The RNA World and the Origins of Life

B. Balen

Cell origin and evolution

❖ Cell is **structural**, **functional** and **reproduction** unit of life

❖ Similarities:

- DNA – genetic material
- surrounded by membranes
- the same basic mechanisms for energy production

Prokaryotic and eukaryotic cells

❖ Differences:
- nucleus
- genome complexity
- organelles
- cytoskeleton
- size

➢**prokaryotic cell** – devoid off nuclear envelope

➢**eukaryotic cell** – nucleus (Greek word - *karyon*) – genetic material separated from cytoplasm

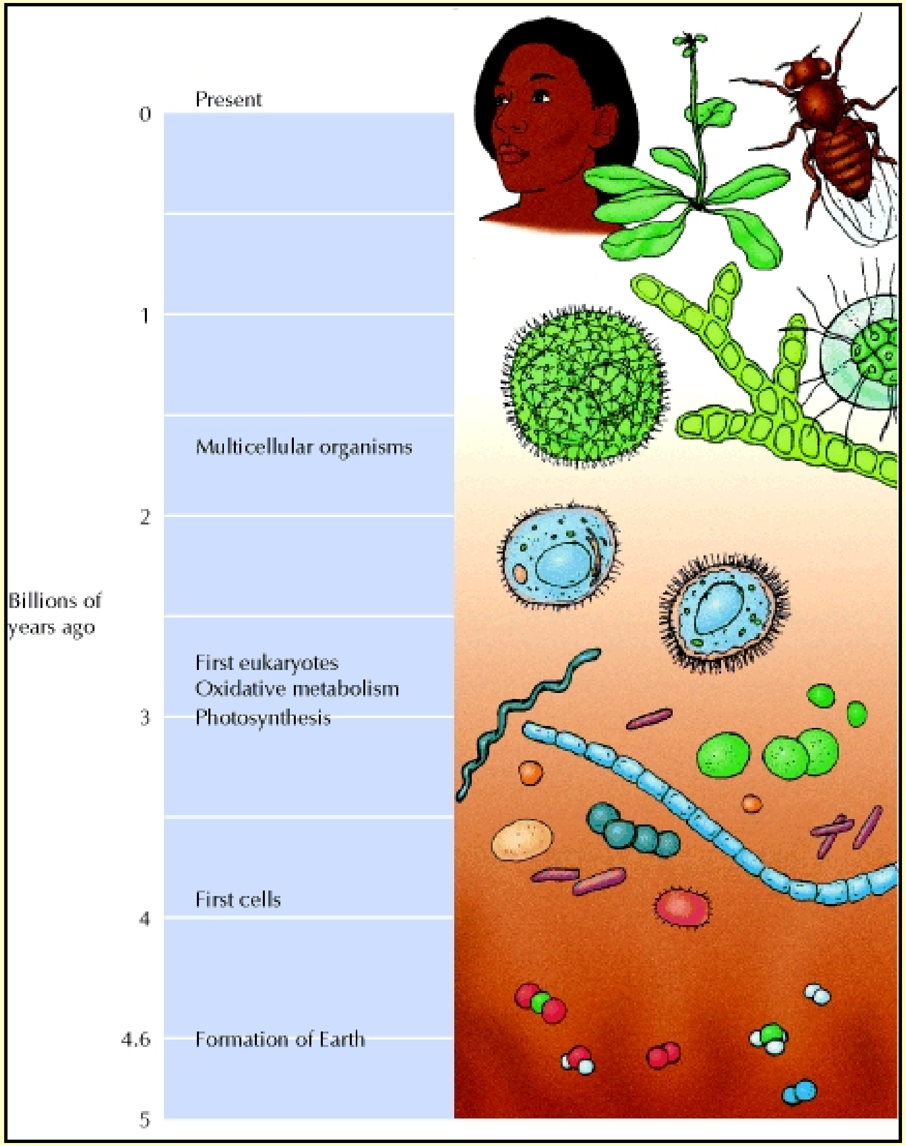
Table 1.1 Prokaryotic and Eukaryotic Cells

Characteristic	Prokaryote	Eukaryote
Nucleus	Absent	Present
Diameter of a typical cell	≈1 μm	10–100 μm
Cytoskeleton	Absent	Present
Cytoplasmic organelles	Absent	Present
DNA content (base pairs)	1×10^6 to 5×10^6	1.5×10^7 to 5×10^9
Chromosomes	Single circular DNA molecule	Multiple linear DNA molecules

From: The Origin and Evolution of Cells

2000. Cooper

TIME SCALE OF EVOLUTION



- ✓ **The same molecular mechanisms direct life of both prokaryotes and eukaryotes!**
- ✓ Life on Earth - 3,8 billion years ago
- ✓ How did the first cell develop? Object of speculations
- ✓ Several important experiments

FIGURE 1.1.
The scale indicates the approximate times at which some of the major events in the evolution of cells are thought to have occurred.
Cooper G.M. 2000

1. **<u>1920-ies</u>** → simple organic molecules can polymerize spontaneously and form macromolecules in conditions of the first atmosphere on Earth

The first atmosphere:

– very little or none of molecular O_2

– mostly CO_2 and N_2

– small quantities of H_2, H_2S, CO

} + sunlight or electric sparks

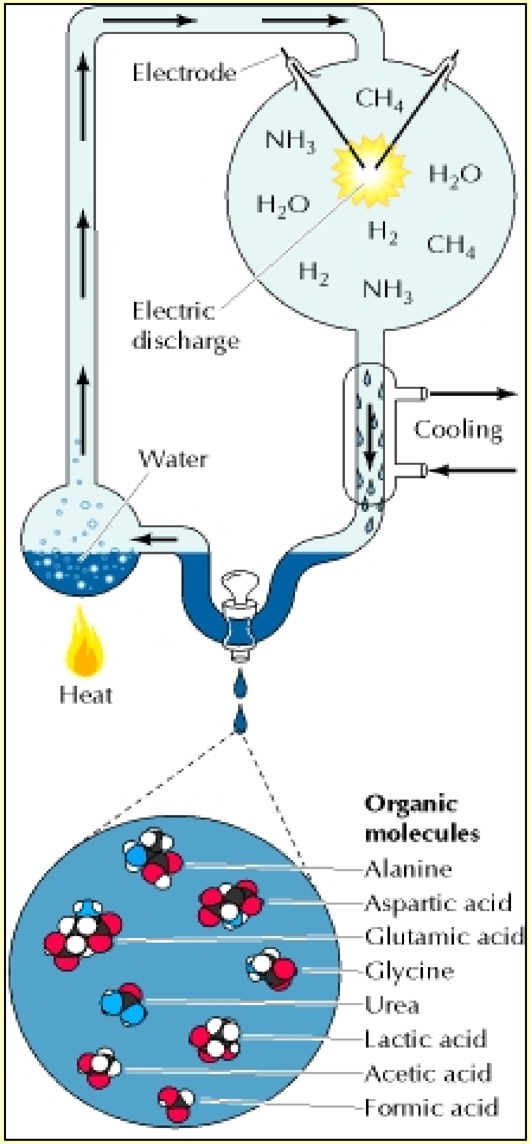
↓

Such an atmosphere provides reducing conditions

↓

Spontaneous formation of organic molecules

2. <u>1950-ies</u> → Spontaneous formation of organic molecules



- **Stanley Miller**

- water vapor was refluxed through an atmosphere (CH_4, NH_3, and H_2) into which electric sparks were discharged

- analysis of the reaction products revealed the formation of:

-a variety of organic molecules

-including the amino acids alanine, aspartic acid, glutamic acid, and glycine

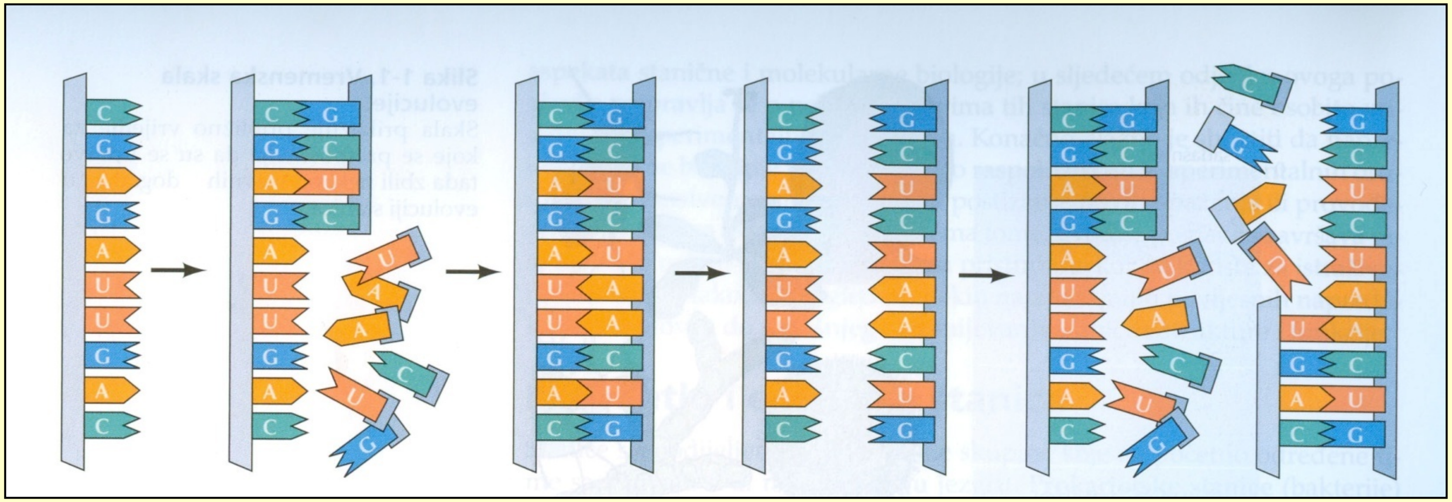
Interestingly, both L and D isomers of amino acids were detected → no contamination!

Only L-forms are ever found in proteins!

FIGURE 1.2; Cooper G.M. 2000

3. **<u>1980-ies</u>** → RNA can direct the synthesis of the complementary chain

- ✓ Sid Altman and Tom Cech
- ✓ spontaneous polimerization of nucleotides



2004. Cooper and Hausman

❖ **hypothesis**:

✓ RNA world existed on Earth before modern cells arose

✓ RNA stored both genetic information and catalyzed the chemical reactions in primitive cells

✓ later in evolutionary time DNA took over as the genetic material and proteins became the major catalysts and structural components of cells

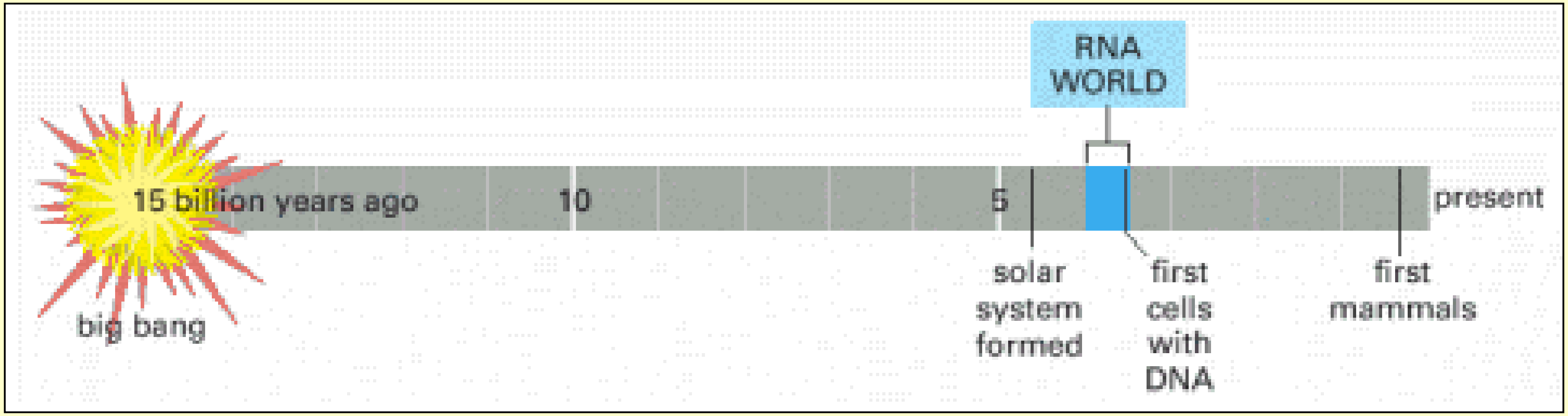


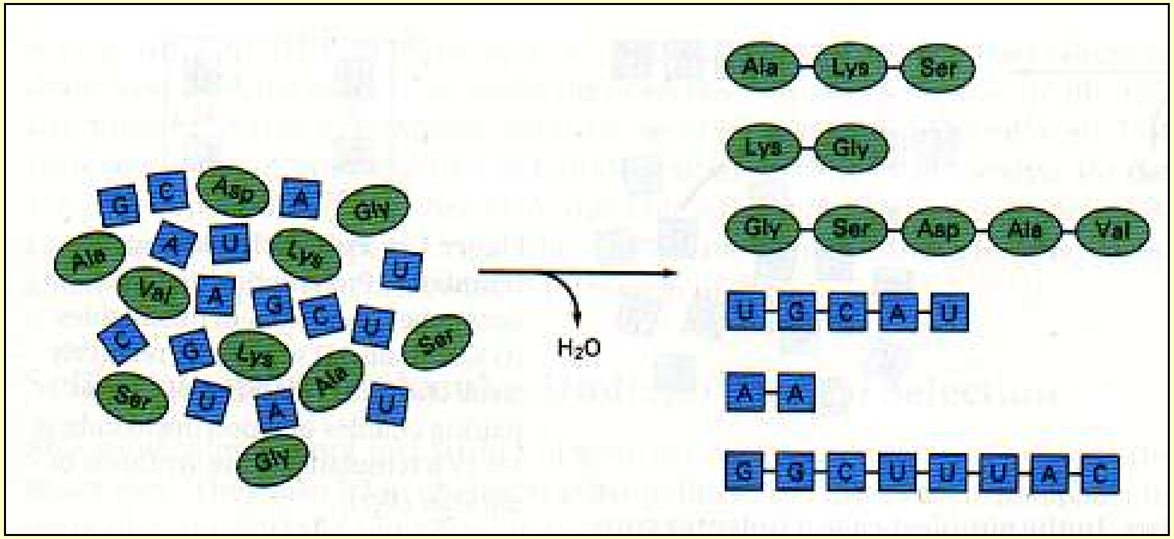
Figure 6-91. Time line for the universe, suggesting the early existence of an RNA world of living systems.

2002 Bruce Alberts, et al.

➢ simple organic molecules can associate and form long polymers

✓ **aa - aa → peptide bond → polypeptides and proteins**

✓ **na - na → phosphodiester bond → polynucleotides (DNA and RNA)**



Spontaneous polymerization - polypeptides and polynucleotides

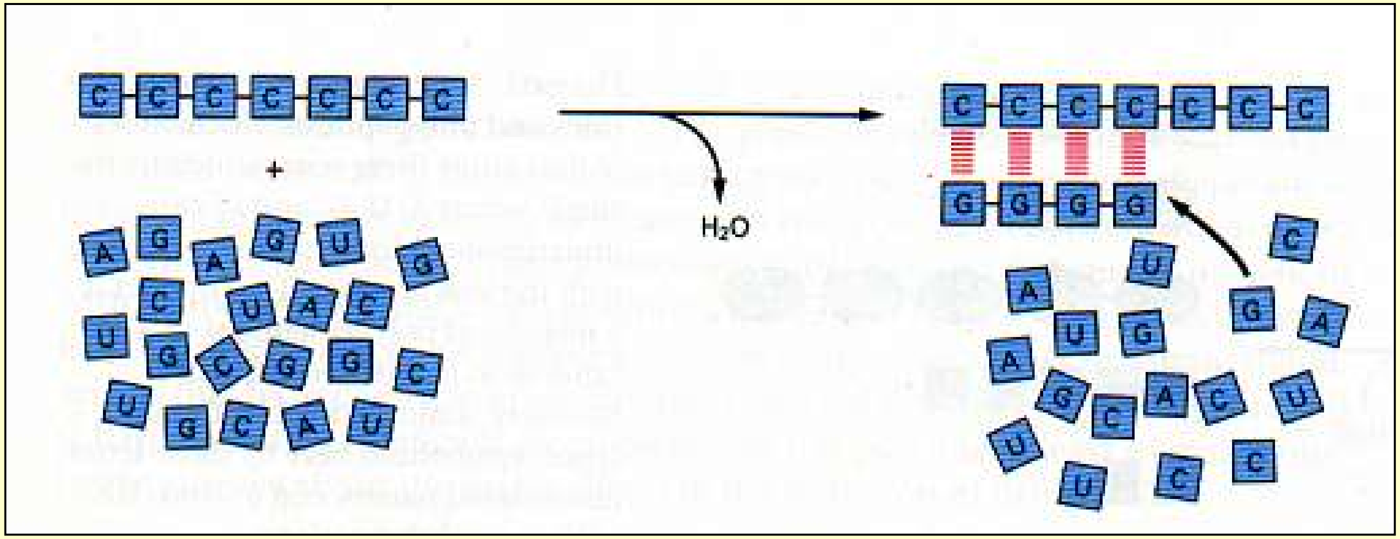
- random sequence

- different length

2002 Bruce Alberts, et al.

✓ polynucleotides have one property that contrasts with those of polypeptides:

They can directly guide the formation of exact copies of their own sequence!

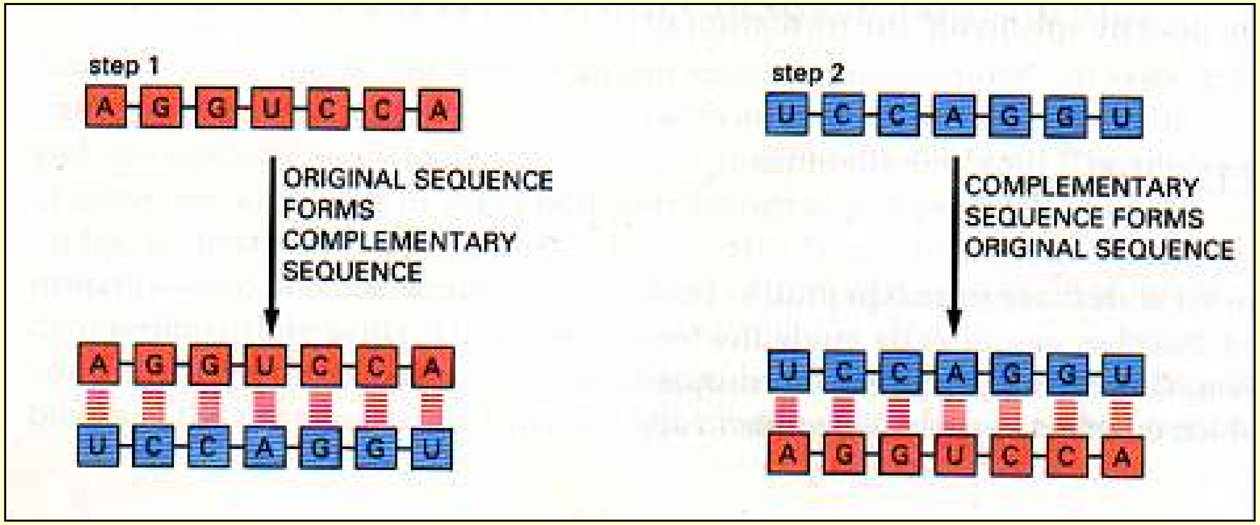


✓ complementary base pairing of nucleotide subunits

✓ one polynucleotide to act as a template for the formation of another
→ complementary templating mechanisms

2002 Bruce Alberts, et al.

✓ complementary templating mechanisms → key role in origin of life on Earth



complementary nucleotides:

A – U

G – C

✓ At the first step original RNA acts as a template for formation of complementary molecule

✓ At the second step complementary molecule can act as a template for synthesis of the molecule identical to the original

2002 Bruce Alberts, et al.

Synthesis of polynucleotides

✓efficient synthesis of polynucleotides requires catalysts to promote the polymerization reaction

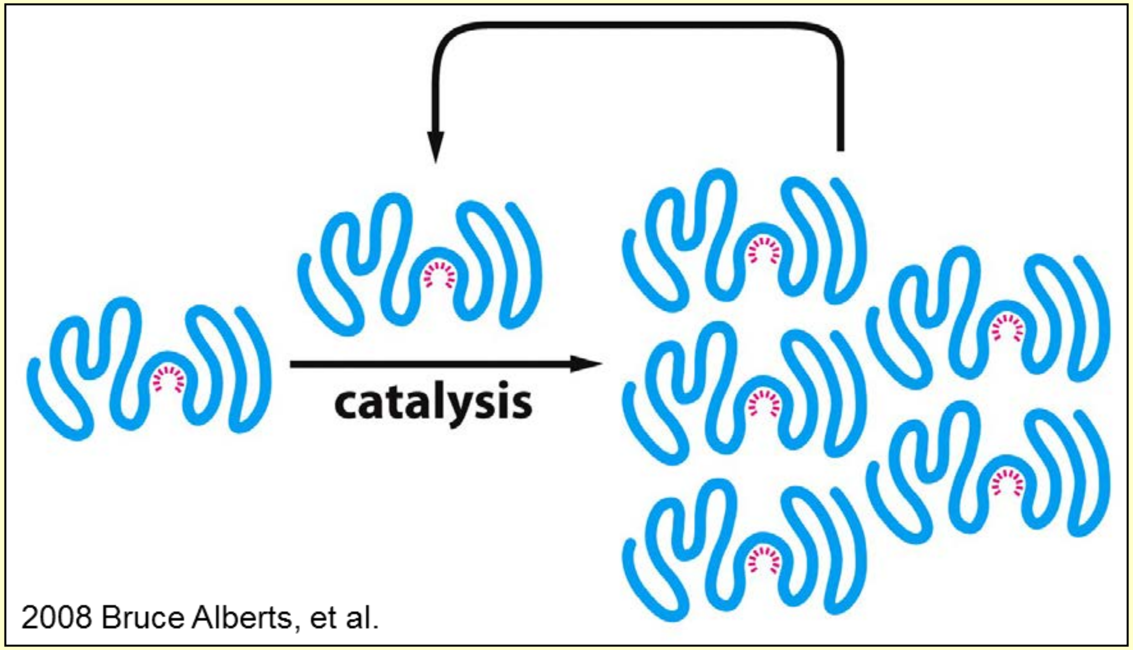
✓ without catalysts, polymer formation is slow, error-prone, and inefficient

✓ today, template-based nucleotide polymerization is rapidly catalyzed by protein enzymes - such as the DNA and RNA polymerases

❖ **How could it be catalyzed before proteins with the appropriate enzymatic specificity existed?**

RNA molecules themselves can act as catalysts

✓discovered in **1982.**



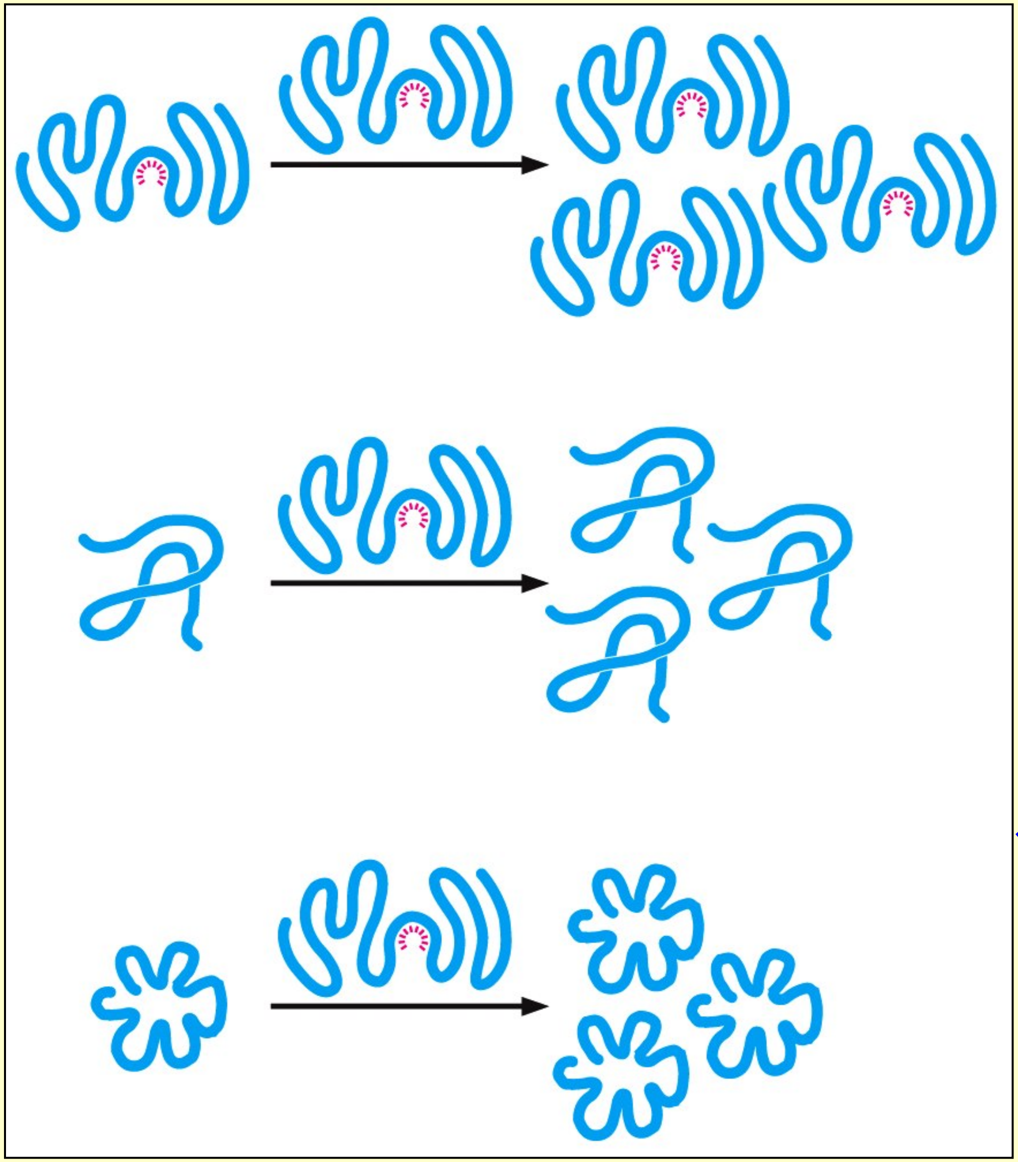
✓ The *red* rays represent the active site of this hypothetical RNA enzyme

Figure 6-99. An RNA molecule that can catalyze its own synthesis.

This hypothetical process would require:

- ✓ catalysis of the production of both a second RNA strand of complementary nucleotide sequence
- ✓ the use of this second RNA molecule as a template to form many molecules of RNA with the original sequence.

RNA can catalyze synthesis of RNA

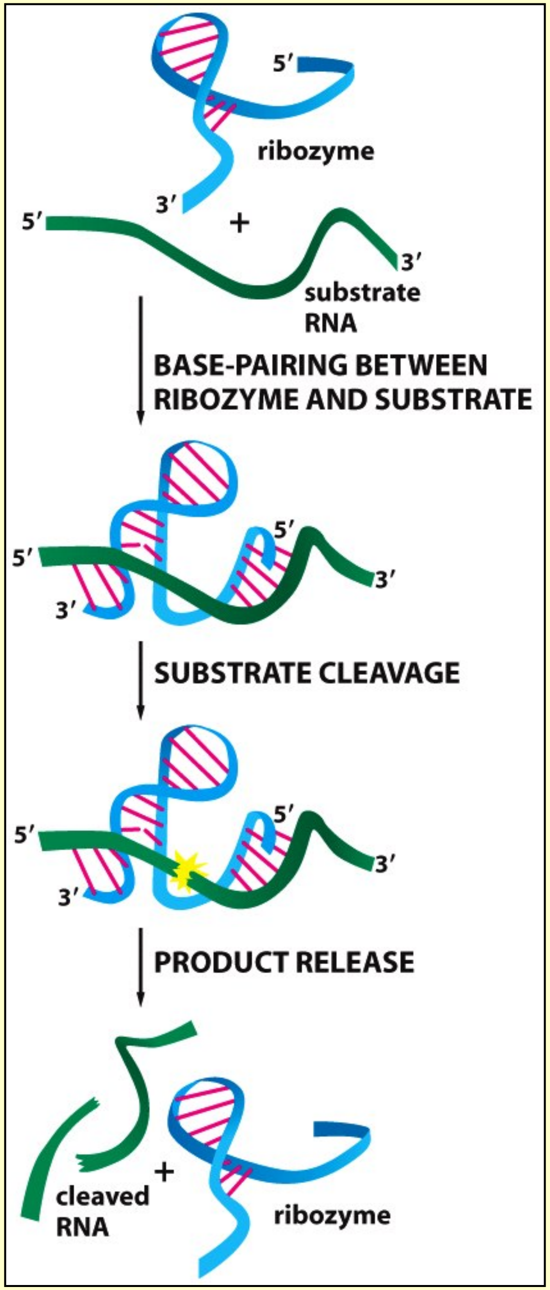


RNA molecule that can catalyze its own synthesis

a set of mutually beneficial RNAs could replicate themselves only if all the RNAs were to remain in the neighborhood of the RNA that is specialized for templated polymerization.

Figure 6-107 *Molecular Biology of the Cell*

A family of mutually supportive RNA molecules, one catalyzing the reproduction of the others.



Ribozyme (**ribo**nucleic acid en**zyme**)
= RNA enzyme
= catalytic RNA

- RNA molecule which can

✓ hydrolyze its own phosphodiester bonds

✓ hydrolyze phosphodiester bonds in other RNA molecules

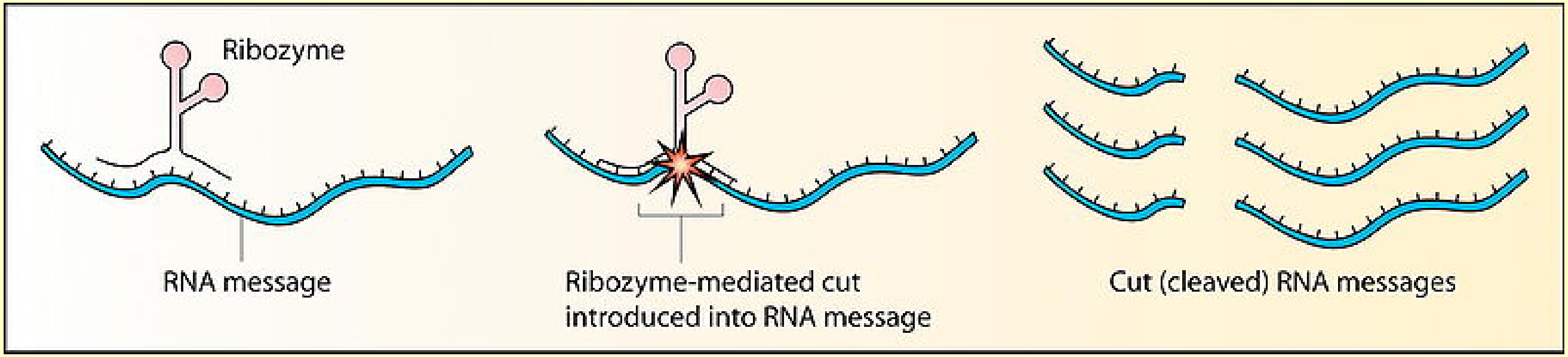
✓ catalyze aminotransferase activities of ribosomes

Figure 6-103.

This simple RNA molecule catalyzes the cleavage of a second RNA at a specific site.

Figure 6-103 *Molecular Biology of the Cell* (© Garland Science 2008)

Ribozymes *in vivo*



- Peptidyl transferase 23S rRNA
- RNase P
- Group I and Group II introns
- GIR1 branching ribozyme
- Leadzyme
- Hairpin ribozyme
- Hammerhead ribozyme
- HDV ribozyme
- Mammalian CPEB3 ribozyme
- VS ribozyme
- *glmS* ribozyme
- CoTC ribozyme

Pre-RNA world - RNA-like polymers

➢the first molecules to possess both catalytic activity and information storage capabilities may have been polymers that resemble RNA but are chemically simpler

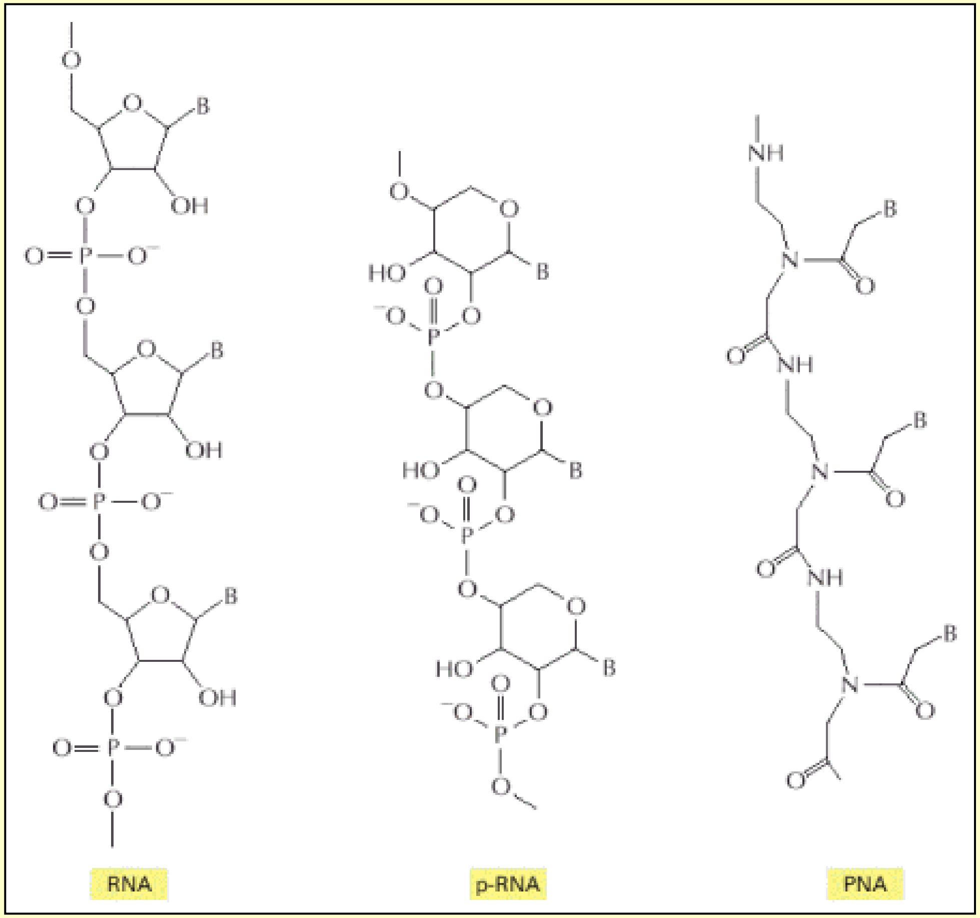


Figure 6-93. Structures of RNA and two related information-carrying polymers.

➢**p-RNA** (pyranosyl-RNA)
→ RNA in which ribose has been replaced by the pyranose

➢**PNA** (peptide nucleic acid)
→ the ribose phosphate backbone of RNA has been replaced by the peptide backbone found in proteins
→ can act as a template for synthesis of complementary RNA

2002 Bruce Alberts, et al.

Important qualities of RNA molecule

- ✓ information coded in nucleotide sequence
- ✓ 3D strucutre

- ✓ 3D strucutre important for
  - stability,
  - activity and
  - replication capability of RNA

RNA as a double-stranded molecule

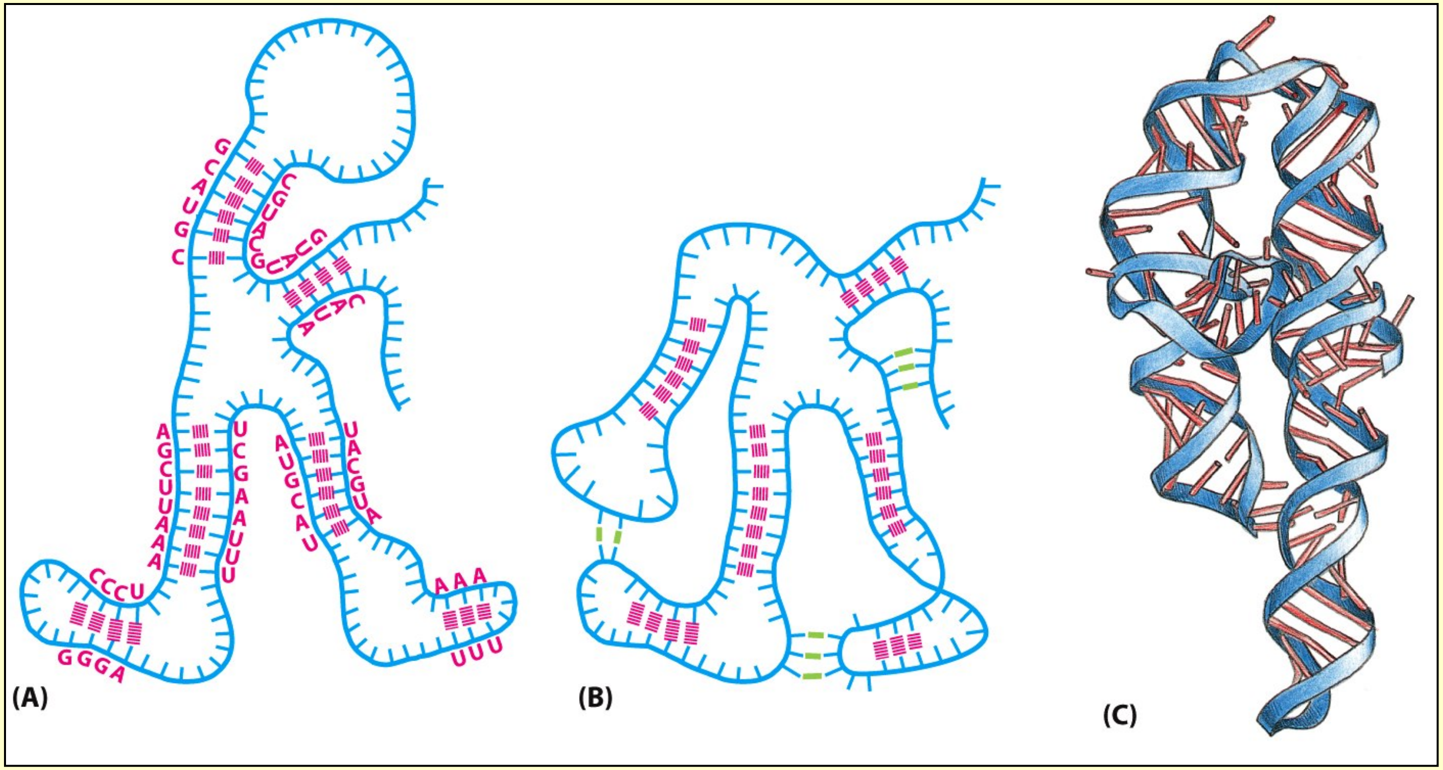


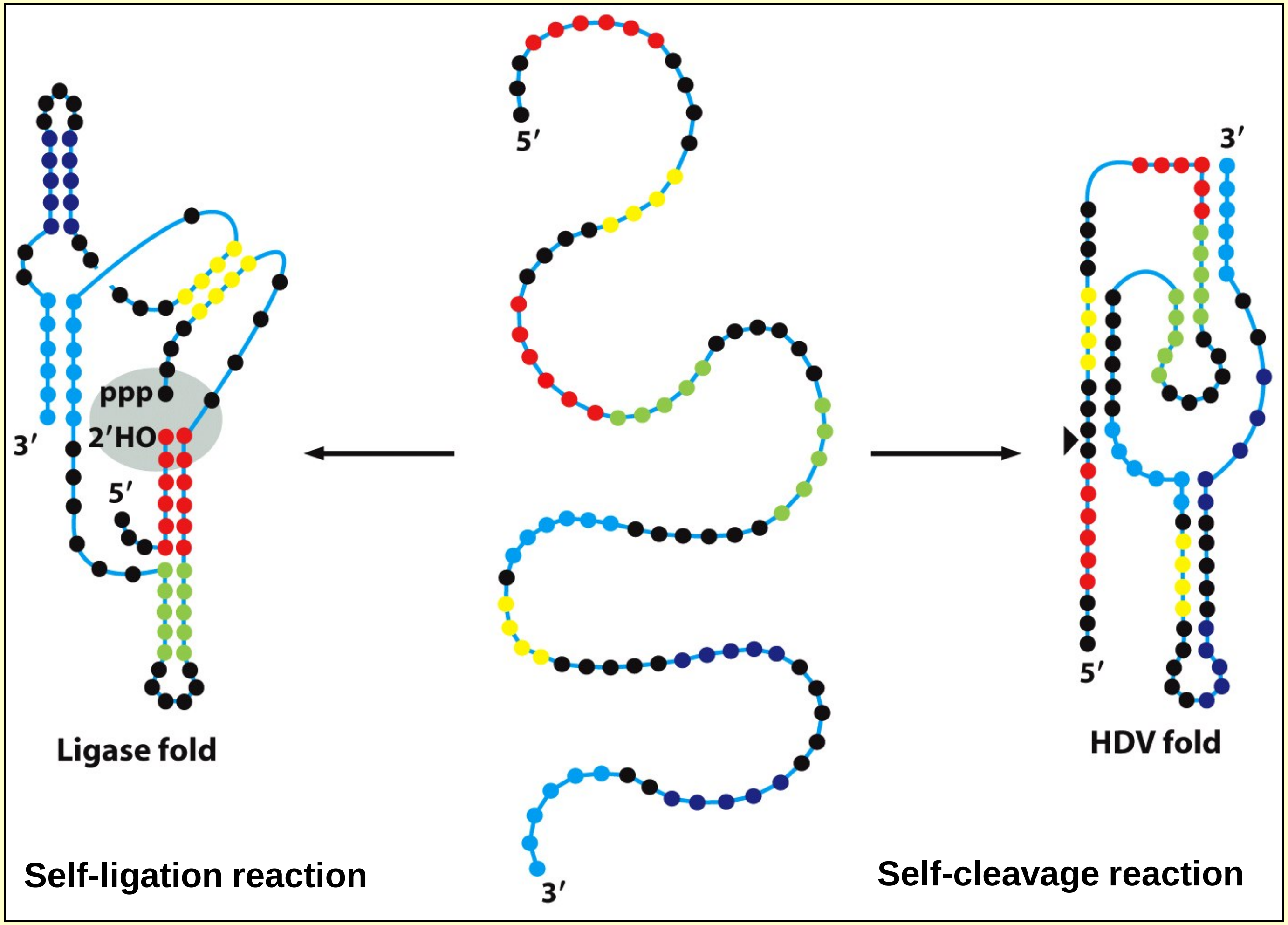
Figure 6-6 *Molecular Biology of the Cell* (© Garland Science 2008)

RNA can fold into specific structures

✓ RNA is largely single-stranded

✓ it often contains short stretches of nucleotides that can form conventional base-pairs with complementary sequences found elsewhere on the same molecule.

RNA that folds into two different ribozymes



- ✓ **hepatitis delta virus (HDV) ribozyme** - non-coding RNA necessary for virus replication
- ✓ active *in vivo*
- ✓ the fastest natural self-cleaving RNA

Figure 6-105 Molecular Biology of the Cell (© Garland Science 2008)

The hypothesis that RNA preceded DNA and proteins in evolution

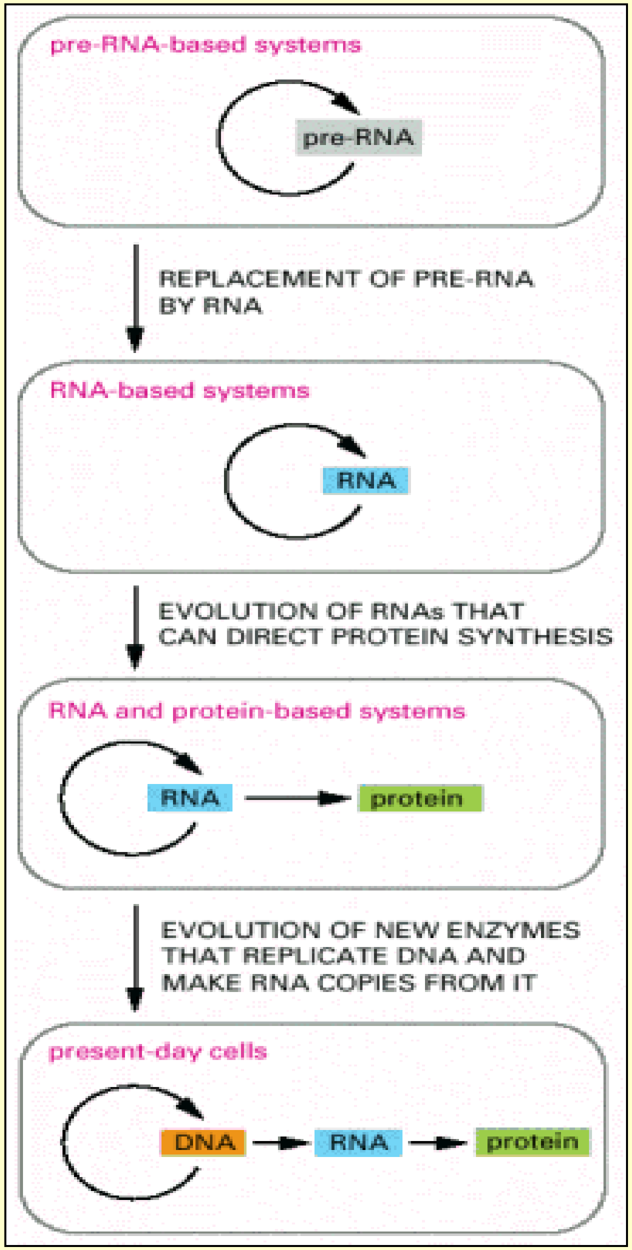


Figure 6-101. 2002 Bruce Alberts, et al.

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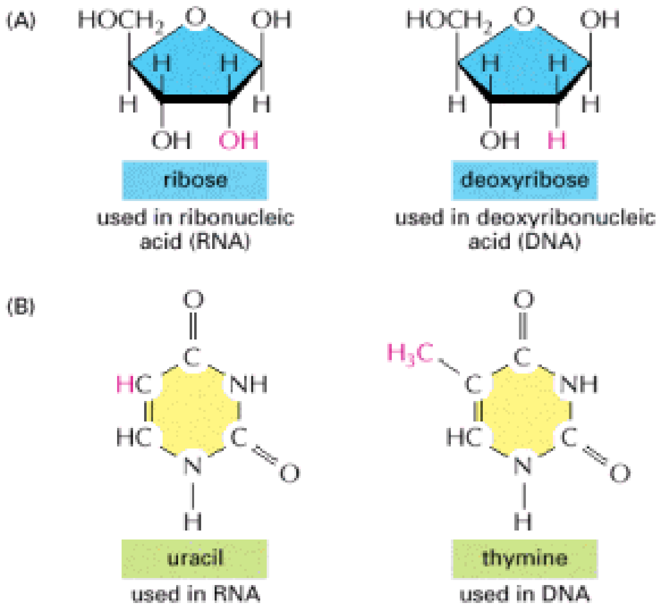
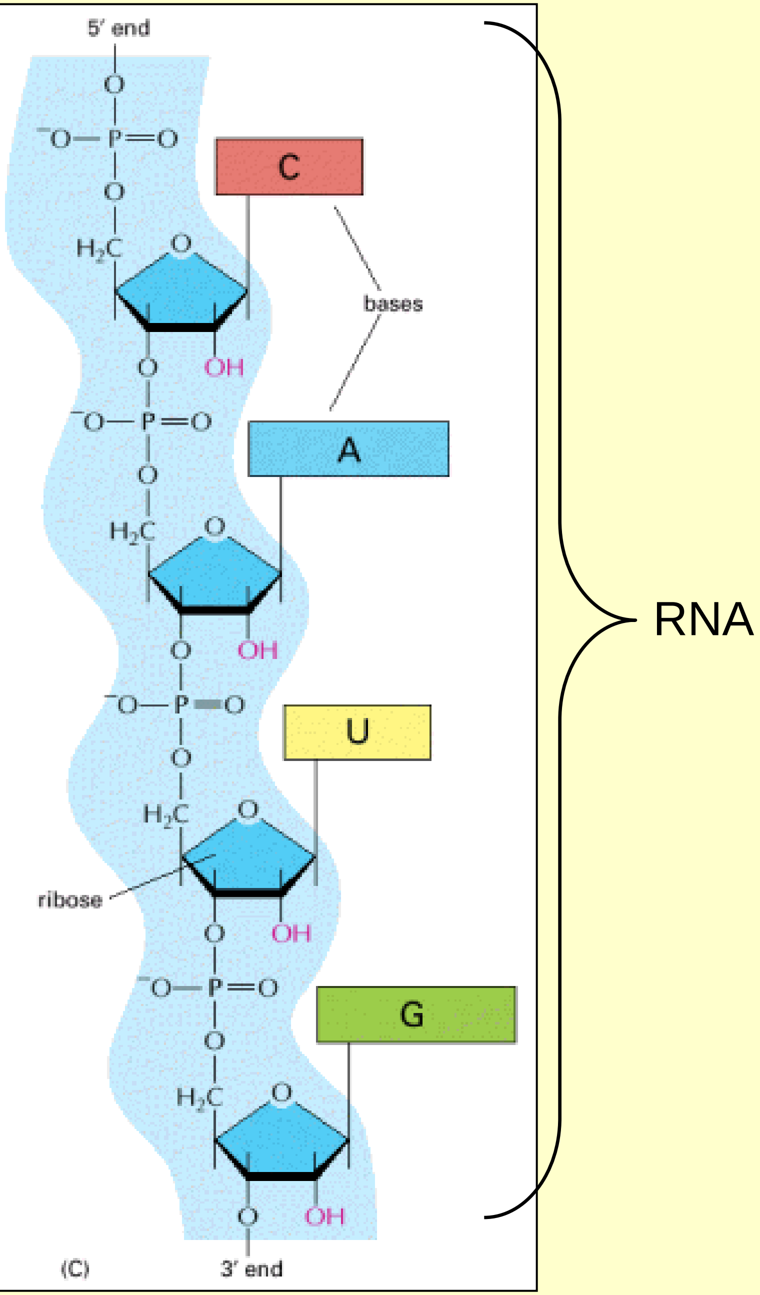
DNA vs RNA





Stability of DNA

- *deoxyribose*
- *thymine*
- *double-stranded structure*

2002 Bruce Alberts, et al.

Sugars

✓ Ribose – easy to produce from HCOH in the conditions of the first atmosphere

✓ Deoxyribose – modern cells: from ribose with enzymes

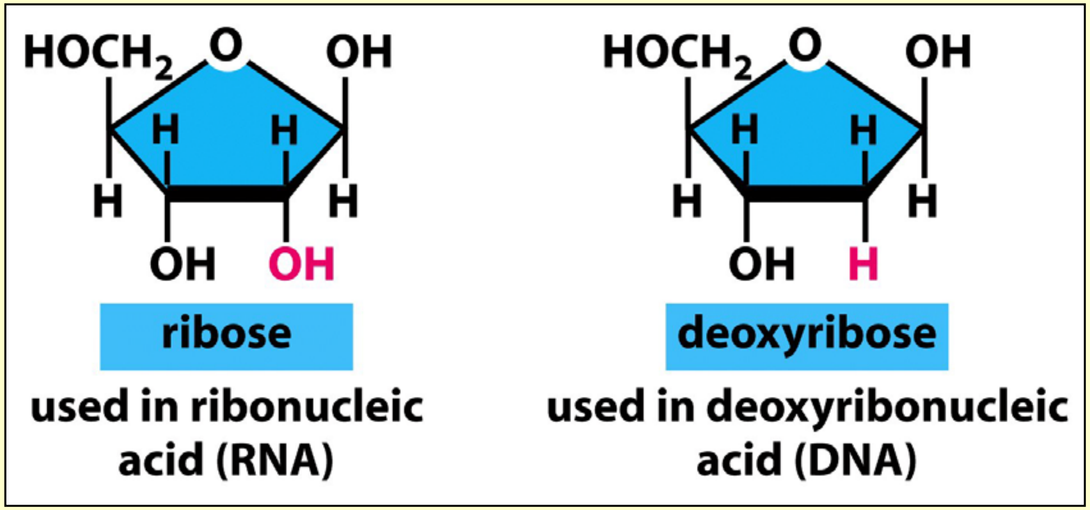


Figure 6-4a *Molecular Biology of the Cell* (© Garland Science 2008)

Bases

- A, G, C
- T (5-methyluracil) instead of U

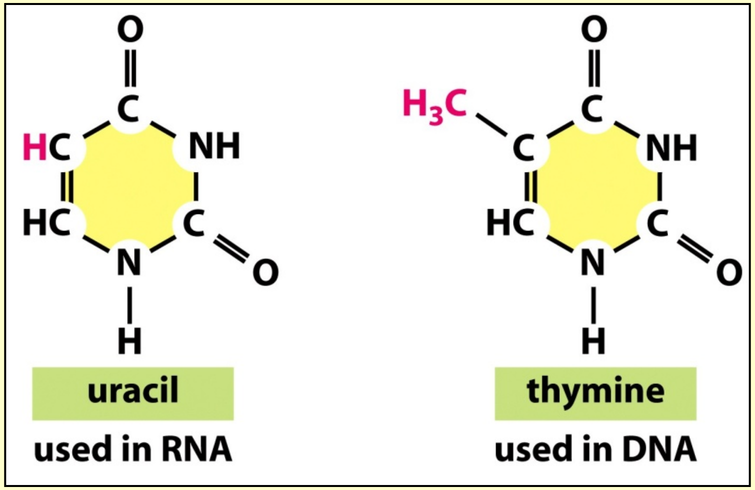


Figure 6-4b *Molecular Biology of the Cell* (© Garland Science 2008)

Question: Why is U methylated to T before incorporation to DNA?

Answer: Methylation protects DNA!
- additional methylations of A and C after DNA synthesis
- methylation makes DNA unrecognizable for nucleases form bacteria and viruses

Thymin protects DNA in another way:
- U is easily paired with all other bases (including U)
- addition of $–CH_3$ group allows T to pair only A - **ensures accuracy of DNA replication!**

Development of the first cell

- ✓ self-replicating RNA surrounded by the phospholipid membrane
- ✓ unit capable for self reproduction and further evolution

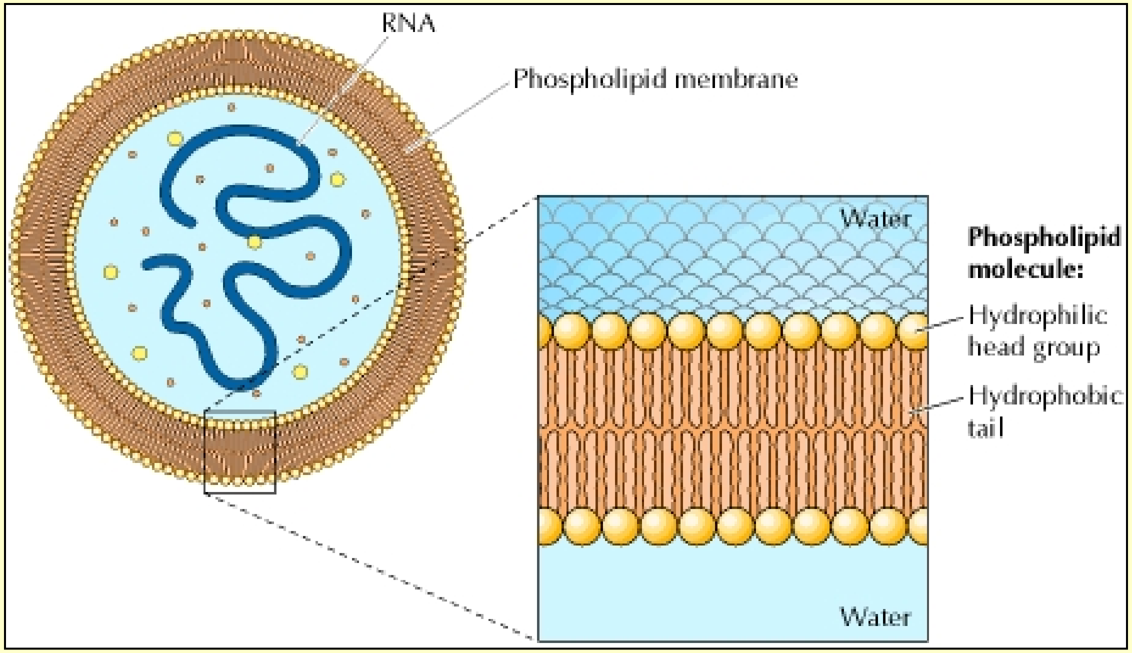
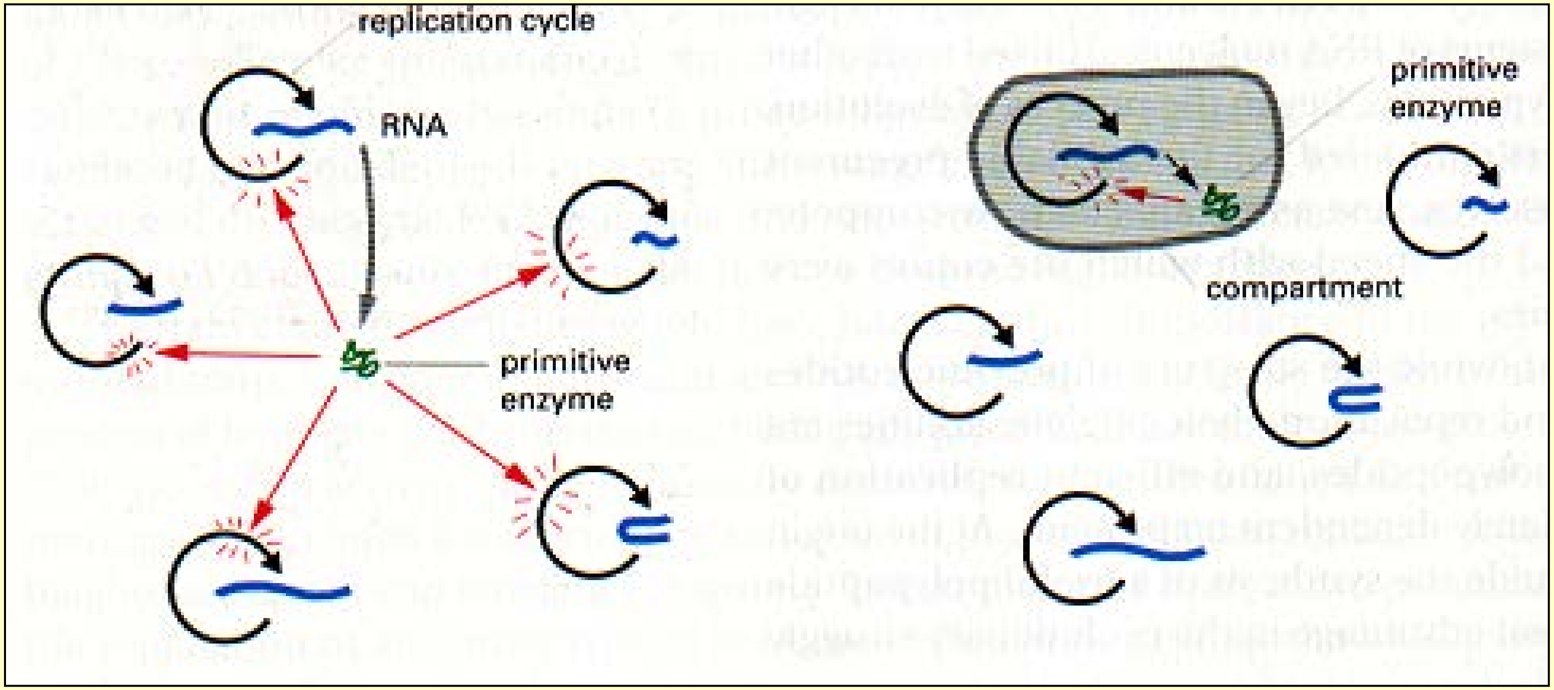


FIGURE 1.4. ENCLOSURE OF SELF-REPLICATING RNA IN A PHOSPHOLIPID MEMBRANE

Cooper GM. 2000.

Evolutionary importance of cell compartments formation



✓ in a mixed population of RNA molecules only one carries information for protein synthesis

✓ when it is placed in membrane surrounded compartment protein accelerates only her reproduction

2002 Bruce Alberts, et al.

Evolution of metabolism

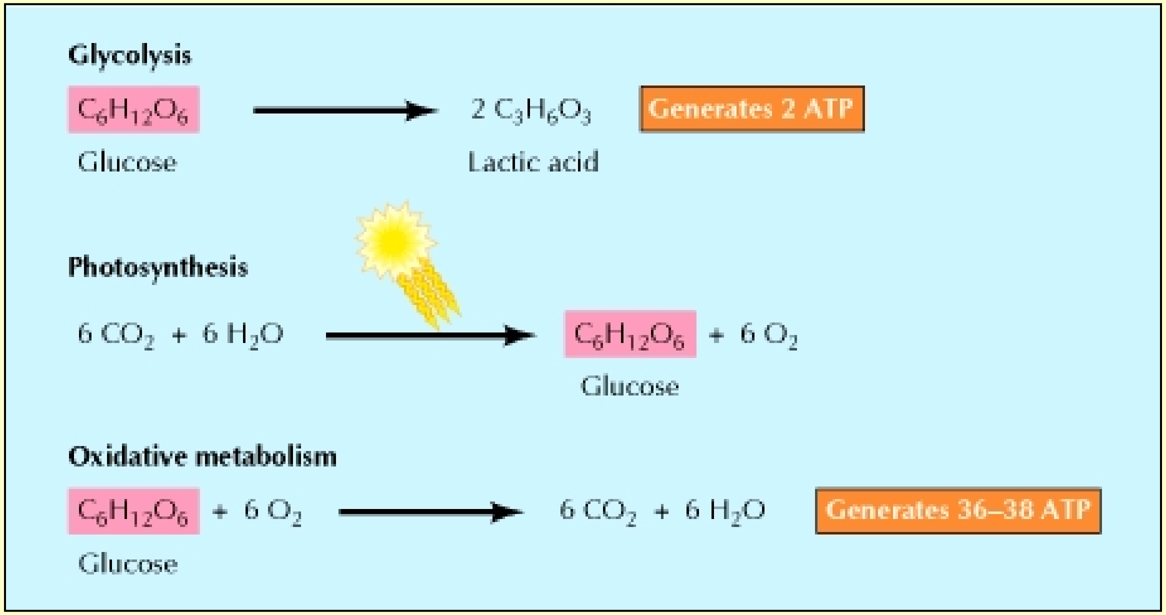


Figure 1.5. Generation of metabolic energy. Cooper GM. 2000.

✓Glycolysis is the anaerobic breakdown of glucose to lactic acid

✓Photosynthesis utilizes energy from sunlight to drive the synthesis of glucose from CO_2 and H_2O, with the release of O_2 as a by-product

✓The O_2 released by photosynthesis is used in oxidative metabolism, in which glucose is broken down to CO_2 and H_2O, releasing much more energy than is obtained from glycolysis.

Living organisms obtain free energy in different ways

Organotrophic (animals, fungi, some bacteria)
→ *trophe* – Greek word - food
→ feed on other living organisms

Fototrophic (plants, algaes and some bacteria)
→ harvest the energy of sunlight
→ altered the chemistry of our environment
(O_2 - product of biosynthetic activity)

Lithotrophic → capture energy form energy-rich systems of inorganic chemicals in the environment
→ microscopic organisms in extreme habitats (deep in the ocean, buried in Earth's crust)
→ aerobic (use molecular O_2)
→ anaerobic (environment similar to early days of of life on Earth)

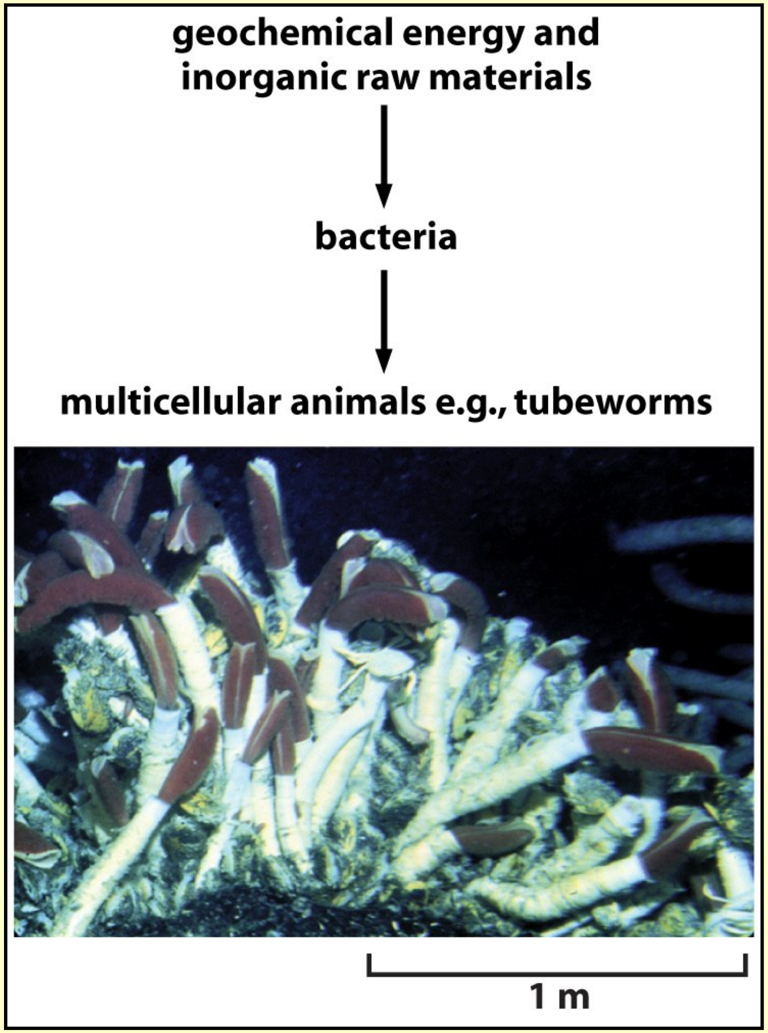
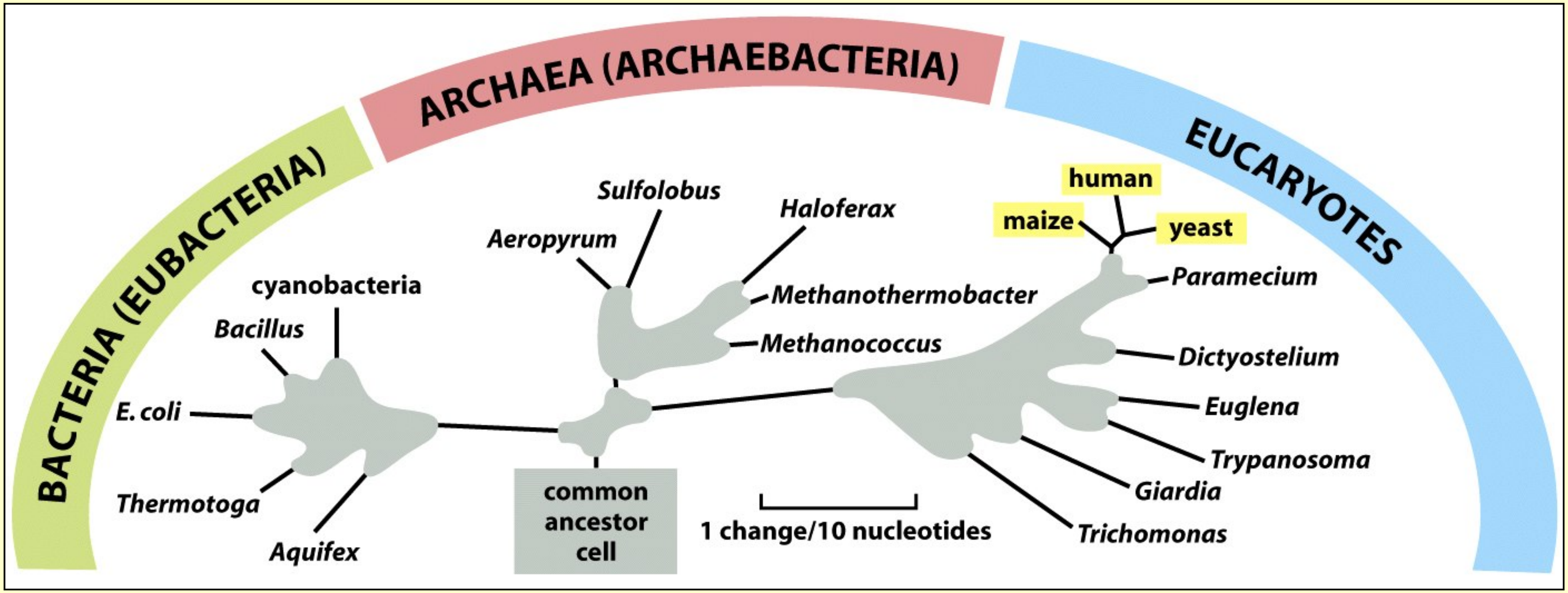


Figure 1-16 *Molecular Biology of the Cell*, Fifth Edition (© Garland Science 2008)

The three major divisions (domains) of the living world



✓ based on comparisons of the nucleotide sequence (about 1500 nucleotides) of a ribosomal RNA subunit 16S RNA in the different species

✓ the lengths of the lines represent the numbers of evolutionary changes that have occurred in this molecule in each lineage

Figure 1-21 *Molecular Biology of the Cell*, Fifth Edition (© Garland Science 2008)

Evolution of cells

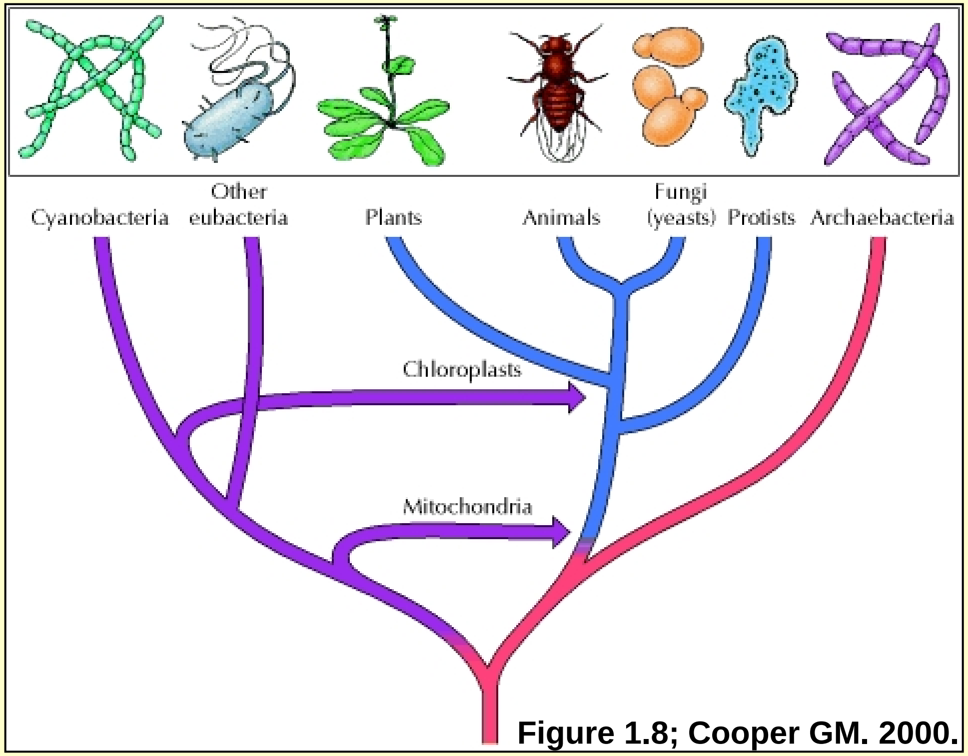


Figure 1.8; Cooper GM. 2000.

✓ present-day cells evolved from a common prokaryotic ancestor along three lines of descent, giving rise to **archaebacteria**, **eubacteria**, and **eukaryotes**

✓ mitochondria and chloroplasts originated from the endosymbiotic association of aerobic bacteria and cyanobacteria, respectively, with the ancestors of eukaryotes

Horizontal gene transfers in early evolution

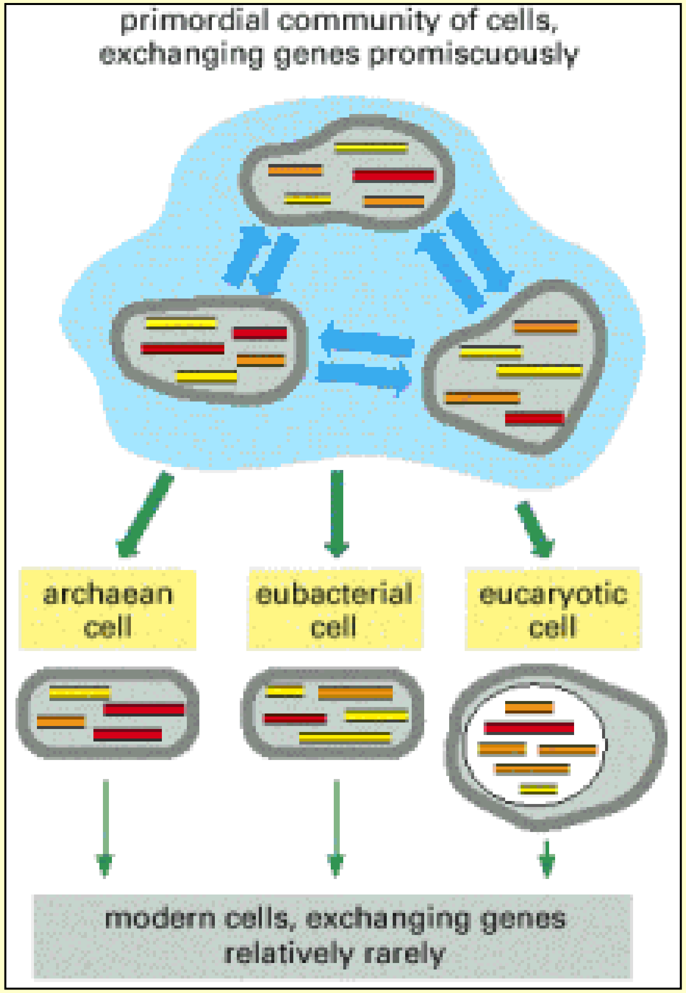


Figure 1-28. 2002 Bruce Alberts, et al.

✓ in early days of life on Earth horizontal gene transfer was frequent between cells

✓In that way archean, eubacterial and eukaryotic cells inherited different but overlapping sets of genes

Prokaryotic cells

✓ small

✓ simple structure

✓ unicellular organisms

✓ genomes small and compact

→ 10^6 – 10^7 nucleotides

→ 1000 – 4000 genes

• **Archaea** → with eukaryotes resembling in mechanisms for replication, transcription and translation

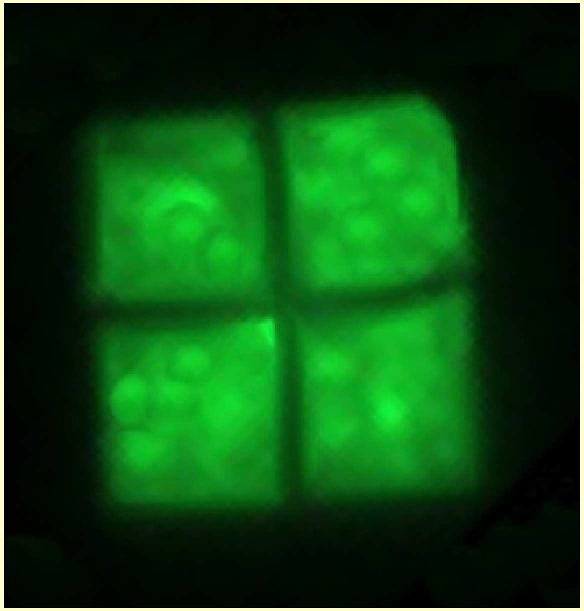
• **Bacteria** → with eukaryotes resembling in metabolism and energy conversion

Archaea

Halobacteriaceae

- **genus *Halobacterium***

- **genus *Haloquadratum***



Eubacteria

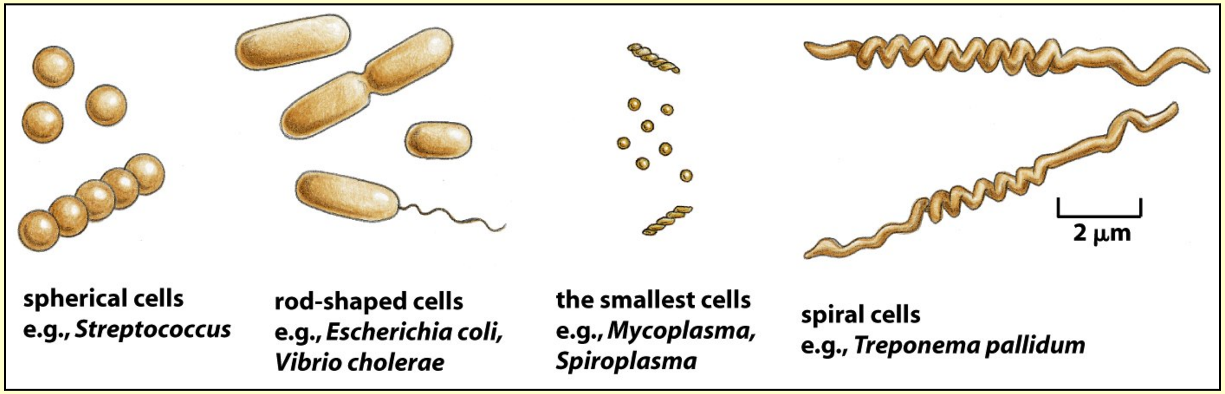
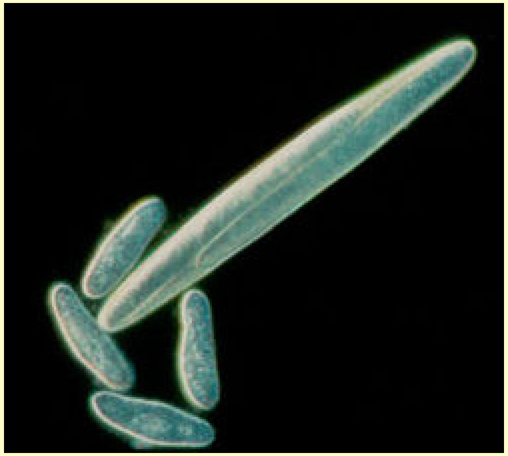


Fig. 1-17. Shapes and sizes of some bacteria. Although most are small, as shown, there are also some giant species. An extreme example is the cigar-shaped bacterium *Epulopiscium fishelsoni*, which lives in the gut of the surgeon fish and can be up to 600 µm long.



2002 Bruce Alberts, et al.

- ✓*Epulopiscium fishelsoni* – one epulo with four Paramecium
- ✓length 200-600 µm; diameter 80 µm

http://schaechter.asmblog.org.

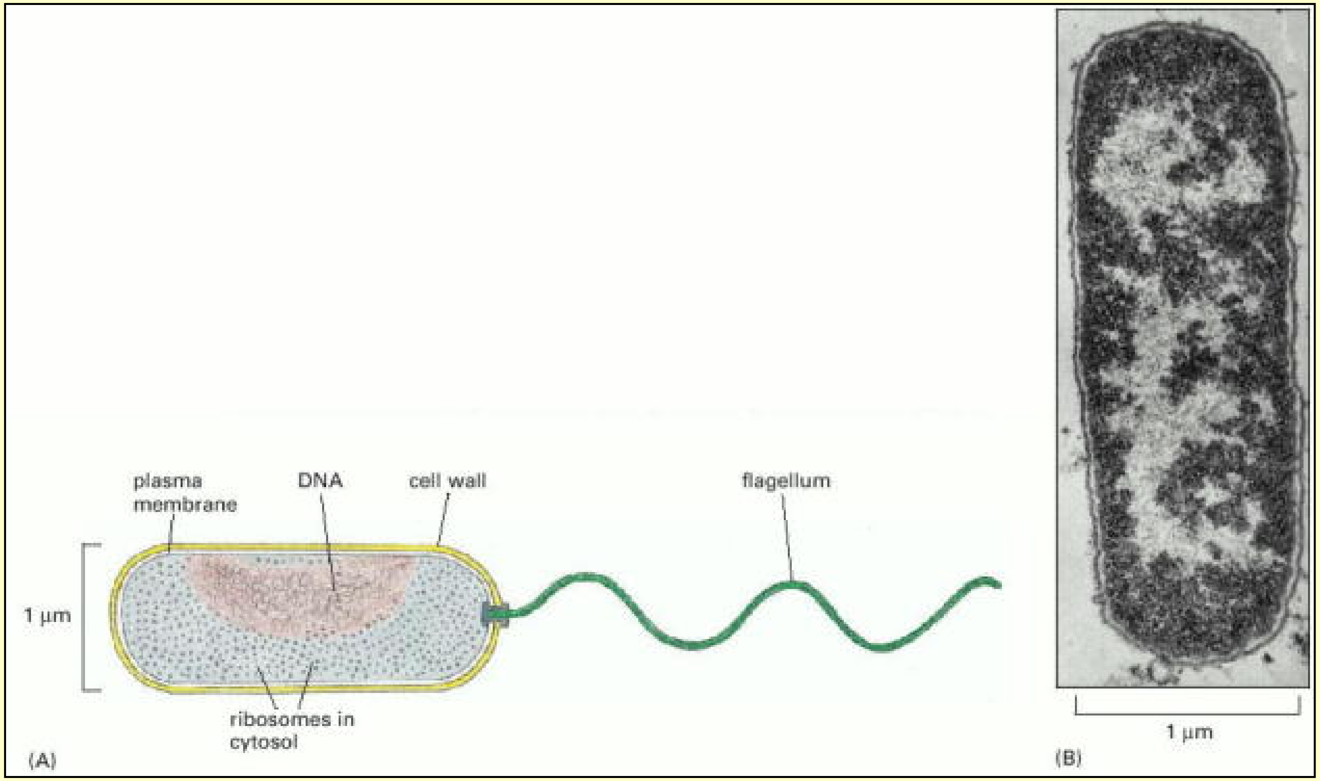


Figure 1-18. The structure of a bacterium.

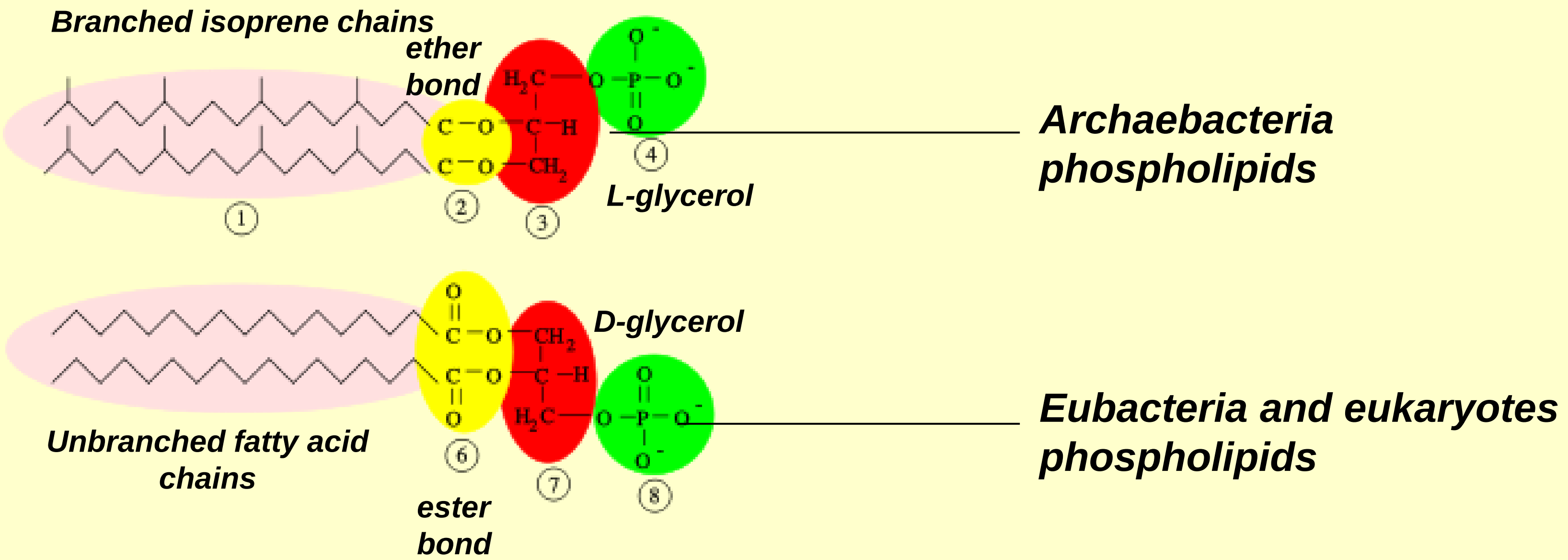
(A) The bacterium *Vibrio cholerae*, showing its simple internal organization. Like many other species, *Vibrio* has a helical appendage at one end—a flagellum—that rotates as a propeller to drive the cell forward.

(B) An electron micrograph of a longitudinal section through the widely studied bacterium *Escherichia coli* (*E. coli*). This is related to *Vibrio* but lacks a flagellum. The cell's DNA is concentrated in the lightly stained region.

2002 Bruce Alberts, et al.

Differences between archaebacteria and eubacteria

- ✓ *archaebacteria - no peptidoglycan (murein) in cell wall*
- ✓ *unique lipid bilayer in cell membranes → differences in lipids*



- ✓ *RNA polymerase of archaea like in eukaryotes*
- ✓ *ribosomal proteins like in eukaryotes*

http://study.com/academy/lesson/archaea-bacteria-similarities-differences.html

Eukaryotic cells

✓ similarities to prokaryotic cells → surrounded by a plasma membrane and ribosomes

✓ difference → more complex:

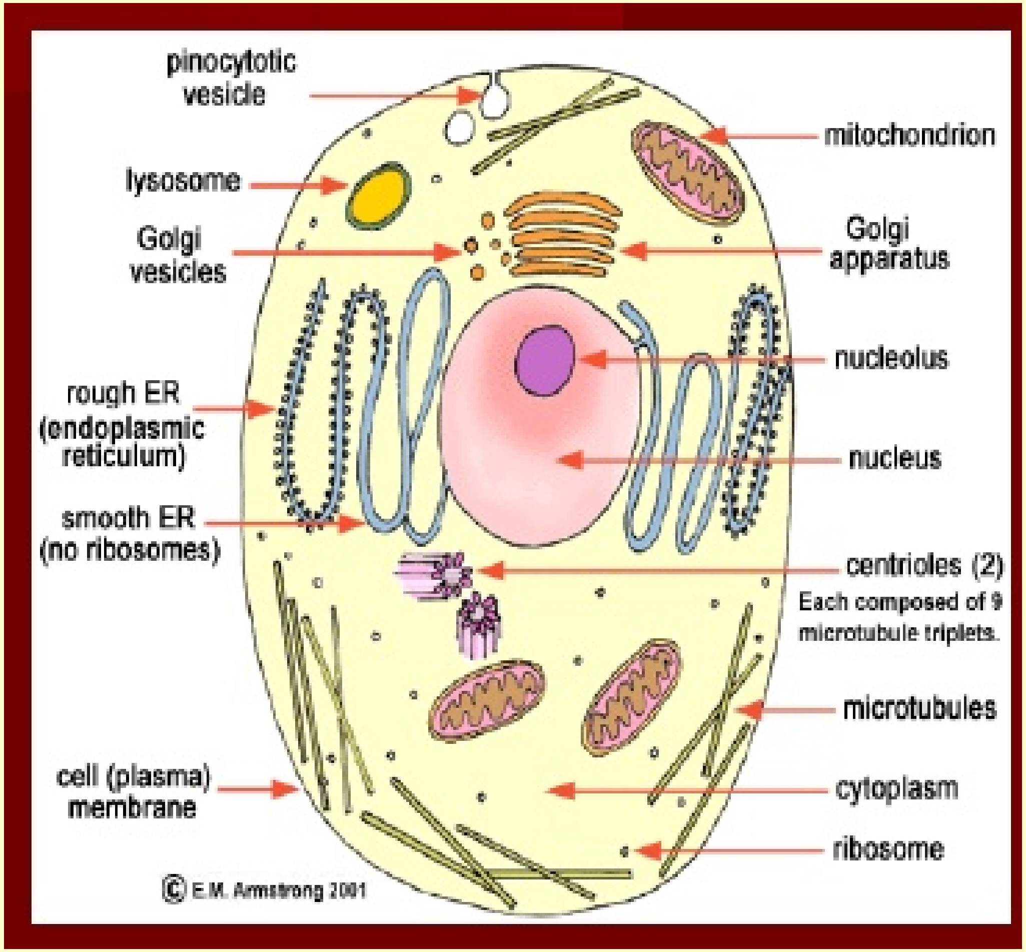
- nucleus
- cytoplasmic organelles
- cytoskeleton

✓ **Nucleus** → the largest organelle (5 μm diameter)

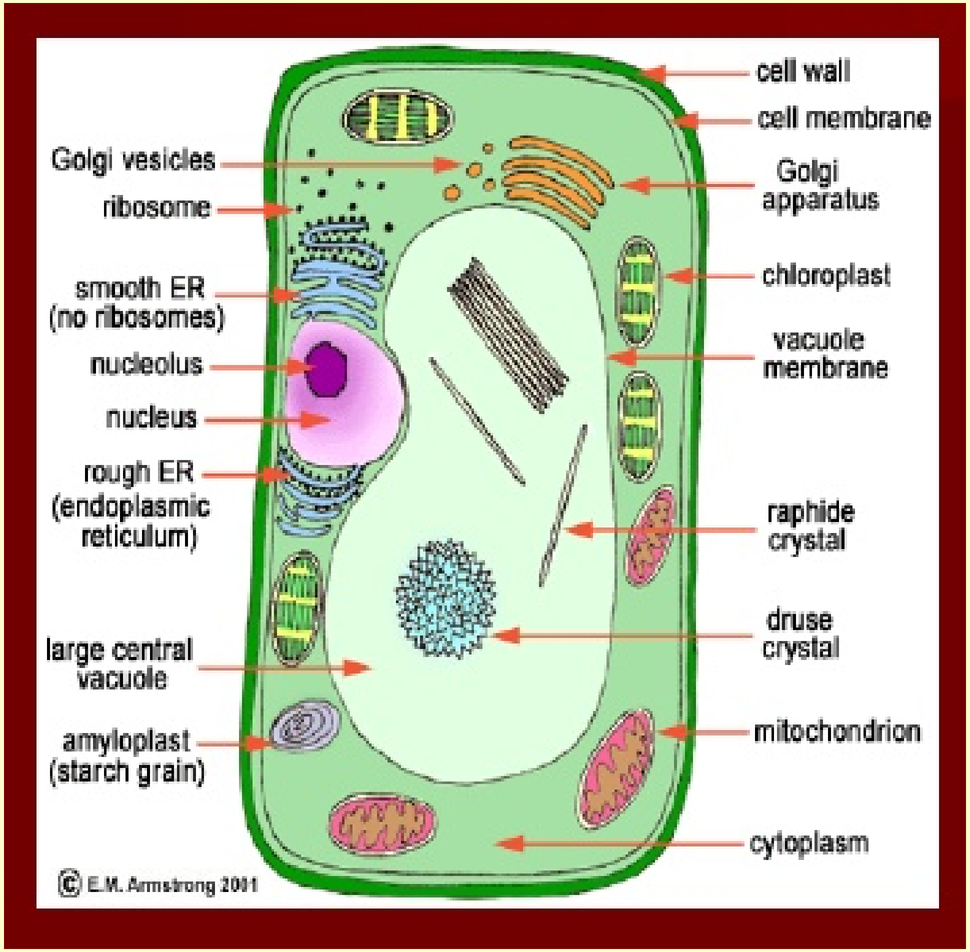
- genetical information
- linear DNA molecule
- DNA replication and RNA synthesis

✓ **Cytoplasm** → different organelles surrounded by membranes

The structure of an animal cell



The structure of a plant cell



Plant cells are surrounded by a cell wall and contain chloroplasts and large vacuoles.

Endosymbiont hypothesis

- ✓ acquirement of organelles surrounded by membrane → important step in evolution of eukaryotic cells
- ✓ eukaryotic cells started out as anaerobic organisms
- ✓ established endosymbiotic relation with ancestors of mitochondrion (purple bacterium) and chloroplast (photosynthetic bacterium)
- ✓ proofs which support this hypothesis:
    - ✓ DNA-containing organelles
    - ✓ similar size like bacteria
    - ✓ binary division (like bacteria)
    - ✓ ribosomes and rRNA resemble bacterial

Mitochondria evolved from bacteria engulfed by ancestral eukaryotic cells

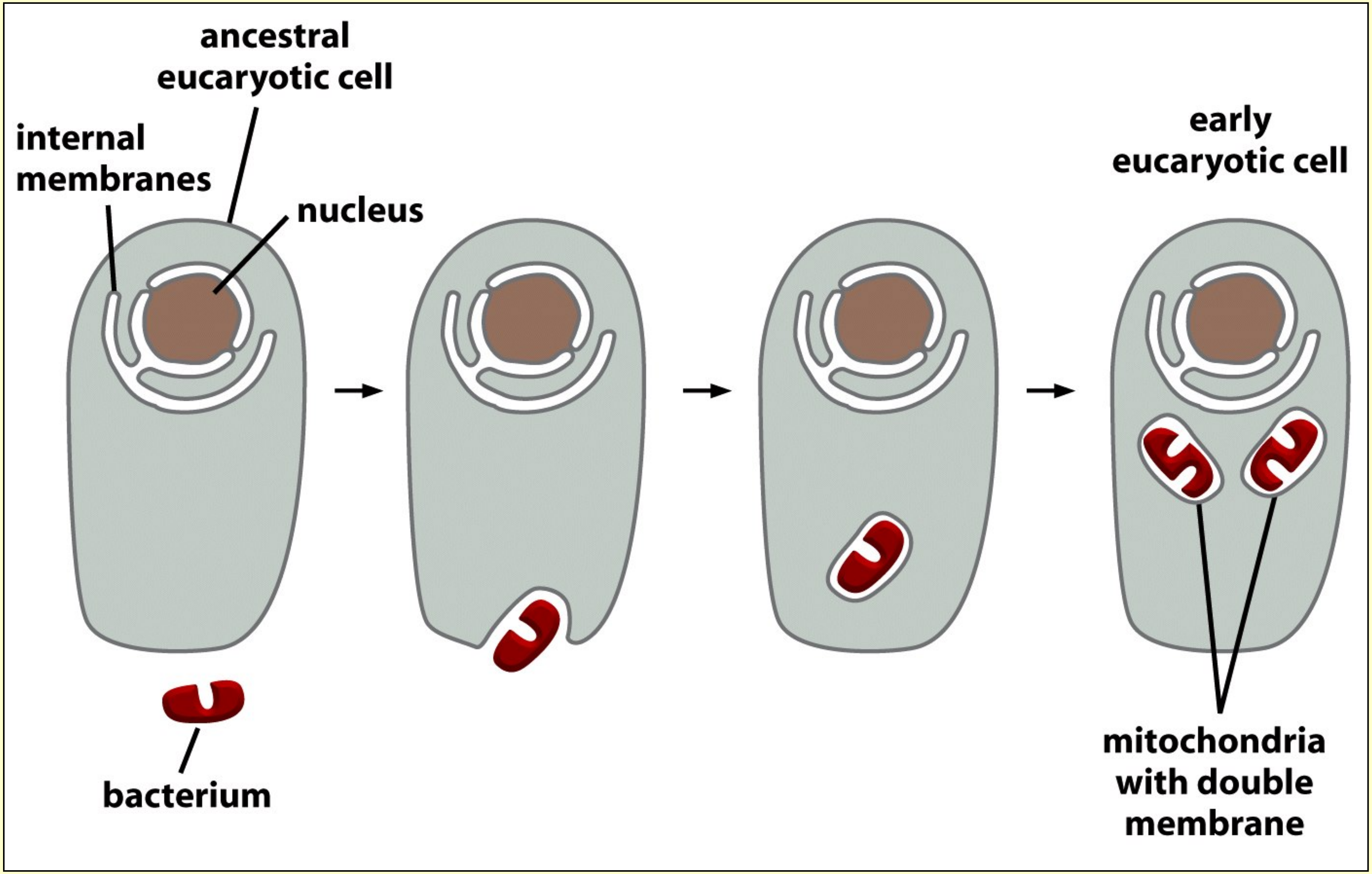


Figure 1-34 *Molecular Biology of the Cell*, Fifth Edition (© Garland Science 2008)

Chloroplasts evolved from bacteria engulfed by ancestral eukaryotic cells

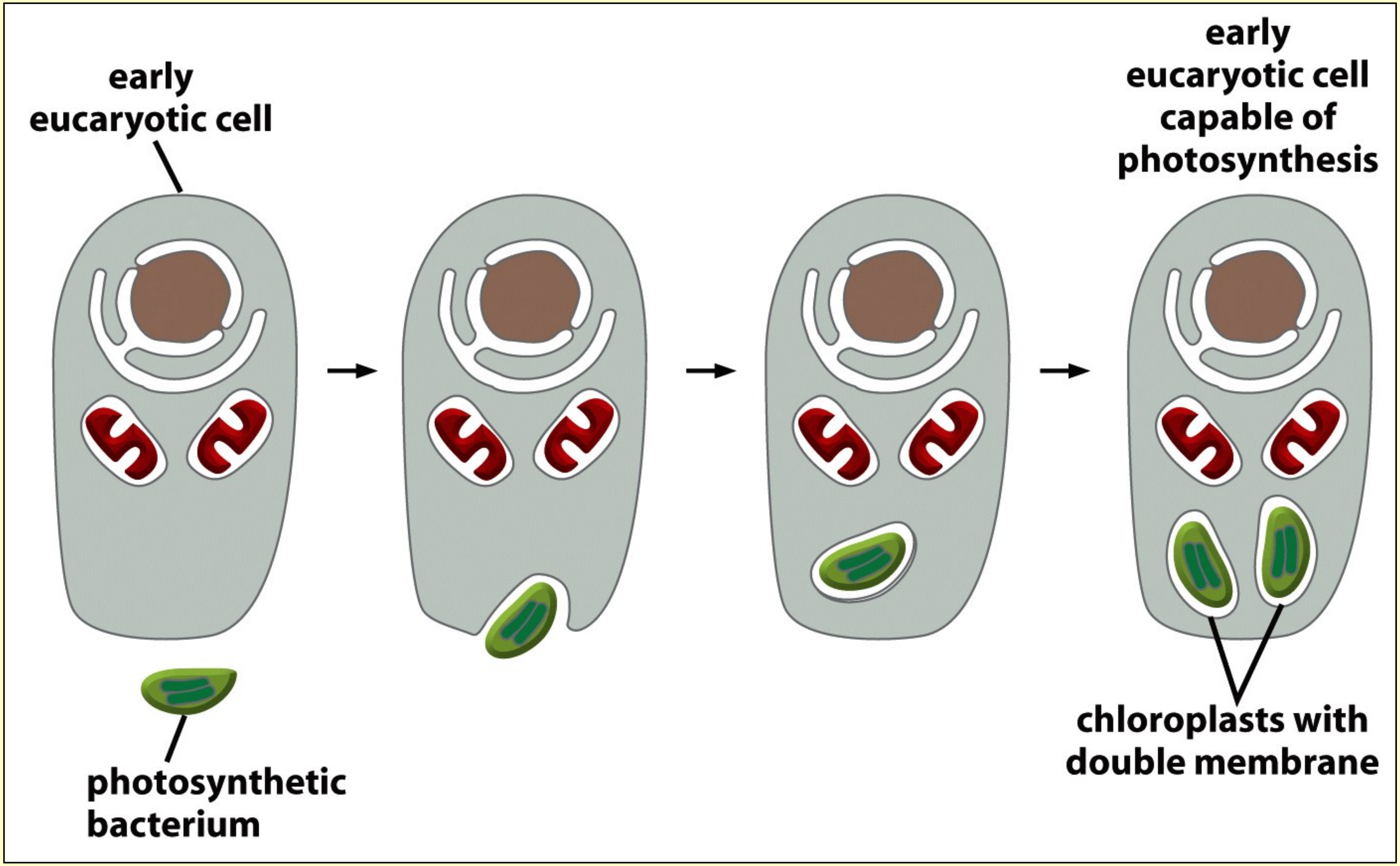
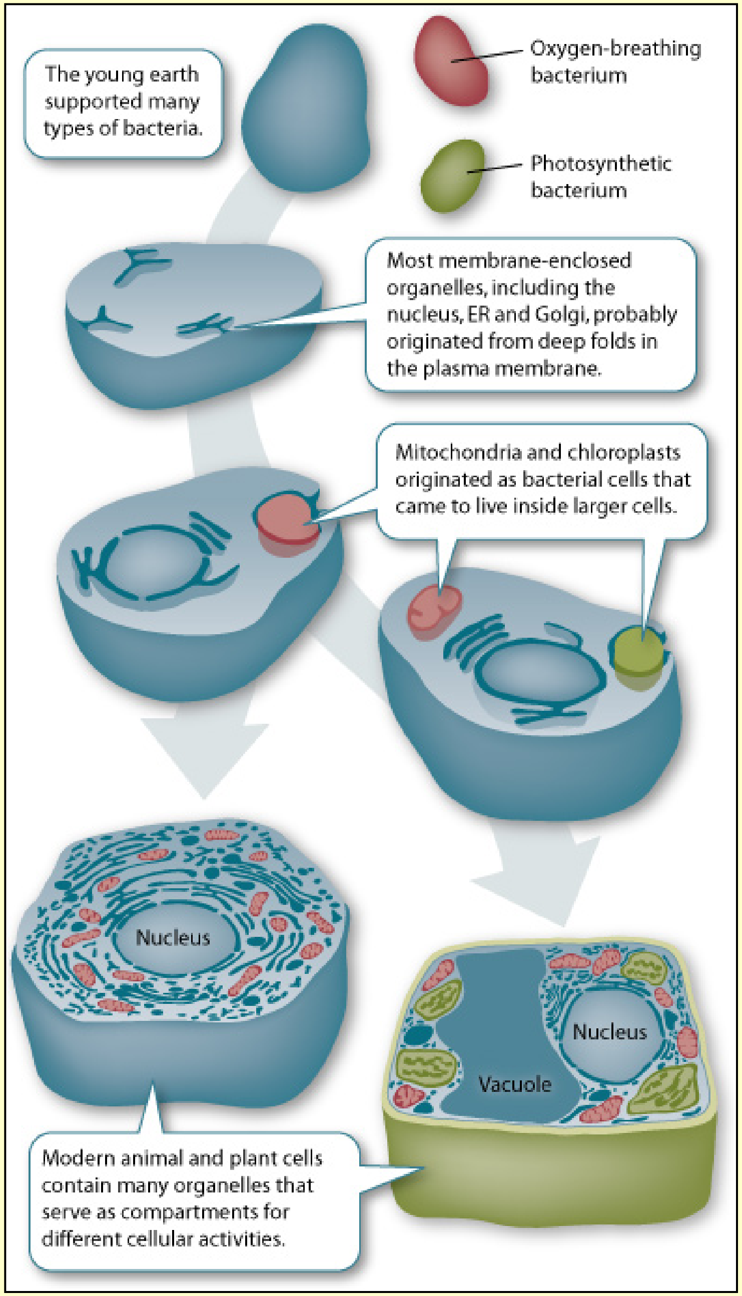


Figure 1-36 *Molecular Biology of the Cell*, Fifth Edition (© Garland Science 2008)

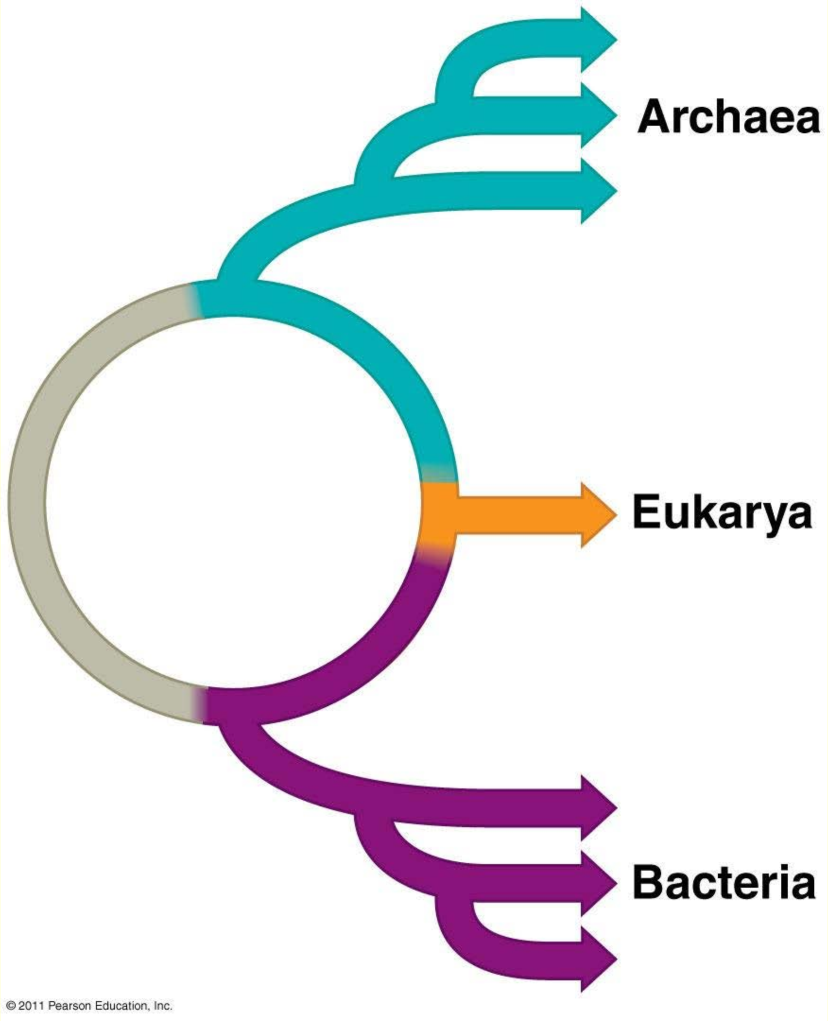


http://learn.genetics.utah.edu/content/begin/cells/organelles/

Animacija

http://www.sumanasinc.com/webcontent/animations/content/organelles.html

Origin of eukaryotes – the circle of life



Hypothesis:

- ✓ *Eukaryotic genomes are the result of the archaea and bacteria genome fusion*
- ✓ *Explanation of the mosaic nature of eukaryotic genome*

1. *Endosymbiotic association of eubacteria and archaebacteria*
2. *Genome fusion – eukaryotic genome with archaeal and bacterial genes*

❖ *Initial endosymbiotic relationship - aerobic eubacteria living in archaebacteria*

❖ *Result:*
- *Mitochondria*
- *Genome of eukaryotic cells*

Differences between eukaryotic and prokaryotic cell in steps leading from gene to protein

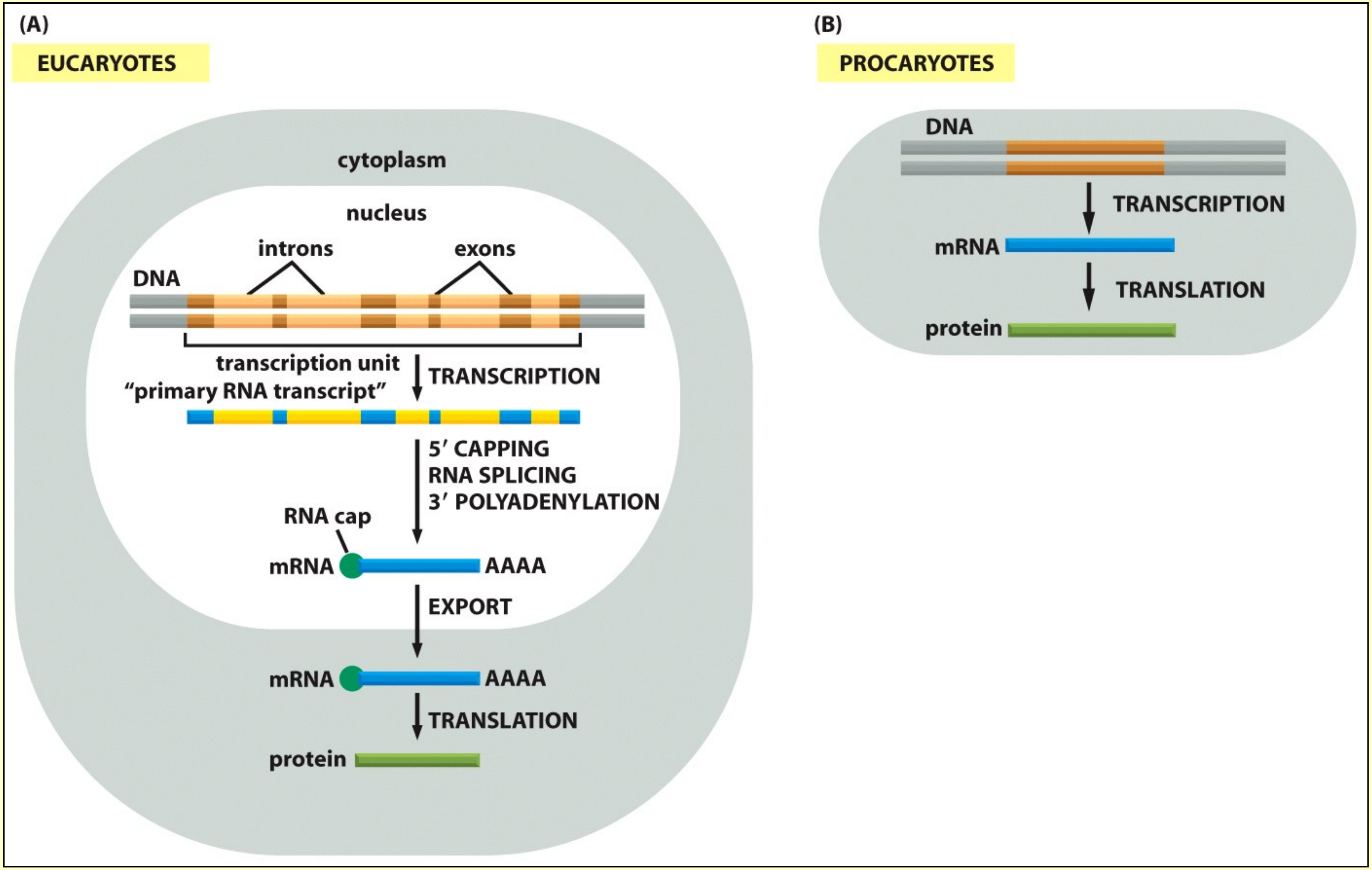


Figure 6-21 Molecular Biology of the Cell (© Garland Science 2008)