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Cell evolution

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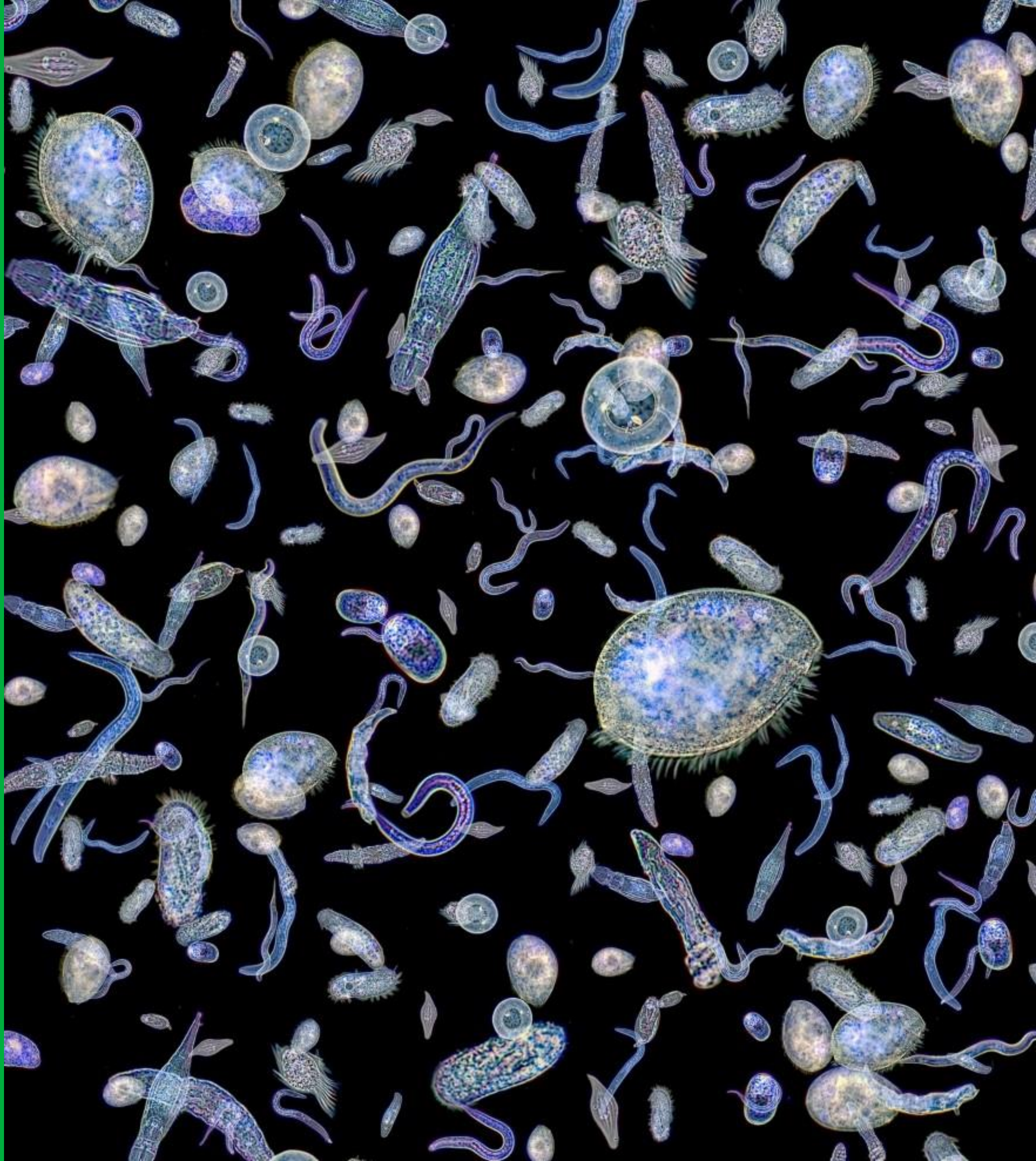
Department of Experimental Biology



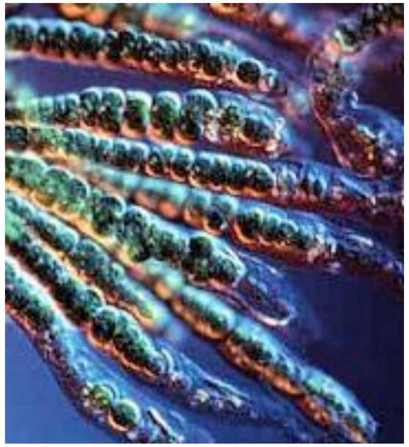
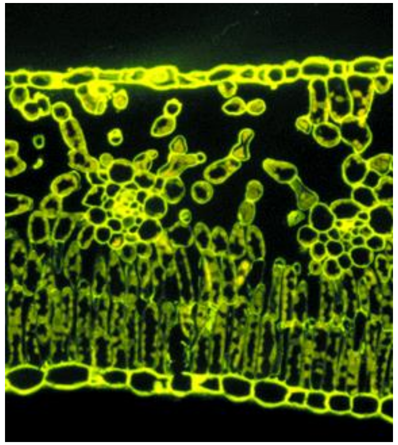
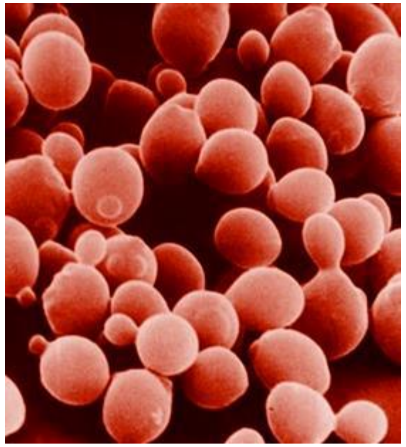
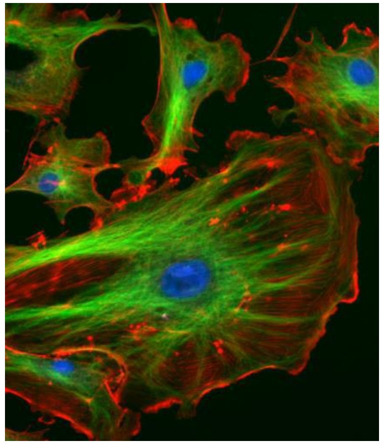
Outline

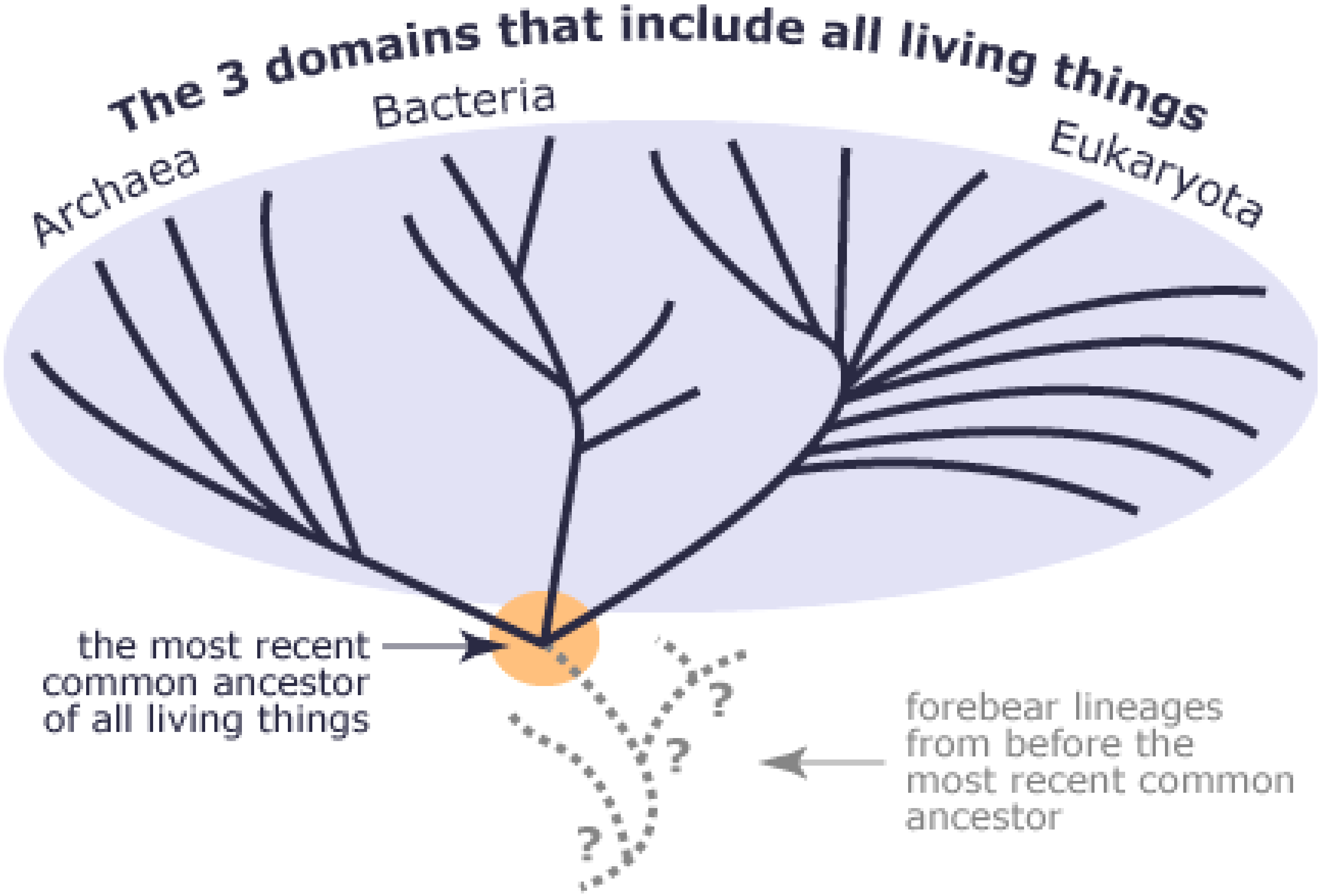
- From simple compounds to the world of RNA, DNA and proteins
- RNA world
- From primordial soup to the first cells
- From prokaryotes to eukaryotes
- Synthetic biology

Cell evolution by natural selection

Last universal cellular ancestor (LUCA)

- Unicellular organism that is ancestral to all current cellular forms of life
- Natural selection requirements: genetic variability, selection of genotypes underlying the highest fitness (reproductive success)



The 3 domains that include all living things
Archaea
Bacteria
Eukaryota
the most recent common ancestor of all living things
?
?
?
forebear lineages from before the most recent common ancestor

From simple compounds to the world of RNA, DNA and proteins

Origin of first complex organic compounds

Alexander Ivanovich Oparin (1894–1980)

- Russian biochemist (Moscow State University)
- **Theory of the origin of life** (1922, in Russian):
  - Strongly reducing atmosphere on early Earth (methane, ammonia, hydrogen and water vapor)
  - Simple carbon compounds and inorganic molecules could react to form “building blocks” – nucleotides, amino acids
  - **Gradual chemical evolution from the primordial soup**: accumulation of these “building blocks” in the water facilitated their further reactions into polymers (with energy of lightning or sun) and their assembly into units/structures capable of self-replication

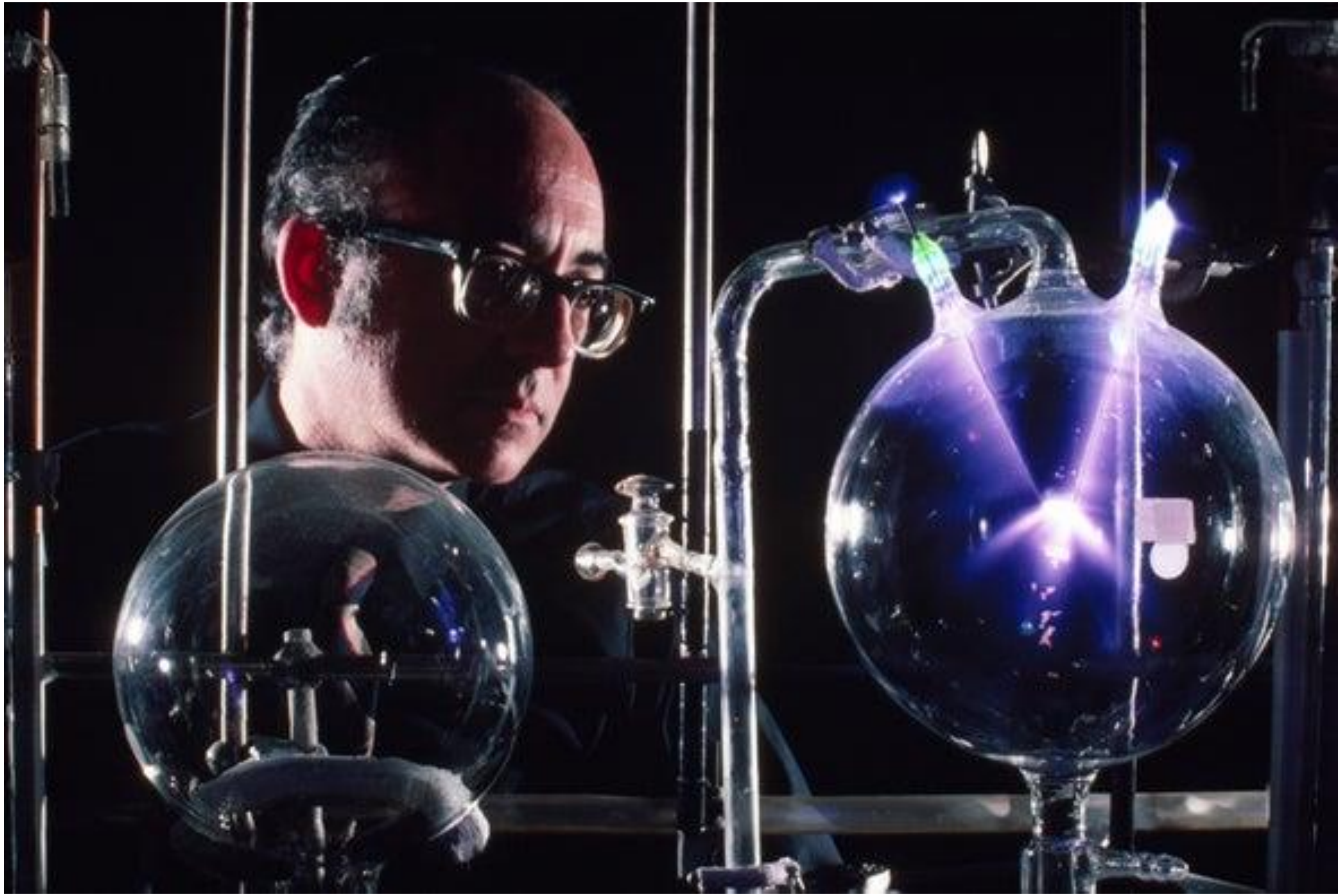
Origin of first complex organic compounds

John Burdon Sanderson Haldane (1892–1964)

- British biologist and mathematician
- Proposed a similar theory: The origin of life (1929, in English)
  - Oparin’s work published in English in 1936

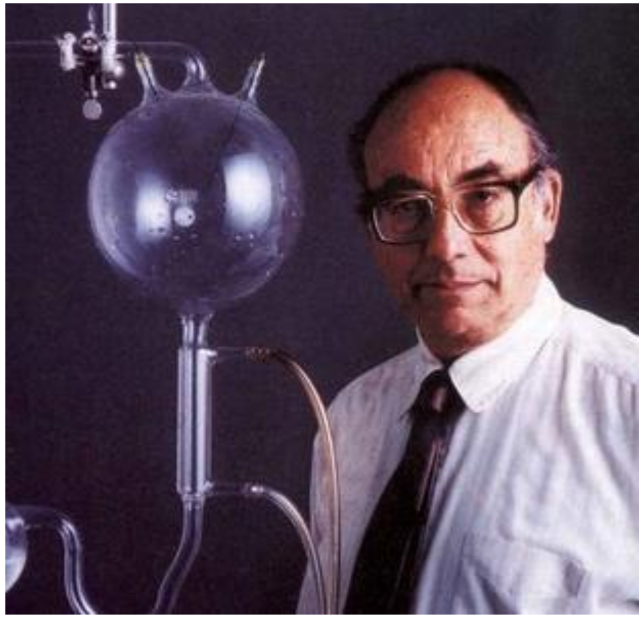
Oparin-Haldane hypothesis

- Cells self-organized from a primordial soup



Miller (Miller-Urey) experiment

- **1953: first experimental evidence of possible origin of life from non-living matter**
- **Stanley Miller** and **Harold Urey**



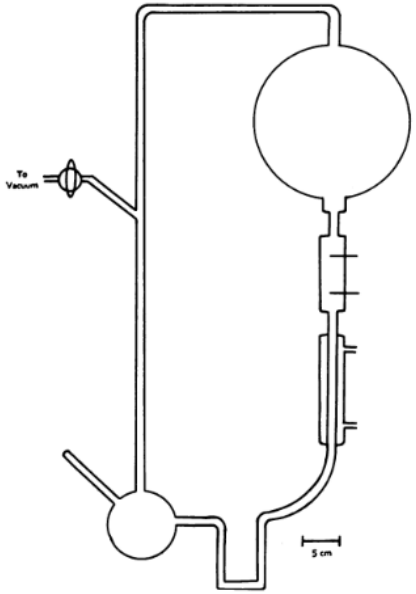


Fig. 1.

A Production of Amino Acids Under Possible Primitive Earth Conditions

Stanley L. Miller[1,2]

G. H. Jones Chemical Laboratory, University of Chicago, Chicago, Illinois

The idea that the organic compounds that serve as the basis of life were formed when the earth had an atmosphere of methane, ammonia, water, and hydrogen instead of carbon dioxide, nitrogen, oxygen, and water was suggested by Oparin (*1*) and has been given emphasis recently by Urey (*2*) and Bernal (*3*).

In order to test this hypothesis, an apparatus was built to circulate CH_4, NH_3, H_2O, and H_2 past an electric discharge. The resulting mixture has been tested for amino acids by paper chromatography. Electrical discharge was used to form free radicals instead of ultraviolet light, because quartz absorbs wavelengths short enough to cause photo-dissociation of the gases. Electrical discharge may have played a significant role in the formation of compounds in the primitive atmosphere.

The apparatus used is shown in Fig. 1. Water is boiled in the flask, mixes with the gases in the 5-l flask, circulates past the electrodes, condenses and empties back into the boiling flask. The U-tube prevents circulation in the opposite direction. The acids

During the run the water in the flask became noticeably pink after the first day, and by the end of the week the solution was deep red and turbid. Most of the turbidity was due to colloidal silica from the glass. The red color is due to organic compounds adsorbed on the silica. Also present are yellow organic compounds, of which only a small fraction can be extracted with ether, and which form a continuous streak tapering off at the bottom on a one-dimensional chromatogram run in butanol-acetic acid. These substances are being investigated further.

At the end of the run the solution in the boiling flask was removed and 1 ml of saturated $HgCl_2$ was added to prevent the growth of living organisms. The ampholytes were separated from the rest of the constituents by adding $Ba(OH)_2$ and evaporating *in vacuo* to remove amines, adding H_2SO_4 and evaporat-

[1] National Science Foundation Fellow, 1952–53.
[2] Thanks are due Harold C. Urey for many helpful suggestions and guidance in the course of this investigation.

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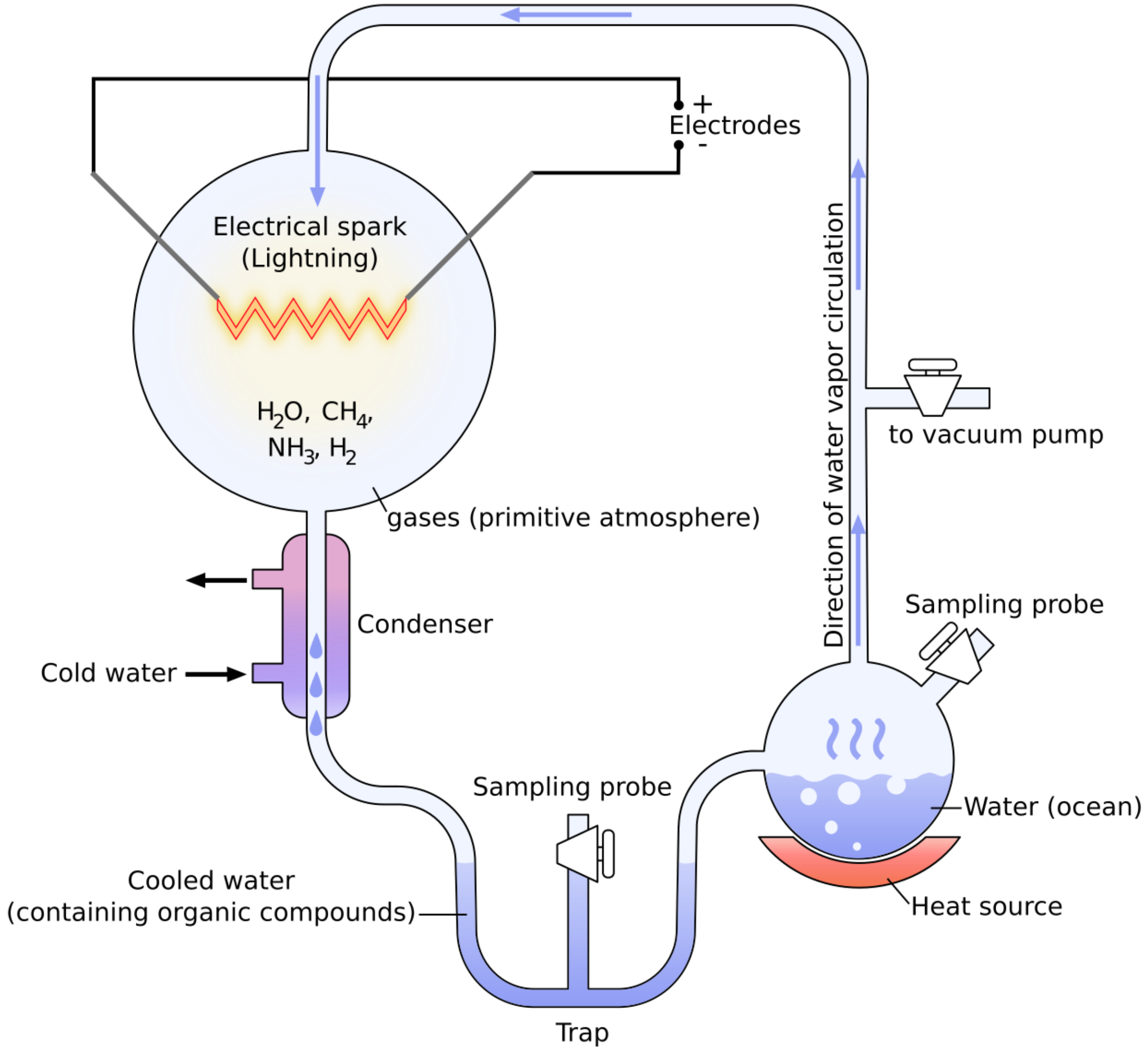
Miller experiment

- Simulated the conditions thought at the time to be present on the early Earth
- **Mixture of gases**: methane, ammonia, hydrogen and water vapor
- **Electrical sparks** (lightnings)
- Water condensation and analysis of the solution



Results of Miller experiment:

- Hydrogen cyanide, formaldehyde
- Formic, lactic, acetic, uric acids
- **Amino acids**
  - 5 reported initially
  - **23** when the original samples re-analyzed in 2008

- Many following variants: **purines and pyrimidines, sugars**

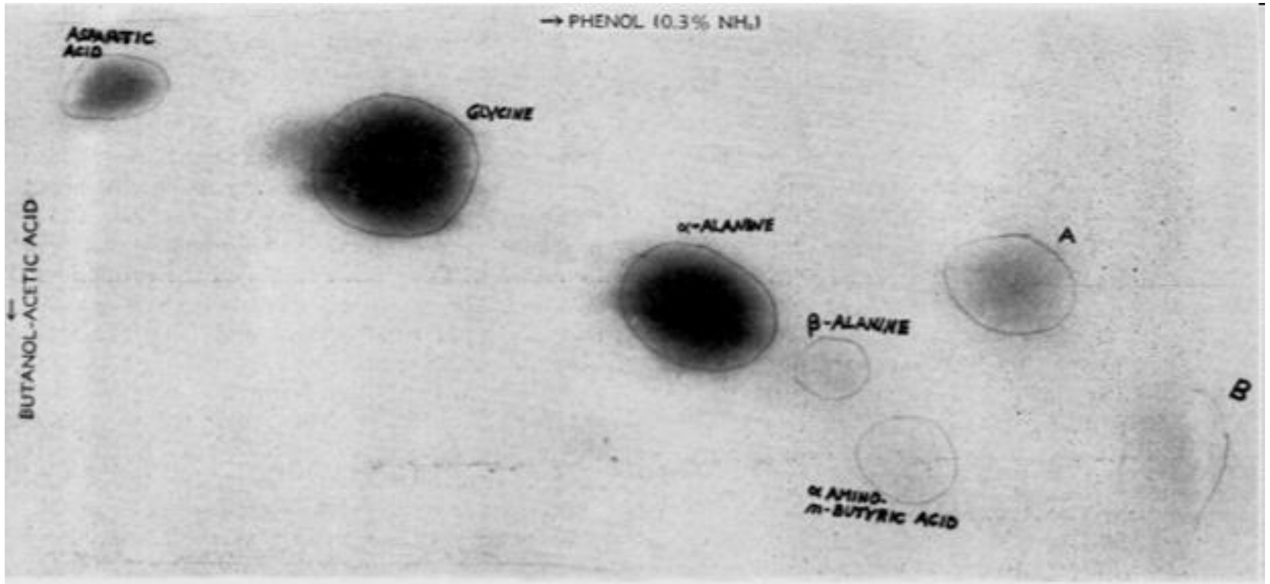
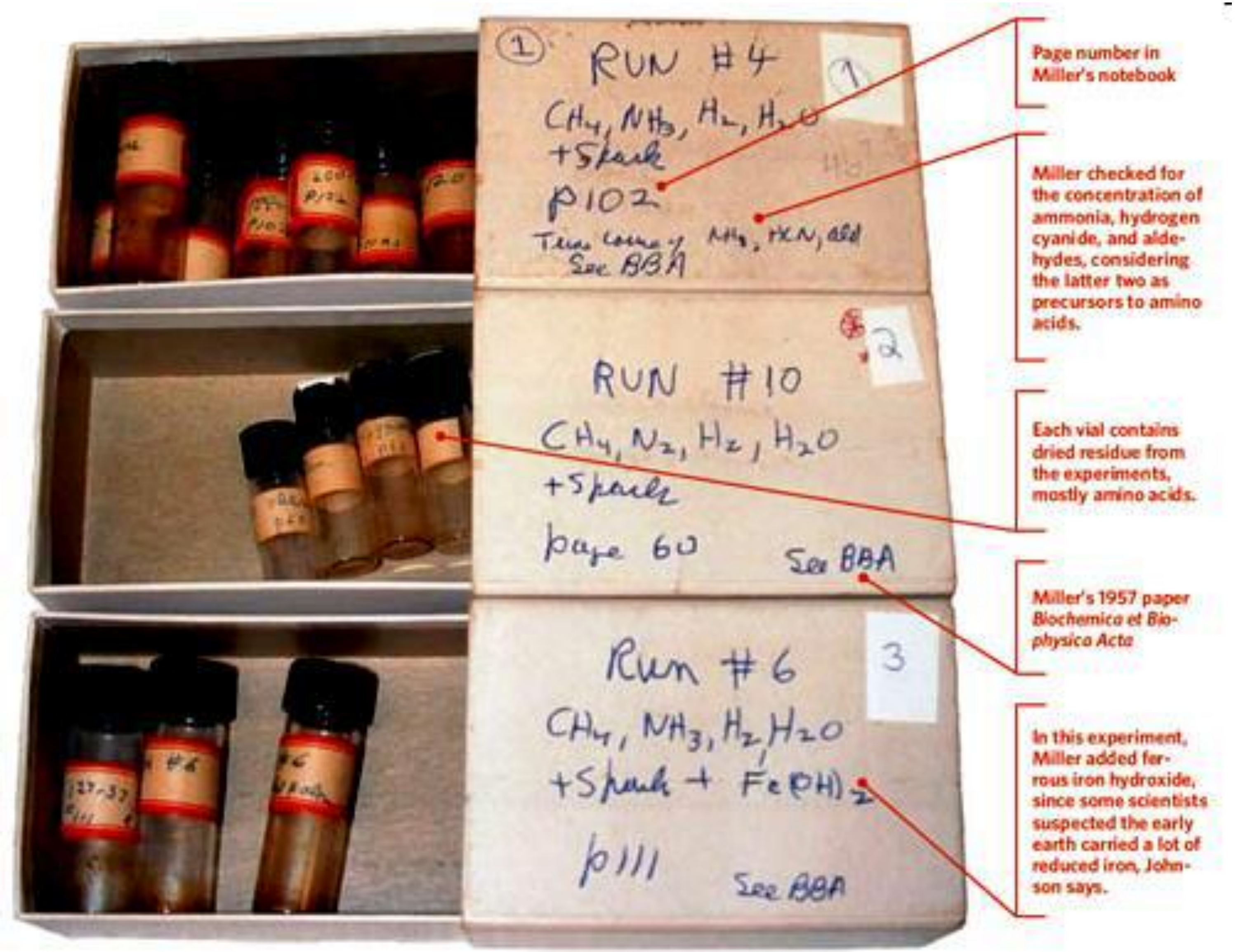


Fig. 2.



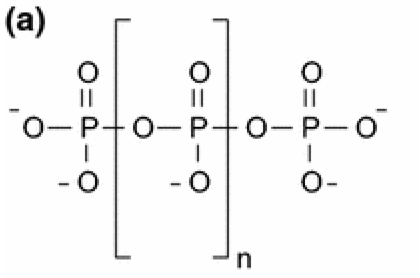
vs.

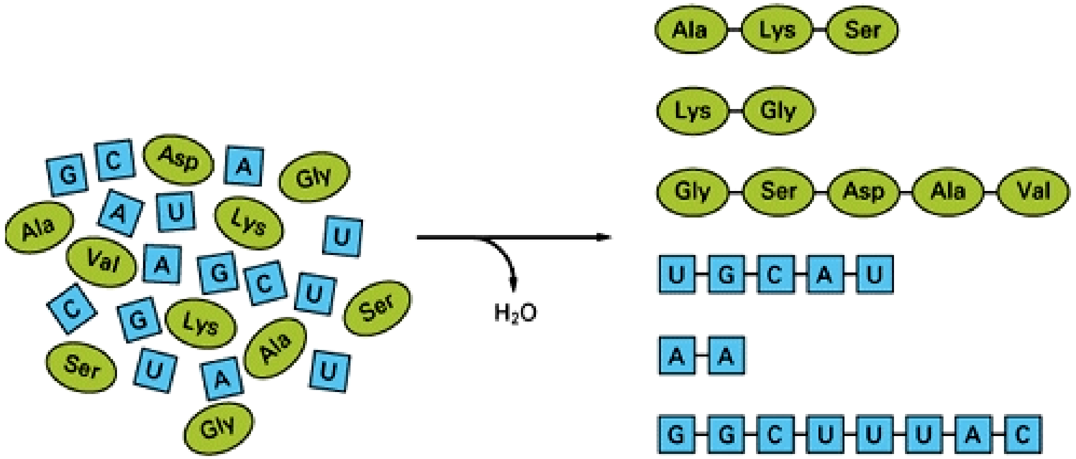
Extraterrestrial organic compounds

- Organic compounds are common in space
- Purines and pyrimidines found in meteorites

Formation of polymers from organic monomers

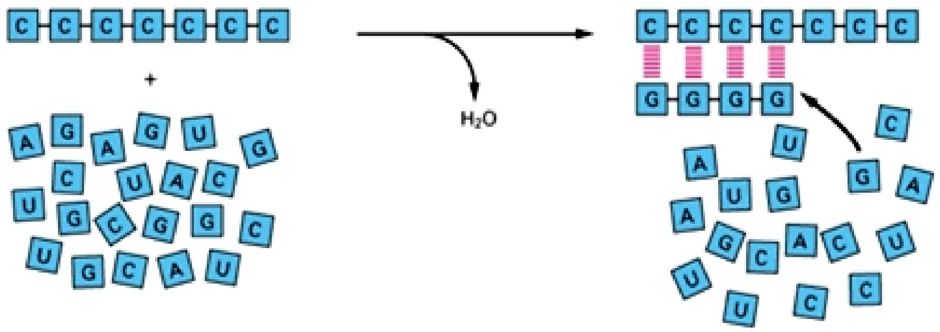
- Heating of the organic monomers
- Catalytic activity of highly concentrated inorganic polyphosphates and other compounds: polyanionic scaffold to assemble macromolecules
- **Selection for autocatalytic activity, self-replication**

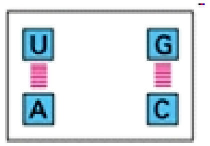


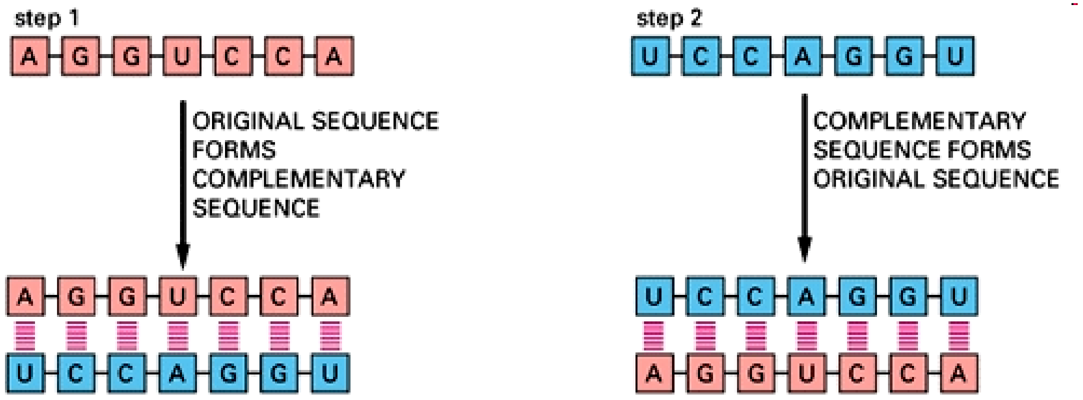


Polynucleotides – templates for self-replication

– Hydrogen bonds – base pairing





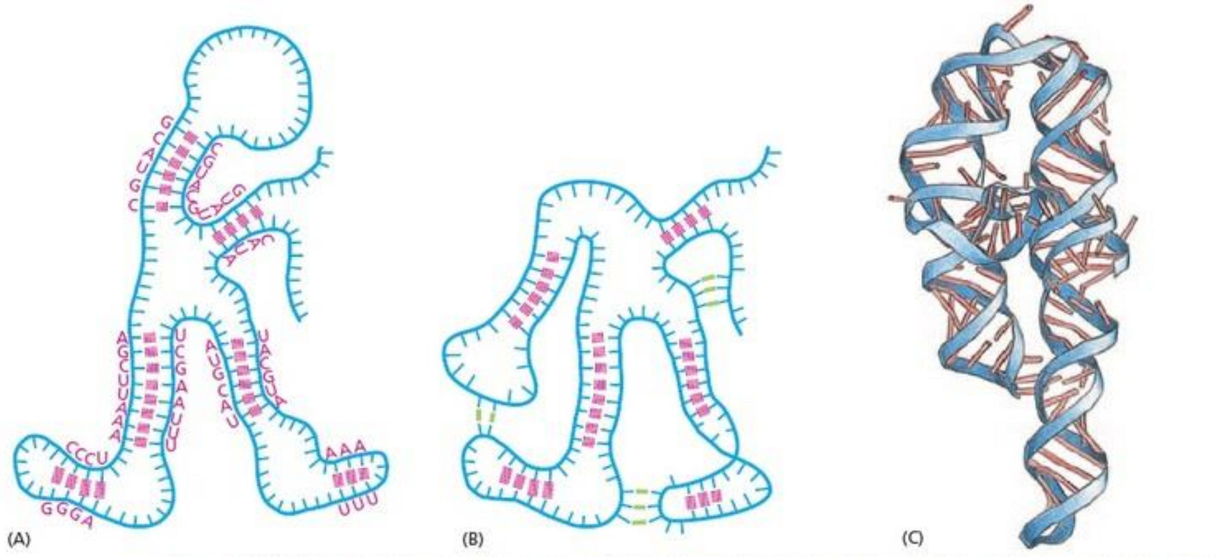


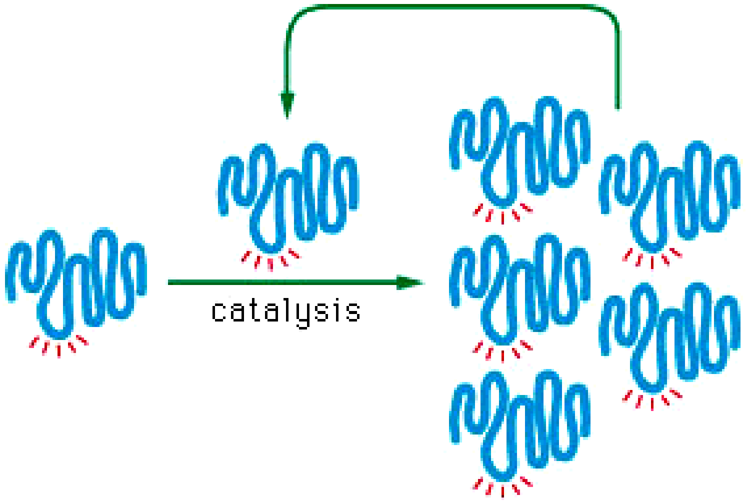
Nucleic acid or protein?

Which came first, the chicken or the egg?

RNA world

- 2 key features of RNA from the evolution perspective:
- **Encodes information** (sequence of nucleotides)
- **Exert different functions** (tertiary structure) **including catalysis**

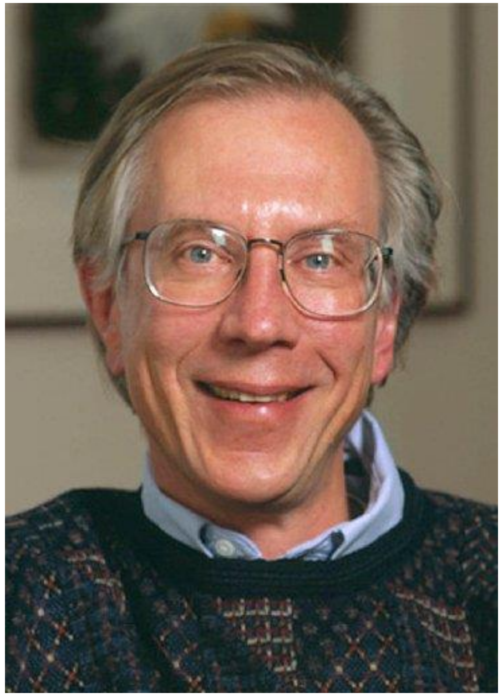




Discovery of ribozymes

- Ribonucleic acid enzymes – RNAs with catalytic functions
- **1989 Nobel Prize in Chemistry**

Mendel Genetics Conference
21 July 2022, Brno



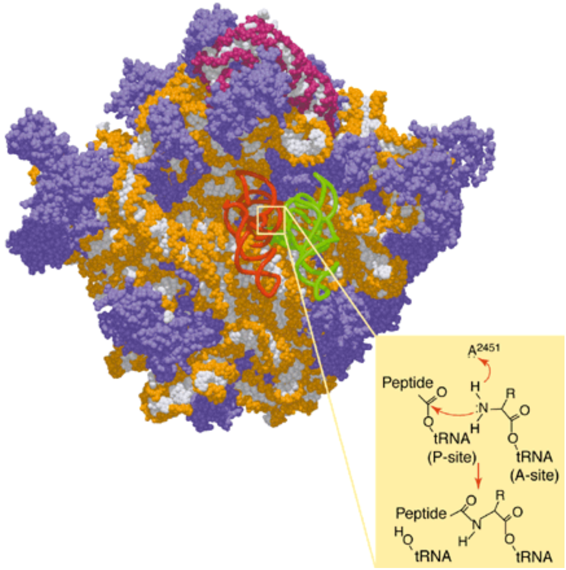
Thomas R. Cech

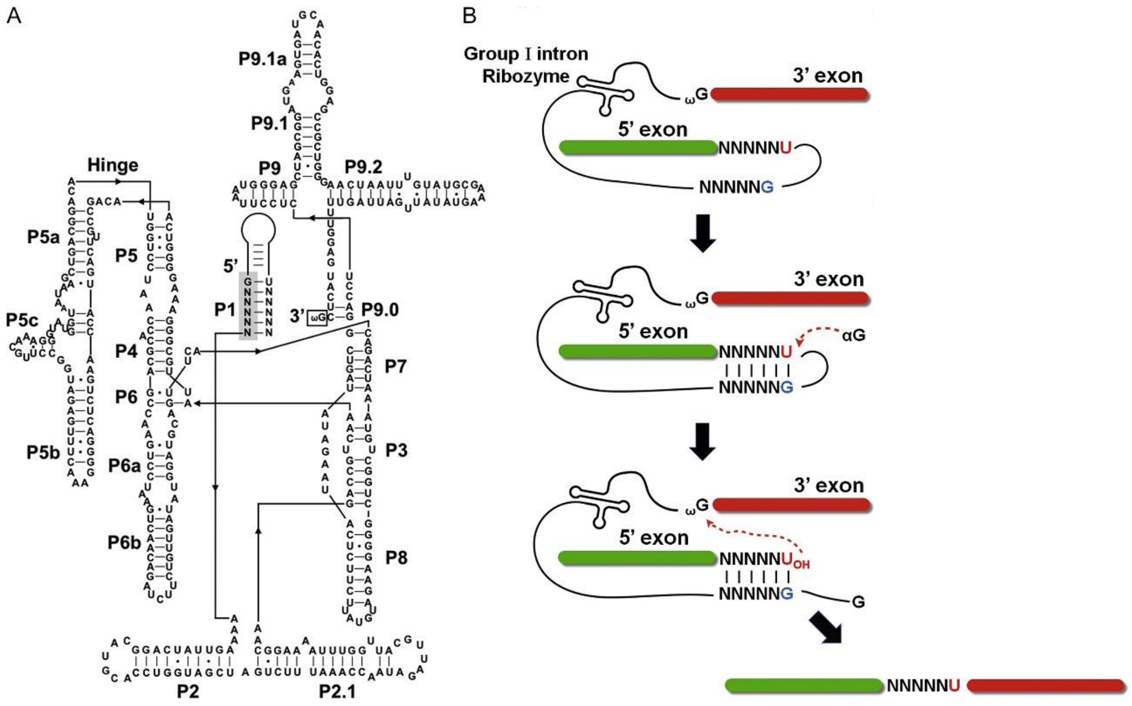
Interesting interview about breaking the paradigm

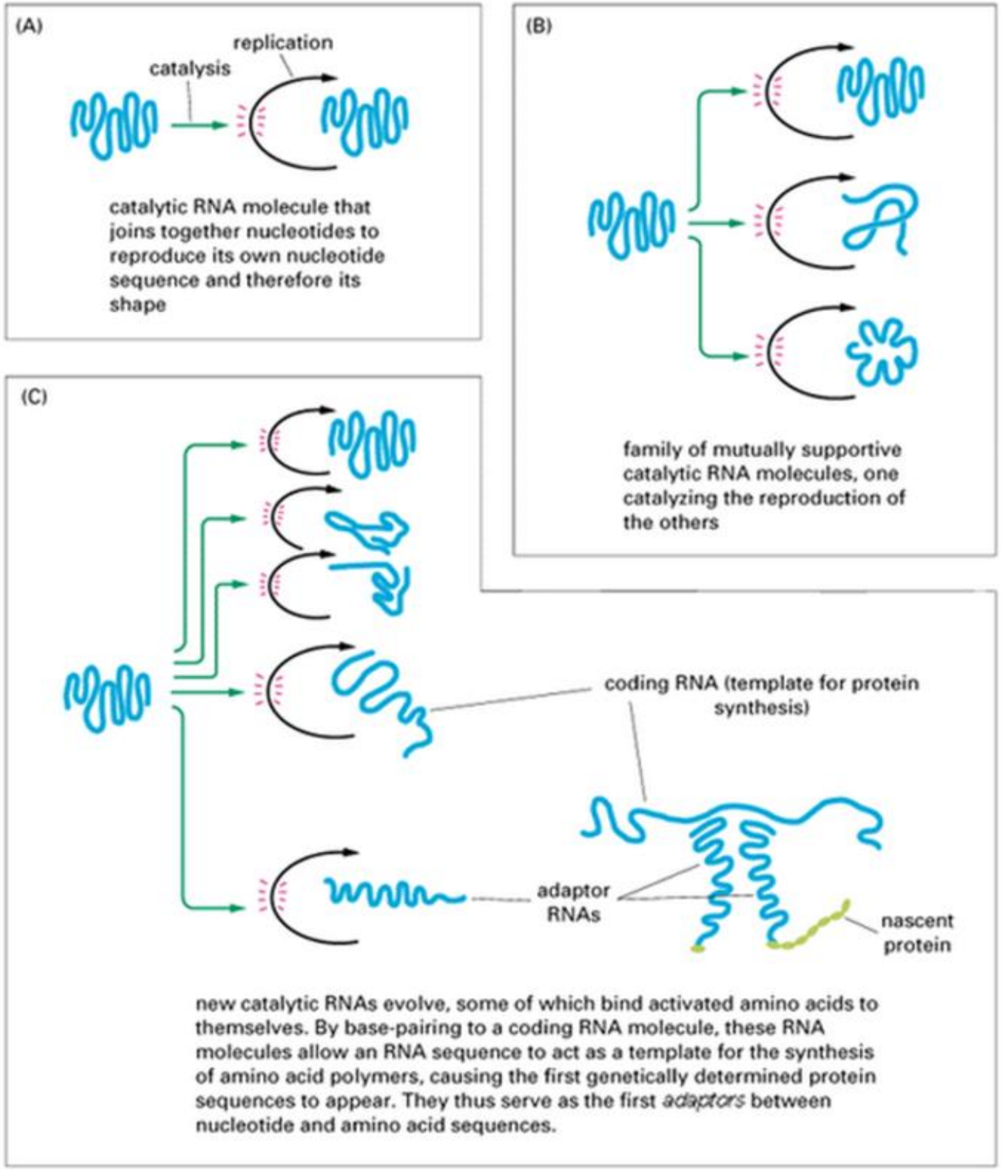
Sidney Altman

Examples of ribozymes

- Self-splicing introns
- **Peptidyl transferase activity of rRNA in ribosomes**



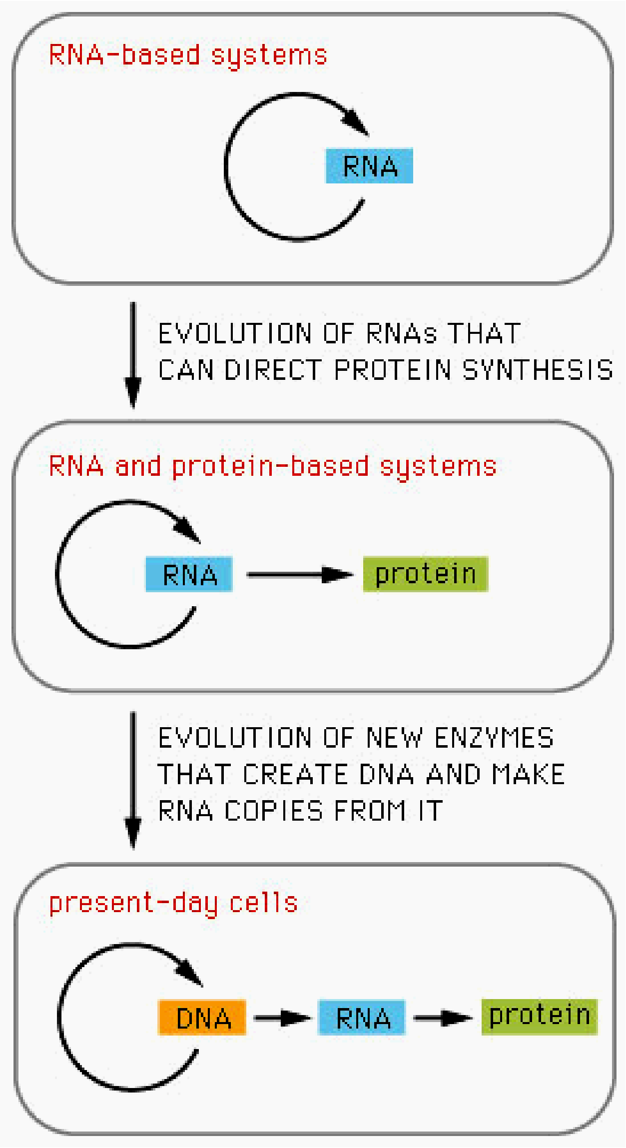




3 essential (and hypothetical) steps in transition from RNA to nucleic acid-protein world

Ribozyme

1. Self-replication of RNA molecule
2. One RNA molecule catalyzes replication of other molecules
3. Evolution of primitive protein synthesis and genetic code



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A prebiotically plausible scenario of an RNA–peptide world

Felix Müller, Luis Escobar, Felix Xu, Ewa Węgrzyn, Milda Nainytė, Tynchtyk Amatov, Chun-Yin Chan, Alexander Pichler & Thomas Carell

Nature **605**, 279–284 (2022) | Cite this article

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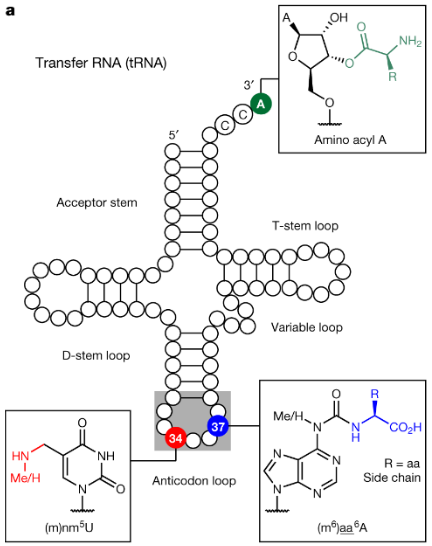
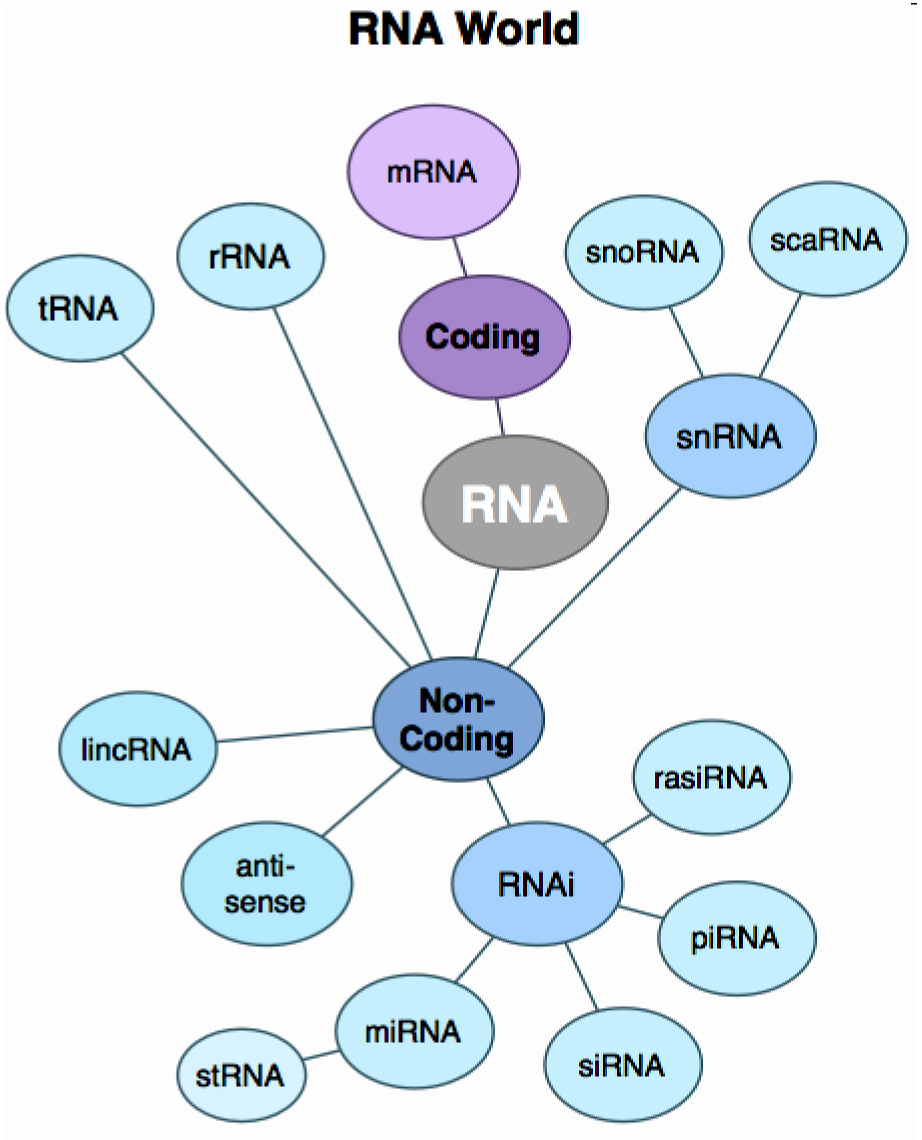


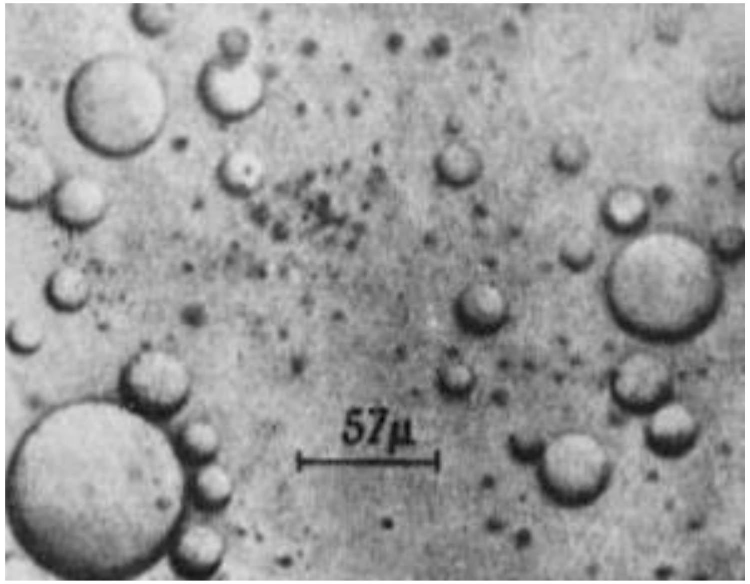
- Non-canonical RNA bases (nowdays in tRNA and rRNA) can bind amino acids and establish peptide synthesis directly on RNA
- Potential origin of ribosome-centered translation


RNA World
mRNA
rRNA
tRNA
Coding
snoRNA
scaRNA
snRNA
RNA
Non-Coding
lincRNA
rasiRNA
anti-sense
RNAi
piRNA
miRNA
stRNA
siRNA

From primordial soup to the first cells

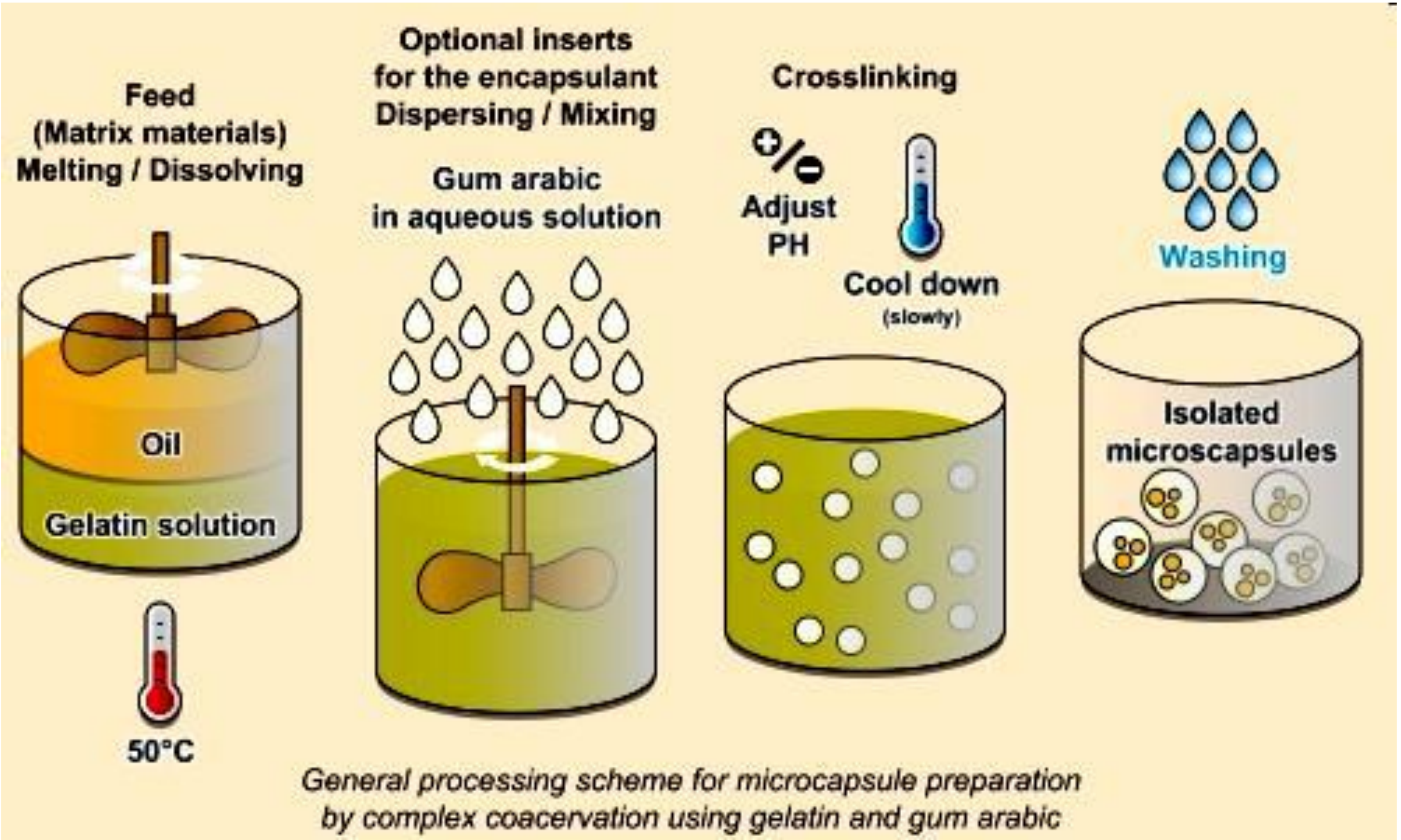
Coacervates

– **Small droplets (condensates = dense phase) of biopolymers** in a dilute phase (generally water in cells)
– Formed through **liquid-liquid phase separation**
– Hendrik G. Bungenberg de Jong



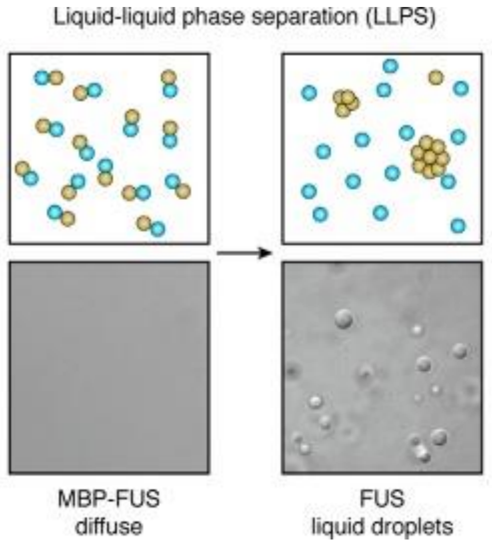
Coacervate droplets formed by interaction between gelatin and gum arabic

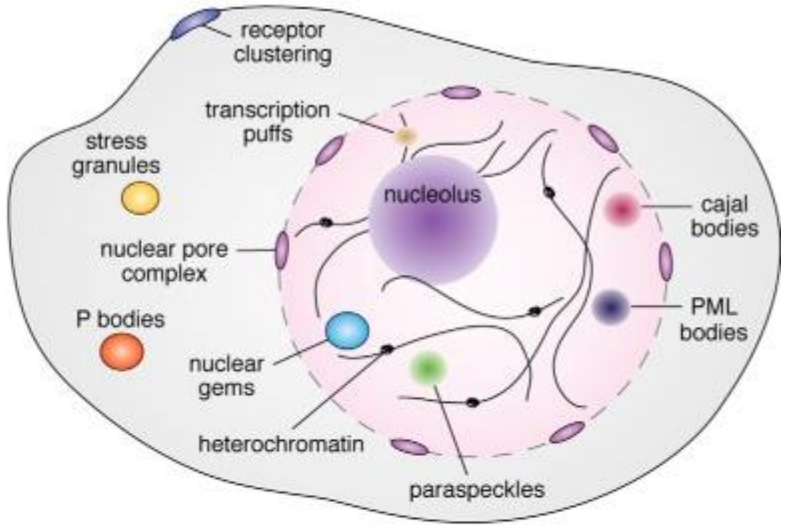
Coacervation process



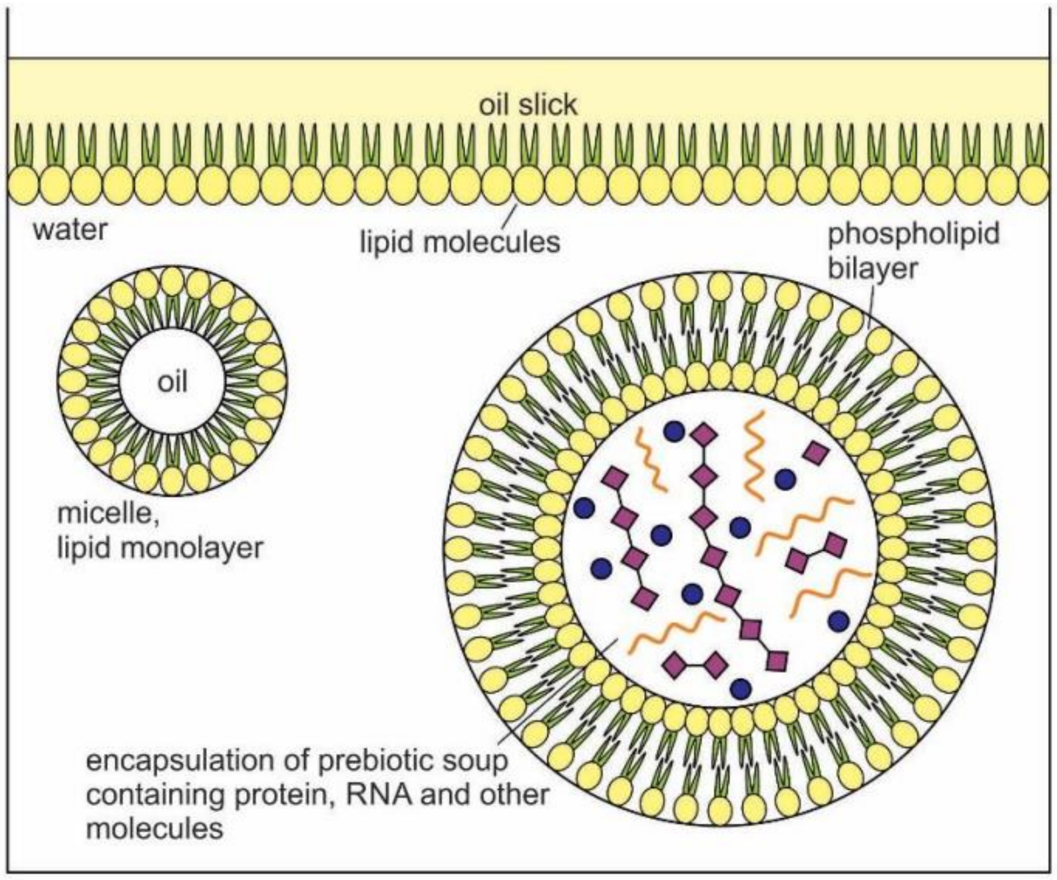
Membraneless organelles

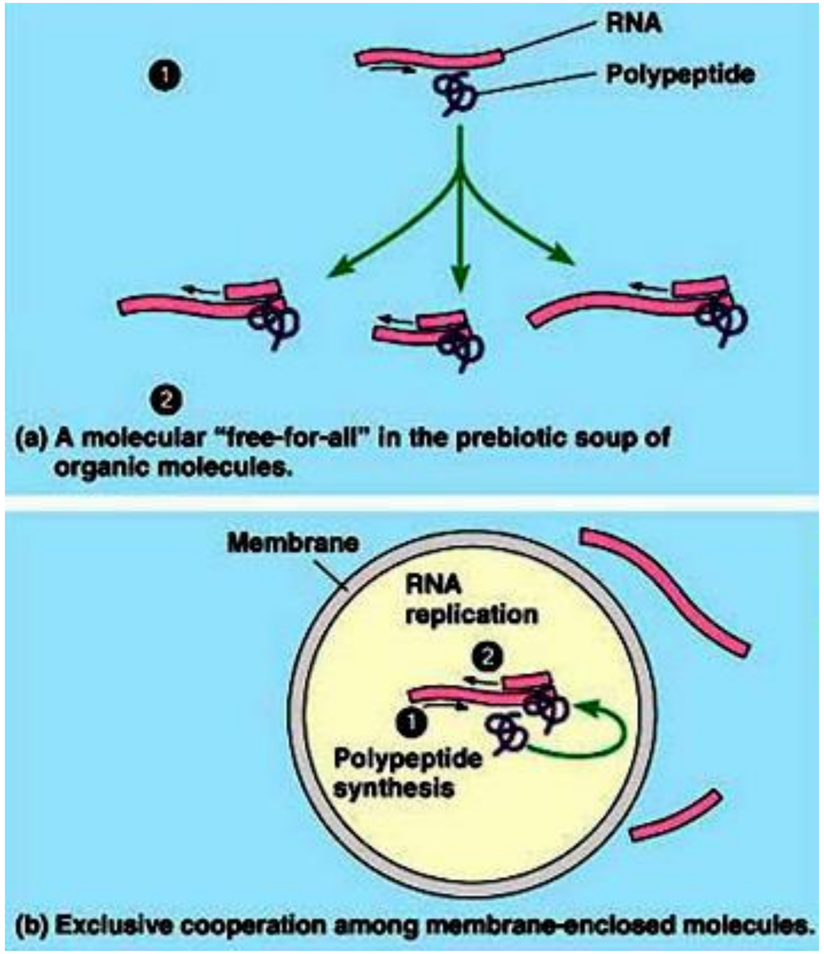
- A. Oparin: *life originated as coacervate drops of organic materials*
- **Membraneless organelles: liquid-like compartments** arising through liquid–liquid phase separation

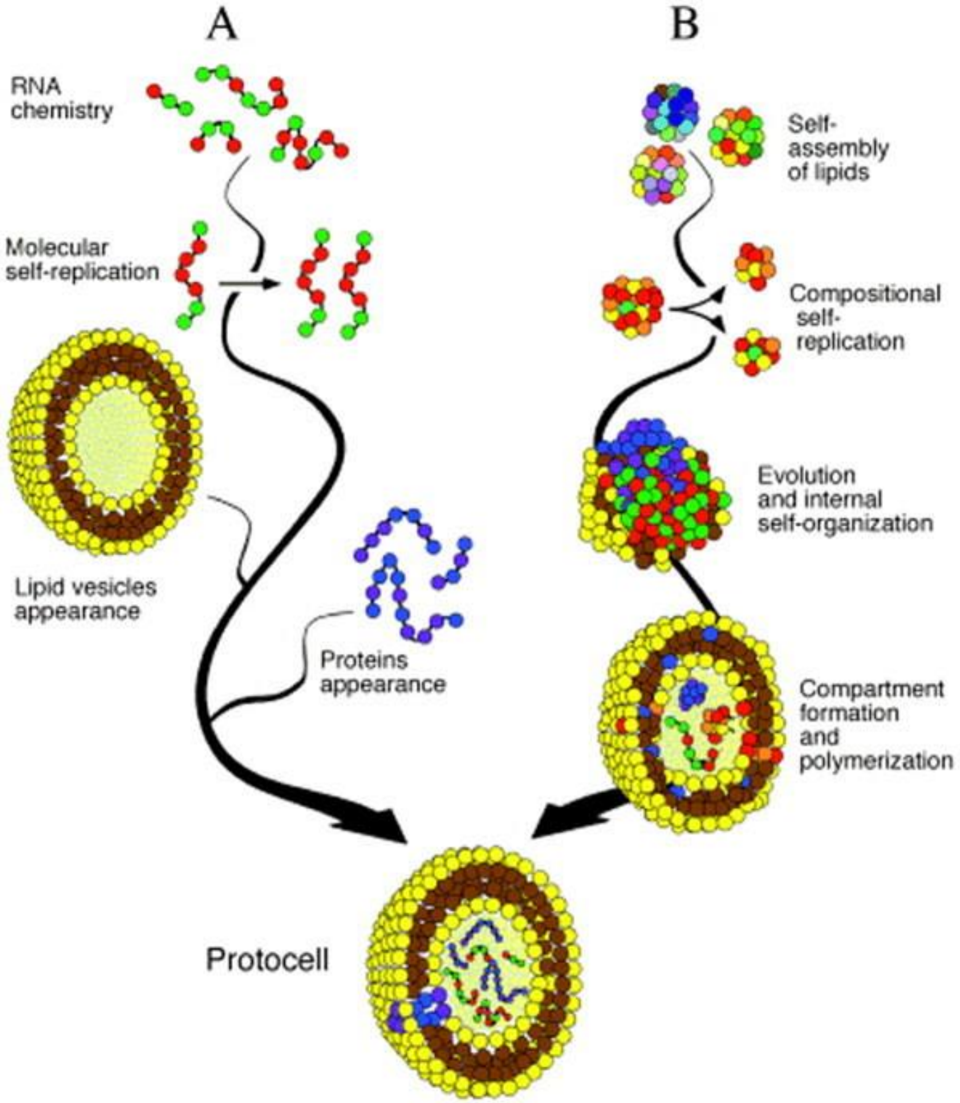




Encapsulation – formation of a protocell



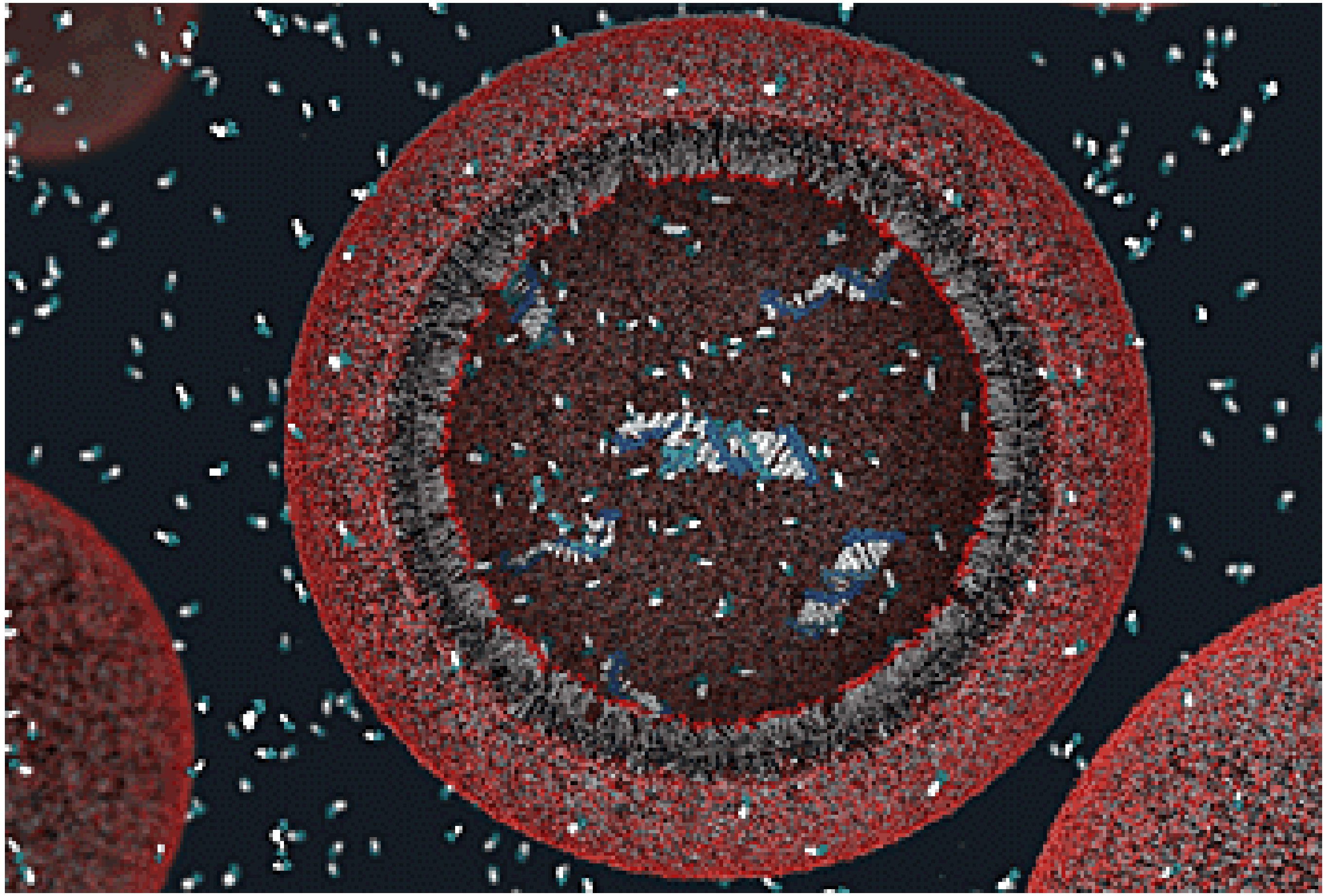


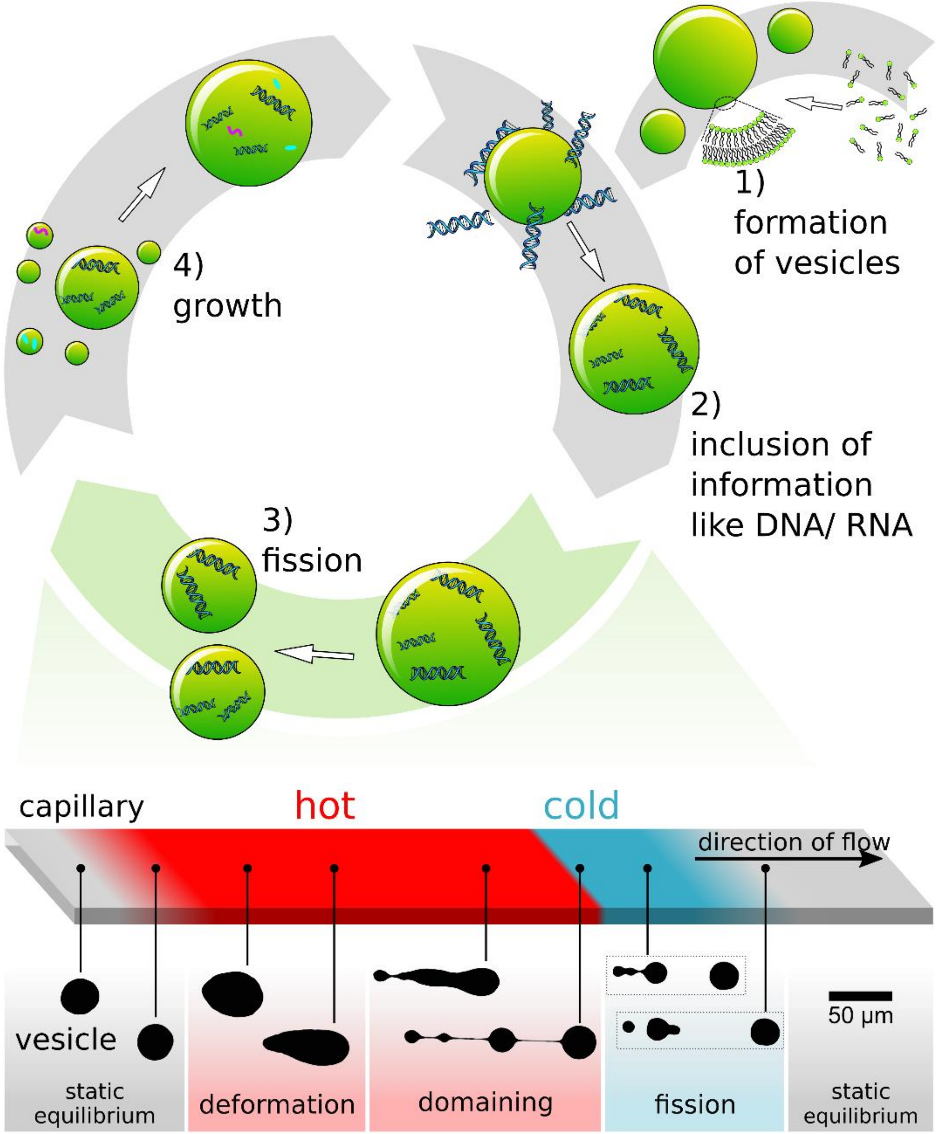


Two ways of protocell assembly from the primordial soup

A. Biopolymer first
B. Lipid world

Division by fission





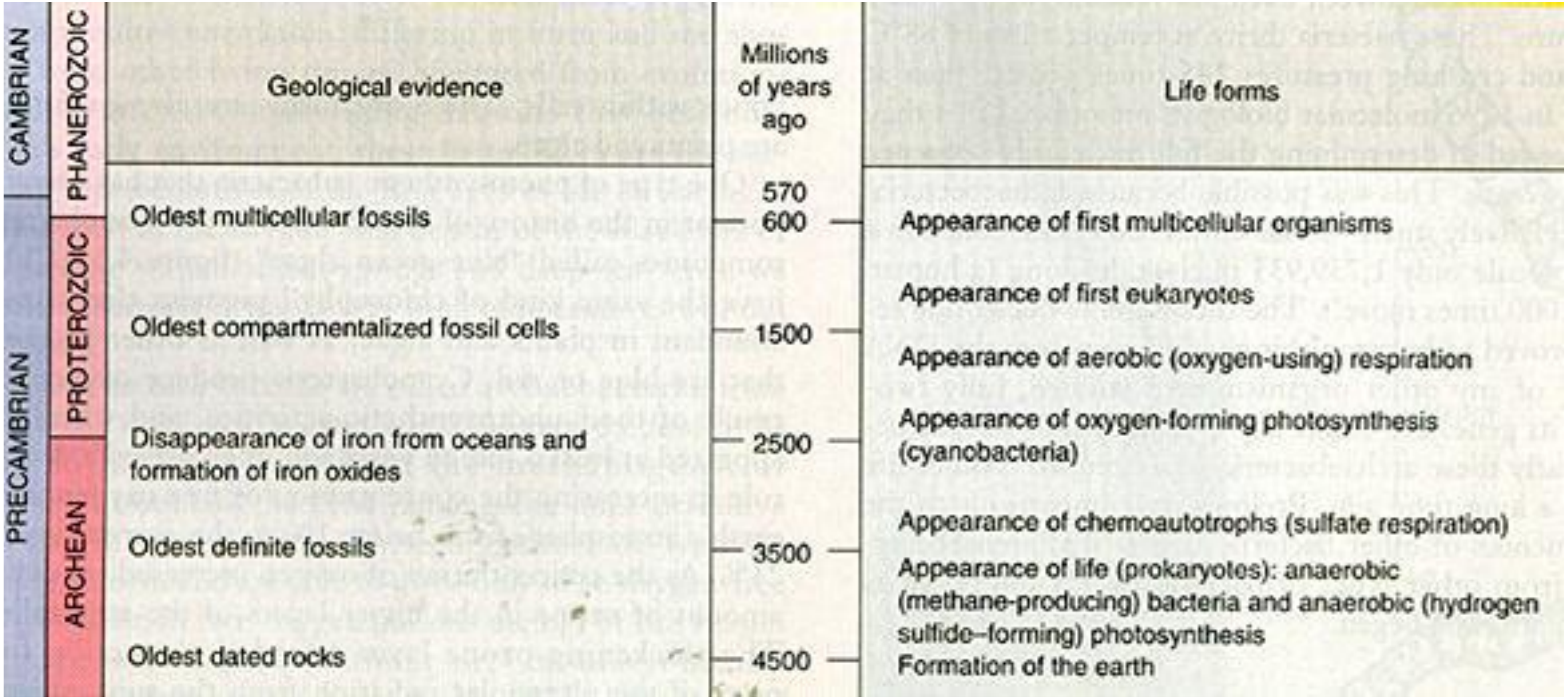
From prokaryotes to eukaryotes

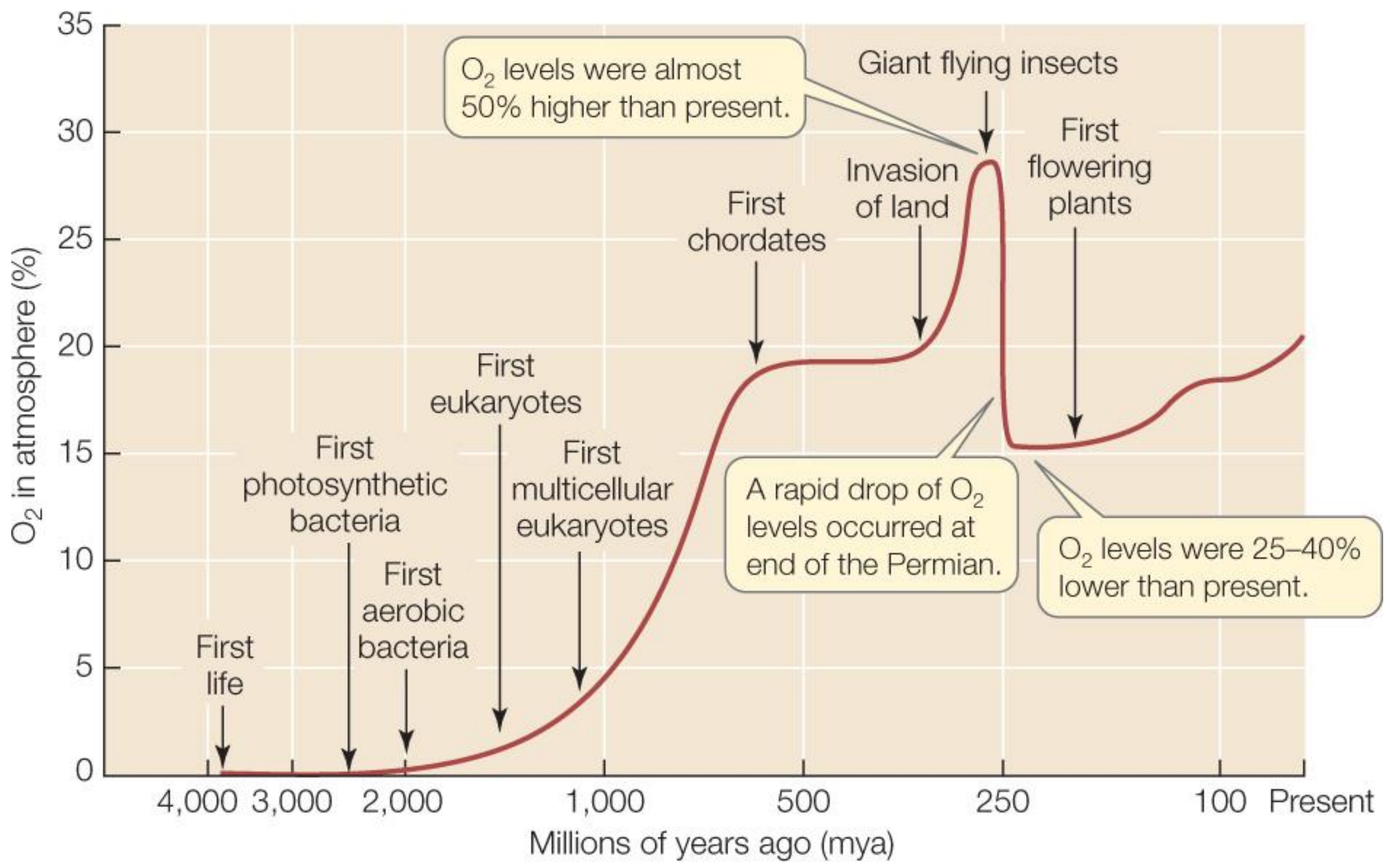
Evolution reconstruction

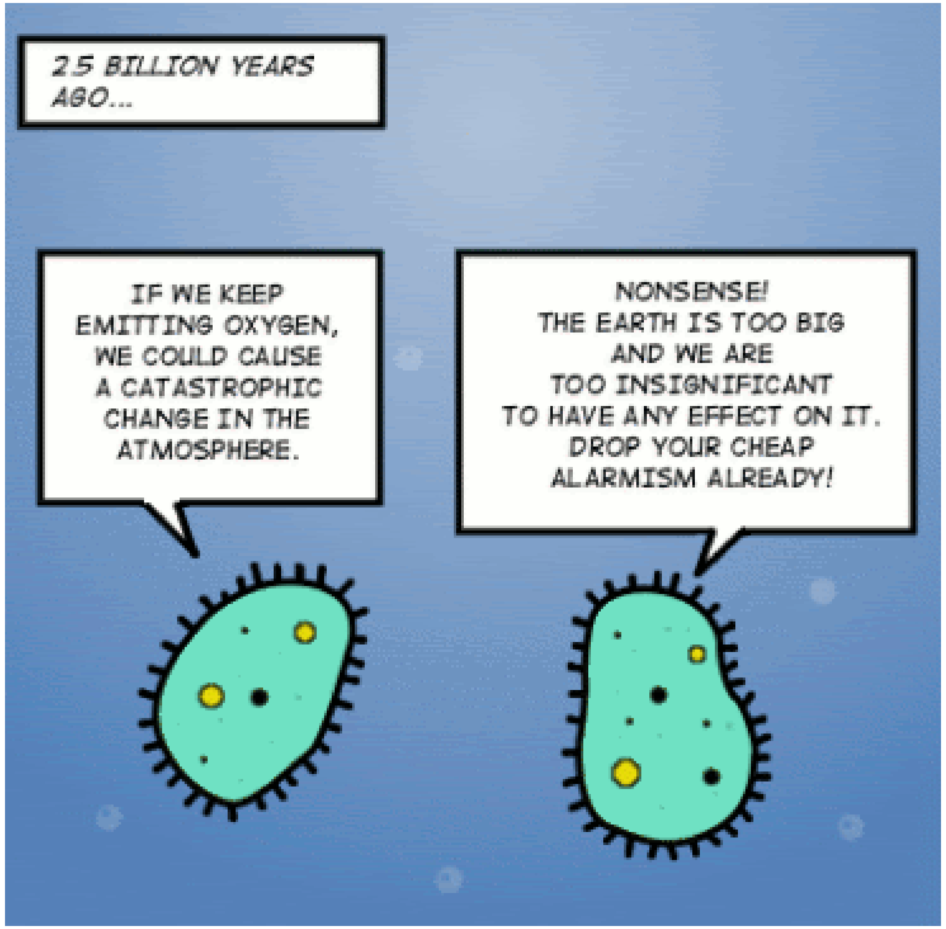
- **Age of fossils**
- Prokaryotic cells: 3.5 billion years
- Eukaryotic cells: 1.5 billion years
- Multicellular organisms: 500 million years

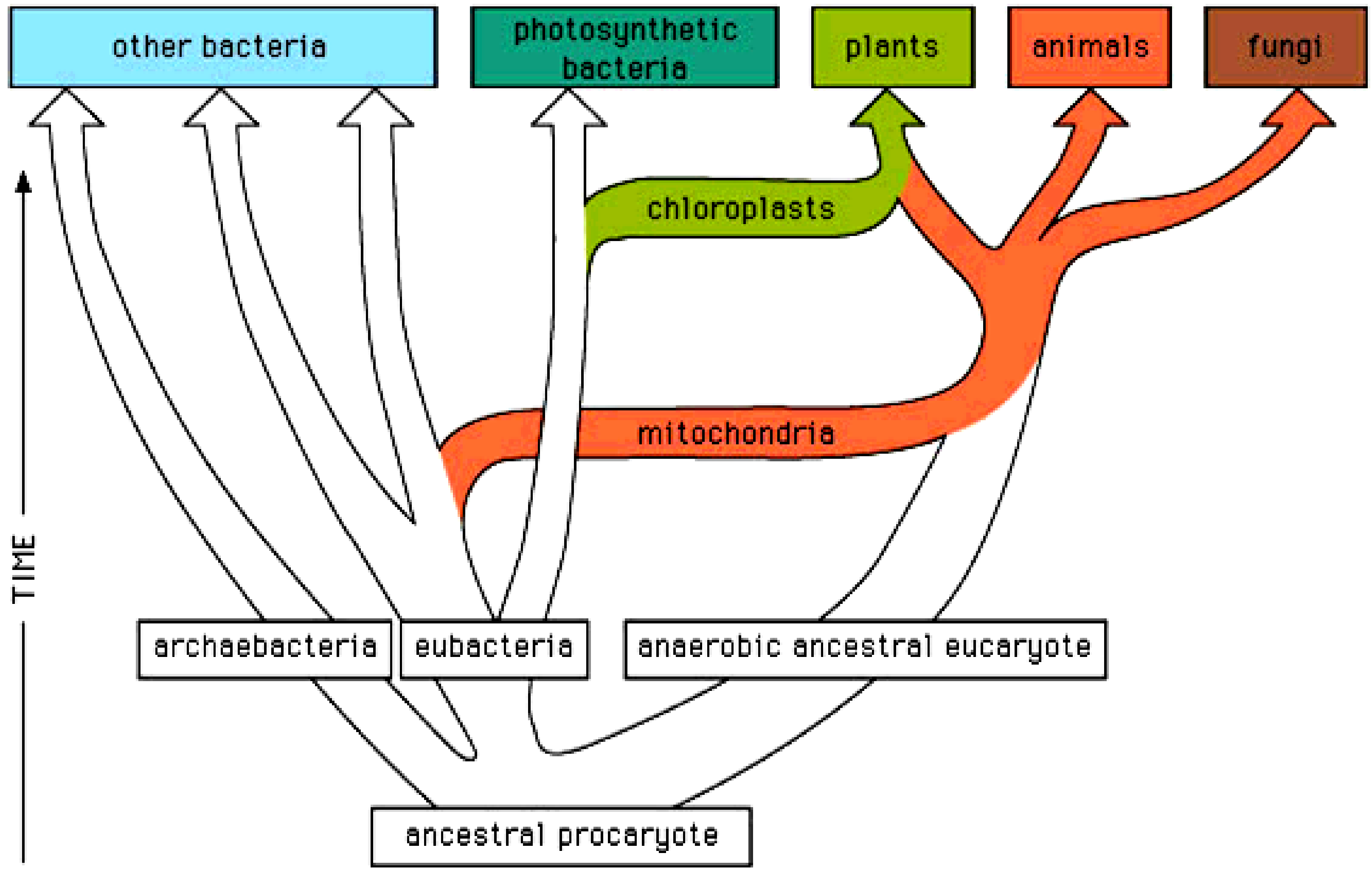
Cyanobacteria fossil

Eukaryotic cell fossil

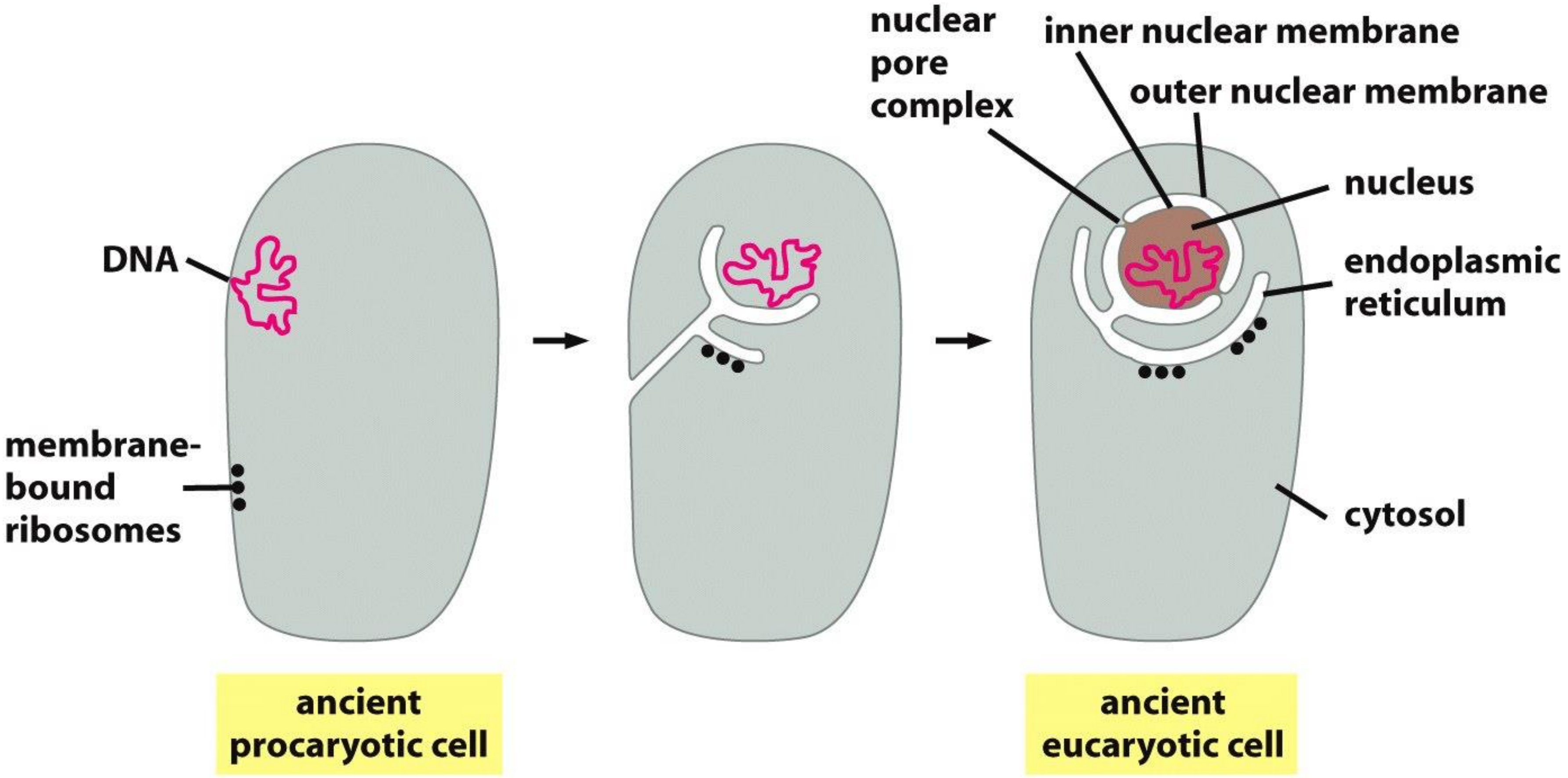

CAMBRIAN
PRECAMBRIAN
PHANEROZOIC
PROTEROZOIC
ARCHEAN
Geological evidence
Millions of years ago
Life forms
Oldest multicellular fossils
Oldest compartmentalized fossil cells
Disappearance of iron from oceans and formation of iron oxides
Oldest definite fossils
Oldest dated rocks
570
600
1500
2500
3500
4500
Appearance of first multicellular organisms
Appearance of first eukaryotes
Appearance of aerobic (oxygen-using) respiration
Appearance of oxygen-forming photosynthesis (cyanobacteria)
Appearance of chemoautotrophs (sulfate respiration)
Appearance of life (prokaryotes): anaerobic (methane-producing) bacteria and anaerobic (hydrogen sulfide–forming) photosynthesis
Formation of the earth


35
30
25
20
15
10
5
0
O_2 in atmosphere (%)
O_2 levels were almost 50% higher than present.
Giant flying insects
First flowering plants
Invasion of land
First chordates
First eukaryotes
First photosynthetic bacteria
First multicellular eukaryotes
A rapid drop of O_2 levels occurred at end of the Permian.
O_2 levels were 25–40% lower than present.
First aerobic bacteria
First life
4,000
3,000
2,000
1,000
500
250
100
Present
Millions of years ago (mya)

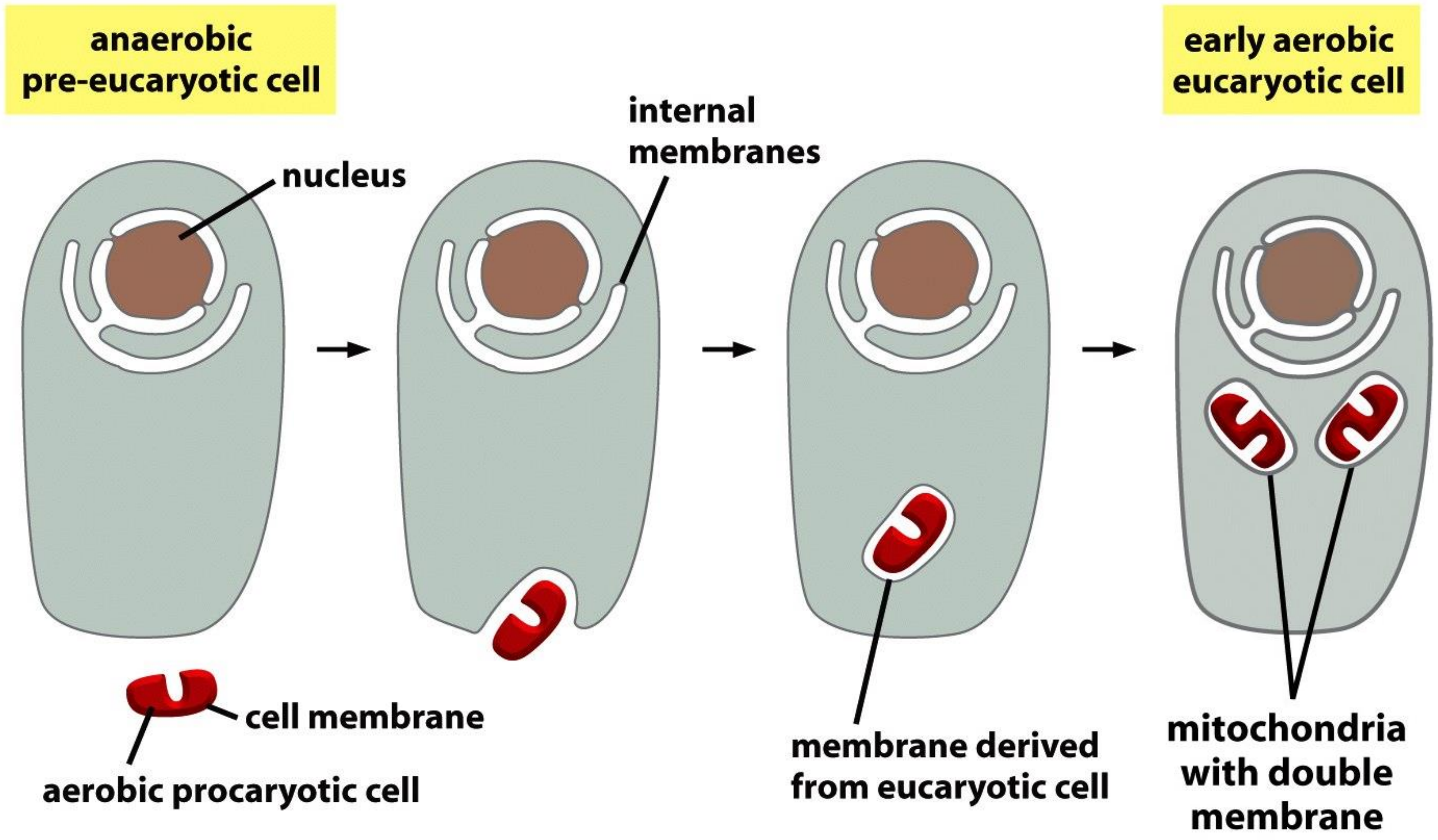

2.5 BILLION YEARS AGO...
IF WE KEEP EMITTING OXYGEN, WE COULD CAUSE A CATASTROPHIC CHANGE IN THE ATMOSPHERE.
NONSENSE! THE EARTH IS TOO BIG AND WE ARE TOO INSIGNIFICANT TO HAVE ANY EFFECT ON IT. DROP YOUR CHEAP ALARMISM ALREADY!


other bacteria
photosynthetic bacteria
plants
animals
fungi
chloroplasts
mitochondria
TIME
archaebacteria
eubacteria
anaerobic ancestral eucaryote
ancestral procaryote

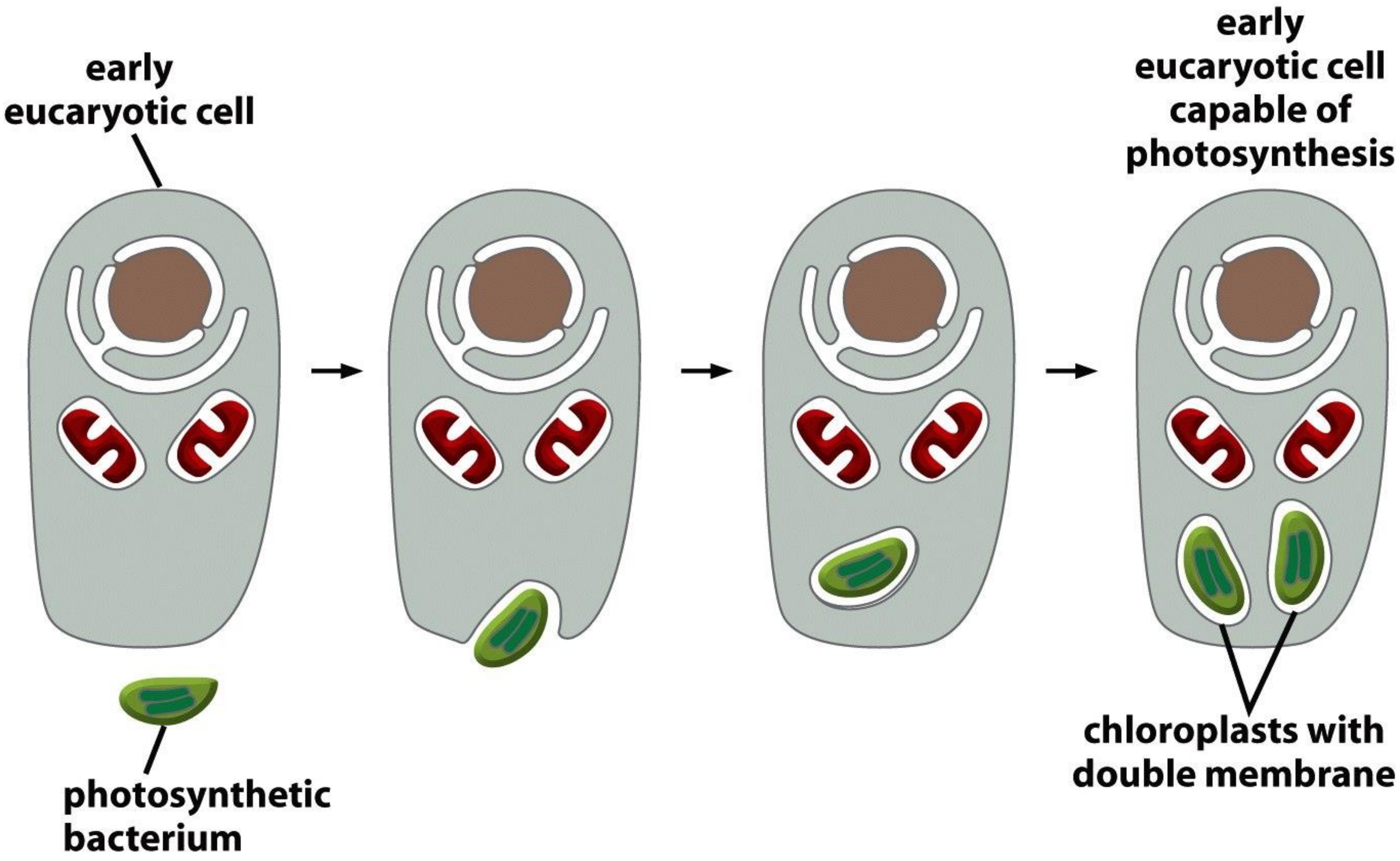
Evolutionary origin of membrane structures and the cell nucleus



Origin of mitochondria

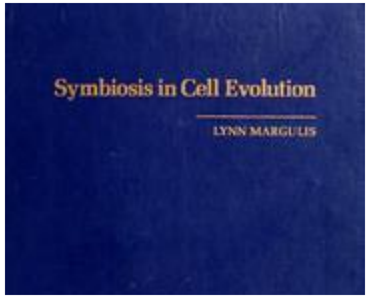


Origin of chloroplasts



Endosymbiotic theory

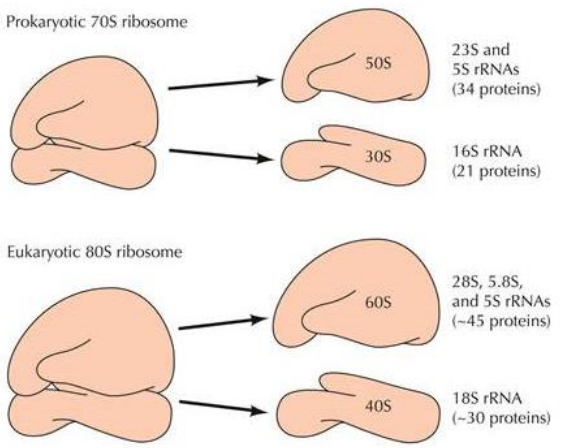
- 1883 – **Andreas W. Schimper**
  - Chloroplasts have many similar characteristics to cyanobacteria
  - Journal footnote: photosynthetic organisms - combination of two separate organisms?
- 1967/81 – **Lynn Margulis**:
- **1967 (Sagan) – „On the origin of mitosing cells“**
- **1981 – Symbiosis in Cell Evolution**
  - All life is bacterial or derives from bacteria by symbiogenesis

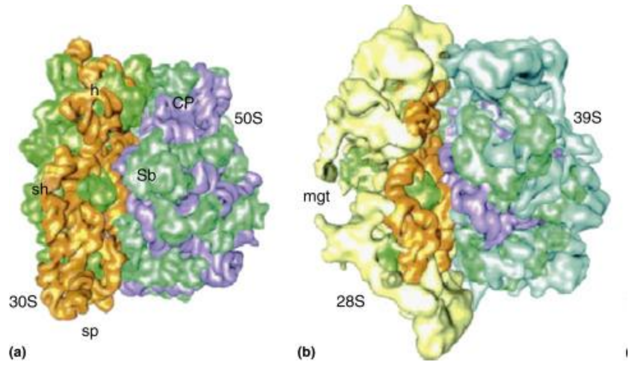


Evidence supporting the endosymbiotic theory

Mitochondria & plastids

- Surrounded by **double membrane**
- Contain own **genome similar to procaryotic**: circular DNA, without histones
- Replication and **division by fission** like bacteria
- **Own protein synthesis apparatus:** ribosomes similar to prokaryotic, rRNAs encoded in the own genome



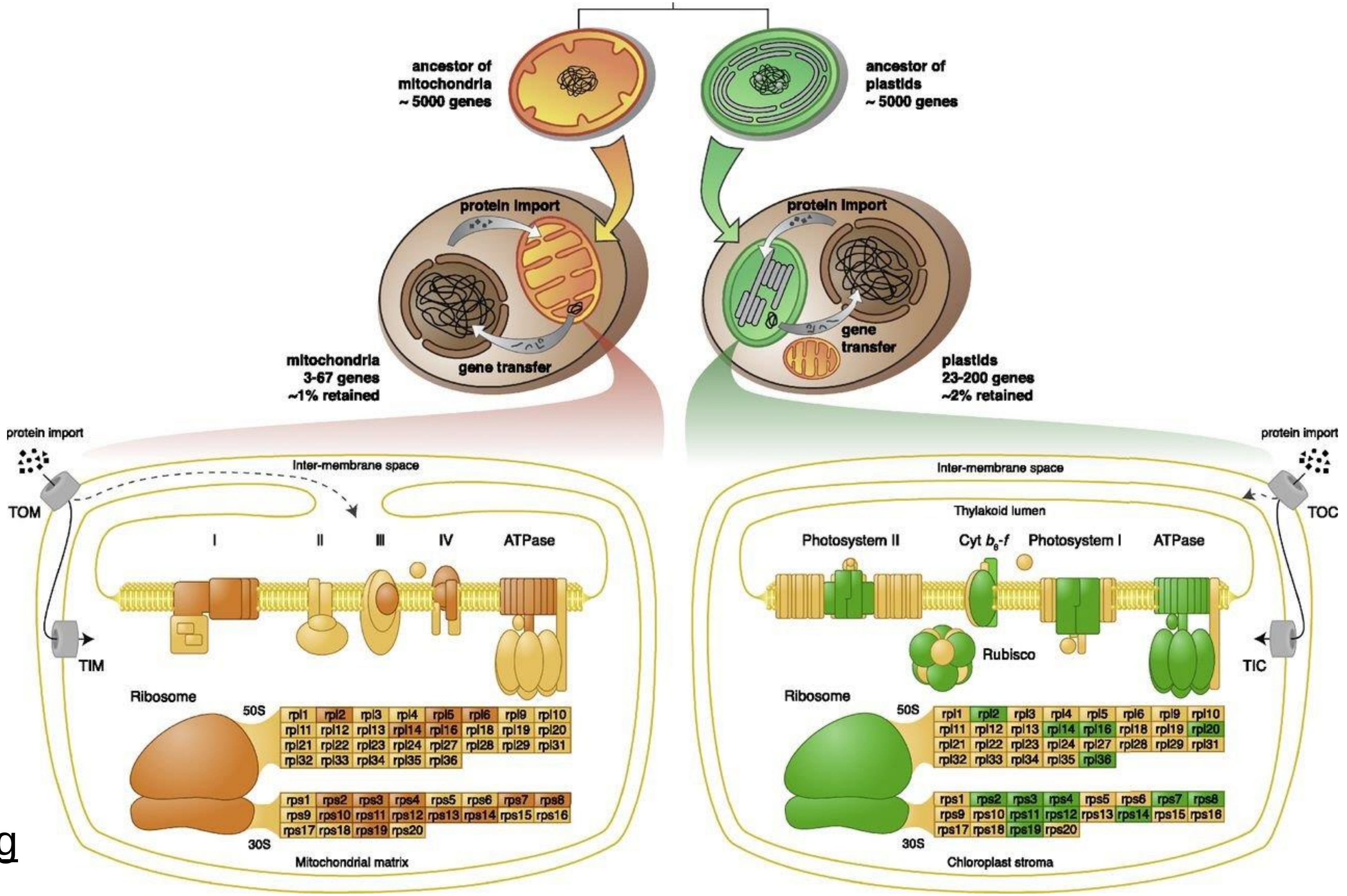


a) *E. coli*

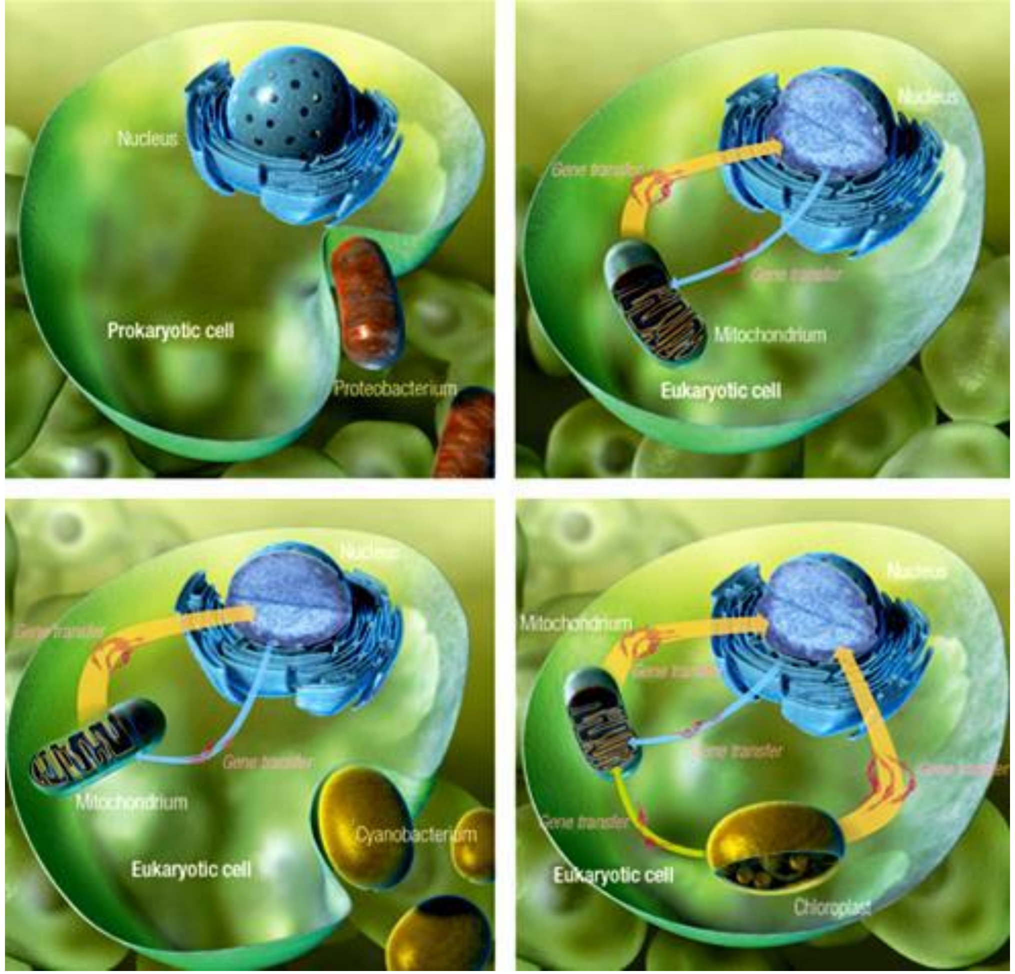
b) Mammalian mitoribosome

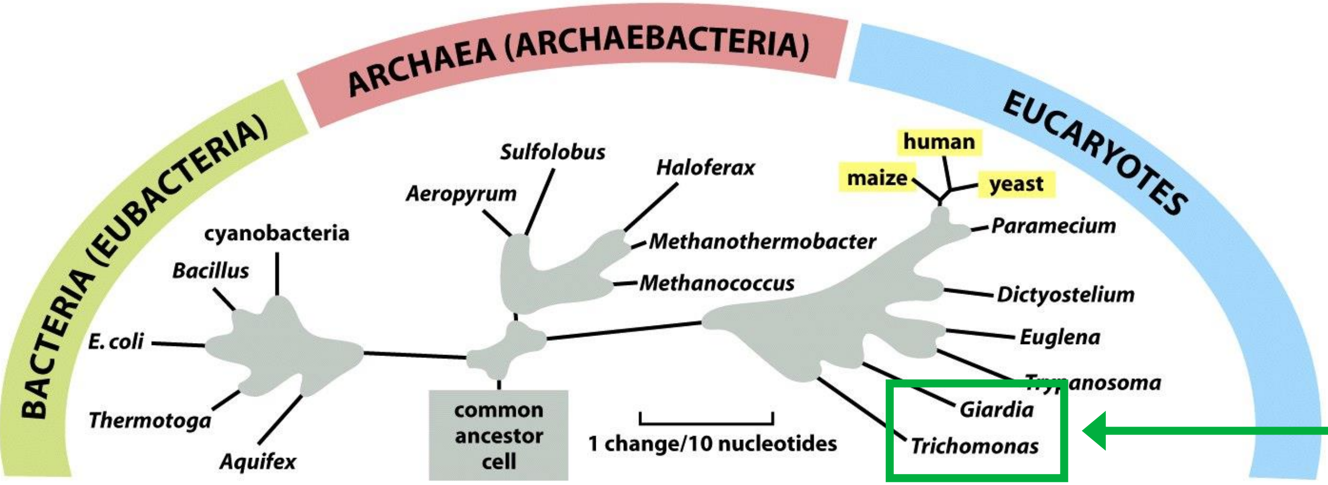
Gene transfer to nucleus

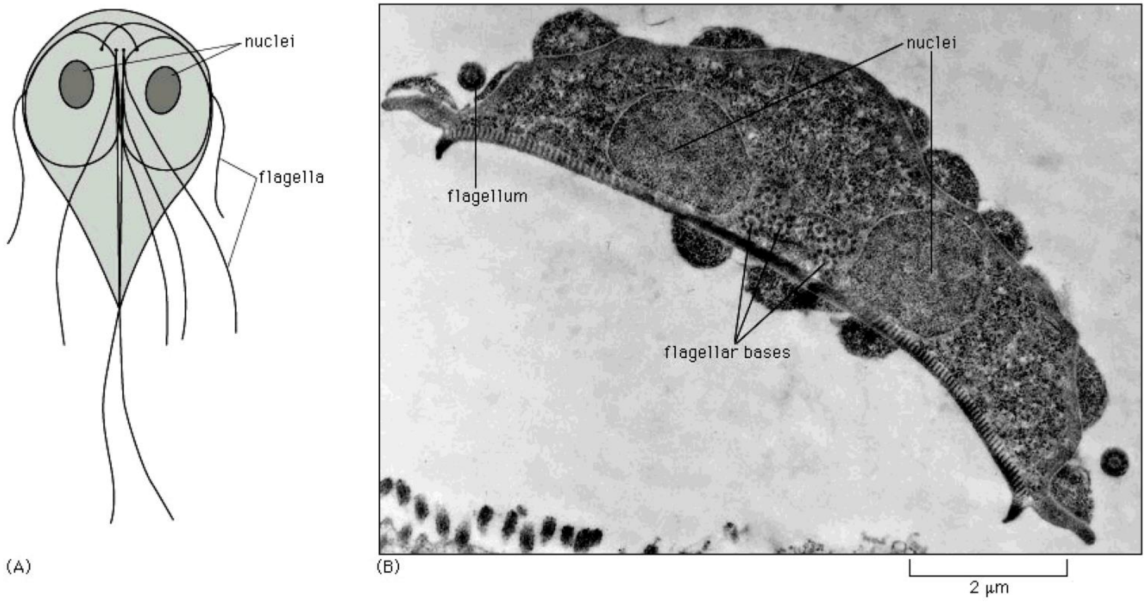
– **Crucial genes retained** in the genome of mitochondria or plastids



Further reading


Nucleus
Prokaryotic cell
Proteobacterium
Nucleus
Gene transfer
Gene transfer
Mitochondrium
Eukaryotic cell
Nucleus
Gene transfer
Gene transfer
Mitochondrium
Cyanobacterium
Eukaryotic cell
Nucleus
Mitochondrium
Gene transfer
Gene transfer
Gene transfer
Gene transfer
Eukaryotic cell
Chloroplast





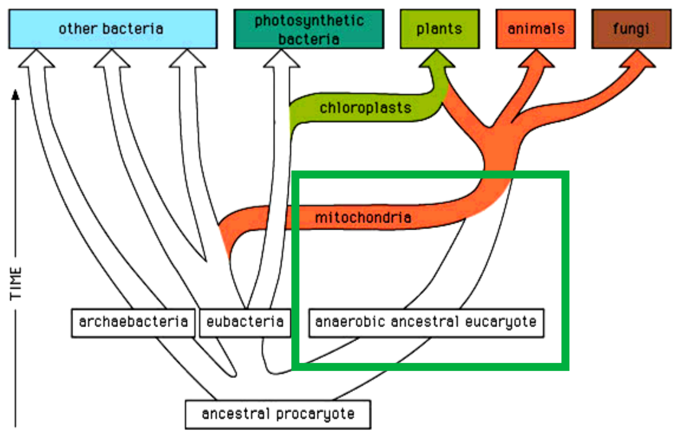
Anaerobic eukaryotes

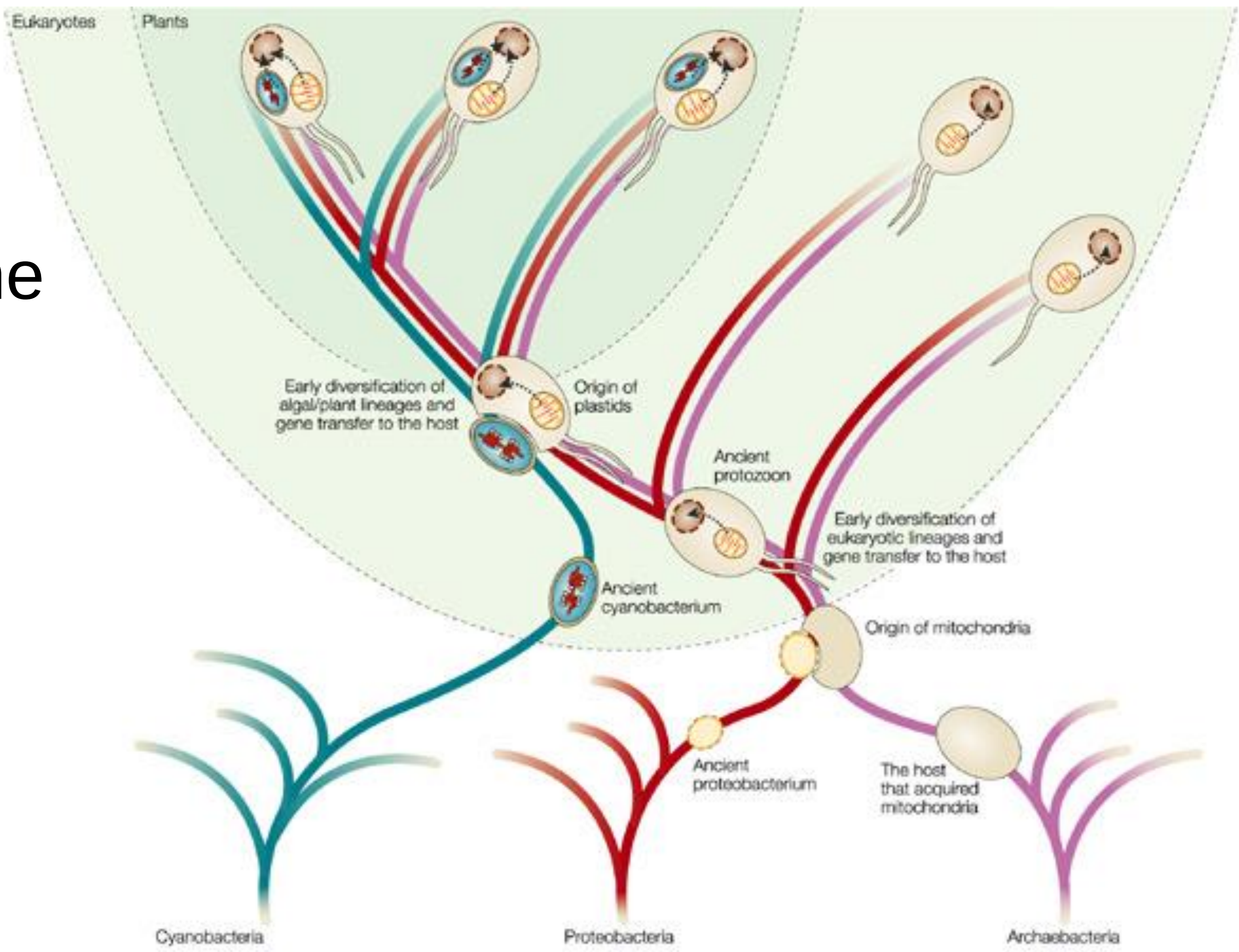
Anaerobic protists

- **Lack conventional mitochondria**: remnants – specific **double membrane organelles** (e.g., mitosome)
- Primitive nature and poorly developed endomembrane system
- Parasitic: **Giardia, Trichomonas**

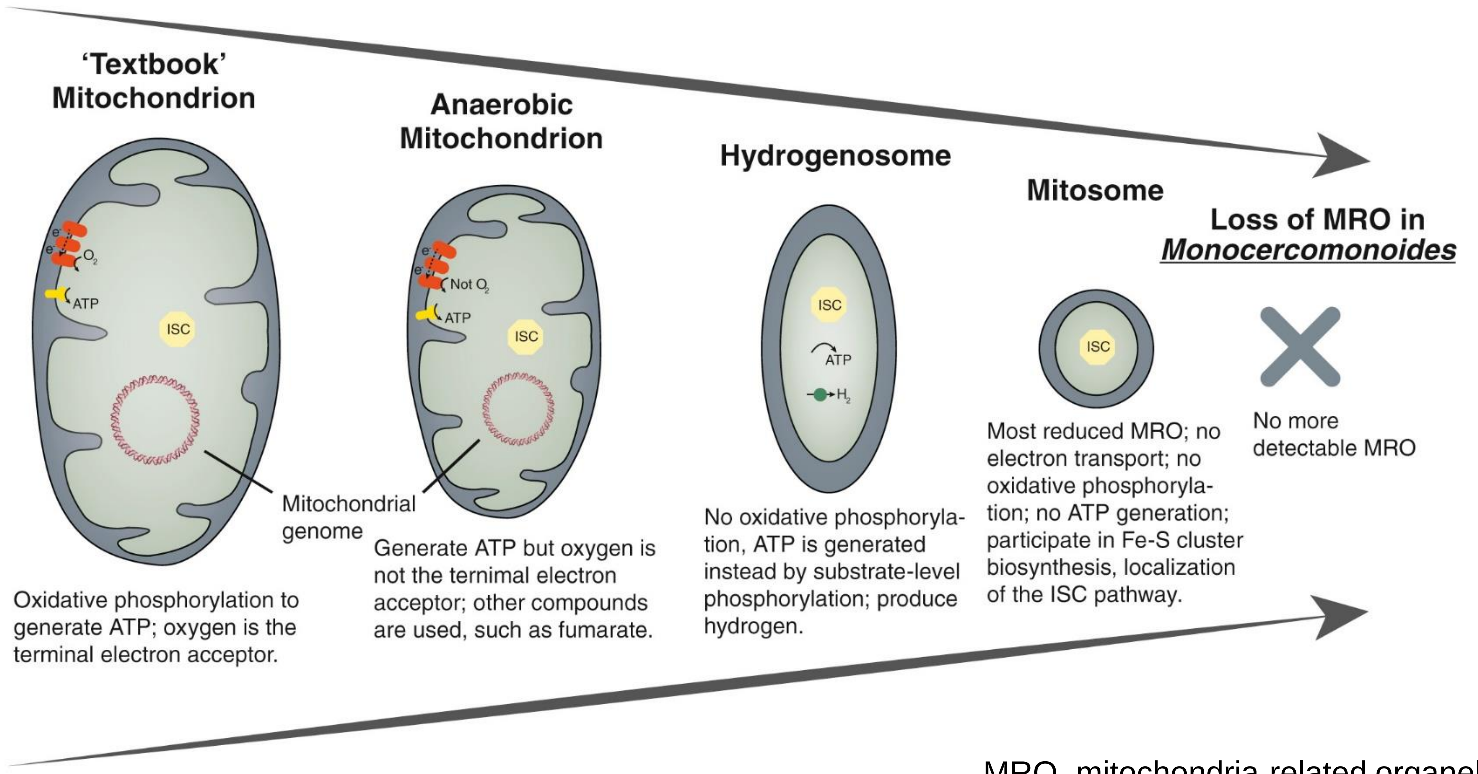
Revisited model

– Endosymbiosis of proteobacterium (mitochondrion) preceded the last eukaryotic common ancestor

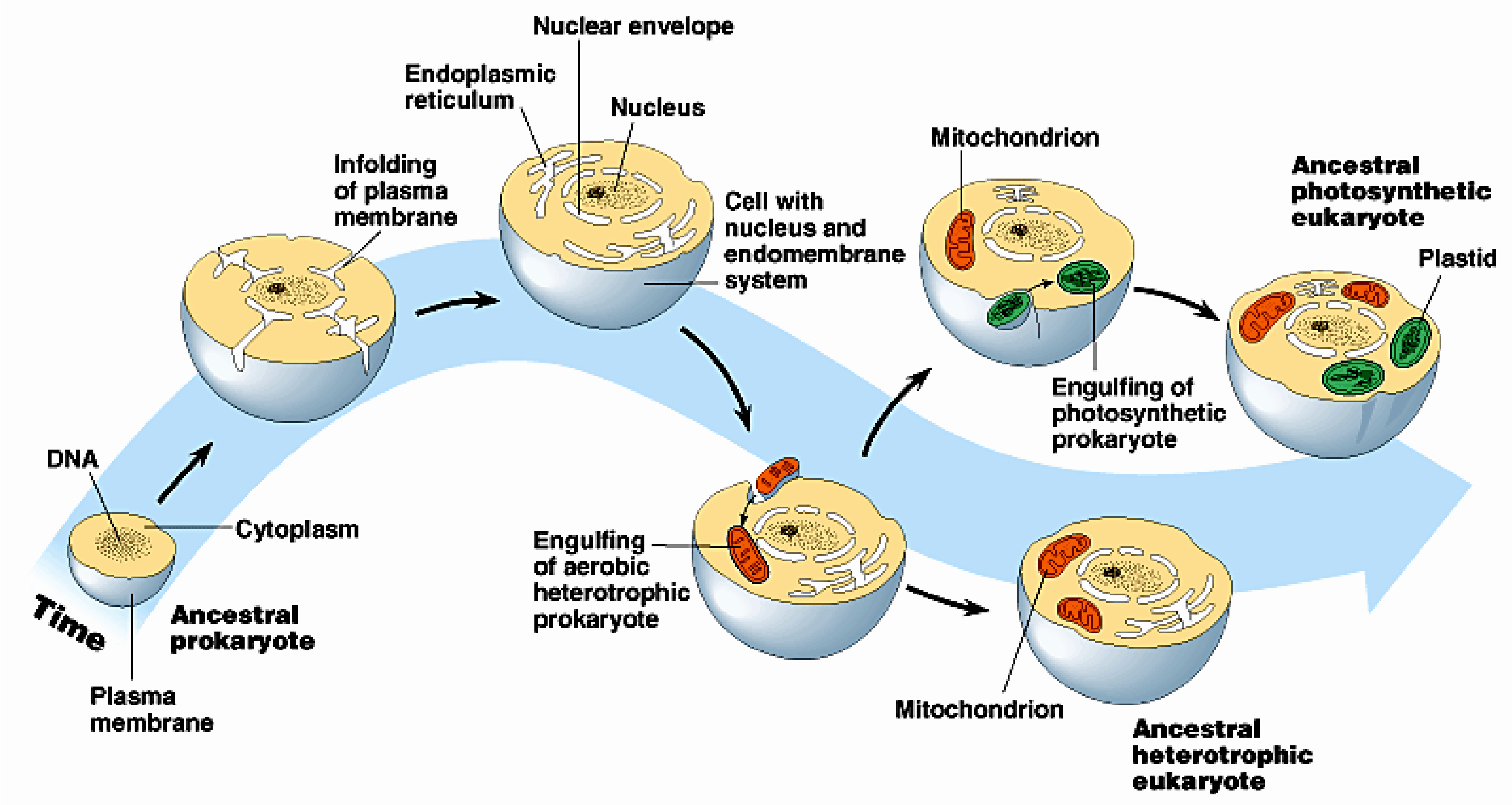




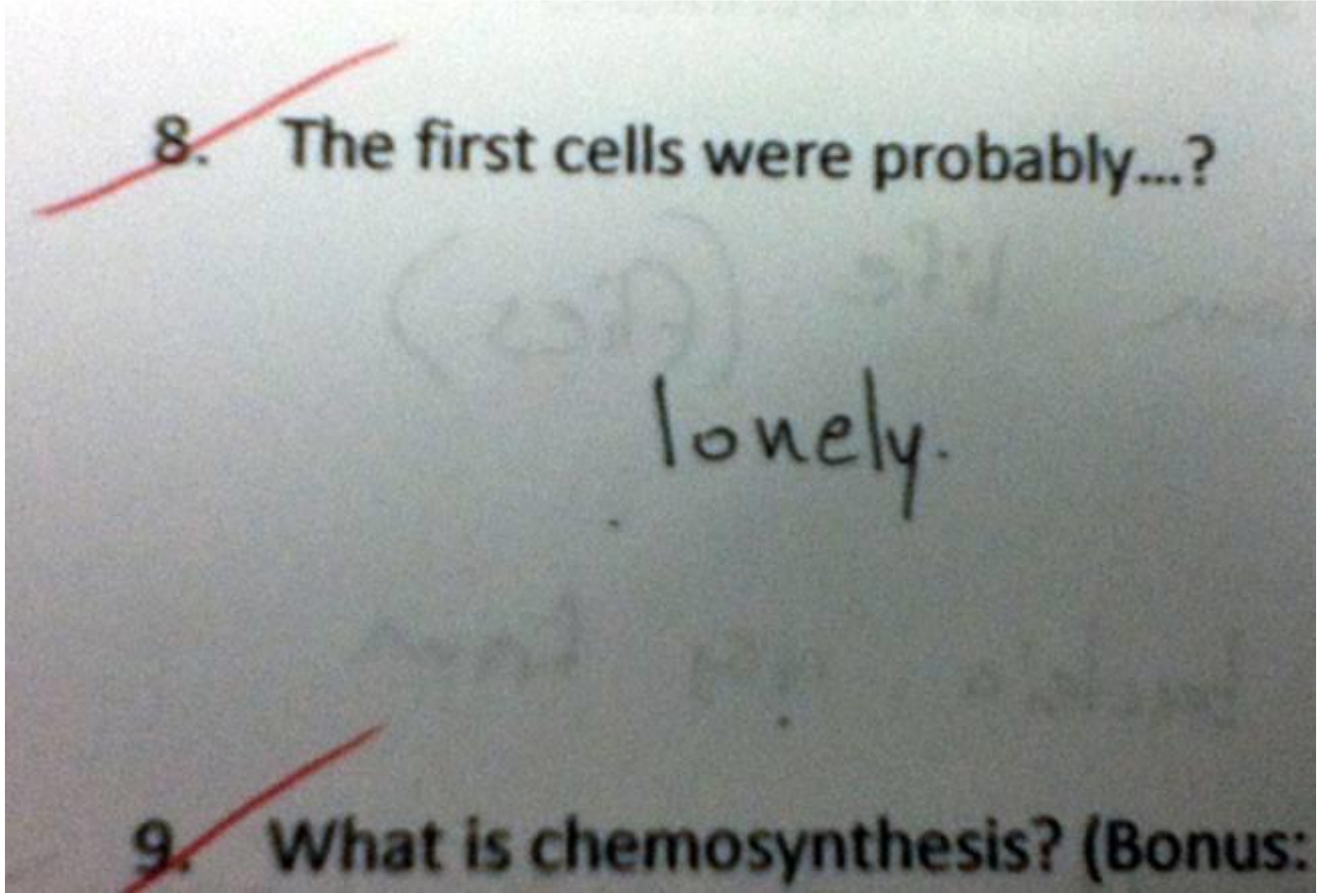
Mitochondria reduced or even lost during the diversification and evolution of eukaryotes



MRO, mitochondria-related organelle



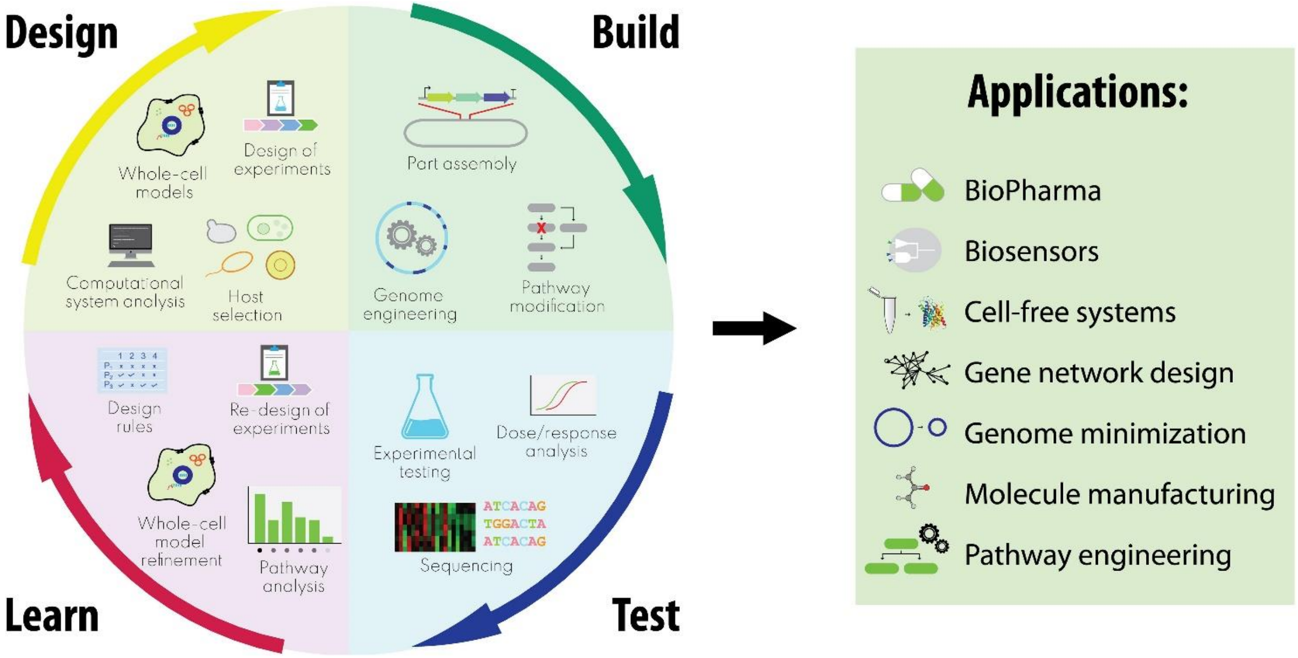
Nuclear envelope
Endoplasmic reticulum
Nucleus
Infolding of plasma membrane
Cell with nucleus and endomembrane system
Mitochondrion
Ancestral photosynthetic eukaryote
Plastid
Engulfing of photosynthetic prokaryote
DNA
Cytoplasm
Time
Ancestral prokaryote
Plasma membrane
Engulfing of aerobic heterotrophic prokaryote
Mitochondrion
Ancestral heterotrophic eukaryote


8. The first cells were probably...?
lonely.
9. What is chemosynthesis? (Bonus:

Synthetic biology

Synthetic biology

- Bi9690en Synthetic Biology
- Aims to create or redesign new biological systems to achieve specific purposes



2010 – First synthetic genome

RESEARCH ARTICLE Science

Creation of a Bacterial Cell Controlled by a Chemically Synthesized Genome

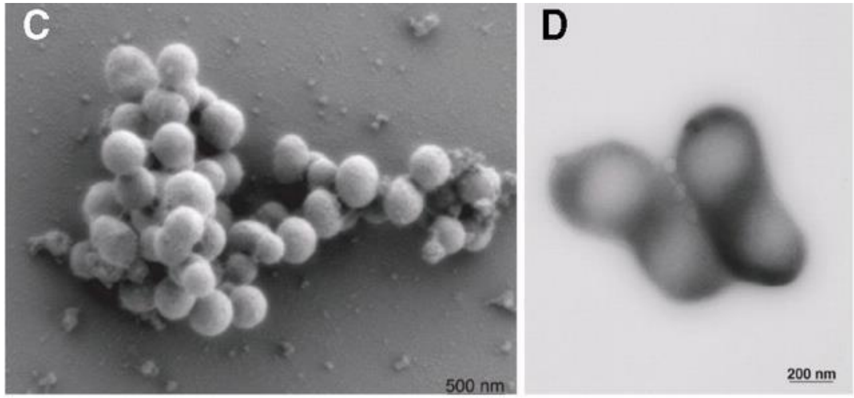
Daniel G. Gibson,[1] John I. Glass,[1] Carole Lartigue,[1] Vladimir N. Noskov,[1] Ray-Yuan Chuang,[1] Mikkel A. Algire,[1] Gwynedd A. Benders,[2] Michael G. Montague,[1] Li Ma,[1] Monzia M. Moodie,[1] Chuck Merryman,[1] Sanjay Vashee,[1] Radha Krishnakumar,[1] Nacyra Assad-Garcia,[1] Cynthia Andrews-Pfannkoch,[1] Evgeniya A. Denisova,[1] Lei Young,[1] Zhi-Qing Qi,[1] Thomas H. Segall-Shapiro,[1] Christopher H. Calvey,[1] Prashanth P. Parmar,[1] Clyde A. Hutchison III,[2] Hamilton O. Smith,[2] J. Craig Venter[1,2*]

We report the design, synthesis, and assembly of the 1.08–mega–base pair *Mycoplasma mycoides* JCVI-syn1.0 genome starting from digitized genome sequence information and its transplantation into a *M. capricolum* recipient cell to create new *M. mycoides* cells that are controlled only by the synthetic chromosome. The only DNA in the cells is the designed synthetic DNA sequence, including "watermark" sequences and other designed gene deletions and polymorphisms, and mutations acquired during the building process. The new cells have expected phenotypic properties and are capable of continuous self-replication.

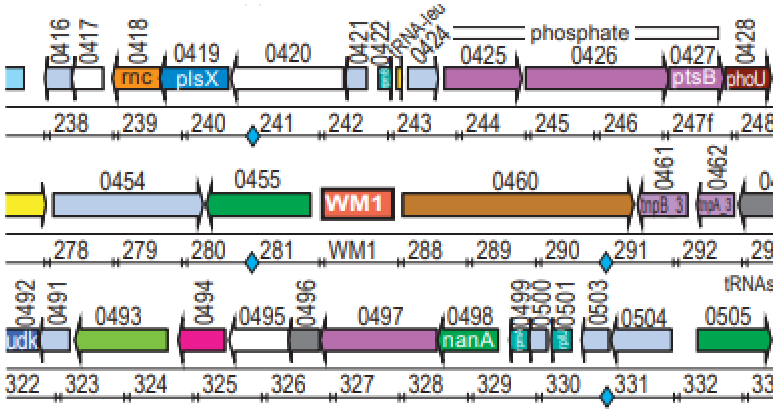
- Design, synthesis and assembly of bacterial chromosome: ***Mycoplasma mycoides*** **JCVI-syn01**
- DNA segments assembled in yeast
- **Chromosome introduced into recipient *Mycoplasma capricolum* to replace its genome**

2010 – First synthetic genome

- **Bacteria able to replicate controlled by the synthetic genome**



- **Comprises watermarks** (encrypted messages)



1. Explanation of the coding system itself
2. URL address for those who deciphered the code
3. Names of all authors and co-workers
4. Famous quotes (James Joyce, Richard Feynman)

A	B	C	D	E	F	G	H	I			L	M	N	O	P		R	S	T	U	V	W		Y	
TAG	AGT	TTT	ATT	TAA	GGC	TAC	TCA	CTG	GTT	GCA	AAC	CAA	TGC	CGT	ACA	TTA	CTA	GCT	TGA	TCC	TTG	GTC	GGT	CAT	TGG

– Watermark one:

– J. CRAIG VENTER INSTITUTE 2009

ABCDEFGHIJKLMNOPQRSTUVWXYZ

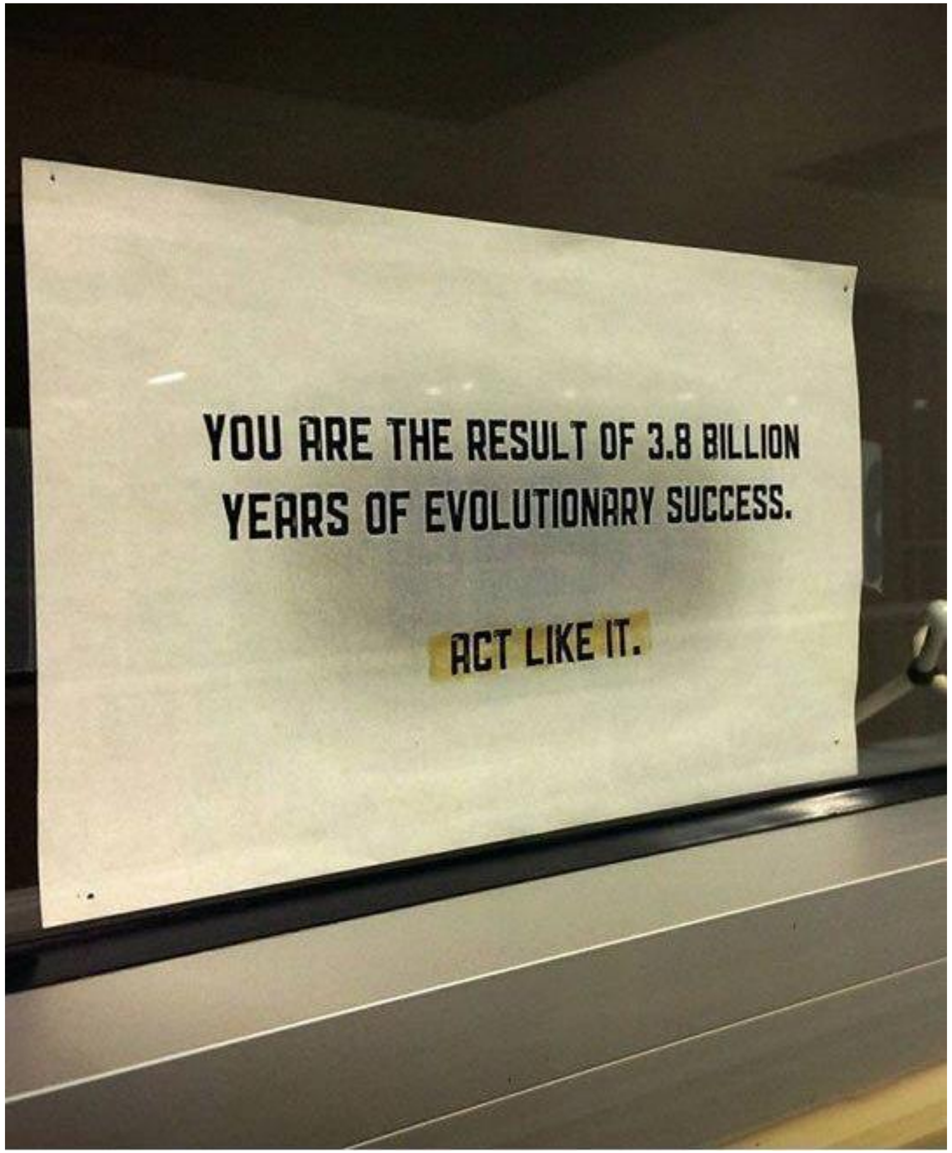
0123456789?@??-??=/:<?>??????"??!'.,

SYNTHETIC GENOMICS, INC.

<!DOCTYPE HTML><HTML><HEAD><TITLE>GENOME TEAM</TITLE></HEAD><BODY><A

HREF="HTTP://WWW.JCVI.ORG/">THE JCVI</A><P>PROVE YOU'VE DECODED THIS WATERMARK BY EMAILING

US <A HREF="MAILTO:XXXXXXXX@JCVI.ORG">HERE!</A></P></BODY></HTML>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