Lecture 4: Structure and Composition (Sept. 15) **4.1**

Reading Assignment for Lectures 3-4: Phillips, Kondev, Theriot (PKT), Chapter 2
Problem Set 1 (due Sept. 24) now posted on the website.

Cellular materials:
At a somewhat more sophisticated level, every branch of physics has its favorite constituent materials (e.g., Phys. 101: wood, air, metal,…), whose structure and properties you need to know to understand what is going on. Of course, everything is made up of atoms and molecules. But, semiconductor device physics requires knowing about Si, Ge, etc. Metallurgy: Fe, Ni, Co, etc.

At the cellular level of biology, important classes of materials include:

- Carbohydrates (starches and sugars): Mainly (but not entirely) structural materials (wood, extracellular matrix)).
- Proteins and amino acids): Structural and functional (enzymes, motors).
- Lipids: Mainly phospholipids in the cell membranes, act as material barriers.
- DNA, RNA (nucleic acids): Information content and transfer.

Plus, combinations of the above like lipoproteins/proteolipids (lipid+protein), lipopolysaccharides (lipid+carbohydrate/sugar), peptidoglycans (proteins+sugars), etc.
Generic properties and specific examples. Where do they come from? How are they made in the cell? What do they do? Physical properties.

Organisms:
We will need to have some examples in mind for our spherical cows.

Prokaryotes (no organelles)

- Archaebacteria
- Eubacteria (including E. coli)

Eukaryotes (organelles)

- Single cell "protists" (including yeast S. cerevisiae and protozoa)
- Multicellular
    - Plants
    - Fungi
    - Animals

See Alberts, Fig. 1-43 (below)

Alberts, Fig. 1-43 Evolutionary Relationships **4.2**

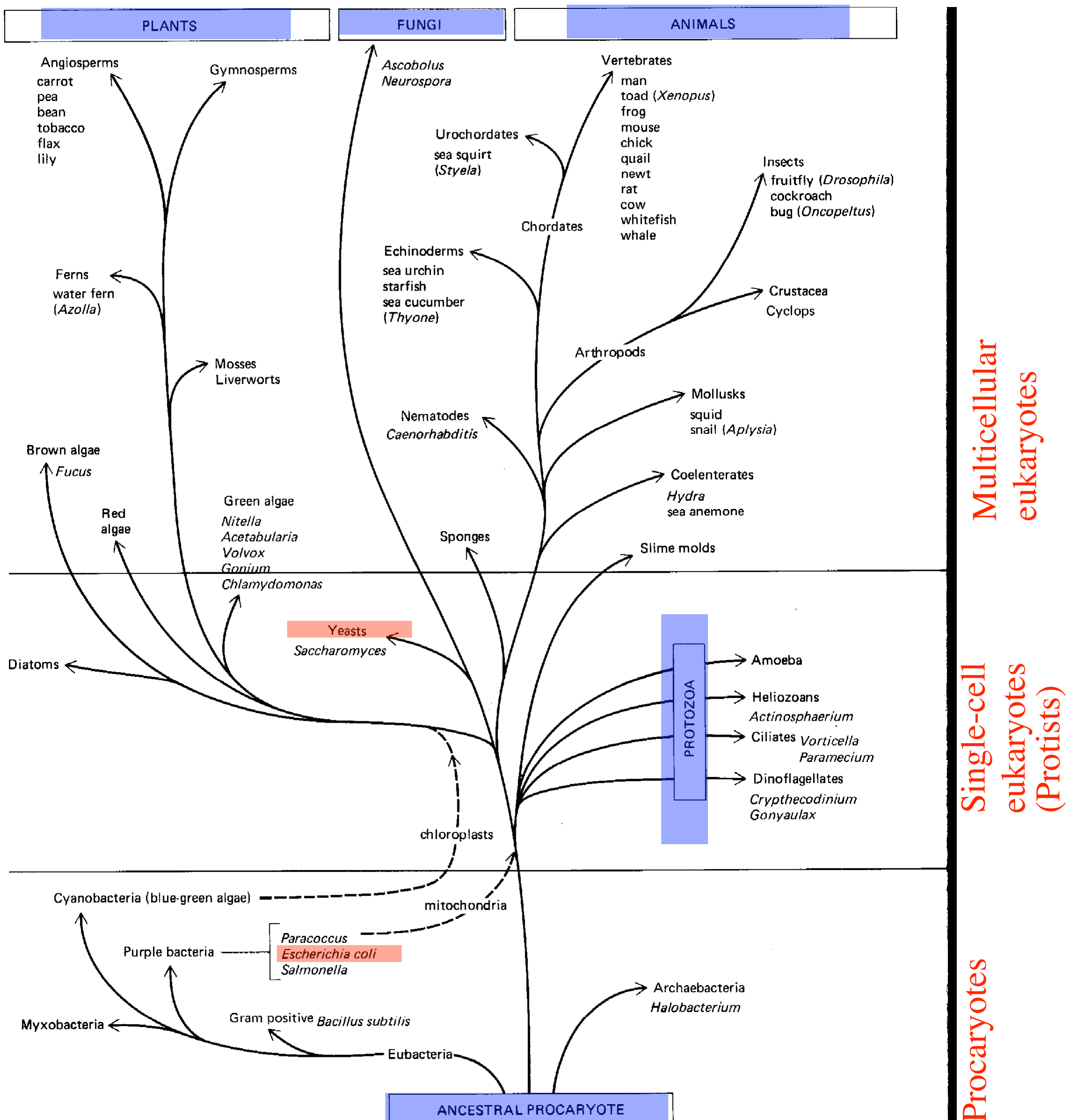
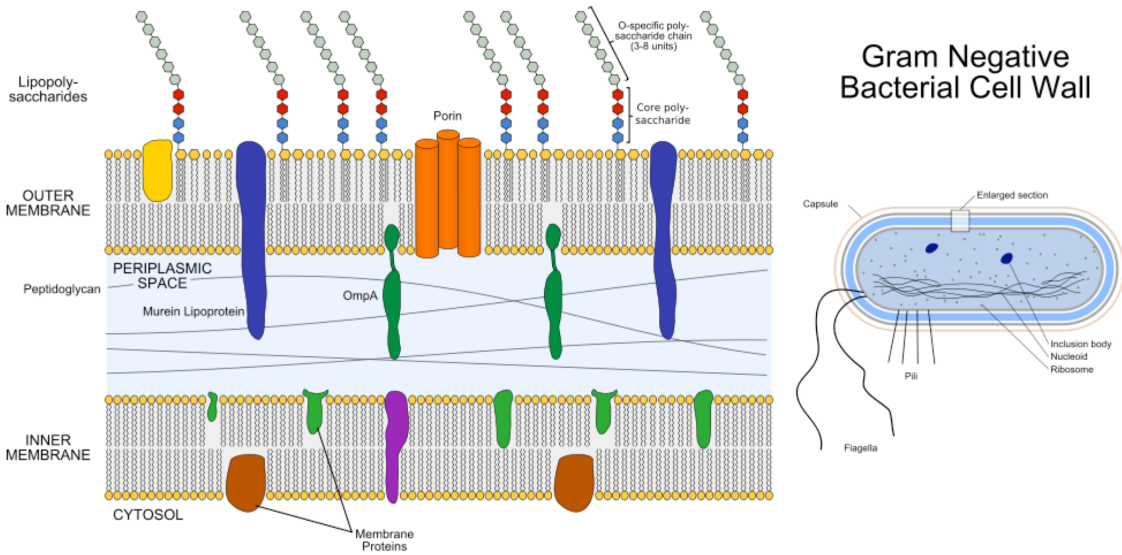


Figure 1–43 Evolutionary relationships among some of the organisms mentioned in this boo branches of the tree show paths common descent but do not ind their length the passage of time. similarly, that the vertical axis of diagram shows major categories organisms and not time.)

PKT use E. coli and S. cerevisiae as their generic examples: **4.3**

E. coli structure:
E. coli bacterium is gram negative (they do not retain crystal violet dye in staining protocol) due to cell-wall structure.

Image from Wikipedia



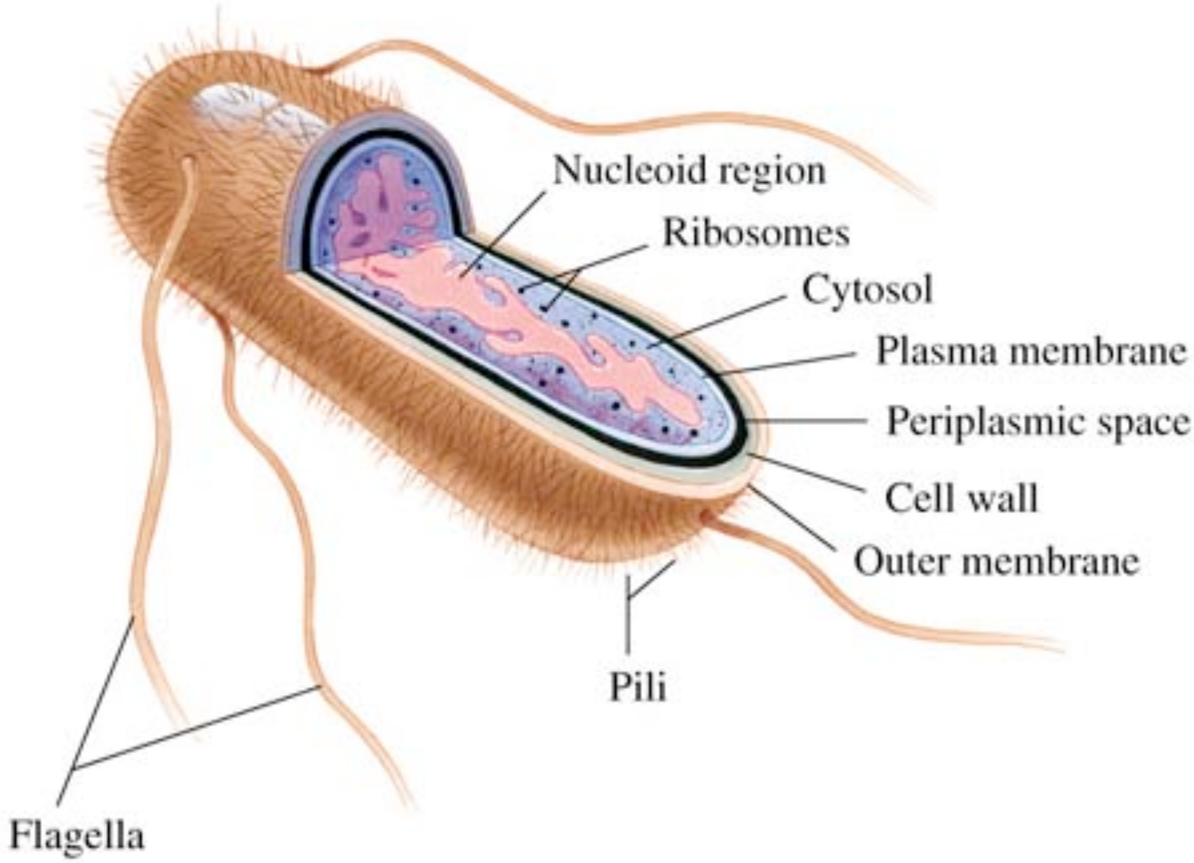
Note:

- Wall structure, including plasma membrane (lipid bilayer)
- Flagella and pili
- Cytosol, including proteins, DNA and ribosomes but no organelles
- Interior is not uniform despite lack of interior compartments
- Interior is very crowded

Image from: http://asymptotia.com/category/books/ **4.4**

E. coli

Image from: http://www.canariculturacolor.com/colibacilosis-aves **4.5**



What is molecular inventory of E. coli?

PKT Table 2.1

Substance	% of total dry weight	Number of molecules
Macromolecule		
Protein	55.0	2.4×10^6
RNA	20.4	
23S RNA	10.6	19,000
16S RNA	5.5	19,000
5S RNA	0.4	19,000
Transfer RNA (4S)	2.9	200,000
Messenger RNA	0.8	1,400
Phospholipid	9.1	22×10^6
Lipopolysaccharide	3.4	1.2×10^6
DNA	3.1	2
Murein	2.5	1
Glycogen	2.5	4,360
Total macromolecules	**96.1**	
Small molecules		
Metabolites, building blocks, etc.	2.9	
Inorganic ions	1.0	
Total small molecules	**3.9**	

Table 2.1 Observed macromolecular census of an *E. coli* cell. (Data from F. C. Neidhardt et al., Physiology of the Bacterial Cell, Sunderland, Sinauer Associates Inc., 1990 and M. Schaechter et al., Microbe, Washington DC, ASM Press, 2006.)

Where do these numbers come from?
Experiments described in PKT Ch. 2. Can estimate based on simple information.

Example: Proteins (PKT p. 33)

Rules of thumb:
1. Dry "weight" is ~30% mass of cell.
2. Protein is ~50% dry weight.
3. Average protein has ~300 amino acids.
4. Average amino acid has mass ~100 Da. ($1\text{Da}=1.66\text{x}10^{-27}$ kg)

Thus, $$N_{protein} = \frac{total\ protein\ mass}{mass\ per\ molecule} = \frac{10^{-15}(0.3)0.5}{300(100)1.66\times10^{-27}} = 3\times10^6 \text{ molecules.}$$

What is total volume of these proteins?
About 15% of the cellular volume (since density similar to water).
It follows that these protein molecules are quite close together:
Suppose equally spaced. What is volume around (and including) each protein?

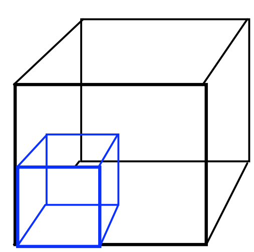
$$V = \frac{total\ protein\ volume}{number\ of\ proteins} = \frac{10^{-18}}{3\times10^6} = 3\times10^{-25}\ m^3,$$

so distance between centers is $D = \sqrt[3]{3\times10^{-25}} \approx 7\times10^{-9}\ m = \boxed{7\ nm}.$

What is space between these proteins?

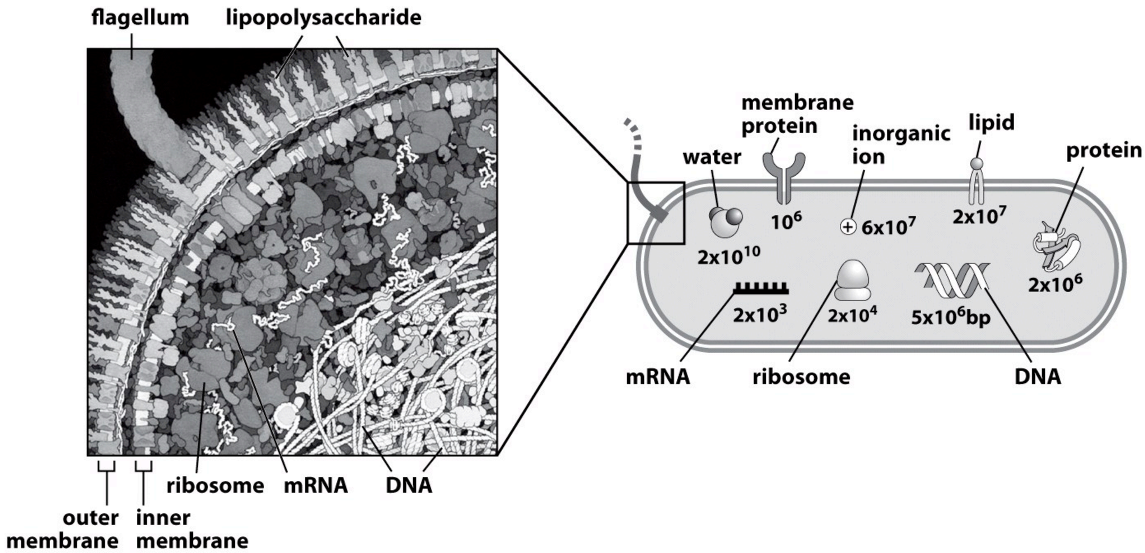
$V_{protein} = 15\%\, V = 4.5\times10^{-26}\ m^3,$

so $D_{protein} = \sqrt[3]{4.5\times10^{-26}} \approx 4\times10^{-9}\ m = \boxed{4\ nm}.$



And, this is only half of the dry weight! The bacterial cell is a very crowded place! The interior of an E. coli bacterium is NOT a dilute solution but a thick soup, almost a gel. See PKT, Fig. 2.2 (below).

PKT, Fig. 2.2



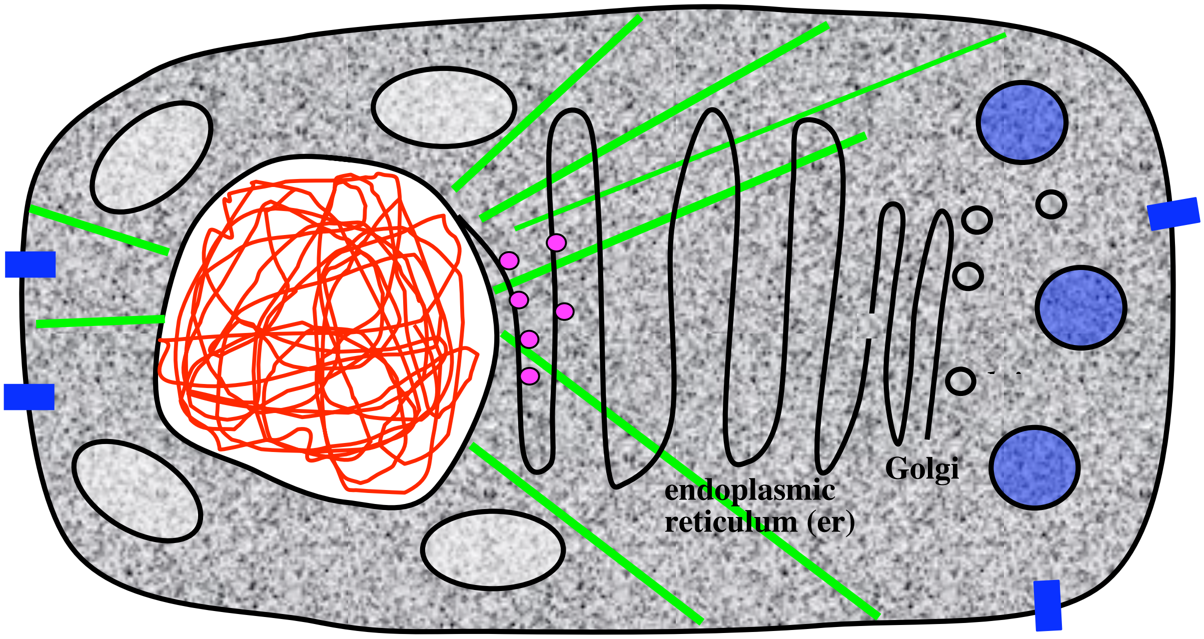
Another useful number which we will need in Chapter 5:

How many carbon atoms in one E. coli?
Typical organic molecule roughly half mass is C.
Since 50% dry mass is protein, just look at typical amino acid.
Also, e.g., glucose $C_6H_{12}O_6$ typical carbohydrate.
Thus, number of C atoms/cell is:

$$N_C = \frac{total\ carbon\ mass}{mass\ per\ atom} = \frac{0.5(0.3)10^{-15}\ g}{12\left(1.66\times10^{-24}\right)\ g/\text{C atom}} = 0.75\times10^{10} \sim \boxed{10^{10}\ \text{C atoms/cell}}$$

(see Lect.??)

Eukaryotic cell:
Generic animal cell (plants are similar but with important characteristic differences)



black lines represent lipid bilayers;
the lipid bilayer surrounding the cell is the plasma membrane or pm

mitochondria (ATP manufacture)

lysosomes and peroxyzomes (digestion)

transport vesicles (from Golgi)

channels, pumps, etc. (functional proteins)

er and Golgi are a set of flattened sack-like membranes which attach to the nuclear membrane

ribosomes are connected to protein synthesis

filaments of various kinds (protein) extend throughout cytosol
(structure and tracks for transport of material)

see also Alberts, pp. 16-17 (attached)

Structure and Function: Themes of Cellular Organization:

1. Everything takes place in an aqueous solution, thus, we will have to spend time discussing what happens when molecules dissolve in water and how this affects their interactions with one another.

2. Membranes: Encapsulation/compartmentalization provides the possibility of specialized environments for chemical processing (e.g., extreme pH's).
Membranes are NOT waterproof!!!! Indeed, they are quite permeable to water.
What they inhibit is transport of molecules which are (a) large and/or (b) charged.

They also provide a "substrate" for many functional proteins (factory floor). Important examples are the specialized channels and pumps which (often actively) transport of the molecules required to prepare the required environments.
Membranes are osmotic barriers: even though the chemical environment may be different on the two sides, the "osmolarity" must balance; otherwise, water will flow. If this balance is not maintained, then the osmotic pressures can easily lead to lysis.

3. Processing is done by protein enzymes, designed to function in these specific environments.
(machines) Number of proteins in genome (enzymes): 500—30,000, depending on organism.
Some are structural (e.g., filaments); most are functional (i.e., enzymes)

4. Distribution of materials: Active vs passive transport
Across membranes: pores, channels, transporters
In membranes
In cytosol: vesicles, motor, filaments
The message is that, except at the shortest distances, passive transport (diffusion down chemical gradients) is too slow to work, so nature uses active (protein-based) machines that "burn" ATP.
We will study diffusion in Chapter 13. But, let me jump ahead:
Let $\sqrt{\langle r^2 \rangle}$ be the rms distance traveled by a solute particle in time t. The rule is that the rms displacement in 3D goes as the square root of time with $\langle r^2 \rangle = 6Dt$, where the "diffusion constant" D [m^2/s] depends on solvent and solute.
A typical D for a lipid or protein in aqueous solution is $D \sim 10^{-12}\ m^2/s$.
(we'll see later how to estimate this)
For a prokaryote with size 1 micron, this means that the time to diffuse across the cell is: $\left(10^{-6}\right)^2 = 6 \times 10^{-12} t$, i.e., t~0.2 s.
For a eukaryotic cell with size 10 microns, this means that the time to diffuse across the cell is: $\left(10^{-5}\right)^2 = 6 \times 10^{-12} t$, i.e., t=20 s.
But, the typical timescale for processes in cells is 1 ms, so even for the bacterium this is slow.
And, for the eukaryote it is hopeless.

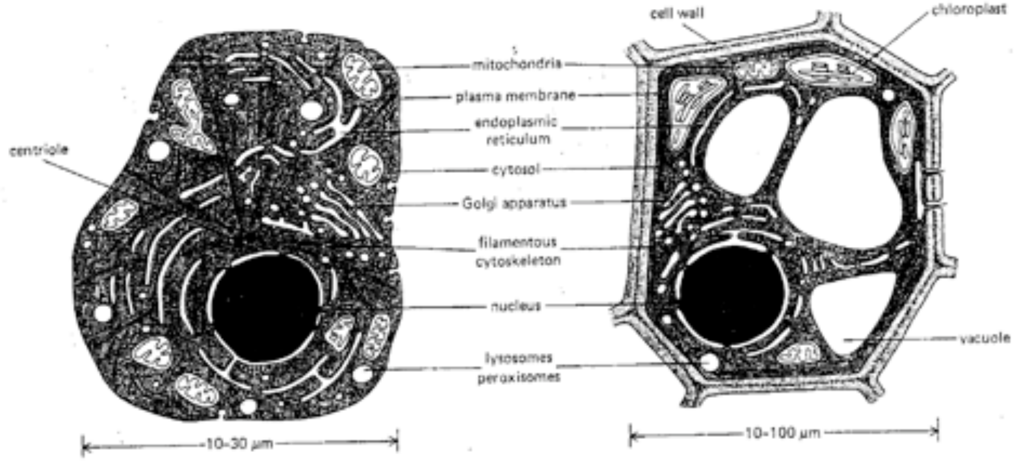
5. Control:
DNA read ("transcribed") by m-RNA, which takes information to ribosomes where proteins are built according to specs provided with the help of t-RNA. ("central dogma")
There is a complex system of feed-back regulating which genes are read and when.
Up-stream non-coding DNA can block or promote transcription.

ANIMAL CELL

thin section of a generalized animal cell

PLANT CELL

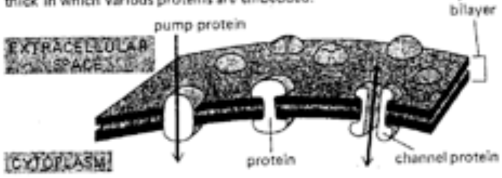
thin section of a generalized cell from a higher plant



THE MEMBRANE SYSTEM OF THE CELL

PLASMA MEMBRANE

The outer boundary of the cell is the plasma membrane, a continuous sheet of phospholipid molecules about 4-5 nm thick in which various proteins are embedded.

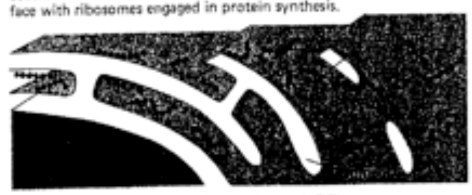


Some of these proteins serve as pumps and channels for transporting specific molecules into and out of the cell.

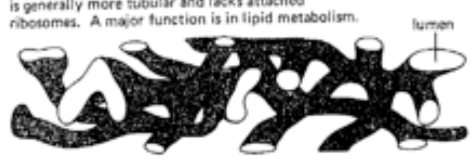
ENDOPLASMIC RETICULUM

Flattened sheets, sacs, and tubes of membrane extend throughout the cytoplasm of eucaryotic cells, enclosing a large intracellular space. The ER membrane is in structural continuity with the outer membrane of the nuclear envelope and it specializes in the synthesis and transport of lipids and membrane proteins.

The rough endoplasmic reticulum (rough ER) generally occurs as flattened sheets and is studded on its outer face with ribosomes engaged in protein synthesis.



The smooth endoplasmic reticulum (smooth ER) is generally more tubular and lacks attached ribosomes. A major function is in lipid metabolism.



GOLGI APPARATUS

A system of stacked, membrane-bounded, flattened sacs involved in modifying, sorting, and packaging macromolecules for secretion or for delivery to other organelles.

Around the Golgi apparatus are numerous small membrane-bounded vesicles (50 nm and larger). These are thought to carry material between the Golgi apparatus and different compartments of the cell.

LYSOSOMES

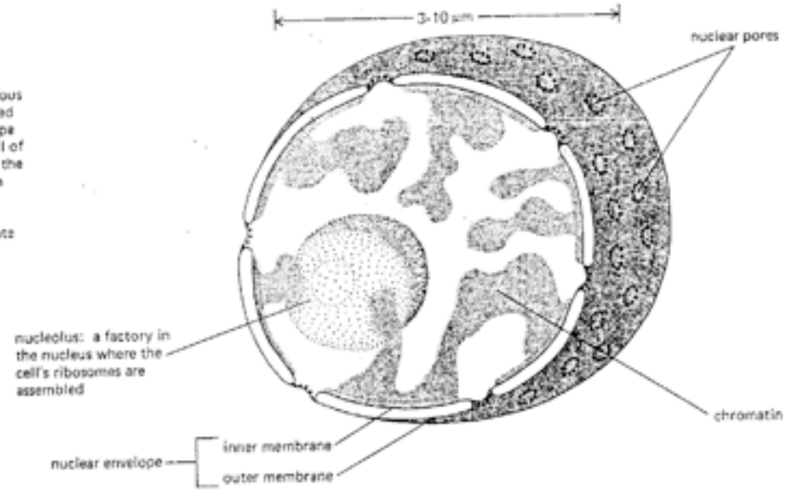
membrane-bounded vesicles that contain hydrolytic enzymes involved in intracellular digestions

PEROXISOMES

membrane-bounded vesicles containing oxidative enzymes that generate and destroy hydrogen peroxide

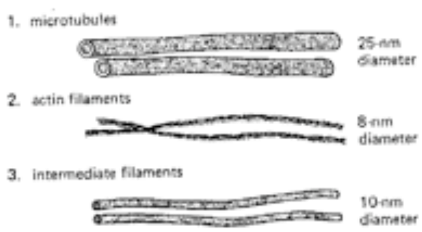
NUCLEUS

The nucleus is the most conspicuous organelle in the cell. It is separated from the cytoplasm by an envelope consisting of two membranes. All of the chromosomal DNA is held in the nucleus, packaged into chromatin fibers by its association with an equal mass of histone proteins. The nuclear contents communicate with the cytosol by means of openings in the nuclear envelope called nuclear pores.



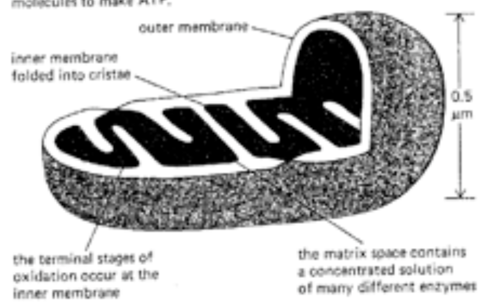
CYTOSKELETON

In the cytosol, arrays of protein filaments form networks that give the cell its shape and provide a basis for its movements. In animal cells the cytoskeleton is often organized from an area near the nucleus that contains the cell's pair of centrioles. Three main kinds of cytoskeletal filaments are:



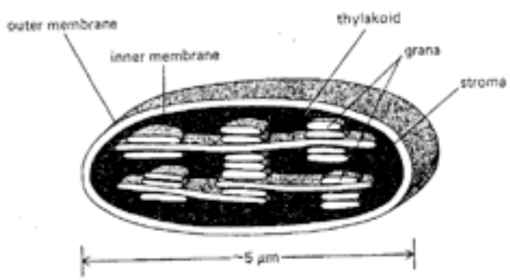
MITOCHONDRIA

About the size of bacteria, mitochondria are the power plants of all eucaryotic cells, harnessing energy obtained by combining oxygen with food molecules to make ATP.

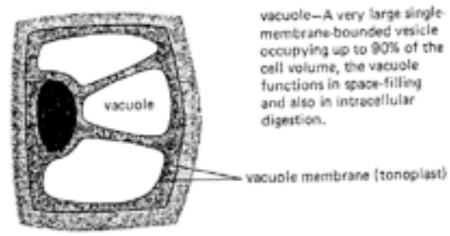


SPECIAL PLANT CELL ORGANELLES

chloroplasts – These chlorophyll-containing plastids are double-membrane-bounded organelles found in all higher plants. An elaborate membrane system in the interior of the chloroplast contains the photosynthetic apparatus.



vacuole – A very large single-membrane-bounded vesicle occupying up to 90% of the cell volume, the vacuole functions in space-filling and also in intracellular digestion.



cell wall – Plant cells are surrounded by a rigid wall composed of tough fibrils of cellulose laid down in a matrix of other polysaccharides.