Chem 352 - Lecture 1
Introduction to Biochemistry

Question for the Day: What characteristics distinguishes living systems from non-living systems?

Introduction

- Biochemistry involves the study of biological system at the molecular level.

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- What biological systems should we study?

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Anything found to be true of E. coli must also be true of elephants.
-Jacques Monod

Introduction

In this introduction we will consider

- History of biochemistry
- Molecules
  - Families of organic molecules and the functional groups that define them
  - Polymers (Macromolecules)
- Energy
- Cells and cellular structures

Introduction

Question:

What is a polymer?

Introduction

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- History of biochemistry
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  - Polymers (Macromolecules)
- Energy
- Cells and cellular structures

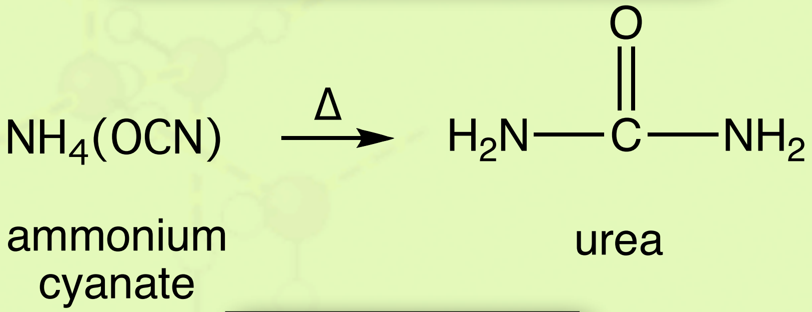
A brief history of Biochemistry

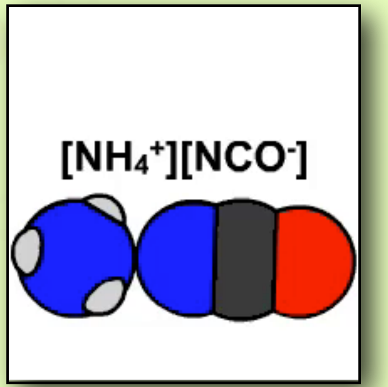
Biochemistry, as with all the sciences, is a human endeavor.

- It is worth recognizing some of the early contributors to biochemistry.

A brief history of Biochemistry

- Fredrich Wöhler (1800-1882)
  - Demonstrated that urea, a compound that had only been associated with living cells, could be synthesized from an inorganic compound outside of a living cell.
  - This led to the recognition that the chemistry that takes place inside a living cell is the same chemistry that takes place outside of the cell.





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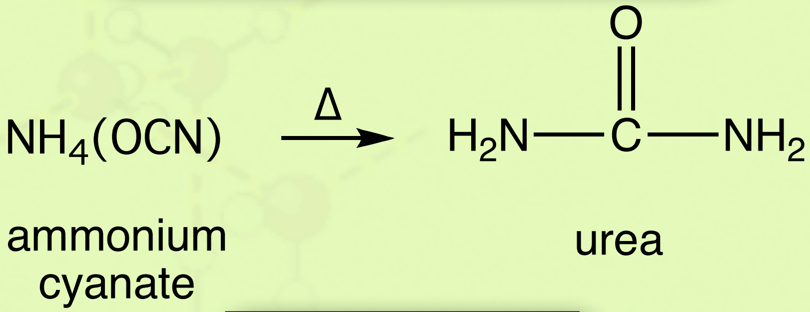
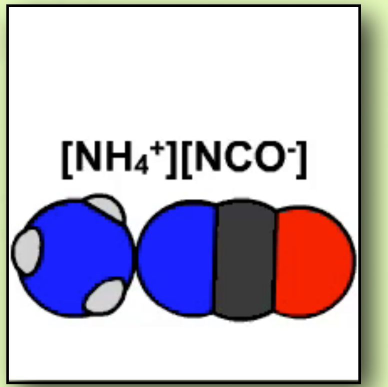




A brief history of Biochemistry

- Eduard Buchner (1860-1917)
  - Showed that the fermentation of sugars by yeast, a process that occurs when making beer, wine and bread, could be carried out with the cell extracts from yeast cells.
  - Living cells were not required to carry out this complex series of reactions.

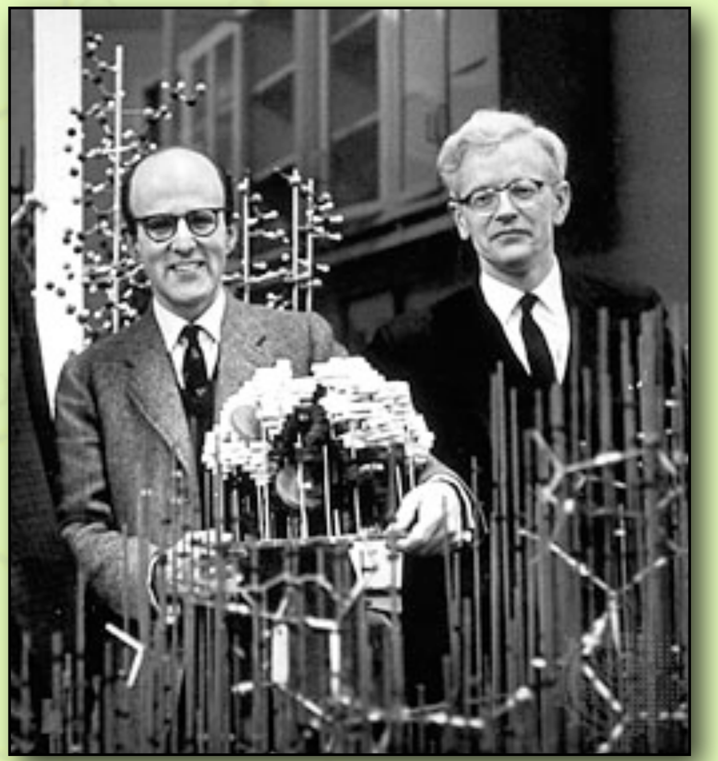
A brief history of Biochemistry

- Emil Fischer (1852-1919)
  - Characterized the catalytic components of yeast extracts that were carrying out the fermentation reactions.
  - We now refer to these biological catalysts as enzymes.
  - His descriptions of the molecular interactions that take place between an enzyme and its substrates and products are, in hindsight, remarkably insightful.

Received the 2nd Nobel Prize awarded in Chemistry (1902)

A brief history of Biochemistry

- Fischer's enzymes turned out to be proteins.
  - Proteins are a major class of biological molecules and turn out to be the real workhorses of a living cell.
  - It was not until the late 1950's that we were first construct models for the 3-dimensional structures of proteins.



Max Perutz (left)
John Kendrew (right)
shared the 1962
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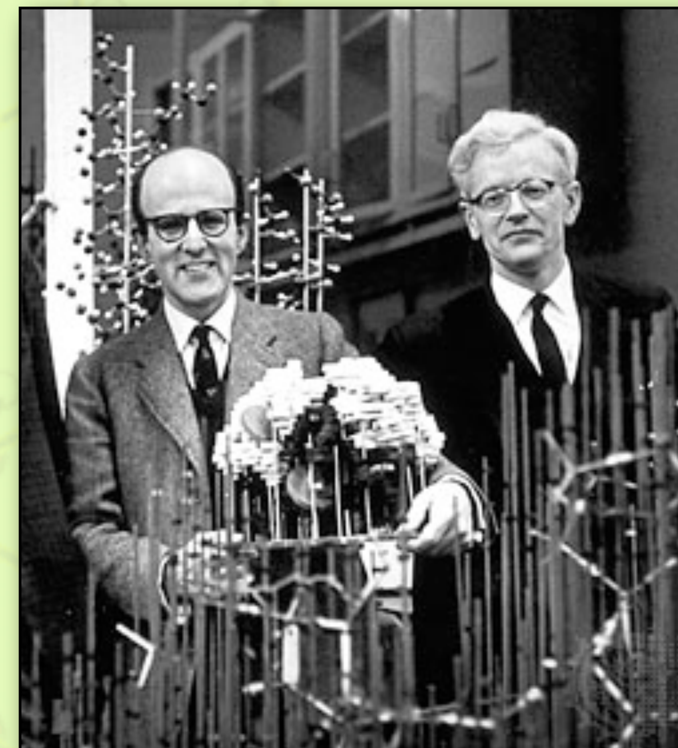

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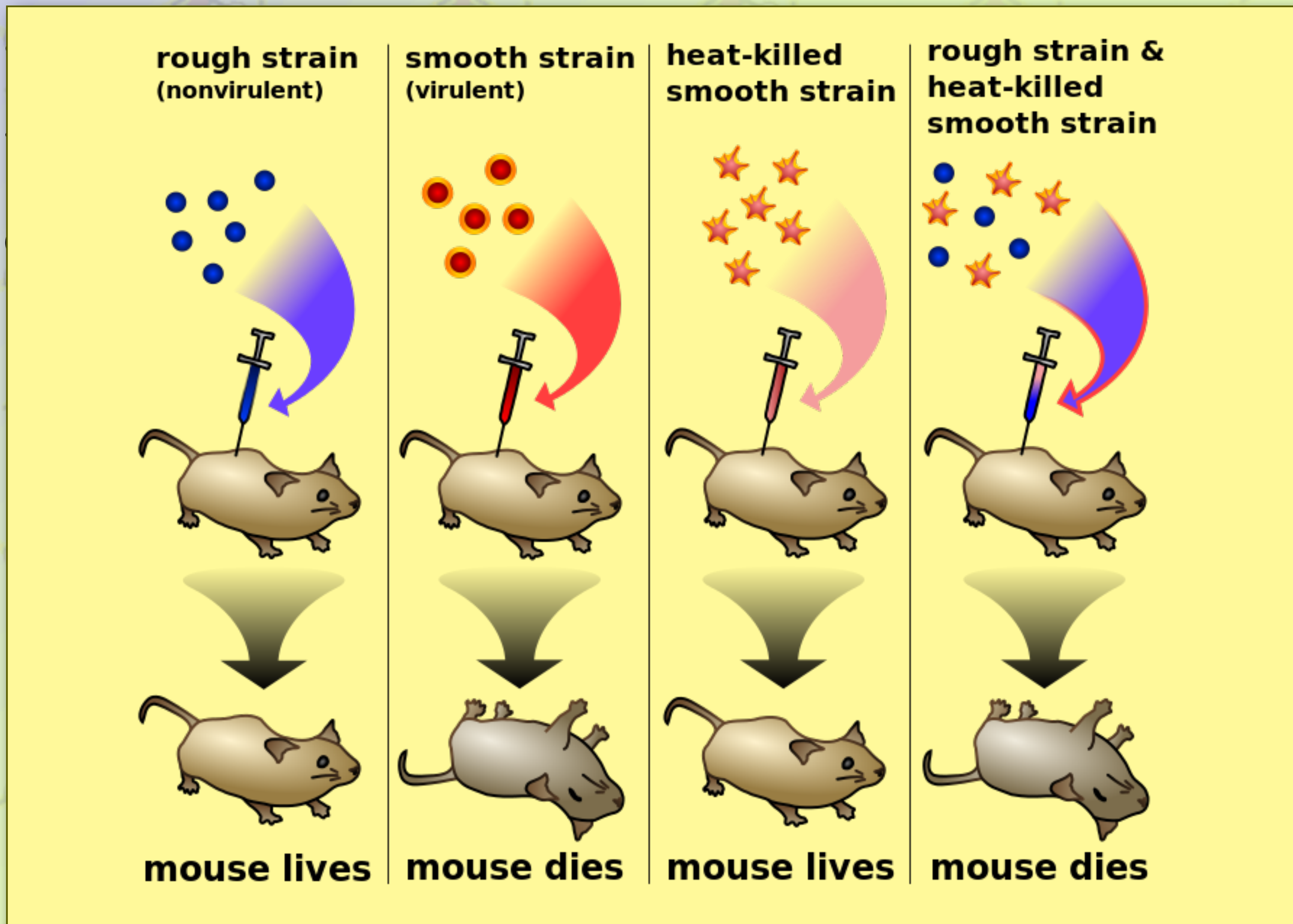
  - In 1944, Oswald Avery, Colin MacLeod and Maclyn McCarty demonstrated that the infectious component of *Streptococcus pneumoniae*, the bacterium that causes pneumonia, was the molecule **deoxyribonucleic acid** (DNA), and not protein.
  - This significant finding provided evidence that DNA is the carrier of the biological information.

A brief history of Biochemistry



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A brief history of Biochemistry

- In 1953, James Watson and Francis Crick proposed an atomic level structure for DNA.
    - Their model met with immediate acceptance because their structure readily explained how DNA can function as an information carrying molecule that is capable of replicating itself as cells divide and multiply.

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A brief history of Biochemistry

- Francis Crick went on to propose that the general flow of information is from DNA to RNA to protein.
  - His model has become known as the "central dogma" of molecular biology.

DNA ⟶ RNA ⟶ Protein

A brief history of Biochemistry

- Darwin's theory of evolution
  - All of modern biology rests on a foundation that Darwin laid with his theory of natural selection.
  - Even though Darwin's theory helps us to understand how all of the forms of life currently found on earth could have evolved from a single cell, starting 3.5 billion years ago,
    - It does not shed light on how that first cell arose.

A brief history of Biochemistry

- Darwin's thoughts on the origins of life:
  - "Probably all the organic beings which have ever lived on this earth have descended from some one primordial form, into which life was first breathed." (from The Origin of the Species, 1859)

A brief history of Biochemistry

- Darwin's thoughts on the origins of life:
  - "But if (and Oh!, what a big if!) we could conceive in some warm little pond, with all sorts of ammonia and phosphoric salts, light heat, electricity, etc., present, that a protein compound was chemically formed ready to undergo still more complex changes, at the present day such matter would be instantly devoured or absorbed, which would not have been the case before living creatures were formed." (Letter to botanist Joseph Hooker, 1871)

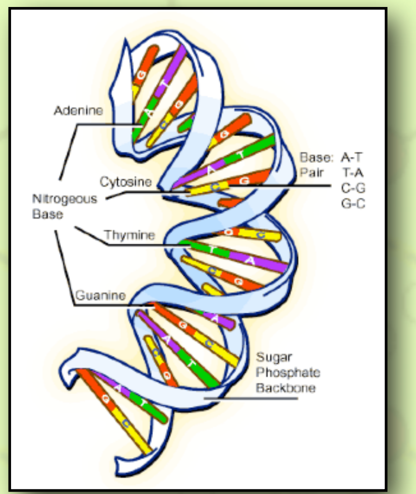
A brief history of Biochemistry

- The origin of life on earth is still one of the big questions in biology.
  - In the Zimmer essay, there is a discussion of the current progress being made to discover how that first cell arose. It is a good introduction to some of the major molecular players that we will encounter this semester.

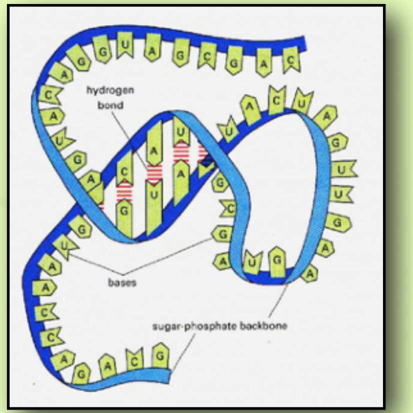
Carl Zimmer, "On the Origin of Life on Earth", Science 2009, 323, 198-199.

A brief history of Biochemistry

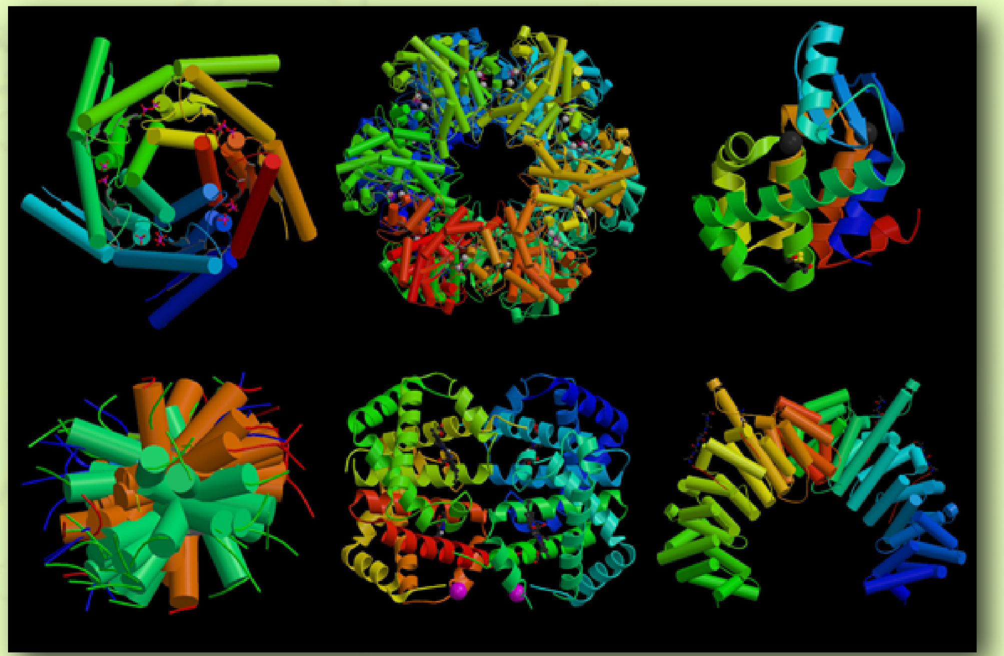
- Just about all organisms use DNA to encode genetic information.



- They copy this information into RNA

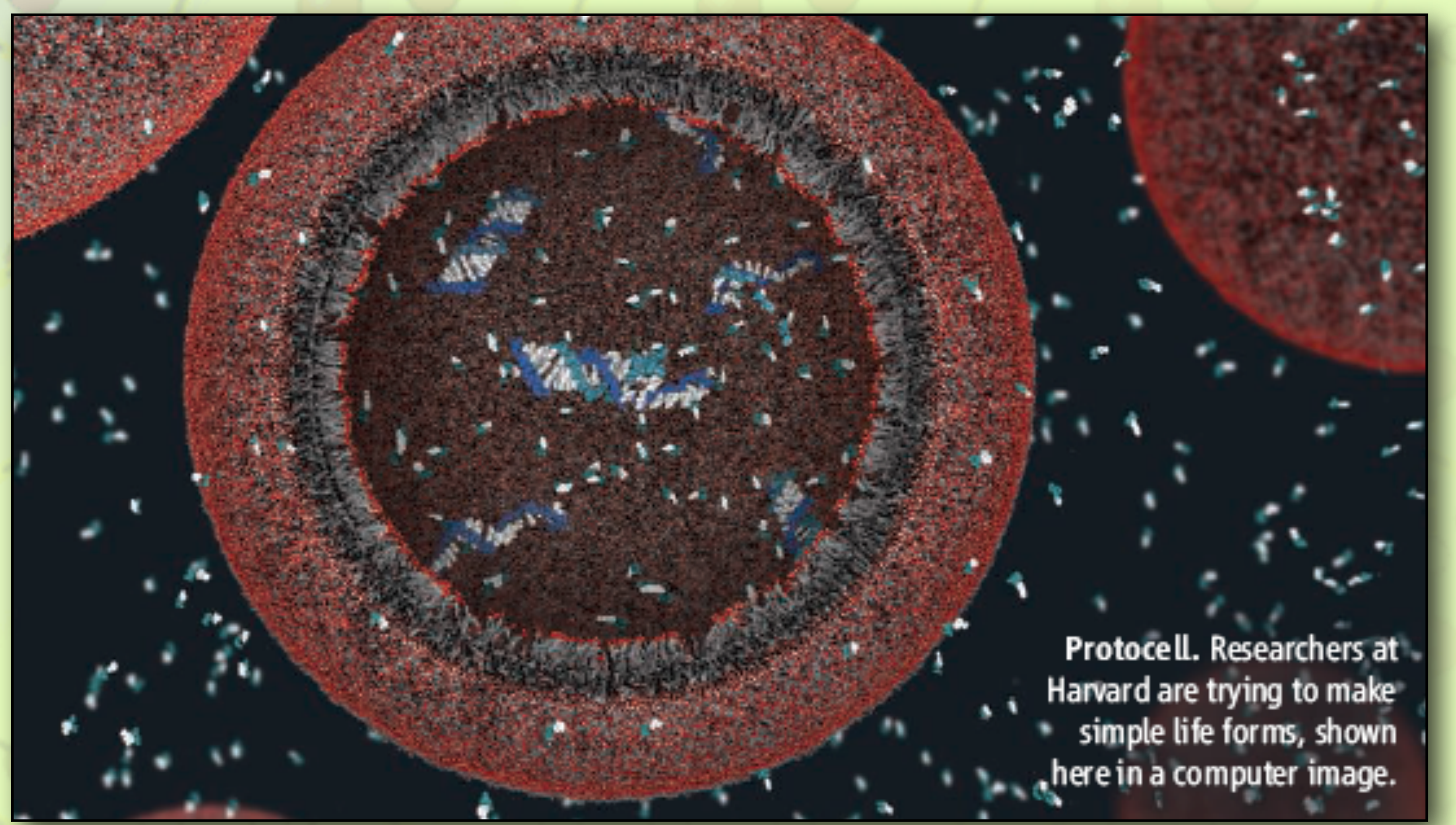


- The RNA is used to make proteins



A brief history of Biochemistry

- The other important component of living cells are membranes.
  - These are made out of lipids.



The Elements of Life

- Since this is a chemistry class, we should probably start with the elements.
  - Approximately 97% of elements found in living systems comprise just six elements:
    - oxygen
    - carbon
    - hydrogen
    - nitrogen
    - phosphorous
    - sulfur

The Elements of Life

IA	IIA	IIIB	IVB	VB	VIB	VIIB	VIIIB			IB	IIB	IIIA	IVA	VA	VIA	VIIA	0
1 H 1.008																	2 He 4.003
3 Li 6.941	4 Be 9.012											5 B 10.81	6 C 12.01	7 N 14.01	8 O 16.00	9 F 19.00	10 Ne 20.18
11 Na 22.99	12 Mg 24.31											13 Al 26.98	14 Si 28.09	15 P 30.97	16 S 32.07	17 Cl 35.45	18 Ar 39.95
19 K 39.10	20 Ca 40.08	21 Sc 44.96	22 Ti 47.87	23 V 50.94	24 Cr 52.00	25 Mn 54.94	26 Fe 55.85	27 Co 58.93	28 Ni 58.69	29 Cu 63.55	30 Zn 65.39	31 Ga 69.72	32 Ge 72.61	33 As 74.92	34 Se 78.96	35 Br 79.90	36 Kr 83.80
37 Rb 85.47	38 Sr 87.62	39 Y 88.91	40 Zr 91.22	41 Nb 92.91	42 Mo 95.94	43 Tc (98)	44 Ru 101.1	45 Rh 102.9	46 Pd 106.4	47 Ag 107.9	48 Cd 112.4	49 In 114.8	50 Sn 118.7	51 Sb 121.8	52 Te 127.6	53 I 126.9	54 Xe 131.3
55 Cs 132.9	56 Ba 137.3	57 * La 138.9	72 Hf 178.5	73 Ta 180.9	74 W 183.8	75 Re 186.2	76 Os 190.2	77 Ir 192.2	78 Pt 195.1	79 Au 197.0	80 Hg 200.6	81 Tl 204.4	82 Pb 207.2	83 Bi 209.0	84 Po (209)	85 At (210)	86 Rn (222)
87 Fr (223)	88 Ra (226)	89** Ac (227)	104 Rf (261)	105 Db (262)	106 Sg (263)	107 Bh (264)	108 Hs (265)	109 Mt (268)	110 (269)	111 (272)	112 (277)	113	114 (285)	115	116 (289)	117	118 (293)

58* Ce 140.1	59 Pr 140.9	60 Nd 144.2	61 Pm (145)	62 Sm 150.4	63 Eu 152.0	64 Gd 157.3	65 Tb 158.9	66 Dy 162.5	67 Ho 164.9	68 Er 167.3	69 Tm 168.9	70 Yb 173.0	71 Lu 175.0
90** Th 232.0	91 Pa 231	92 U 238.0	93 Np (237)	94 Pu (244)	95 Am (243)	96 Cm (247)	97 Bk (247)	98 Cf (251)	99 Es (252)	100 Fm (257)	101 Md (258)	102 No (259)	103 Lr (262)

The Compounds of Life

- Water, H_2O, comprises up to 75% of the mass of a living cell.

- Most of the solid material, the other 25%, is made up of carbon-based molecules.

•

The Compounds of Life

- Organic molecules are grouped into **families** according to the **functional groups** they contain.

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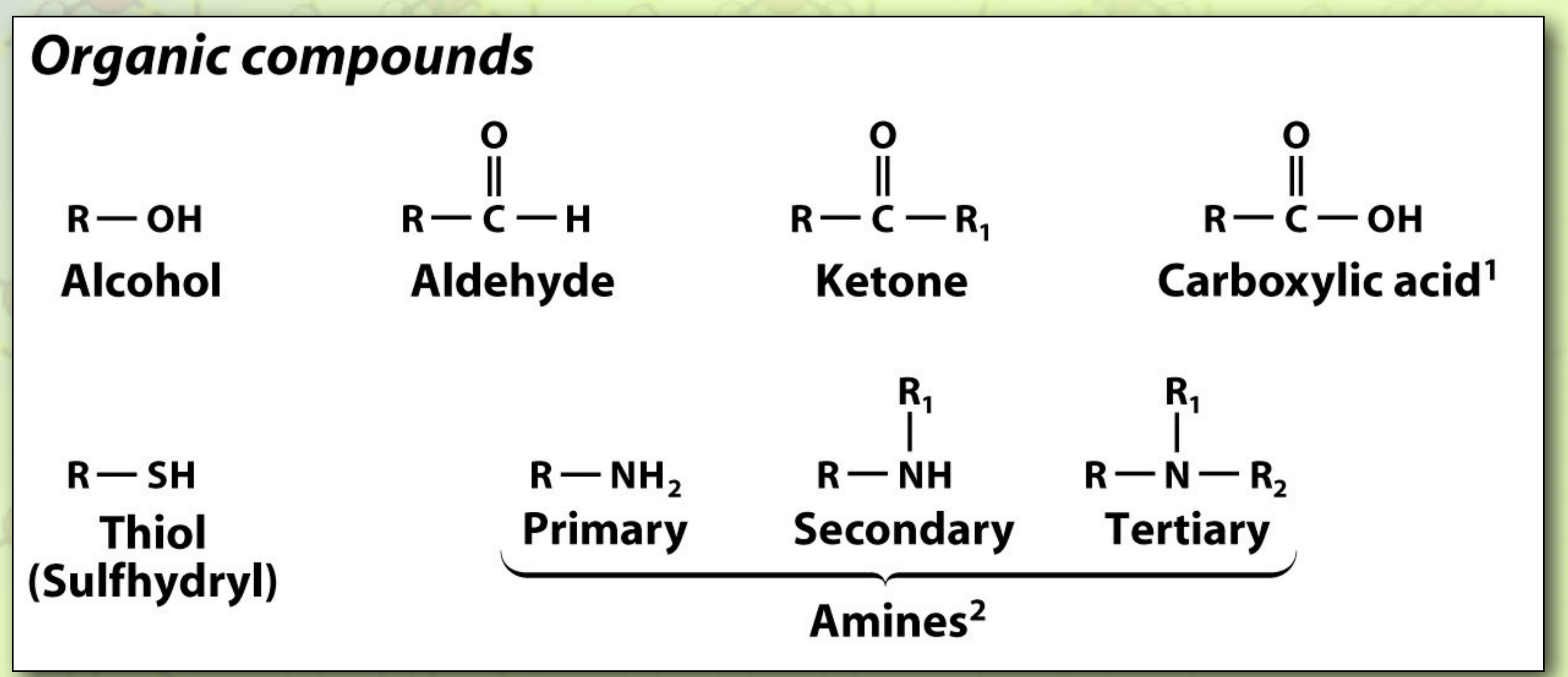

The Compounds of Life

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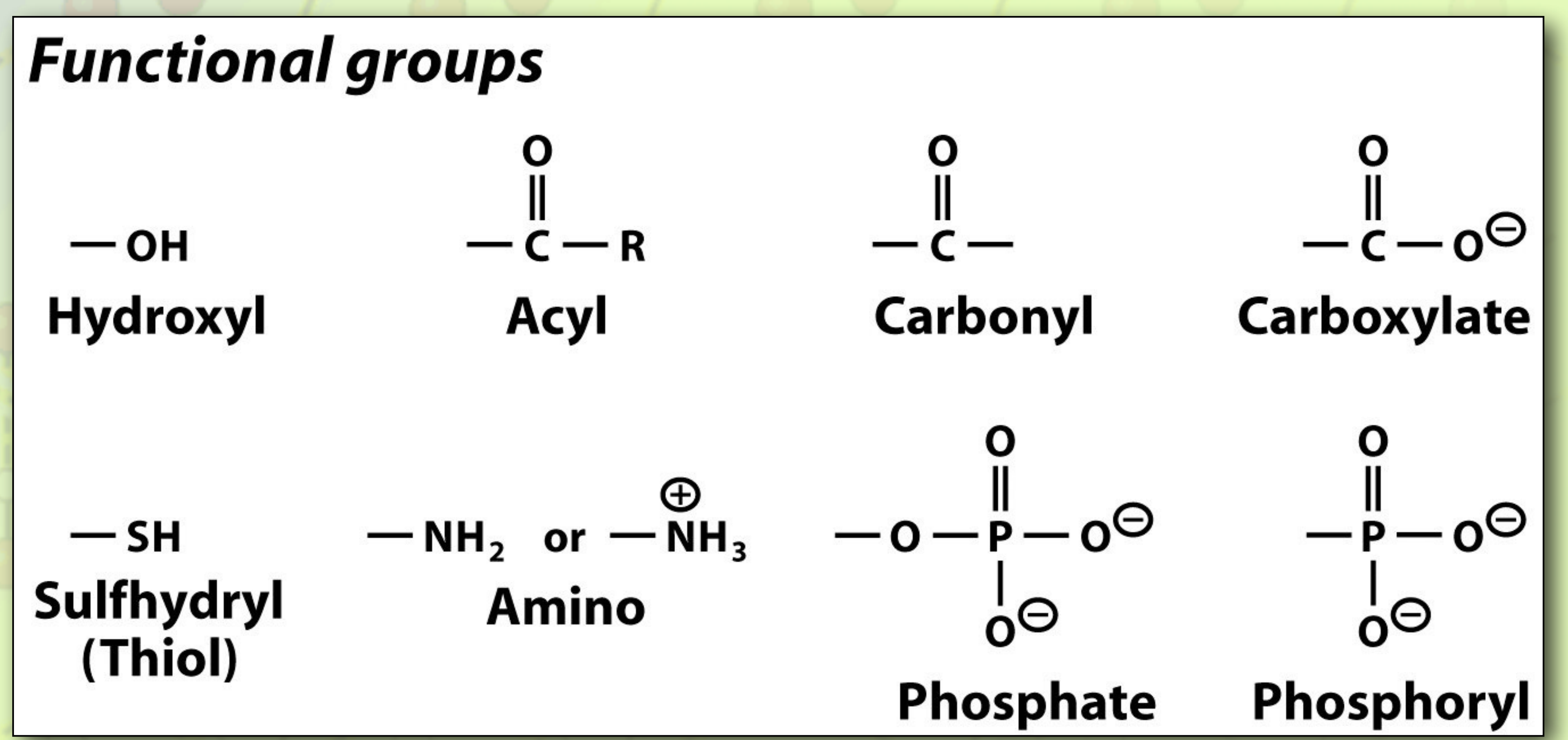
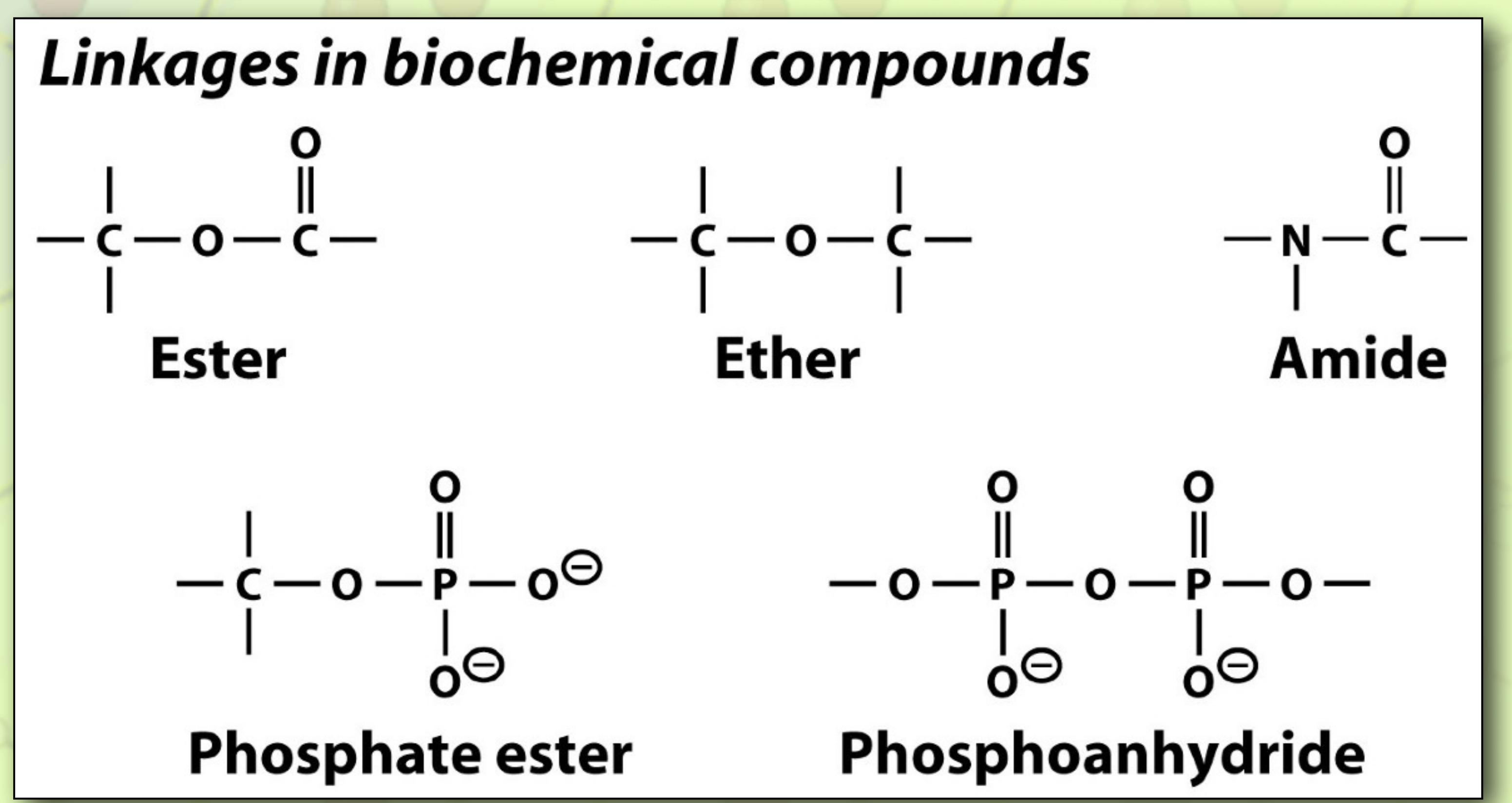


The Compounds of Life

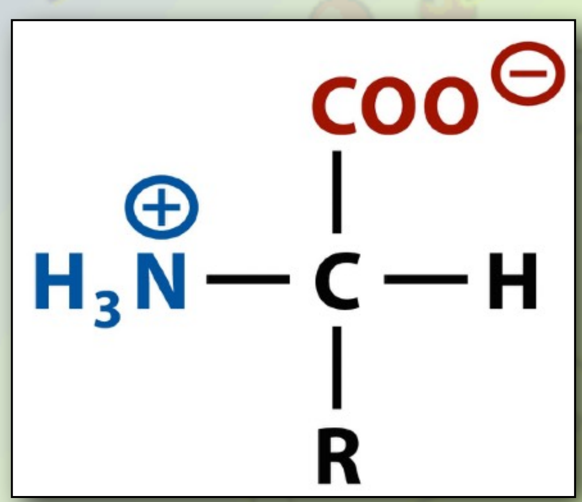
- Some of the functional groups combine with others to form new functional groups.
- 

Biological Macromolecules

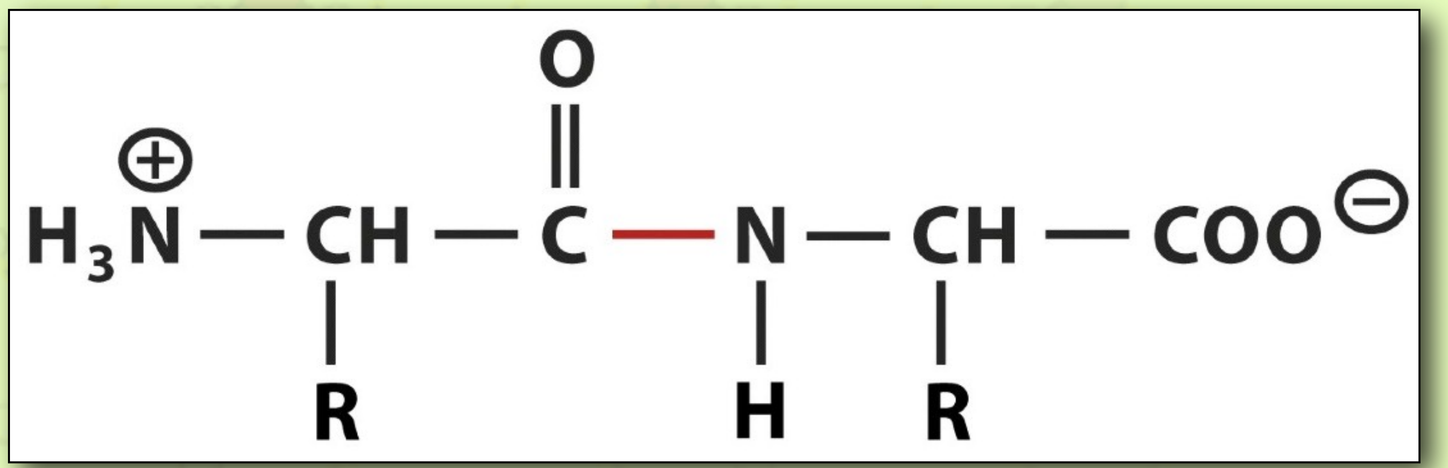
- The large biological molecules (macromolecules), such as proteins, nucleic acids and polysaccharides, are **polymers**.
  - Polymers are made by joining together monomers, much like beads on a string.
    - Proteins are polymers of **amino acids**
    - Polysaccharides are polymers of **monosaccharides**.
    - Nucleic acids are polymers of **nucleotides**.

Biological Macromolecules

- Proteins are polymers of **amino acids**



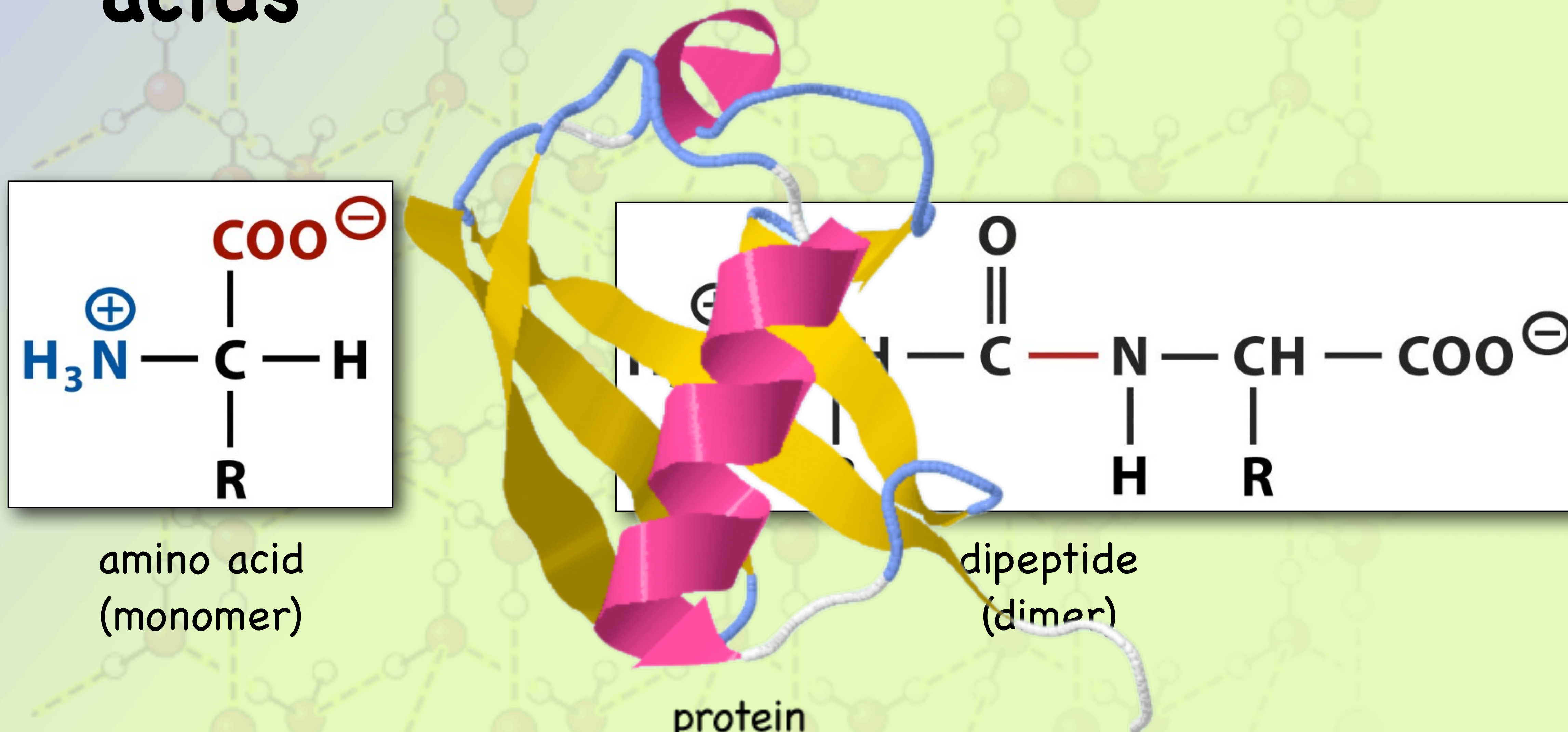
amino acid
(monomer)



dipeptide
(dimer)

Biological Macromolecules

- Proteins are polymers of **amino acids**



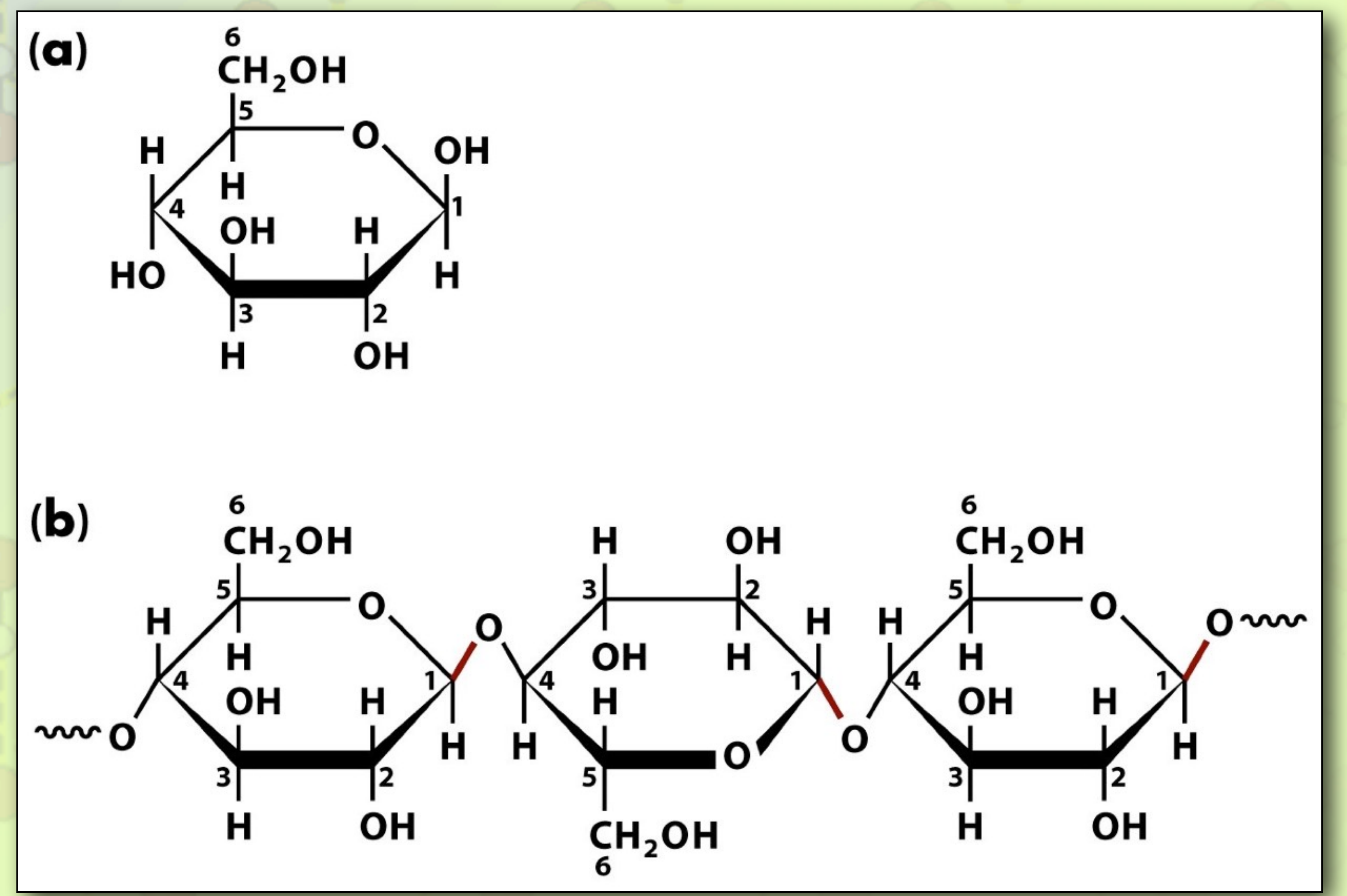
amino acid (monomer)

dipeptide (dimer)

protein (polypeptide)

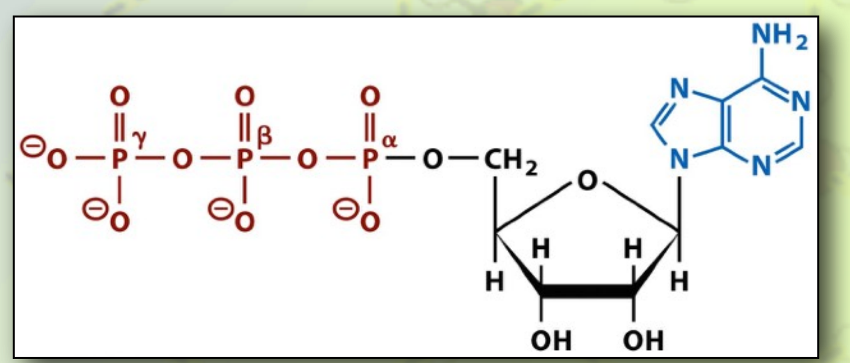
Biological Macromolecules

- Polysaccharides are polymers of **monosaccharides**.

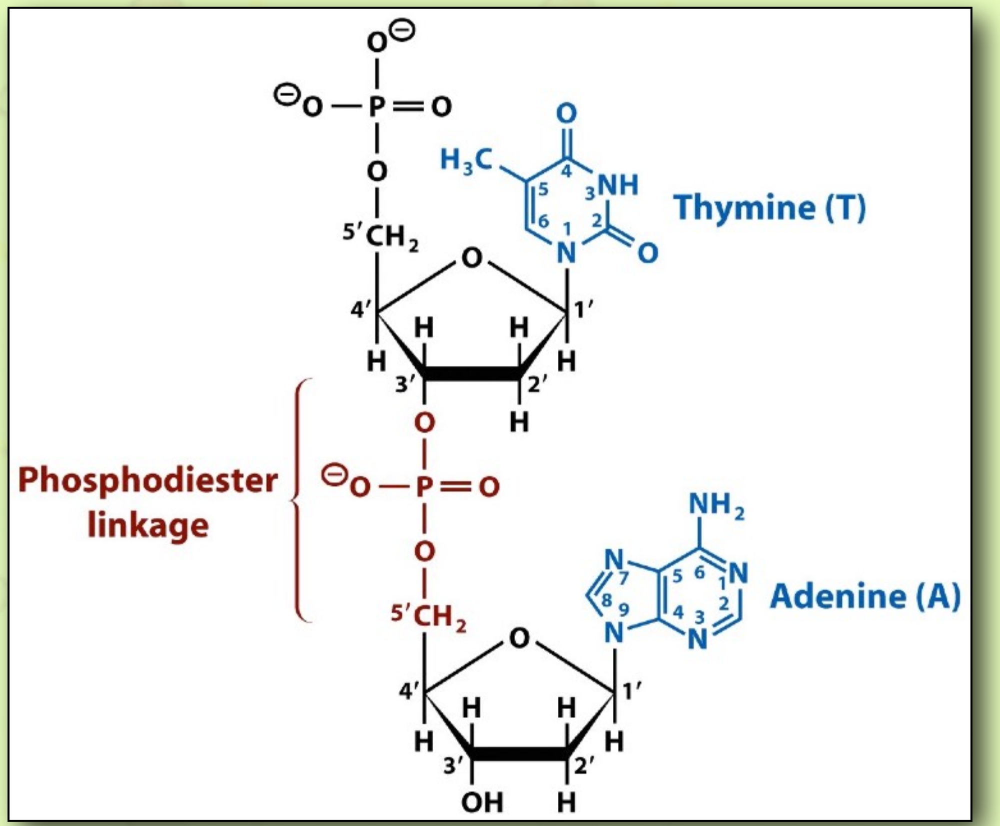


Biological Macromolecules

- Nucleic acids are polymers of **nucleotides**



nucleotide
(monomer)



dinucleotide
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Biological Macromolecules

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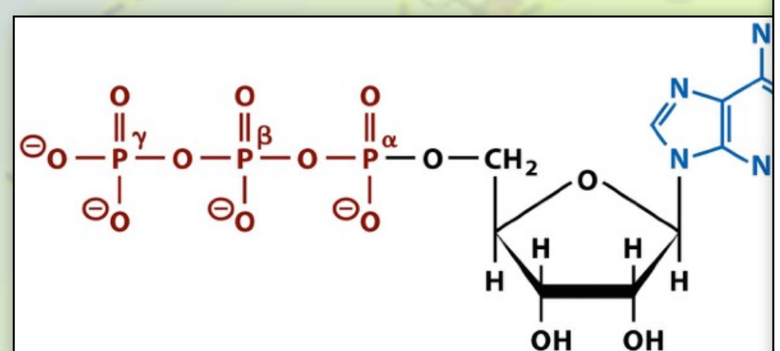
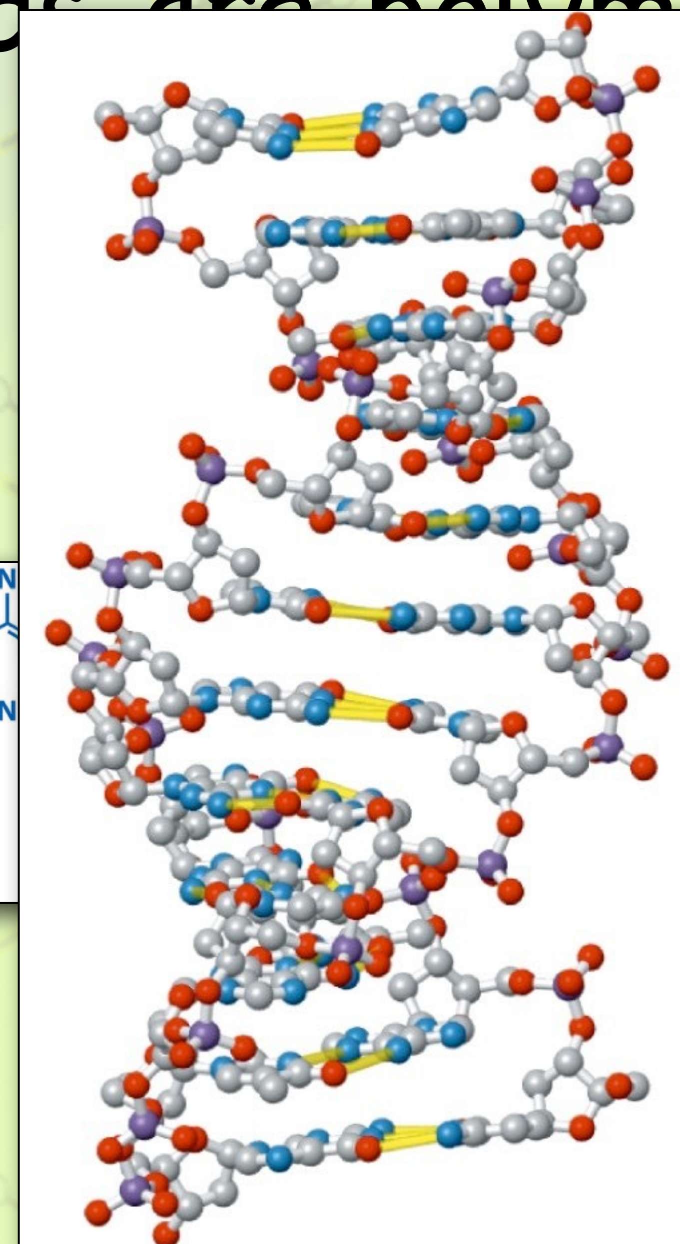
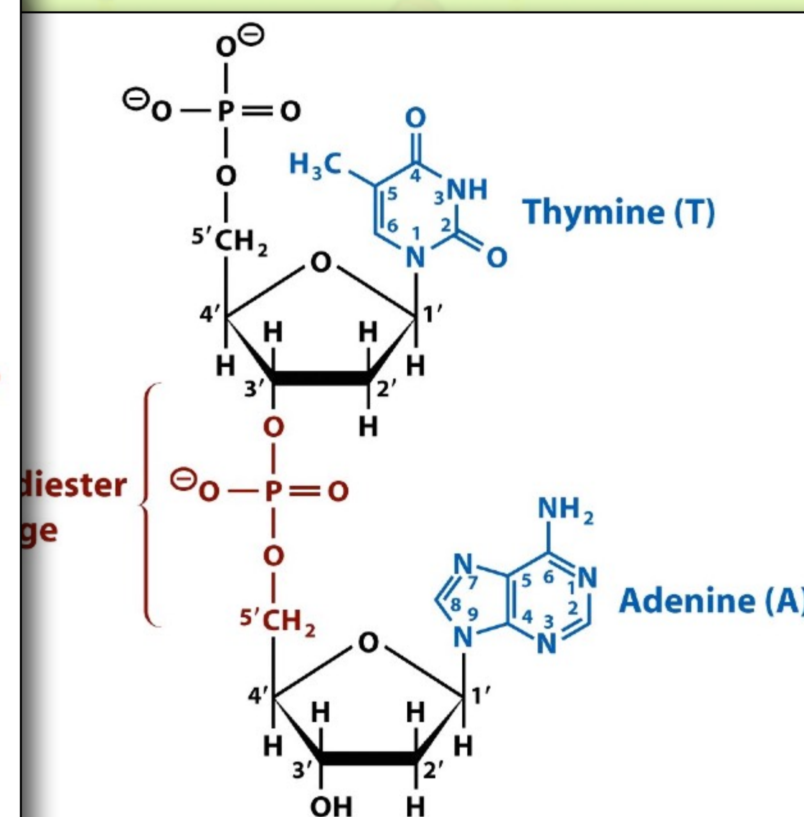


nucleotide
(monomer)



polynucleotide
(polymer)



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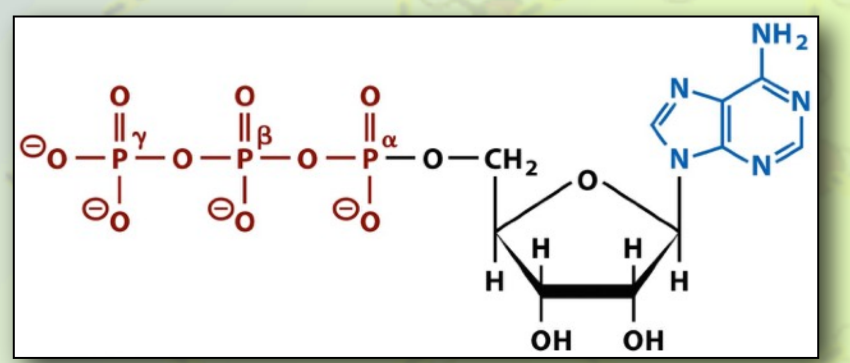

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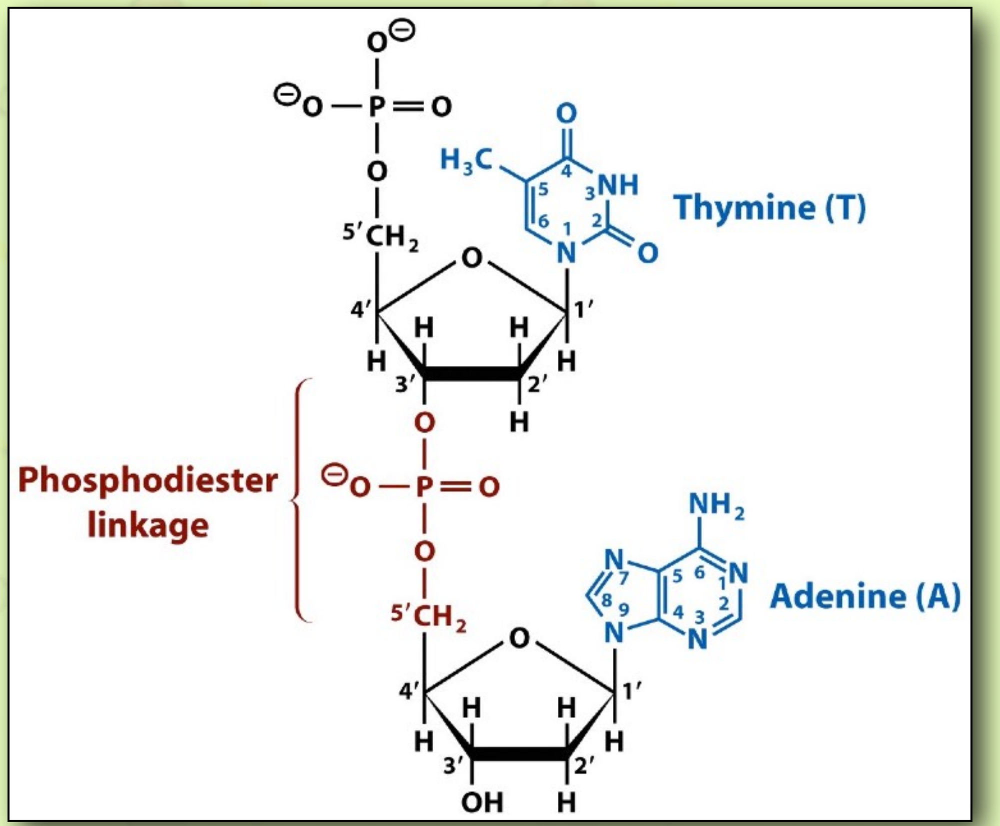


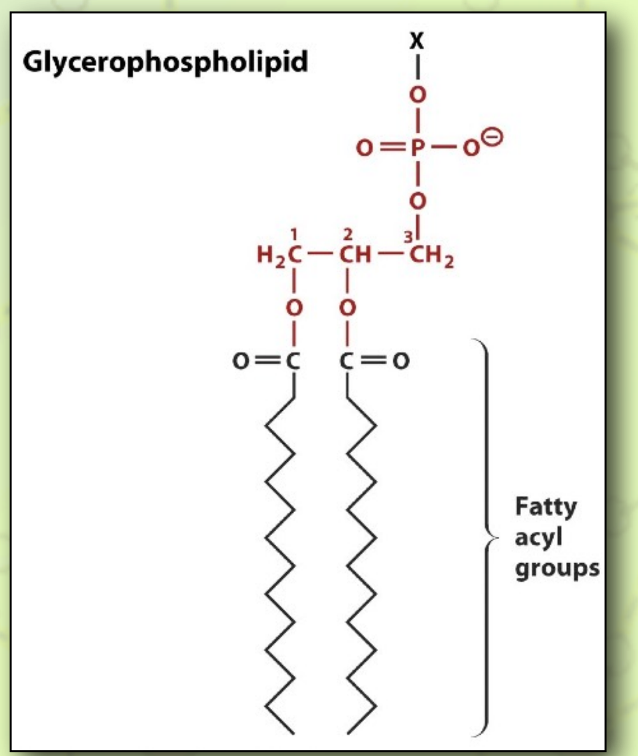
dinucleotide
(dimer)

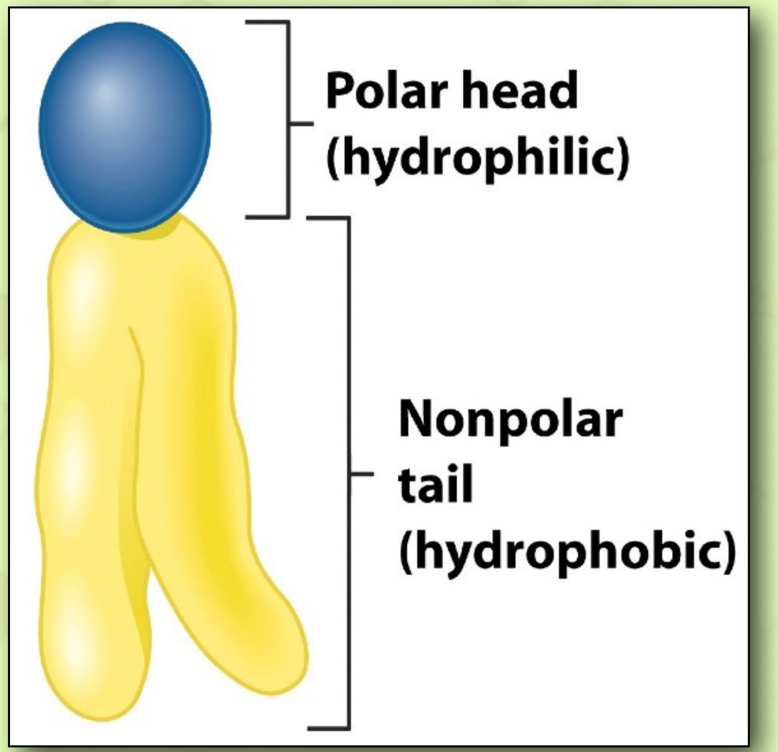
Other Biological Molecules

- Lipids are another important class of biological molecule
  - **Lipids** are not grouped according to a common structure, but rather are grouped according to a **common physical property**.
  - They are non-polar molecules, which are insoluble in water.

Other Biological Molecules

- An important group of lipids are the phospholipids
  - Phospholipids are not polymers, but they do aggregate in the presence of water to form membranes.





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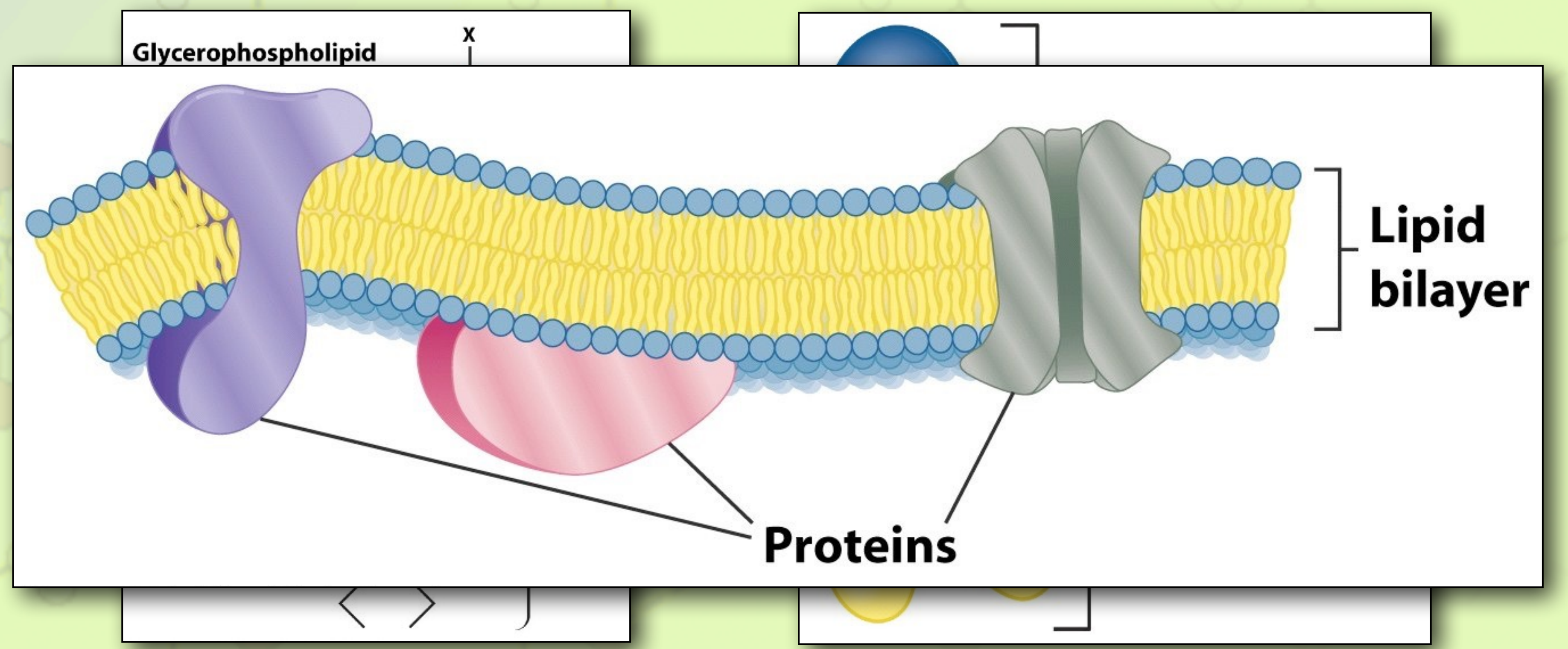

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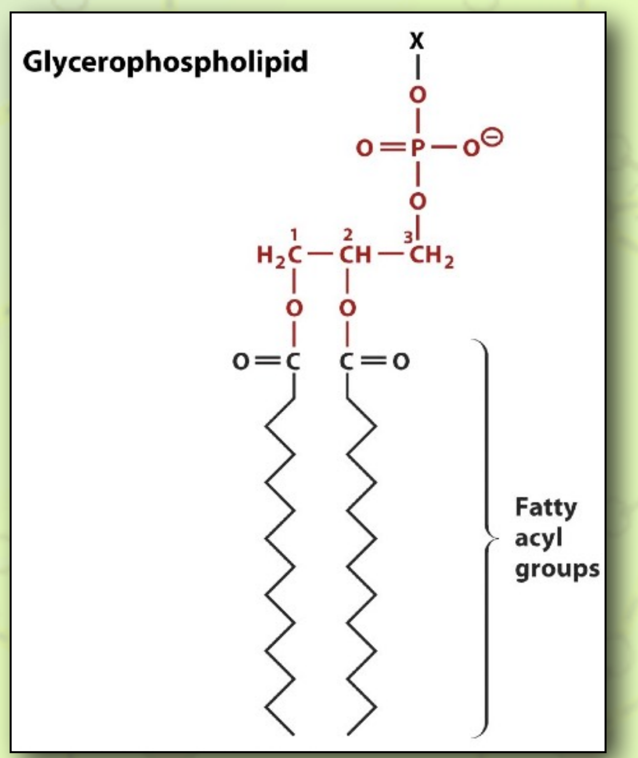

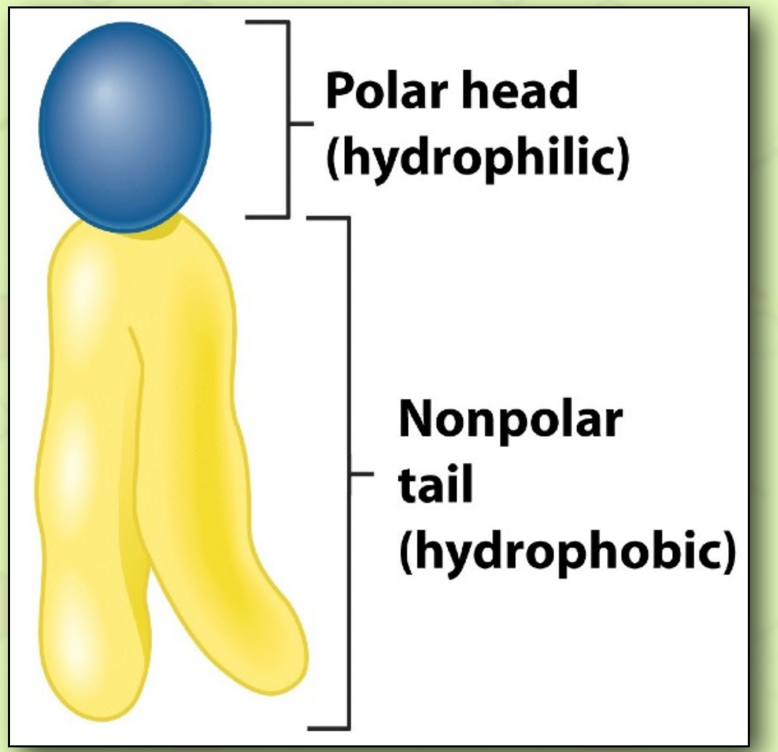

Energy

- The sun is the ultimate source of energy for nearly every organism on the earth.
  - **Photosynthesis** is the process by which some organisms are able to utilize the light energy from the sun to synthesize organic molecules.
  - Other organisms can then extract the energy from theses molecule to meet their own needs.

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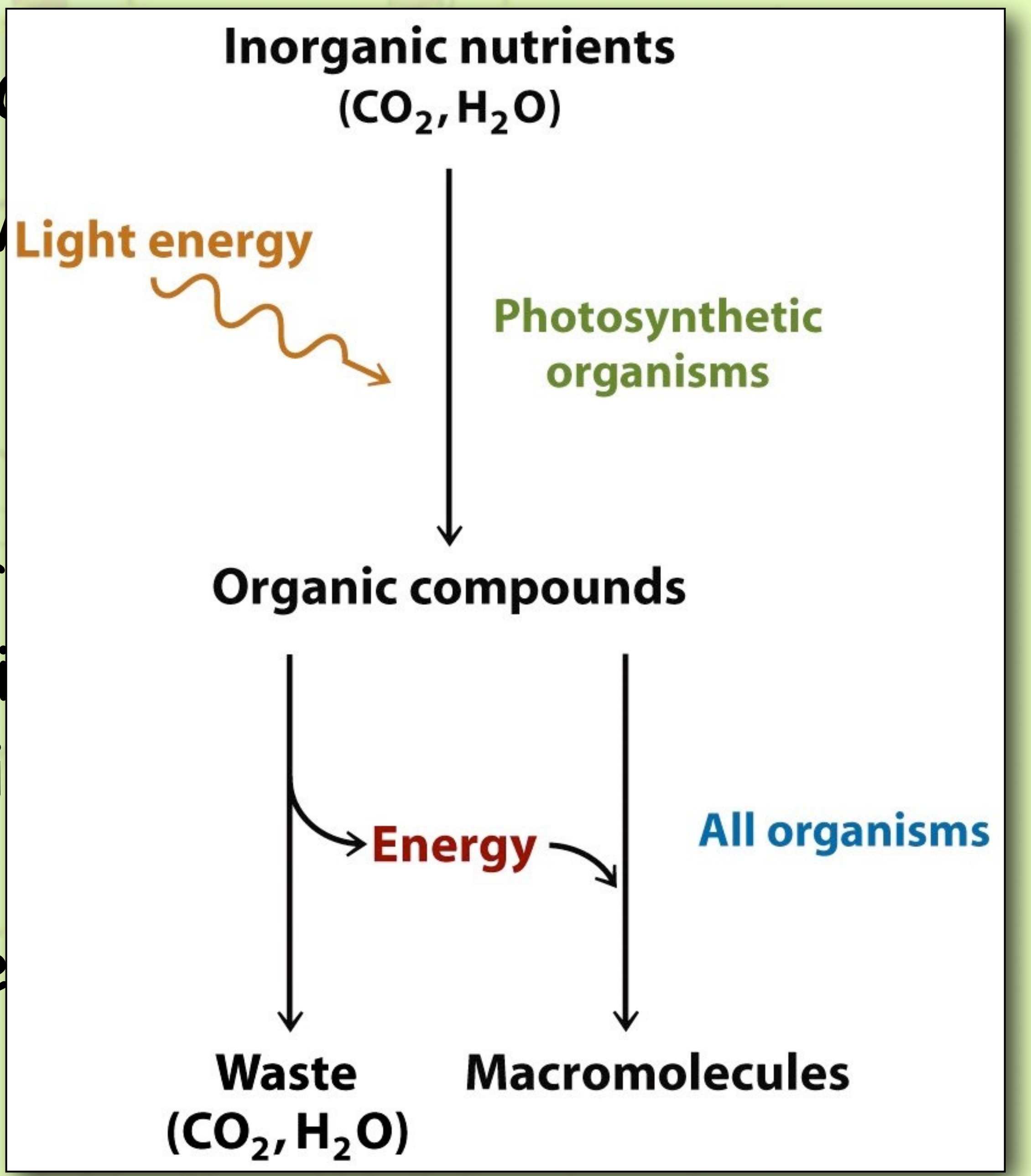

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Energy

- The sum total of all of the reactions that take place in a living cell is called metabolism.
  - **Catabolism** is the subset of metabolism that is involved in breaking down organic molecules to extract chemical energy.
  - **Anabolism** is the subset of metabolism that makes new molecules using the energy obtained from catabolism.

Energy

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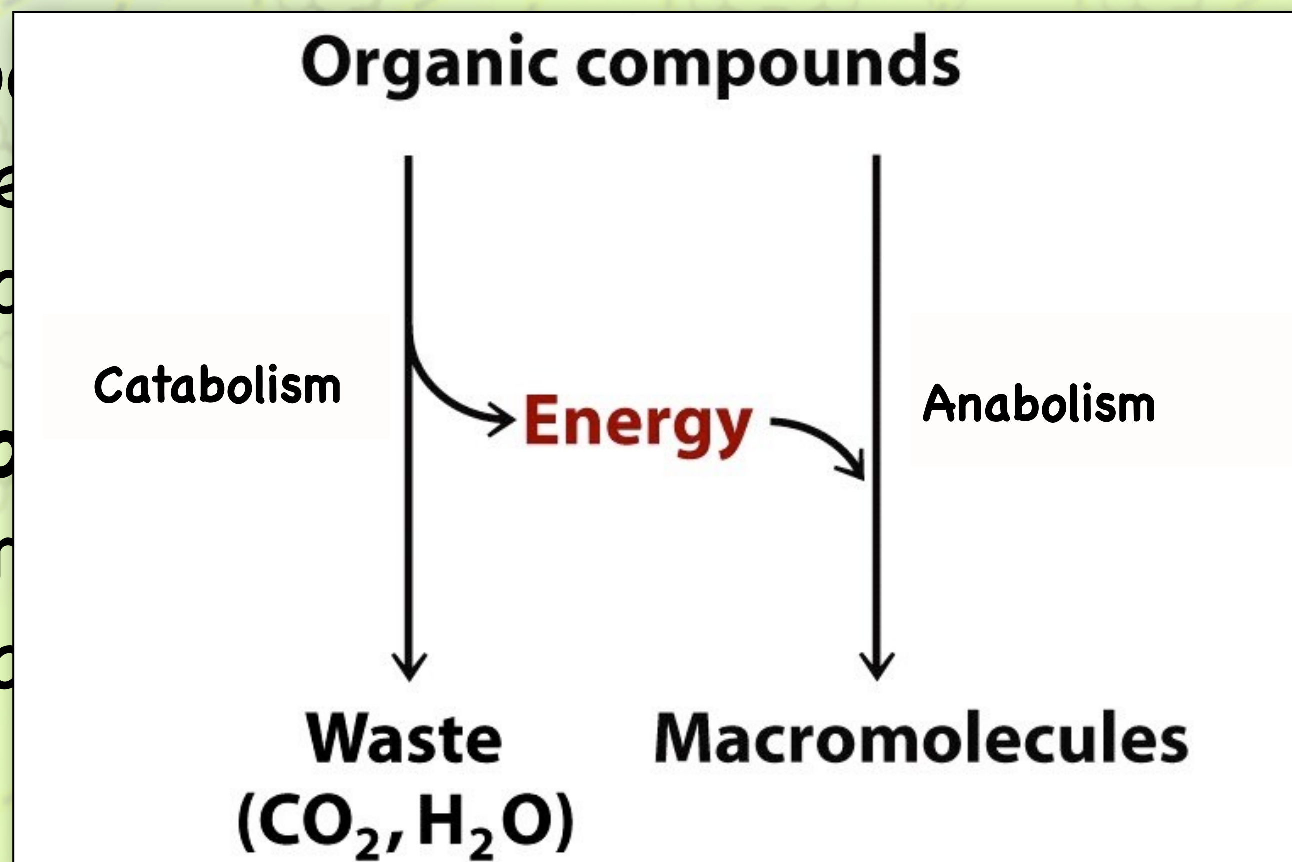
  - **Catab**… that is involve… cules to extrac…
  - **Anabo**… that makes new m… ed from catabo…



Energy

- **Thermodynamics vs Kinetics**
  - **Thermodynamics** is used to assess if a system is at equilibrium, and if not, which direction it needs to move to reach equilibrium.
  - **Kinetics** tells us how fast a system that is not at equilibrium will approach equilibrium

Energy

- Reaction Rates
  - For chemical reactions, the speed, or rate of a reaction is dependent on the relative concentrations of the reactants and the products of the reaction.
  - Enzymes, as catalysts, can speed up the rate of a reaction.
  - All reactions are striving to reach equilibrium

$$aA + bB \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} cC + dD$$

$$\frac{k_1}{k_{-1}} = \frac{[C]^c [D]^d}{[A]^a [B]^b} = K_{eq}$$

Thermodynamics

- **Thermodynamic** can be used to tell us where an equilibrium is.
  - Thermodynamics is the study the transformations of heat, work and energy.
  - There are different ways to measure energy, the one that will be of most useful to us is the **Gibb's free energy (G).**

Thermodynamics

- All molecules have free energy
  - For molecules in solution, the free energy is influenced by composition, temperature and concentration.
  - The change in the free energy for a reaction, ΔG, is the difference between the sum of the free energies of the products and reactants in a reaction.

$$\Delta G = \left(G_C + G_D\right) - \left(G_A + G_B\right)$$

(products) (reactants)

Thermodynamics

- Under the conditions for most reactions that take place in a cell, the ΔG has two components
  - Δ**H**, the change in **enthalpy** or heat content
  - Δ**S**, the change in the **entropy**, or order of the system.

$$\Delta G = \Delta H - T\Delta S$$

where T is temperature, and is constant

Thermodynamics

- If the pressure is also constant, ΔG can be used to tell us which way a reaction needs to proceed order to reach equilibrium.
  - When $\Delta G < 0$ (free energy is released)
  - When $\Delta G > 0$ (free energy is absorbed)
  - When $\Delta G = 0$

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    $$A + B \longleftarrow C + D$$

  - When $\Delta G = 0$

    $$A + B \rightleftharpoons C + D$$

Thermodynamics

- The actual free energies for the reactants and products in a reaction are not knowable.
  - The free energies, however, do depend in a predictable way on the concentrations of the reactants and products.
  - Instead, free energies are determined relative to an arbitrary **standard state**.
  - The free energy of the standard state is called **standard state free energy ($G°$)**.

Thermodynamics

- The free energies at states other than the standard state varies with concentration in a predictable way.

$$aA + bB \rightleftharpoons cC + dD$$

$$\Delta G = \Delta G^{0'} + RT \ln\left(\frac{[C]^c [D]^d}{[A]^a [B]^b}\right)$$

Thermodynamics

- For solutions, the standard state is defined as [A] = [B] = [C] = [D] = 1M.

$$\Delta G = \Delta G^{0'} + RT\ln\left(\frac{[C]^c[D]^d}{[A]^a[B]^b}\right)$$

At the standard state:

$$\Delta G = \Delta G^{0'} + RT\ln\left(\frac{(1\text{M})(1\text{M})}{(1\text{M})(1\text{M})}\right)$$

$$\Delta G = \Delta G^{0'} + RT\ln(1)$$

$$\Delta G = \Delta G^{0'}$$

Energy

- The standard free energy change can be determined from the equilibrium concentrations of the reactants and products in a reaction.

$$\text{when } \Delta G = 0 \text{ (at equlilibrium)}$$

$$\Delta G^{\circ}{}' = -RT \ln\left(\frac{[\mathrm{C}]^c[\mathrm{D}]^d}{[\mathrm{A}]^a[\mathrm{B}]^b}\right)_{eq}$$

$$\Delta G^{\circ}{}' = -RT \ln\left(K_{eq}\right)$$

The Cell

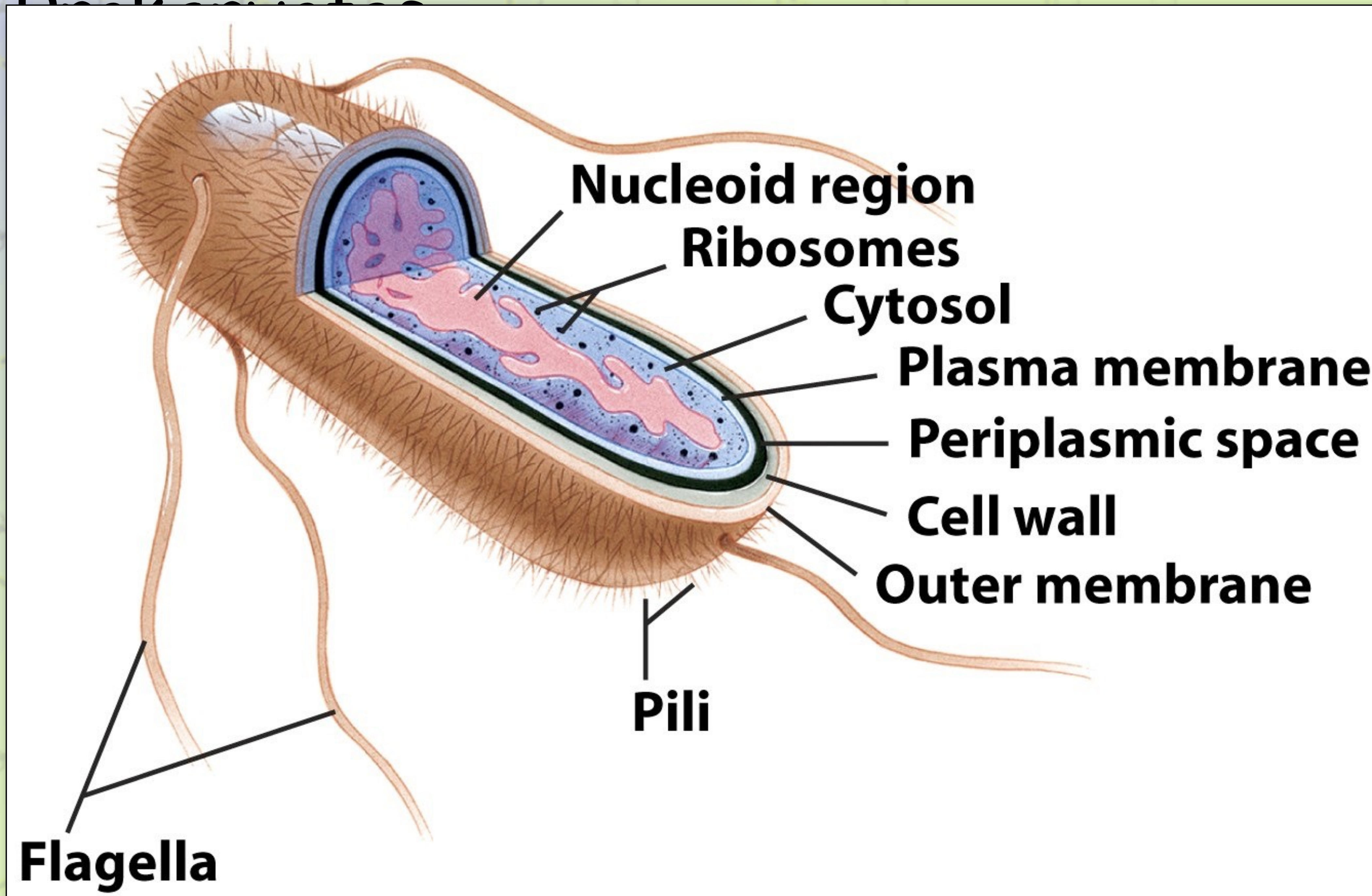
- The fundamental unit for living systems is the cell.
  - There a two basic cell types, **prokaryotic** and **eukaryotic**.

The Cell

- Prokaryotes
  - These were the first to evolve some 3.6 billion years ago.
  - The have simpler cell structure.
  - These organisms are always unicellular
  - They have an cell or plasma membrane, but no internal membrane structures
  - They typically have a single, circular chromosome
  - They have pili for attaching to surfaces and flagella for motility

The Cell

- Prokaryotes



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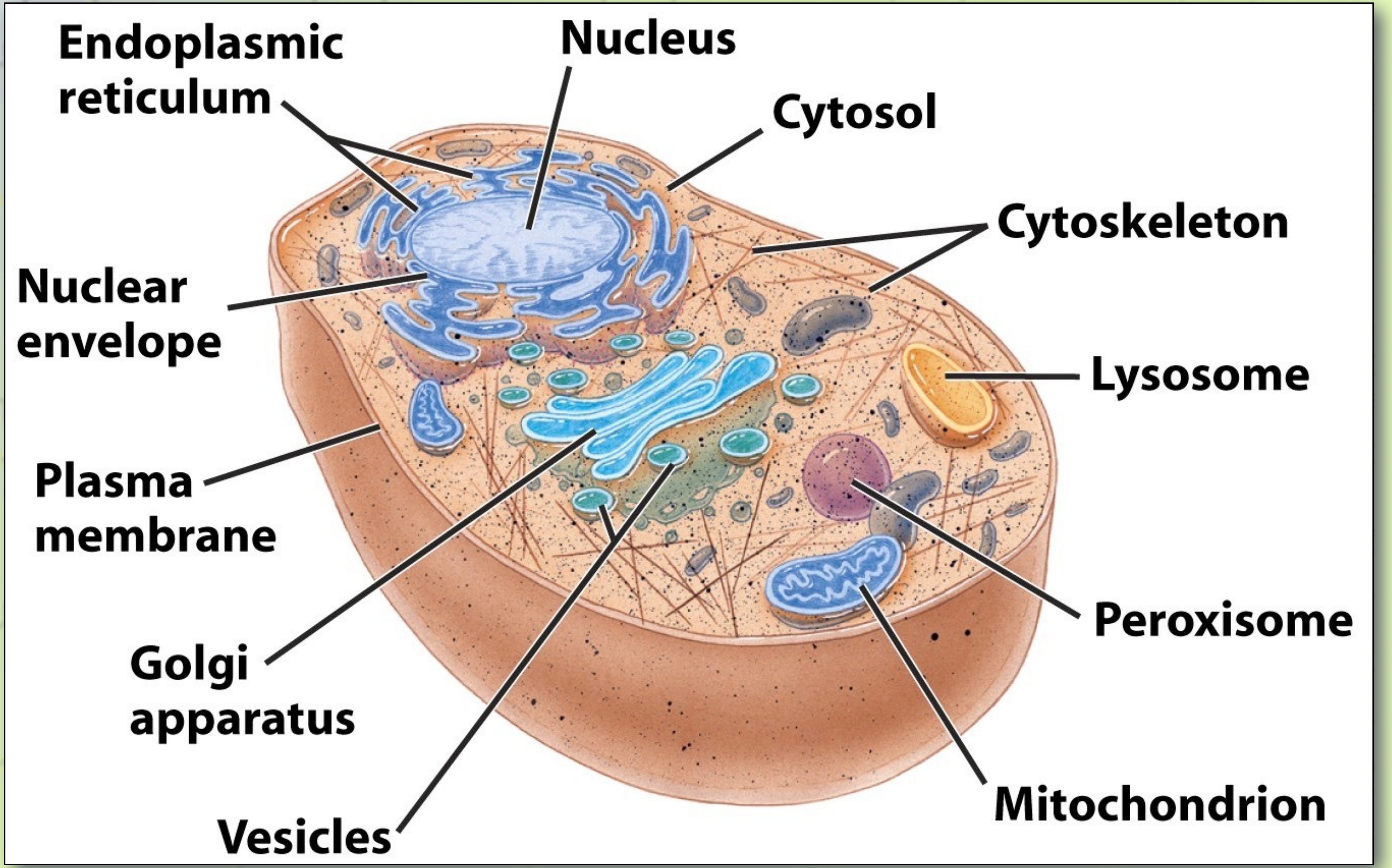
The Cell

- Eukaryotes have a much more complex cell.
  - The evolved around 2 billion years ago.
  - These organisms can be multicellular, starting 1 billion years ago.
  - These cells have volumes that are about 1000 times larger than a prokaryotic cell.
  - In addition to a plasma membrane, they have membrane enclosed structures called **organelles** within the cell, which have dedicated functions

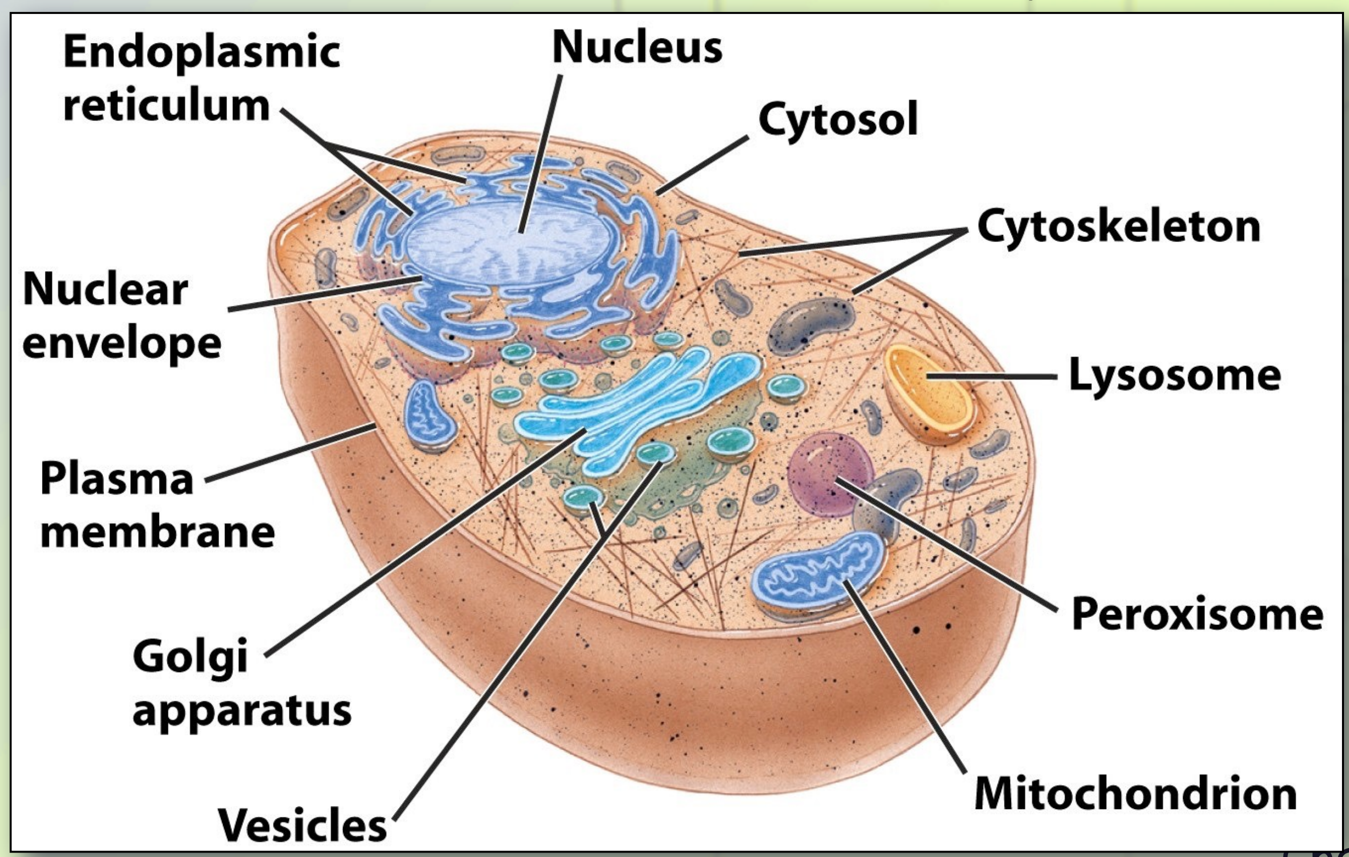
The Cell

- Eukaryotes have a much more complex cell.



The Cell

- Some of the organelles include
  - The **endoplasmic reticulum (ER)**
  - The **golgi apparatus**
  - The **mitochondria**
  - The **chloroplasts**



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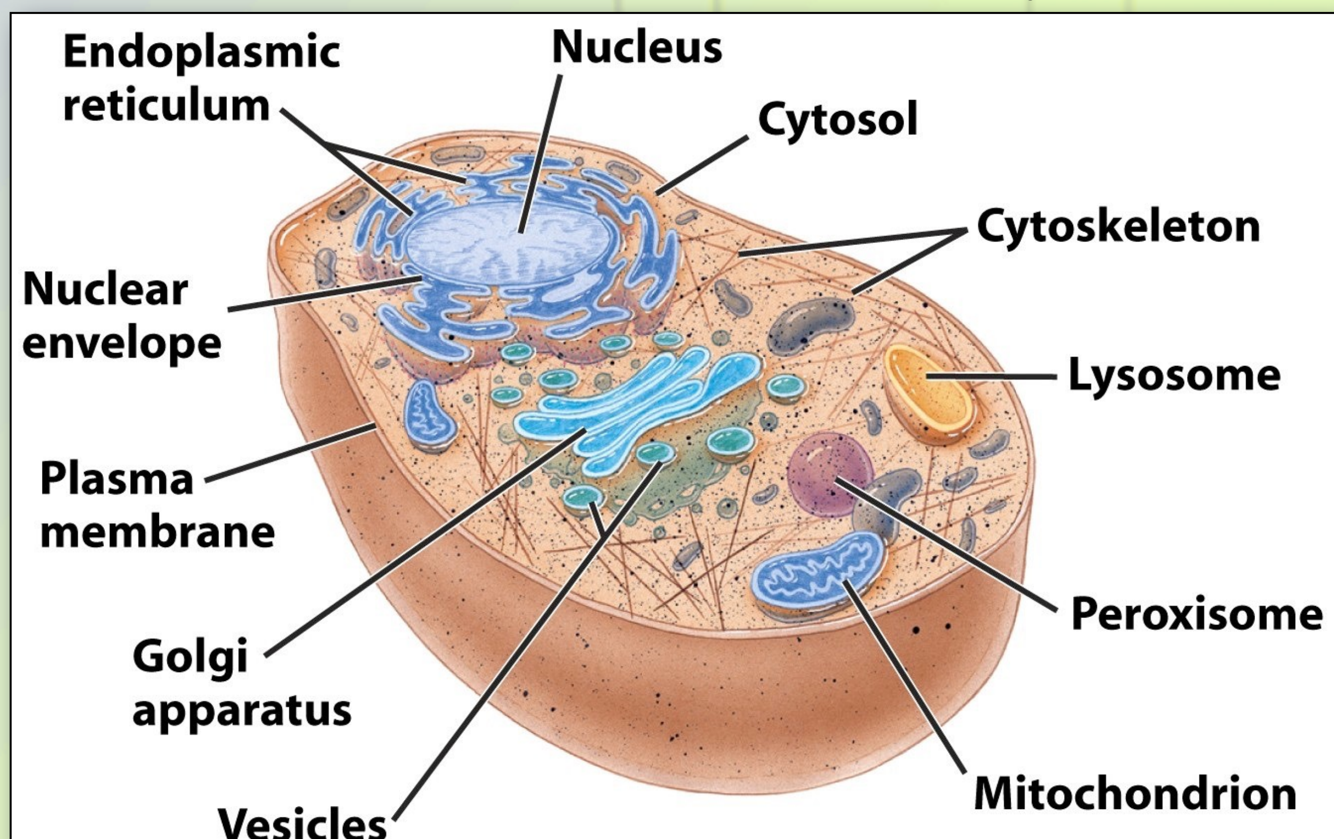

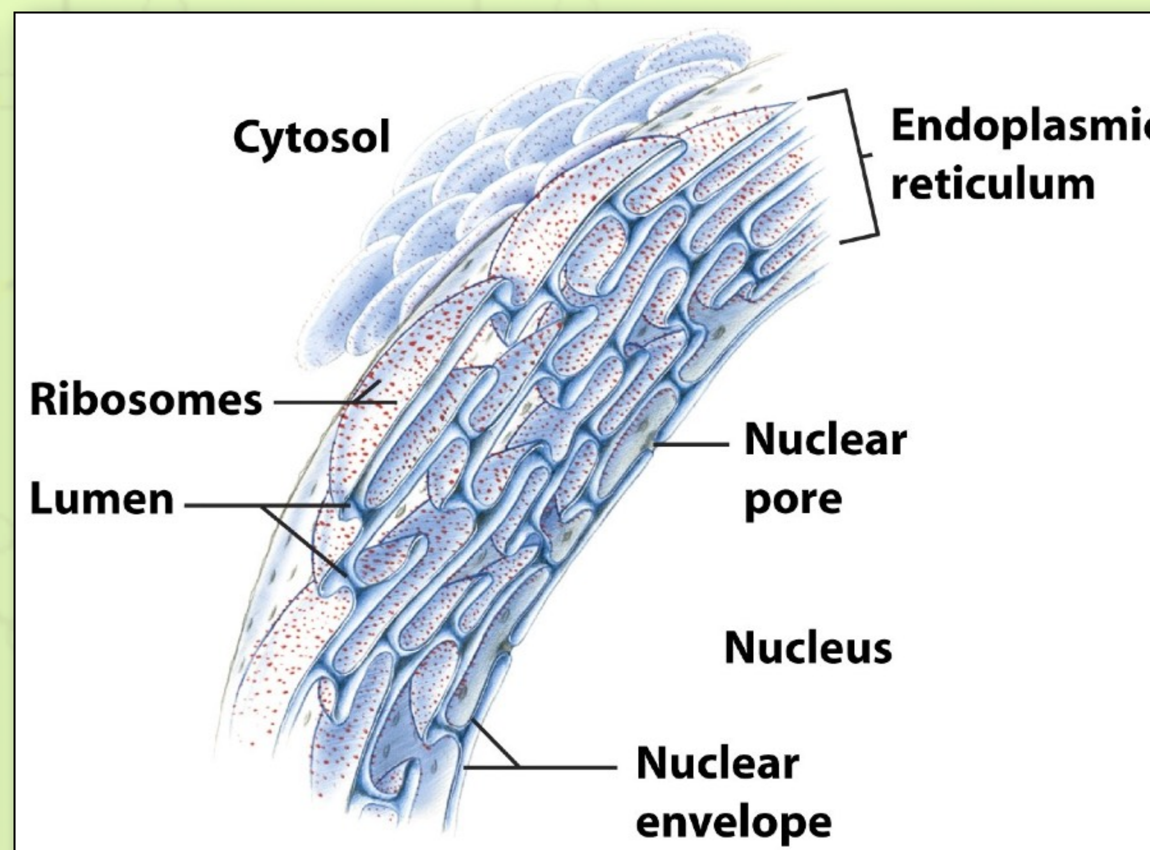

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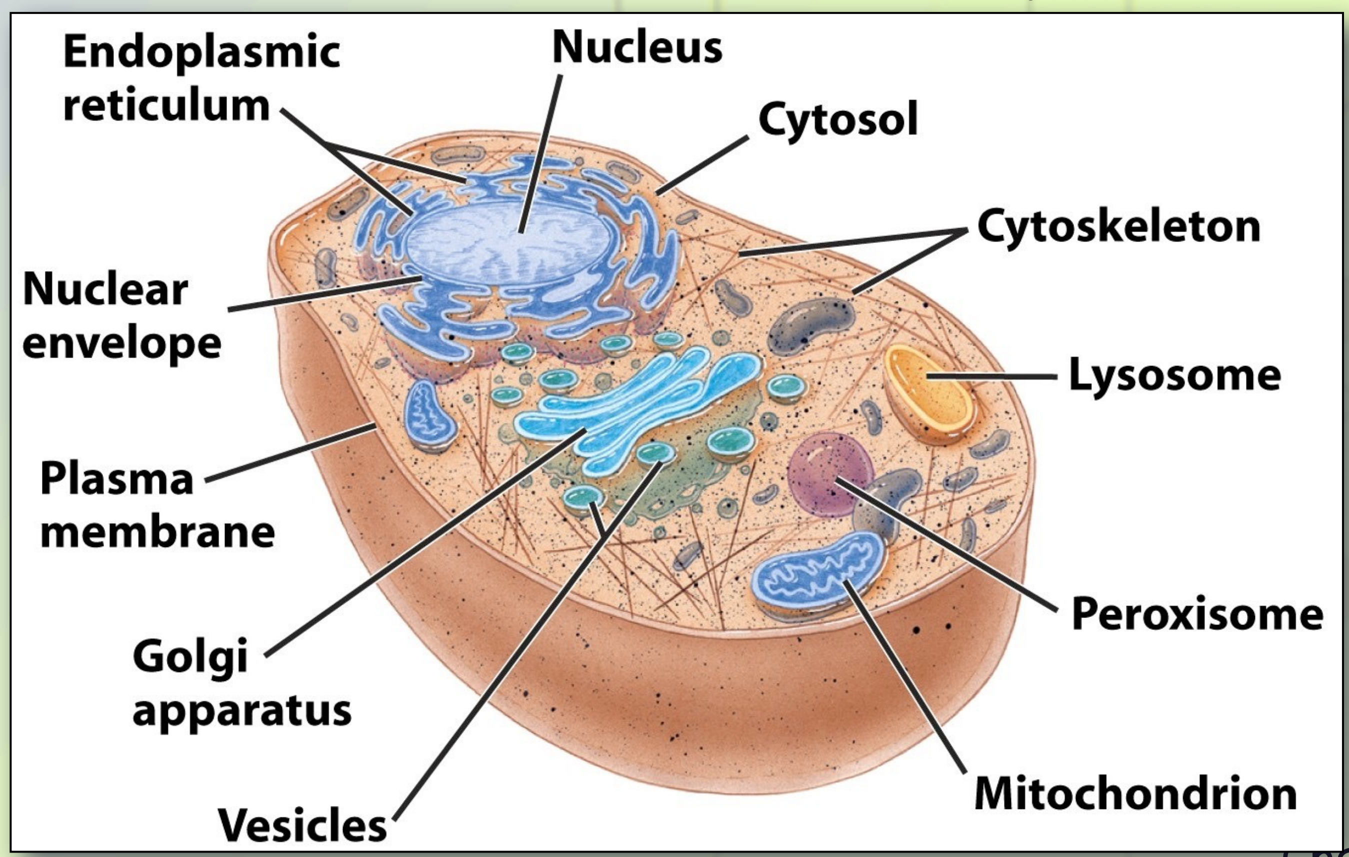

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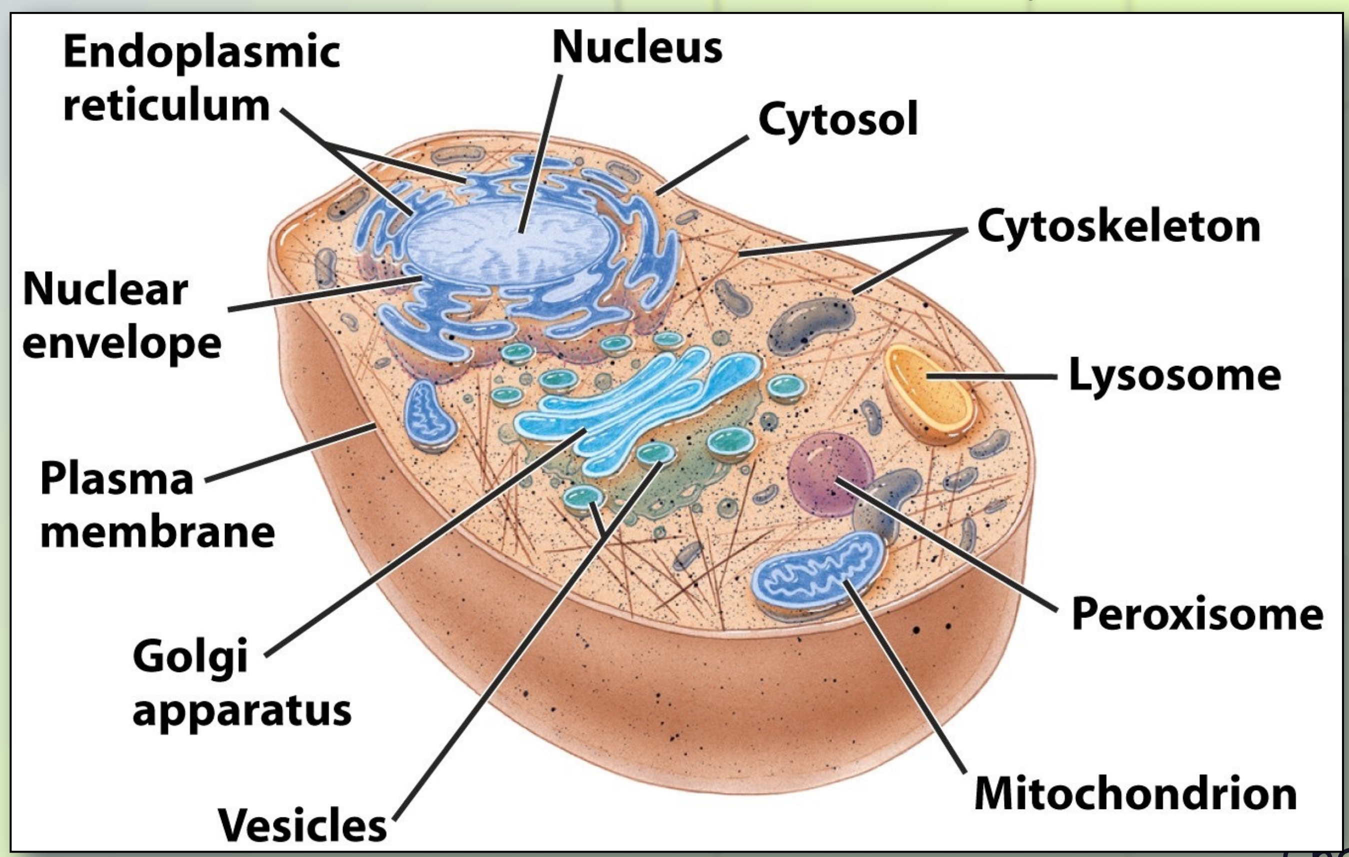

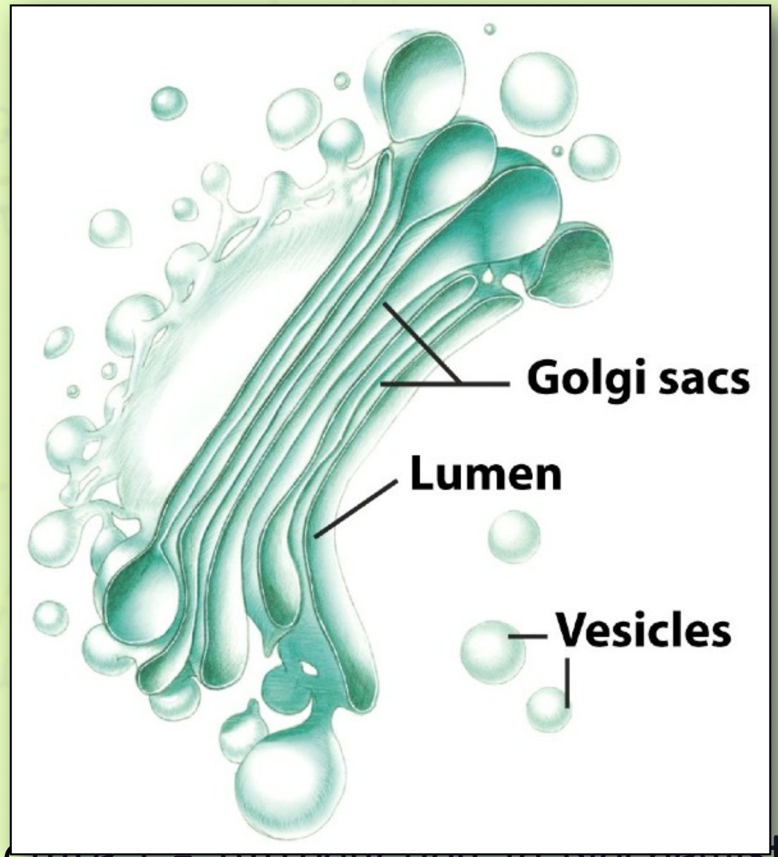

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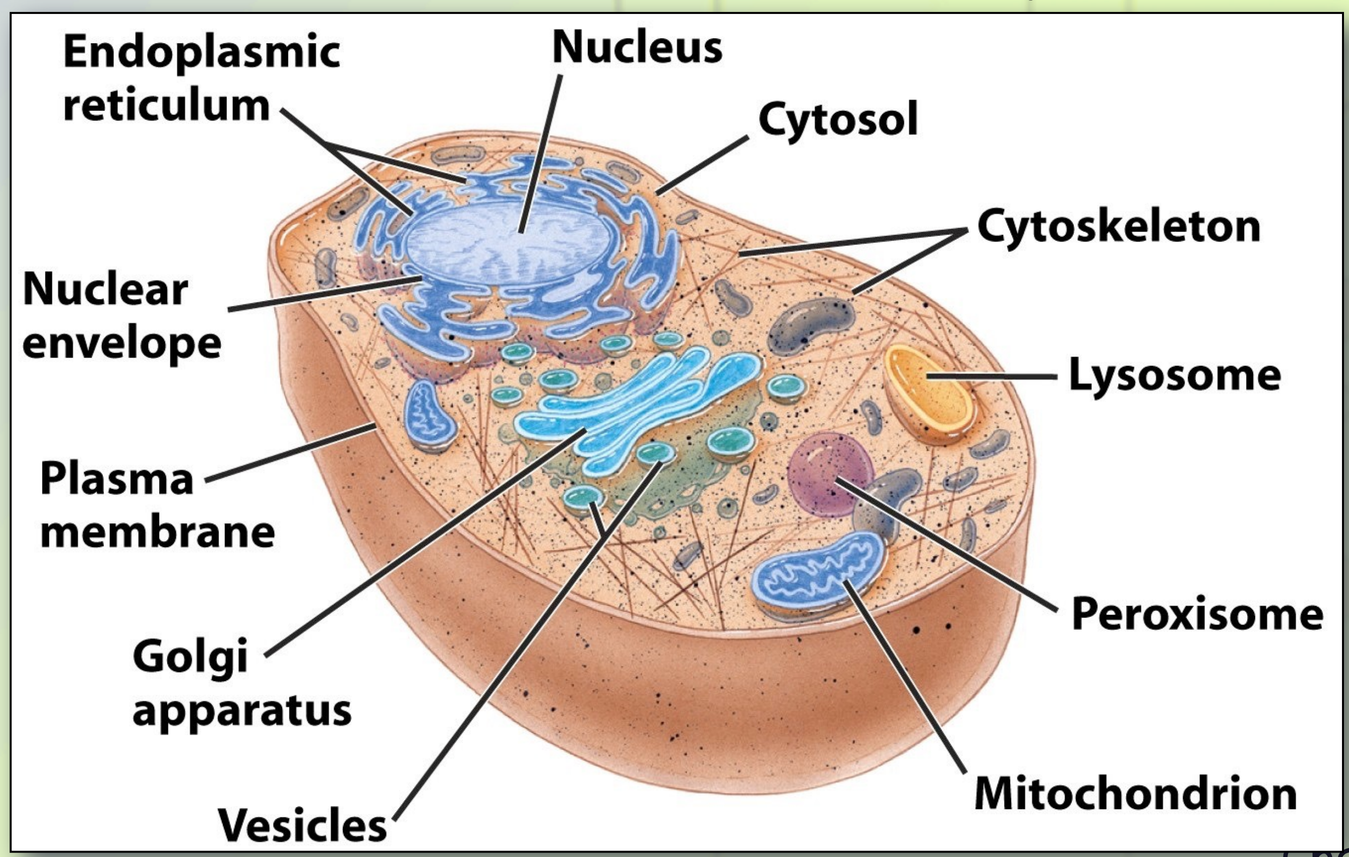

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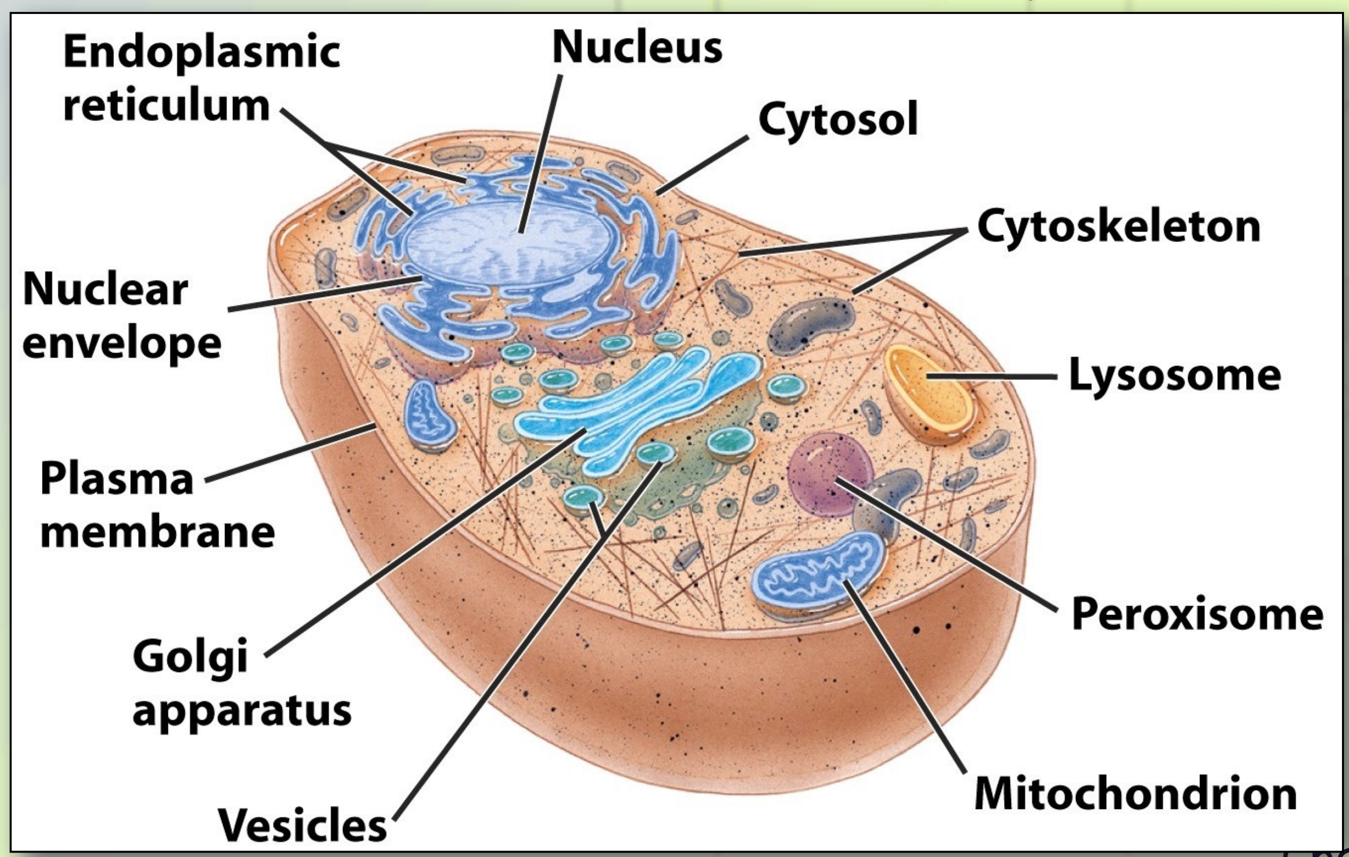

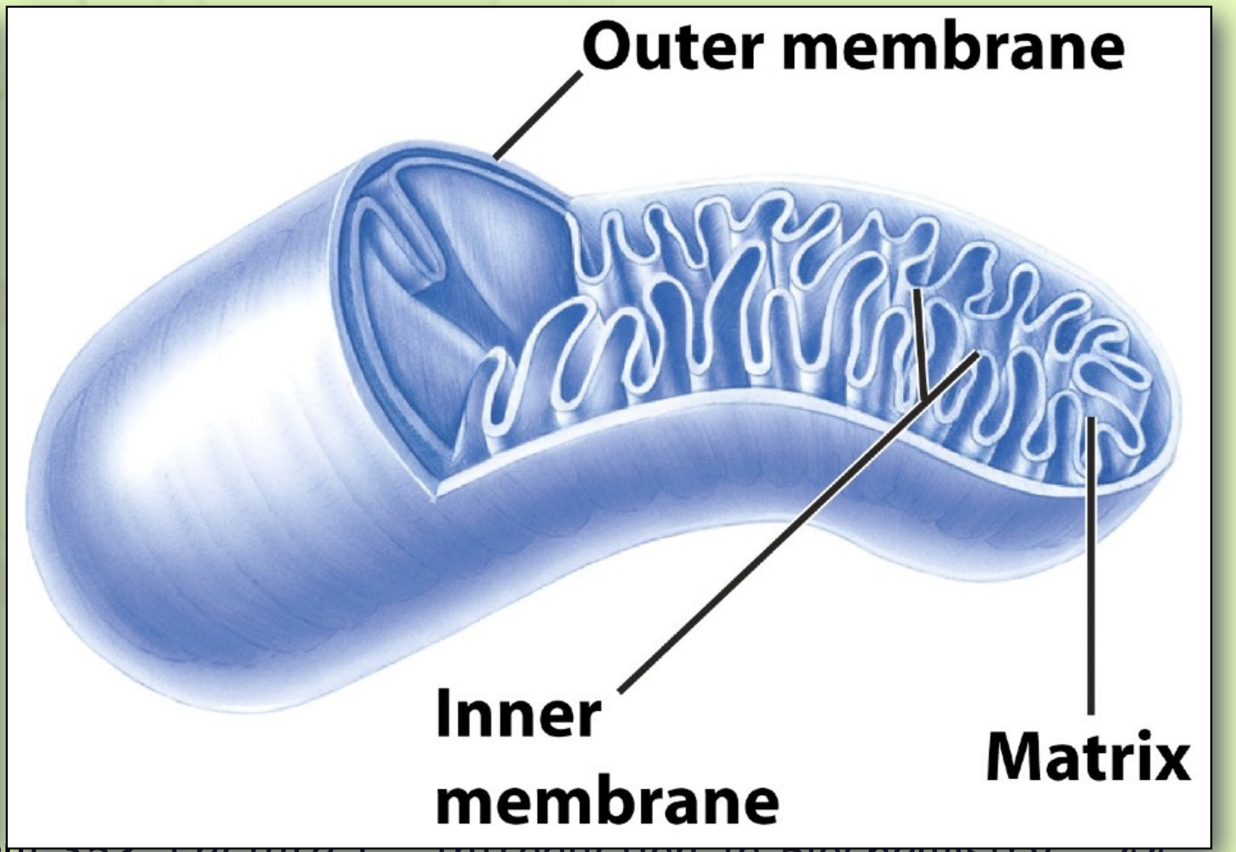

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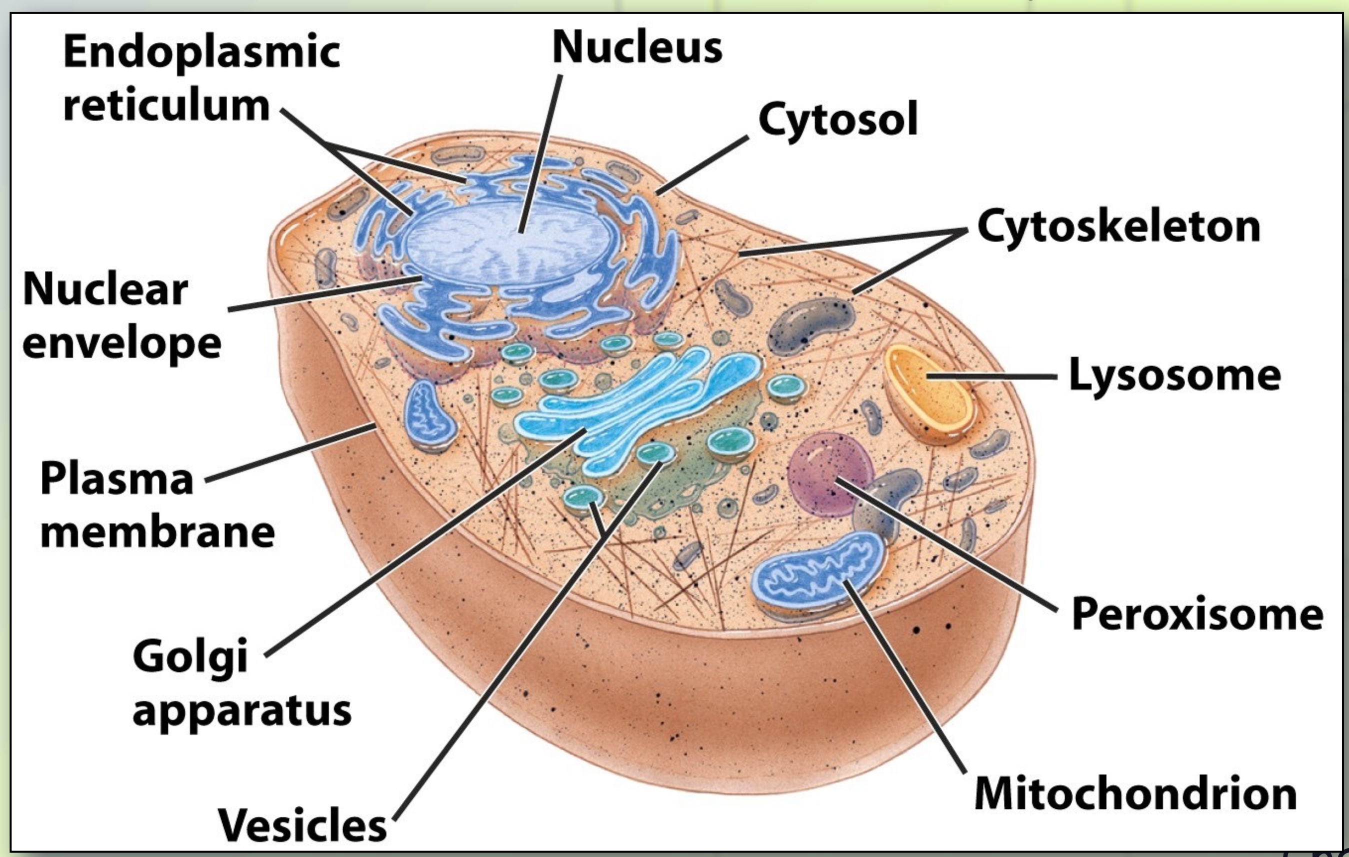

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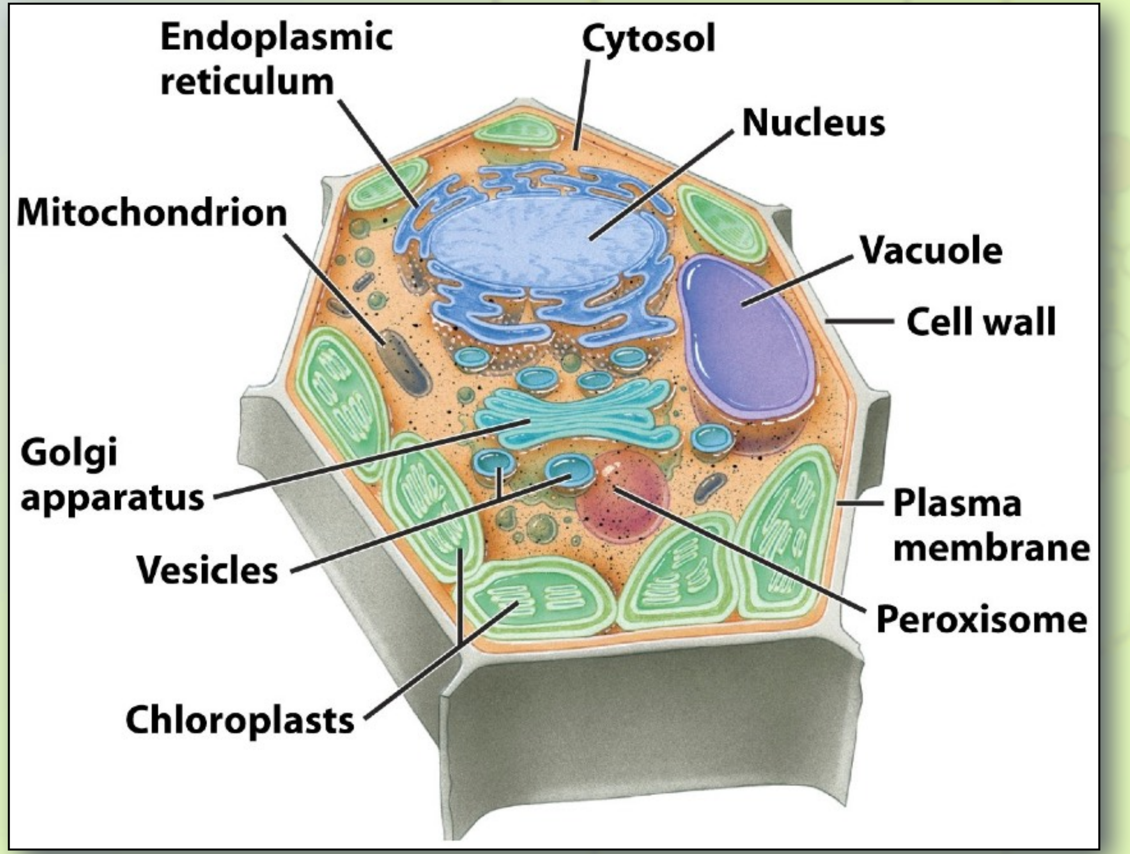

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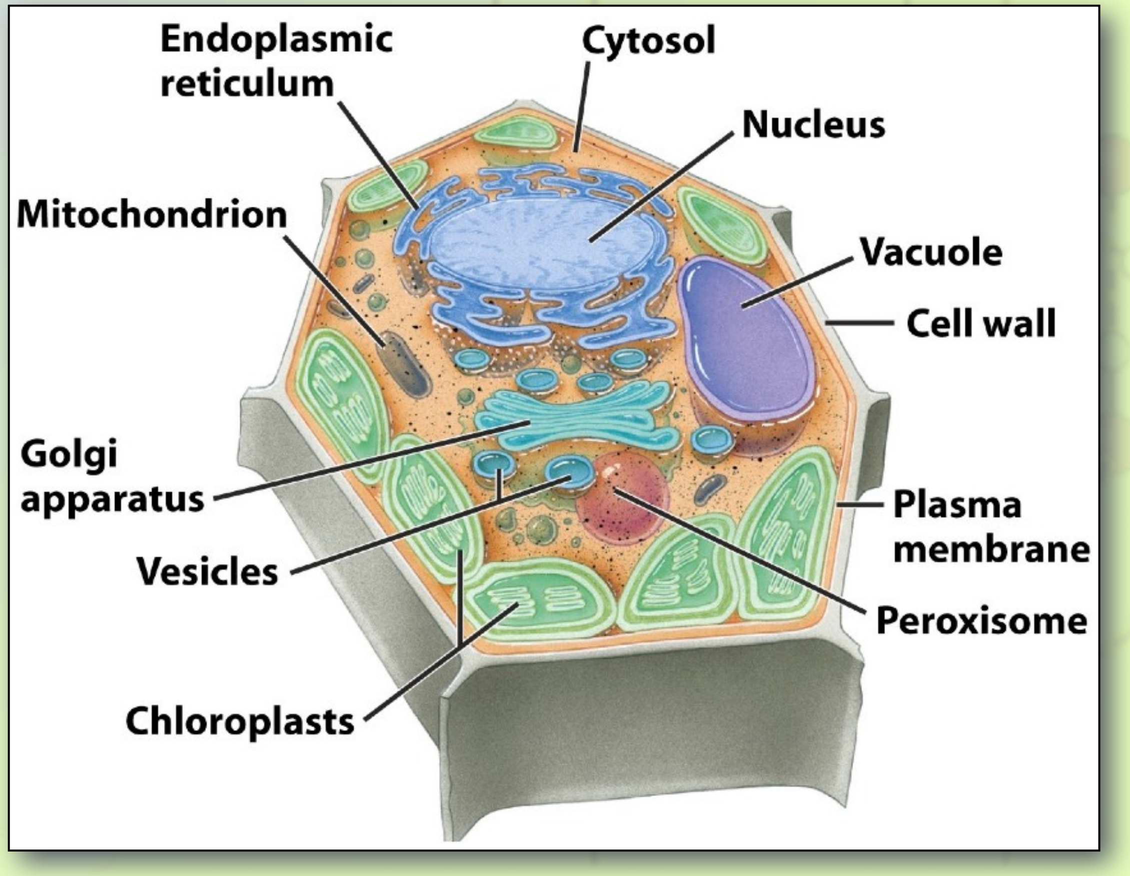
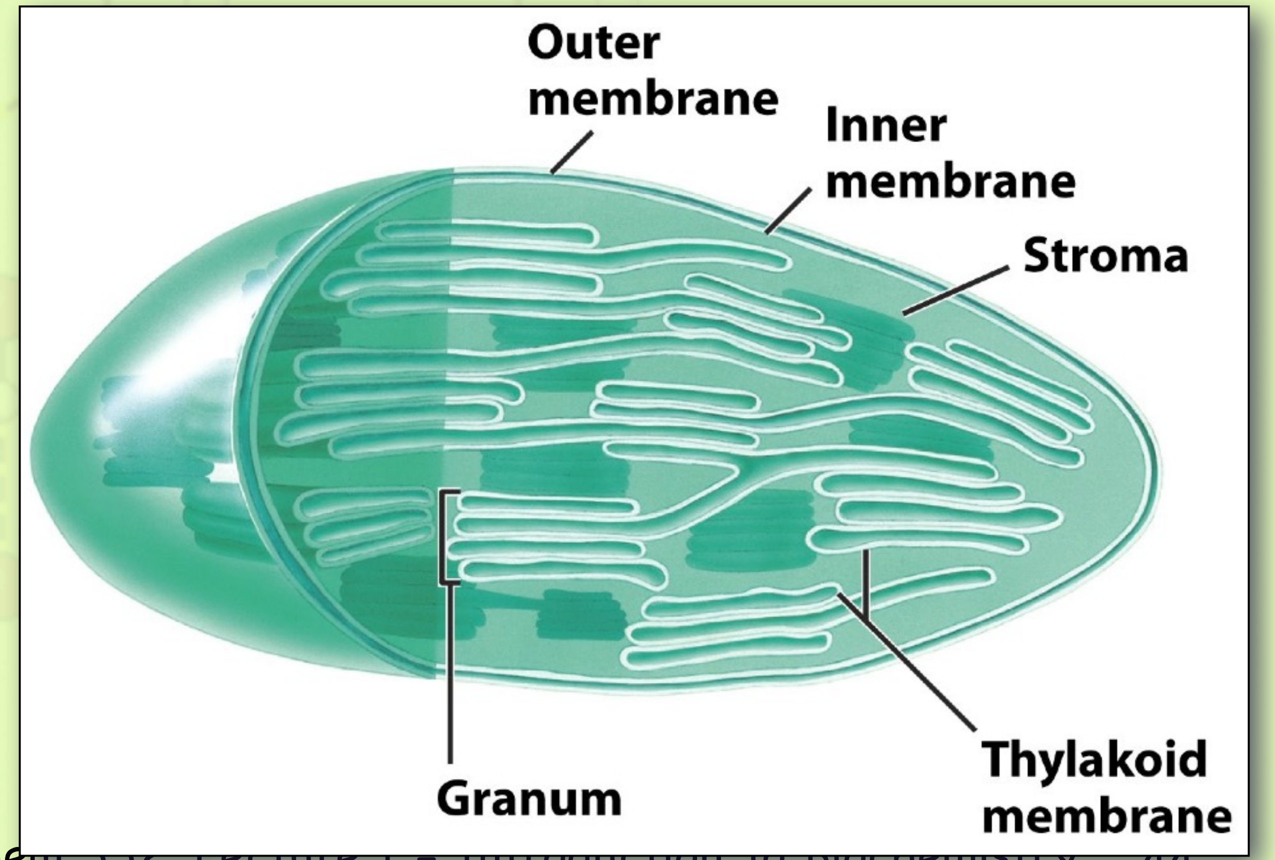




Science Podcast on Cyanobacteria

- Science Magazine website (www.sciencemag.org)
- Podcast on Cyanobacteria
  - Provides an introduction to many of the terms we will be using this semester.

Prokaryotes and Eukaryotes

Body's Hardworking Microbes Get Some Overdue Respect

HUMANS HAVE BEEN DOING BATTLE WITH bacteria since the 1800s, thwarting disease with antibiotics, vaccines, and good hygiene with mixed success. But in 2000, Nobel laureate Joshua Lederberg called for an end to the "We good; they evil" thinking that has fueled our war against microbes. "We should think of each host and its parasites as a superorganism with the respective genomes yoked into a chimera of sorts," he wrote in *Science* in 2000.

His comments were prescient. This past decade has seen a shift in how we see the microbes and viruses in and on our bodies. There is increasing acceptance that they are us, and for good reason. Nine in 10 of the cells in the body are microbial. In the gut alone, as many as 1000 species bring to the body 100 times as many genes as our own DNA carries. A few microbes make us sick, but most are commensal and just call the human body home. Collectively, they are

This appreciation has dawned gradually, as part of a growing recognition of the key role microbes play in the world. Microbiologists sequencing DNA from soil, seawater, and other environments have discovered vast numbers of previously undetected species. Other genomics research has brought to light incredible intimacies between microbes and their hosts—such as a bacterium called *Buchnera* and the aphids inside which it lives. A study in 2000 found that each organism has what the other lacks, creating a metabolic interdependency.

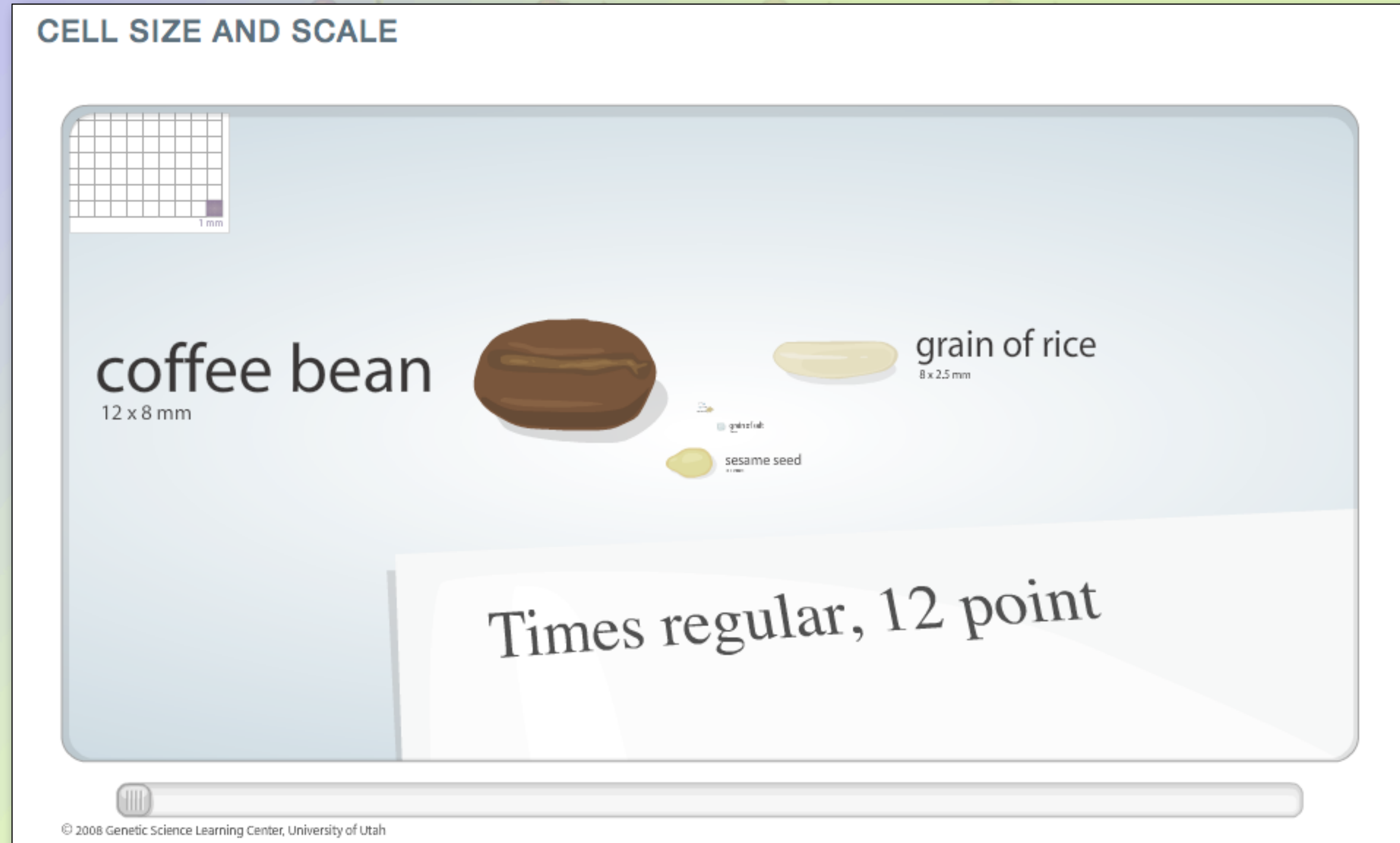
One of the first inklings that microbiologists were missing out on the body's microbial world came in 1999, when David Relman of Stanford University in Palo Alto, California, and colleagues found that previous studies of bacteria cultured from human gums had seriously undercounted the diversity there. Turning to samples taken from the gut and from stools, the researchers iden-

sequenced 500 relevant microbial genomes out of a planned 3000.

Some of these microbes may play important roles in metabolic processes. In 2004, a team led by Jeffrey Gordon of Washington University School of Medicine in St. Louis, Missouri, found that germ-free mice gained weight after they were supplied with gut bacteria—evidence that these bacteria helped the body harvest more energy from digested foods. Later studies showed that both obese mice and obese people harbored fewer Bacteroidetes bacteria than their normal-weight counterparts.

The microbiome is also proving critical in many aspects of health. The immune system needs it to develop properly. What's more, to protect themselves inside the body, commensal bacteria can interact with immune cell receptors or even induce the production of certain immune system cells. One abundant gut bacterium, *Faecalibacterium prausnitzii*, proved to have anti-inflammatory properties, and its abundance seems to help protect against the recurrence of Crohn's disease. Likewise, Sarkis Mazmanian of the California Institute of Technology in Pasadena

Putting Things in Perspective



The Cell

Biochemistry and Molecular Biology Education
Vol. 37, No. 6, pp. 325–332, 2009

Miniseries: Illustrating the Machinery of Life

Escherichia coli*

Received for publication, August 21, 2009, and in revised form, September 15, 2009

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From the Department of Molecular Biology, The Scripps Research Institute, La Jolla, California

Diverse biological data may be used to create illustrations of molecules in their cellular context. I describe the scientific results that support a recent textbook illustration of an *Escherichia coli* cell. The image magnifies a portion of the bacterium at one million times, showing the location and form of individual macromolecules. Results from biochemistry, electron microscopy, and X-ray crystallography were used to create the image.

Keywords: Cellular biology, molecular biology, molecular visualization, textbook, diagrams.

"A clear picture of the interior of a living cell that shows the average distribution of molecules at the proper scale, the proper concentration and with no missing parts, seems to me to be central to the understanding of the workings of life." This is how I began my 1991 article that presented several illustrations of *Escherichia coli* [1]. At the time, there was just enough information to create a convincing picture of the environment inside liv- highly dependent on the environmental conditions of the cell. I settled on a hybrid approach. I took the concentrations of macromolecules from the same sources that I used in the 1991 article. This includes the overall value of 70% water for the cell, as well as the number of proteins, RNA, lipids, and other molecules. I also used the same values for the concentrations for the major players in protein synthesis, transport, and energy production. I

Molecular Resources

- Marvin
  - A tool for drawing and analyzing small molecules
- The Protein Data Bank (PDB)
  - A database where you can find and observe the structures of biological macromolecules and aggregates of these molecules.
  - Not limited to proteins

Next up

- Lecture 2 - Water
  - Water's physical properties
    - Boiling point and Melting point
    - Intermolecular interactions
  - Water's chemical properties
    - pH and acids & bases

- Reading
  - Chapter 2 of Moran et al.