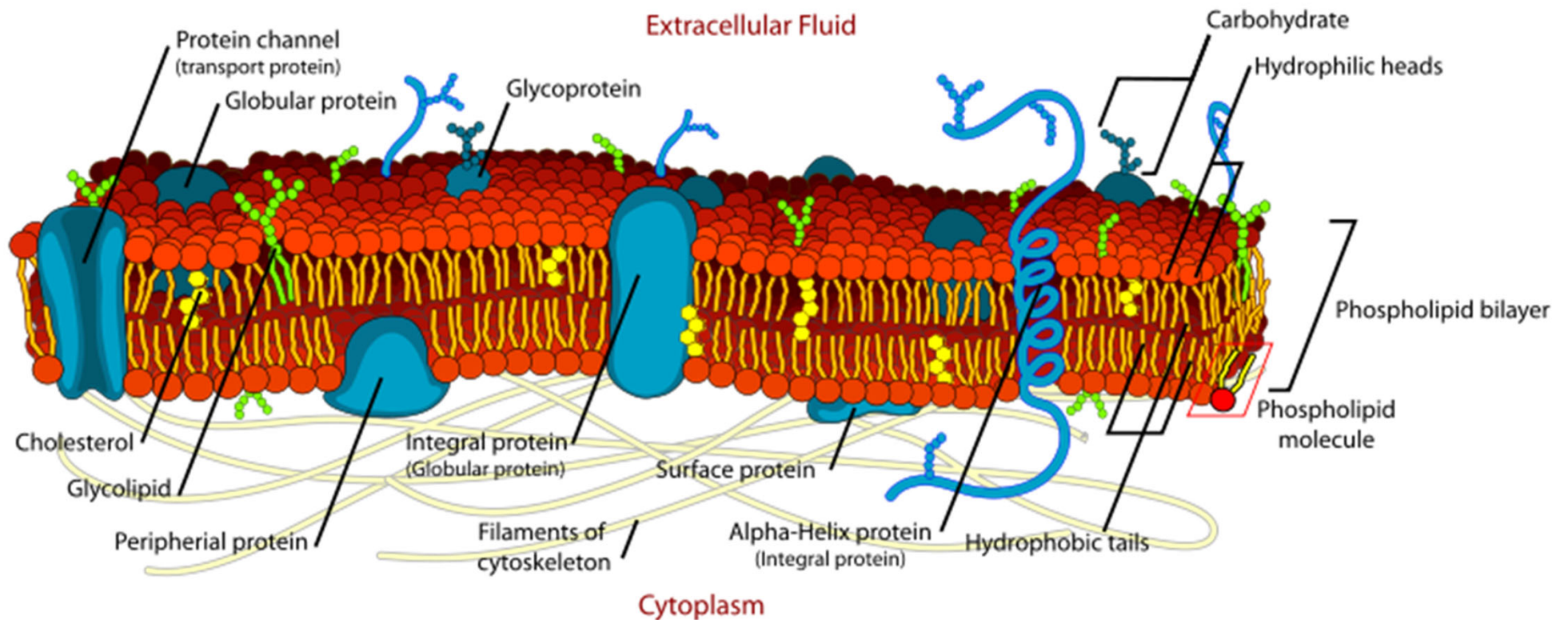
Transmission



Scanning

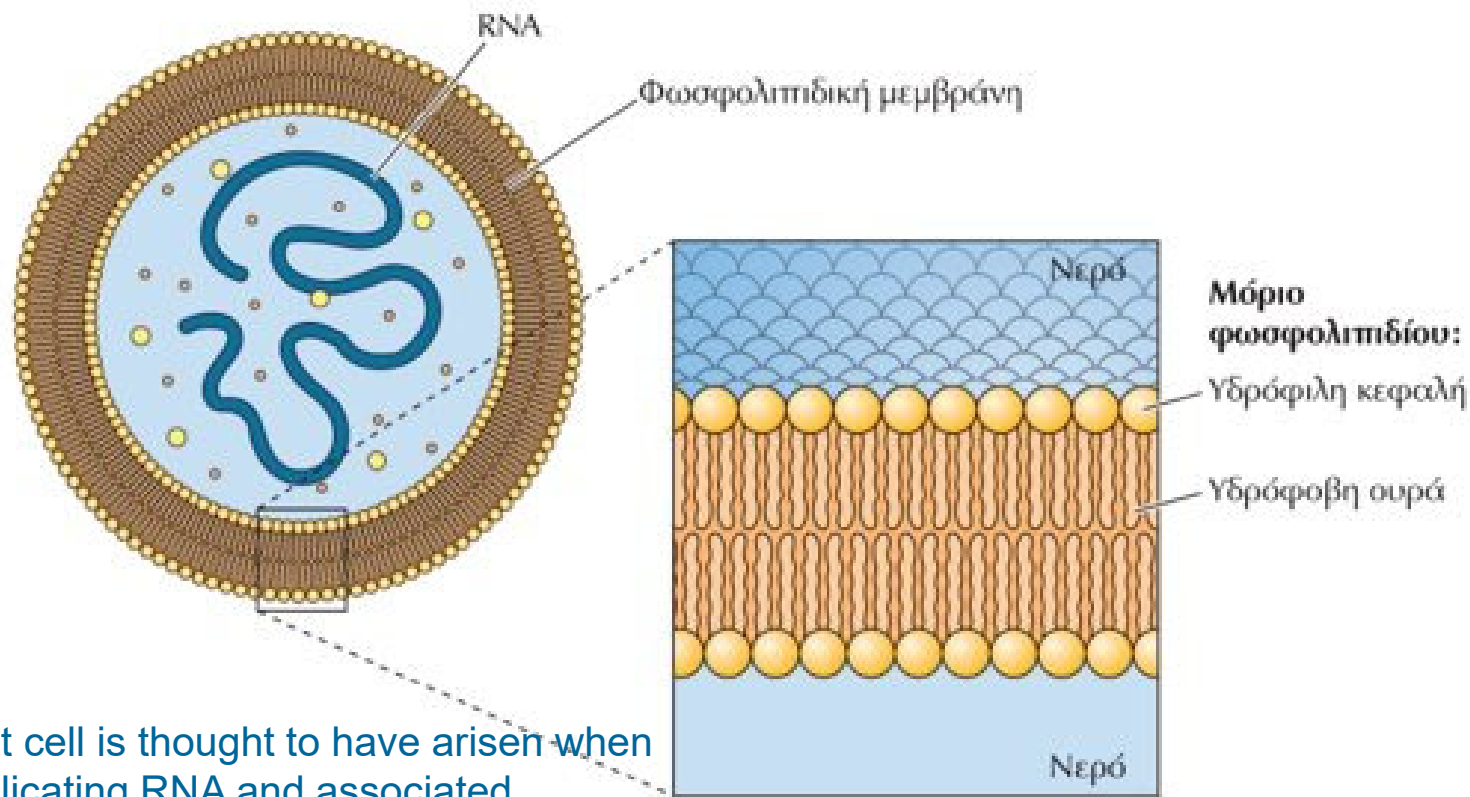


All cells are surrounded by a plasma membrane



A bilayer made of phospholipids. Each phospholipid has two long hydrophobic tails attached to a hydrophilic head. The hydrophobic tails are buried inside the lipid bilayer, while the hydrophilic heads face water on both sides. The plasma membrane also contains proteins and other lipids (e.g. glycolipids and, in animal cells, cholesterol).

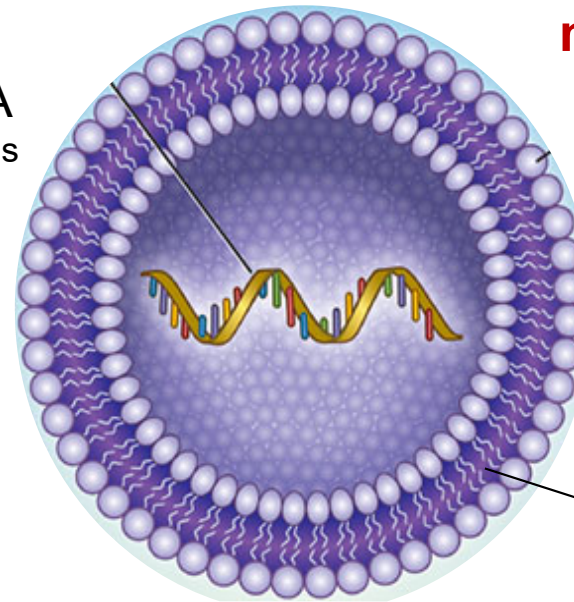
All cells contain genetic material (DNA) and ribosomes



The first cell is thought to have arisen when self-replicating RNA and associated molecules became enclosed within a phospholipid membrane.

mRNA vaccines

mRNA
(encodes
spike
protein)

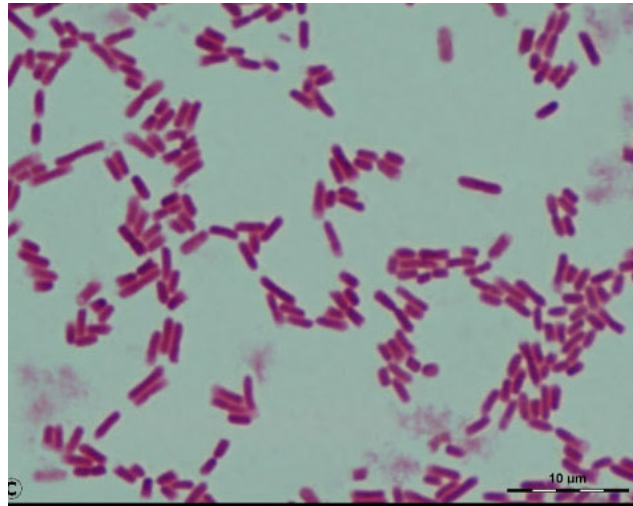


Lipid nanoparticle
Lipid Nanoparticle (LNP)
(nanometer scale)

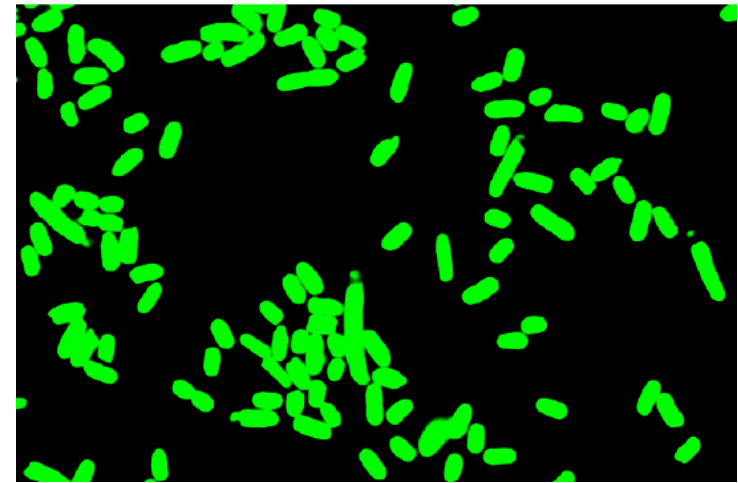
Prokaryotic cell

Escherichia coli

Light

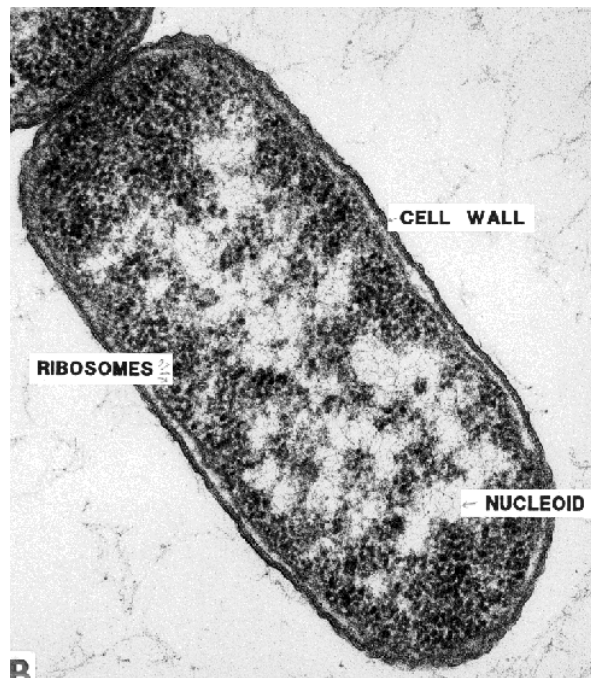


Bright-field

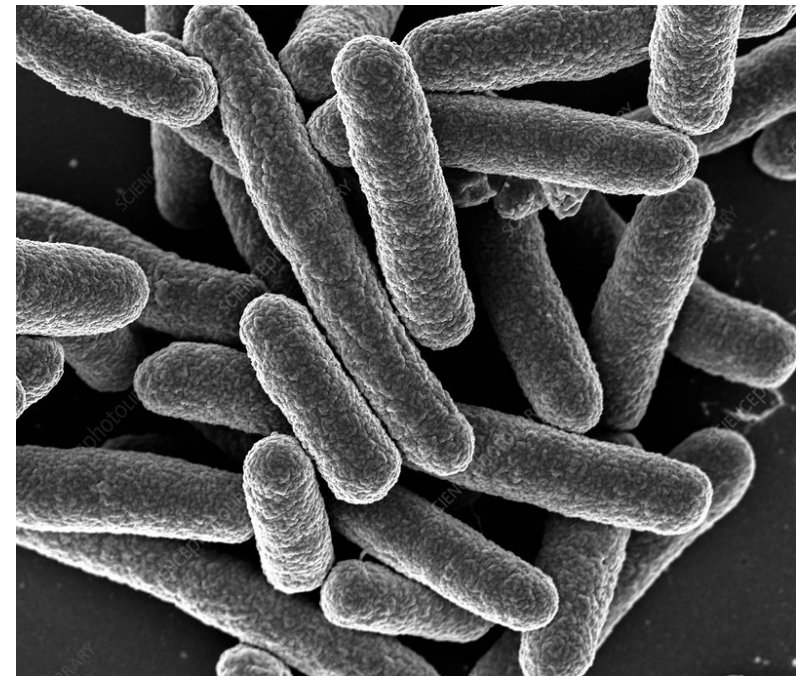


Fluorescence

Electron

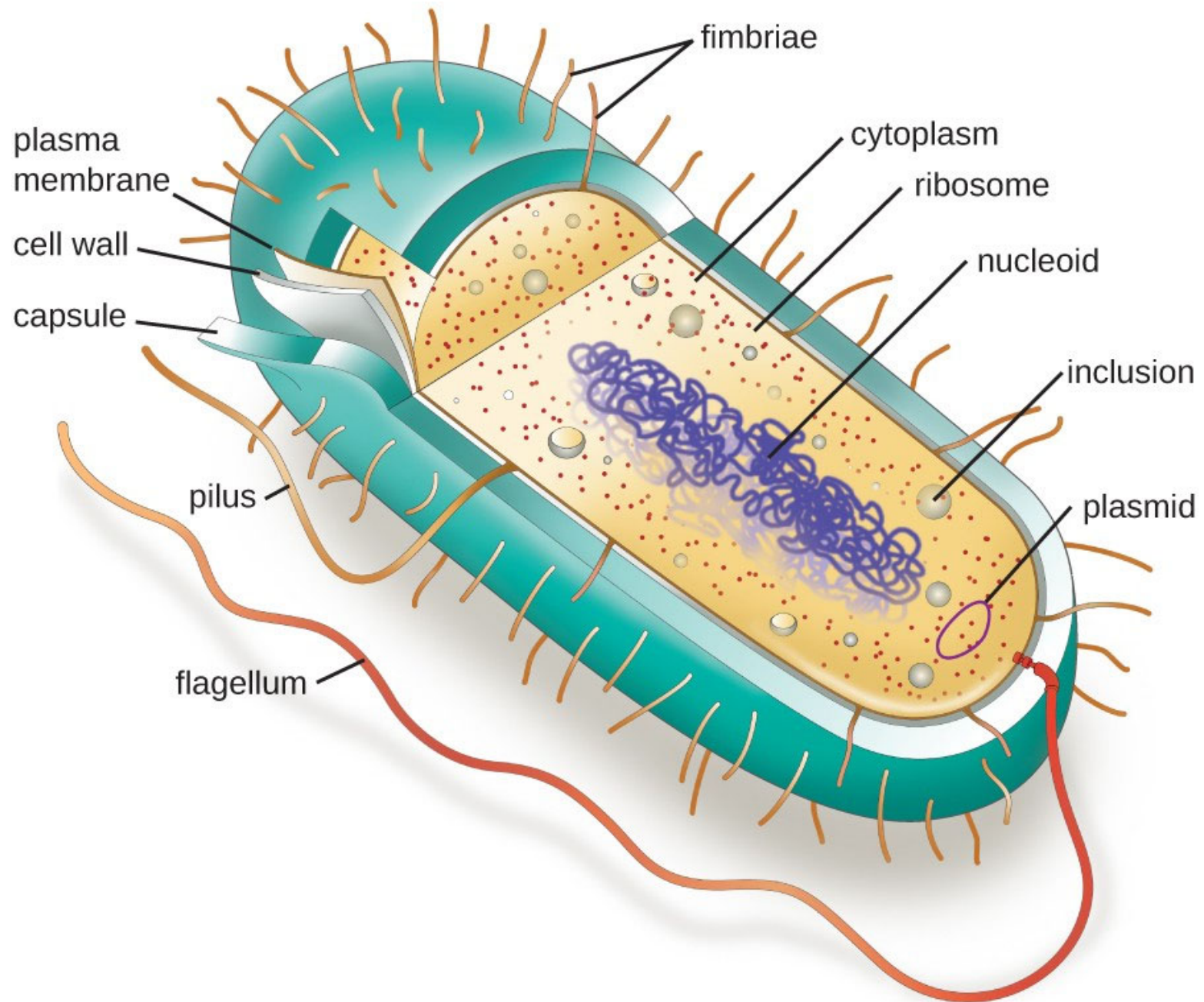


Transmission



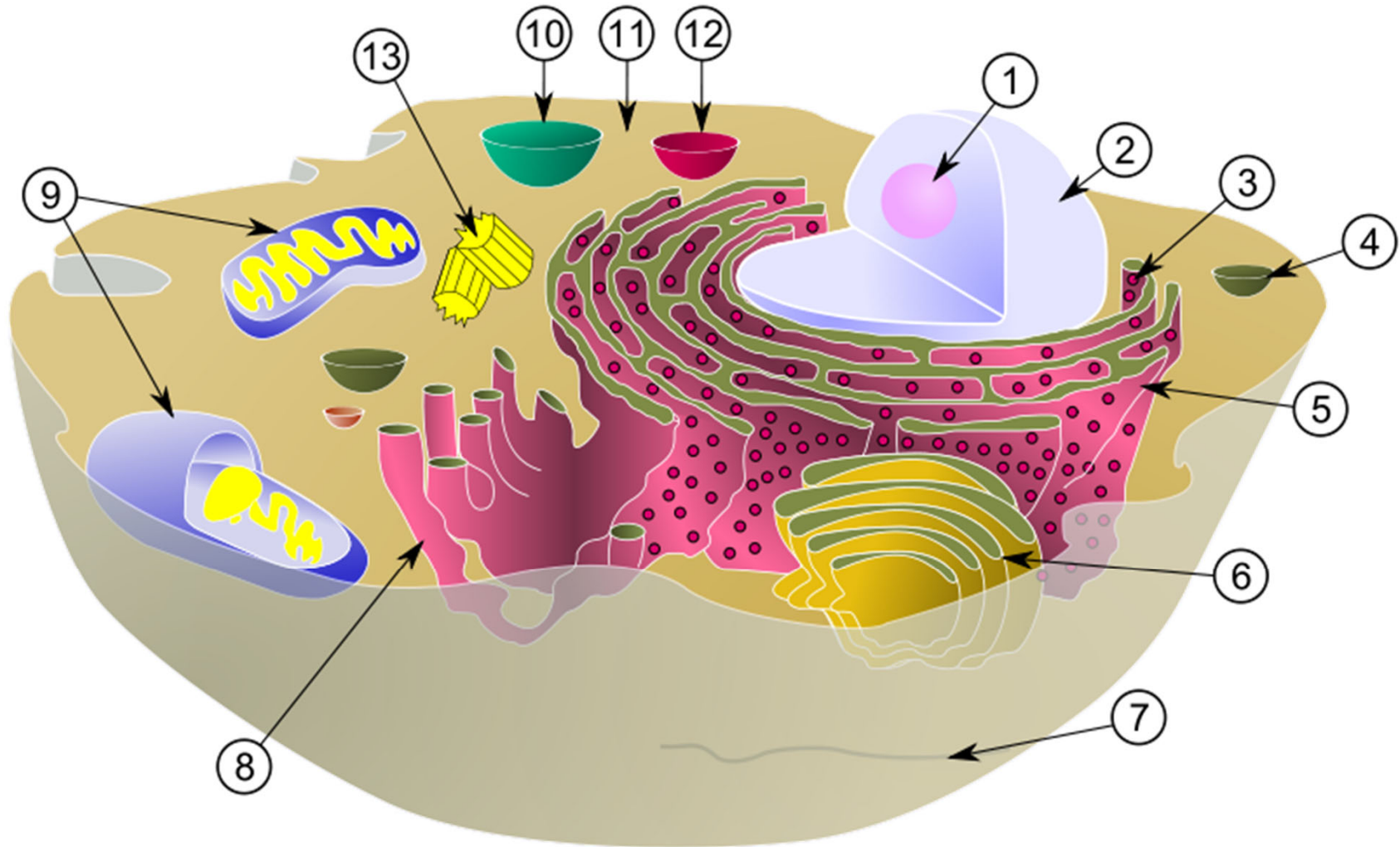
Scanning

Prokaryotic cell



Eukaryotic (animal) cell

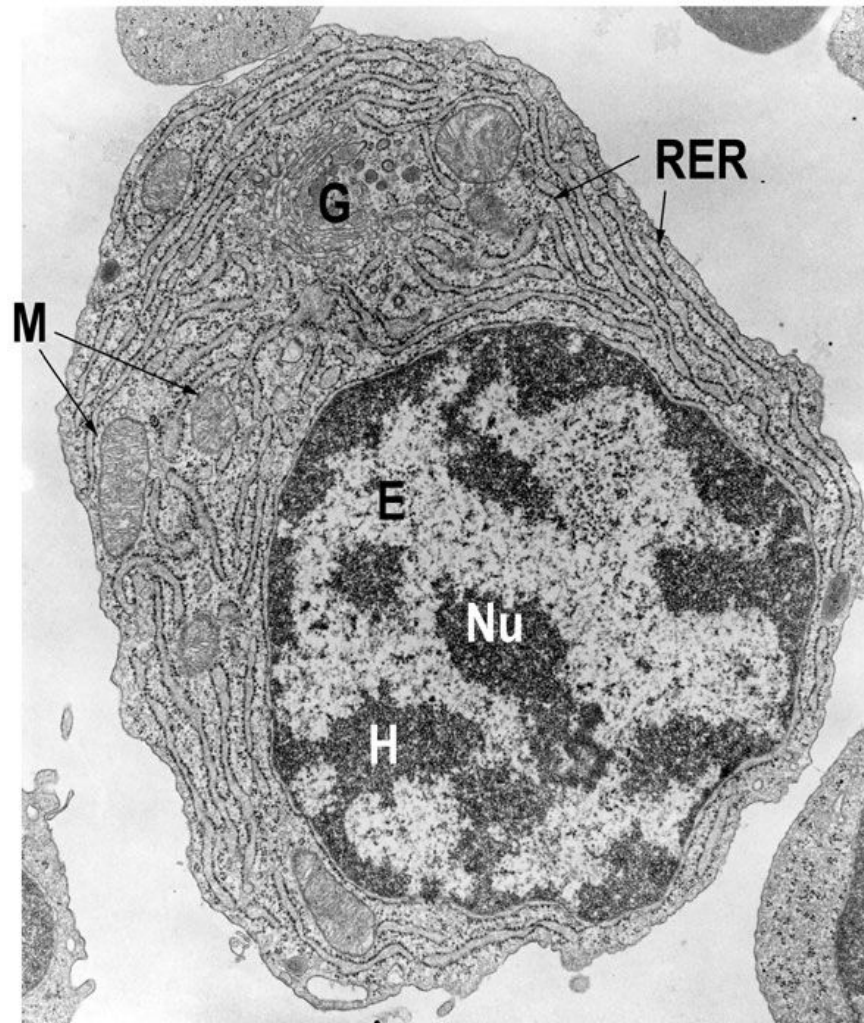
Internal membranes and organelles (cellular regions with specific structures and functions, usually enclosed by a single or double membrane)



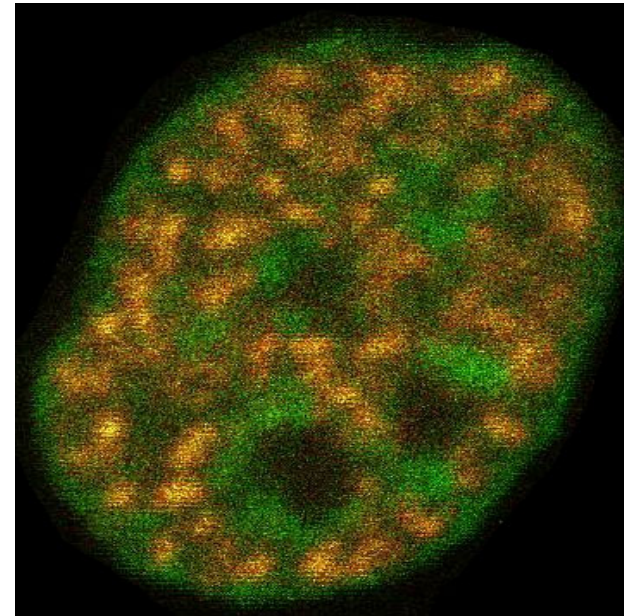
1. Nucleolus, 2. Nucleus, 3. Ribosome, 4. Vesicle, 5. Rough endoplasmic reticulum, 6. Golgi apparatus, 7. Cytoskeleton, 8. Smooth endoplasmic reticulum, 9. Mitochondrion, 10. Lysosome, 11. Cytosol, 12. Peroxisome, 13. Centrosome

Nucleus

The cell's genetic information is stored in the nucleus
Replication, transcription (pre-mRNA, tRNA, rRNA, etc.) and RNA processing



Nu-nucleus, E-euchromatin, H-heterochromatin, M-mitochondria, RER-rough endoplasmic reticulum, G-golgi complex



10 μ m

Double membrane and nuclear pores

Nuclear envelope

Nuclear lamina

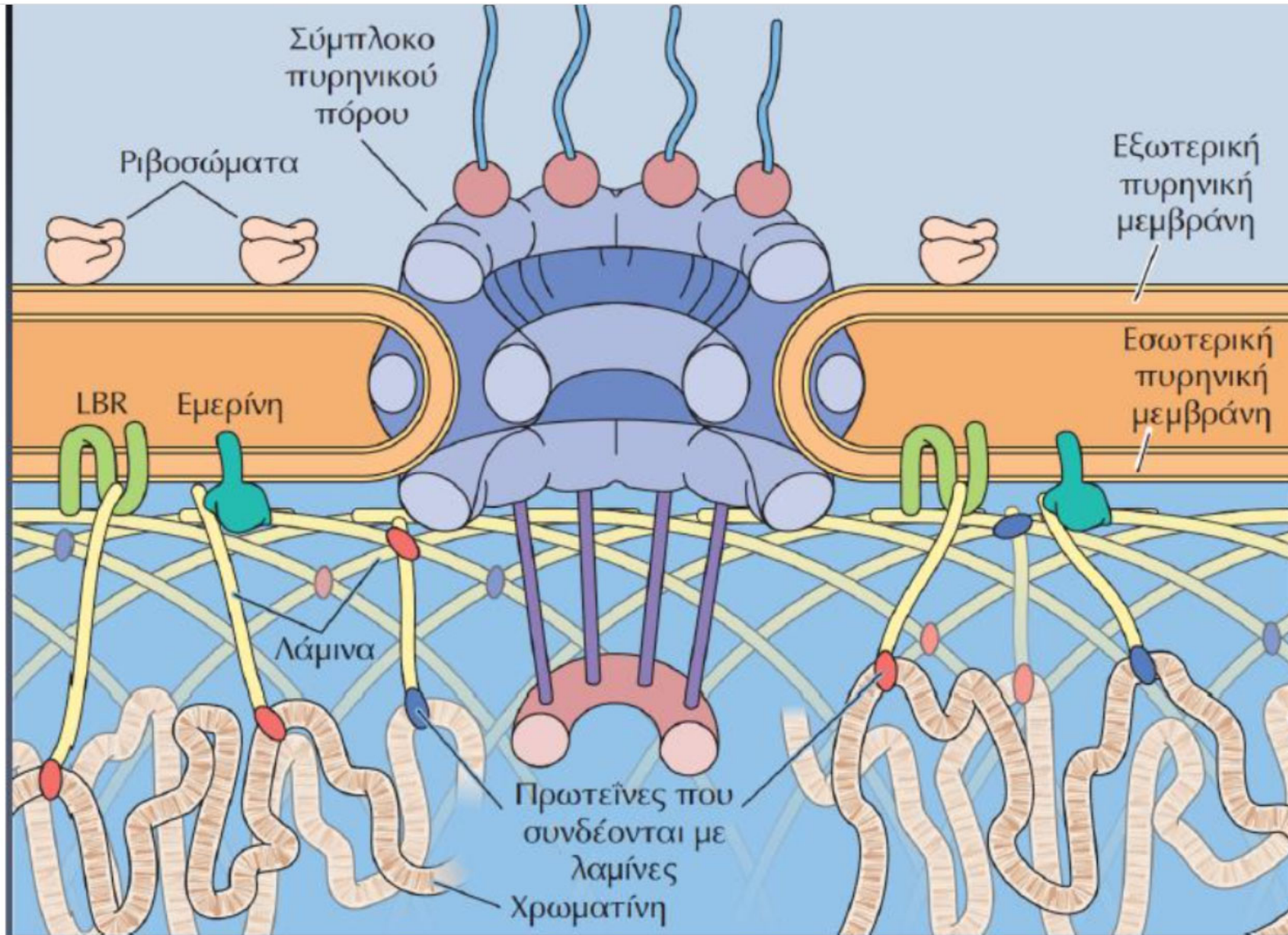
Nucleoplasm

Euchromatin/heterochromatin

Replication factories

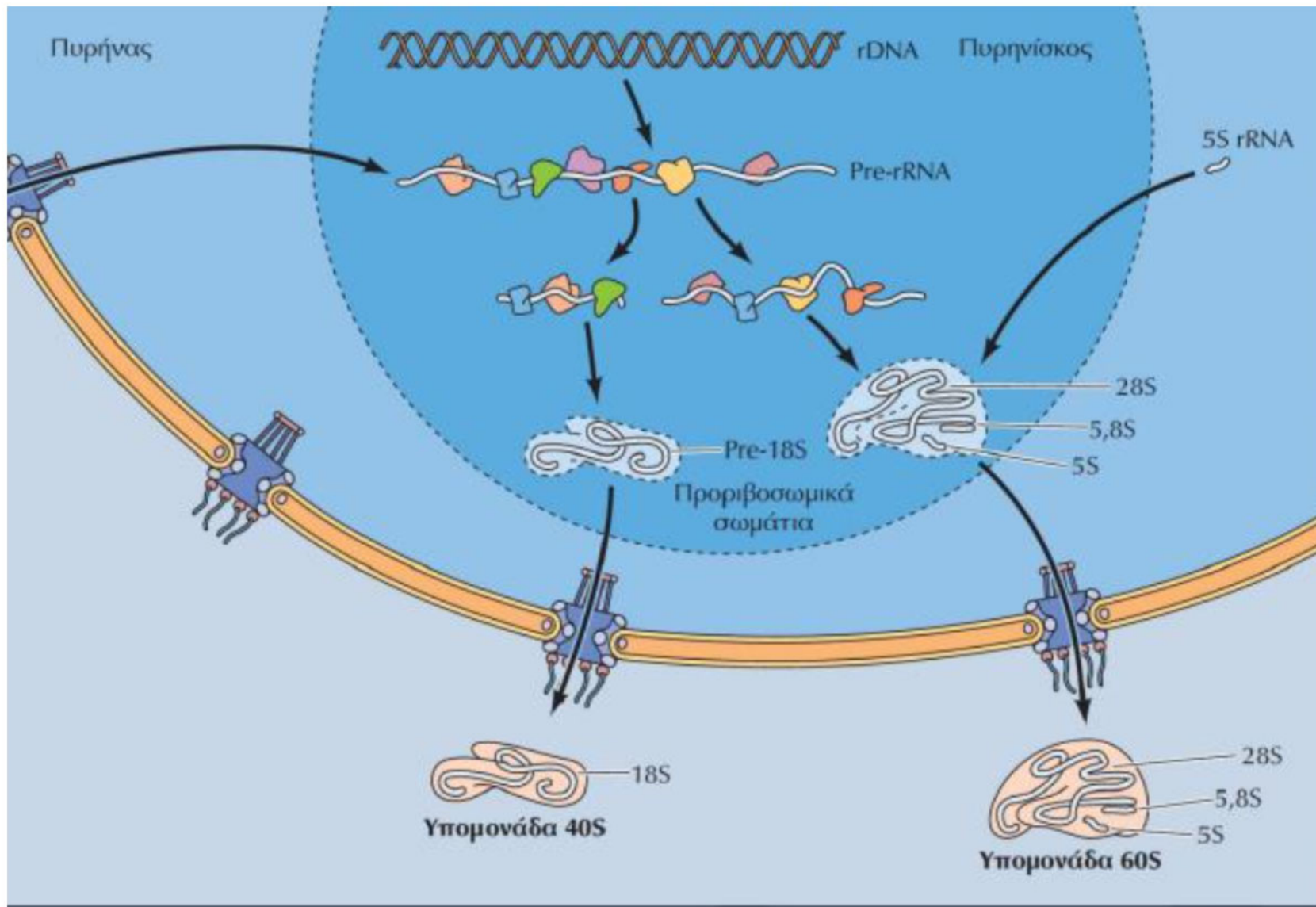
Nucleoli (sites of ribosome production)

Nuclear envelope = nuclear membranes and nuclear pores



Nucleolus

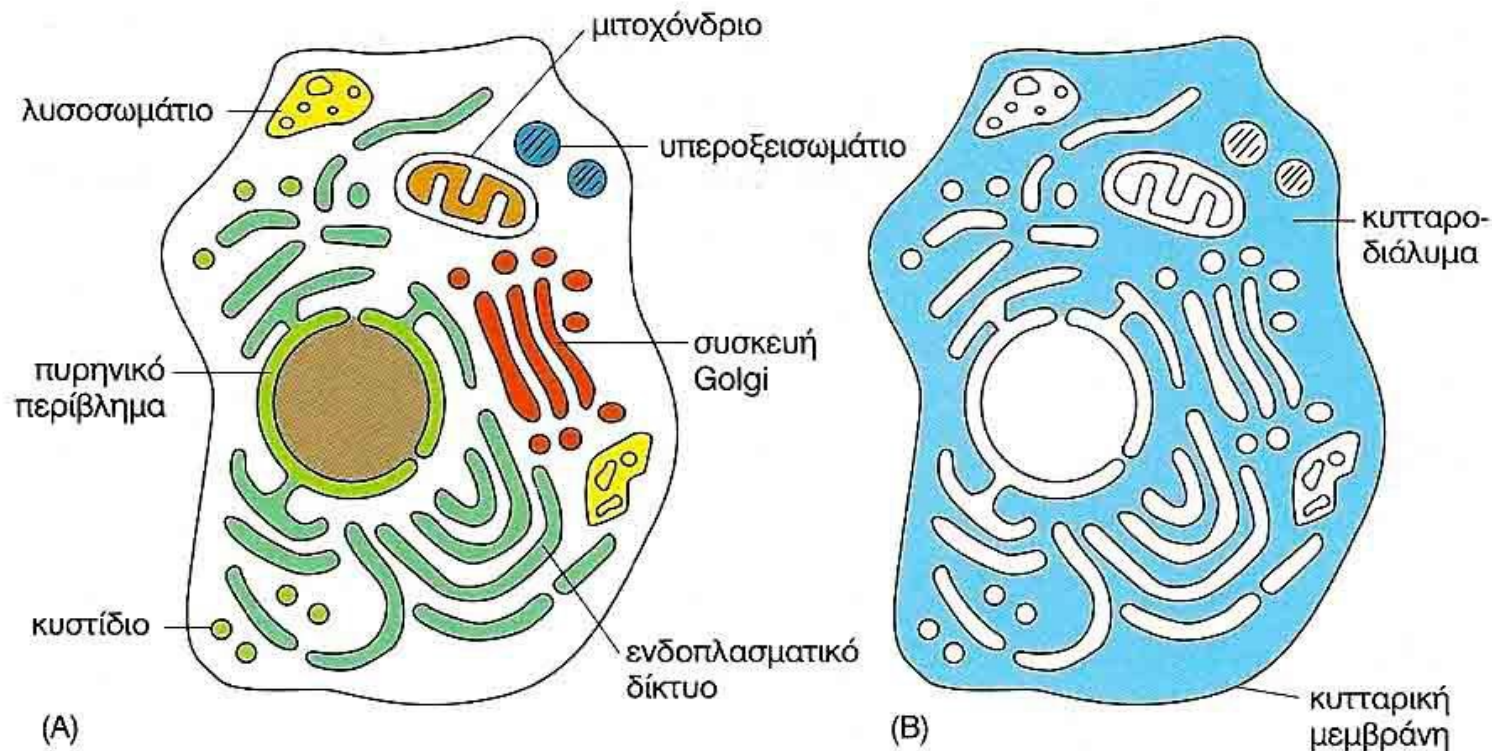
Ribosome production site: the ribosomal RNA genes (on the five acrocentric chromosome pairs in humans) are transcribed; precursor rRNAs are processed and assemble with ribosomal proteins imported from the cytoplasm. The ribosomal subunits (40S and 60S) leave for the cytoplasm through nuclear pores.



Cytoplasm: the contents of the cell outside the nucleus, including organelles

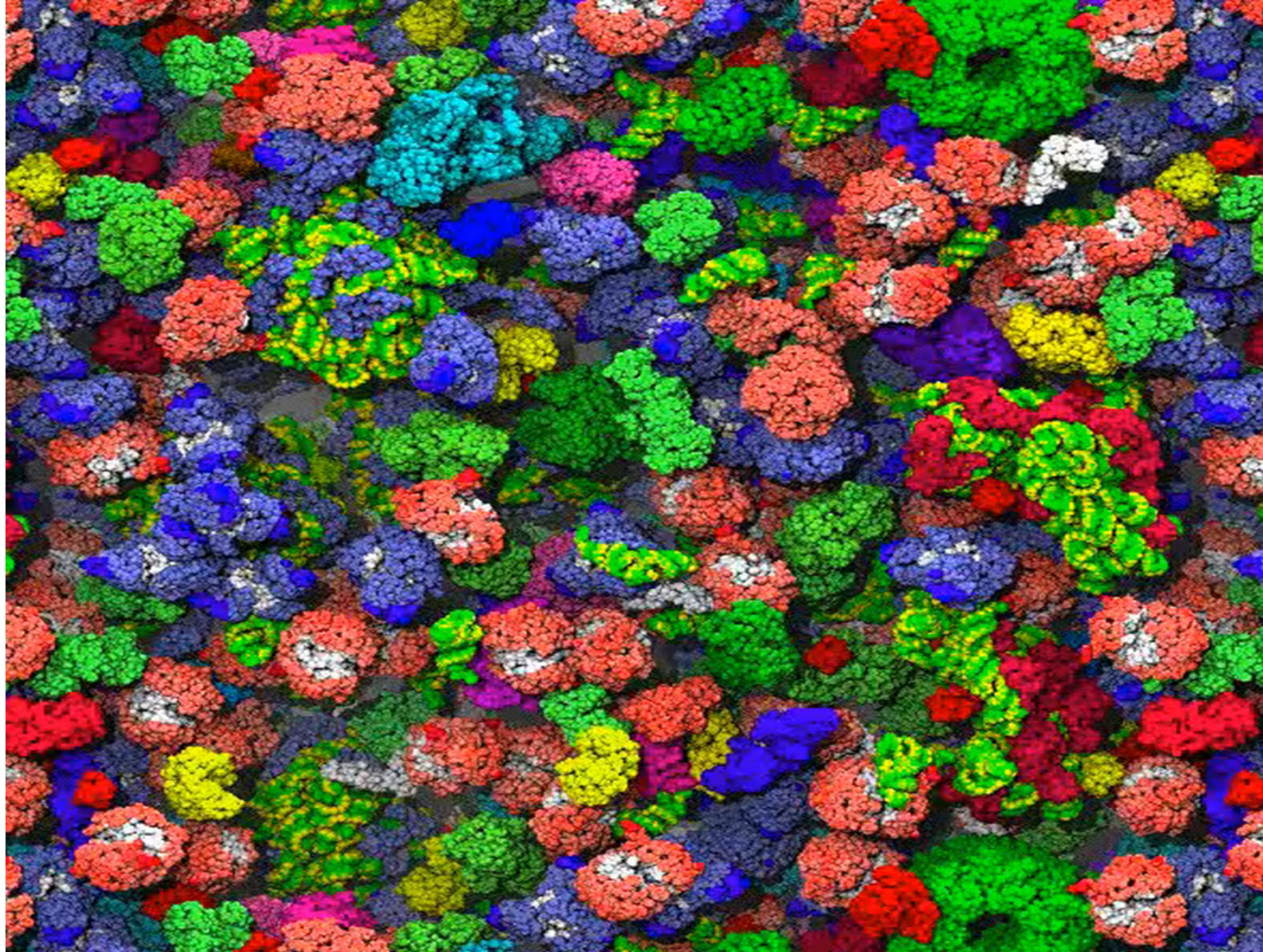
Organelles: dynamic cellular structures with specific functions, usually enclosed by a single or double membrane

Cytosol: the contents remaining after the nucleus and organelles are removed



Cytosol

cytosol



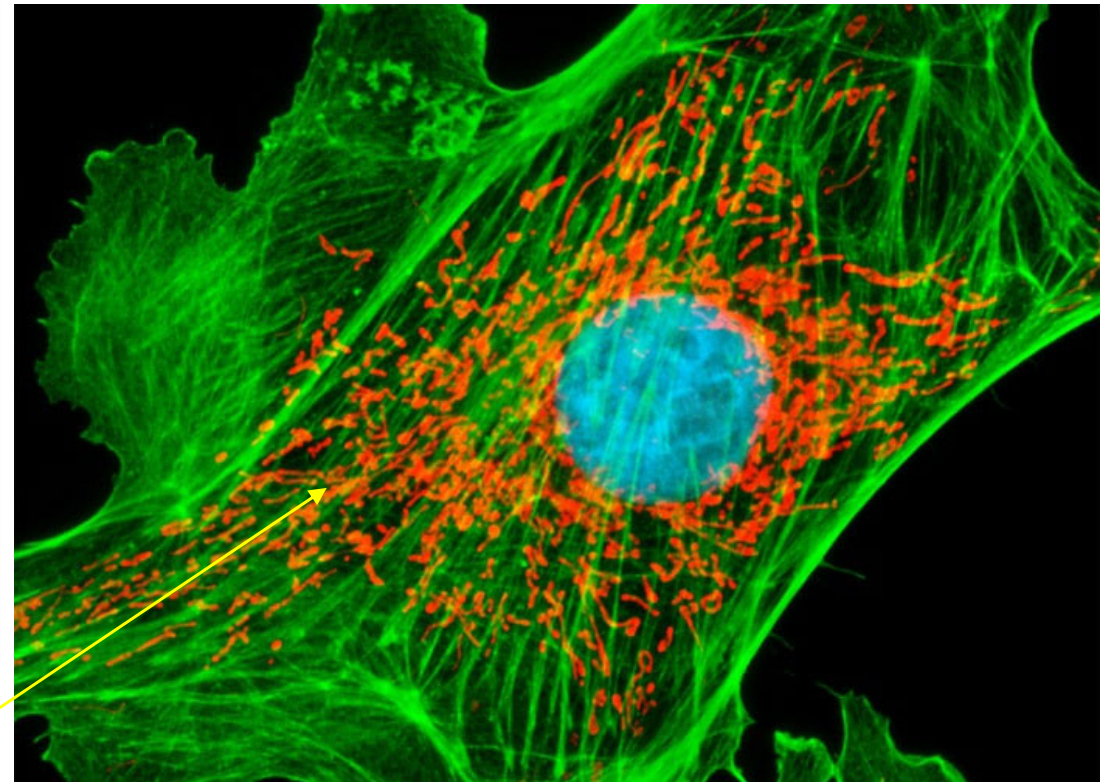
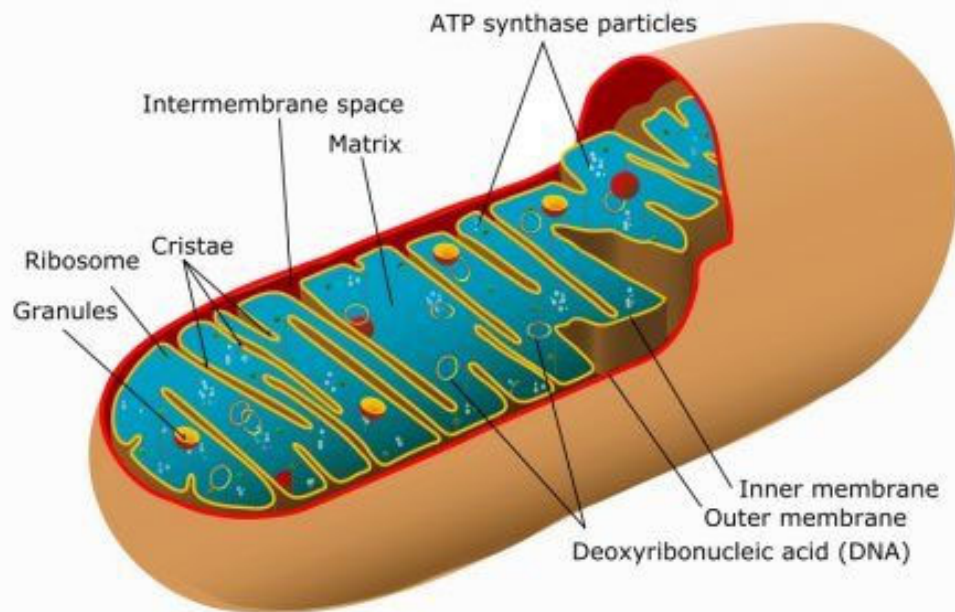
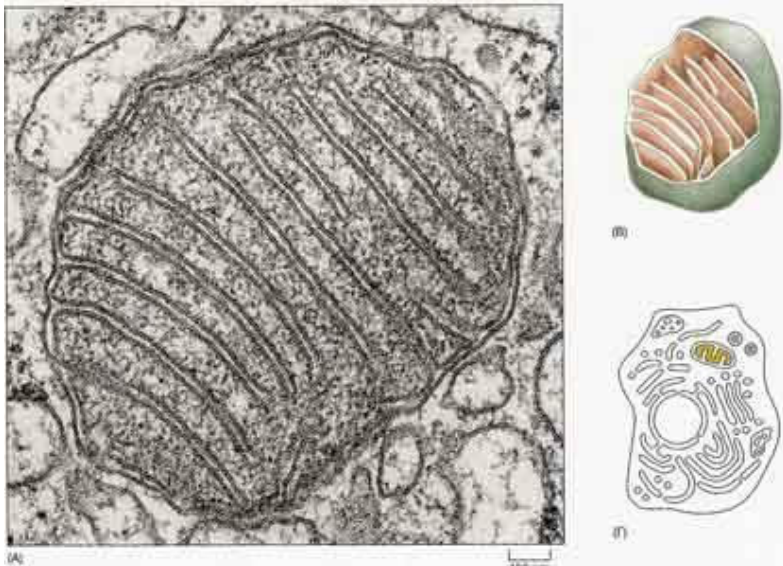
Mitochondria

Energy production and cellular respiration

Enclosed by a double membrane; the inner membrane forms cristae, where oxidative phosphorylation occurs

They have their own genetic material (mtDNA, encoding 13 proteins), ribosomes and a slightly modified genetic code

Metabolic reactions (e.g. the Krebs cycle), transcription and translation occur in the matrix

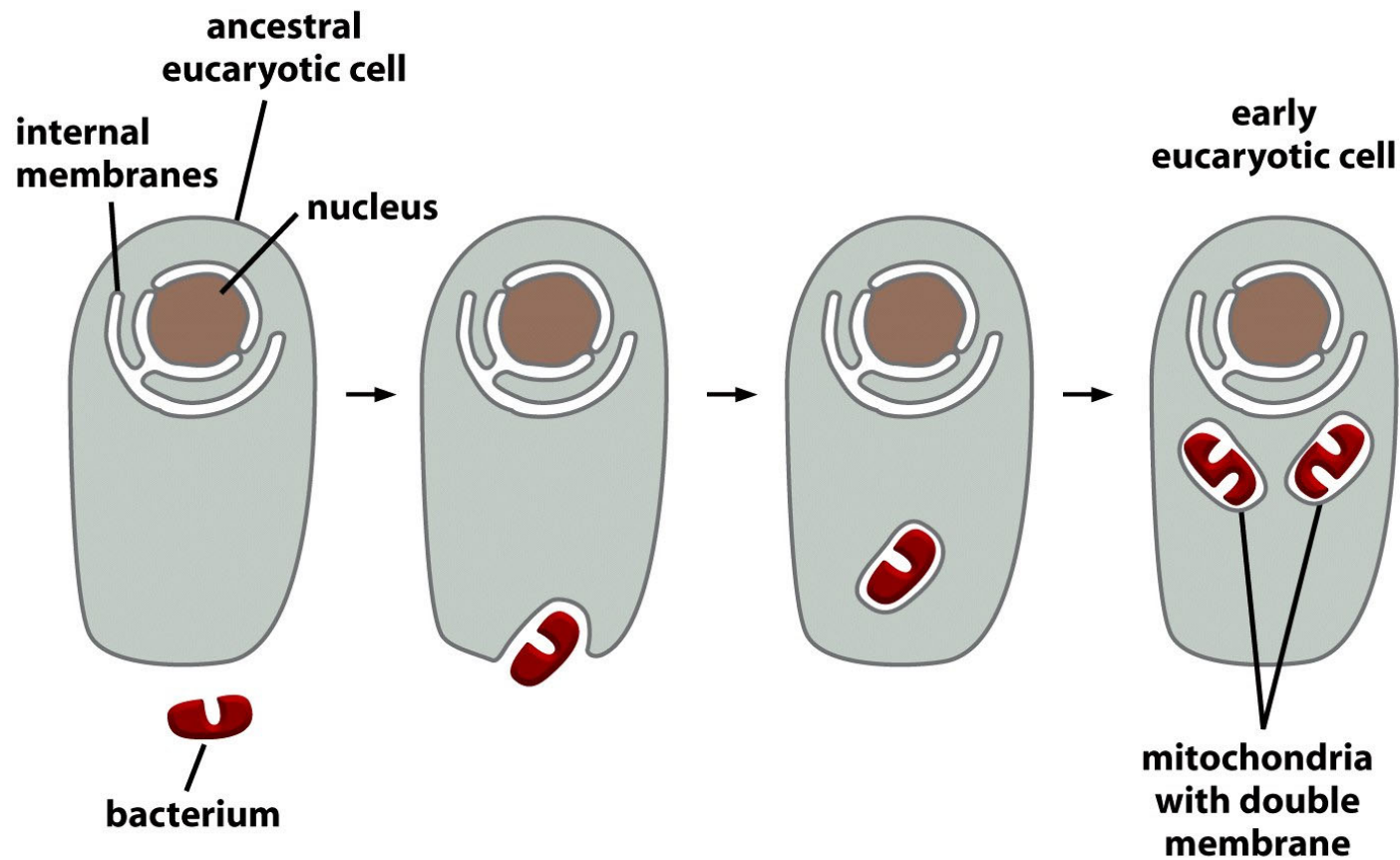


Mitochondria

Mitochondria

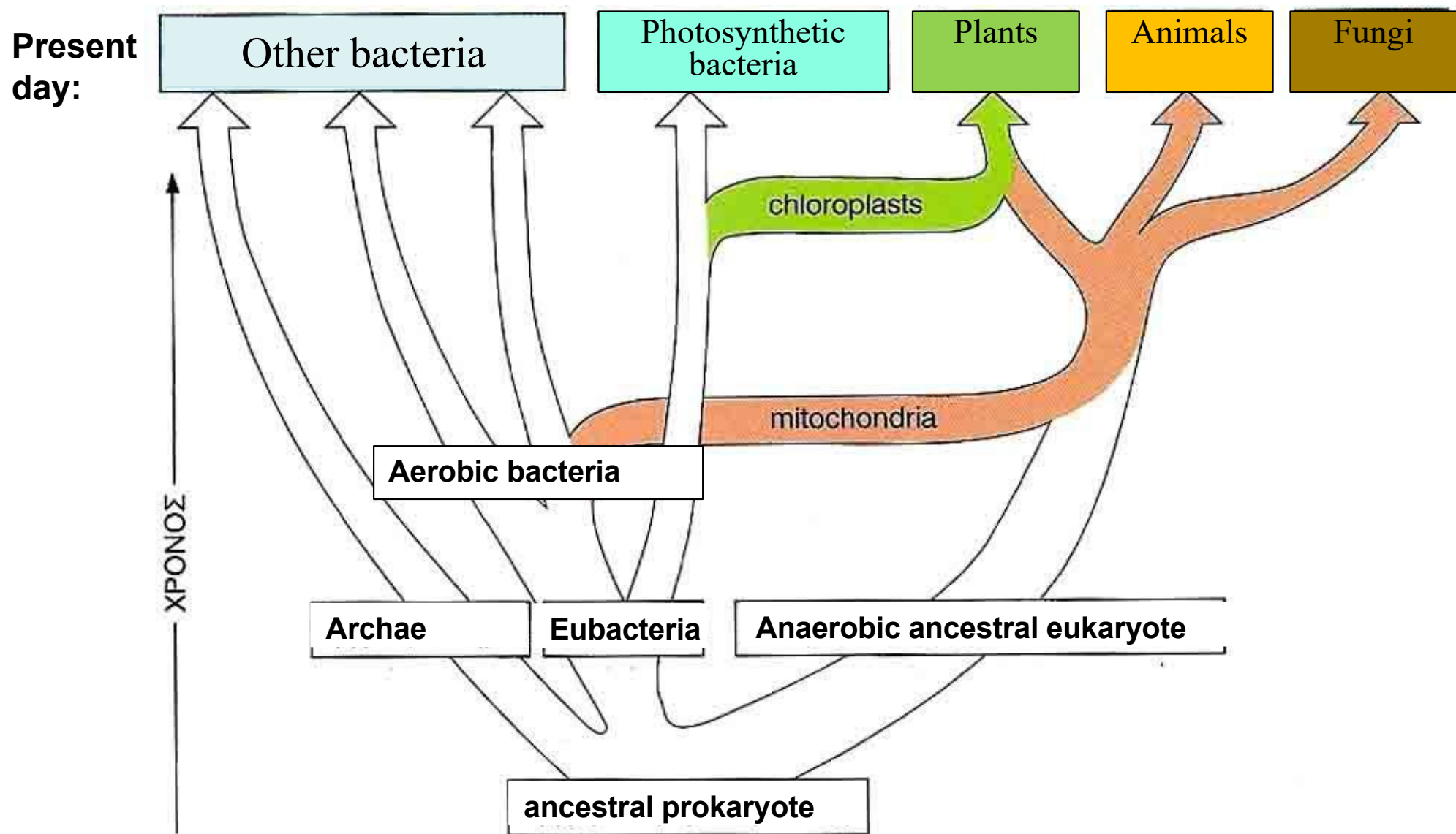
Theory of origin

From bacteria engulfed by an ancestral eukaryote



A similar origin is proposed for chloroplasts

Evolutionary tree

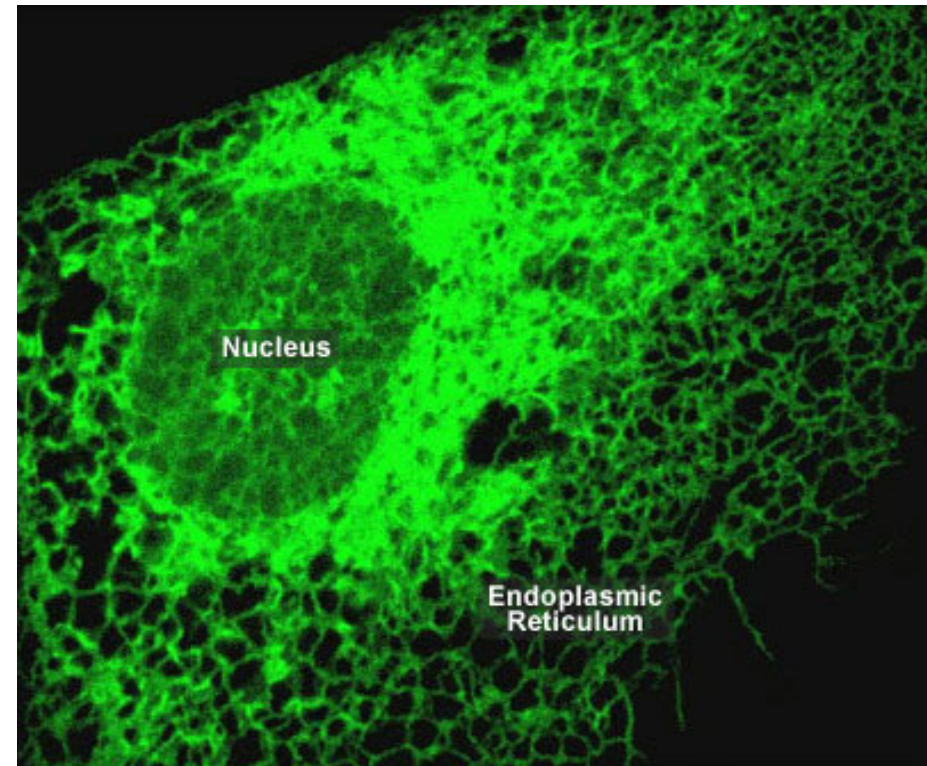
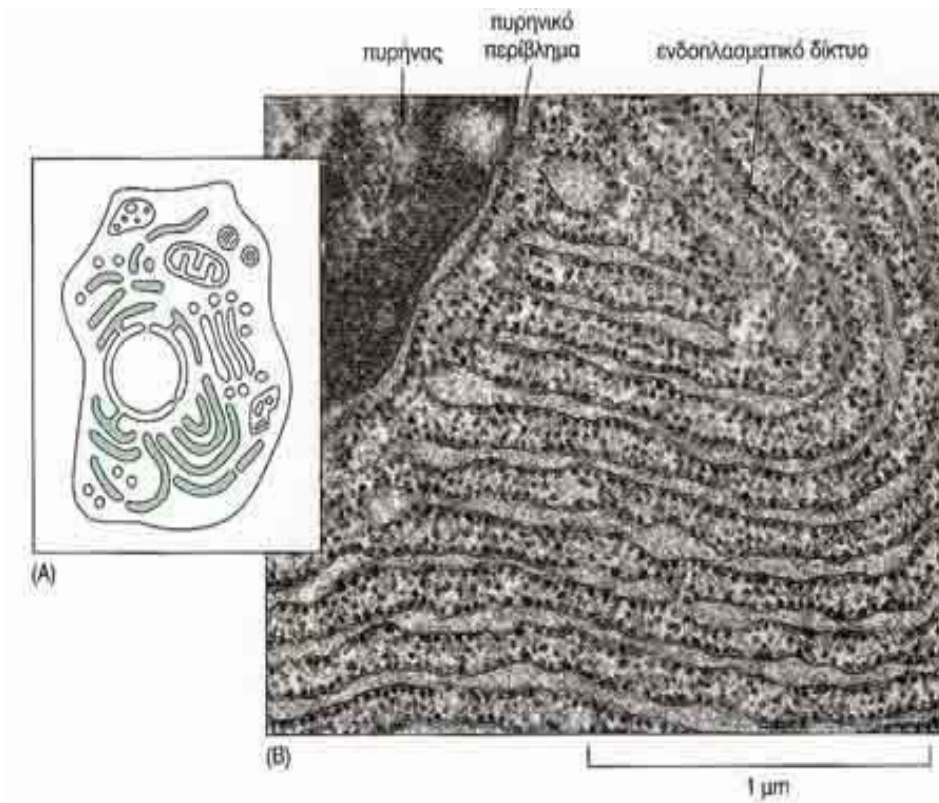


Early eukaryotes were anaerobic and acquired mitochondria (around 1.5 billion years ago), and later chloroplasts

Endoplasmic reticulum (ER)

Rough ER: bears attached ribosomes; synthesizes membrane and secreted proteins

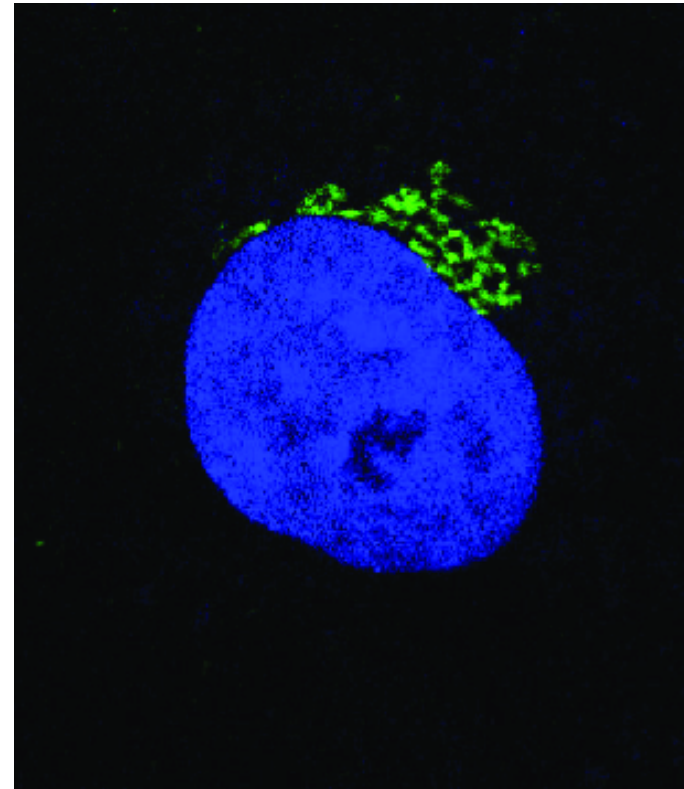
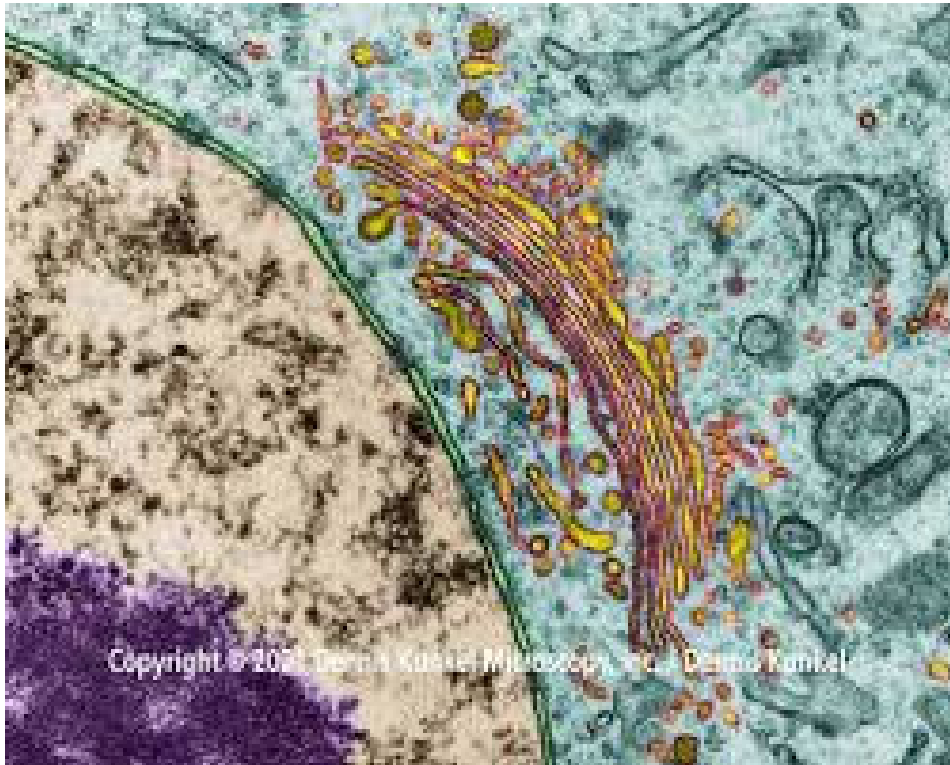
Smooth ER: lipid and steroid synthesis; drug metabolism



Golgi apparatus

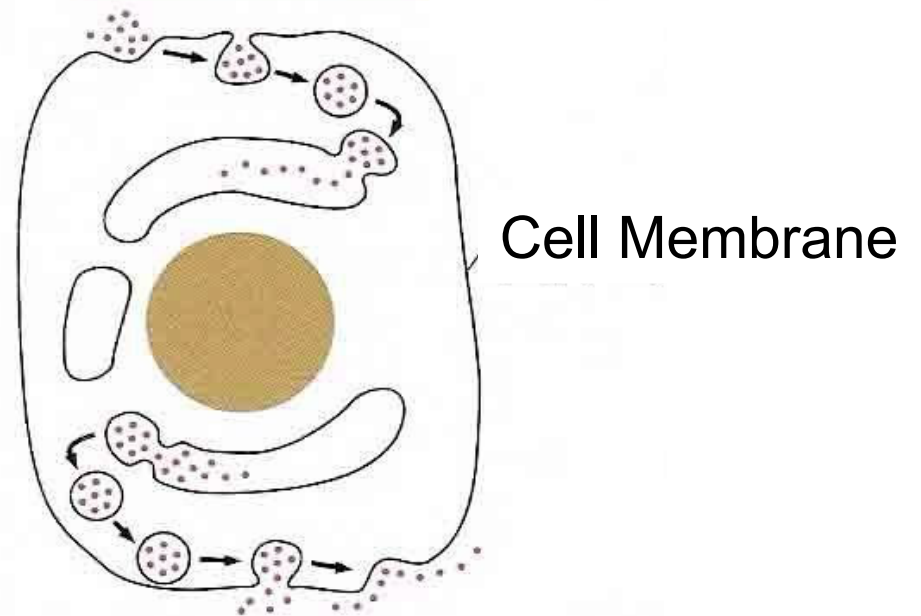
Stacks of flattened membrane-bound sacs, often near the nucleus

Receives proteins from the ER in vesicles and modifies them
e.g. insulin



Intracellular membranes form a network that enables regulated communication between the extracellular environment and cellular structures

Entry: endocytosis

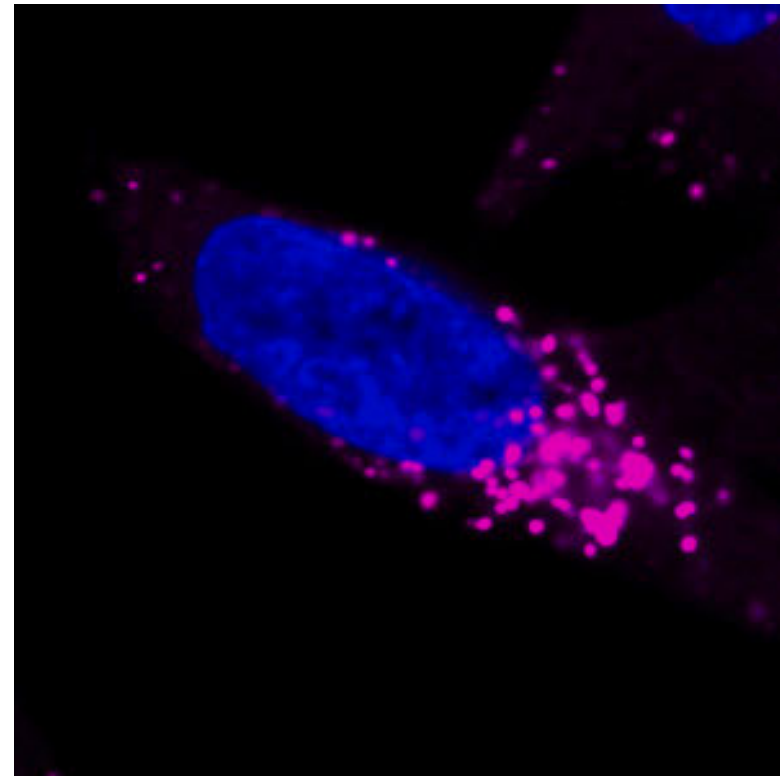
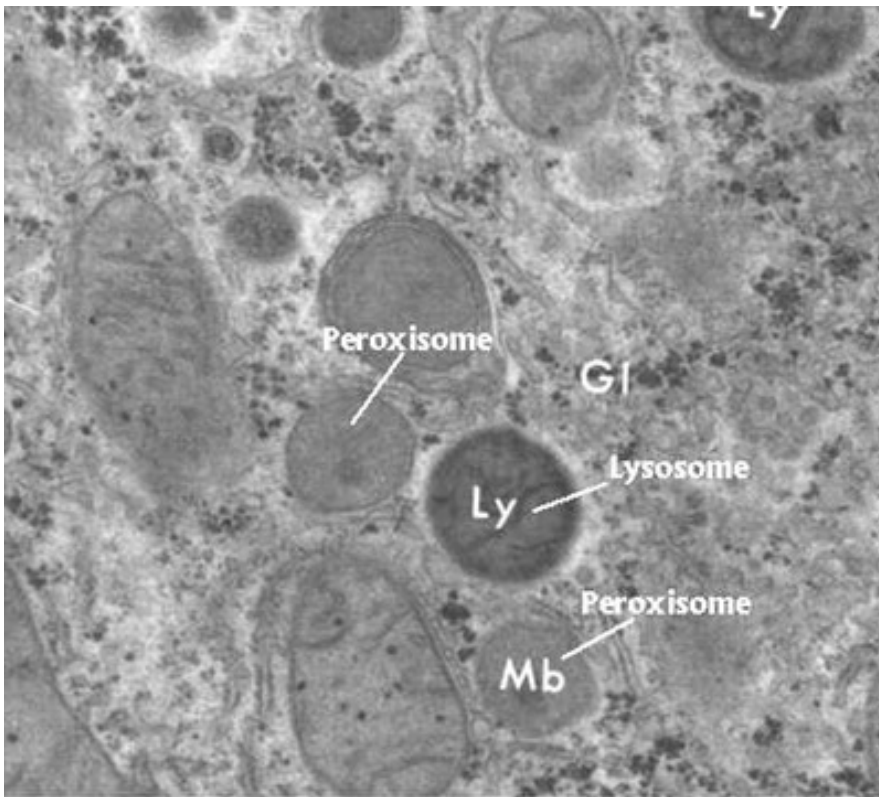


Exit: exocytosis

Lysosome

Single membrane

Cellular digestion: breaks down biomolecules from outside and inside the cell

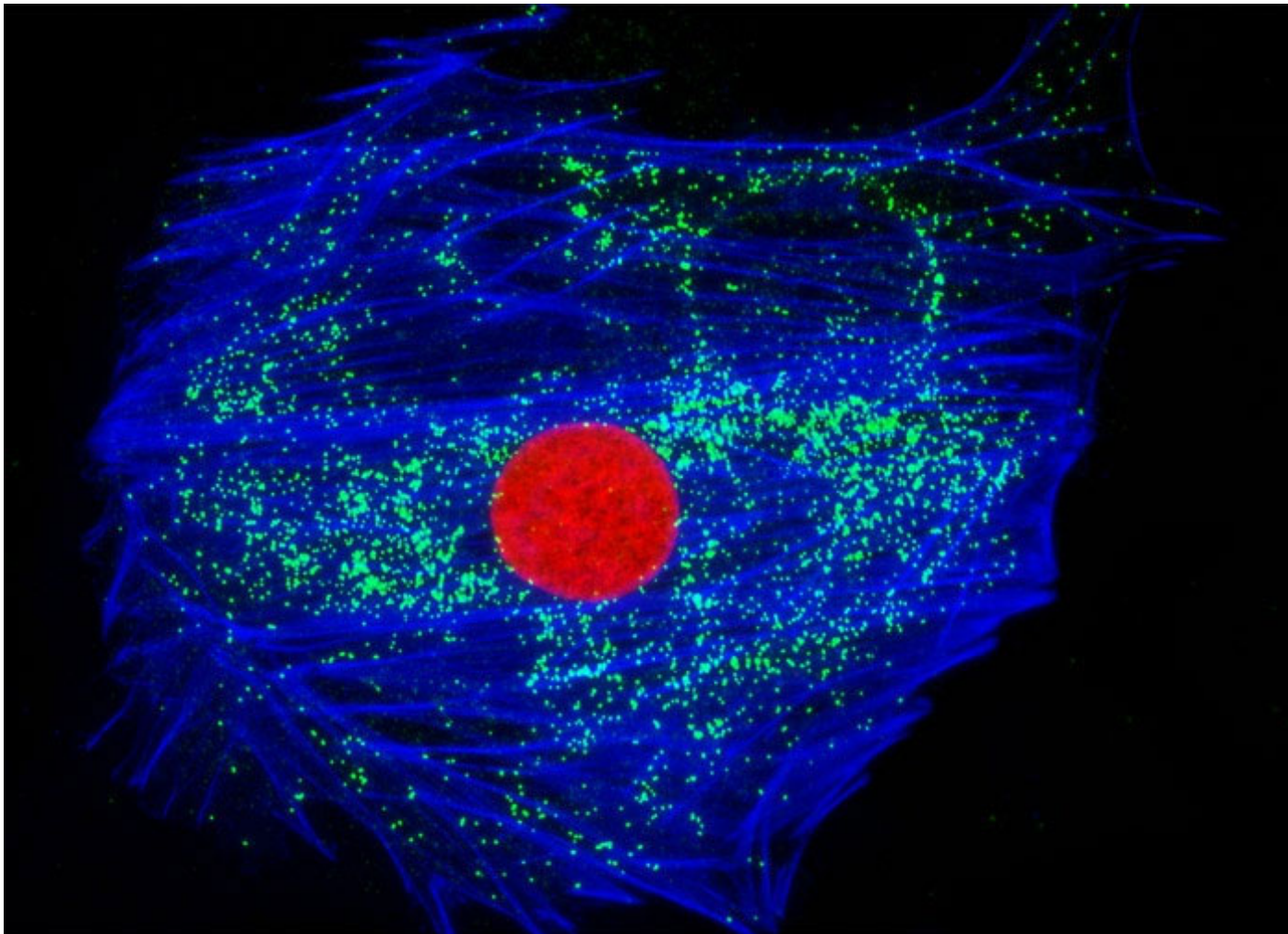


Peroxisome

Small organelles (0.3–1.5 μm), enclosed by a single membrane

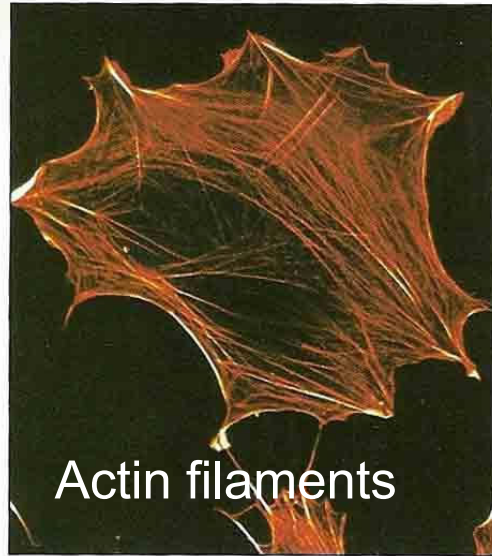
Contains enzymes that catalyse the breakdown of hydrogen peroxide (H_2O_2), including catalase; important for protection against oxidative stress

Other biosynthetic and oxidative reactions, mainly involving lipids



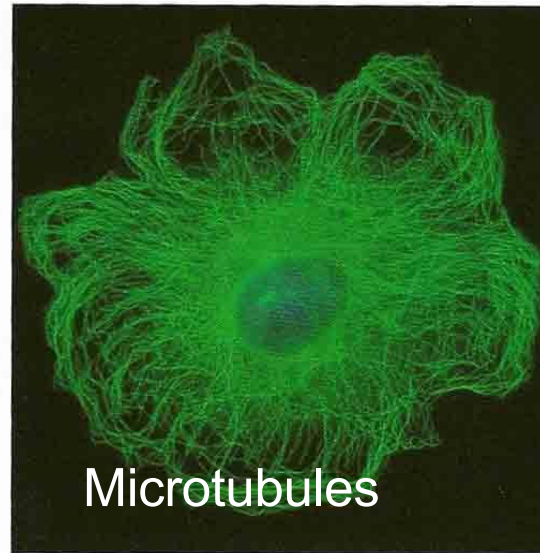
Cytoskeleton

Filaments that help determine cell shape, cell movement, transport of substances and vesicles within the cell, and cell division

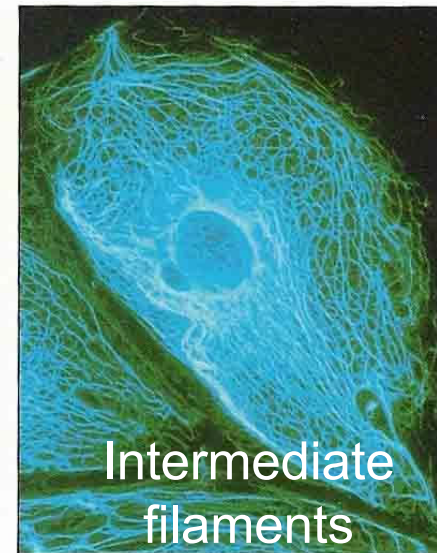


(A)

50 μm

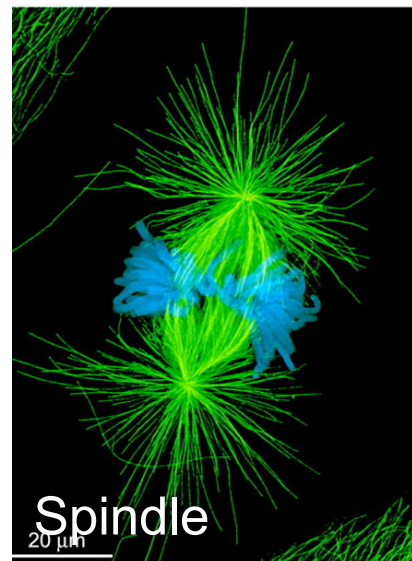
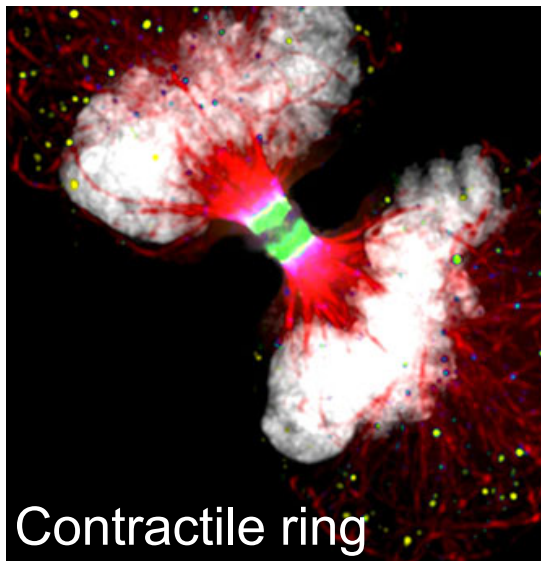


(B)



(C)

Interphase
(interphase)



Cell division

Model organisms

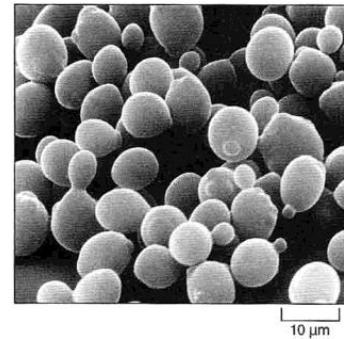
Advantages:

- Inexpensive, easy and rapid culture under controlled, simple laboratory conditions
- Short generation time
- Less complex genome
- Suitable for genetic analysis
- Simpler structure and function
- Fewer (or no) ethical concerns in experimentation

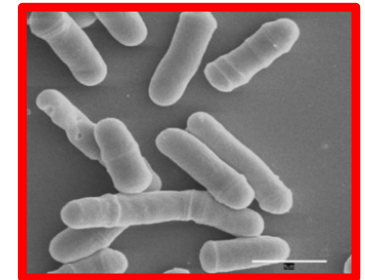
The bacterium *Escherichia coli*



The fungus *Saccharomyces cerevisiae*



Schizosaccharomyces pombe



The plant *Arabidopsis thaliana*



The nematode *Caenorhabditis elegans*



The insect *Drosophila melanogaster*

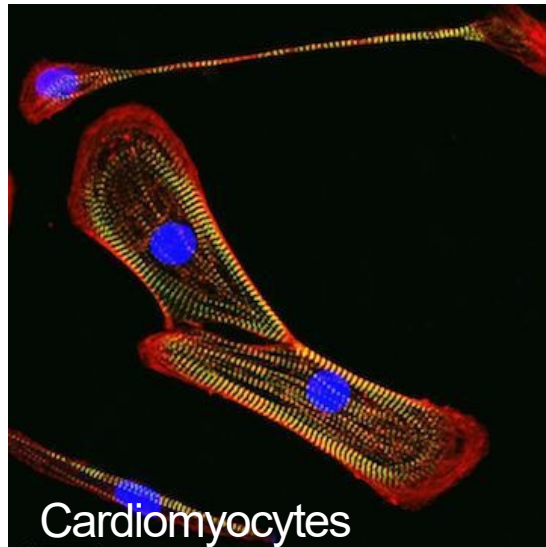


The mouse *Mus musculus*

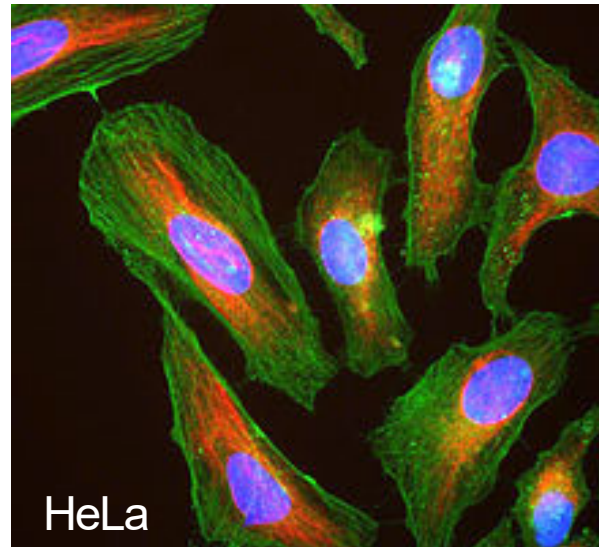
- Model organisms are research tools for understanding the fundamental processes of life.
- They are useful experimental models for identifying disease-related genes and testing treatments.

Human cells in culture

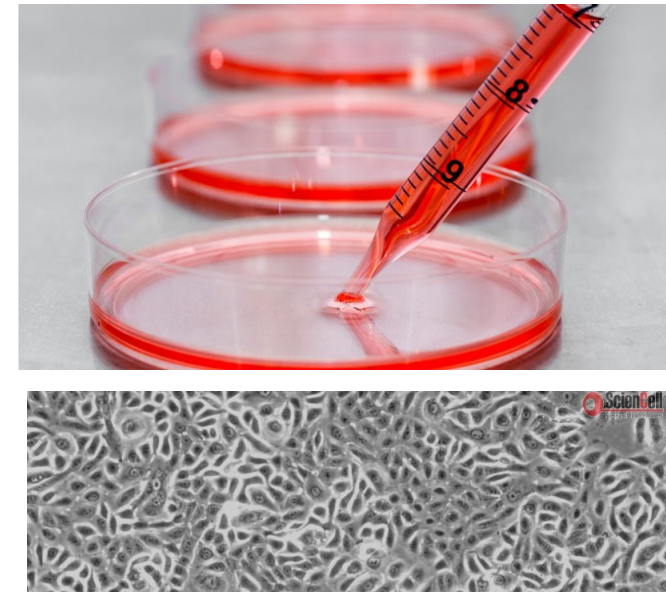
Normal cells



Cancer cells



Cell culture



Human populations and diseases



For the tutorial

1. Review the lecture slides and the main points and terminology in the textbook
2. *On the course eClass page, under Links (on the left), watch the animation Inner Life of a Cell (music version), and if you are keen to learn more, watch the full narrated version*

See

1. How to... read, take notes, follow lectures and prepare for exams