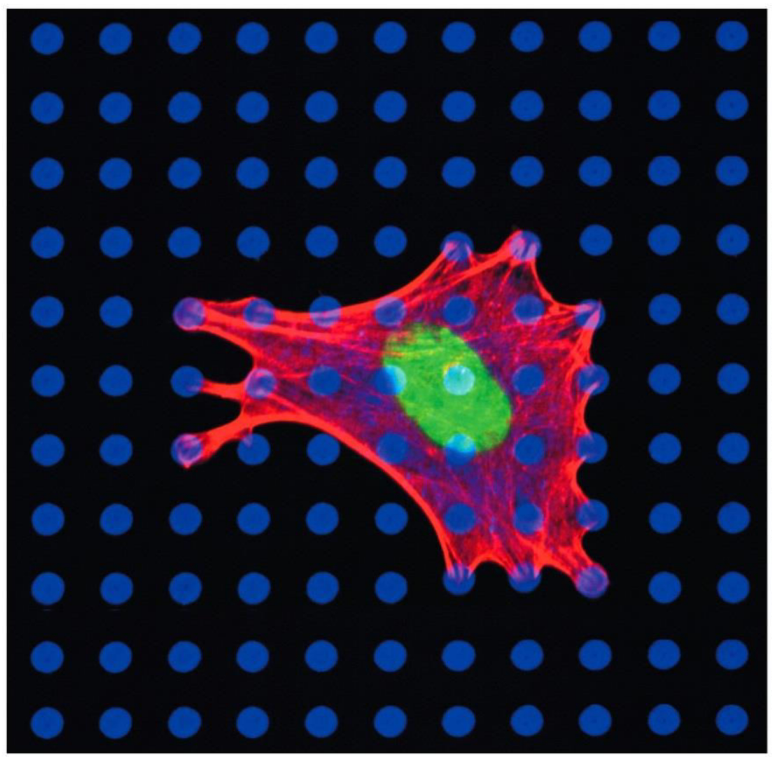
CHAPTER 1

Introduction to Cell Biology



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Keys

- Outline the early history of Cell Biology.
- Distinguish the basic properties of all cells.
- Describe the differences between prokaryotic and eukaryotic cells.
- Specify the types of prokaryotic cells.
- Emphasize cell specialization as it relates to eukaryotic cells.
- Discuss the relevance of multicellularity and the significance of cellular differentiation.
- Review the dimensions important to Cell Biology.
- Clarify the structure and function of the different types of viruses.
- Define the mechanisms by which viral infections proceed.
- Explain the traits that distinguish viroids from viruses.

Introduction

- Cells are the topic of intense study.
- The study of cells requires creative instruments and techniques.
- Cell biology is *reductionist,* based on the premise that studying the parts of the whole can explain the character of the whole.

(1.1) The Discovery of Cells

- The discovery of cells followed from the invention of the **microscope** by Robert Hooke, and its refinement by Anton Leewenhoek.

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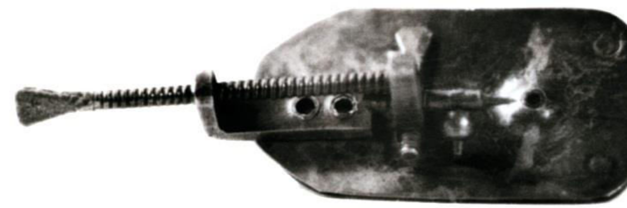
Hooke: double lens microscope



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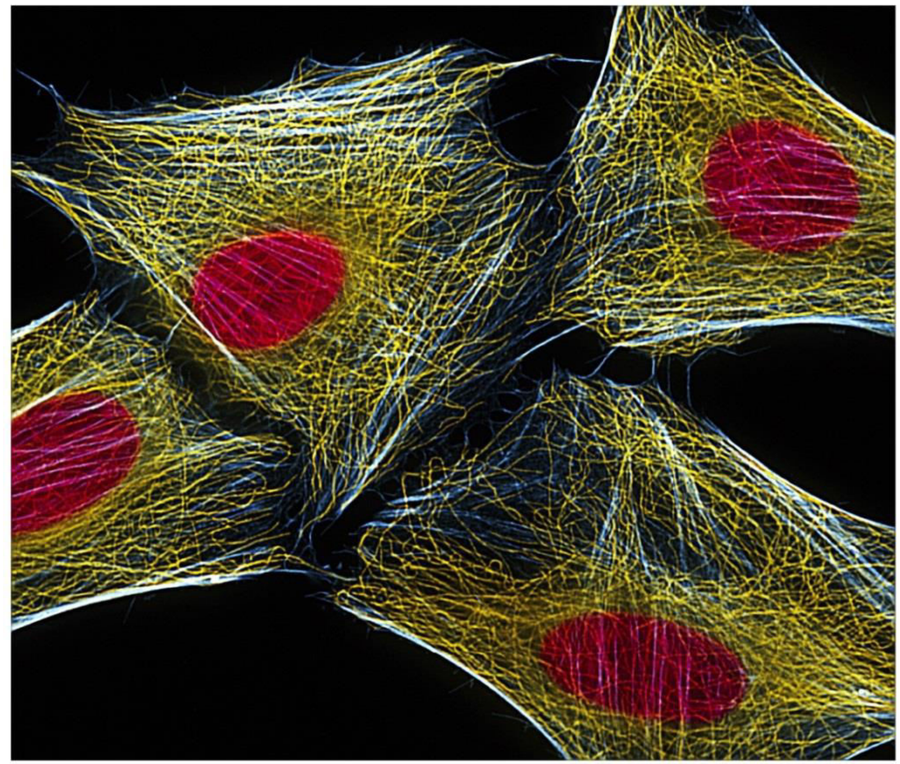
Leewenhoek: single lens microscope

- **Cell theory** was articulated in the mid-1800s by Schleiden, Schwann and Virchow.
  - All organisms are composed or one or more cell.
  - The cell is the structural unit of life.
  - Cells arise from pre-existing cells by division.

(1.2) Basic Properties of Cells

- Life is the most basic property of cells.
- Cells can grow and reproduce in culture for extended periods.
  - HeLa cells are cultured tumor cells isolated from a cancer patient (Henrietta Lacks) by George Gey in 1951.
  - Cultured cells are an essential tool for cell biologists.

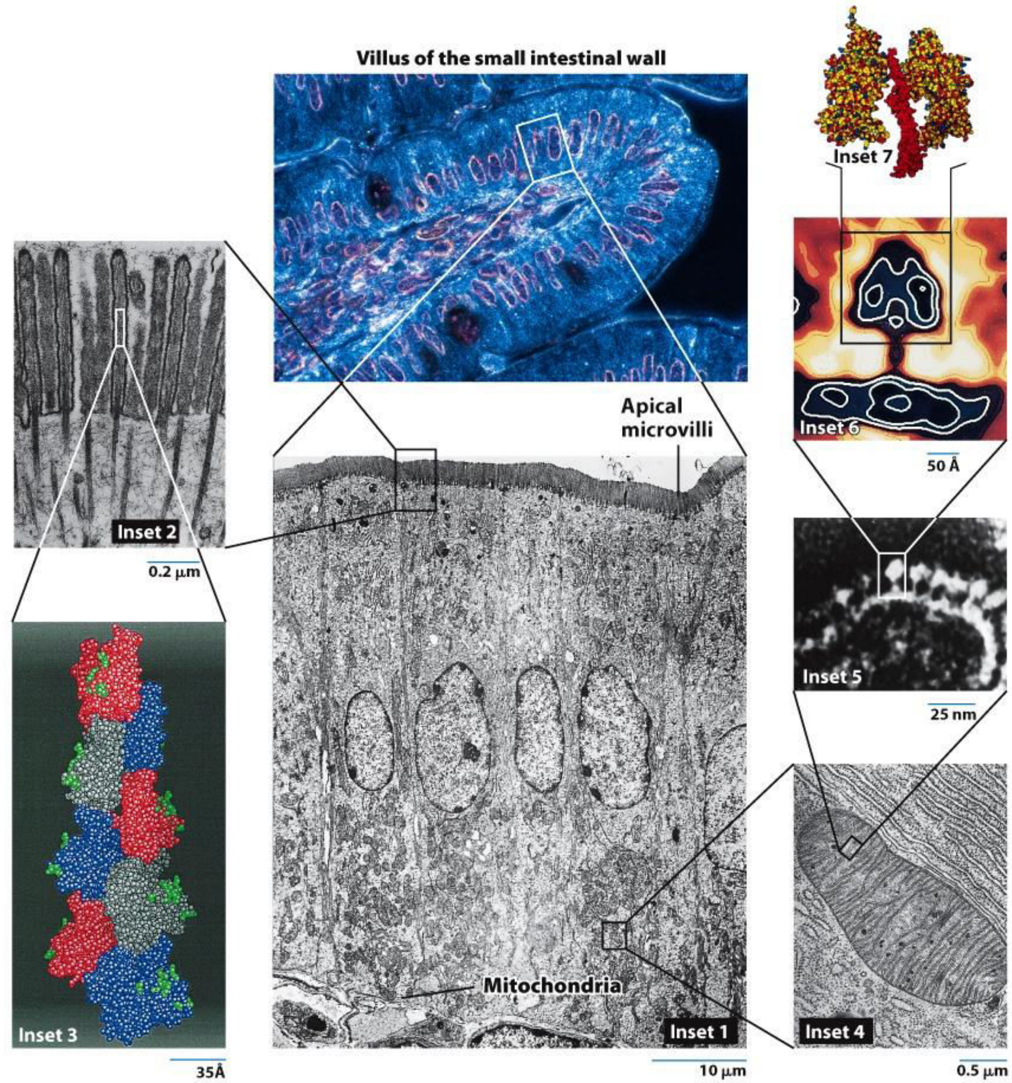


Torsten Wittmann/Photo Researchers, Inc.

HeLa: first human cells for extended culturing

Basic Properties of Cells

- Cells Are Highly Complex and Organized
  - Cellular processes are highly regulated.
  - Cells from different species share similar structure, composition and metabolic features that have been conserved throughout evolution.



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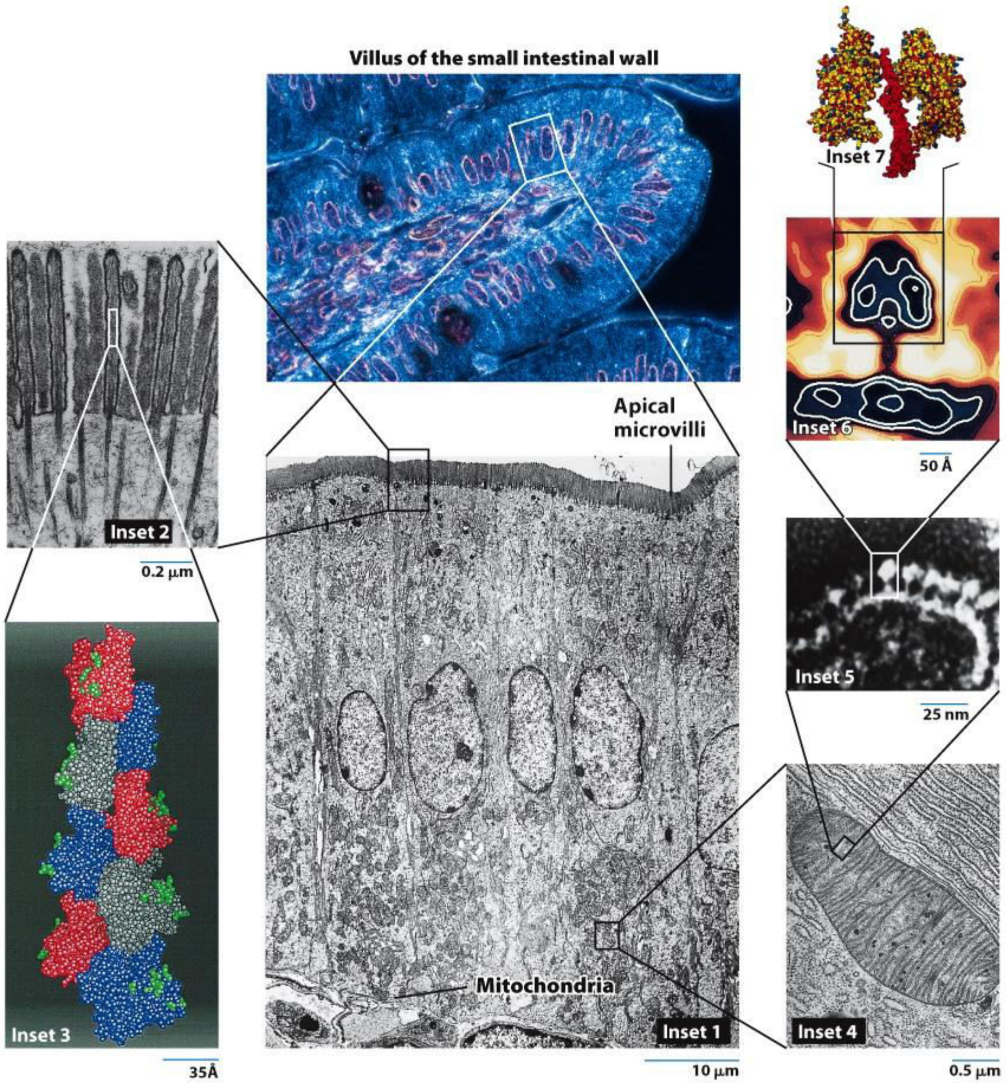
Levels of cellular and molecular organization

Basic Properties of Cells

- Cells Possess a Genetic Program and the Means to Use It
  - Genes encode information to build each cell, and the organism.
  - Genes encode information for cellular reproduction, activity, and structure.



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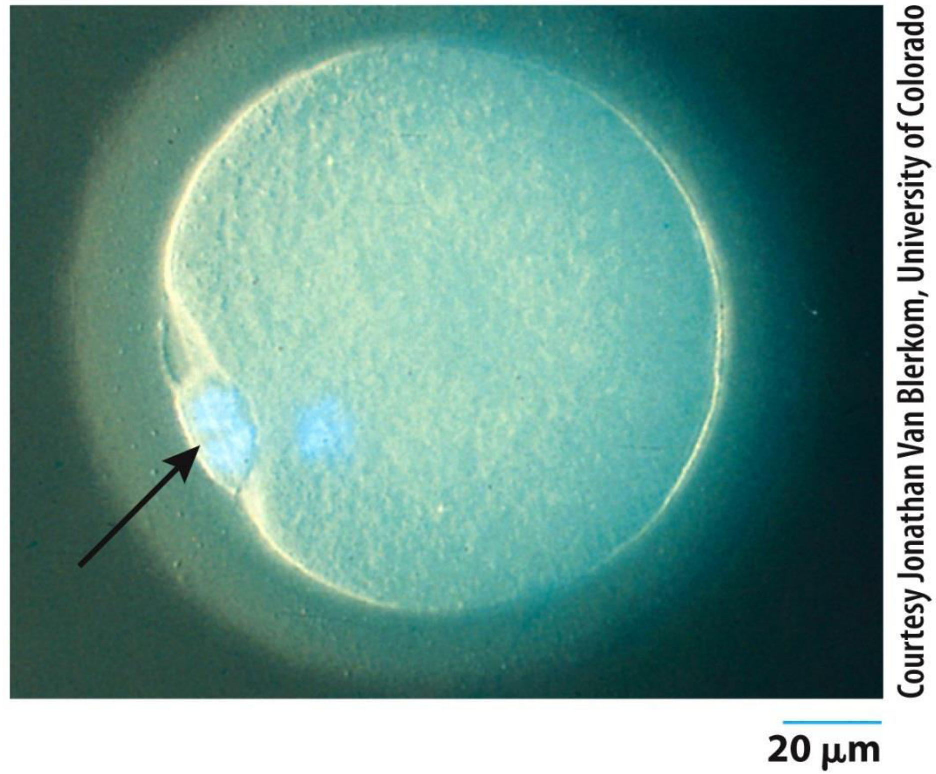
Levels of cellular and molecular organization

Basic Properties of Cells

- Cells Are Capable of Producing More of Themselves
  - Cells reproduce, and each daughter cells receives a complete set of genetic instructions.



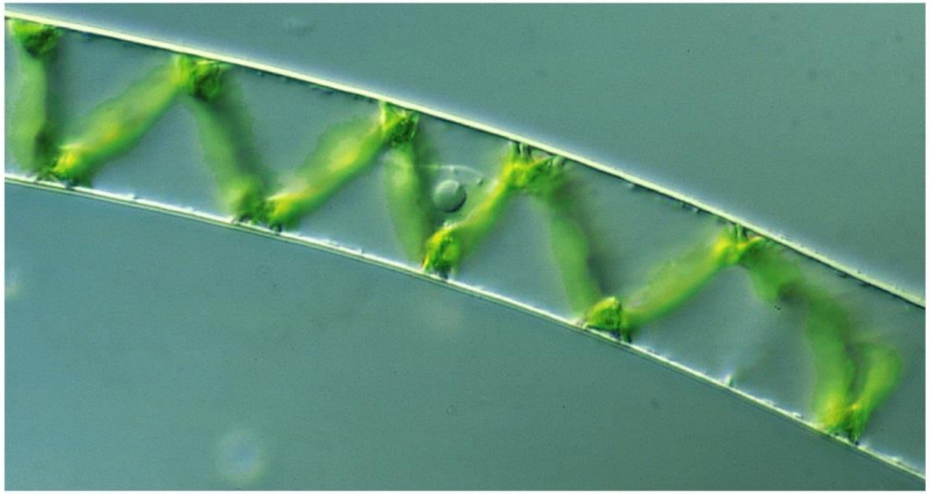
Mammalian oocyte after unequal cell division to produce polar body (arrow)

Basic Properties of Cells

- Cells Acquire and Utilize Energy
  - Photosynthesis provides fuel for all living organisms.
  - Animal cells derive energy from the products of photosynthesis, mainly in the form of glucose.
  - Cell can convert glucose into ATP—a substance with readily available energy.

Basic Properties of Cells

- Cells Acquire and Utilize Energy
- Cells Carry Out a Variety of Chemical Reactions
- Cells Engage in Mechanical Activities
- Cells Are Able to Respond to Stimuli
- Cells Are Capable of Self-Regulation
- Cells Evolve



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Spirogyra: alga with ribbon-like chloroplast for photosynthesis

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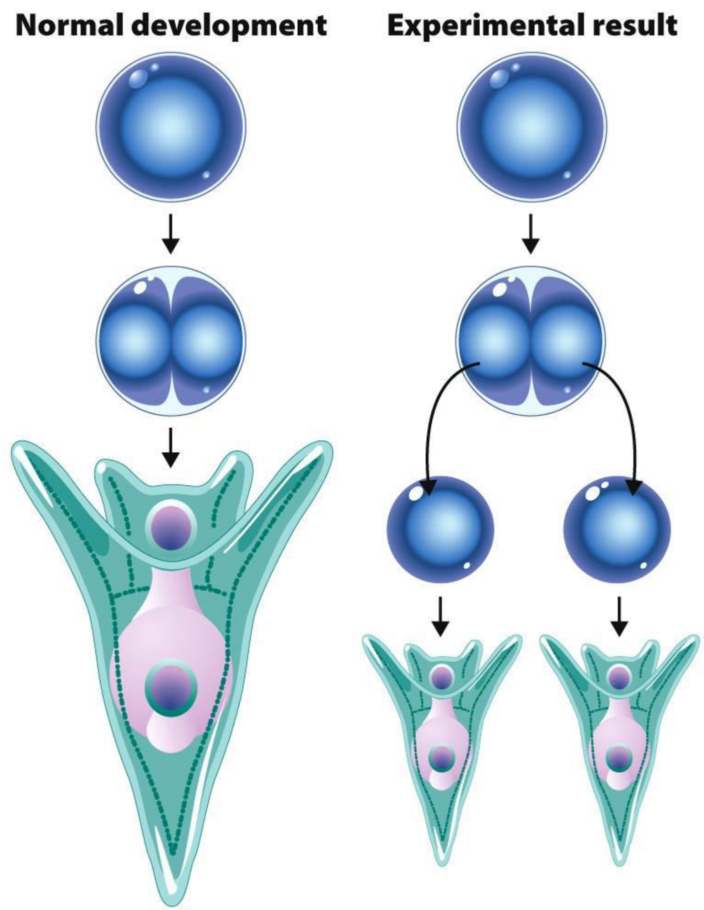

Self-regulated development in the sea urchin during normal (L) and cell separation experiments (R)

Basic Properties of Cells

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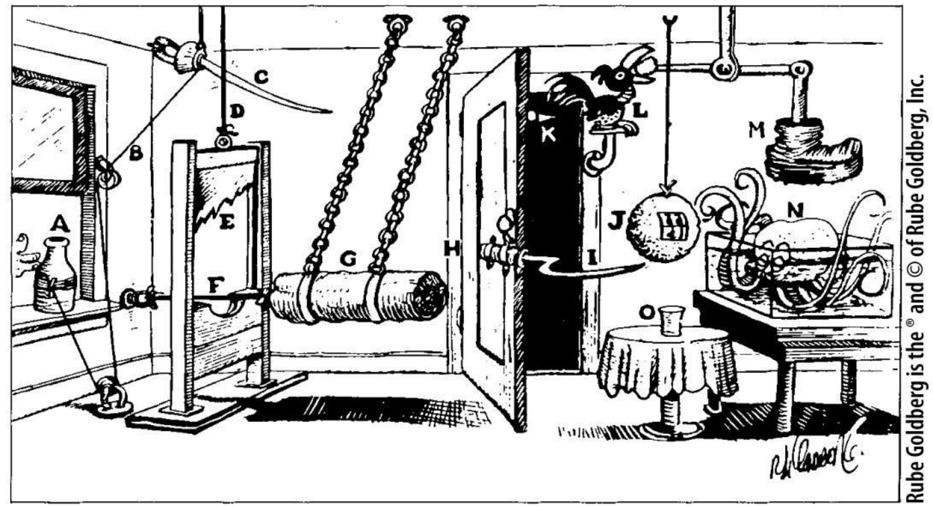
Orange Juice Squeezing Machine



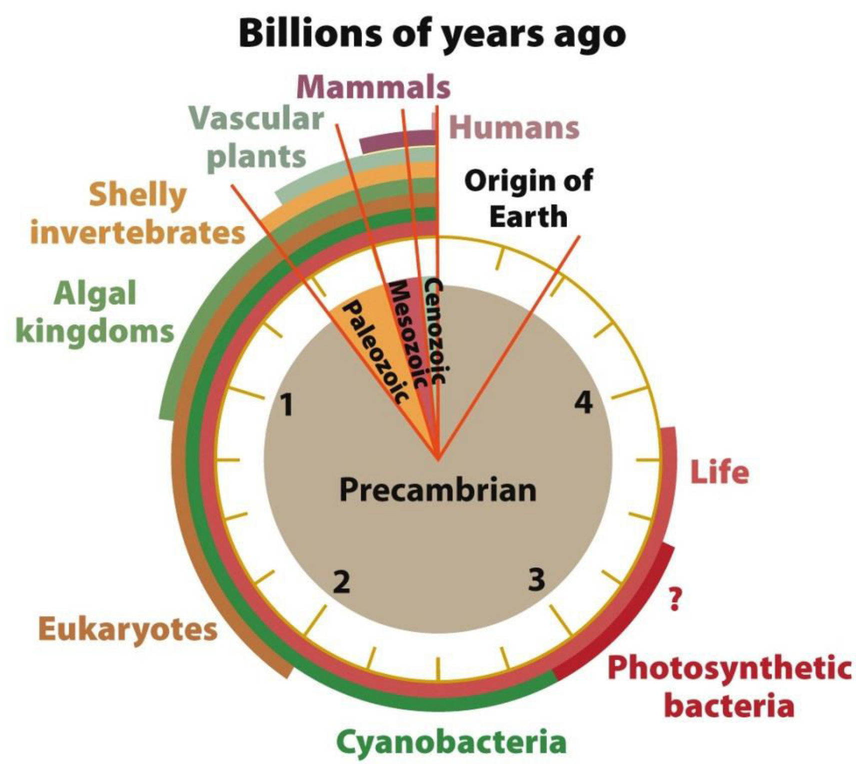
Professor Butts steps into an open elevator shaft and when he lands at the bottom he finds a simple orange squeezing machine. Milkman takes empty milk bottle (**A**), pulling string (**B**) which causes sword (**C**) to sever cord (**D**) and allow guillotine blade (**E**) to drop and cut rope (**F**) which releases battering ram (**G**). Ram bumps against open door (**H**), causing it to close. Grass sickle (**I**) cuts a slice off end of orange (**J**)–at the same time spike (**K**) stabs "prune hawk" (**L**) he opens his mouth to yell in agony, thereby releasing prune and allowing diver's boot (**M**) to drop and step on sleeping octopus (**N**). Octopus awakens in a rage and, seeing diver's face which is painted on orange, attacks it and crushes it with tentacles, thereby causing all the juice in the orange to run into glass (**O**).

Later on you can use the log to build a log cabin where you can raise your son to be President like Abraham Lincoln.

Cellular activities as a sequential series of events or 'chain reaction.'

(1.3) Two Fundamentally Different Classes of Cells

- Prokaryotic and eukaryotic are distinguished by their size and type of **organelles**.
- Prokaryotes are all bacteria, which arose ~3.7 billion years ago.
- Eukaryotes include protists, animals, plants and fungi.



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Bio-geological clock: Proposed appearance time for major groups of organisms

Comparison: Prokaryotic & Eukaryotic Cells

***Table 1.1* A Comparison of Prokaryotic and Eukaryotic Cells**

Features held in common by the two types of cells:

- **Plasma membrane of similar construction**
- **Genetic information encoded in DNA using identical genetic code**
- **Similar mechanisms for transcription and translation of genetic information, including similar ribosomes**
- **Shared metabolic pathways (e.g., glycolysis andTCA cycle)**
- **Similar apparatus for conservation of chemical energy as ATP (located in the plasma membrane of prokaryotes and the mitochondrial membrane of eukaryotes)**
- **Similar mechanism of photosynthesis (between cyanobacteria and green plants)**
- **Similar mechanism for synthesizing and inserting membrane proteins**
- **Proteasomes (protein digesting structures) of similar construction (between archaebacteria and eukaryotes)**

Comparison: Prokaryotic & Eukaryotic Cells

Table 1.1 A Comparison of Prokaryotic and Eukaryotic Cells

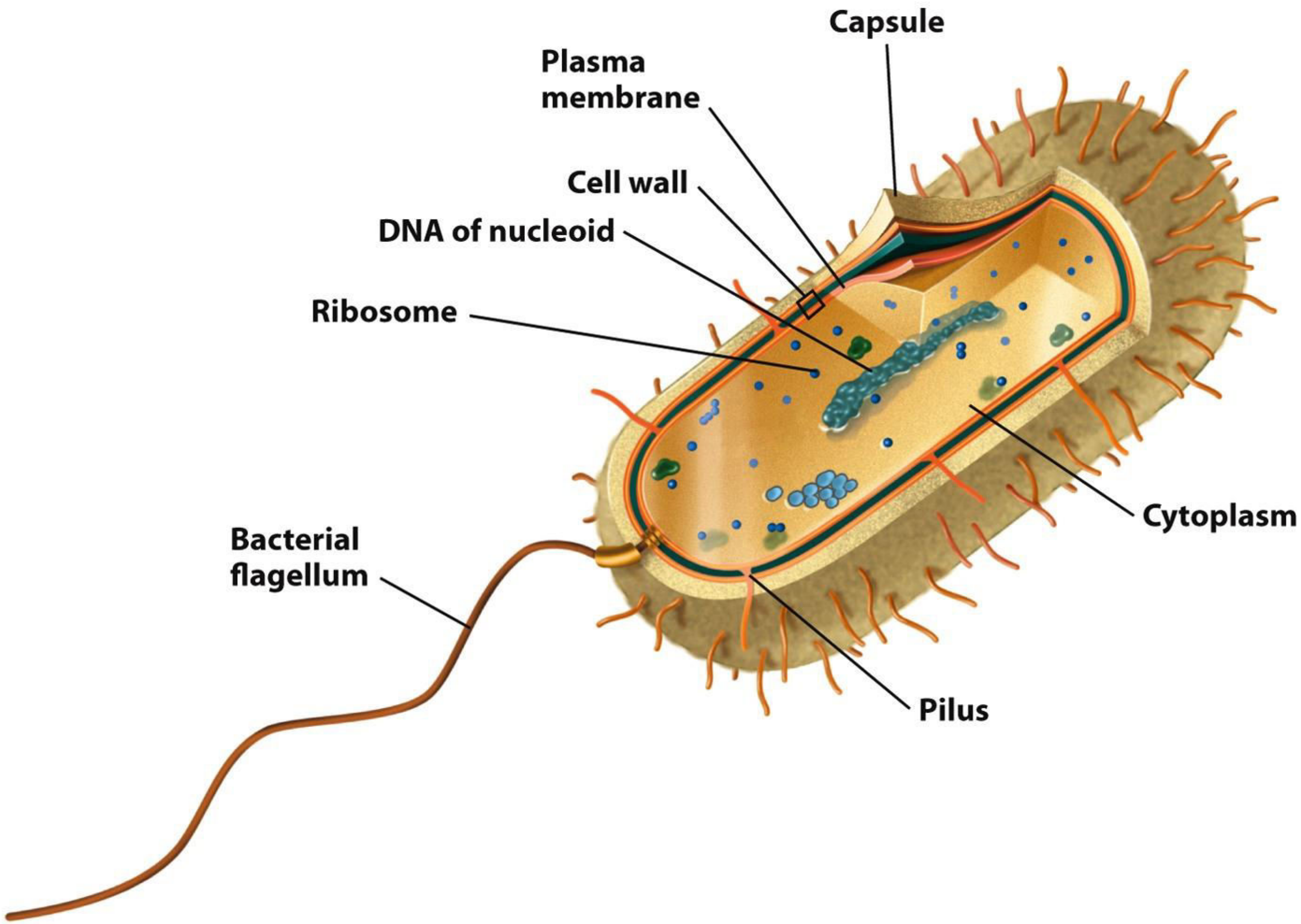
Features of eukaryotic cells not found in prokaryotes:

- Division of cells into nucleus and cytoplasm, separated by a nuclear envelope containing complex pore structures
- Complex chromosomes composed of DNA and associated proteins that are capable of compacting into mitotic structures
- Complex membranous cytoplasmic organelles (includes endoplasmic reticulum, Golgi complex, lysosomes, endosomes, peroxisomes, and glyoxisomes)
- Specialized cytoplasmic organelles for aerobic respiration (mitochondria) and photosynthesis (chloroplasts)
- Complex cytoskeletal system (including microfilaments, intermediate filaments, and microtubules) and associated motor proteins
- Complex flagella and cilia
- Ability to ingest particulate material by enclosure within plasma membrane vesicles (phagocytosis)
- Cellulose-containing cell walls (in plants)
- Cell division using a microtubule-containing mitotic spindle that separates chromosomes
- Presence of two copies of genes per cell (diploidy), one from each parent
- Presence of three different RNA synthesizing enzymes (RNA polymerases)
- Sexual reproduction requiring meiosis and fertilization

Basic Properties of Cells

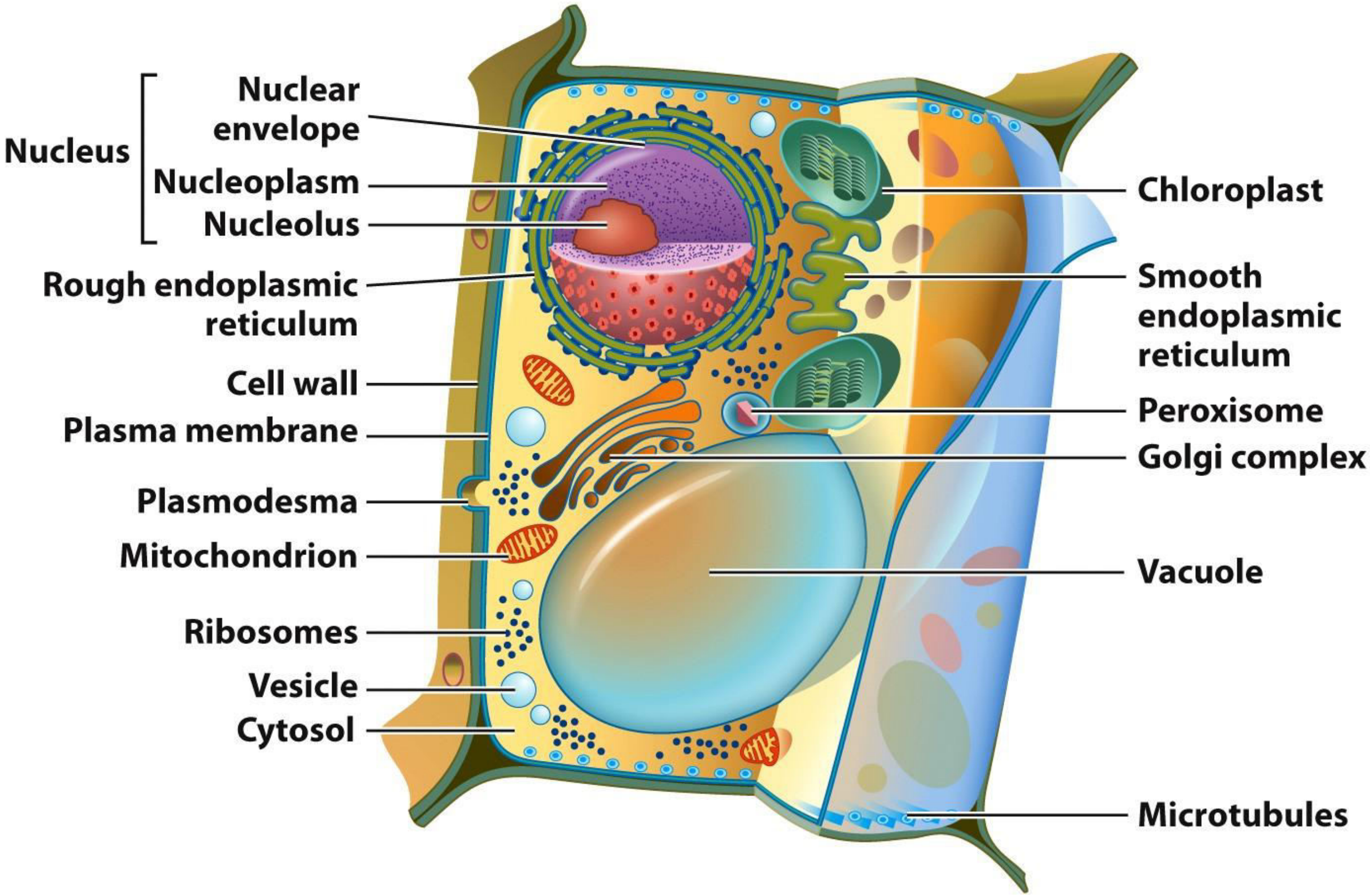
- Characteristics that distinguish prokaryotic and eukaryotic cells
  - **Complexity**: Prokaryotes are relatively simple; eukaryotes are more complex in structure and function.
  - **Cytoplasm**: Eukaryotes have membrane-bound organelles and complex cytoskeletal proteins. Both have ribosomes but they differ in size.
  - **Cellular reproduction**: Eukaryotes divide by mitosis; prokaryotes divide by simple fission.
  - **Locomotion**: Eukaryotes use both cytoplasmic movement, and cilia and flagella; prokaryotes have flagella, but they differ in both form and mechanism.
  - **Genetic material**:
    - *Packaging*: Prokaryotes have a nucleoid region whereas eukaryotes have a membrane-bound nucleus.
    - *Amount*: Eukaryotes have much more genetic material than prokaryotes.
    - *Form*: Eukaryotes have many chromosomes made of both DNA and protein whereas prokaryotes have a single, circular DNA.

The structure of cells



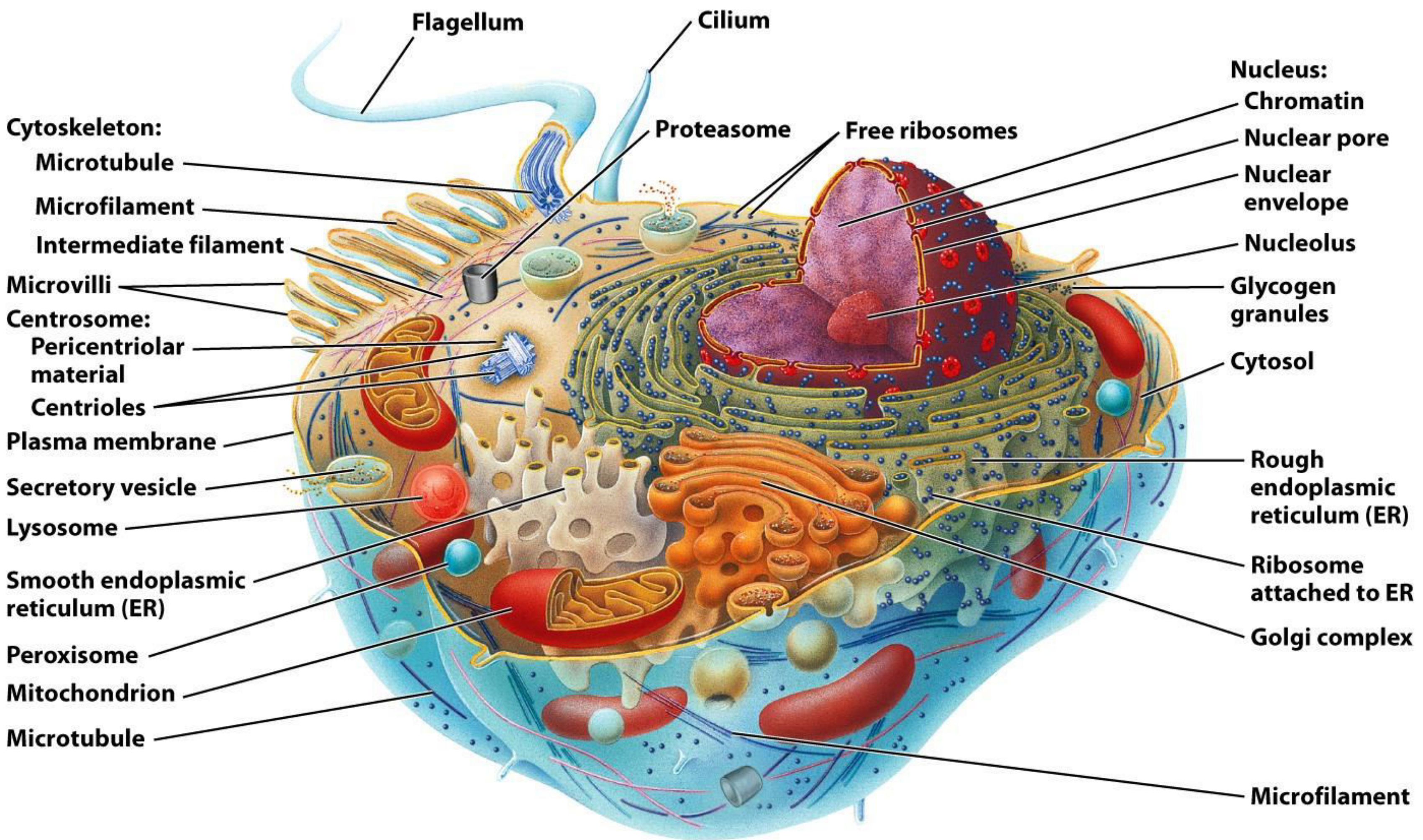
Bacterium

The structure of cells

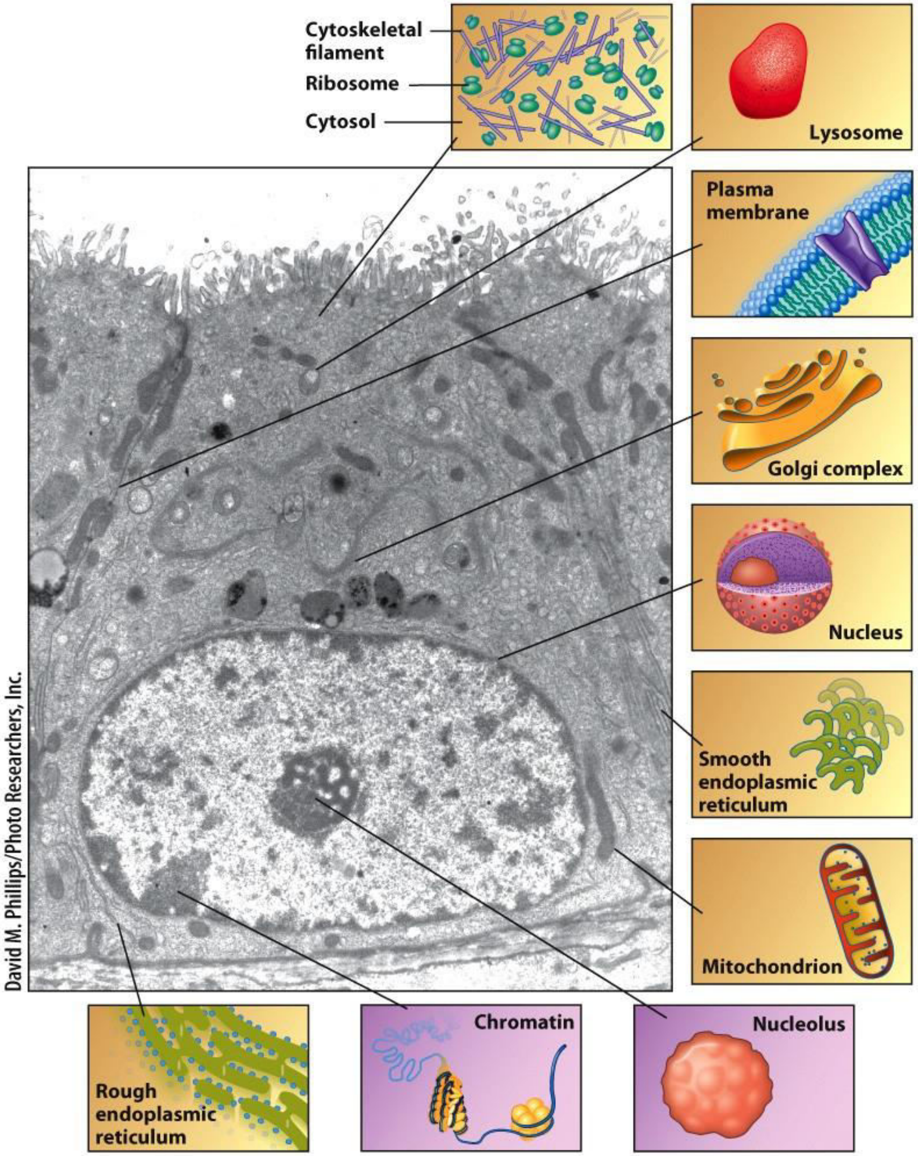


Plant cell

The structure of cells

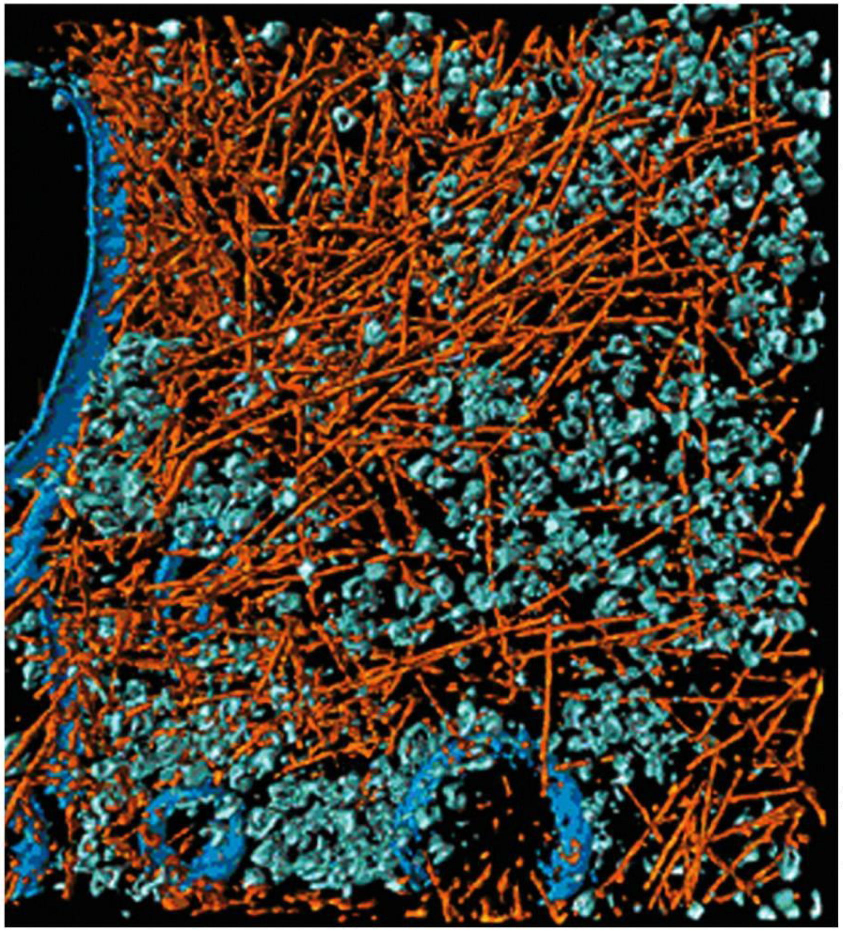


Animal cell



Eukaryotic cell structure: Epithelial cell from the male rat reproductive tract

Cytoplasm: A crowded compartment in a eukaryotic cell

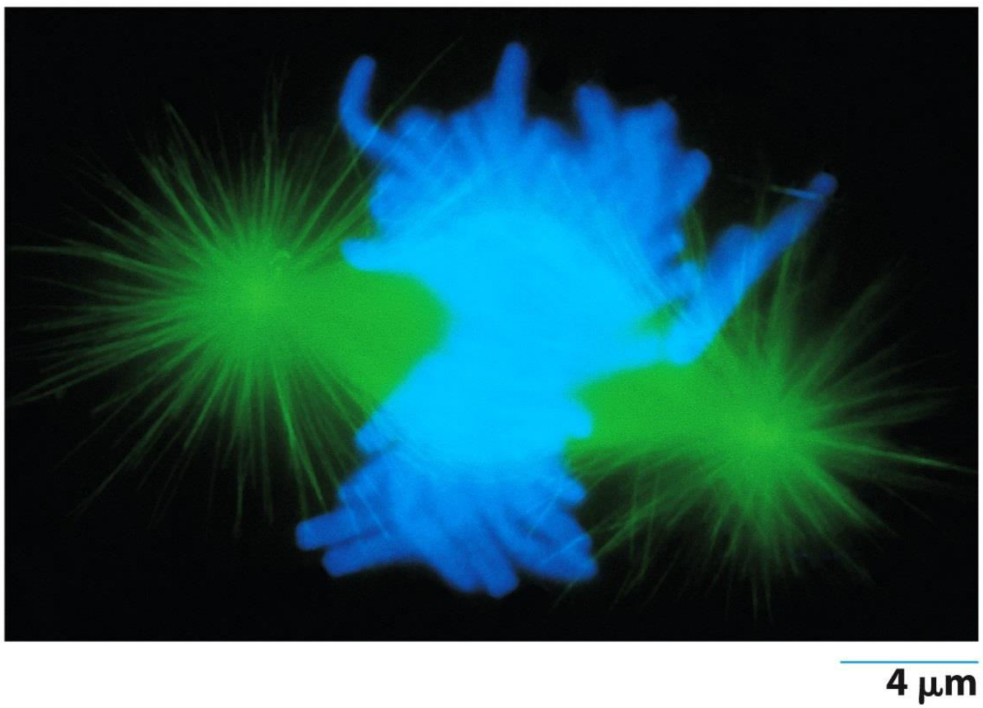


From O. Medalia, et al, Science 298: 1211, 2002, Figure 3a. © 2002, reprinted with permission from AAAS.Photo provided courtesy of Wolfgang Baumeister

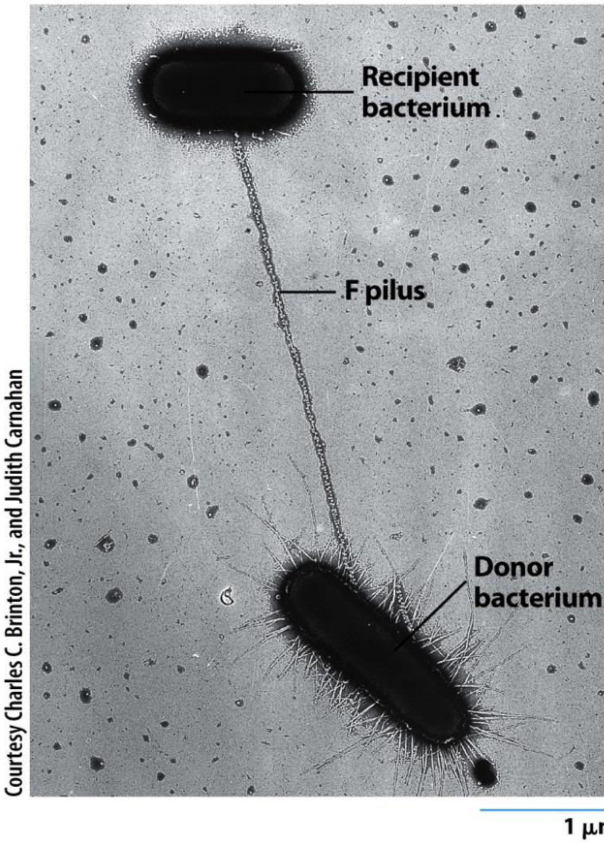
Colorized electron micrograph of a frozen single-celled eukaryote

Cytoskeleton: Red
Ribosomes: Green
Cell membrane: Blue

Cellular reproduction: Eukaryotes and prokaryotes



Courtesy Conly Rieder

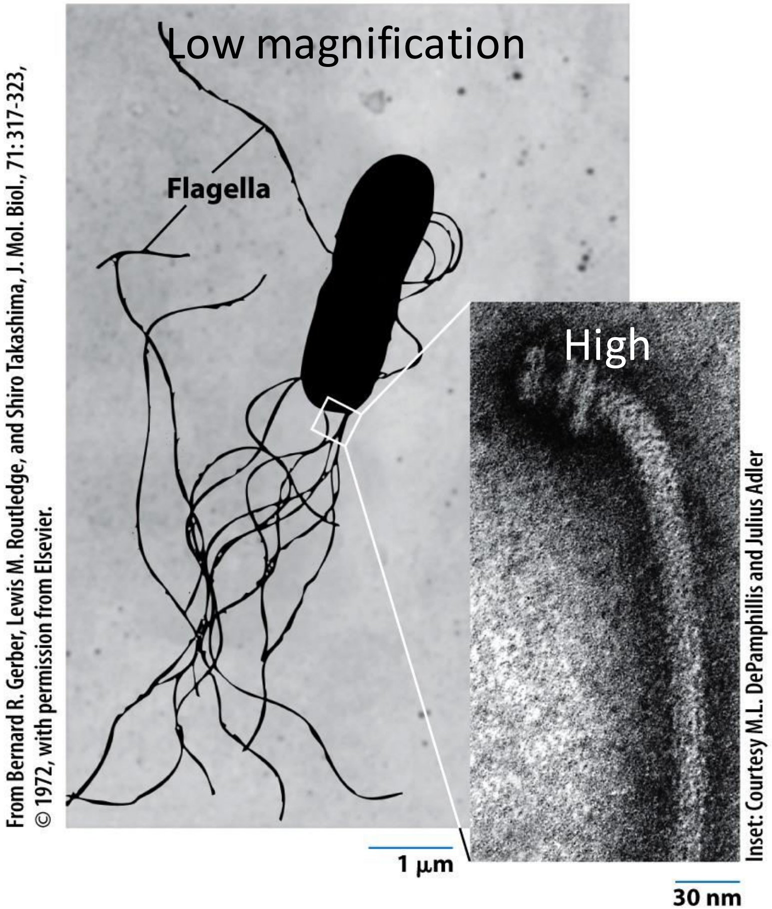


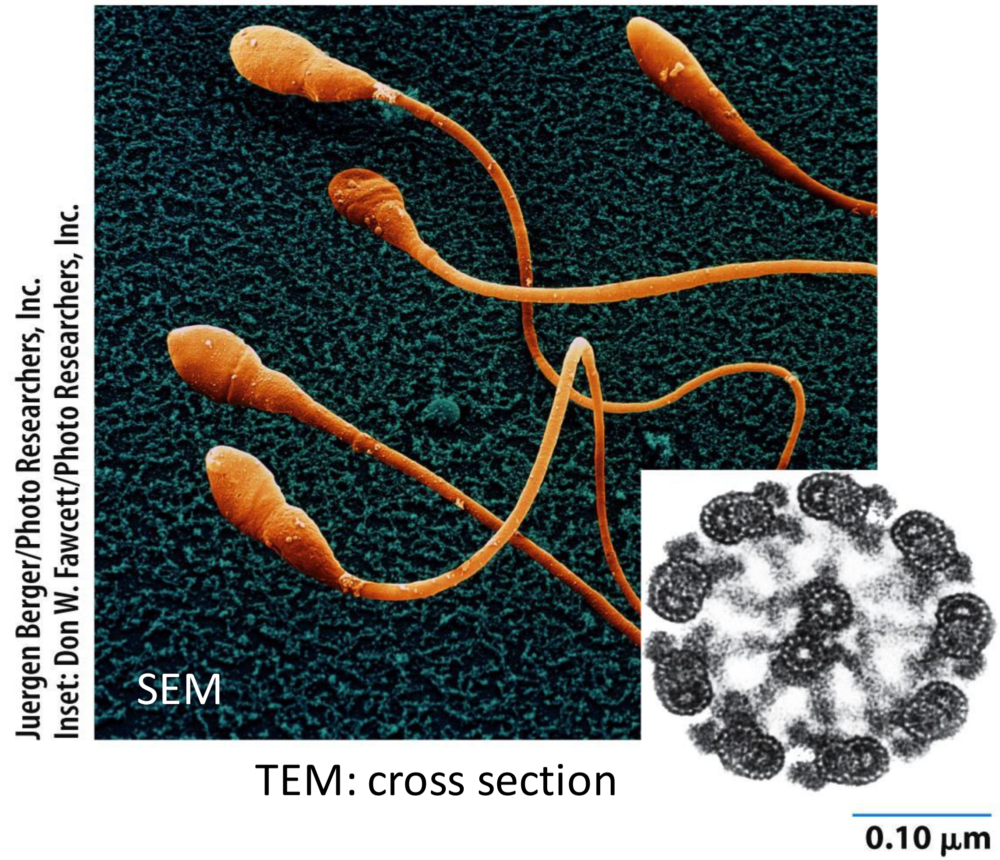
Courtesy Charles C. Brinton, Jr., and Judith Carnahan

<u>Cell division in eukaryotes</u>
DNA (blue) and microtubules (green) of two daughter cells.

<u>Bacterial conjugation</u>
Sharing of DNA through the F pilus

Flagella: differences between prokaryotes and eukaryotes





Salmonella bacterium
Multiple flagella for locomotion

Human sperm cells
Single flagella

Basic Properties of Cells

- Types of Prokaryotic Cells

  1. Domain Archaea: Methanogens, Halophiles, Acidophiles, Thermophiles

  2. Domain Bacteria

- Includes the smallest known cells – mycoplasma
- Includes cyanobacteria – some photosynthetic bacteria
  - Cyanobacteria gave rise to green plants and an oxygen-rich atmosphere.
  - Some bacteria capable of **nitrogen fixation**.

Cyanobacteria: electron micrograph

Cyanobacteria in polar bear coats

Basic Properties of Cells

- Prokaryotic Diversity
  - Prokaryotes are identified and classified on the basis of specific DNA sequences.
  - Recent evidence indicates that prokaryotes are more diverse and numerous than previous thought.

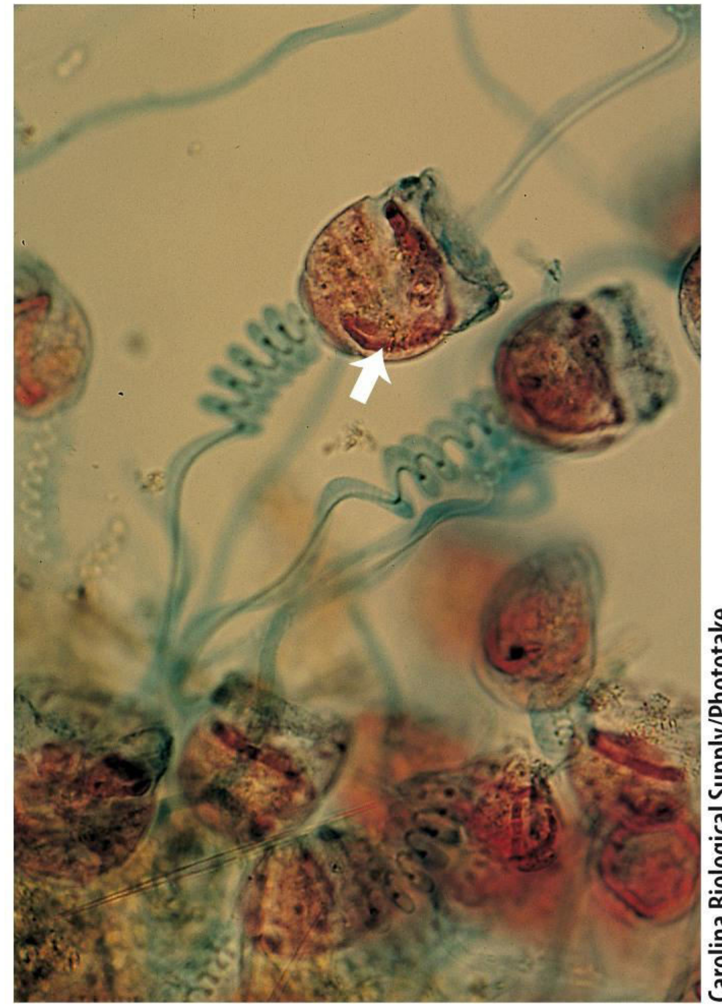
Table 1.2 ***Number and Biomass of Prokaryotes in the World***

Environment	No. of prokaryotic cells, $\times 10^{28}$	Pg of C in prokaryotes*
Aquatic habitats	12	2.2
Oceanic subsurface	355	303
Soil	26	26
Terrestrial subsurface	25–250	22–215
Total	415–640	353–546

*1 Petagram (Pg) = 10^{15} g.
Source: W. B. Whitman et al., *Proc. Nat'l. Acad. Sci. U.S.A.* 95:6581, 1998.

Basic Properties of Cells

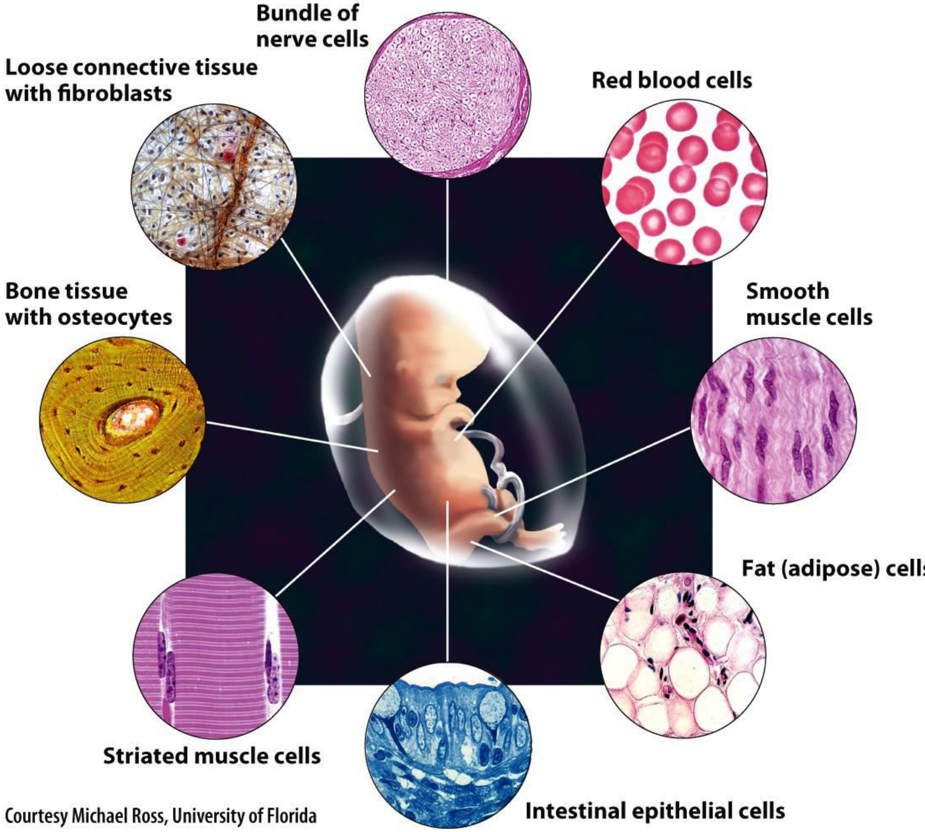
- Types of Eukaryotic Cells: Cell Specialization
  - *Unicellular* eukaryotes are complex single-celled organisms. *Vorticella* have a contractile ribbon in the stalk and a large macronucleus (arrow in figure) that contains multiple copies of its genes.



Vorticella, a complex ciliated protist

Basic Properties of Cells

- Types of Eukaryotic Cells: Cell Specialization
  - *Multicellular* eukaryotes have different cell types for different functions.
    - **Differentiation** occurs during embryonic development in other multicellular organisms.
    - Numbers and arrangements of organelles relate to the function of the cell.
    - Despite differentiation, cells have many features in common.



Pathways of cell differentiation

Basic Properties of Cells: Model Organisms

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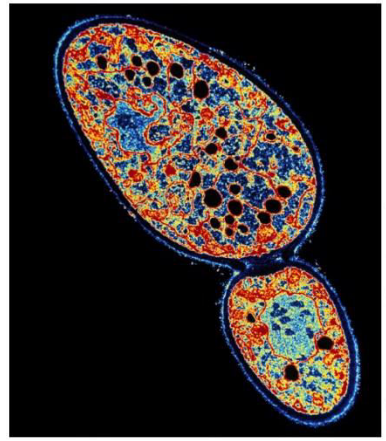
Escherichia coli (bacterium)



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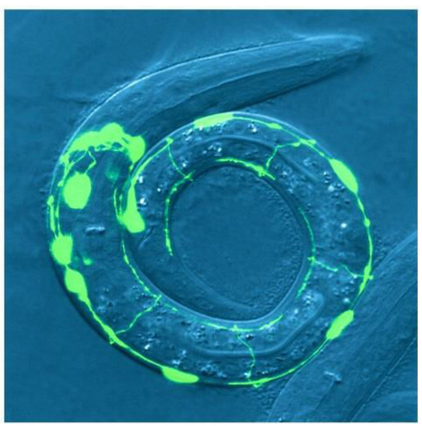
Saccharomyces (yeast)

Jean Claude Revy/Phototake

Arabidopsis (mustard plant)



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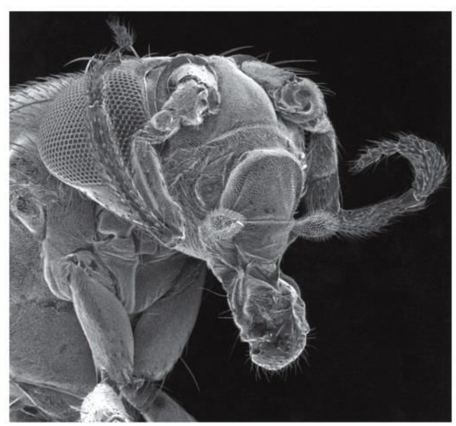
Caenorhabditis elegans (nematode)



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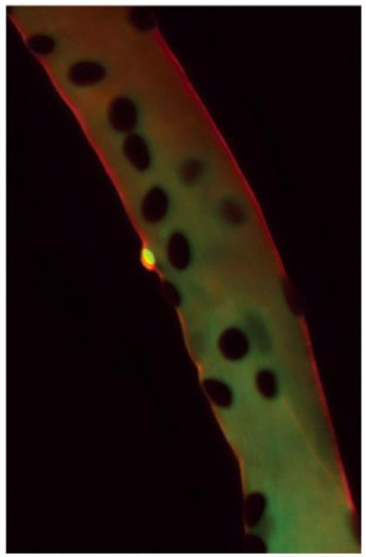
Drosophila (fruit fly)

Ted Spiegel/ © Corbis

Mus musculus (mouse)

The Human Perspective:
The Prospect of Cell Replacement Therapy

Adult muscle stem cell (yellow) present in differentiated muscle fiber with stained blue nuclei.



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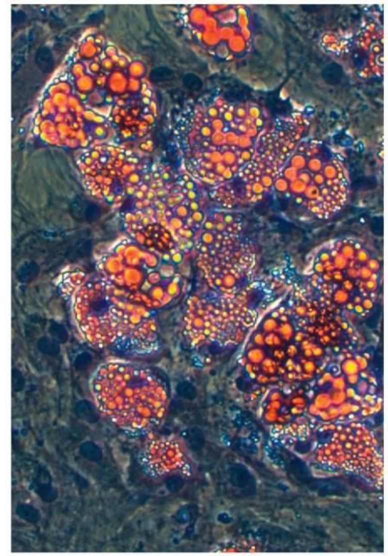


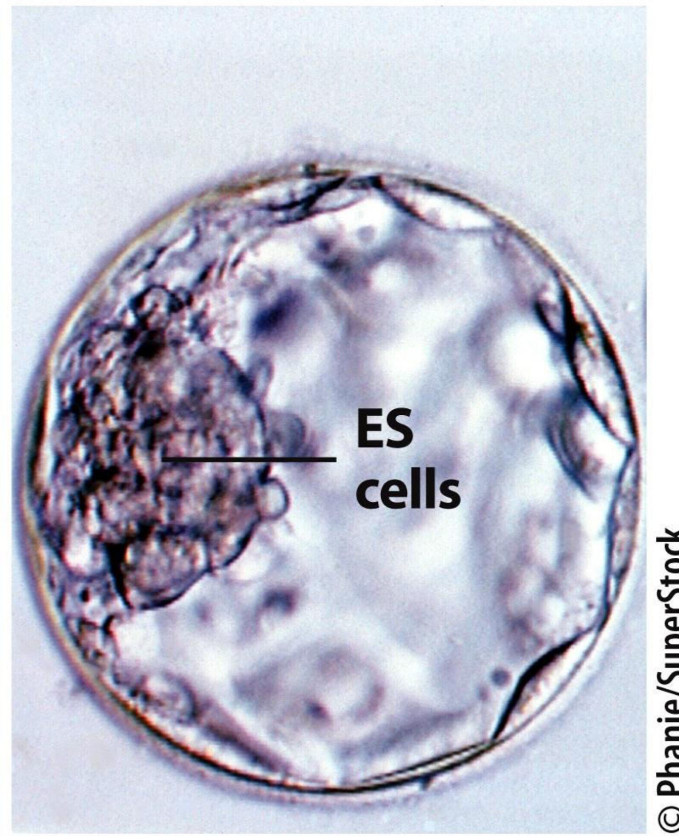
Courtesy Thermo Fisher Scientific

Adult muscle stem cells differentiating into adipose cells in culture.

- **Stem cells** are undifferentiated cells capable of self-renewal and differentiation.
  - Adult stem cells can be used to replace damaged or diseased adult tissue.
    - **Hematopoietic stem cells** can produce blood cells in bone marrow.
    - Neural stem cells may be sued to treat neurodegenerative disorders.

The Human Perspective: The Prospect of Cell Replacement Therapy

- **Embryonic stem (ES) cells** have even greater potential for differentiation (*pluripotent*) than adult stem cells.
  - ES cells must be differentiated *in vitro.*
  - The use of ES cells involves ethical considerations.



Isolation of ES cells from blastocysts

The Human Perspective:
The Prospect of Cell Replacement Therapy

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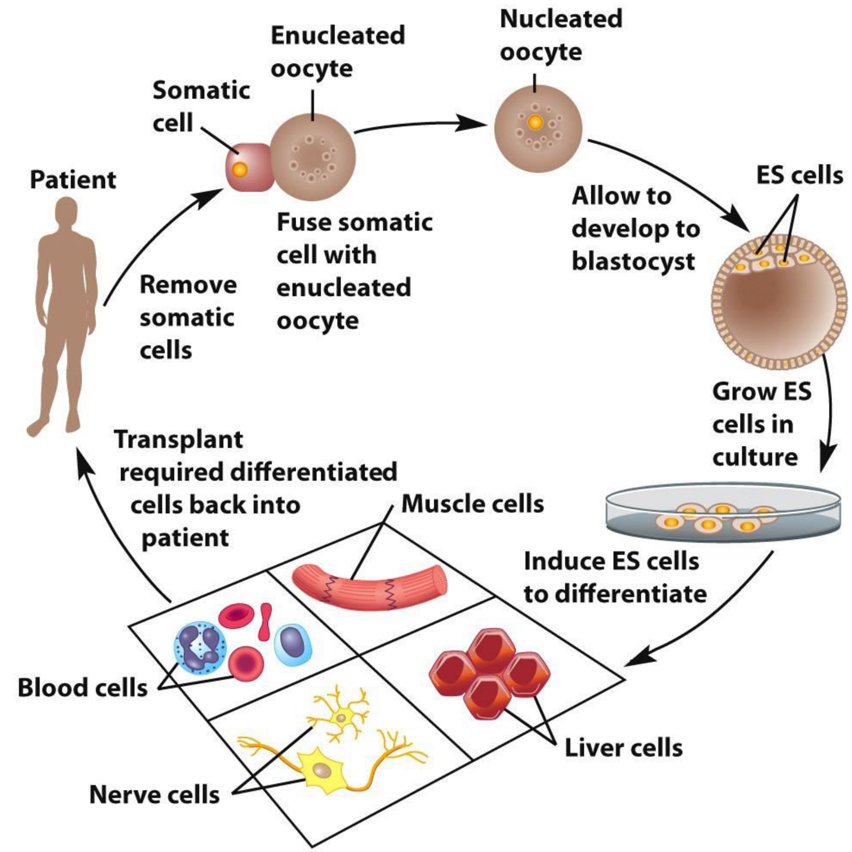
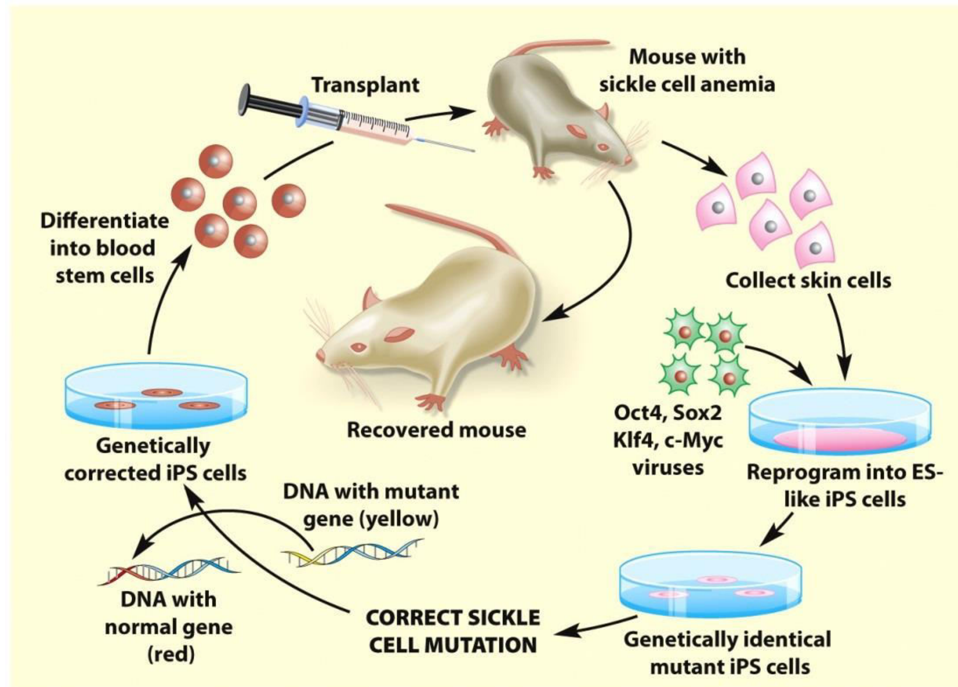


A procedure for obtaining differentiated cells for use in cell replacement therapy

The Human Perspective: The Prospect of Cell Replacement Therapy

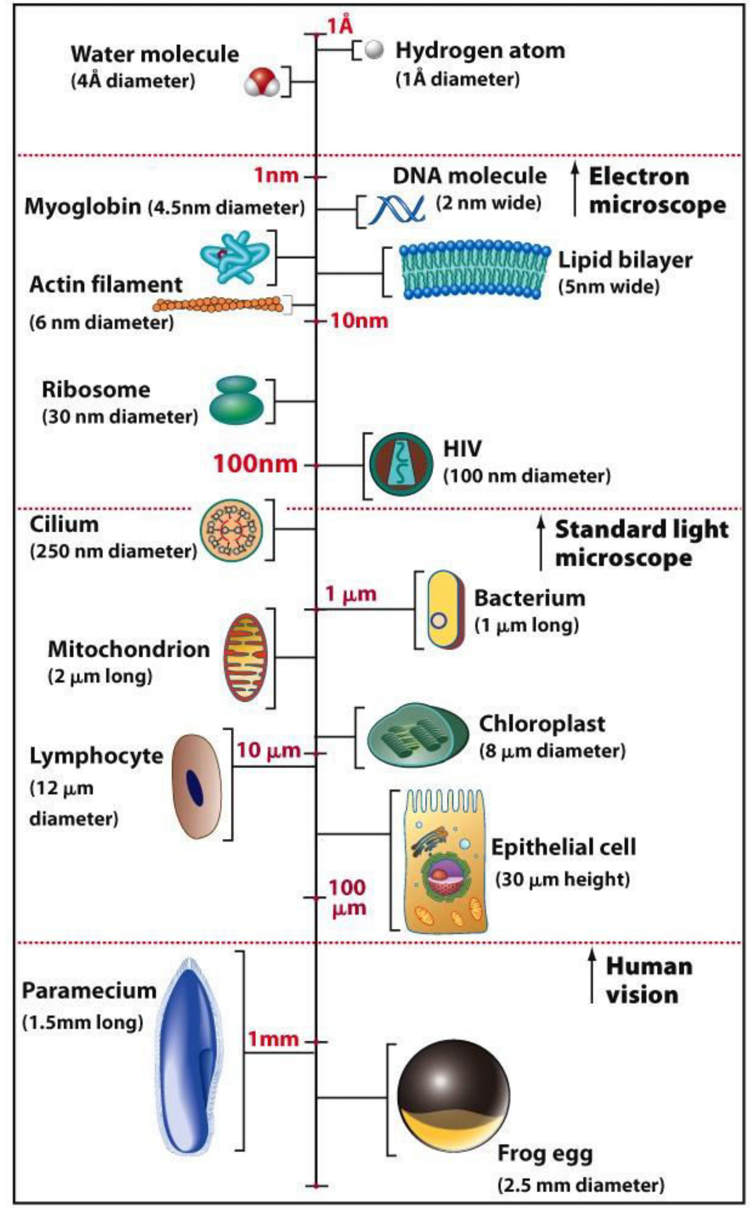
- *Induced pluripotent (iPS) cells* has been demonstrated in culture.
  - Involves reprogramming a fully differentiated cell into a pluripotent stem cell.
  - These cells have been used to correct certain disease conditions in experimental animals.
  - Studies to reveal the mechanism of *iPS* could have significant medical applications.



Steps taken to generate *iPS* for use in correcting the inherited disease sickle cell anemia in mice

Basic Properties of Cells

- The Sizes of Cells and Their Components
  - Cells are commonly measured in units of **micrometers** (1 μm = 10^{-6} meter) and **nanometers** (1 nm = 10^{-9} meter).
  - Cell size is limited:
    - By the volume of cytoplasm that can be supported by the genes in the nucleus.
    - By the volume of cytoplasm that can be supported by exchange of nutrients.
    - By the distance over which substances can efficiently travel through the cytoplasm via *diffusion*.



Relative sizes of cells and cell components

Basic Properties of Cells

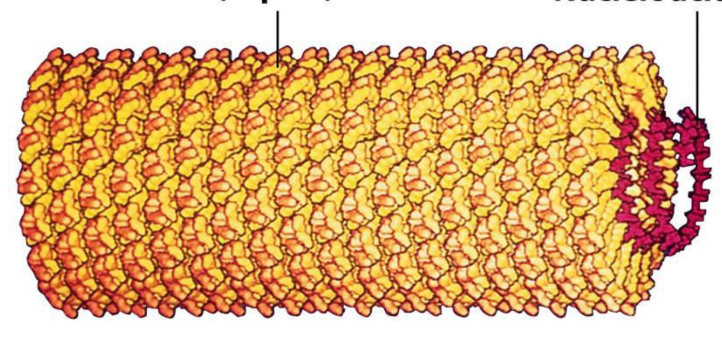
- **Synthetic Biology** is a field oriented to create a living cell in the laboratory.
  - A more modest goal is to develop novel life forms, beginning with existing organisms.
  - Possible applications to medicine, industry, or the environment.
  - Prospect is good after replacing the genome of one bacterium with that of a closely related species.

Courtesy Jakob C. Schweizer

<u>Synthetic biology toolbox</u>:
Nucleic acids, proteins, and lipids

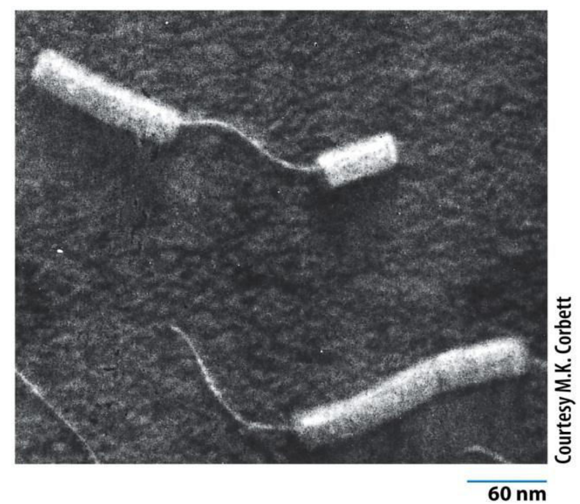
(1.4) Viruses

- **Viruses** are pathogens.
- Viruses are intracellular obligate parasites.
- A **virion** is a virus particle outside the host cell.
- Viral structure:
  - Genetic material and can be single-stranded DNA or RNA.
  - Protein *capsid* surrounds the genetic material.
  - A lipid envelope may surround the capsid in some viruses.
- **Viroids** are pathogens, each consisting of a small, naked RNA molecule.
- Viroids cause disease by interfering with gene expression in host cells.



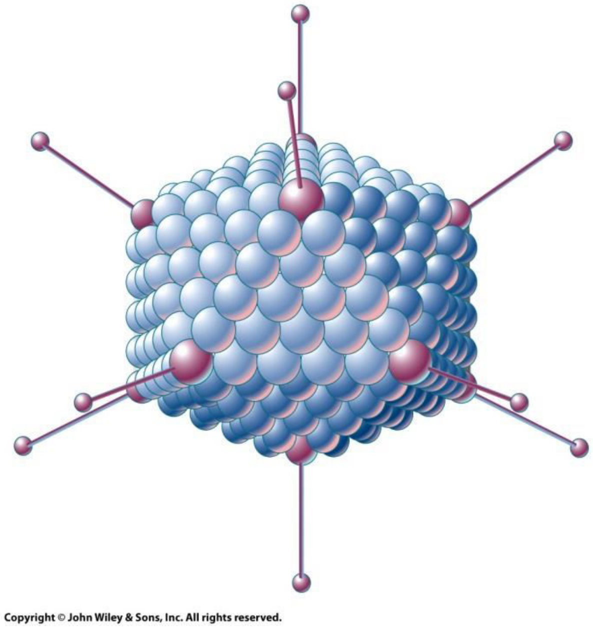
Courtesy Gerald Stubbs and Keiichi Namba and Donald Caspar

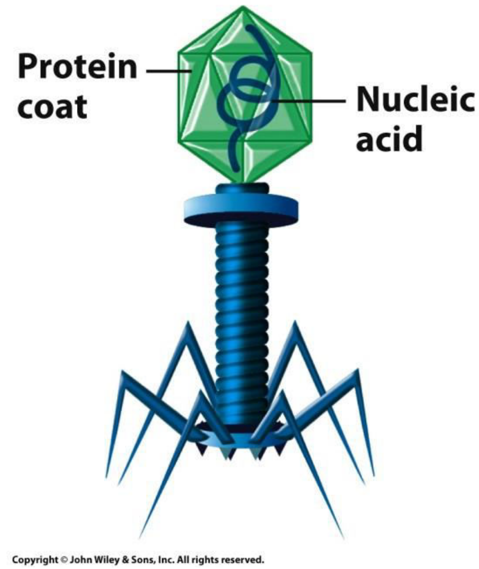
RNA-based Tobacco mosaic virus (TMV)

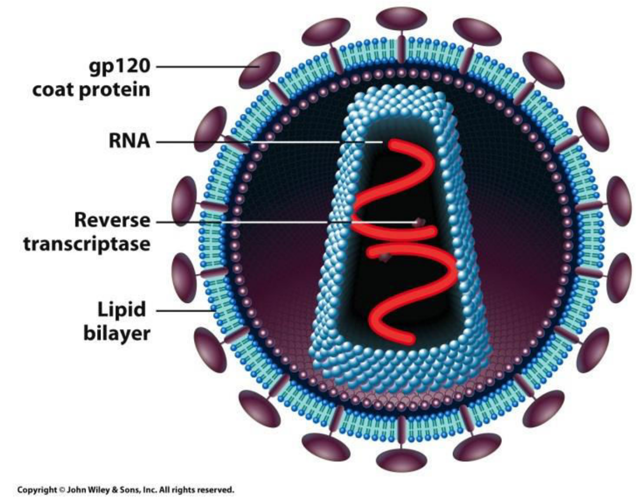


Electron microscopy: TVM

Viruses: Host infection diversity







Adenovirus

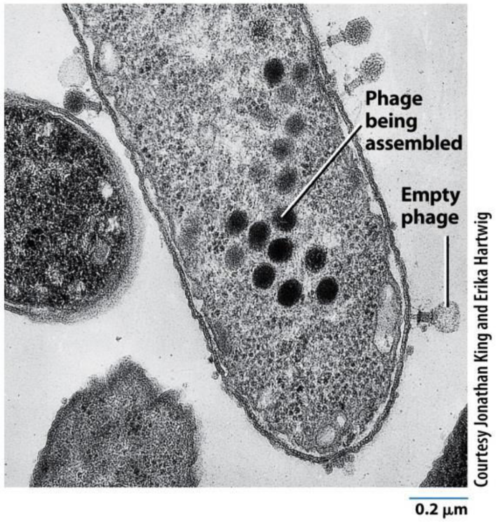
Human immunodeficiency virus (HIV)

T-even bacteriophage

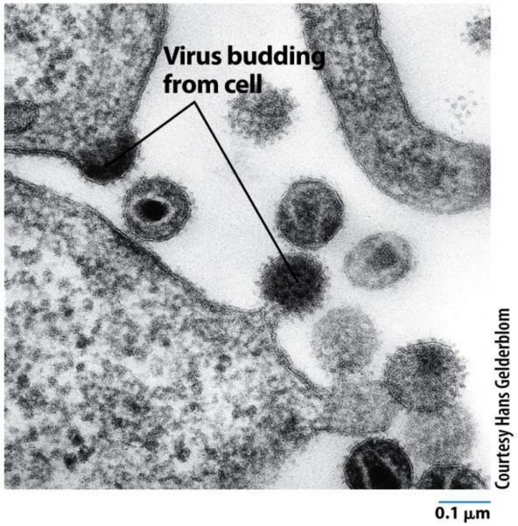
- Virus and host
  - Viruses have surface proteins that bind to the surface of the host cell.
  - Viral specificity for a certain host is determined by the virus' surface proteins.

Viruses

- Viral infection types:
  - *Lytic* infection: the virus redirects the host into making more virus particles, the host cell *lyses* and releases the viruses.
  - *Integration*: the virus integrates its DNA (called a **provirus**) into the host cell's chromosomes.
    - Infected host may behave normally until external stimulus activates provirus, leading to lysis.
    - Host may give rise to viral progeny by budding.
    - Host may become malignant.



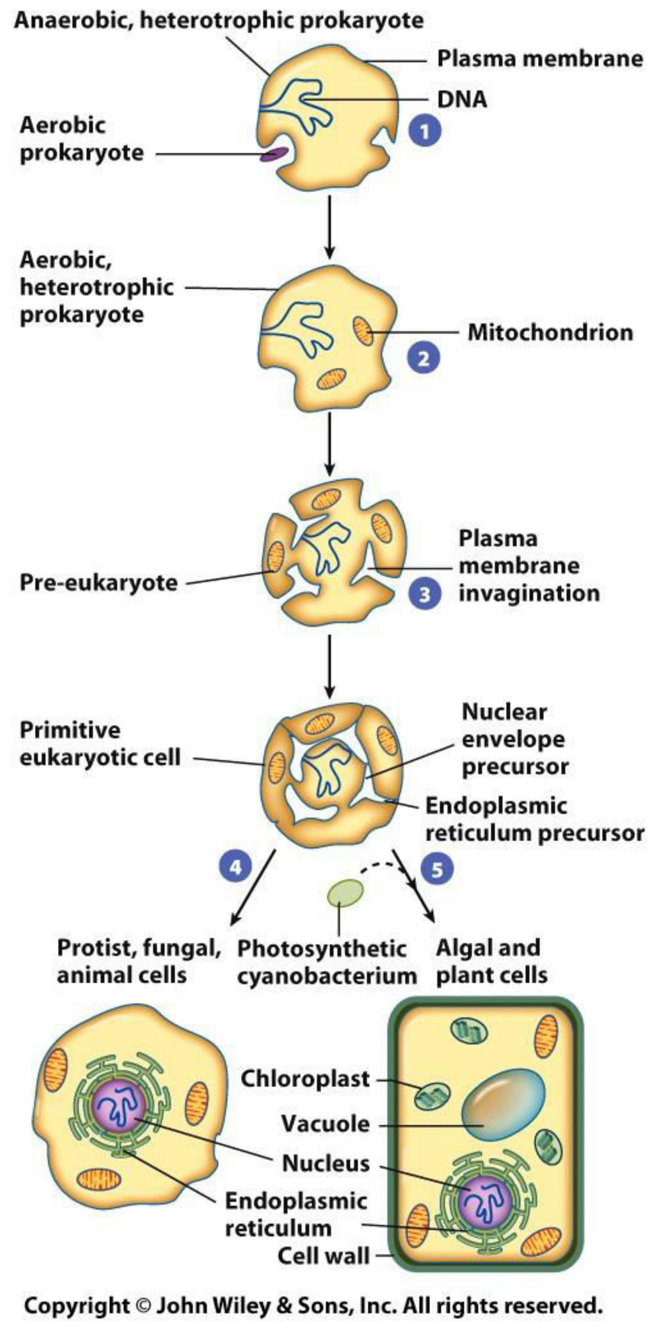
Bacteriophage infection of bacterium (late stage)



HIV infection of human lymphocyte (late stage)

Experimental Pathways: The Origin of Eukaryotic Cells

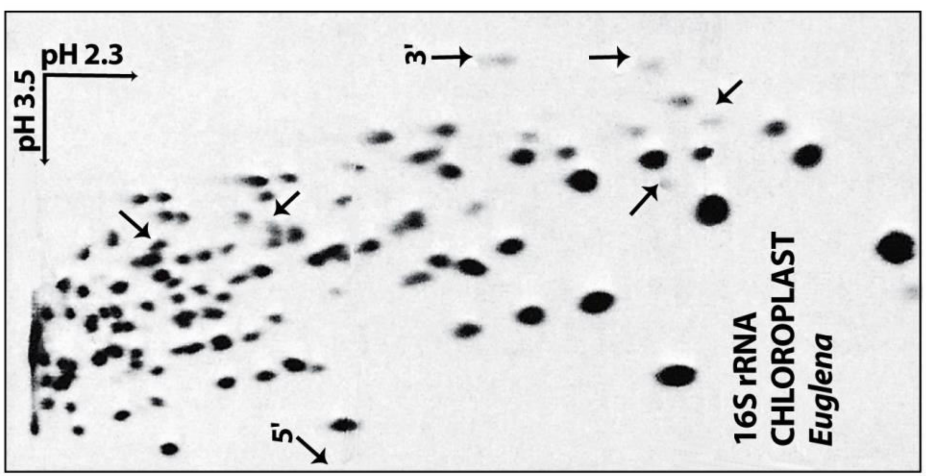
- Prokaryotic cells arose first and gave rise to eukaryotic cells.
- **Endosymbiont Theory**: organelles in eukaryotic cells (mitochondria and chloroplasts) evolved from smaller prokaryotic cells.



A model depicting possible steps in endosymbiosis

Experimental Pathways:
The Origin of Eukaryotic Cells

- Evidence to support endosymbiont theory
  - Absence of eukaryote species with organelles in an intermediate stage of evolution.
  - Many symbiotic relations are known among different organisms.
  - Organelles of eukaryotic cells contain their own DNA.
  - Nucleotide sequences of rRNAs from eukaryotic organelles resembled that of prokaryotes.
  - Organelles duplicate independently of nucleus.



Courtesy Carl Woese, University of Illinois

Two-dimensional gel fingerprint of a T1 digest of chloroplast 16S ribosomal RNA

Nucleotide Sequence Similarities Between Representative Member of the Three Primary Kingdoms

Table 1 Nucleotide Sequence Similarities between Representative Members of the Three Primary Kingdoms

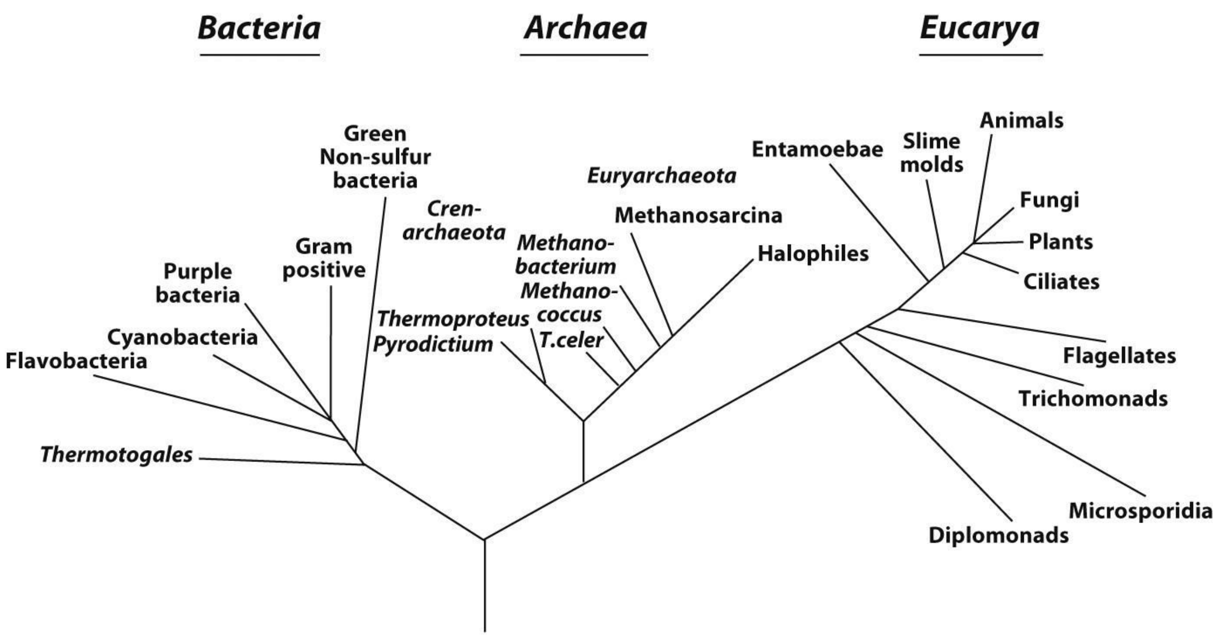
	1	2	3	4	5	6	7	8	9	10	11	12	13
1. *Saccharomyces cerevisiae*, 18S	—	0.29	0.33	0.05	0.06	0.08	0.09	0.11	0.08	0.11	0.11	0.08	0.08
2. *Lemna minor*, 18S	0.29	—	0.36	0.10	0.05	0.06	0.10	0.09	0.11	0.10	0.10	0.13	0.08
3. L cell, 18S	0.33	0.36	—	0.06	0.06	0.07	0.07	0.09	0.06	0.10	0.10	0.09	0.07
4. *Escherichia coli*	0.05	0.10	0.06	—	0.24	0.25	0.28	0.26	0.21	0.11	0.12	0.07	0.12
5. *Cholorbium vibrioforme*	0.06	0.05	0.06	0.24	—	0.22	0.22	0.20	0.19	0.06	0.07	0.06	0.09
6. *Bacillus firmus*	0.08	0.06	0.07	0.25	0.22	—	0.34	0.26	0.20	0.11	0.13	0.06	0.12
7. *Corynebacterium diptheriae*	0.09	0.10	0.07	0.28	0.22	0.34	—	0.23	0.21	0.12	0.12	0.09	0.10
8. *Aphanocapsa* 6714	0.11	0.09	0.09	0.26	0.20	0.26	0.23	—	0.31	0.11	0.11	0.10	0.10
9. Chloroplast (Lemna)	0.08	0.11	0.06	0.21	0.19	0.20	0.21	0.31	—	0.14	0.12	0.10	0.12
10. *Methanebacterium thermoautotrophicum*	0.11	0.10	0.10	0.11	0.06	0.11	0.12	0.11	0.14	—	0.51	0.25	0.30
11. *M. ruminantium* strain M-1	0.11	0.10	0.10	0.12	0.07	0.13	0.12	0.11	0.12	0.51	—	0.25	0.24
12. *Methanobacterium sp.*, Cariaco isolate JR-1	0.08	0.13	0.09	0.07	0.06	0.06	0.09	0.10	0.10	0.25	0.25	—	0.32
13. *Methanosarcina barkeri*	0.08	0.07	0.07	0.12	0.09	0.12	0.10	0.10	0.12	0.30	0.24	0.32	—

Source: C. R. Woese and G. E. Fox, *Proc. Nat'l. Acad. Sci. U.S.A.* 74:5089, 1977.

Experimental Pathways: The Origin of Eukaryotic Cells

- New ideas about the origin of eukaryotic cells
  - Based on nucleotide sequences of single genes, Woese proposed three major cell lineages:
    - Bacteria: include Gram positive, Gram negative, and cyanobacteria.
    - Archaea: include halophiles, thermophiles, methanogens and acidophiles.
    - Eucarya: include plants, animals, fungi, and protists.

Experimental Pathways: The Origin of Eukaryotic Cells



A phylogenetic showing based on rRNA sequence comparisons showing the three domains of life

- Based on whole genomes, many organisms appear to be genetic mosaics.
  - *Lateral gene transfer* (LGT) results in organisms with both parental DNA and DNA from other organisms in the environment.
  - Bacteria and Eucarya show evidence of LGT in their genomes.