Life Science 3

Introduction of Molecular Biology

Instructor: April Pyle, Ph.D. (1st half) and Randy Wall, Ph.D. (2nd half)
Textbook: Watson 7th edition- Molecular Biology of the Gene

Administration issues please see: Life Sciences Core Curriculum Office
Hershey Hall Room 222
Office Hours: Monday-Friday 9-12PM & 1-4PM
Email: lscore@lifesci.ucla.edu

Syllabus

LIFE SCIENCES 3 (LS 3.2)
Introduction to Molecular Biology, Spring 2016
Tue & Thu 3:30-4:45pm, La Kretz 110
Dr. April Pyle & Dr. Randolph Wall

Lecture	Date	Topics	Reading
Pyle	March 29	Molecular Components	51-75
Pyle	April 31	Protein Structure	121-144
Pyle	April 5	Protein Function & Techniques	173-189
Pyle	April 7	DNA Structure	77-104
Pyle	April 12	DNA Replication	257-311
Pyle	April 14	RNA Structure	107-118
Pyle	April 19	Transcription	429-464
Pyle	April 21	Regulation of Prokaryotic Transcription	615-653
Pyle	April 26	Regulation of Eukaryotic Transcription	657-698
Pyle	April 28	Review for Midterm Exam	
Pyle	May 2	Midterm Exam (5-7:50pm)	
Wall	May 3	Eukaryotic Genes & mRNA Processing	457-462, 467-476, 480-487, 491- 493, 503-506
Wall	May 5	Translation I: Genetic Code & tRNA	513-519, 573-583, 590
Wall	May 10	Translation II: Ribosomes & Protein synthesis	509-513, 519-549, 567-569
Wall	May 12	Viruses & the New Central Dogma	798-802
Wall	May 17	Restriction Enzymes & DNA Mapping	147-154
Wall	May 19	Recombinant DNA Cloning & PCR	154-159,
Wall	May 24	Screening Libraries & Microarrays	153, 169-173
Wall	May 26	Sequencing Genes & Genomes/the Transcriptome & RNA silencing	159-168, 199-208, 711-731
Wall	May 31	Comparative Genomics	769-773
Wall	June 2	Final Exam Review	
Wall	June 6	Final Exam (6:30-9:30pm)	

Text: Molecular Biology of the Gene (Seventh Edition), Cold Spring Harbor Press.
J. D. Watson, T.A. Baker, S. P. Bell, A. Gann, M. Levine, & R. Losick

Course Material

Lecture notes- powerpoint slides/course notes

Text book (Watson 7th edition)- only for additional reading

Audio/Video podcasts

https://ccle.ucla.edu/ (Course website)

Grading- 2 EXAMS

Pyle	May 2, 2016	5-7:50pm	Midterm Exam
Wall	Jun 6, 2016	6:30-9:30pm	Final Exam

Make-up Policy:
No make up examination will be given. If you are unable to take an examination due to illness or other emergency, you are responsible for contacting the Life Sciences Core Curriculum Office before the examination. You are required to have written verification from a physician regarding the illness or emergency.

Policies

- Exams will cover predominately lectures and textbook as a reference.
- Re-grade requests are accepted only with demonstrated error (rare). Requests must be submitted to Core office by Friday of week following exam with typed explanation of issue.
- Entire exam will be re-graded by TA.
- Exams will be left with the TA.
- No excuses for missing exam. No-Make-up exams-contact LS Core if emergency.

Office Hours and Class Help

Pyle Office Hours: Fri (10-12pm)
BSRB (Basic Science Replacement Bldg) 277A (office)

LS3 TA's: (see TA's for office hrs)

Life Sciences Core Curriculum Office
Hershey Hall Room 222
Office Hours: Monday-Friday 9-12PM & 1-4PM
Email: lscore@lifesci.ucla.edu

Assessment (not graded): Surveys via email and Concept Inventory (CI) exam will be given in discussion sections (1st and 10th week) to assess class learning in LS3. This is not a part of your grade but participation would be appreciated.

Lecture 1

Molecular Components

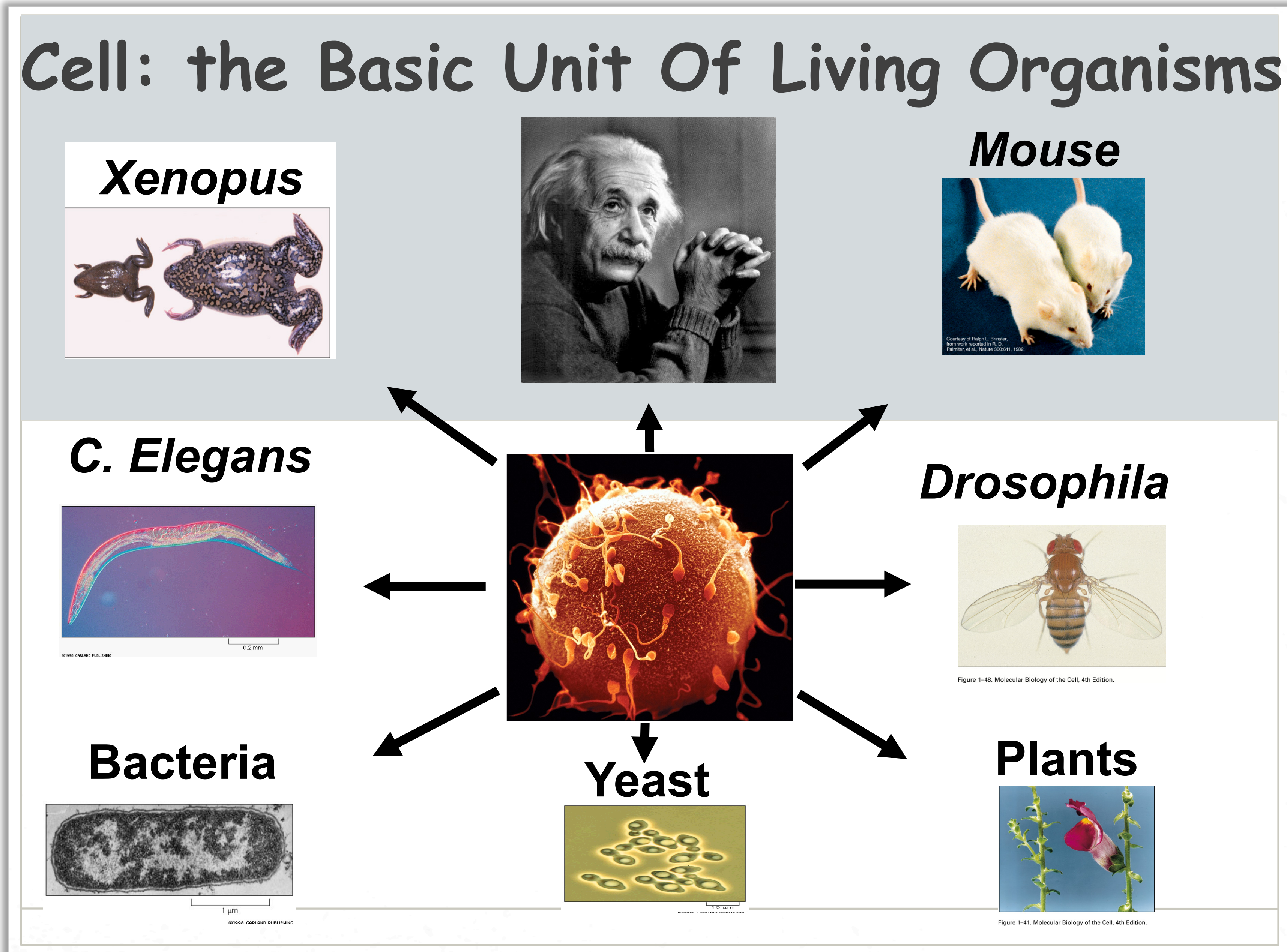
March 29, 2016

Pyle

Why study molecular biology?

Molecular biology seeks to understand the physical and chemical basis of life.

- Growth
- Division
- Specialization
- Movement
- Interactions


Cell: the Basic Unit Of Living Organisms
Xenopus
Mouse
Courtesy of Ralph L. Brinster, from work reported in R. D. Palmiter, et al., Nature 300:611, 1982.
C. Elegans
0.2 mm
Drosophila
Figure 1–48. Molecular Biology of the Cell, 4th Edition.
Bacteria
1 µm
Yeast
Plants
Figure 1–41. Molecular Biology of the Cell, 4th Edition.

Example Prokaryotic Cell Features in Bacteria

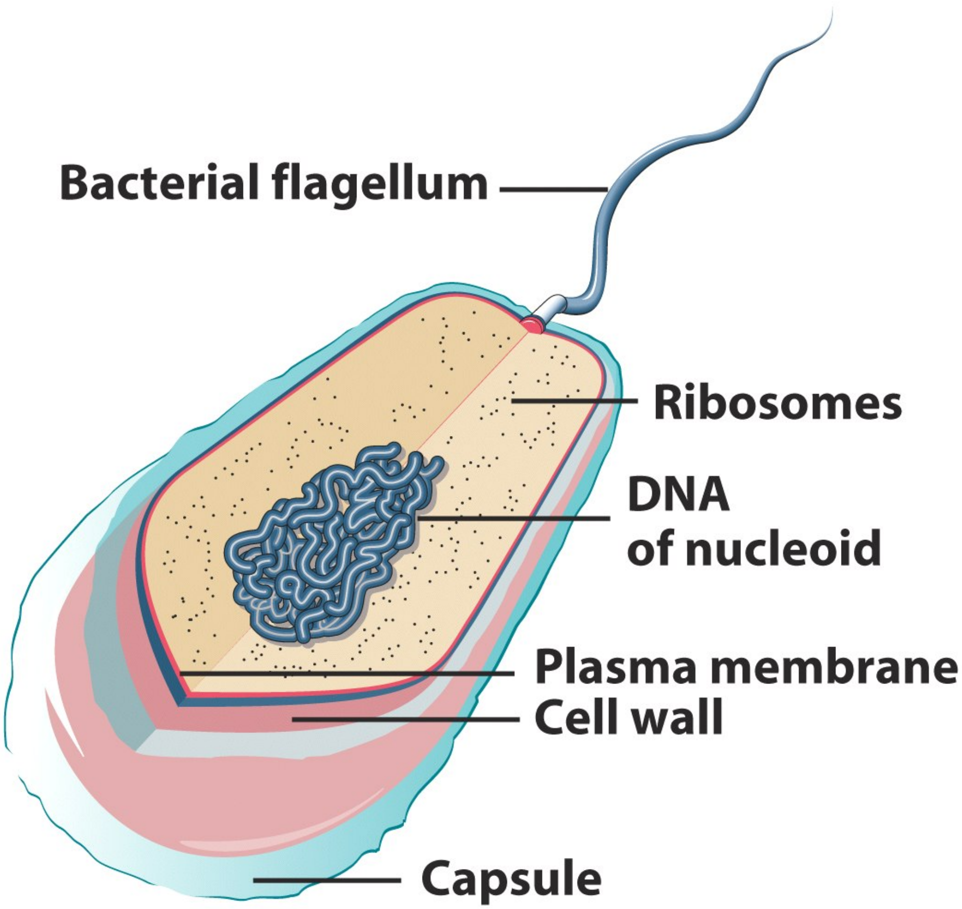


Figure 1-8a Cell and Molecular Biology, 5/e (© 2008 John Wiley & Sons)

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 and TCA 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)

Table 1-1 part 1 Cell and Molecular Biology, 5/e

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 fluid and particulate material by enclosure within plasma membrane vesicles (endocytosis and 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

Table 1-1 part 2 Cell and Molecular Biology, 5/e

Eukaryotic Key Features of Complexity

-Complex Nuclear Structure

-Chromosome compaction/ accessory proteins

-Complex membrane organelles

-Complex cytoskeletal components

-Increased Plasma membrane complexity and activity of protein Regulation (secretory, vesicles, Transport)

-Nobel Prize in Medicine awarded to Rothman, Schekman, and Südof-2013 for this work!! (vesicles and transport in cells)

-Integrated and controlled cell cycle

-Increase in enzymes regulating key aspects of molecular biology

Eukaryotic Cell Structure and Function

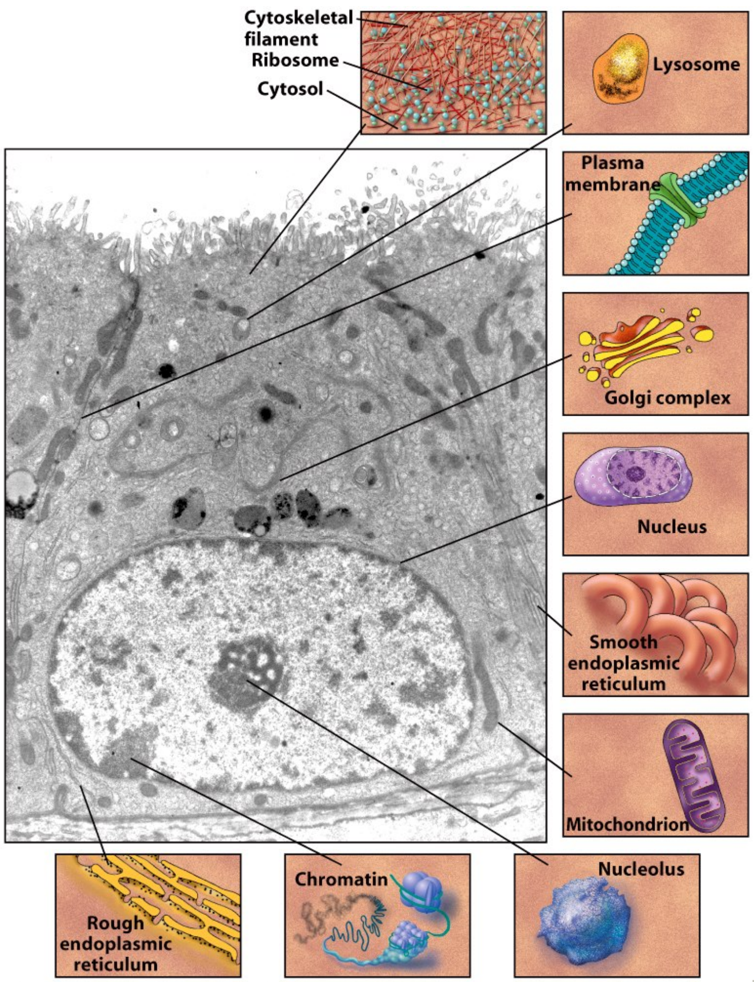


Figure 1-10 Cell and Molecular Biology, 5/e (© 2008 John Wiley & Sons)

Cytoskeleton- Motility:composed of microtubules, Microfilaments and intermediate filaments.

Ribosome-large complex of RNA molecules, the Engine of protein synthesis or translation

Lysosome-small organelle, functions in degradation of materials internalized by endocytosis/autophagy

Golgi complex-stacks of flattened, interconnected Compartments that function in processing and sorting of proteins and lipids

Nucleus- houses DNA organized into chromosomes, synthesis of RNA and ribosome assembly

Smooth endoplasmic reticulum-lacks ribosomes, functions in lipid synthesis

Rough endoplasmic reticulum-associated with ribosomes, functions in synthesis and processing of secreted and membrane proteins

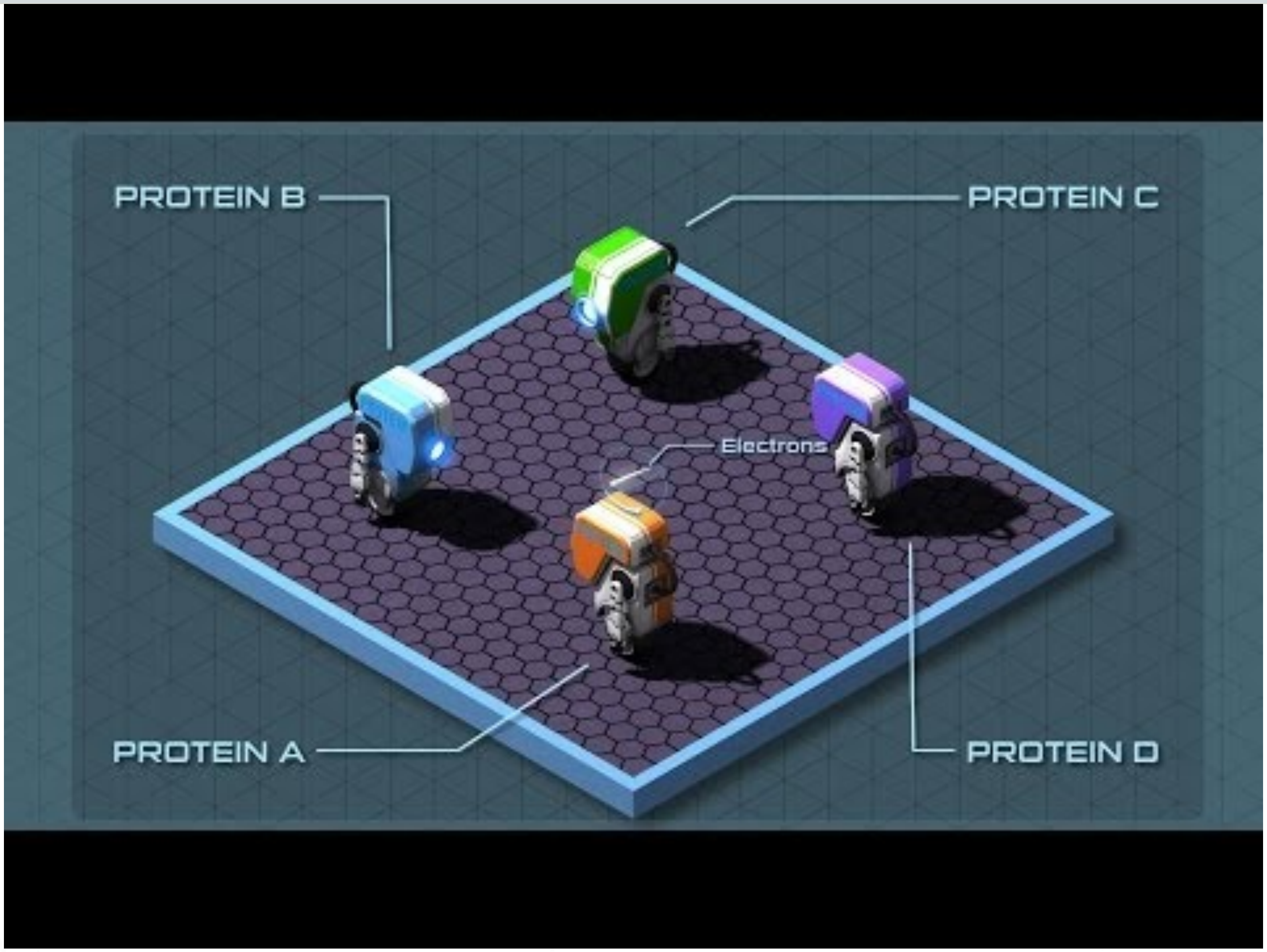
Mitochondria- powerhouse organelle that produces most ATP (energy) of cell

Nucleolus-site of rRNA synthesis, processing and ribosome subunit assembly

Chromatin-complex of DNA, histones, and non histone Proteins from which chromosomes are formed

Plasma membrane- lipid and protein bilayer of cell membrane

The operating system of life..

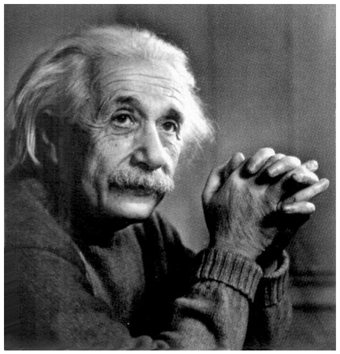


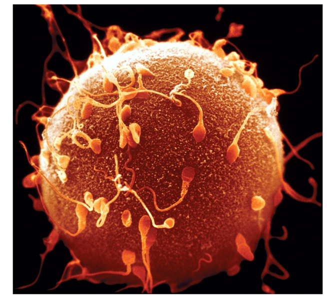
Cells are almost like tiny factories run by robots, with the nucleus, DNA, proteins, lipids, vitamins and minerals all playing critical roles.

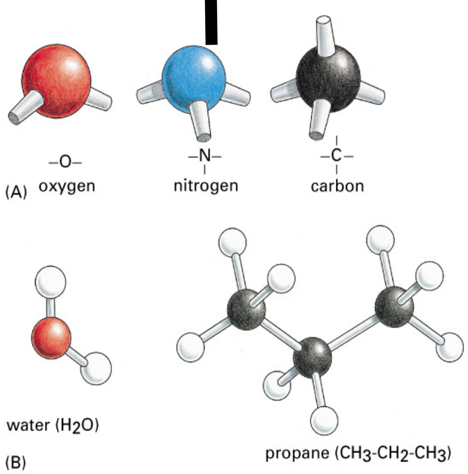
In this TED ED, George Zaidan and Charles Morton lay out the blueprint of a cell and explain how molecular binds all life together.

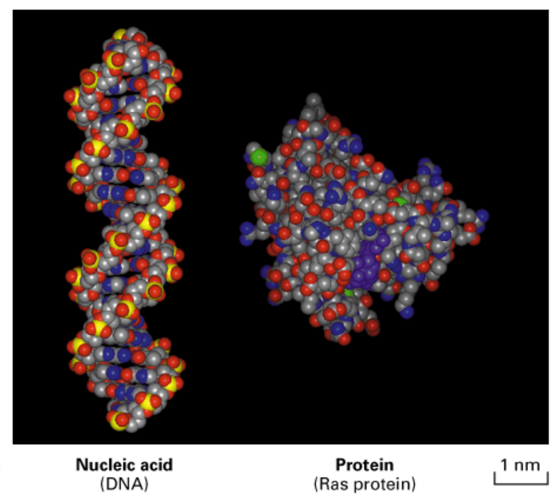
http://ed.ted.com/lessons/the-operating-system-of-life-george-zaidan-and-charles-morton

Macromolecules are the building blocks of every cell









All cells are made up of the same kinds of macromolecules

DNA - <u>D</u>eoxyribo<u>n</u>ucleic <u>a</u>cid, stores information as genes

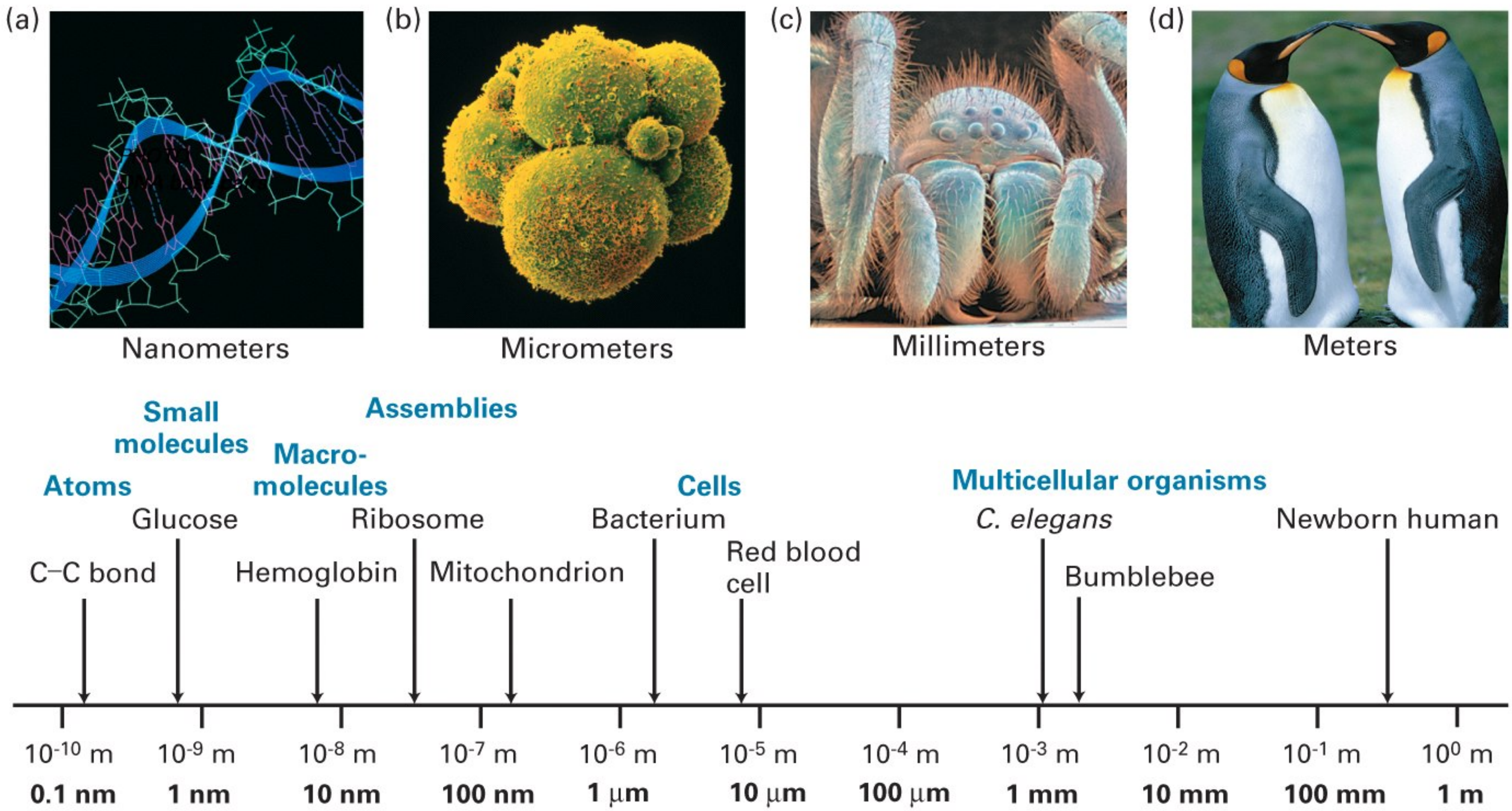
RNA - <u>R</u>ibo<u>n</u>ucleic <u>a</u>cid, used for information transfer from DNA to protein

Protein -functional molecules involved in all cellular processes

Lipids- diverse group of naturally occurring organic compounds that are related by their solubility in nonpolar organic solvents and insolubility in water, ex. fatty acid, phospholipids

Polysacharrides-a carbohydrate composed of many monosaccharide units, ex. starch, glycogen, and cellulose

Biomolecules in cells are the chemical basis of all organisms



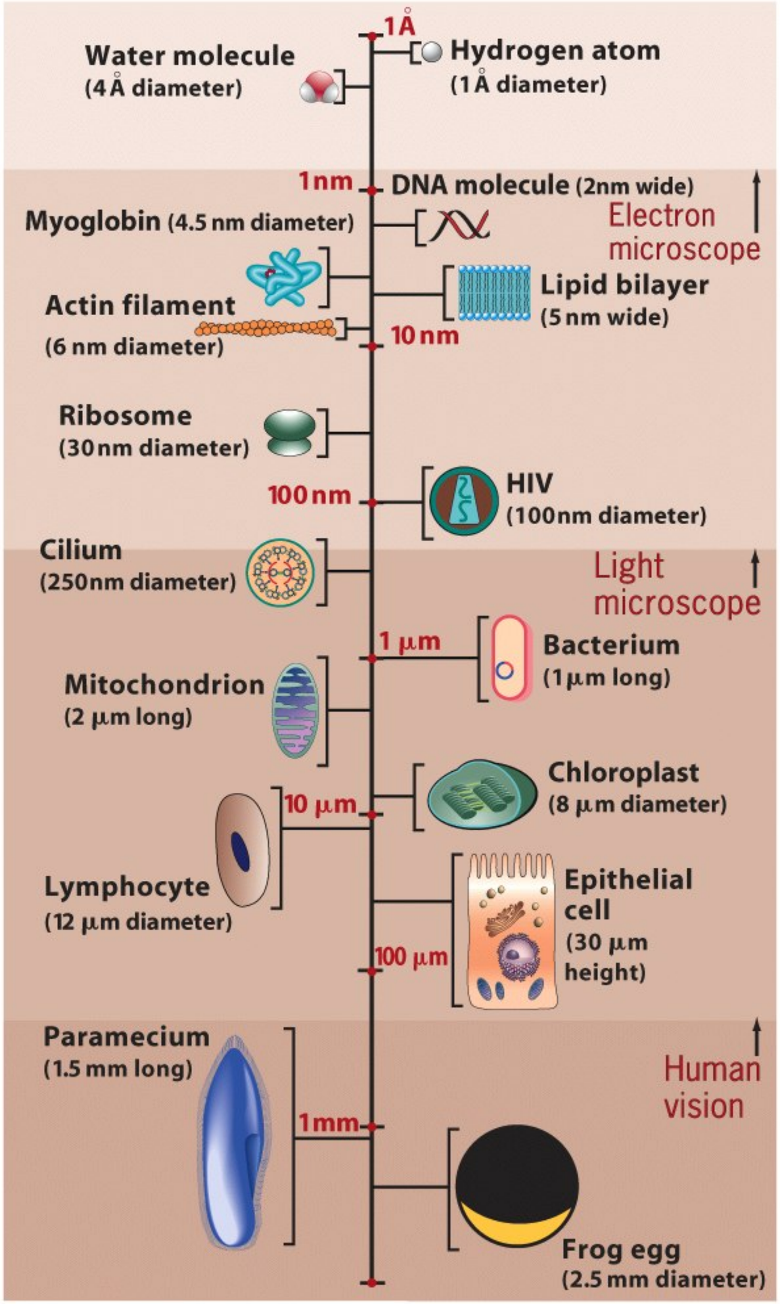


Figure 1-19 Cell and Molecular Biology, 5/e (© 2008 John Wiley & Sons)

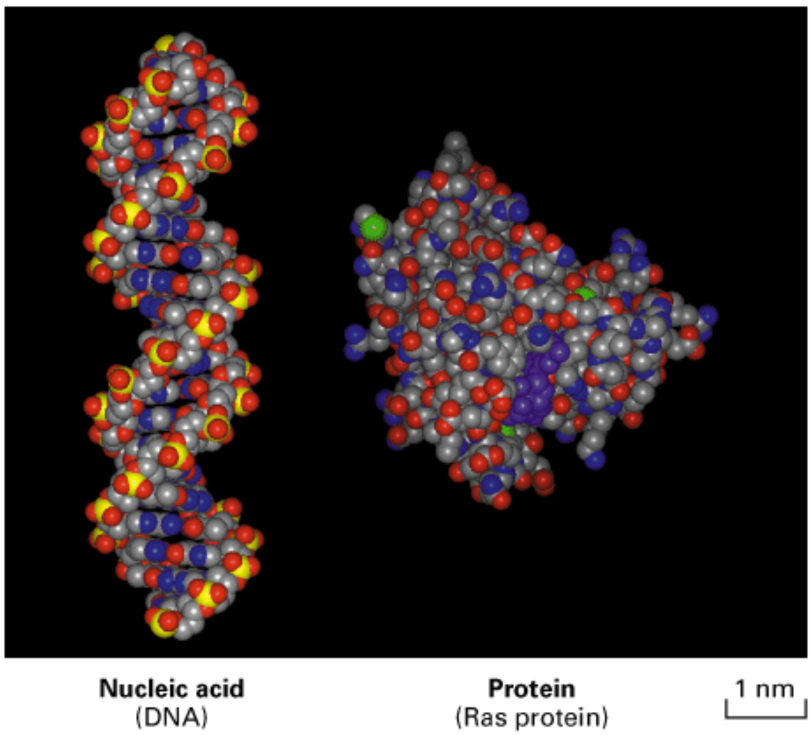
Microscopy: Visualizing Cells and Cell Components

Electron Microscope- viruses, lipids, actin, DNA

Light Microscope- bacteria, cells, mitochondria

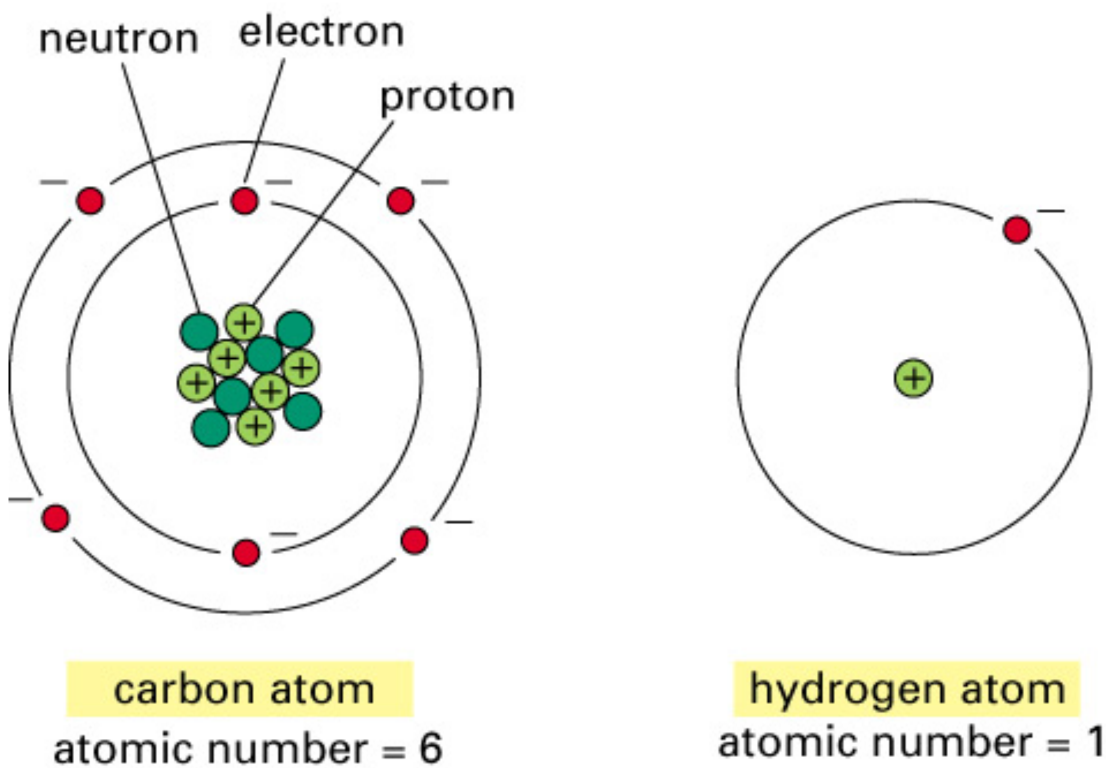
Human Vision- eggs, embryos, mice

Macromolecules



- Macromolecules have a mass of greater than a few thousand daltons
- Typically have a higher order structure
- Chemical interactions regulate stability of macromolecules

Atoms in Macromolecules



Six most popular atoms in living systems:
Hydrogen,
Carbon,
Nitrogen,
Phosphorus,
Oxygen
Sulfur

Types & Properties of Chemical bonds that regulate the interaction between two atoms:

Covalent bonds

-- **Two atoms interact by sharing electrons**

-- **Strong, hold atoms in a molecule together (intra-molecular bonding)**

-- **Bond strength is ~110 kcal / mol, it is the energy needed to break a bond,**

-- **Single bond: two atoms sharing 1 pairs of electrons, free rotate**

-- **Double bonds: two atoms sharing 2 pairs of electrons, can not rotate**

Noncovalent bonds

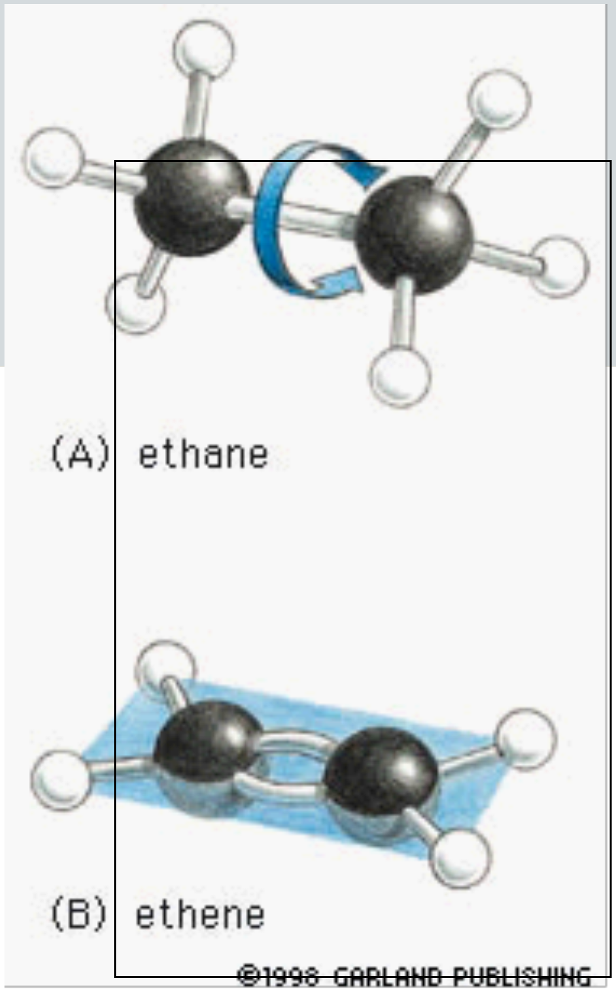
-- **Interactions between atoms not involved with electron sharing**

-- **weak bonds, but many working together can stabilize 3D structure of a large molecule (intra-molecular bonding).**

-- **help molecules bind to other molecules (inter-molecule interactions).**

-- **particularly important for biomolecules**

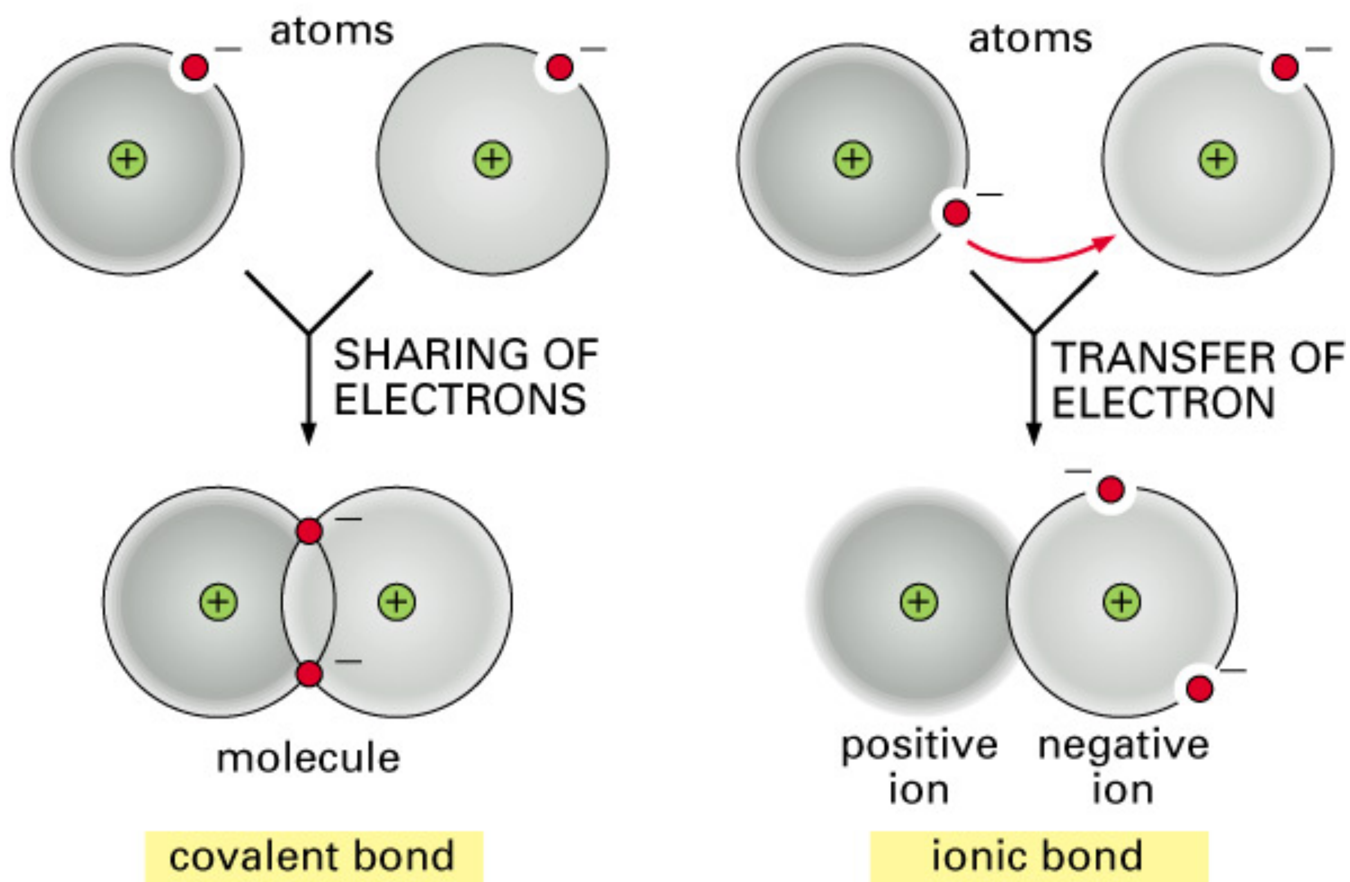
Examples of Covalent Bonds



Single bond

Double bond

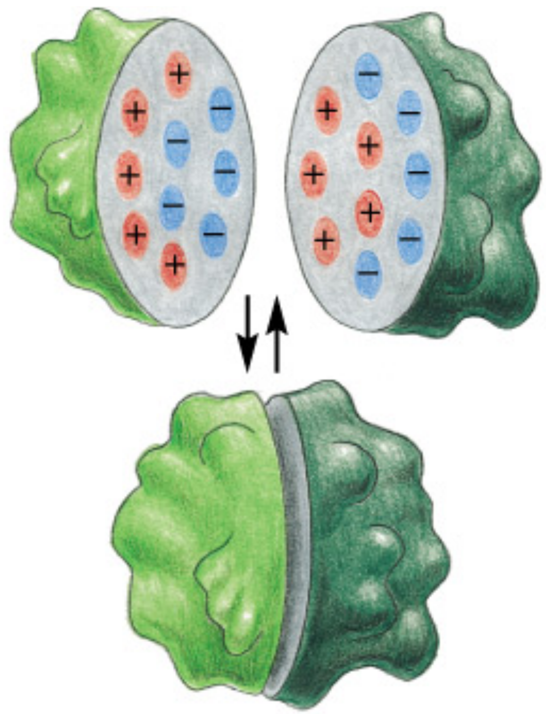
Covalent bond vs ionic (noncovalent) bond



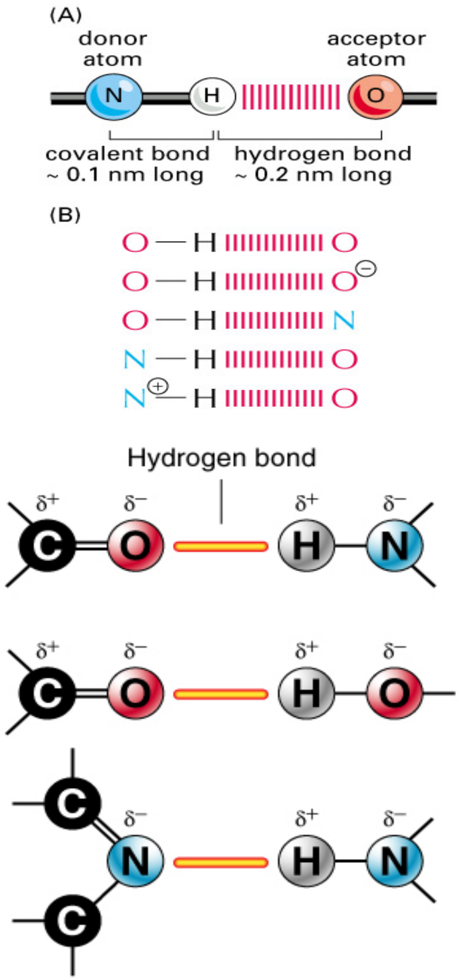
Four types of noncovalent bonds

(1) Ionic bonds

- attractive force between positively and negatively charged atoms
- in ionic bonds, atoms gain or lose electrons completely to its partner
- strongest noncovalent bond



(2) Hydrogen bonds



-H bond is the electrical attraction between a hydrogen atom of one molecule and negatively charged atom in another molecule. It forms when a hydrogen atom is "sandwiched" between two electron-attracting atoms such as O and N.

e.g. O-H···O, N-H··O,

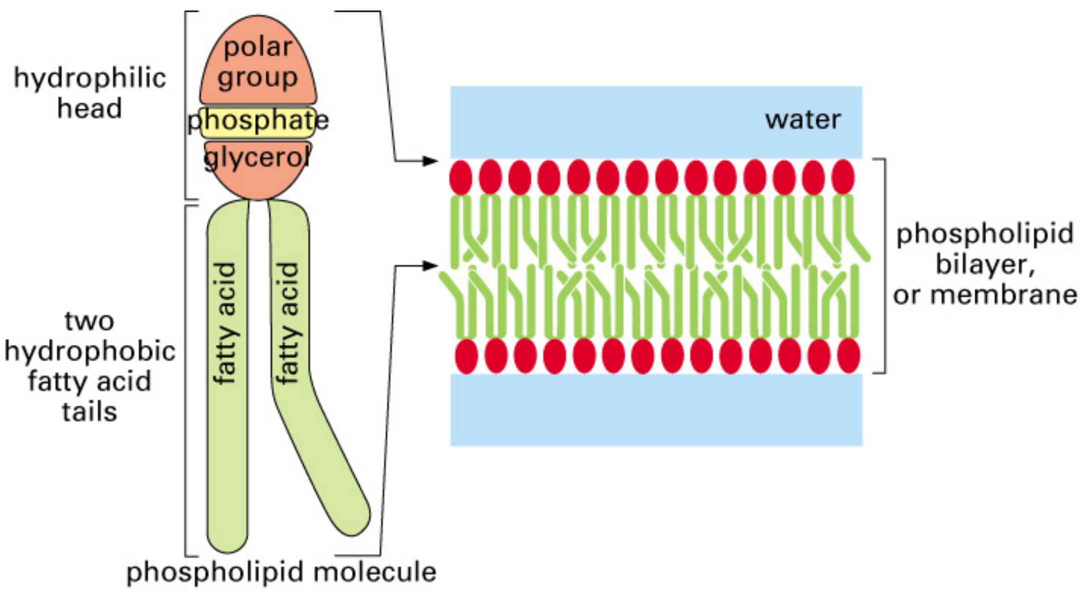
- H bond is particularly important for the high-order structures of polymers such as the secondary structure of protein and RNA and the double strand structure of DNA.
- H_2O molecules (in water) stick to each other and others by H bonds.

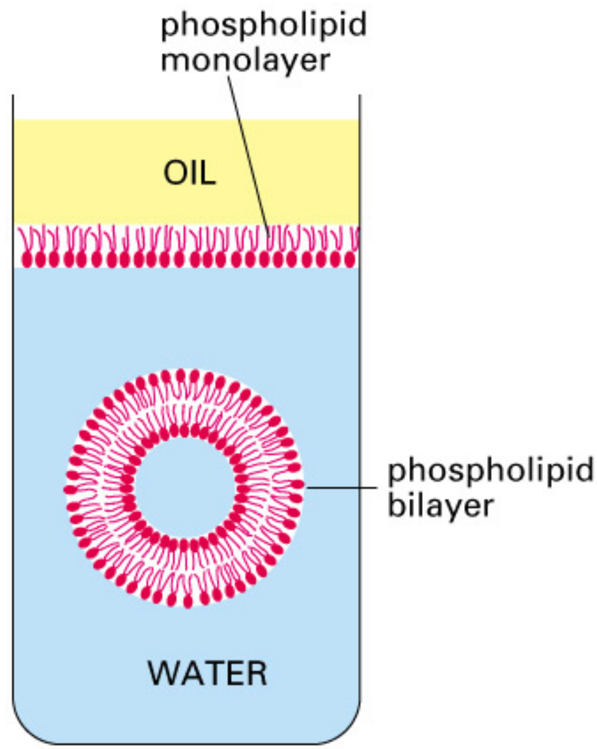
(3) Hydrophobic interactions

-force that causes nonpolar portions of molecules to stay away from water molecules

-In contrast to other bonds that form because the two parties "love" each other, the hydrophobic interaction is formed because all parties "hate" water and they all get pushed together.

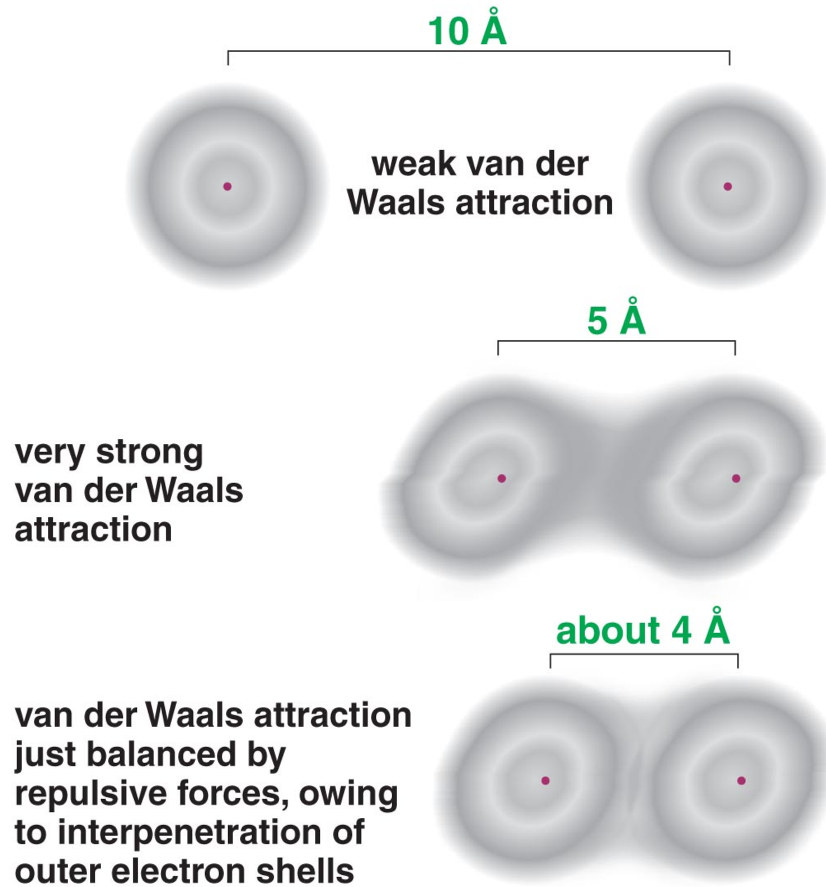
"the enemy of my enemy is my friend"



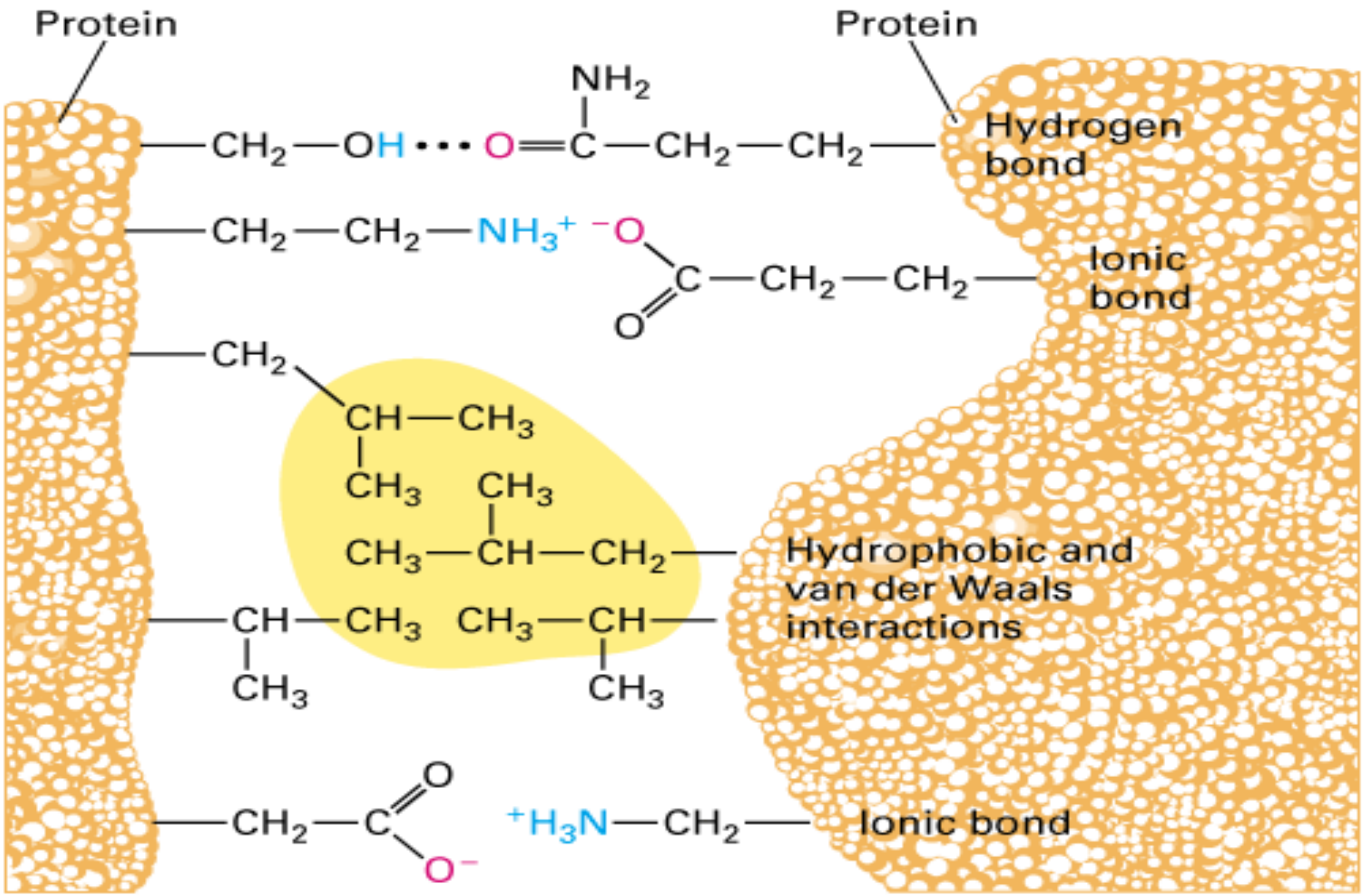


(4) Van der Waal Forces

-Weak attractive forces through transient dipoles in the electron clouds of all atoms.
-Attraction decreases rapidly with increasing distance.
However, atoms repel one another when they are too close.

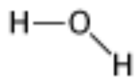


Examples of Non-Covalent Bonds



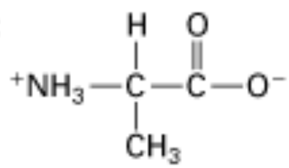
Distribution of Living Matter Components

(a) Water, ions, and small molecules (77%)

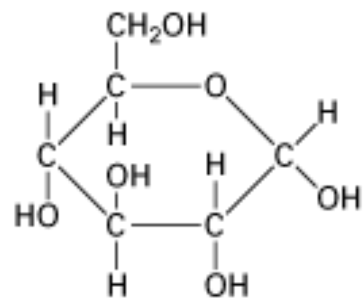
Water (70%): 

Inorganic ions (1%): Na^+ Cl^- K^+ $H_2PO_4^-$

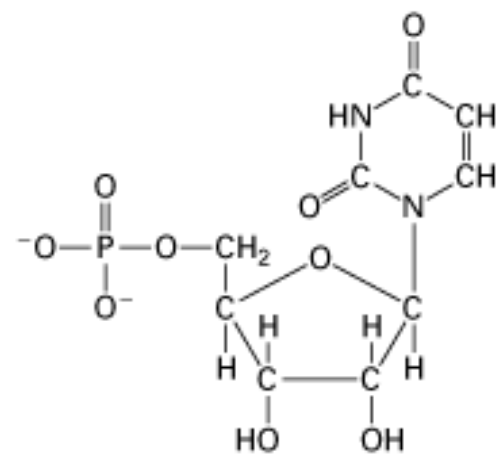
Small molecules (6%):



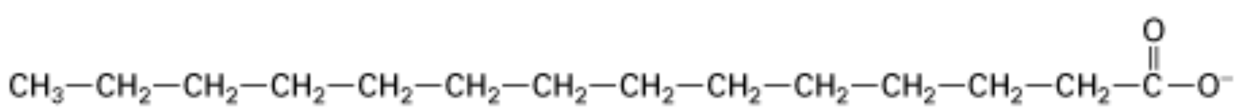
Amino acid
(alanine)



Sugar
(glucose)



Nucleotide
(uradine monophosphate)

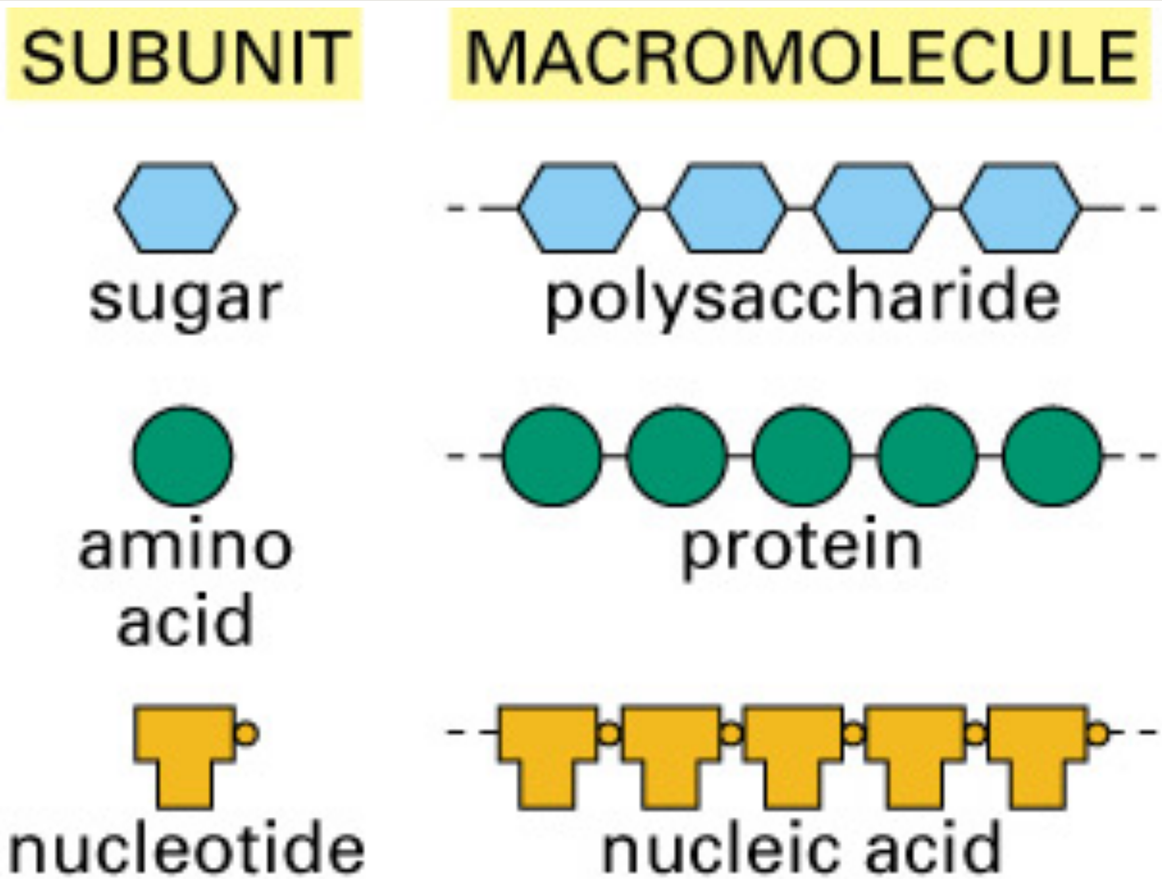


Fatty acid (myristic acid)

Examples of “Small” molecules or biomolecules that make up the subunits of macromolecules

- Sugar: glucose, ribose, etc
- fatty acid: oleic acid (C_{18}), etc
- Amino acids: glycine, methione, etc
- base: adenine (A), guanine (G), cytosine (C), thymine (T), uracil (U)

Macromolecules are polymers made up of individual subunits or monomers



Functional Groups give Biomolecules Unique Properties

Table 2.2 Functional Groups

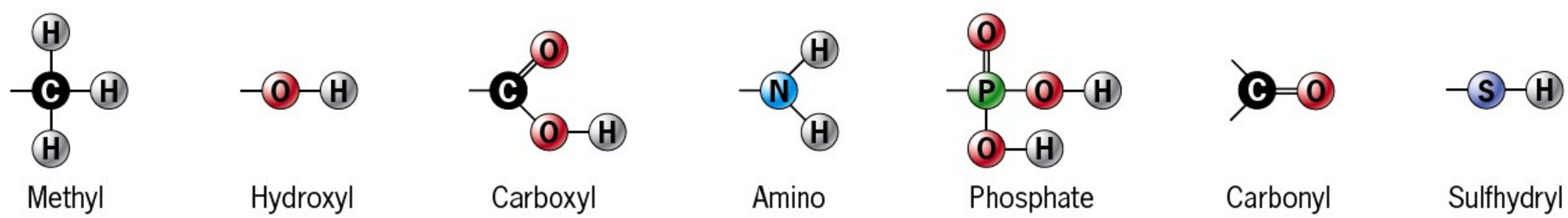
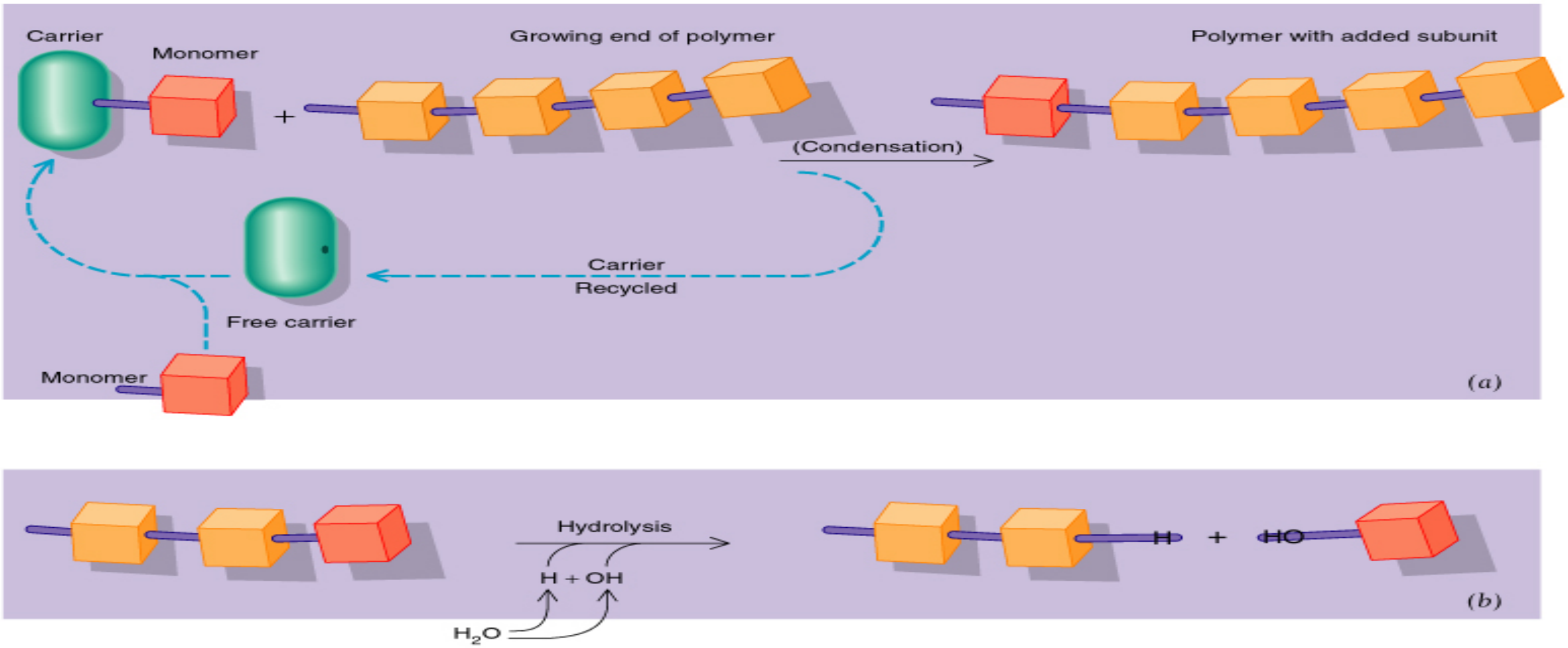


Table 2-2 Cell and Molecular Biology, 5/e (© 2008 John Wiley & Sons)

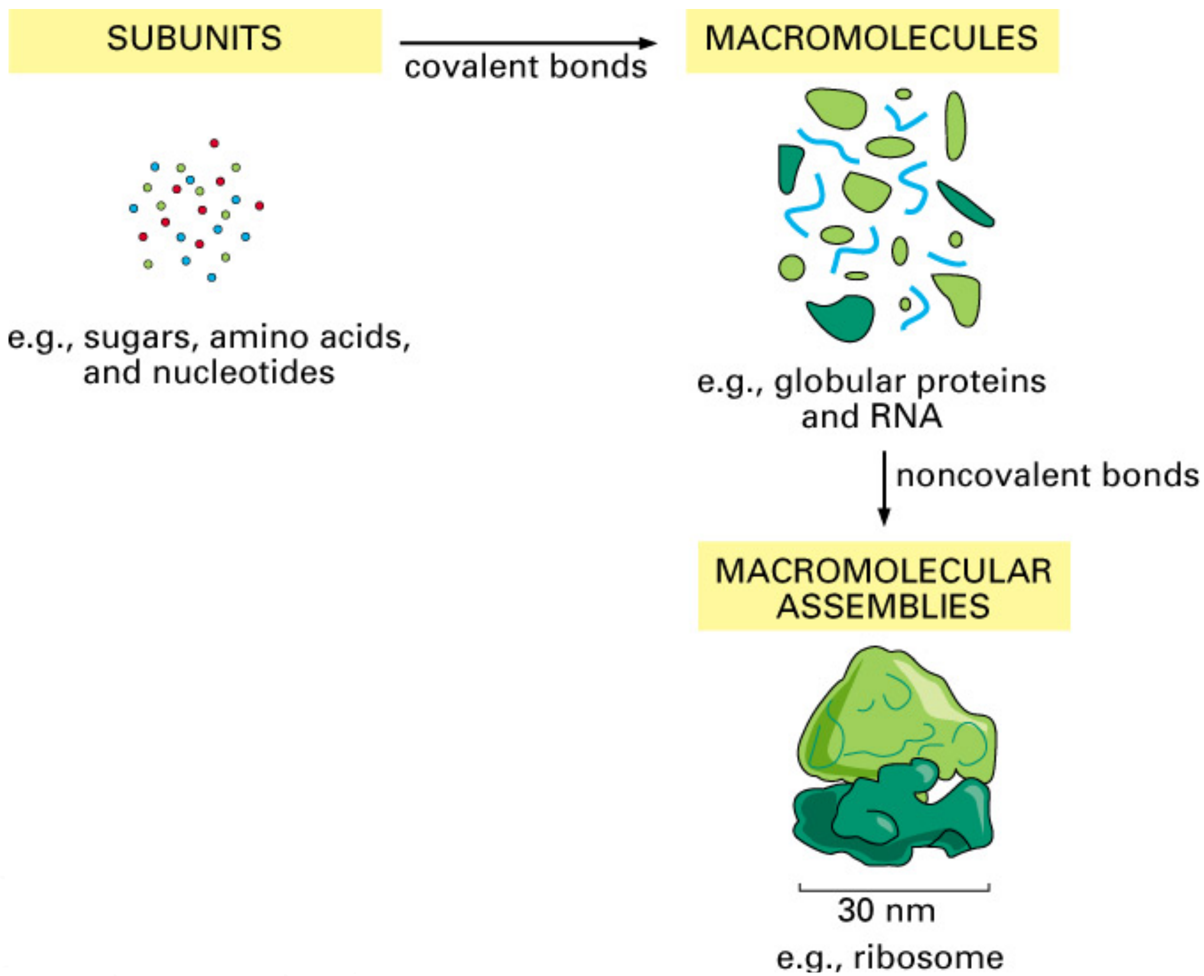
Functional groups can change:
Physical properties
Chemical reactivity
Solubility in solution
Two common functional bonds are:
Ester bonds
Amide bonds

Schematic of Polymer Formation



-In hydrolysis, water is added to break covalent bond between monomers and in condensation, water is removed to bond them together.
-Condensation reactions store energy and hydrolysis typically releases energy

Both covalent and non-covalent bonds are involved in formation of a macromolecular complex



Four most important macromolecules of cells

Polymer--Many copies of small biomolecules (monomer) linked covalently to form polymers, MWs are often in kD (10^3 Dalton).

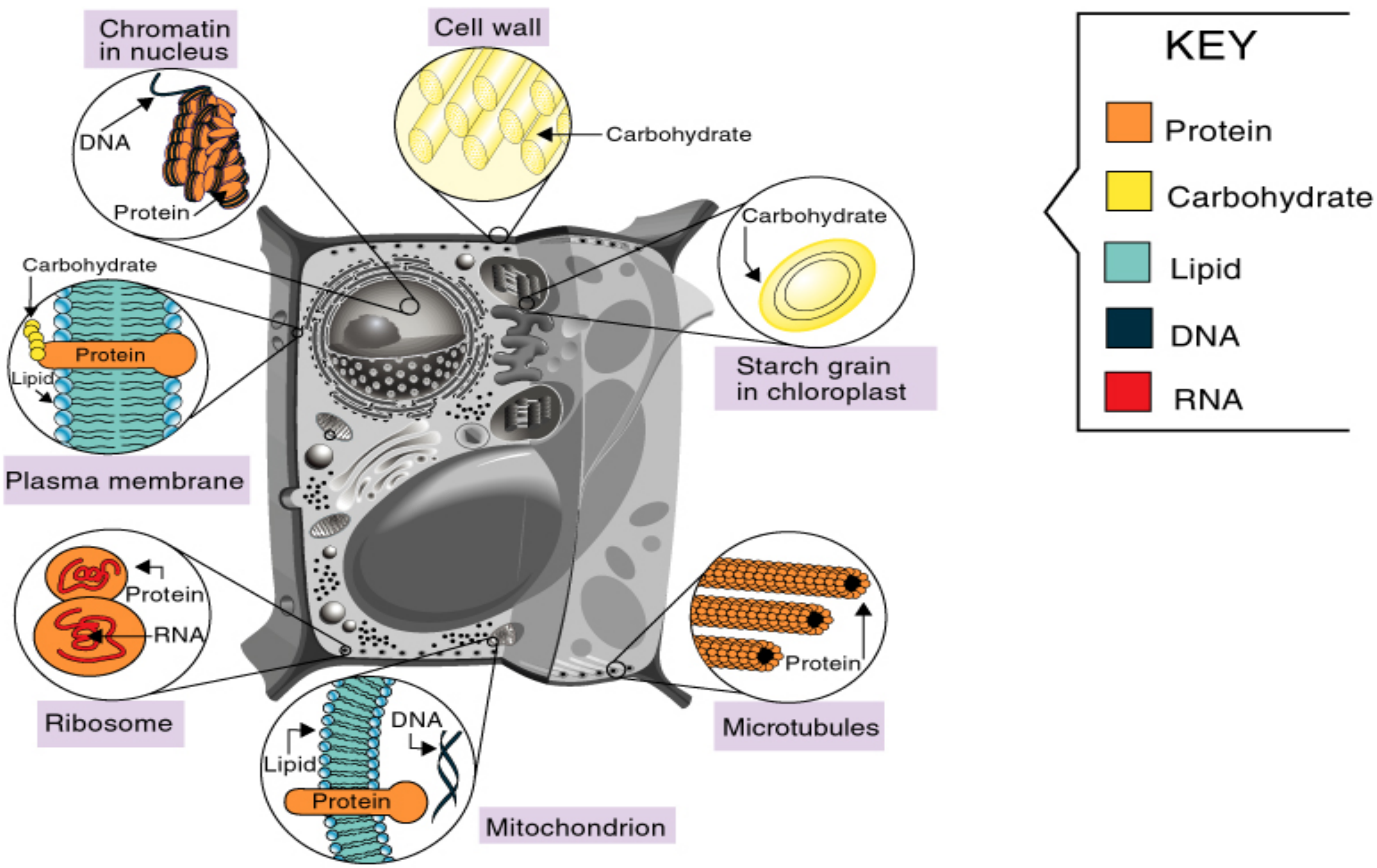
Polysaccharide – polymers of sugars
Polysaccharides are structure and energy materials of the cell.

Proteins –polymers of amino acids, often measured by kilodalton (kD). Proteins are the workforce of the cell.

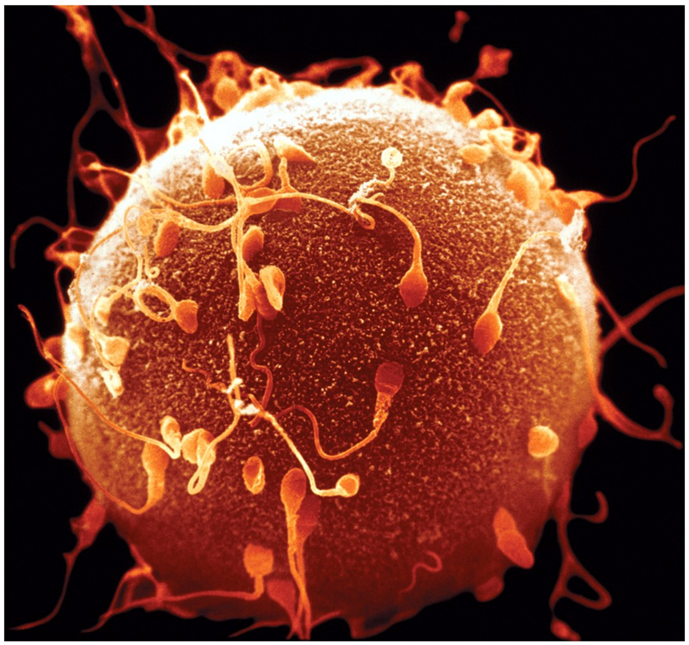
DNA/RNA–polymers of deoxyribonucleotides/ribonucleotides
DNA/RNA are the genetic material of the cell.

lipid—major classes: fatty acids, phospholipids, steroids, and triglycerides- important for enery storage and make up the cell membranes.

Where are biomolecules found in the cell?



How do we get from one cell to Einstein?



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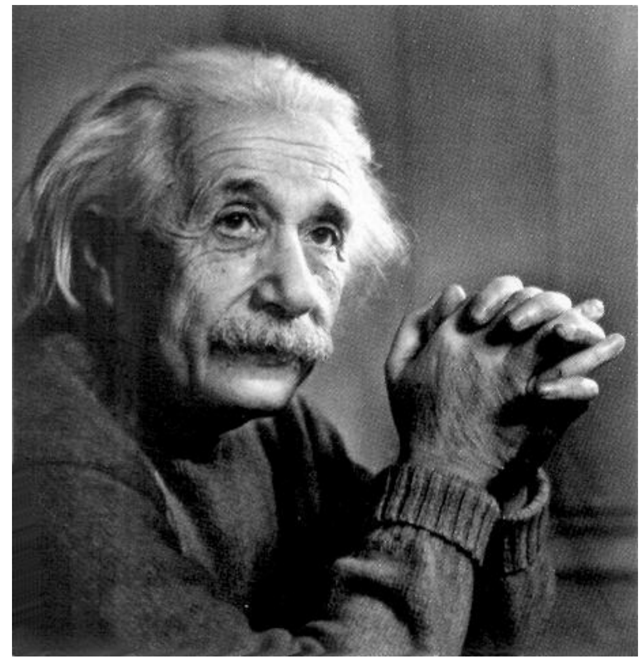
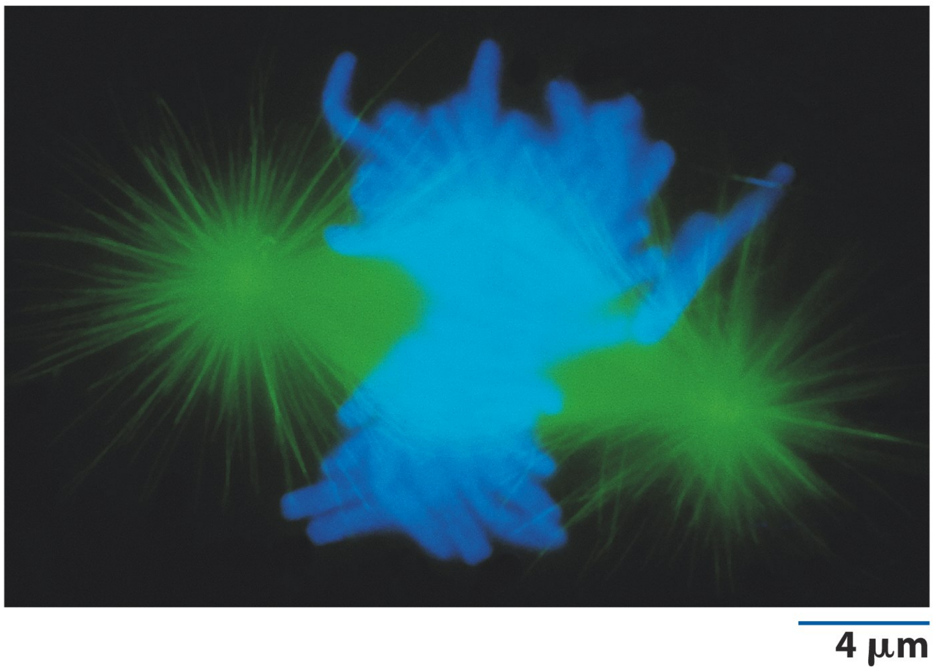


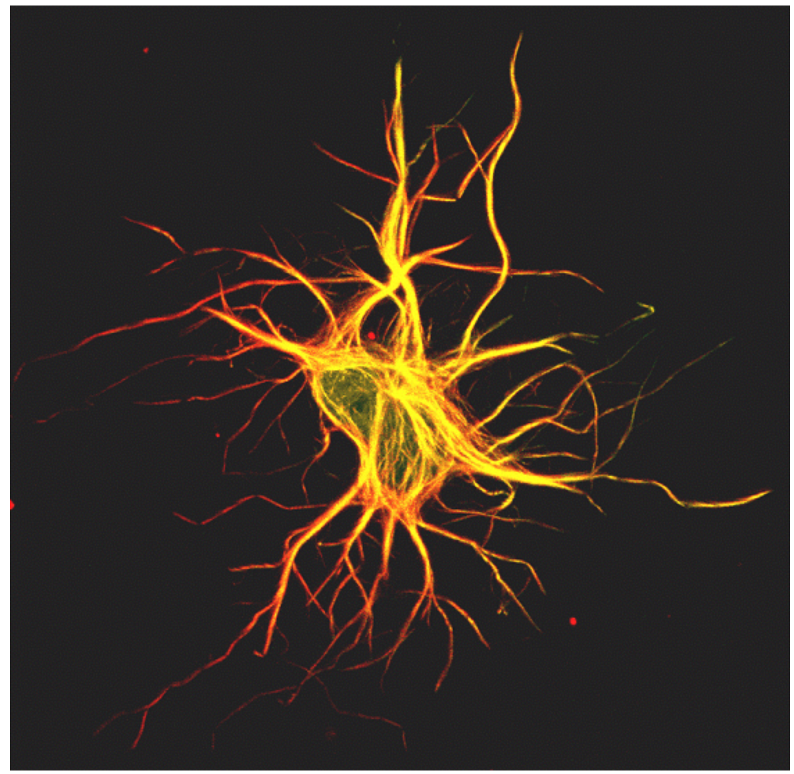
1 Cell

10^{14} Cells

Cell Division and Differentiation!!

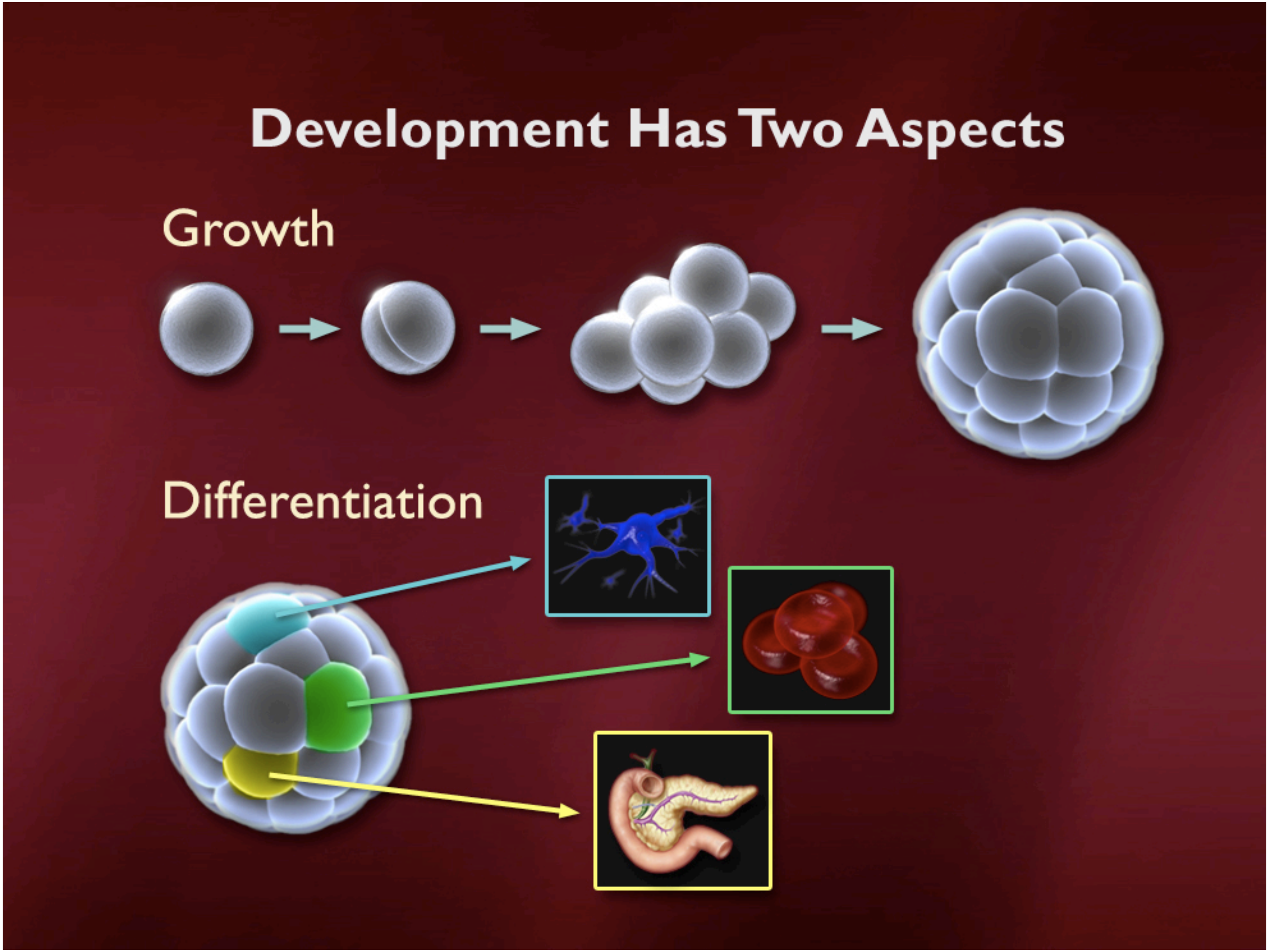


Cell in Metaphase during Division



Differentiated Neurons


HHMI


Development Has Two Aspects
Growth
Differentiation

Cell Division

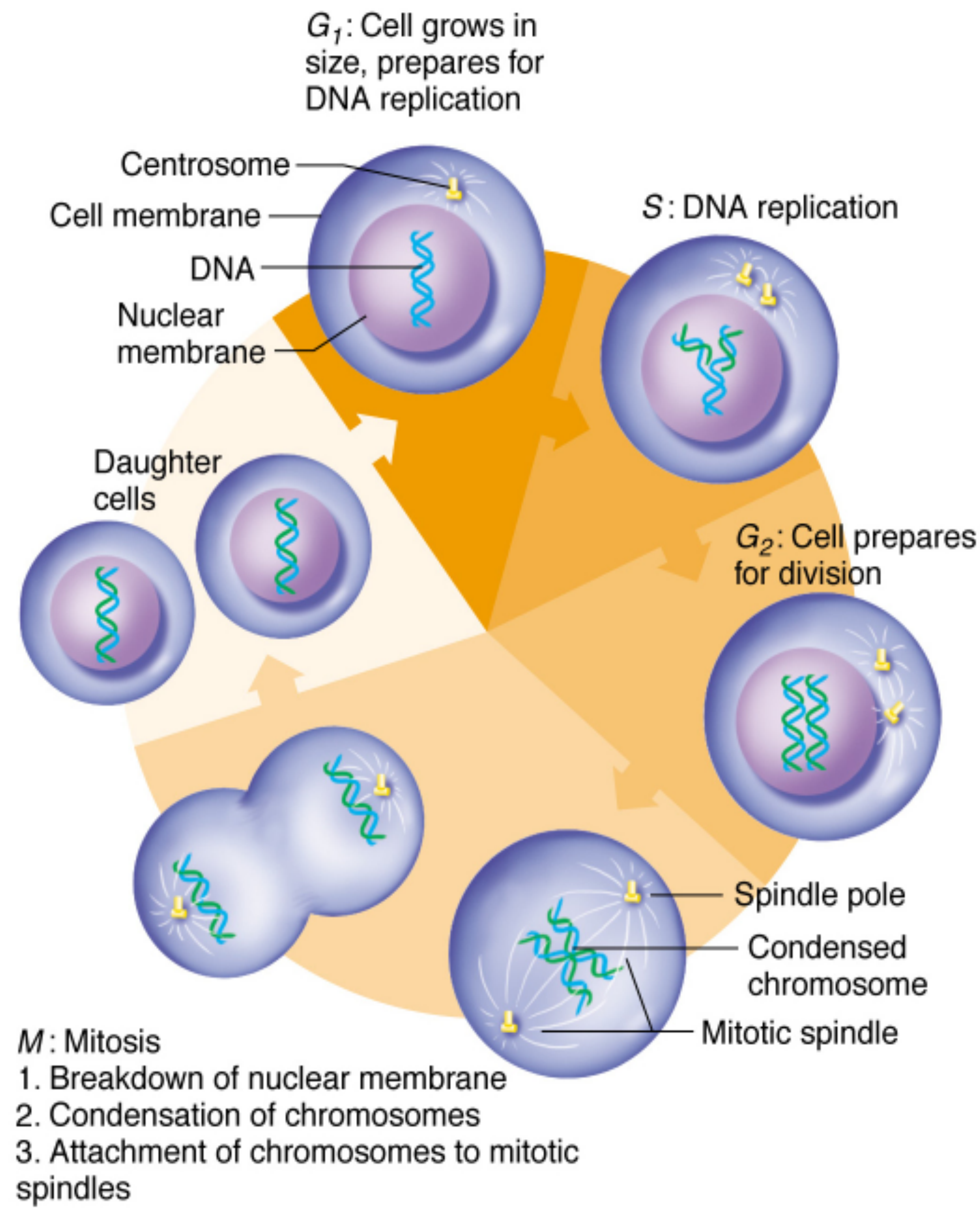
A process by which a cell duplicates its own material and divides into two cells.

G1

G2/M

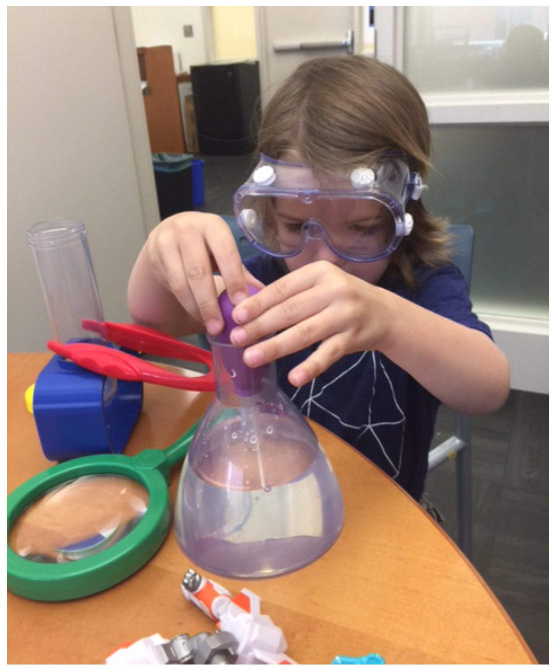
S

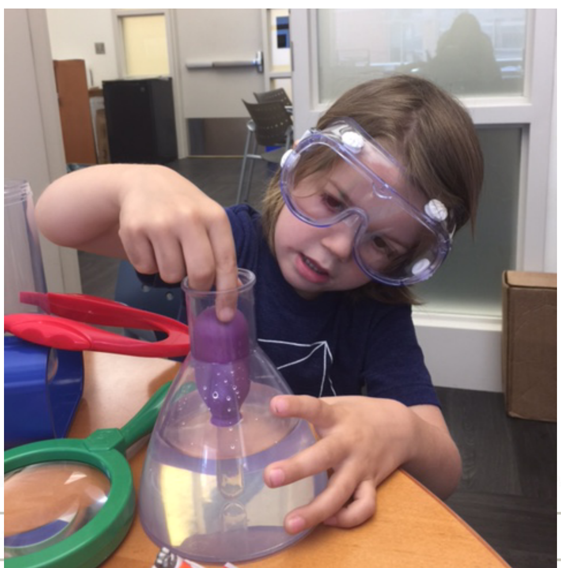
What happens if the cell progresses abnormally through this cycle??





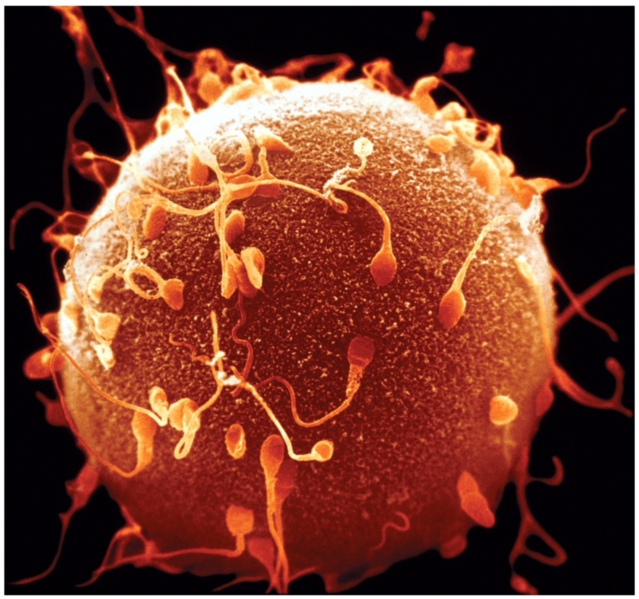
Scientist in action!





Differentiation: A process by which a cell undergoes a change to become a specialized cell type

What are the gene regulatory mechanisms that specify this change?



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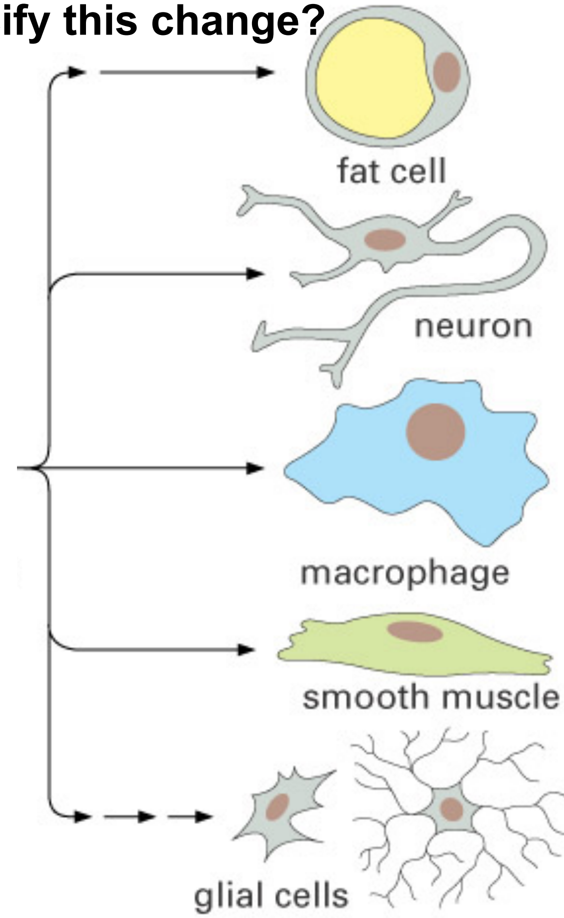


~ 20,000 genes

~ 20,000 genes

SubTypes of Cell Differentiation: Specialized Cells have Unique Cell Functions

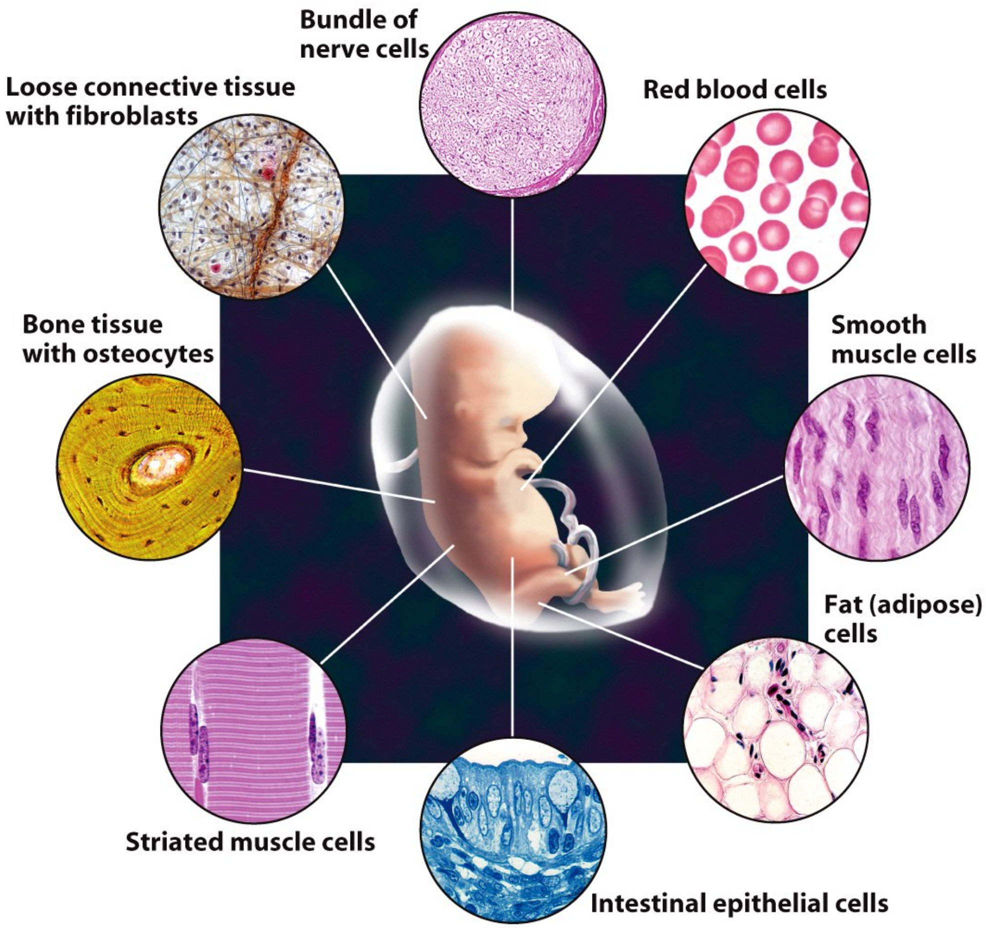
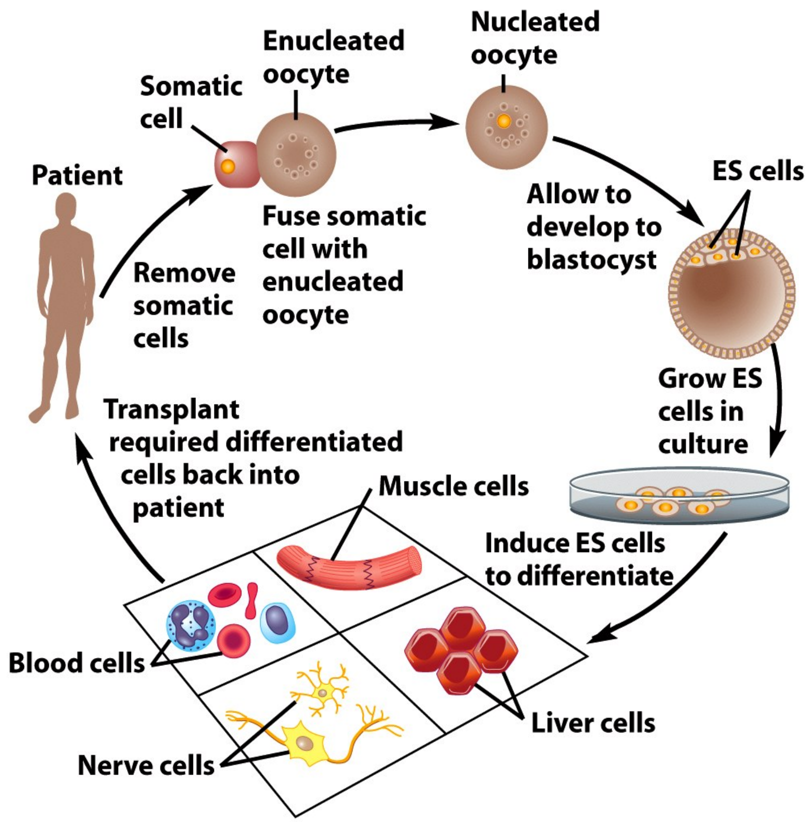
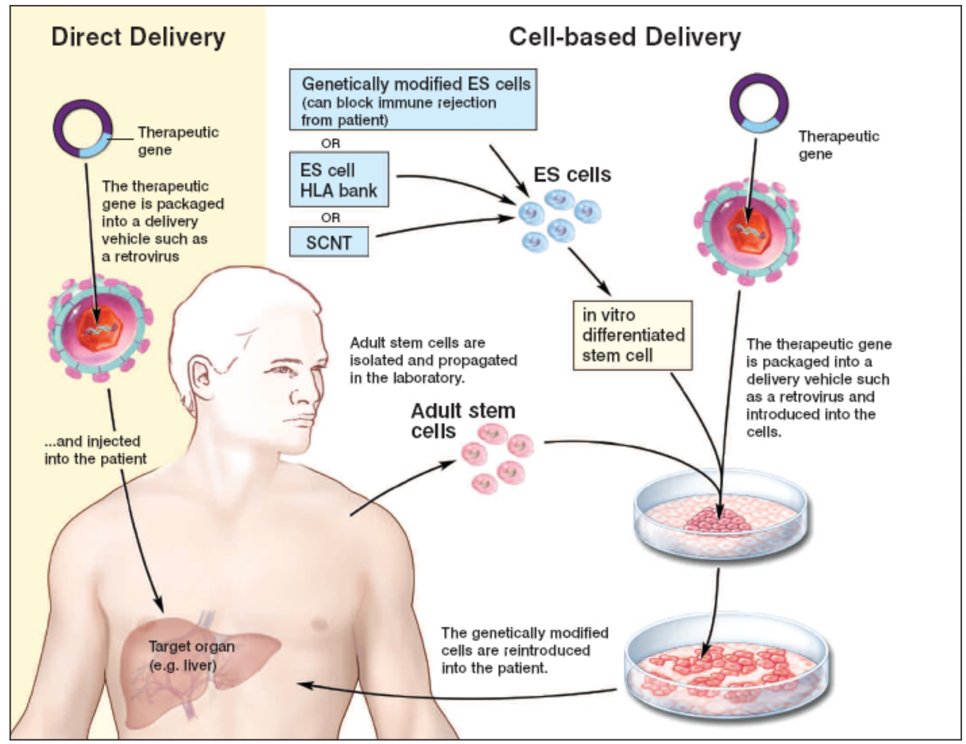


Figure 1-17 Cell and Molecular Biology, 5/e (© 2008 John Wiley & Sons)

What happens if your cells become diseased? Differentiated Cells Can be used for Cell Replacement Therapy



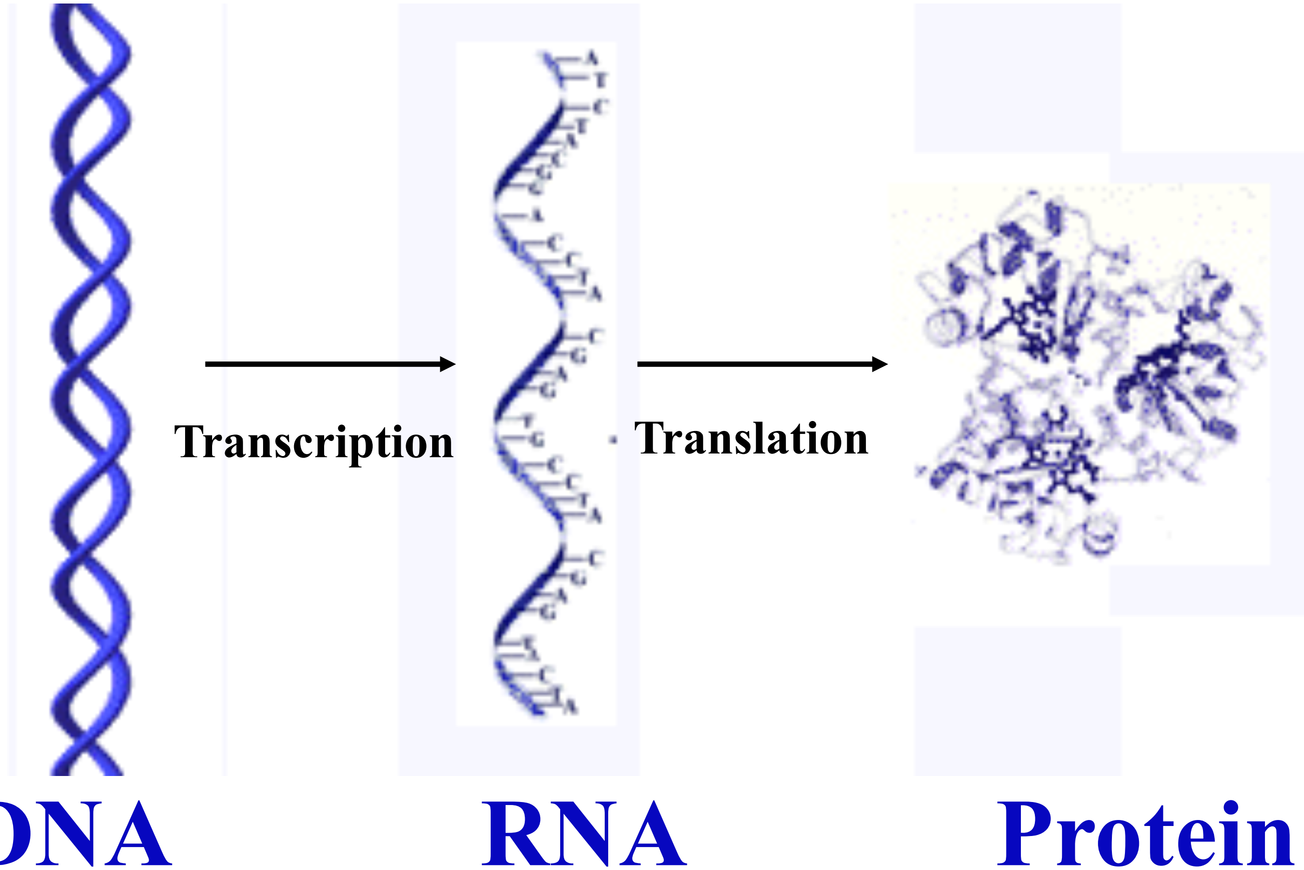
Human Perspective figure 2 Cell and Molecular Biology, 5/e (© 2008 John Wiley & Sons)



Somatic Cell Nuclear Transfer or Human Embryonic Stem Cell Based Therapies

Induced Pluripotent Stem Cells (iPSCs & Cell Replacement Therapy

Central Dogma of Molecular Biology



Macromolecules are key players that regulate every aspect of molecular biology!

Course Overview

1. Structure and function of
   DNA, RNA, and protein

2. Basic Molecular Biology Processes
   Replication
   Transcription
   Translation
   Regulation of gene expression
   Genetic variations
   Transcriptome and RNA silencing

3. Molecular Biology Methods
   Protein purification and analysis
   Recombinant DNA technology

Implications & Critical Thinking-1

- DNA is the building block of genes
- Genes are linked to chromosomes
- Diversity can be generated by mutations in the DNA sequence
- Mutations can also lead to disease
- What happens if mutations occur in the DNA sequence?
- How does a mutation at the gene level affect the protein?