



Foundations of Biochemistry – Dental Course



Text: Nelson & Cox-Lehninger


Principles of Biochemistry (5th ed 2008)



Objectives

1. Recognize that cells are composed of structural and functional units:
 - a. Plasma membrane
 - b. Cytoplasm
 - c. Cytosol
 - d. Ribosomes
 - e. Small metabolites
 - f. Coenzymes
 - g. Nucleus
 - h. Genome
2. Recognize that life consists of 3 domains:
 - a. Archaeobacteria
 - b. Eubacteria
 - c. Eukaryotes
3. Distinguish between components of Eukaryotes and Prokaryotes.

- 
4. Classify organisms according to energy and carbon acquisition:
 - a. Phototrophs
 - b. Chemotrophs
 - c. Autotrophs
 - d. Heterotrophs
 - i. Lithotrophs
 - ii. Organotrophs
 5. Identify common bonds in biomolecules and dissociation energies
Recognize the importance of sunlight as energy source for life.
 6. Recognize common functional groups of biomolecules.
 7. Identify molecular components in *E. coli* cell:
 - a. By percentage weight.
 - b. By number of different molecular species.
- 



8. Recognize that complex molecules are often linear polymers of simple molecules.

- a. 3D structures
- b. Optical activity

[Note Sections 1.3 Physical Foundation and Section 1.4 Genetic Foundation will be covered in depth at appropriate times during the course]

9. Recognize that heritable instructions allow evolution.

- a. Mutations
- b. A biotic production of biomolecules
- c. Landmarks in the evolution of life in earth.

10. Identify organisms in which Genomes have been sequenced.

11. Recognize importance of genomic comparisons in biology and medicine.

[Form a discussion of benefits and/or risks of genomic research].



Table 1.2**Biomolecular Dimensions**

The dimensions of mass* and length for biomolecules are given typically in daltons and nanometers,† respectively. One dalton (D) is the mass of one hydrogen atom, 1.67×10^{-24} g. One nanometer (nm) is 10^{-9} m, or 10 Å (angstroms).

Biomolecule	Length (long dimension, nm)	Mass	
		Daltons	Picograms
Water	0.3	18	
Alanine	0.5	89	
Glucose	0.7	180	
Phospholipid	3.5	750	
Ribonuclease (a small protein)	4	12,600	
Immunoglobulin G (IgG)	14	150,000	
Myosin (a large muscle protein)	160	470,000	
Ribosome (bacteria)	18	2,520,000	
Bacteriophage ϕ x174 (a very small bacterial virus)	25	4,700,000	
Pyruvate dehydrogenase complex (a multienzyme complex)	60	7,000,000	
Tobacco mosaic virus (a plant virus)	300	40,000,000	6.68×10^{-5}
Mitochondrion (liver)	1,500		1.5
<i>Escherichia coli</i> cell	2,000		2
Chloroplast (spinach leaf)	8,000		60
Liver cell	20,000		8,000

*Molecular mass is expressed in units of daltons (D) or kilodaltons (kD) in this book; alternatively, the dimensionless term *molecular weight*, symbolized by M_r , and defined as the ratio of the mass of a molecule to 1 dalton of mass, is used.

†Prefixes used for powers of 10 are

10^6	mega M	10^{-3}	milli m
10^3	kilo k	10^{-6}	micro μ
10^{-1}	deci d	10^{-9}	nano n
10^{-2}	centi c	10^{-12}	pico p
		10^{-15}	femto f

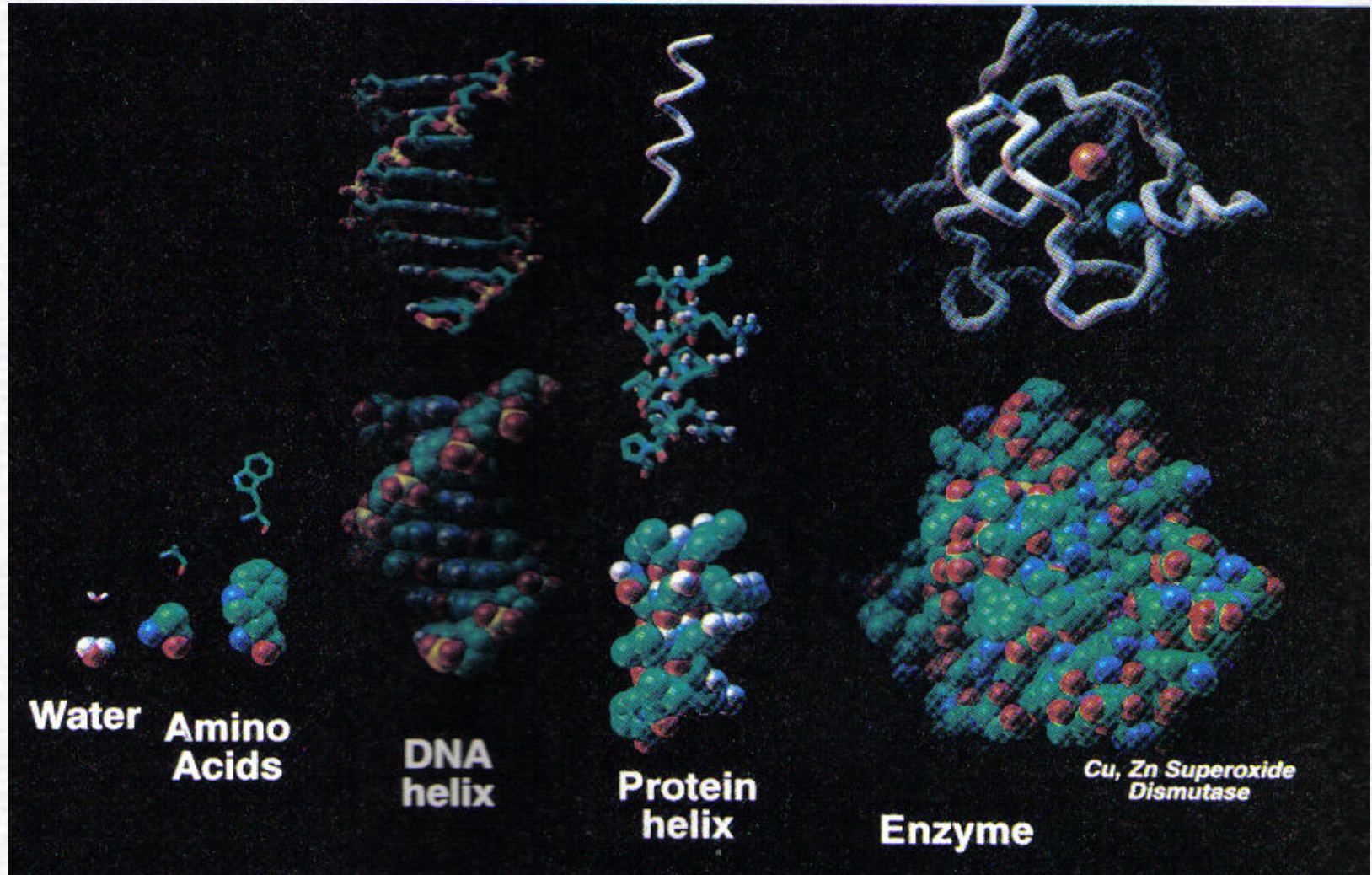
† Prefixes used for powers of 10 are

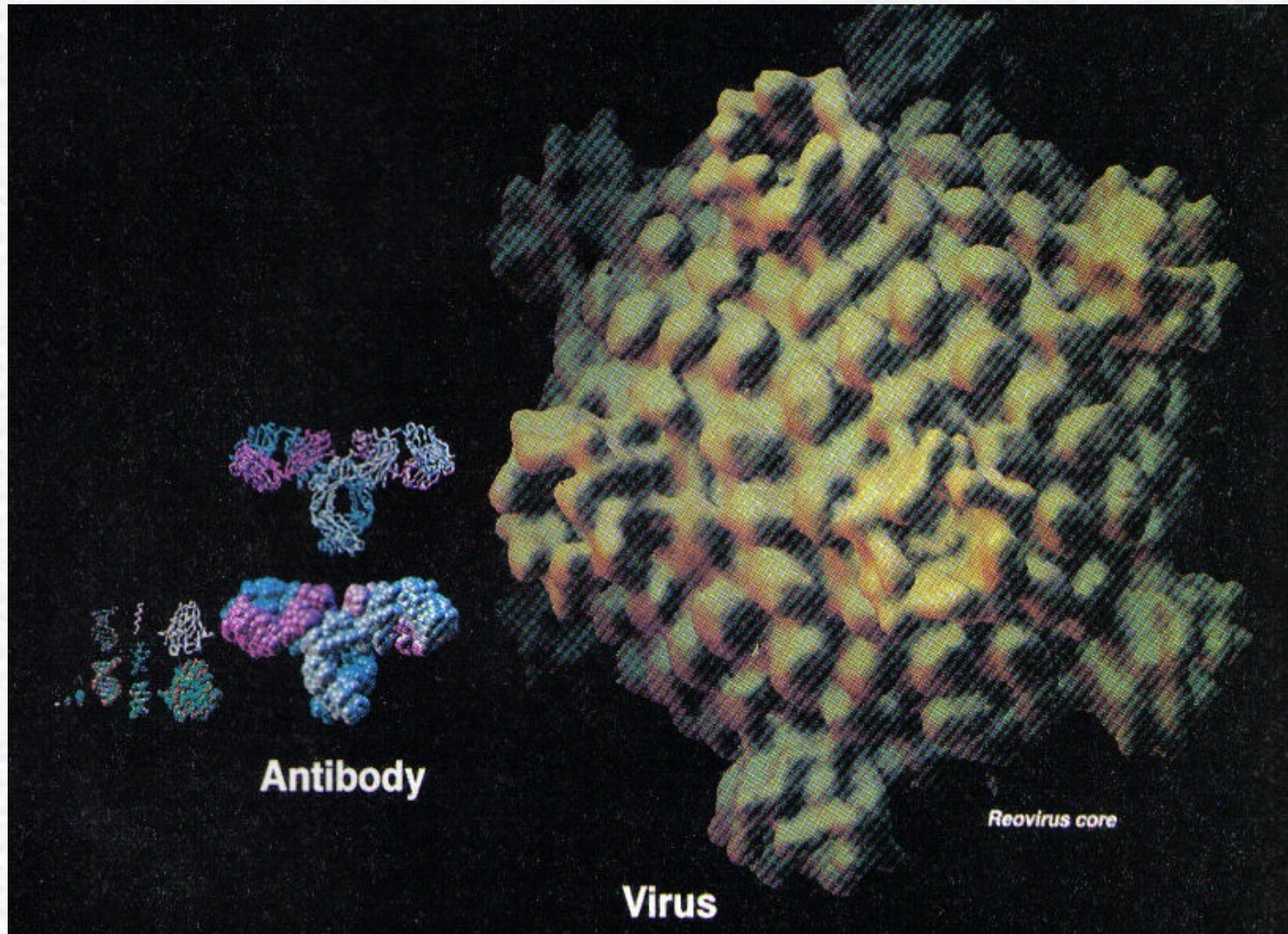
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10^{-2}	centi	c	10^{-12}	pico	p
			10^{-15}	femto	f

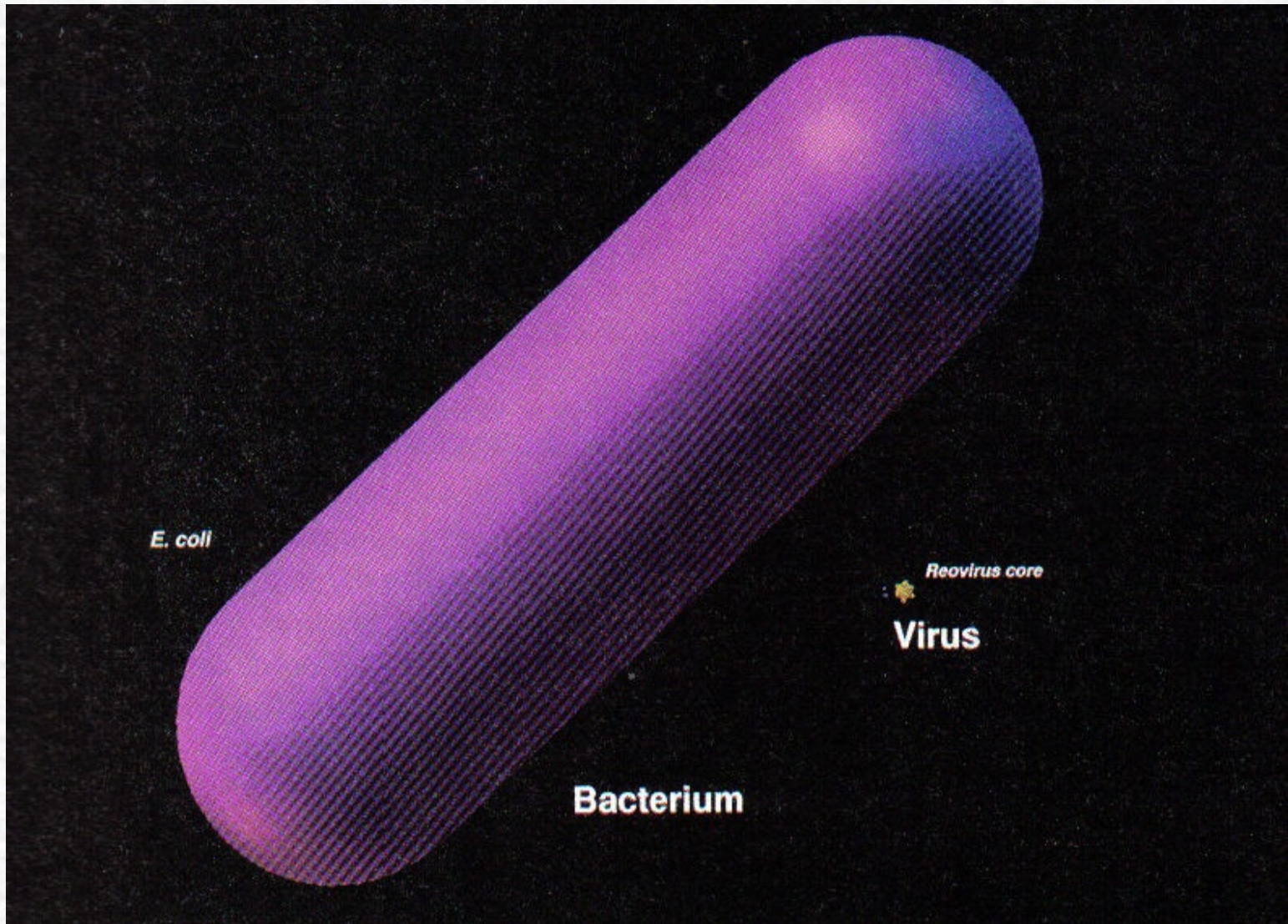
Å Angstrom = 10^{-8} cm

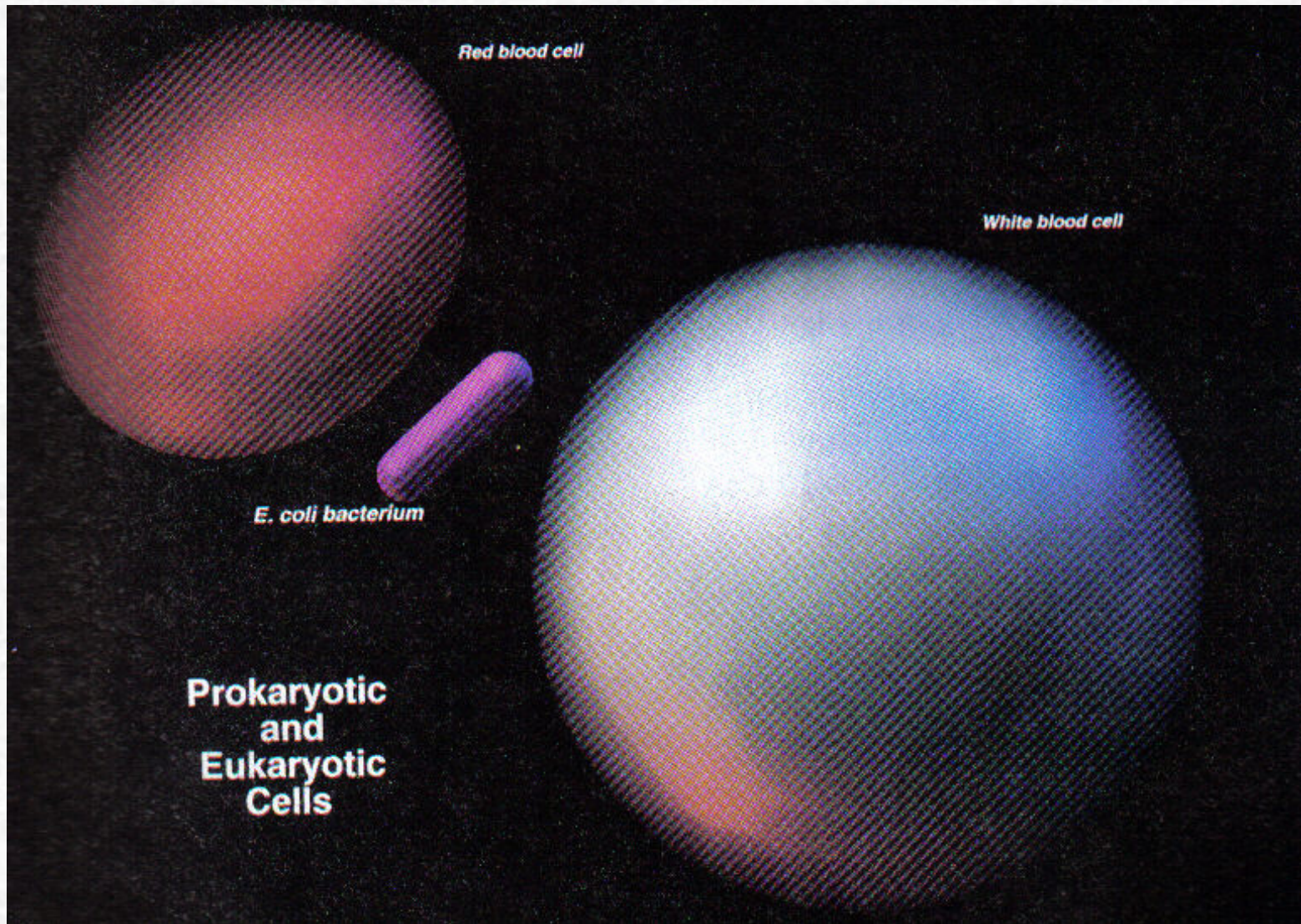
Part per million (ppm) = 1mg/L

Comparative Sizes of Biomolecules, Viruses and Cells









Examples of nanoparticles used in medicine

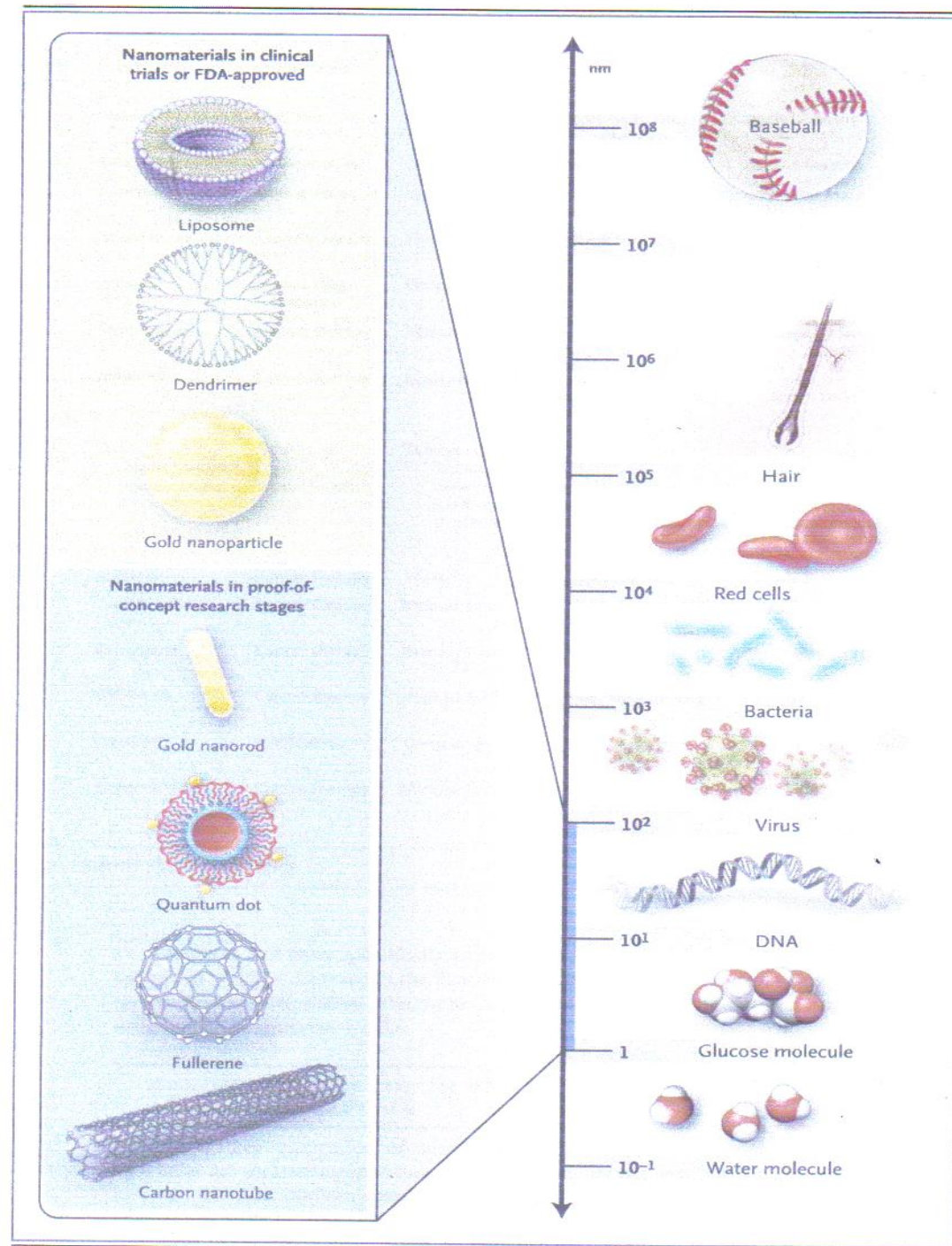


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			10^{-15}	femto	f

Electron microscope resolution
= 0.05nm or 0.5Å



What is the Fundamental
Source of All Life on Earth?



ENERGY OUTPUT FROM SUN

- 3.8×10^{23} kw-hr energy per hr
- 170,000 TW strike earth (TW=trillion watts)
- One third of enegy reflected back into space
- Current useable energy is ca 13 TW
- By 2050 ca 43 TW of energy will be needed

Type of radiation

Wavelength

Gamma rays

X rays

UV

Infrared

Microwaves

Radio waves

< 1 nm

100 nm

< 1 millimeter

1 meter

Thousands of meters

Visible light

Yellow

Violet

Blue

Cyan

Green

Orange

Red

Wavelength (nm)

380

430

500

560

600

650

750

Energy (kJ/einstein)

300

240

200

170

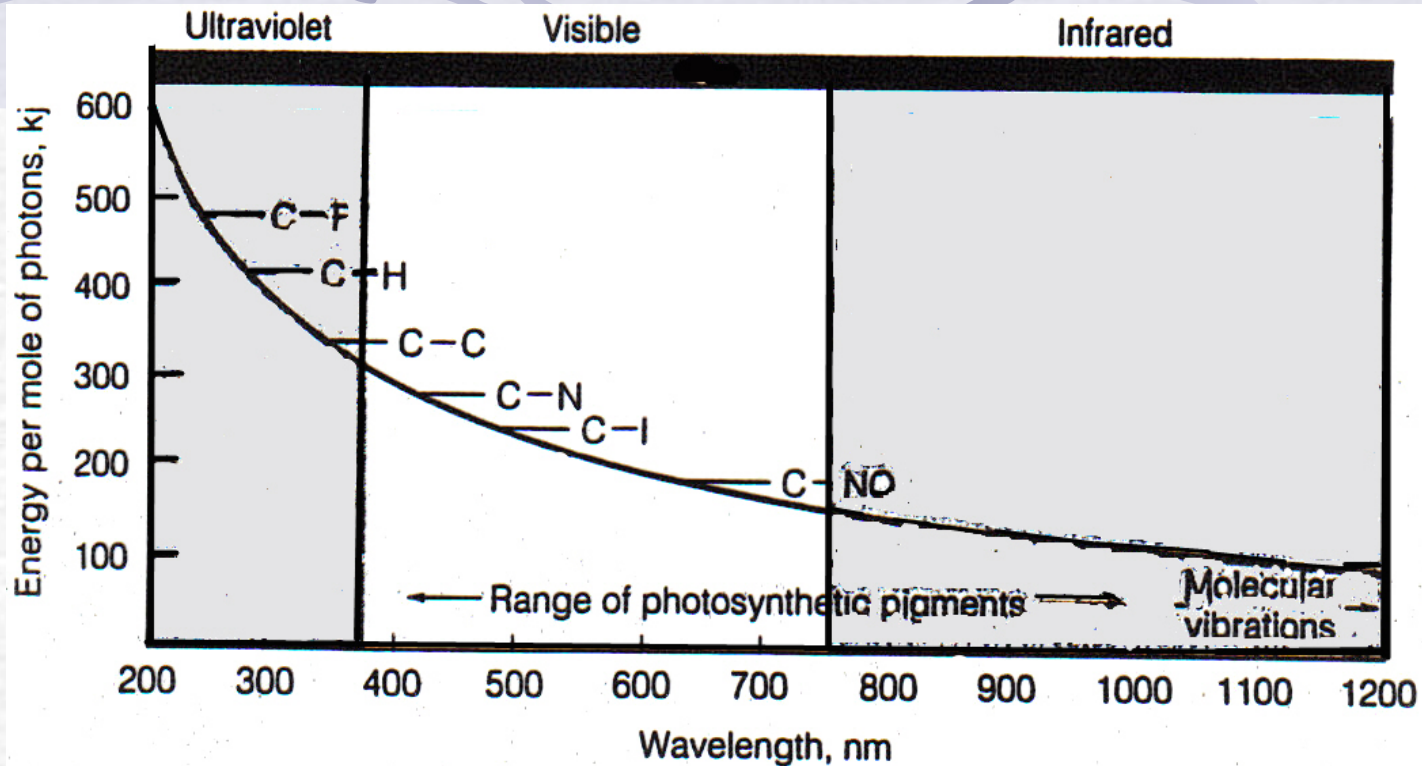


Figure 19.6

Energy per mole of photons (einstein) as a function of wavelength, compared with energies of several chemical bonds. Light in the UV and visible range has enough energy to directly break chemical bonds, whereas light in the long-wavelength portion of infrared region of the spectrum only causes heat-producing molecular vibrations.

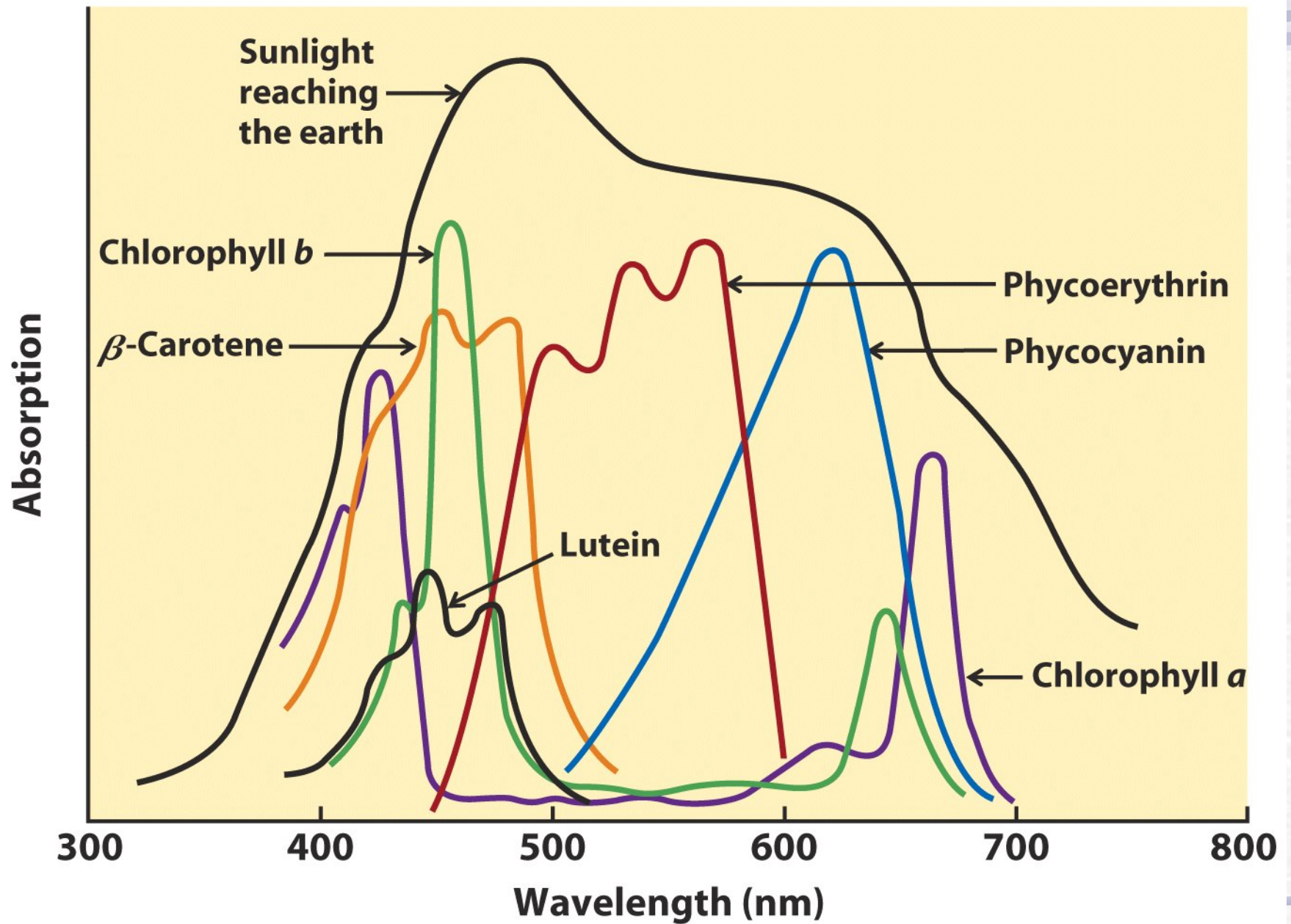
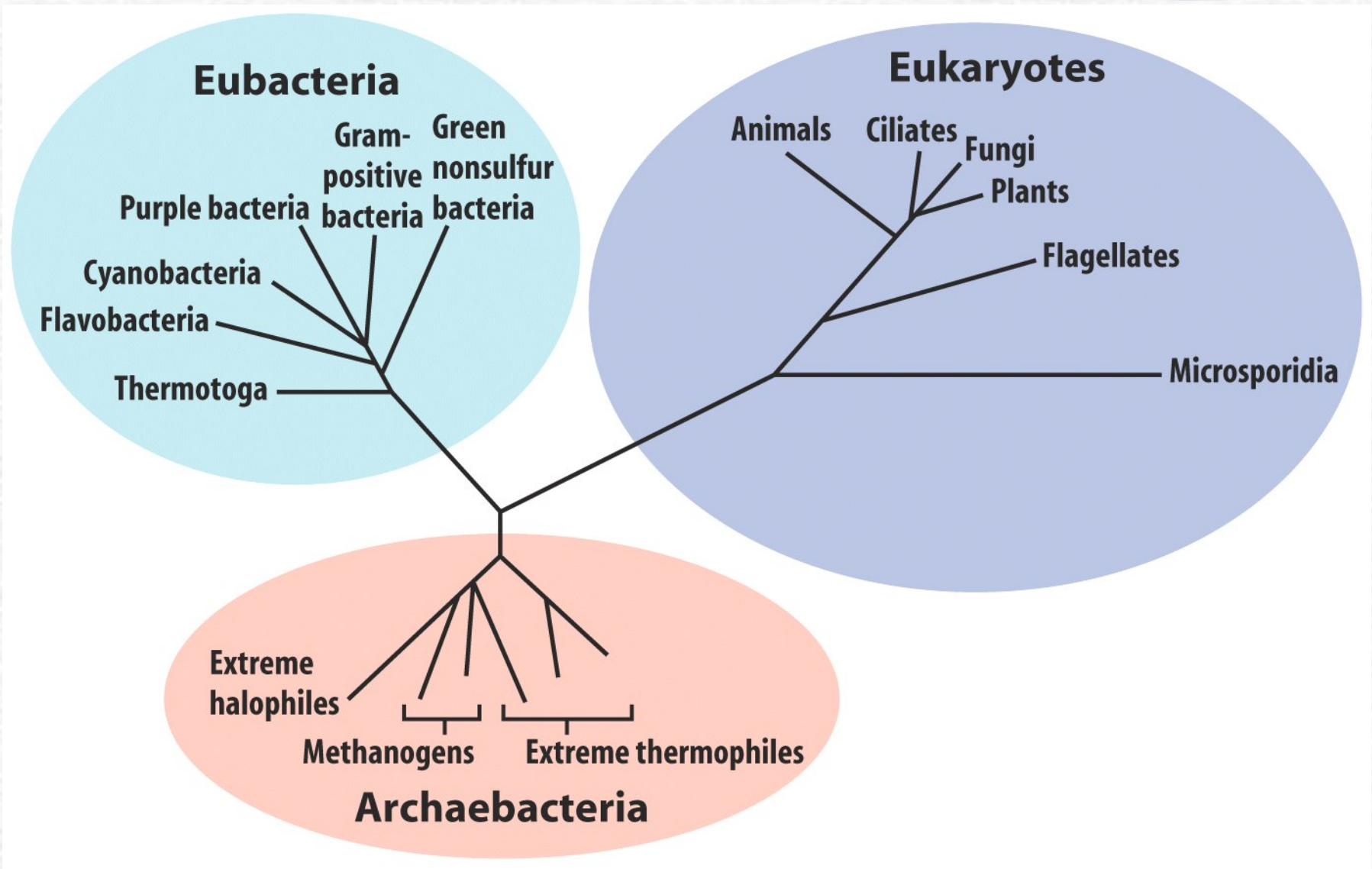


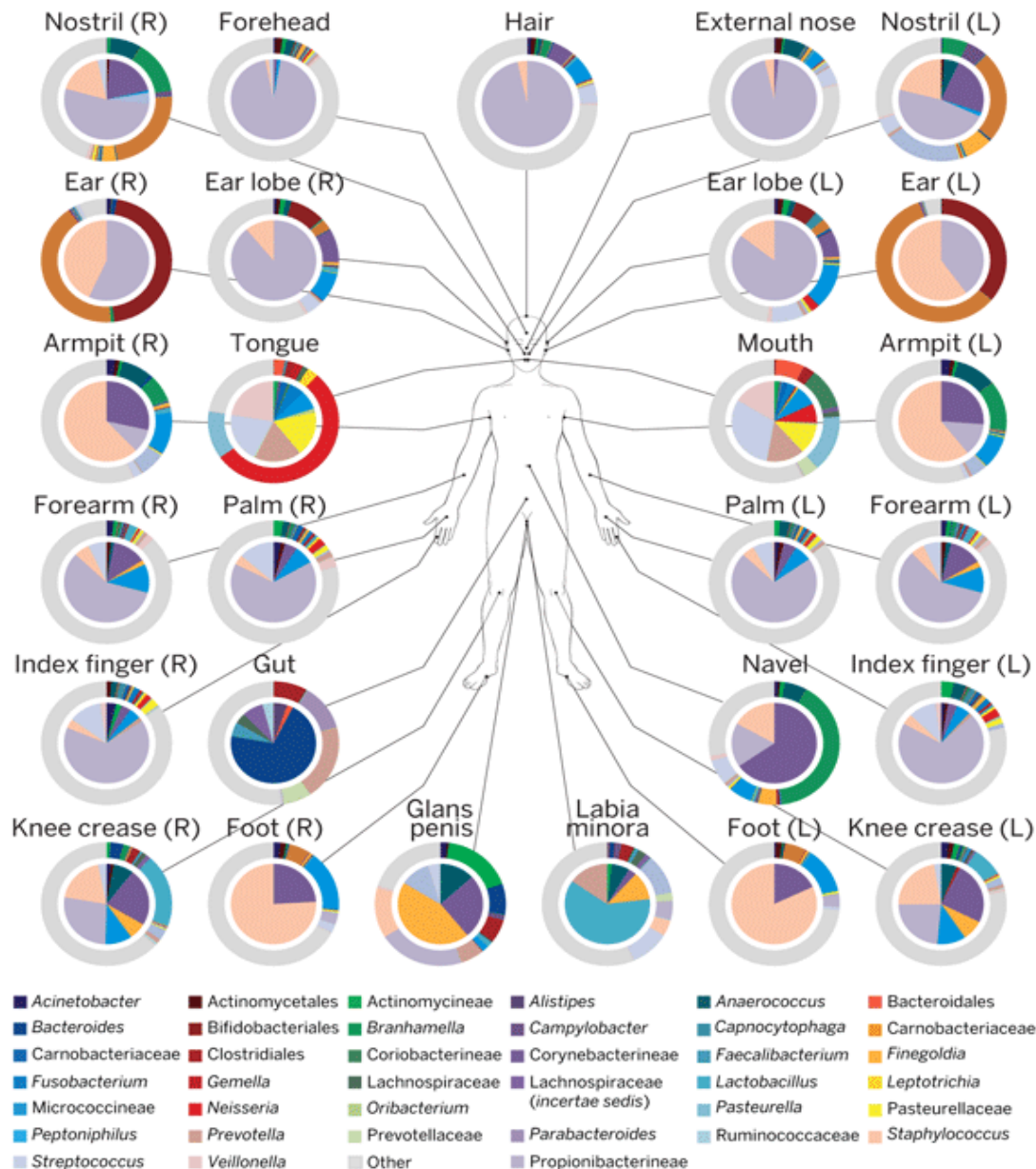
TABLE 1-1 Strengths of Bonds Common in Biomolecules

Type of bond	Bond dissociation energy* (kJ/mol)	Type of bond	Bond dissociation energy (kJ/mol)
Single bonds		Double bonds	
O—H	470	C=O	712
H—H	435	C=N	615
P—O	419	C=C	611
C—H	414	P=O	502
N—H	389		
C—O	352	Triple bonds	
C—C	348	C≡C	816
S—H	339	N≡N	930
C—N	293		
C—S	260		
N—O	222		
S—S	214		

*The greater the energy required for bond dissociation (breakage), the stronger the bond.



MAP OF MICROBIOME In a survey of bacteria from 27 sites in nine healthy adults, researchers found that certain lineages of bacteria were common to all subjects (represented in the inner circles), whereas many more bacterial lineages were found in some people but not others (represented in the outer circles).



Microbes co-inhabiting our bodies outnumber human cells by a factor of 10.

They account for 90% of all protein-encoding cells

They protect us from pathogens, synthesize essential vitamins, enzymes for digestion and contribute to such human factors as obesity, food digestion and pill metabolism.

Imbalances of microbes can result in auto-immune diseases such as Crohn's and skin disorders like eczema and psoriasis.



In the mouth, bacteria in saliva can be different from that on the teeth.

In fact, bacteria on one tooth may be different from the tooth next to it.



TABLE 1-3 Comparison of Prokaryotic and Eukaryotic Cells

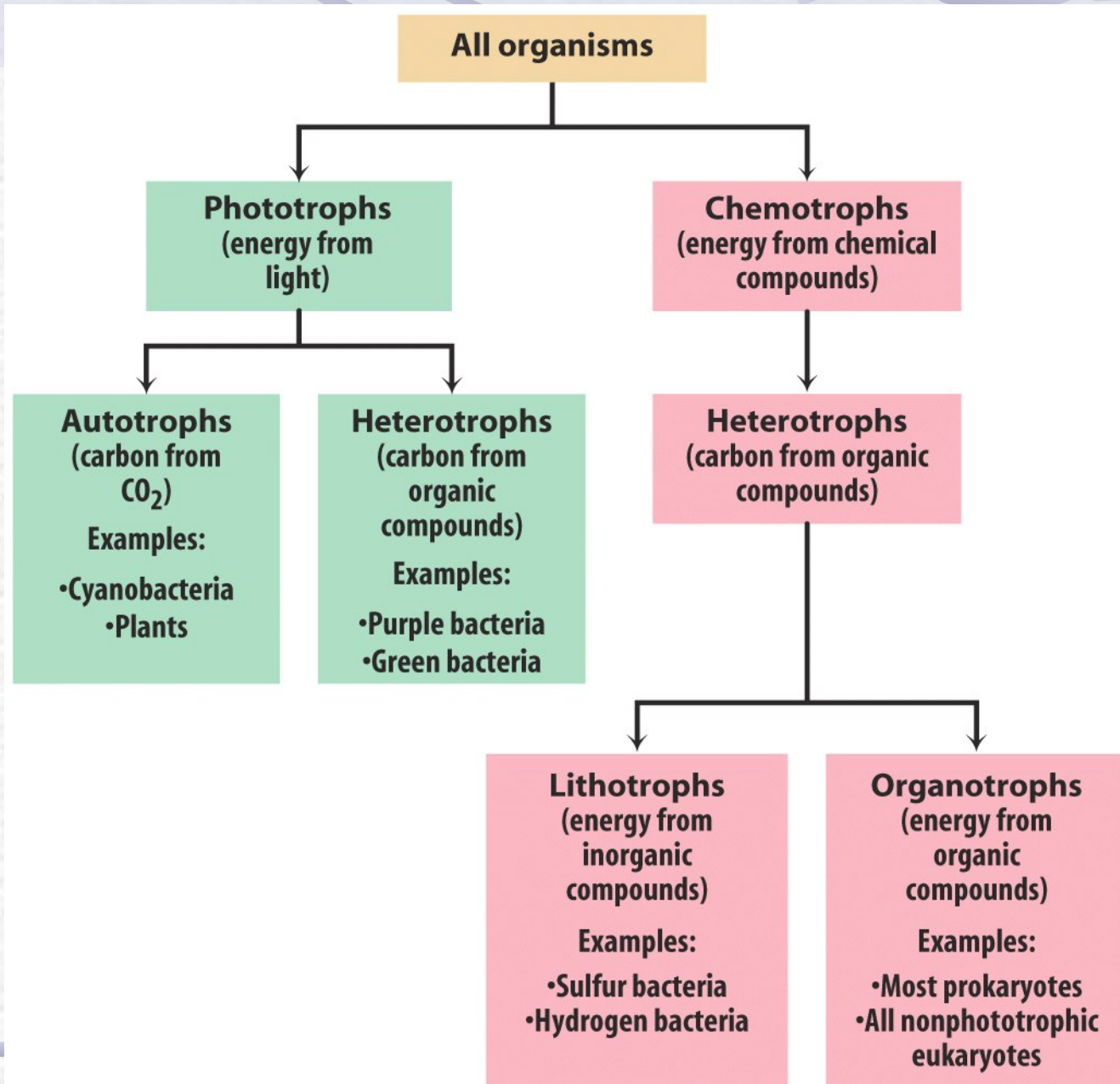
<i>Characteristic</i>	<i>Prokaryotic cell</i>	<i>Eukaryotic cell</i>
Size	Generally small (1–10 μm)	Generally large (5–100 μm)
Genome	DNA with nonhistone protein; genome in nucleoid, not surrounded by membrane	DNA complexed with histone and nonhistone proteins in chromosomes; chromosomes in nucleus with membranous envelope
Cell division	Fission or budding; no mitosis	Mitosis, including mitotic spindle; centrioles in many species
Membrane-bounded organelles	Absent	Mitochondria, chloroplasts (in plants, some algae), endoplasmic reticulum, Golgi complexes, lysosomes (in animals), etc.
Nutrition	Absorption; some photosynthesis	Absorption, ingestion; photosynthesis in some species
Energy metabolism	No mitochondria; oxidative enzymes bound to plasma membrane; great variation in metabolic pattern	Oxidative enzymes packaged in mitochondria; more unified pattern of oxidative metabolism
Cytoskeleton	None	Complex, with microtubules, intermediate filaments, actin filaments
Intracellular movement	None	Cytoplasmic streaming, endocytosis, phagocytosis, mitosis, vesicle transport

Table 13-1. Metabolic Functions of Eukaryotic Organelles

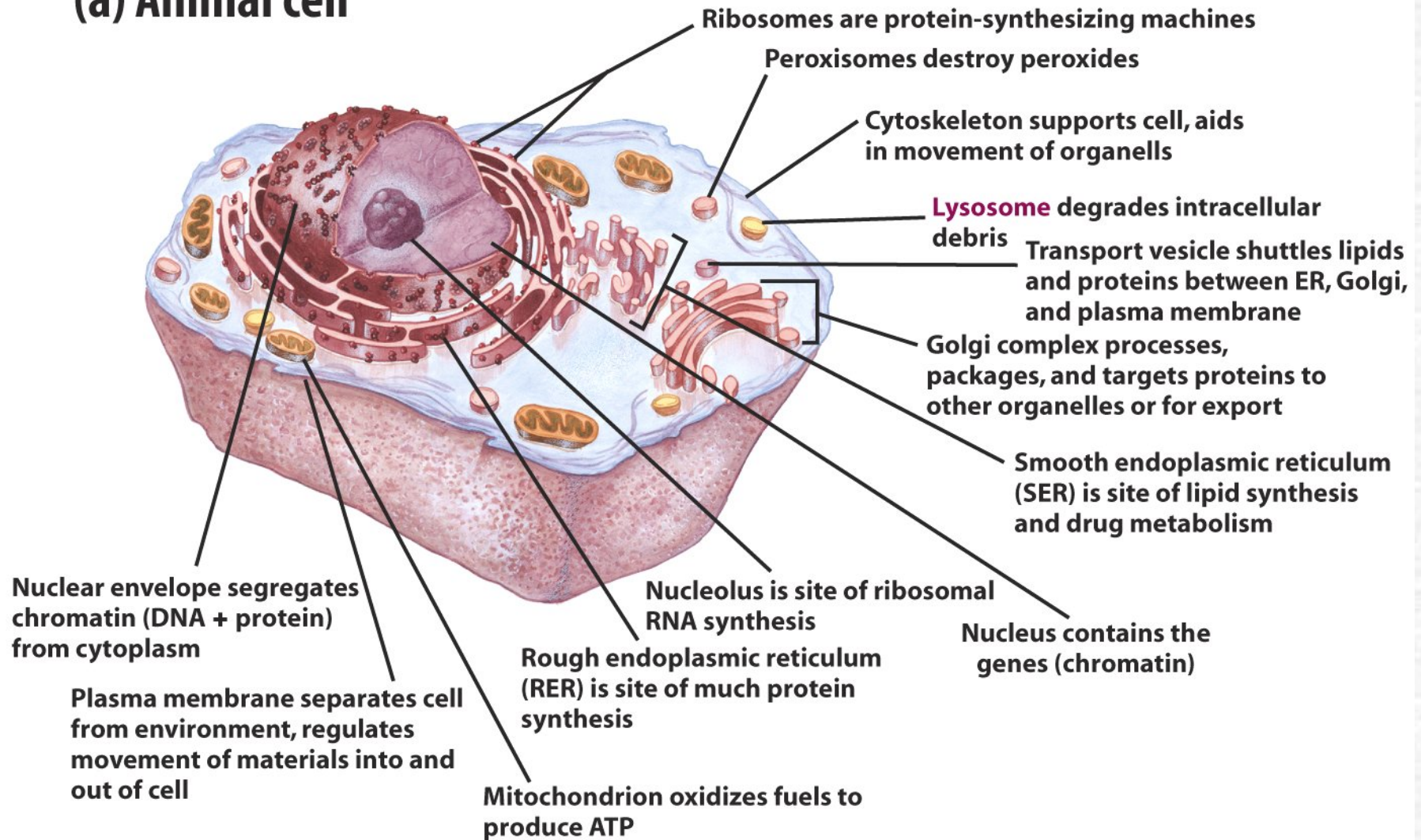
<i>Organelle</i>	<i>Function</i>
Mitochondrion	Citric acid cycle, oxidative phosphorylation, fatty acid oxidation, amino acid breakdown
Cytosol	Glycolysis, pentose phosphate pathway, fatty acid biosynthesis, many reactions of gluconeogenesis
Lysosomes	Enzymatic digestion of cell components and ingested matter
Nucleus	DNA replication and transcription, RNA processing
Golgi apparatus	Posttranslational processing of membrane and secretory proteins; formation of plasma membrane and secretory vesicles
Rough endoplasmic reticulum	Synthesis of membrane-bound and secretory proteins
Smooth endoplasmic reticulum	Lipid and steroid biosynthesis
Peroxisomes (glyoxysomes in plants)	Oxidative reactions catalyzed by amino acid oxidases and catalase; glyoxylate cycle reactions in plants

TABLE 1-2 **Molecular Components of an
E. coli Cell**

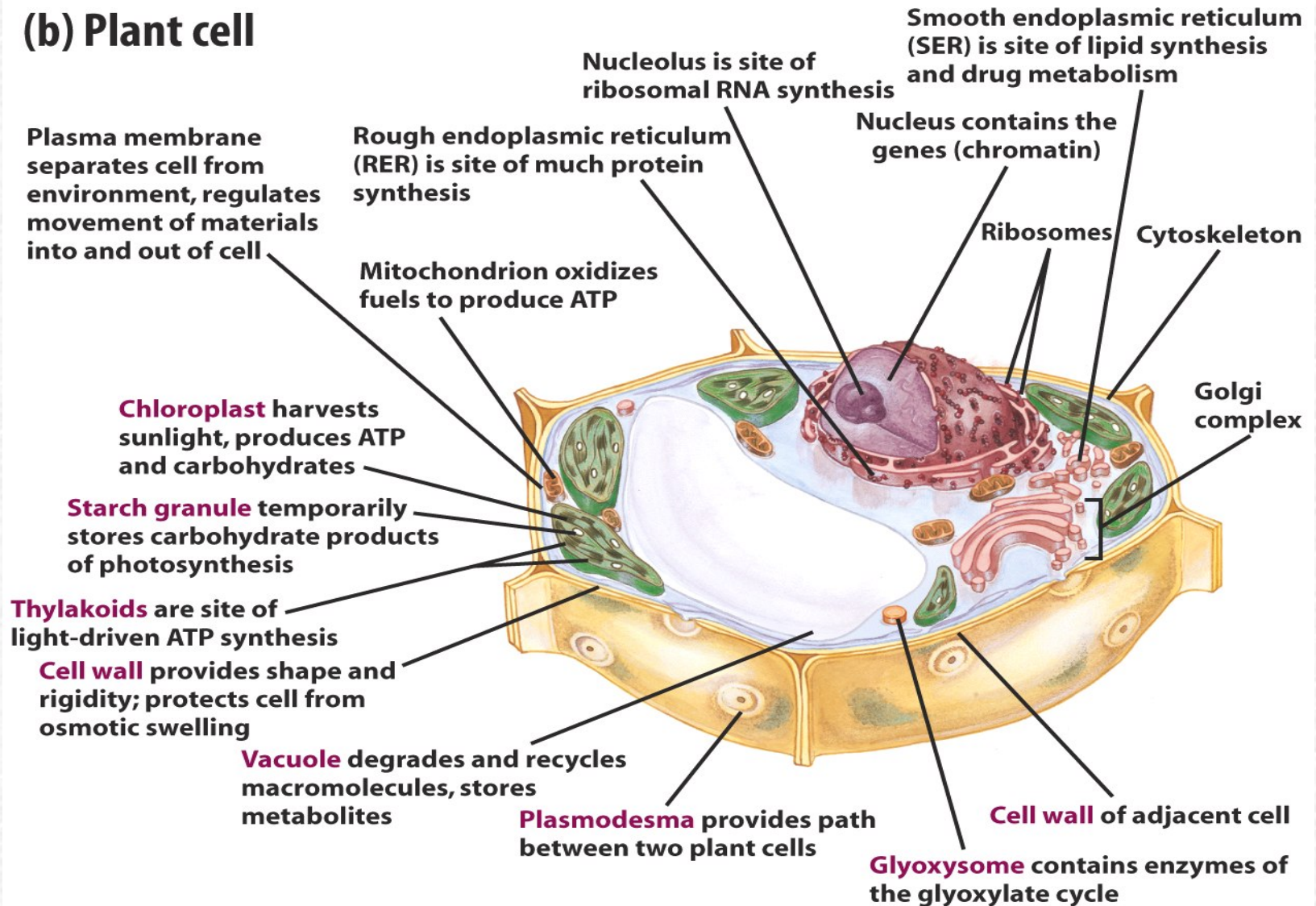
	<i>Percentage of total weight of cell</i>	<i>Approximate number of different molecular species</i>
Water	70	1
Proteins	15	3,000
Nucleic acids		
DNA	1	1
RNA	6	>3,000
Polysaccharides	3	5
Lipids	2	20
Monomeric subunits and intermediates	2	500
Inorganic ions	1	20

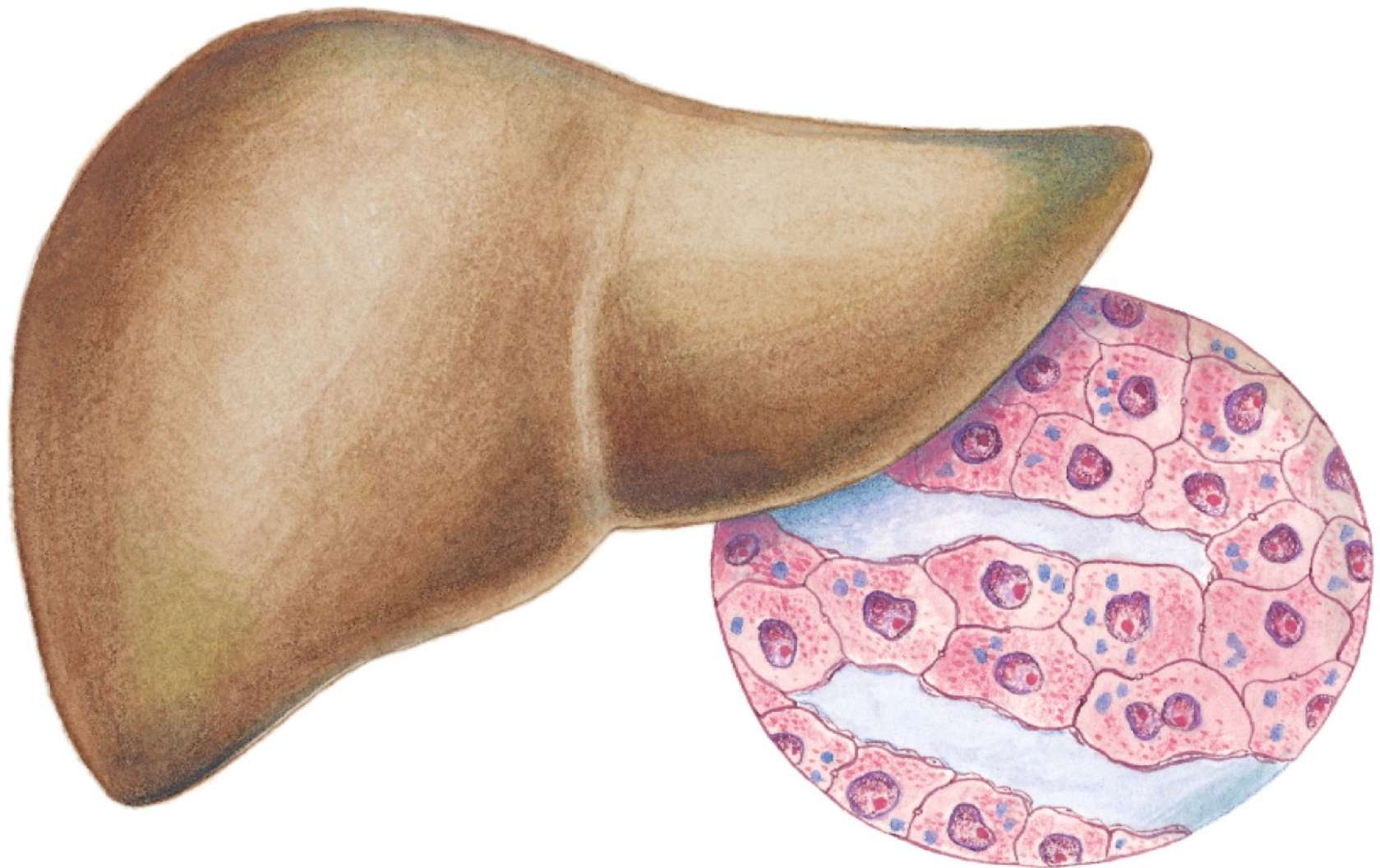


(a) Animal cell



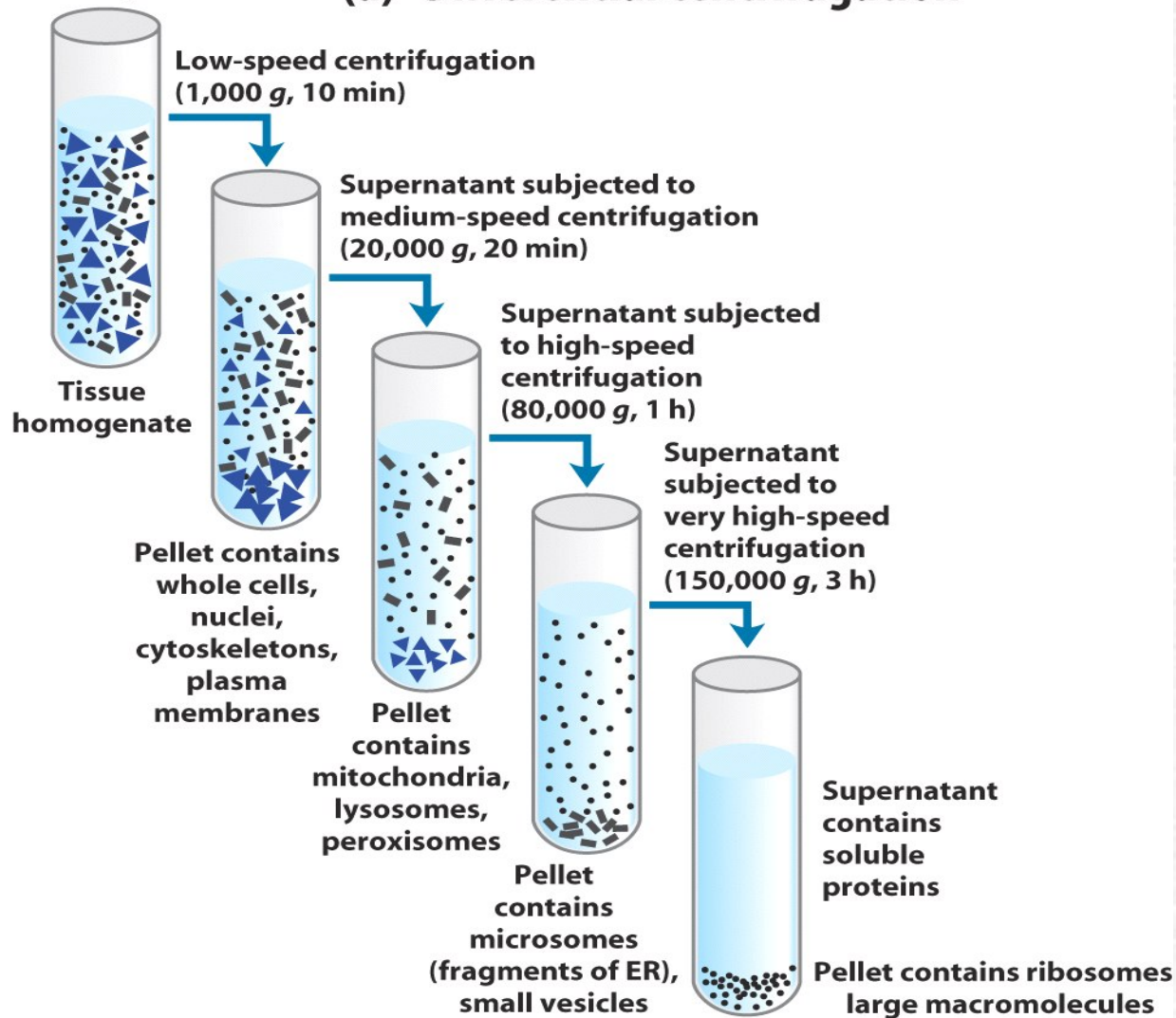
(b) Plant cell



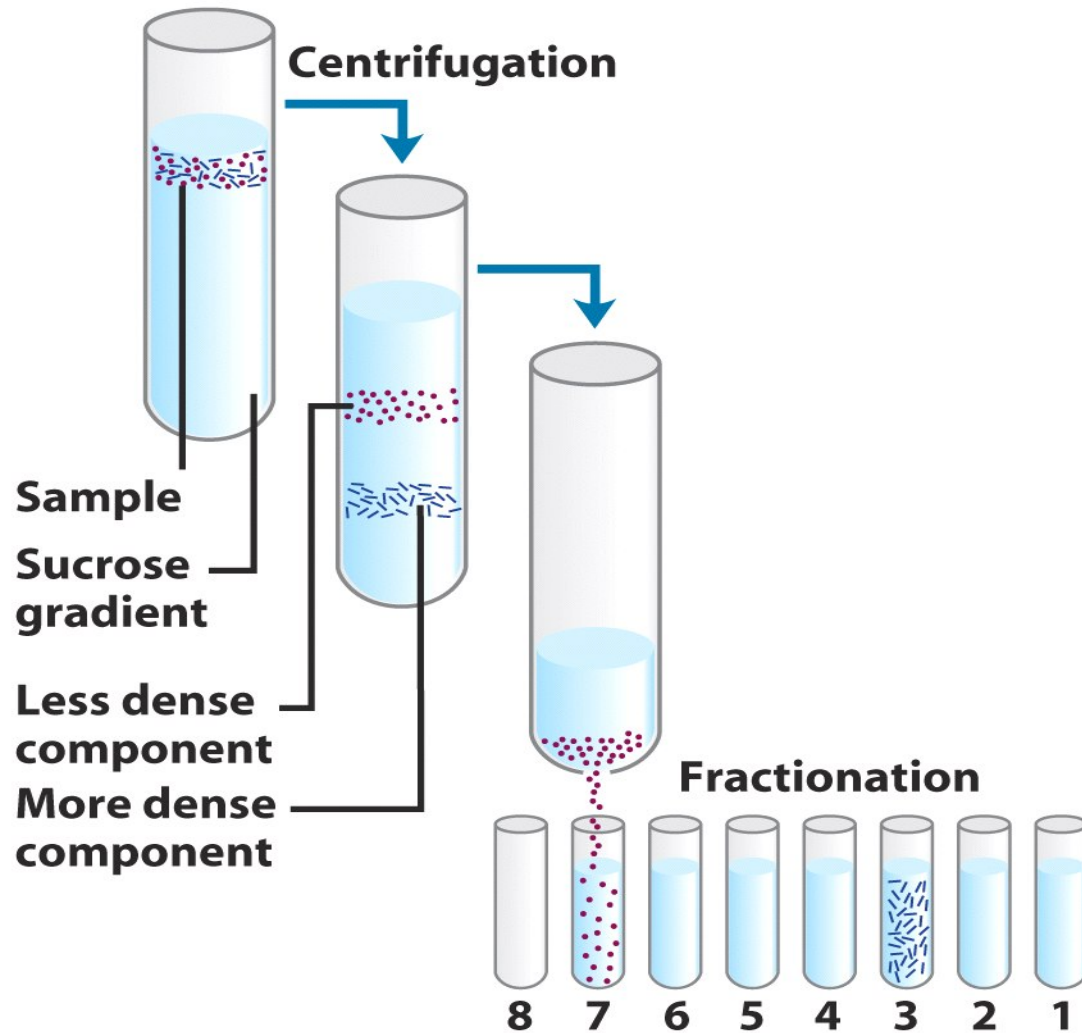


Tissue homogenization

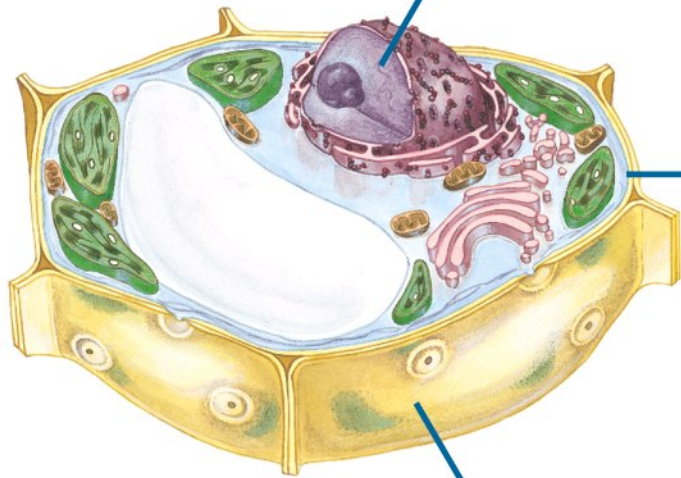
(a) Differential centrifugation



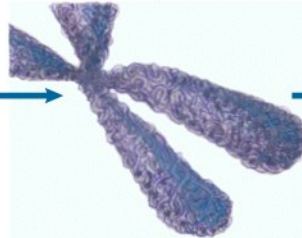
(b) Isopycnic (sucrose-density) centrifugation



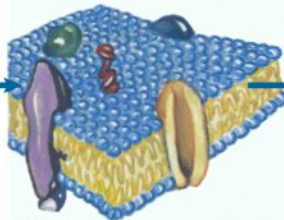
**Level 4:
The cell
and its organelles**



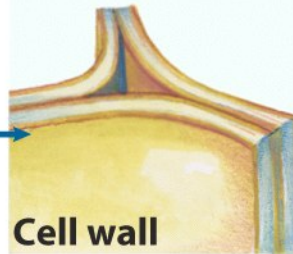
**Level 3:
Supramolecular
complexes**



Chromosome

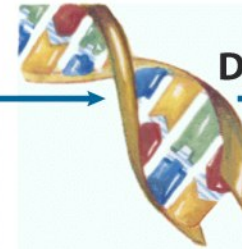


Plasma membrane



Cell wall

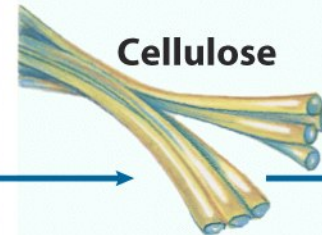
**Level 2:
Macromolecules**



DNA

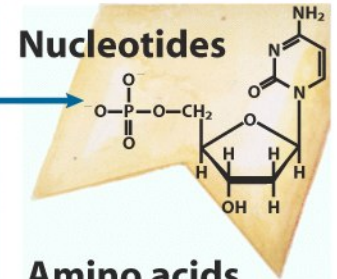


Protein

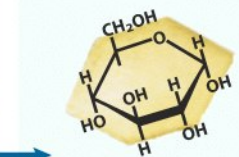
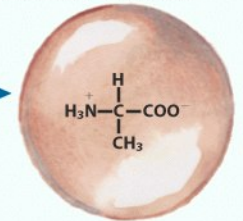


Cellulose

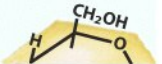
**Level 1:
Monomeric units**



Amino acids



Sugars



Grown in Arsenic

Researchers isolated arsenic-tolerant bacteria from Mono Lake, an ancient and alkaline California lake. The bacteria were gradually starved of phosphorus, an element thought to be essential for life, and fed more and more arsenic. Over time the bacteria began to grow and multiply by replacing the phosphorus in their bodies with arsenic atoms.

At right, images of several normal and arsenic-grown bacteria. The arsenic-grown microbes appear larger because the extra arsenic seems to make them grow empty internal spaces.

At right, images of two individual microbes. The researchers used radioactive tracers to detect the relative amounts of phosphorus and arsenic in each bacterium.

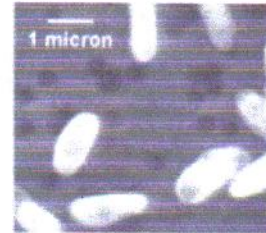
The normal bacterium has high levels of phosphorus, while the arsenic-grown one has almost none.

Amount of phosphorus
None High

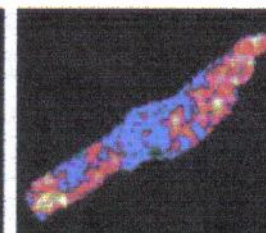
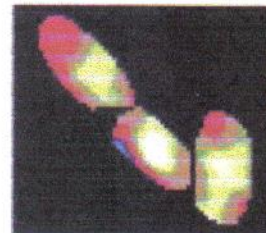
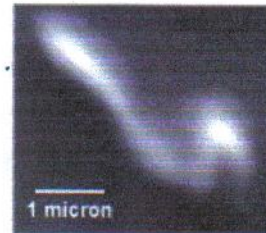
The normal bacterium also has low levels of arsenic, while the arsenic-grown one has much higher levels.

Amount of arsenic
None High

NORMAL BACTERIA



ARSENIC-GROWN



Source: Science

THE NEW YORK TIMES; IMAGES BY SCIENCE

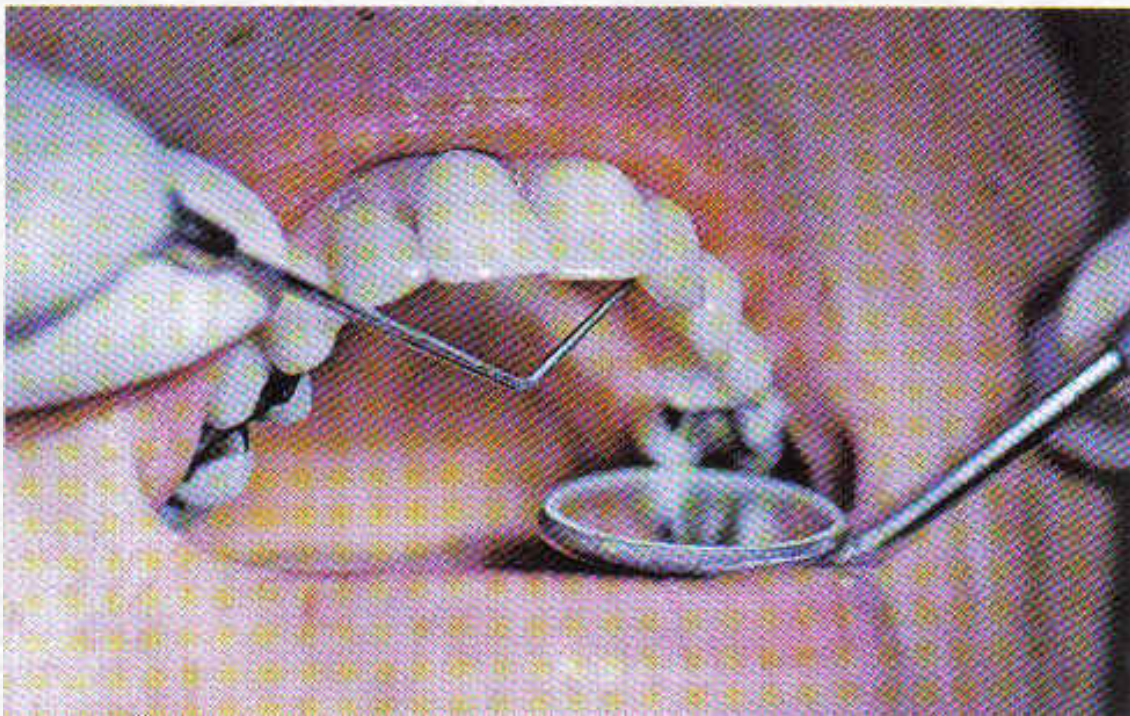
RECOMMEND

Six elements are the most essential for life: C, H, O, N, P, S
A microbe in California can substitute As for P as part of DNA

1 H																	2 He		
3 Li	4 Be													5 B	6 C	7 N	8 O	9 F	10 Ne
11 Na	12 Mg													13 Al	14 Si	15 P	16 S	17 Cl	18 Ar
19 K	20 Ca	21 Sc	22 Ti	23 V	24 Cr	25 Mn	26 Fe	27 Co	28 Ni	29 Cu	30 Zn	31 Ga	32 Ge	33 As	34 Se	35 Br	36 Kr		
37 Rb	38 Sr	39 Y	40 Zr	41 Nb	42 Mo	43 Tc	44 Ru	45 Rh	46 Pd	47 Ag	48 Cd	49 In	50 Sn	51 Sb	52 Te	53 I	54 Xe		
55 Cs	56 Ba		72 Hf	73 Ta	74 W	75 Re	76 Os	77 Ir	78 Pt	79 Au	80 Hg	81 Tl	82 Pb	83 Bi	84 Po	85 At	86 Rn		
87 Fr	88 Ra		Lanthanides Actinides																

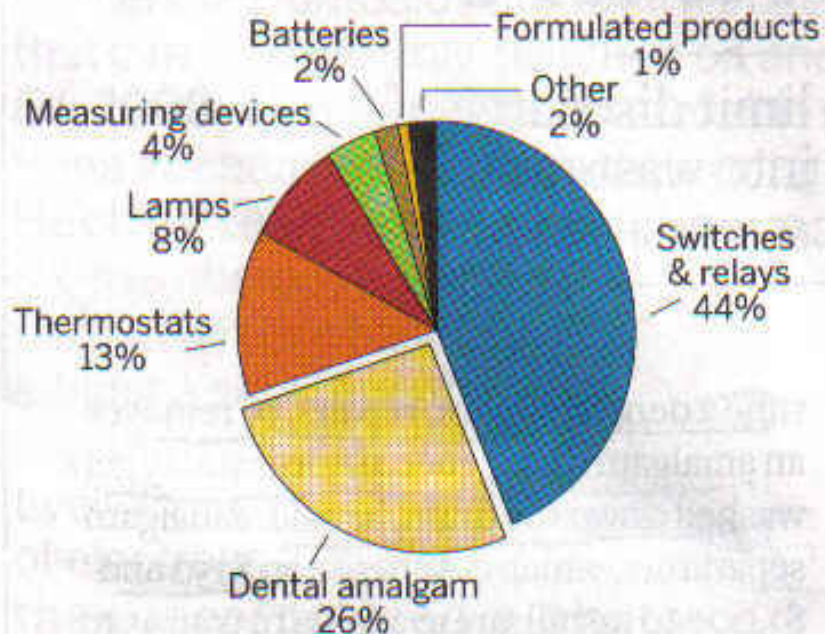
Bulk elements
 Trace elements

Hg- Americans are walking around with more than 1,000 tons of mercury in their mouths



MERCURY MARKET

More than a quarter of mercury is used in dental amalgams



2004 U.S. demand = 234,268 lb


SOURCE: "Trends in Mercury Use in Products," June 2008, Northeast Waste Management Officials' Association

Amalgam separators are available for between \$750 and \$3,000 which can trap about 95 – 99% of Hg in drain wash but most states do not require them.

Ultimate Disposal of Mercury in Teeth (what happens to fillings in cremated corpses?)

Crematoria in Europe must filter Hg released from dental amalgams; In the US the EPA does not regulate Hg emissions from smokestacks however about 6,600 # ' s (3.3 tons) of Hg were released into the environment in 2005.

This problem may last until about 2055 when Hg fillings fall out of use.

- 
- So if there may be a problem with amalgams, what other options are available?
 - Resin-based dental materials can be used but these commonly contain Bisphenol A (BPA) which can be intra-orally released from the biting surface of the teeth.
 - Children with higher cumulative exposure to BPA derivatives demonstrated impaired psychosocial behavior compared to children treated with amalgams. (Ref. Pediatrics 2011-3374)

➤ Lesson: BE AWARE of RISK OF FILLING TYPE

BIOMOLECULES

KEY TERMS

Functional Groups: Groups of atoms added to carbon skeletons, which confer specific properties in the molecule.

Stereoisomers - order of bonding is the same but special relationship between atoms is different.

Geometric (cis-trans) - differ in arrangement of substituent groups around double bond.

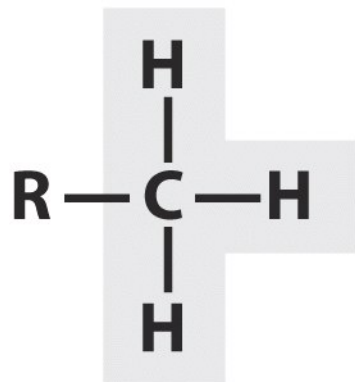
Chiral Center - Asymmetric carbon atom - i.e. 4 different substituents.

Enantiomers - mirror images

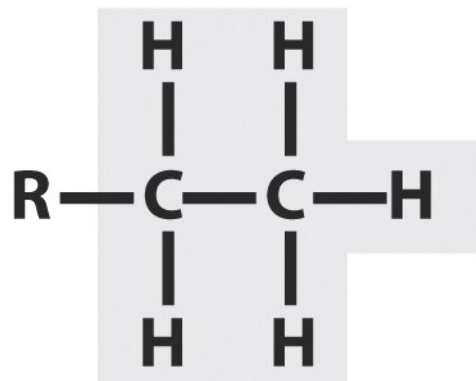
Diastereomers - non-mirror images

Racemic mixtures - no optical rotation

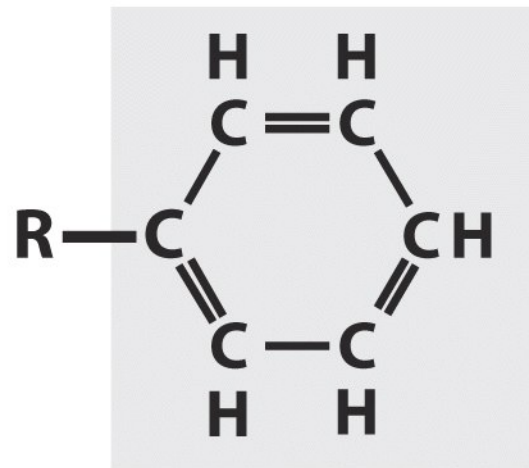
Methyl



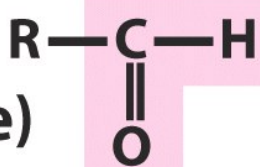
Ethyl



Phenyl



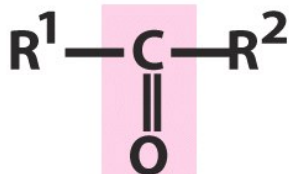
Carbonyl
(aldehyde)



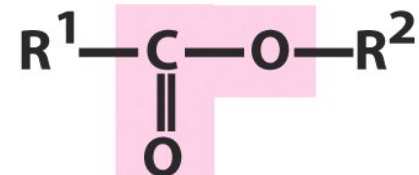
Ether



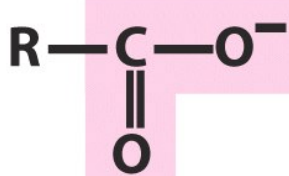
Carbonyl
(ketone)



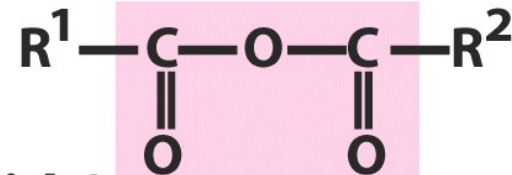
Ester



Carboxyl



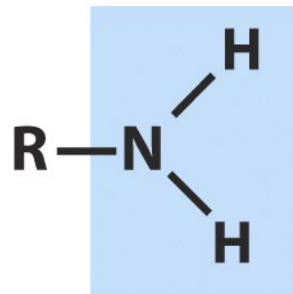
Anhydride
(two carboxylic acids)



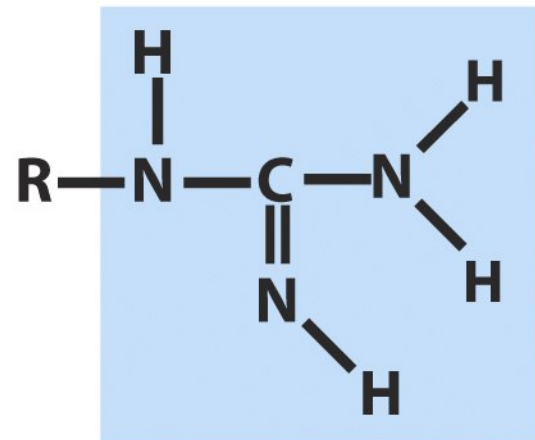
Hydroxyl
(alcohol)



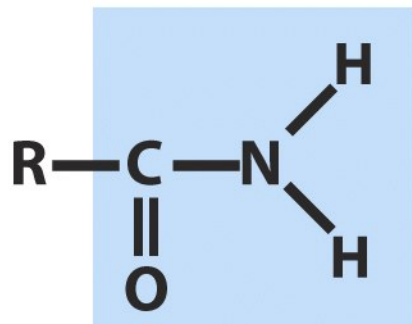
Amino



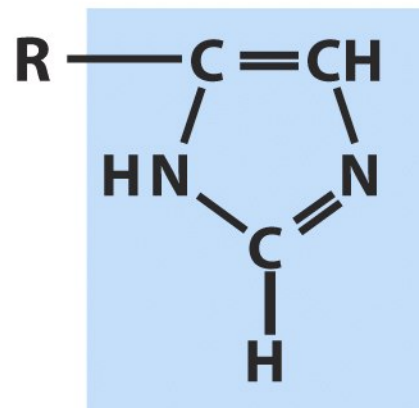
Guanidino



Amido



Imidazole



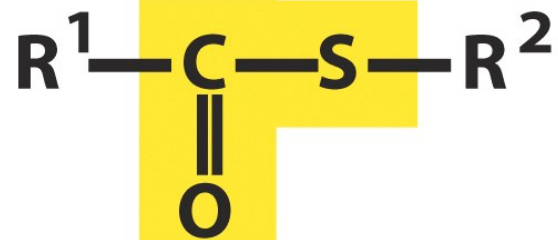
Sulfhydryl



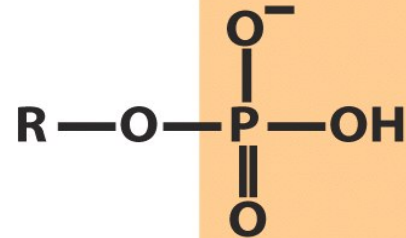
Disulfide



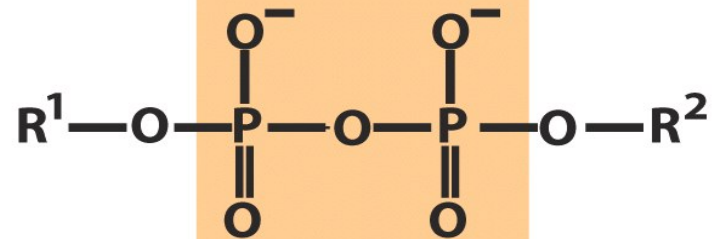
Thioester



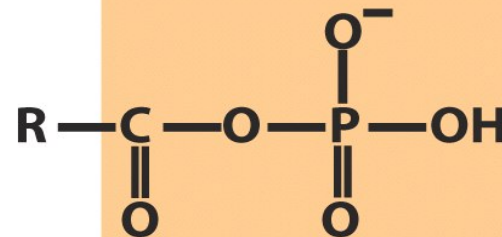
Phosphoryl



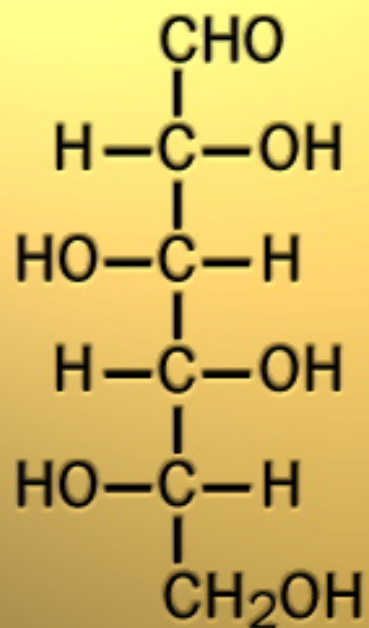
Phosphoanhydride



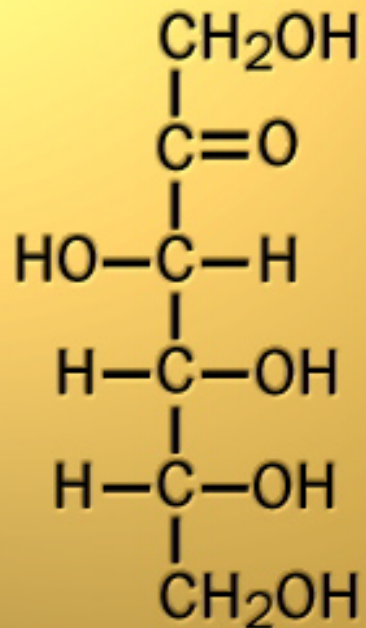
Mixed anhydride
(carboxylic acid and
phosphoric acid;
also called acyl phosphate)



Structural Isomers

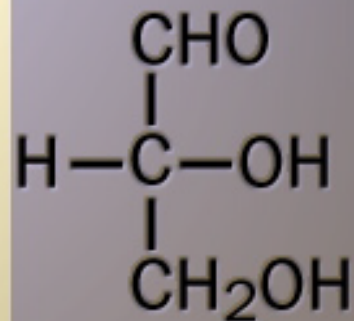


D-Glucose

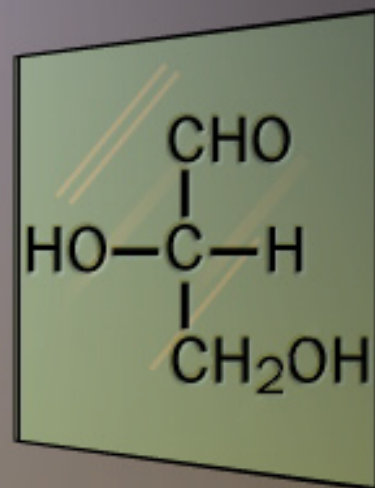


D-Fructose

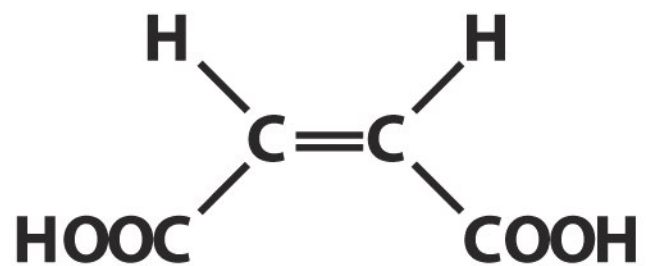
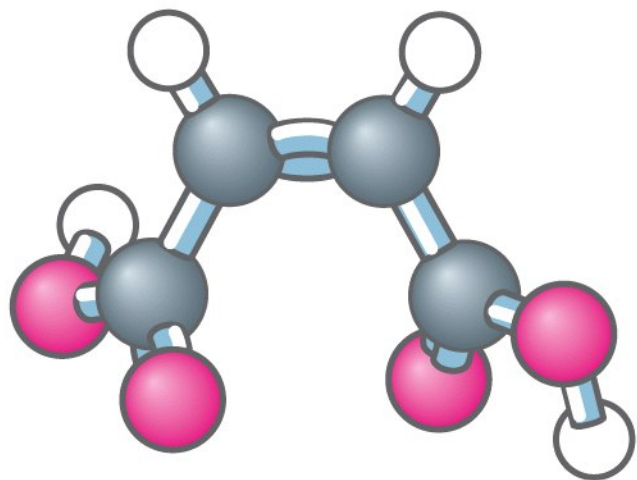
Optical Isomers (enantiomers)



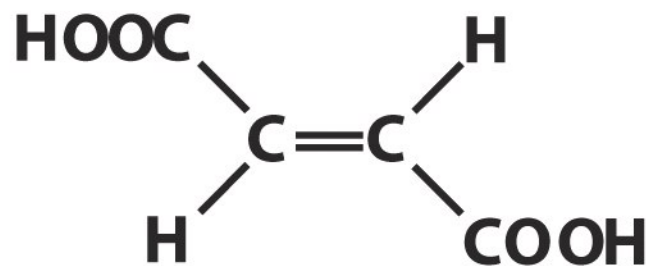
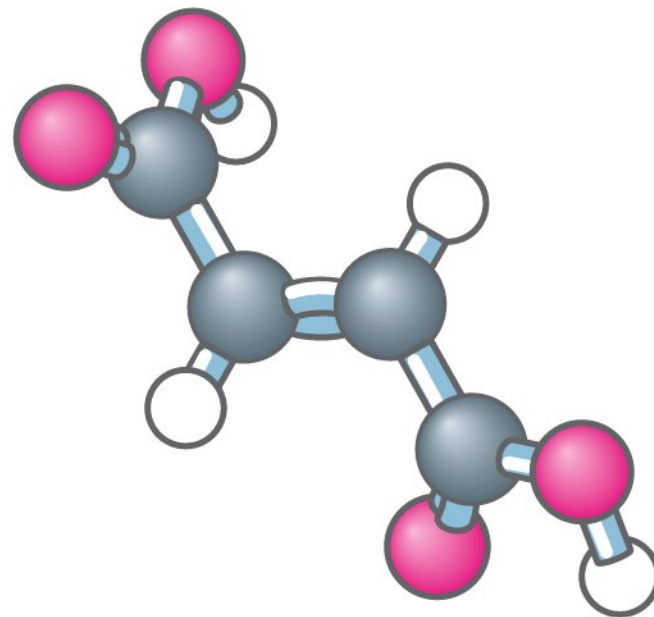
D-Glyceraldehyde



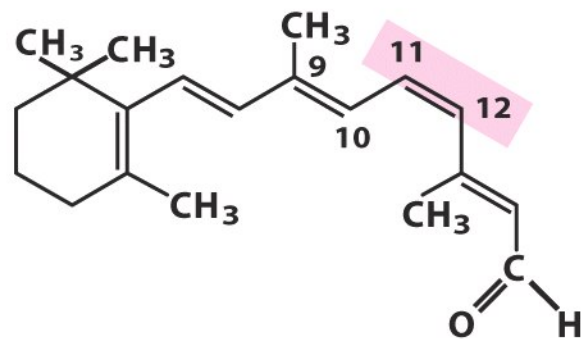
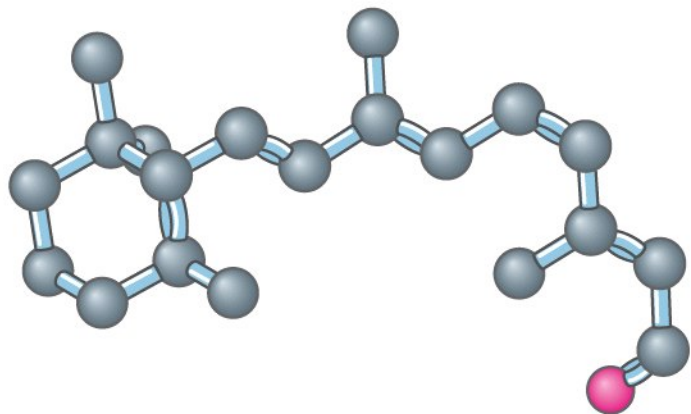
L-Glyceraldehyde



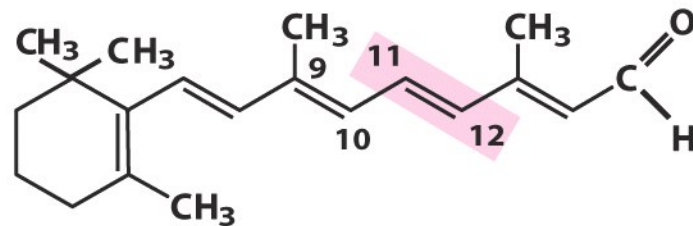
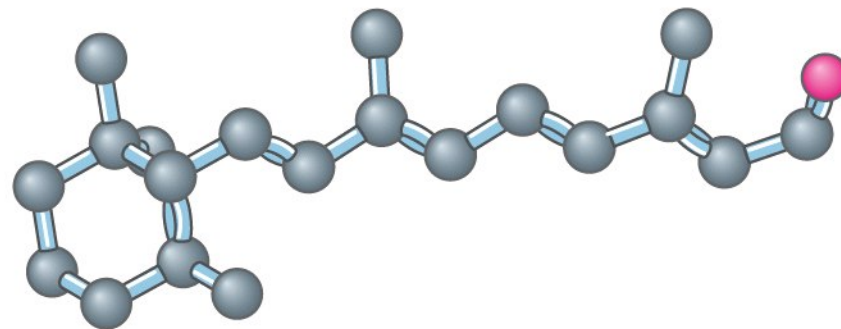
Maleic acid (cis)



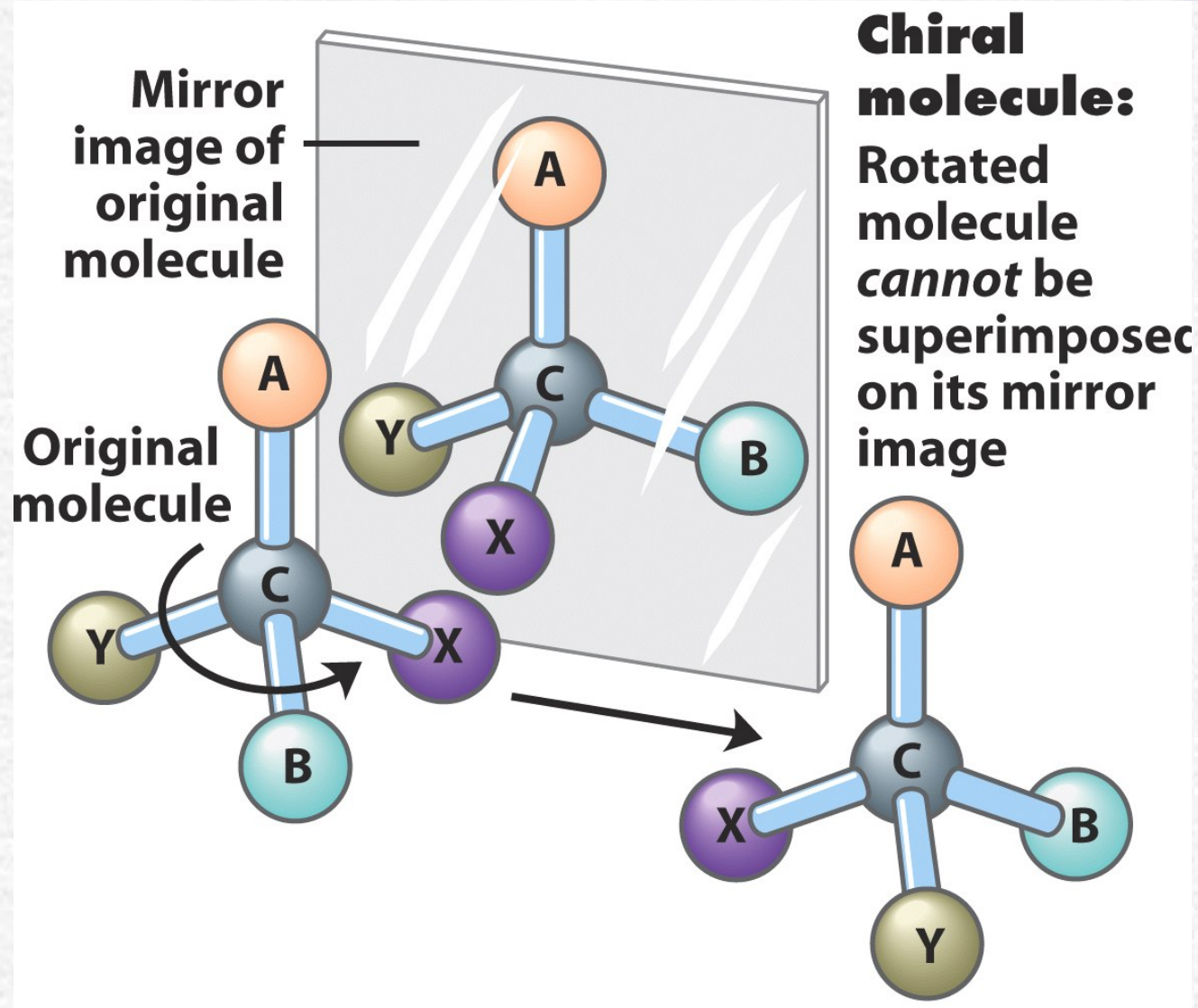
Fumaric acid (trans)

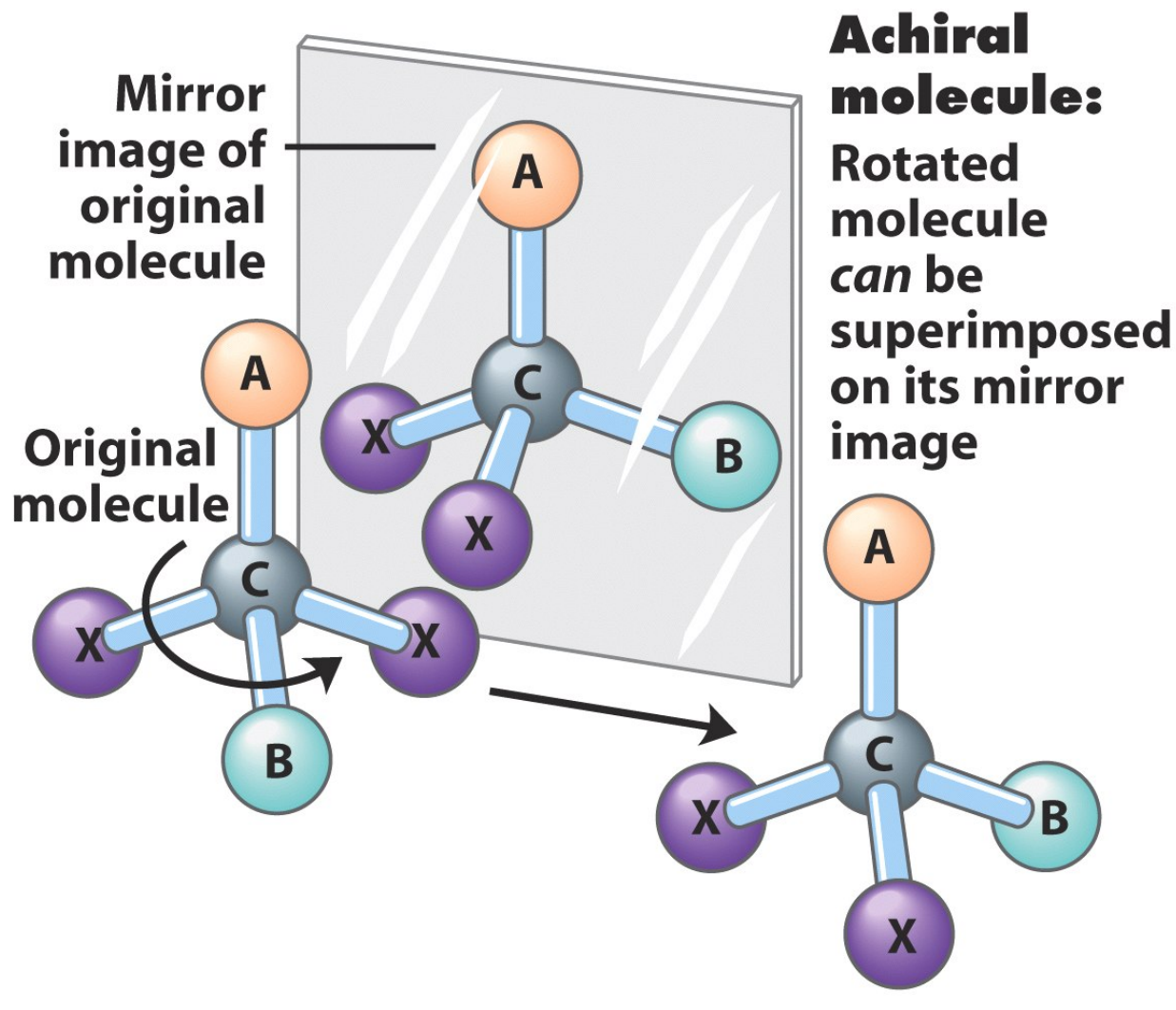


11-*cis*-Retinal

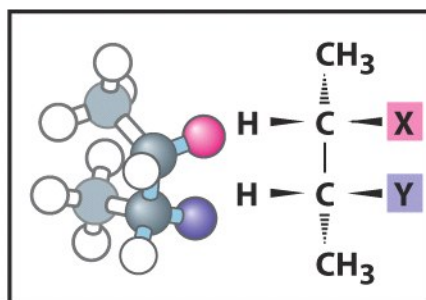
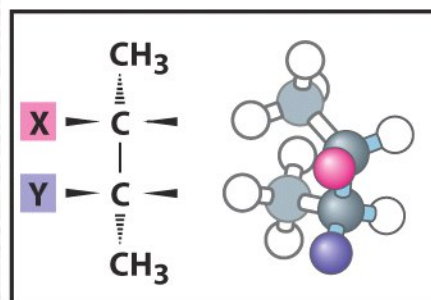


All-*trans*-Retinal

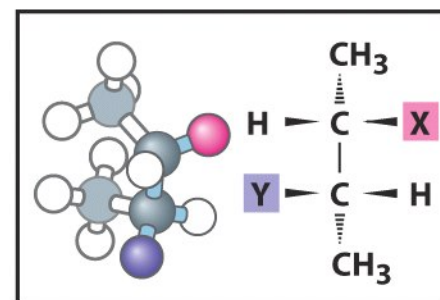
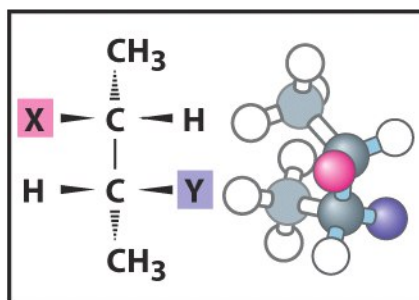




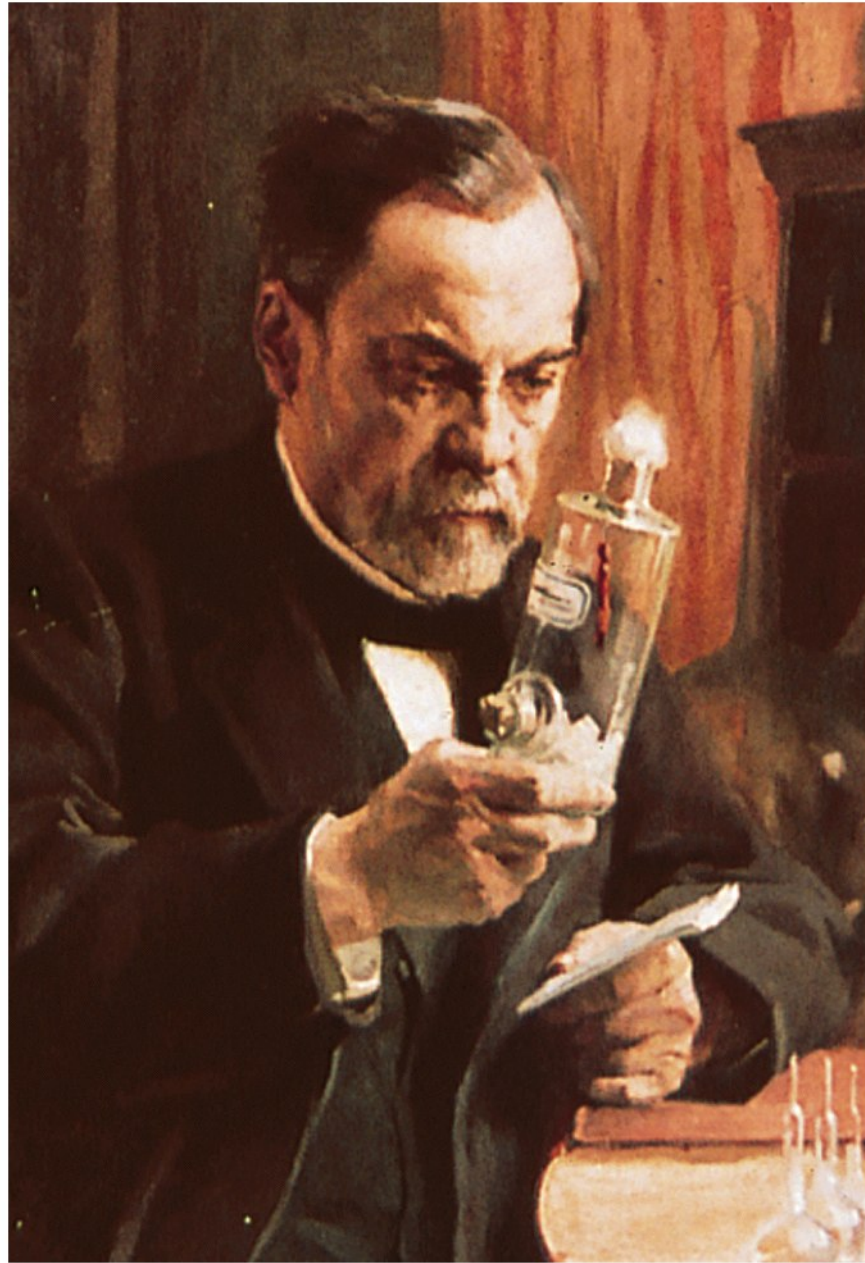
Enantiomers (mirror images)

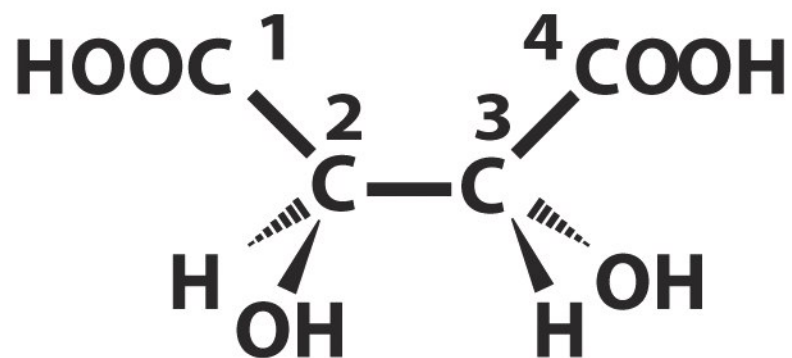


Enantiomers (mirror images)

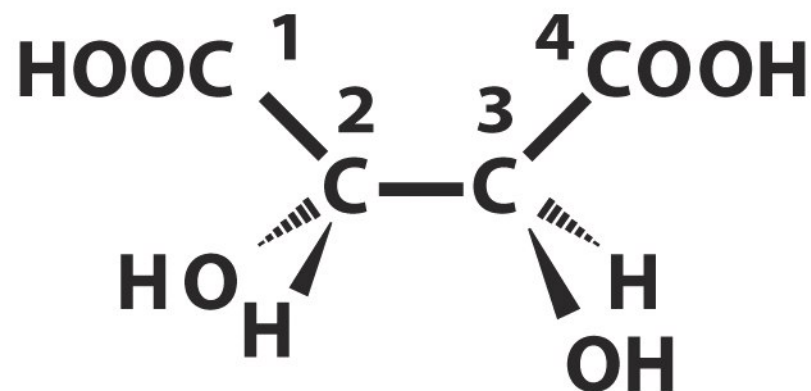


Diastereomers (non-mirror images)

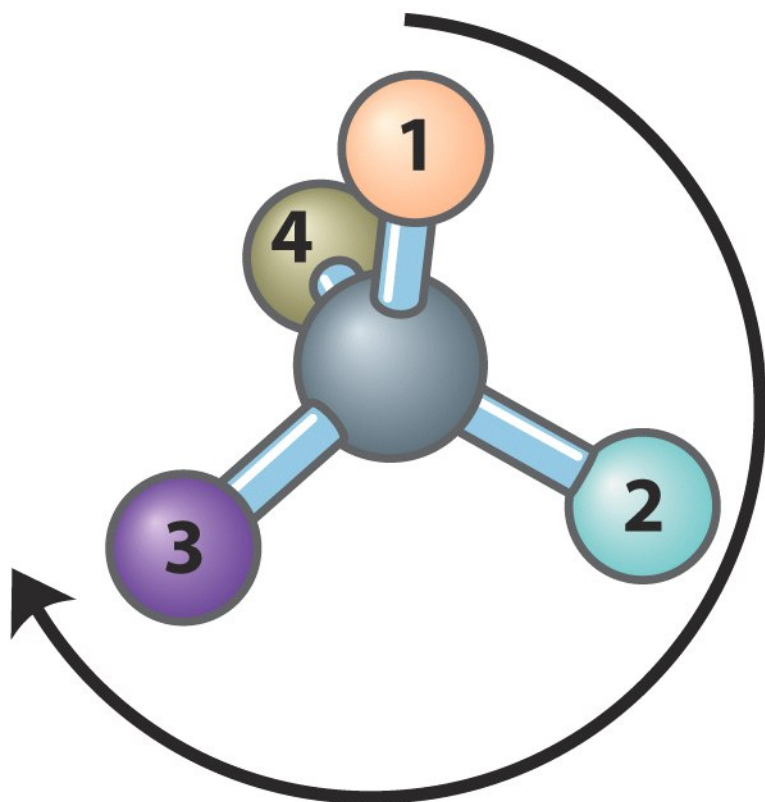




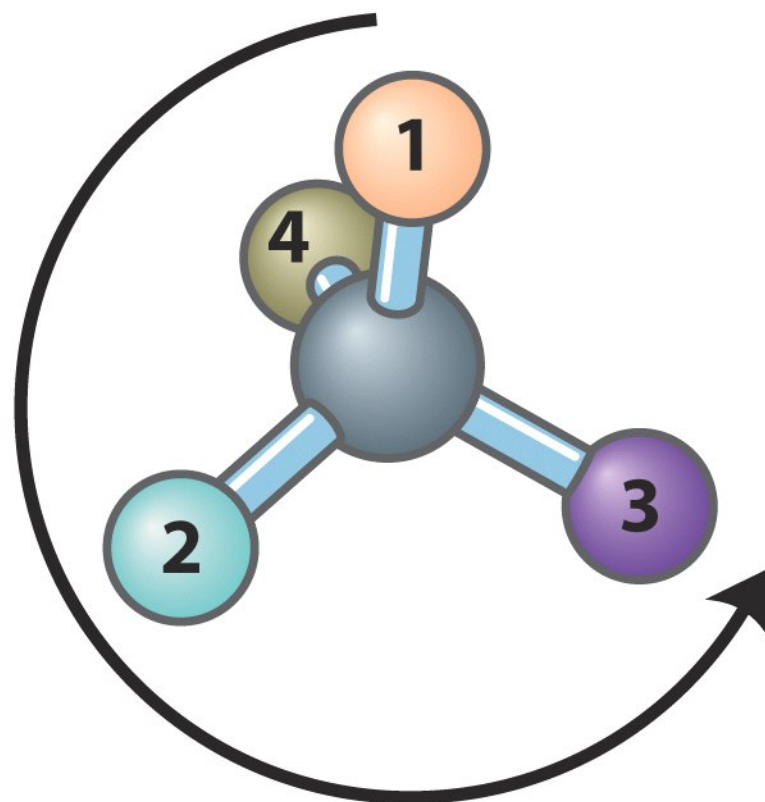
**(2R,3R)-Tartaric acid
(dextrorotatory)**



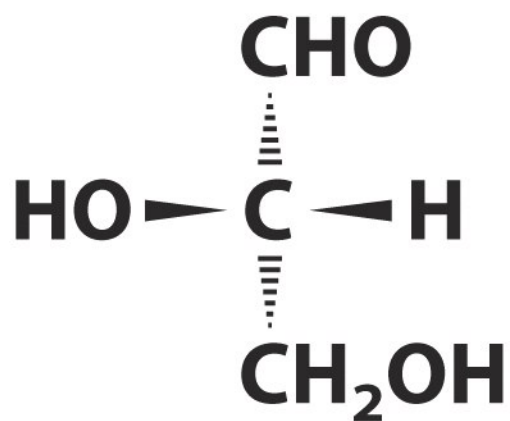
**(2S,3S)-Tartaric acid
(levorotatory)**



Clockwise
(*R*)

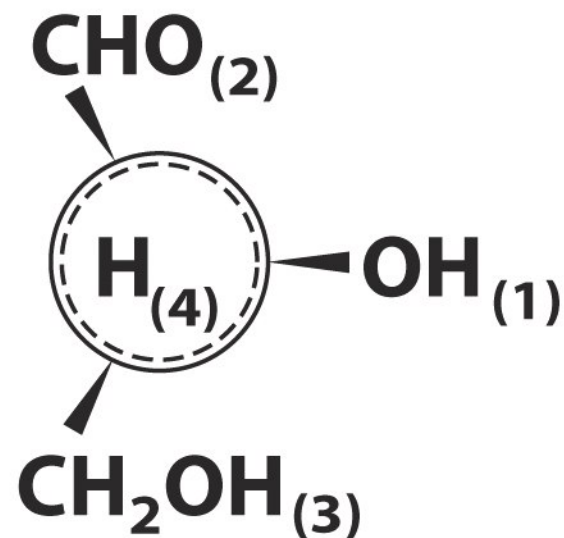


Counterclockwise
(*S*)

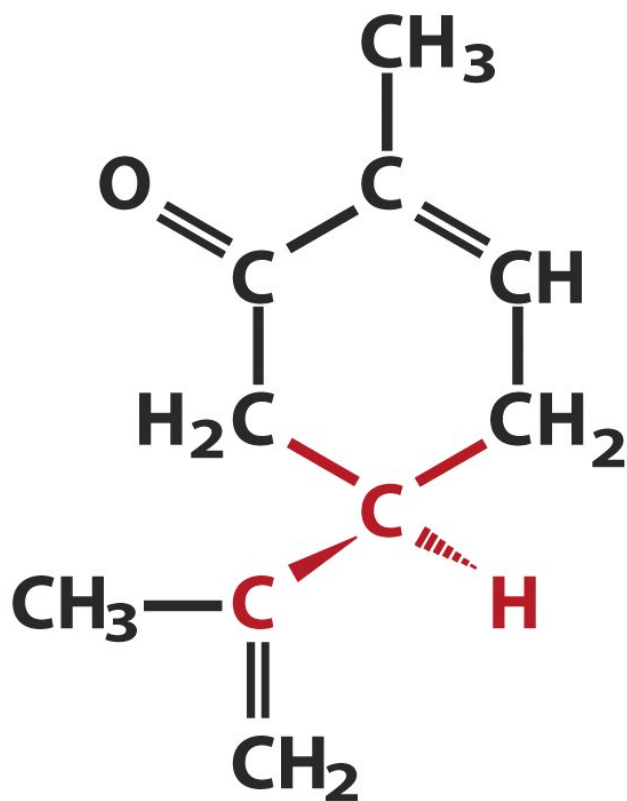


L-Glyceraldehyde

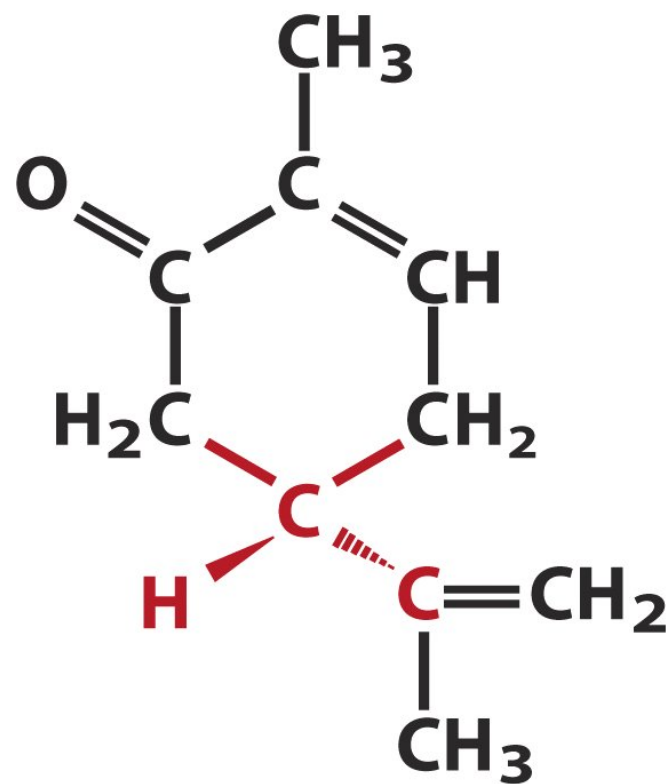
≡



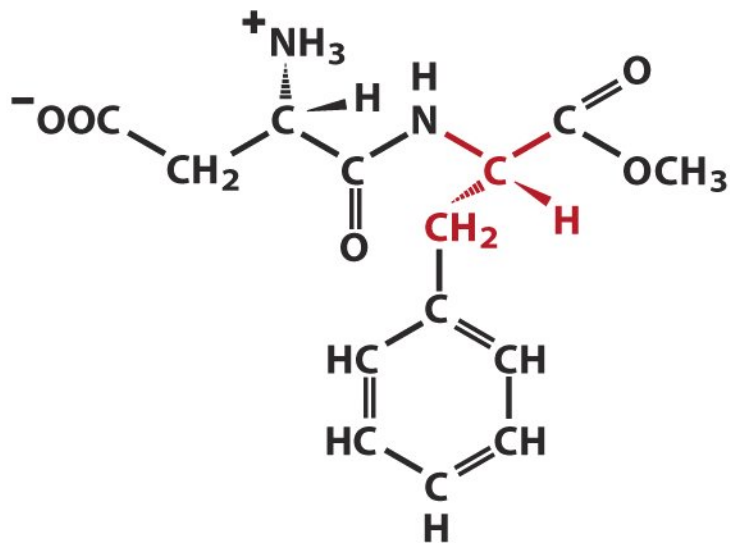
(S)-Glyceraldehyde



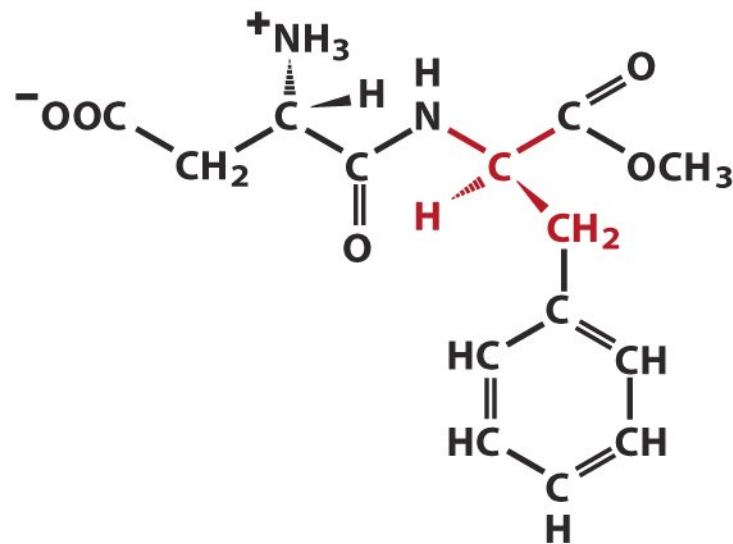
(R)-Carvone
(spearmint)



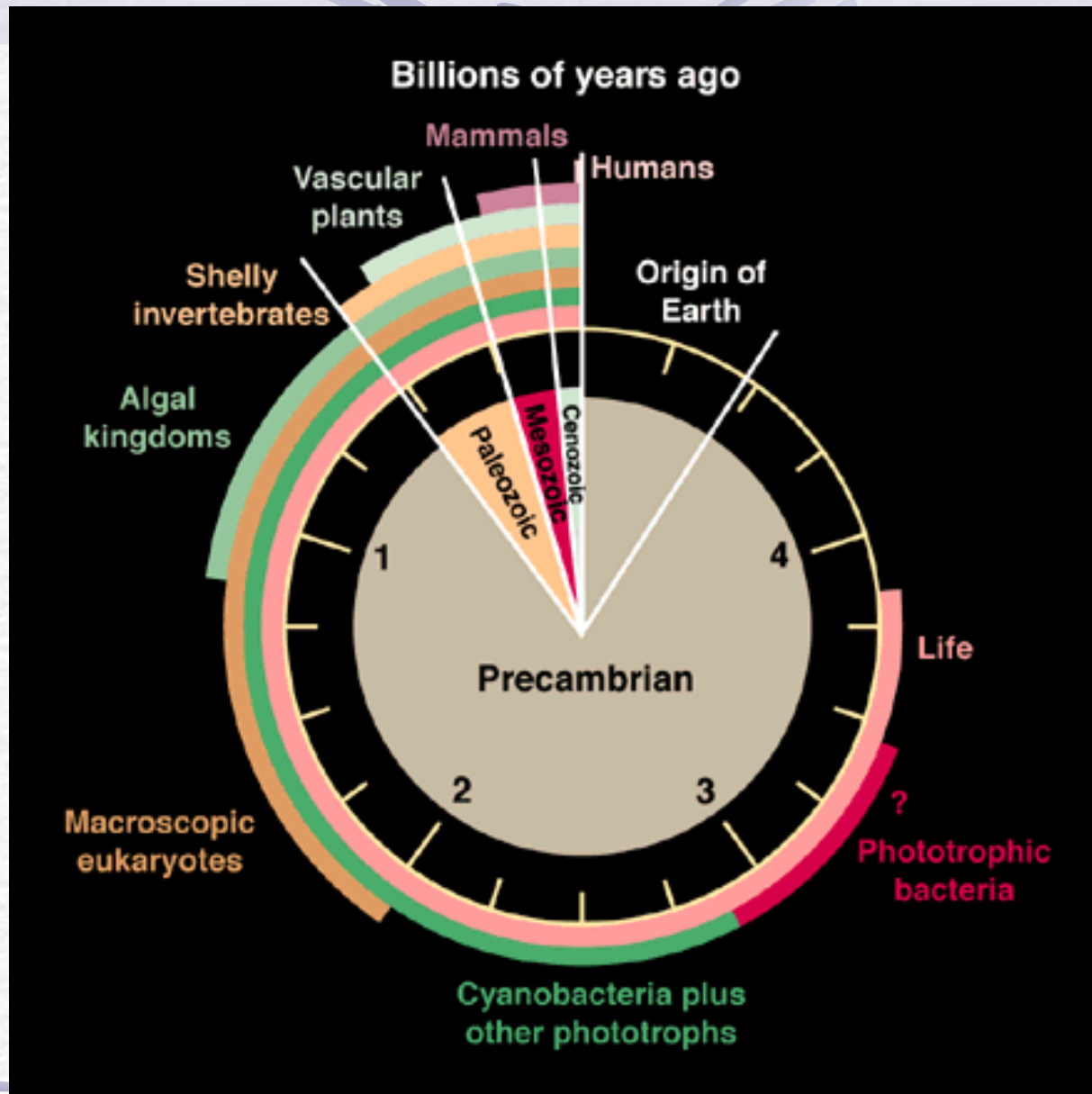
(S)-Carvone
(caraway)



L-Aspartyl-L-phenylalanine methyl ester
(aspartame) (sweet)



L-Aspartyl-D-phenylalanine methyl ester
(bitter)



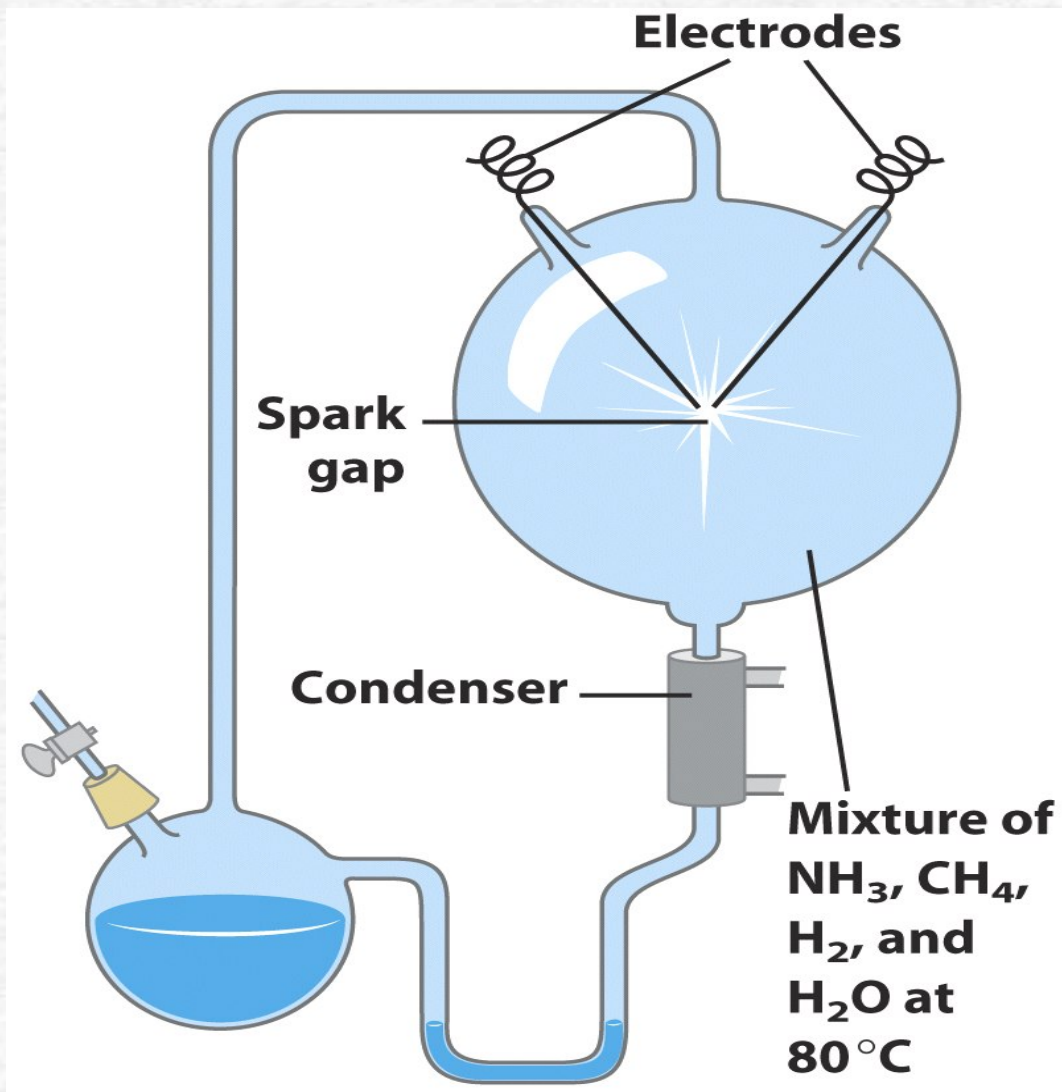


table 3-6

Some Products Formed under Prebiotic Conditions

Carboxylic acids	Nucleic acid bases	Amino acids	Sugars
Formic acid	Adenine	Glycine	Straight and branched pentoses and hexoses
Acetic acid	Guanine	Alanine	
Propionic acid	Xanthine	α -Aminobutyric acid	
Straight and branched fatty acids (C ₄ –C ₁₀)	Hypoxanthine	Valine	
Glycolic acid	Cytosine	Leucine	
Lactic acid	Uracil	Isoleucine	
Succinic acid		Proline	
		Aspartic acid	
		Glutamic acid	
		Serine	
		Threonine	

Source: From Miller, S.L. (1987) Which organic compounds could have occurred on the prebiotic earth? *Cold Spring Harb. Symp. Quant. Biol.* **52**, 17–27.

**Creation of prebiotic soup, including nucleotides,
from components of Earth's primitive atmosphere**



**Production of short RNA molecules
with random sequences**



**Selective replication of self-duplicating
catalytic RNA segments**



**Synthesis of specific peptides,
catalyzed by RNA**



**Increasing role of peptides in RNA replication;
coevolution of RNA and protein**



**Primitive translation system develops,
with RNA genome and RNA-protein catalysts**



Genomic RNA begins to be copied into DNA



**DNA genome, translated on RNA-protein complex
(ribosome) with protein catalysts**

TABLE 1-4 Some Organisms Whose Genomes Have Been Completely Sequenced

Organism	Genome size (millions of nucleotide pairs)	Biological interest
<i>Mycoplasma pneumoniae</i>	0.8	Causes pneumonia
<i>Treponema pallidum</i>	1.1	Causes syphilis
<i>Borrelia burgdorferi</i>	1.3	Causes Lyme disease
<i>Helicobacter pylori</i>	1.7	Causes gastric ulcers
<i>Methanococcus jannaschii</i>	1.7	Grows at 85 °C!
<i>Haemophilus influenzae</i>	1.8	Causes bacterial influenza
<i>Methanobacterium thermo- autotrophicum</i>	1.8	Member of the Archaea
<i>Archaeoglobus fulgidus</i>	2.2	High-temperature methanogen
<i>Synechocystis</i> sp.	3.6	Cyanobacterium
<i>Bacillus subtilis</i>	4.2	Common soil bacterium
<i>Escherichia coli</i>	4.6	Some strains cause toxic shock syndrome
<i>Saccharomyces cerevisiae</i>	12.1	Unicellular eukaryote
<i>Plasmodium falciparum</i>	23	Causes human malaria
<i>Caenorhabditis elegans</i>	97.1	Multicellular roundworm
<i>Anopheles gambiae</i>	278	Malaria vector
<i>Mus musculus domesticus</i>	2.5×10^3	Laboratory mouse
<i>Homo sapiens</i>	2.9×10^3	Human

Introduction to “-omics”

Def. The term –omics represents the rigorous study of various collections of molecules, biological processes or physiological and structures such as systems, represented most prominently by genomics.

The human genome encodes over 30,000 genes and generates more than 100,000 functionally distinct proteins. Most genes have small sequence differences (polymorphisms) that occur between individuals at about every 1,500 base pairs. SNPs make up about 90% of all human genetic variability.

Allele – any one of a number of alternate forms of the same gene

Genotype – the genetic material in the chromosome

Phenotype – properties of an organism that are produced by interaction with the environment

Genetic Variation and Dental Care JADA 140:896, 2009

Dental care – related anxiety, fear of dental pain and avoidance of dental care may be influenced by genetic variations.

An example is naturally red haired persons who have a melanocortin-1 receptor gene variant which causes them to be resistant to subcutaneous local anesthetics (ie tooth-numbing drugs like novocaine).

Consequently, these persons experience troublesome episodes during dental procedures, develop a fear of dental care and avoid all future checkups.

(a possible solution is to use a relaxant such as valium during treatments)

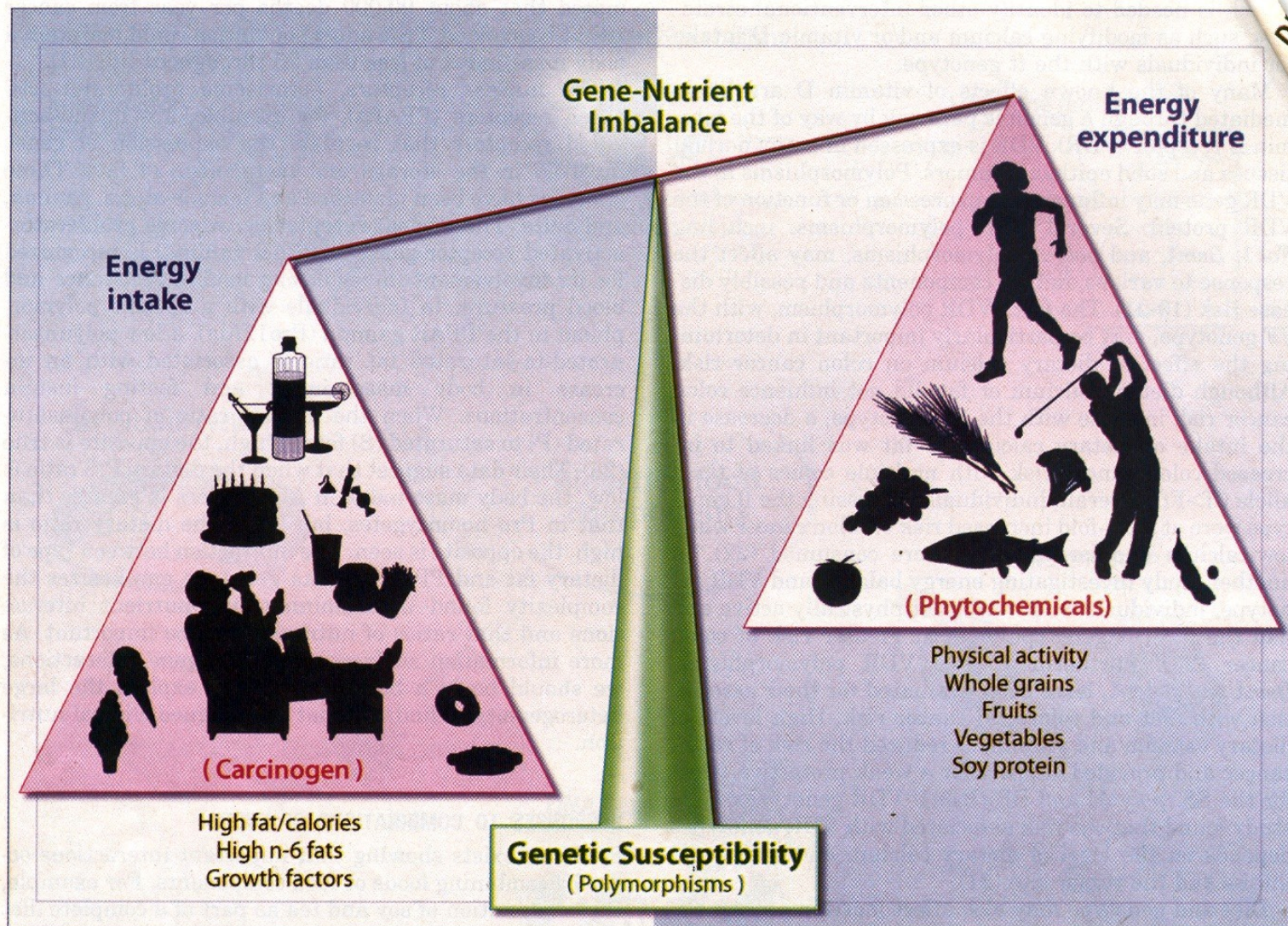
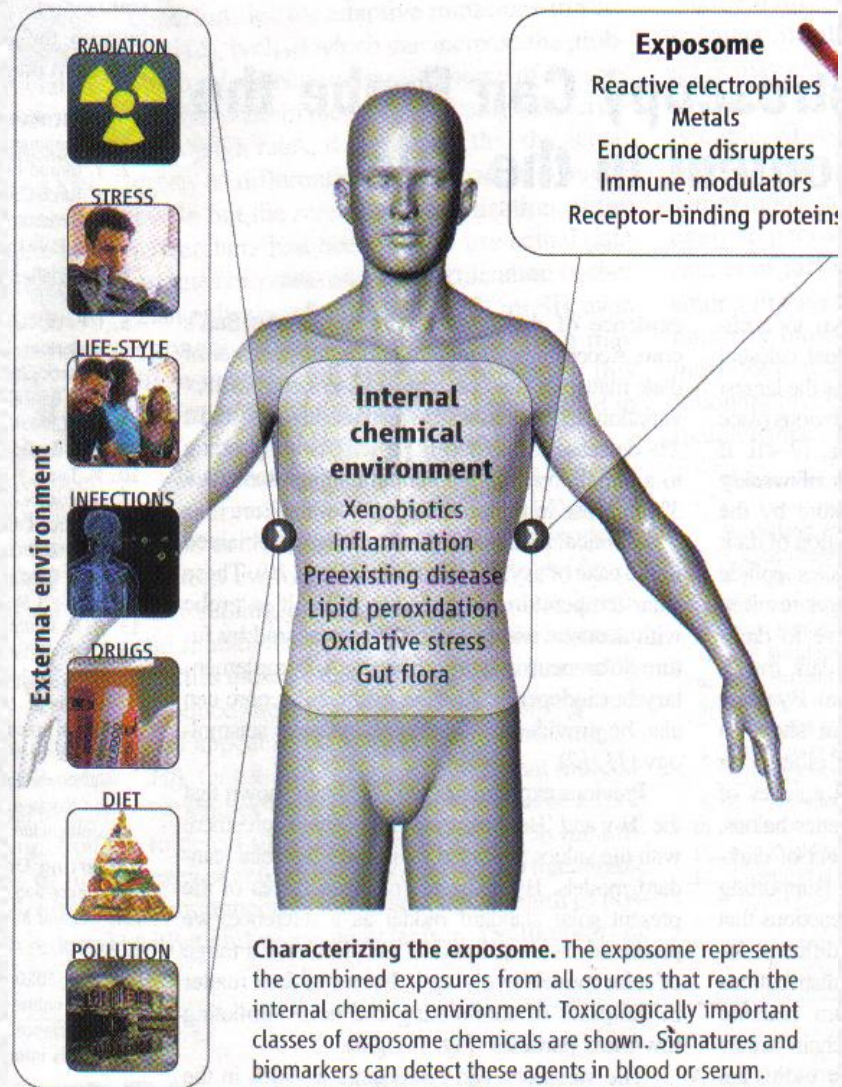


Figure 4. Certain genetic polymorphisms can shift the balance of energy intake and energy expenditure and thereby influence bioenergetics and obesity. Higher energy intakes, a low polyunsaturated-to-saturated fat ratio, insulin resistance, and a sedentary lifestyle leading to obesity are risk factors for chronic diseases, such as heart disease, diabetes, and cancer, depicted when the scale is sloping downward. The right side of the scale portrays lifestyle including physical activity and a diet rich in whole grains, fruits, vegetables, and soy protein, which are associated with less risk for obesity and chronic disease. Gene-nutrient imbalances may explain the morbidity and mortality associated with obesity.

70-90 % of risk for diseases is due to environmental exposures. The term EXPOSOME refers to the totality of environmental exposures from conception onward.





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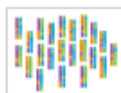
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Health & Traits



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What People Are Saying

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Genetic Tests Available

Abdominal aneurism	Lung cancer
Alzheimers disease	Lupus
Arterial fibrulation	Macular degeneration
Brain aneurism	Melanoma
Breast cancer	Multiple sclerosis
Celiac disease	Obesity
Crohn's disease	Osteoarthritis
Deep vein thrombosis	Prostate cancer
Diabetes type 2	Psoriasis
Glaucoma	Restless leg syndrome
Graves' disease	Rheumatoid arthritis
Heart attack	Sarcoidosis
Hemochromatosis	Stomach cancer (diffuse)
Lactose intolerance	

Cost \$500 (2009)



Practice Exercises


CHAPTER 1



A 1% solution of NaF equals how many ppm's?

- a. 1
- b. 10
- c. 100
- d. 1000
- e. 10,000

$1\% = 1\text{g}/100\text{ ml} = 10\text{g}/\text{L} \times 1000\text{mg}/\text{g} = 10,000\text{mg}/\text{L}$
 $1\text{ ppm} = 1\text{ mg}/\text{L}$ so ans is 10,000 ppm (e)





1. A Eukaryotic cell is homogenized and centrifuged at 150,000 xg for 1 hour. The pellet will contain all of the following EXCEPT which one?

- a. Organelles
 - b. Ribosomes
 - c. Enzymes**
 - d. Mitochondria
 - e. Endoplasmic reticulum
- 





2. The basic difference between prokaryotes and eukaryotes is:

- Presence of a nuclear envelope.
 - Bacteria have a nucleoid which has no membrane.
 - Eukaryotes have a nucleus which has a double membrane.
- 



3. Small cells have a (large, small) surface/volume ratio
so O_2 diffusion is (easy, difficult).

- Small cells have a large surface/volume ratio so
 O_2 diffusion is easy.
 - Large cells have a small surface/volume ratio
so O_2 diffusion is difficult.
- 




■ Anabolic activity takes place in which of the following? (hint check ALL that are correct)

- A. Cytosol
 - B. Lysosomes
 - C. Mitochondria
 - D. RER
 - E. SER
- 



4. An example of a level 3 supramolecular complex is:

- a. DNA
 - b. Cellulose
 - c. Plasma membrane**
 - d. The cell
 - e. Nucleotide
- 





5. The plasma membrane is a barrier to free passage of:

- a. Na^+
- b. K^+
- c. Polar molecules
- d. Charged molecules
- e. All of these**




6. Both plant and animal cells contain:

- a. Thylakoid membrane
 - b. Central vacuole
 - c. Glyoxysomes
 - d. Chloroplasts
 - e. Rough endoplasmic reticulum**
- 




7. An element essential for life with the highest molecular weight is:

- a. Chromium
 - b. Copper
 - c. Iodine**
 - d. Iron
 - e. Selenium
- 



8. Which of the following is characterized as an essential trace element?

- a. Aluminum
 - b. Chlorine
 - c. Hydrogen
 - d. Magnesium**
 - e. Sodium
- 

9. For a chiral carbon atom which substrate has
(a) the highest, (b) the lowest priority?

a. -NH

b. -CHO

c. CH_2OH

d. -OH (highest)

e. $-\text{CH}_3$ (lowest)

10. The primitive atmosphere of earth contained all the following gases, EXCEPT which one?


a. H_2O

b. O_2

c. NH_3

d. CH_4

e. H_2



11. Genome sequences have been obtained for all the following species, EXCEPT which one?

- a. Fruit fly
 - b. Roundworm
 - c. Rice
 - d. Mouse
 - e. All of these have been sequenced**
- 