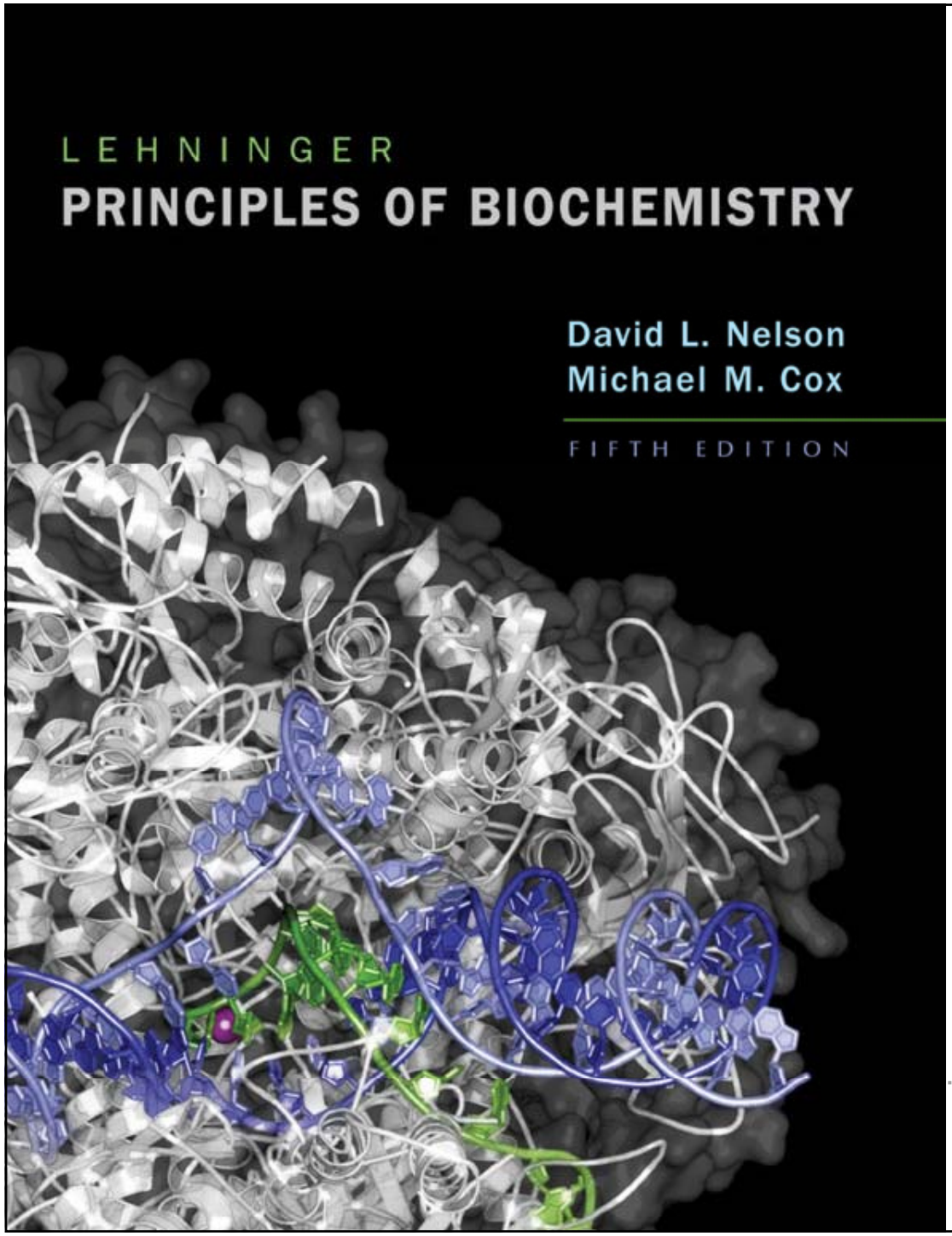


WELCOME TO THE BIOCHEMISTRY WORLD

生化科技學系

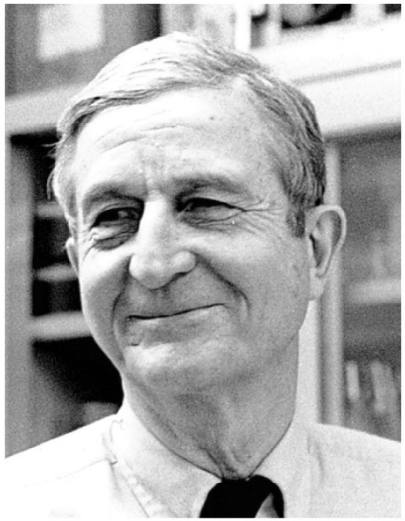
張 世 宗

shihchung@ntu.edu.tw

RNA polymerase II from yeast, bound to DNA and in the act of transcribing it into RNA (PDB ID 1I6H)

About the textbook

The discovery in 1948 by **Eugene Kennedy** and **Albert Lehninger**: mitochondria are the site of oxidative phosphorylation



Eugene P. Kennedy
1919-

Albert L. Lehninger
1917–1986

Albert Lehninger: wrote the 1st edition in 1982

Eugene Kennedy: Lehninger's student

David Nelson: Kennedy's post-doc

Michael Cox: Nelson's colleague

- Intracellular structures and the fatty acid oxidase system of rat liver.
  Kennedy EP, Lehninger AL.
  J Biol Chem. 1948

- The products of oxidation of fatty acids by isolated rat liver mitochondria
  Kennedy EP, Lehninger AL.
  J Biol Chem. 1950

Some organisms whose genomes have been completely sequenced

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

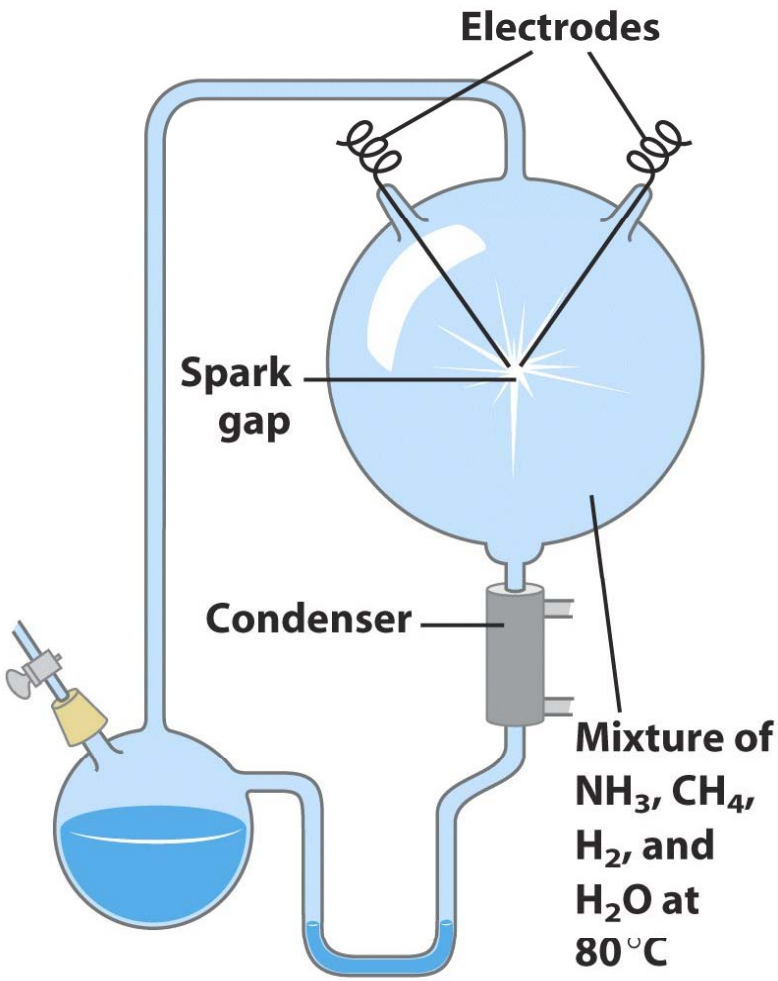
Chapter 1

The Foundations of Biochemistry

Biochemistry describes in **molecular terms** the structures, mechanisms, and chemical processes **shared by all organisms** and provides **organizing principles** that underlie life in all its diverse forms, principles we refer to collectively as **the molecular logic of life**.

The origin of life on earth

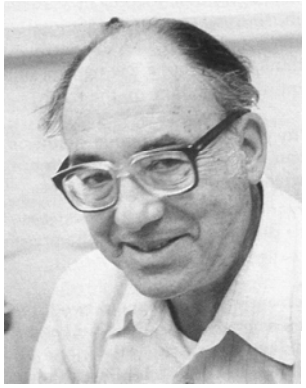
Miller–Urey experiment



A production of amino acids under possible primitive earth conditions.
Miller SL.
Science. 1953 May 15

Organic compound synthesis on the primitive earth.
Miller SL, Urey HC.
Science. 1959 Jul 31

Origin of Life.
Miller SL, Urey HC.
Science. 1959 Dec 11



Miller, SL

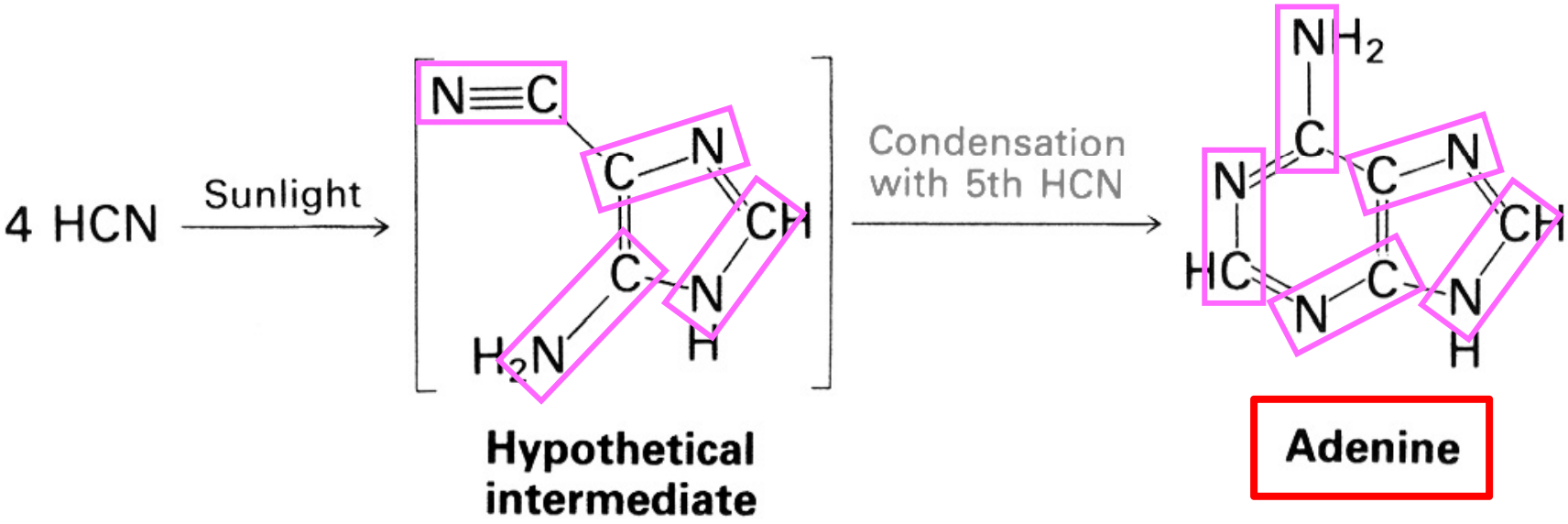
HCN, AMINO ACIDS, NUCLEOTIDES

1953年
一名化學系的研究生

HCN, AMINO ACIDS, NUCLEOTIDES

Miller–Urey experiment

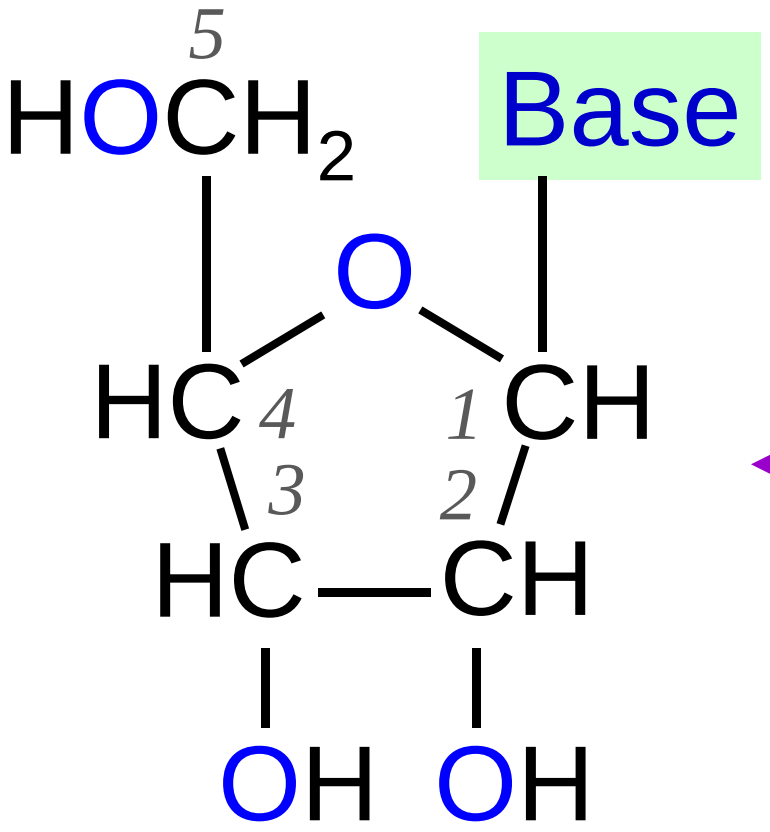
鹼基可能由數個 HCN 組成

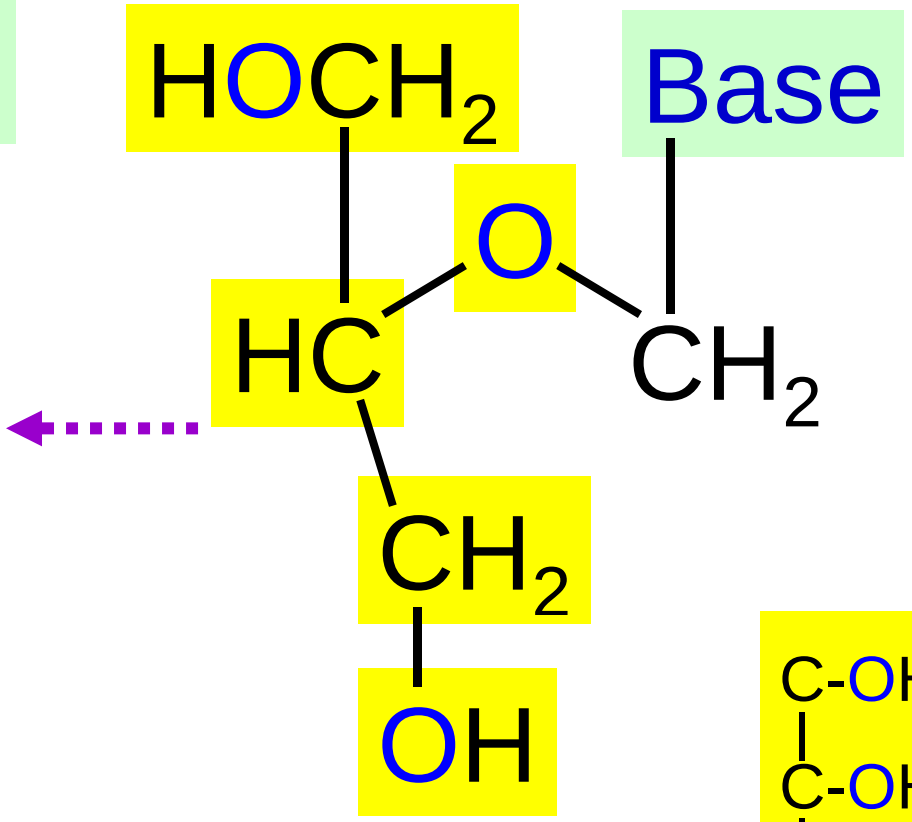


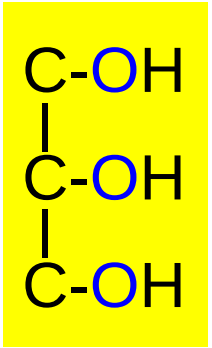
▲ **Figure 26-4** Adenine can be formed from hydrogen cyanide (HCN) in sunlight, although the route of synthesis has not been completely worked out. When heated, HCN and ammonia yield adenine. [See S. L. Miller and L. E. Orgel, 1973, *The Origins of Life on Earth*, Prentice-Hall, p. 105.]

Darnell et al (1990) Molecular Cell Biology (2e) p.1053

甘油可能形成最早的核酸骨架



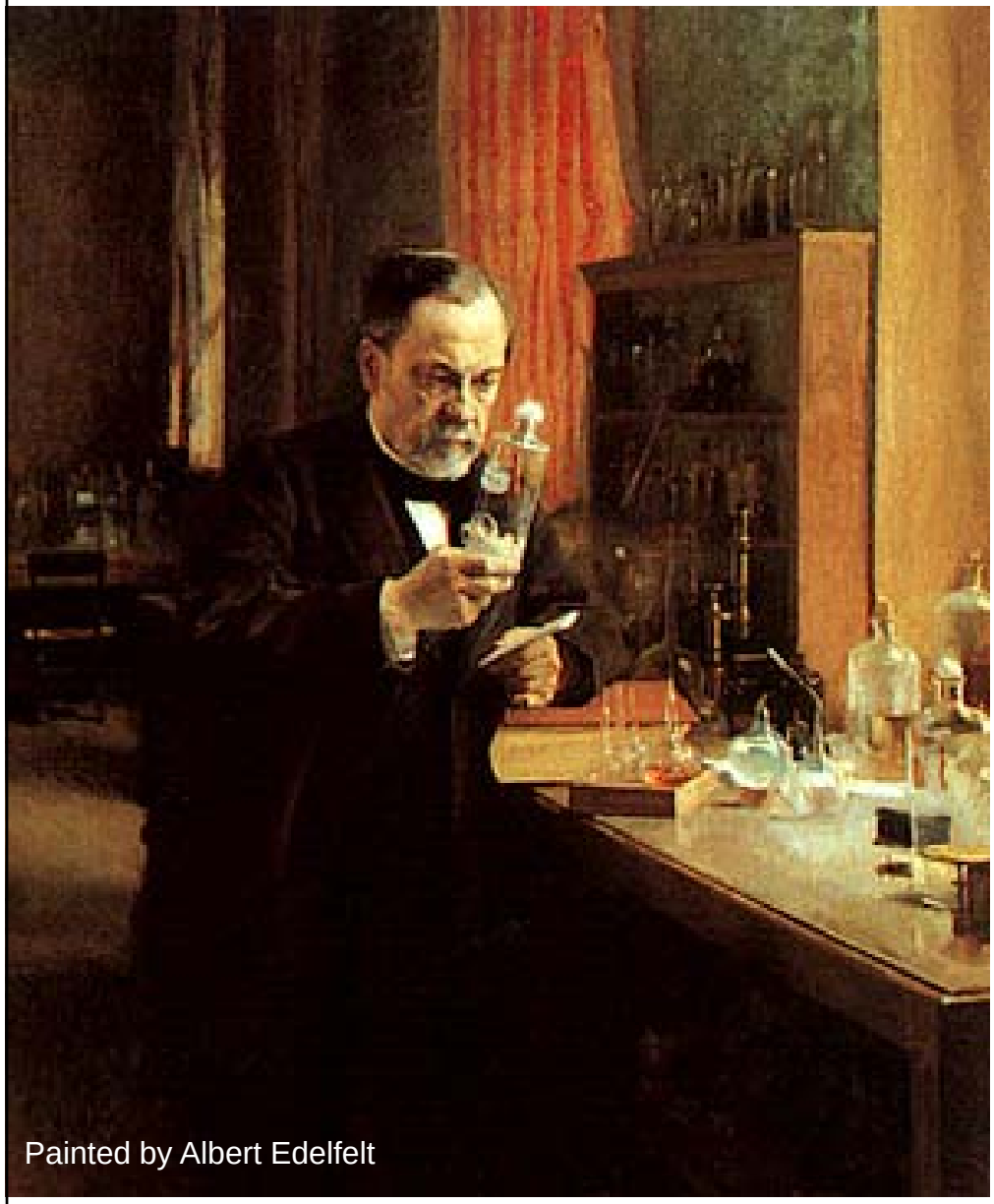




甘 油

核糖組成核酸骨架

Adapted from Darnell et al (1990) Molecular Cell Biology (2e) p.1054



Painted by Albert Edelfelt

Louis Pasteur 巴斯德

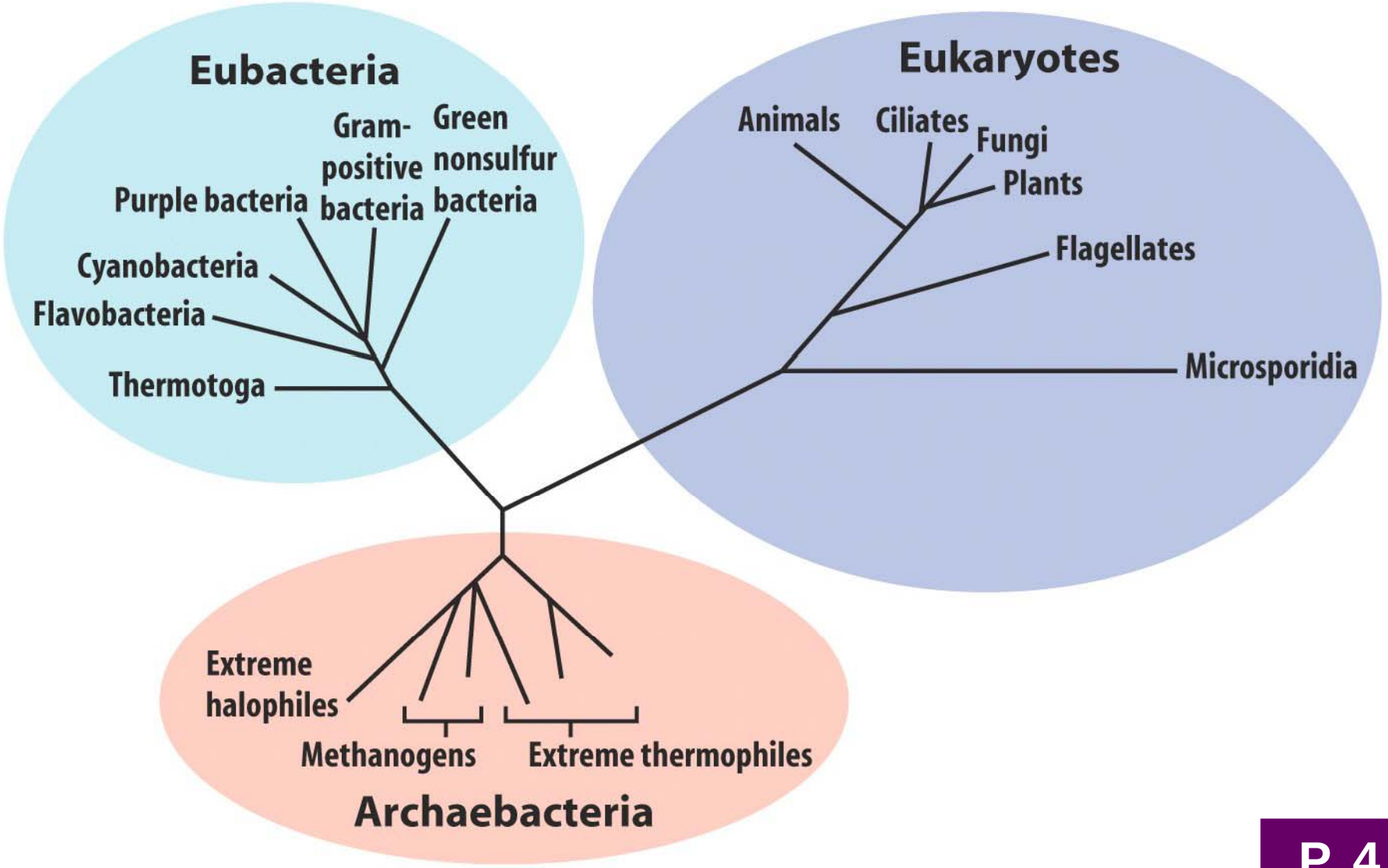
1822-1895

- **Pasteurization of food**
- **Developed vaccines for Rabies** 狂犬病, **Diphtheria** 白喉, **Anthrax** 炭疽

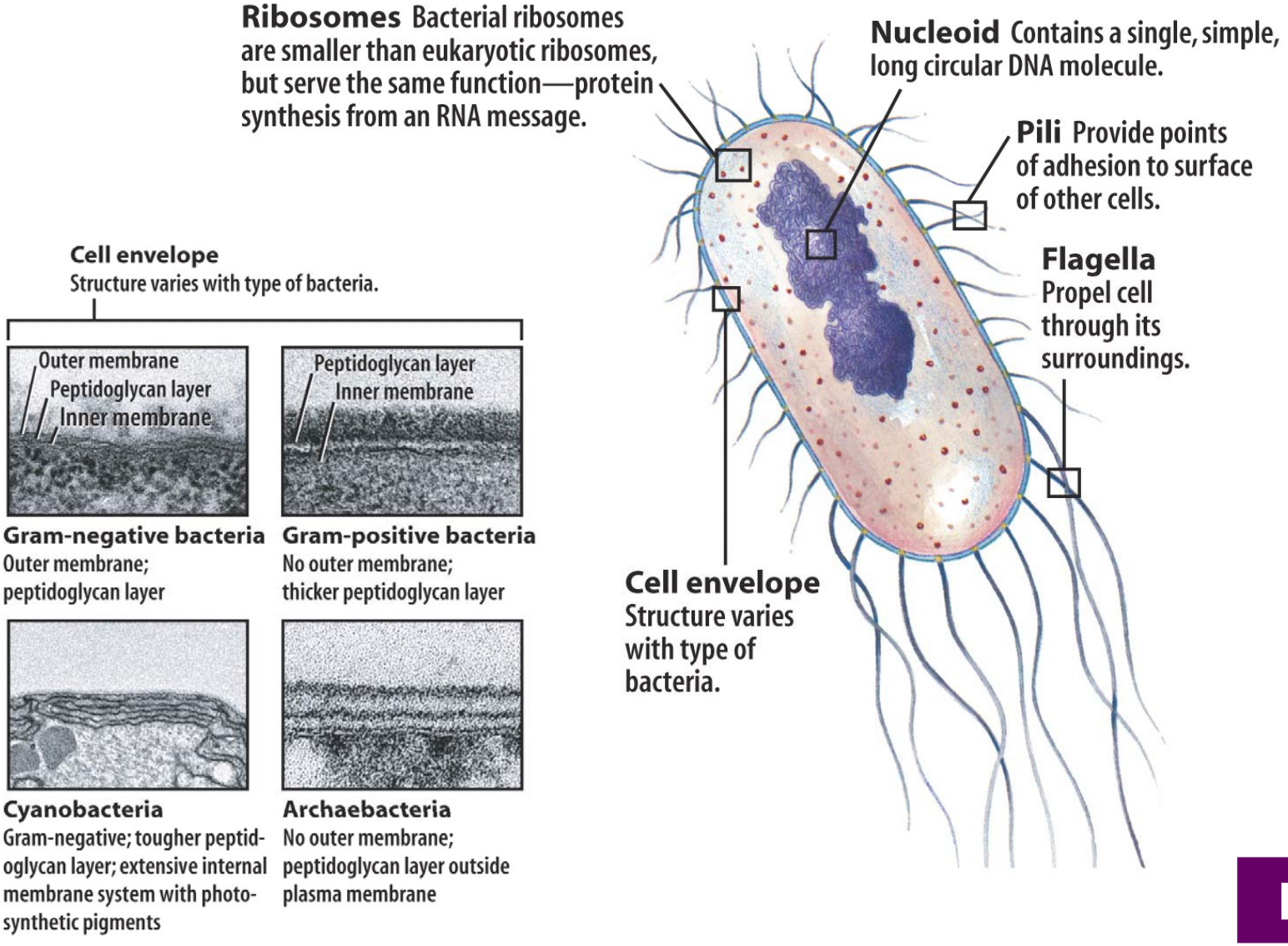
Portrait of Pasteur's father by young Louis

"The more I study nature, the more I stand amazed at the work of the Creator."

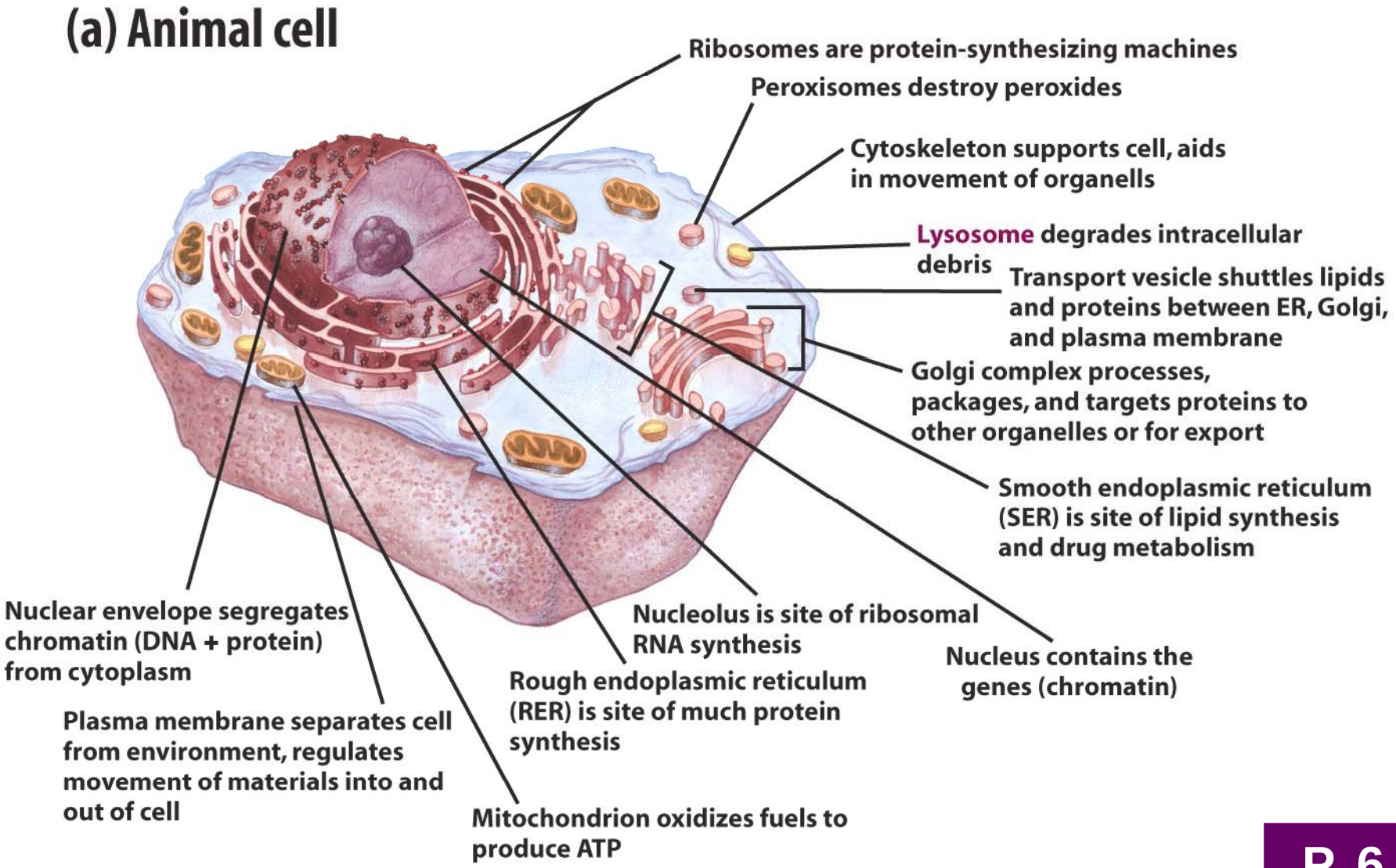
Phylogeny of the three domains of life



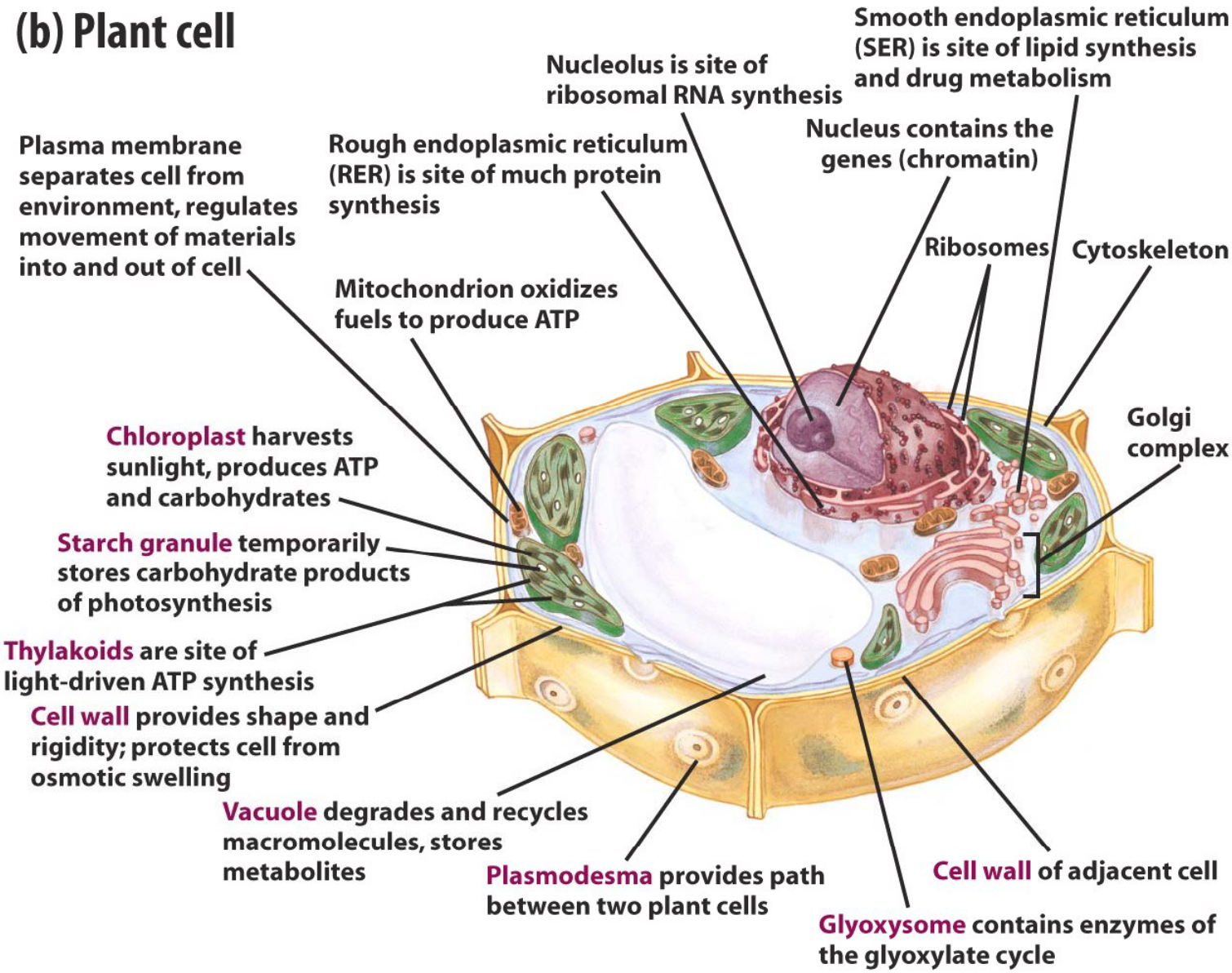
Common structural features of bacterial cells



Cell structure of an animal cell



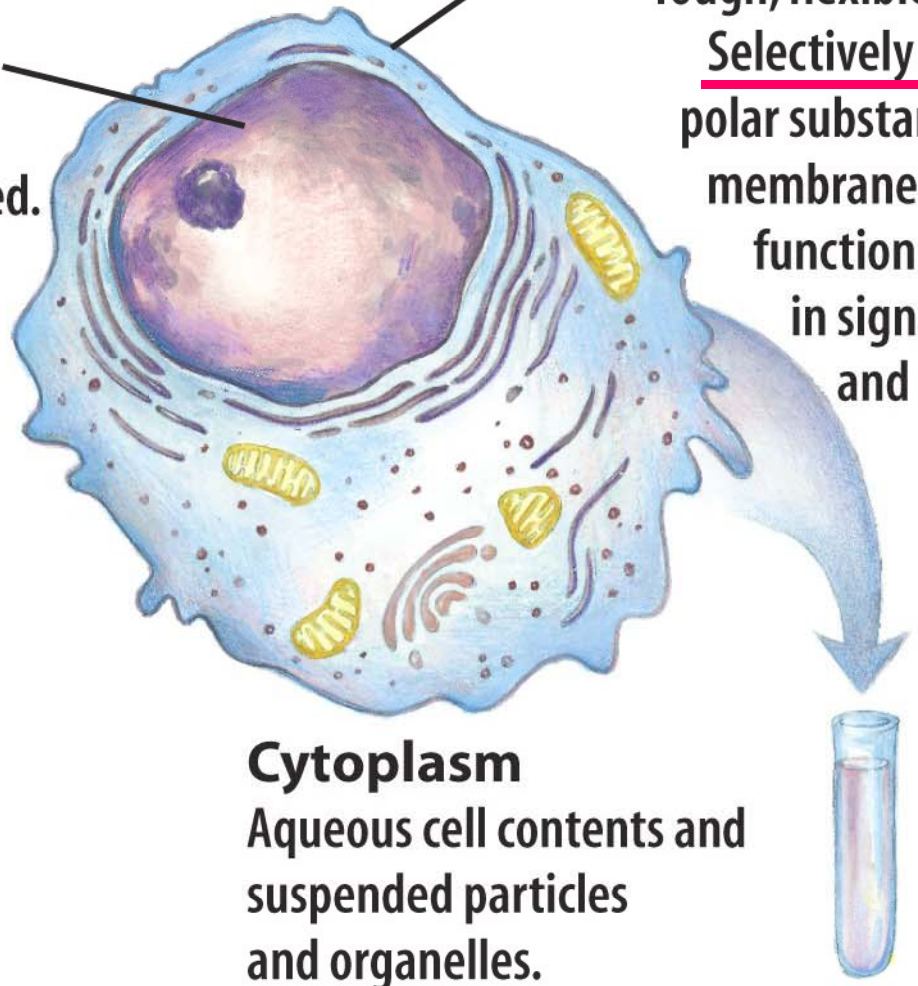
Cell structure of a plant cell



Common features of Eukaryotic cells

Nucleus (eukaryotes) or nucleoid (bacteria)
Contains genetic material– DNA and associated proteins. Nucleus is membrane-bounded.

Plasma membrane
Tough, flexible lipid bilayer. Selectively permeable to polar substances. Includes membrane proteins that function in transport, in signal reception, and as enzymes.



Cytoplasm
Aqueous cell contents and suspended particles and organelles.

Cytoplasm

Aqueous cell contents and suspended particles and organelles.

Theodor Svedberg, Swedish chemistry, 1926

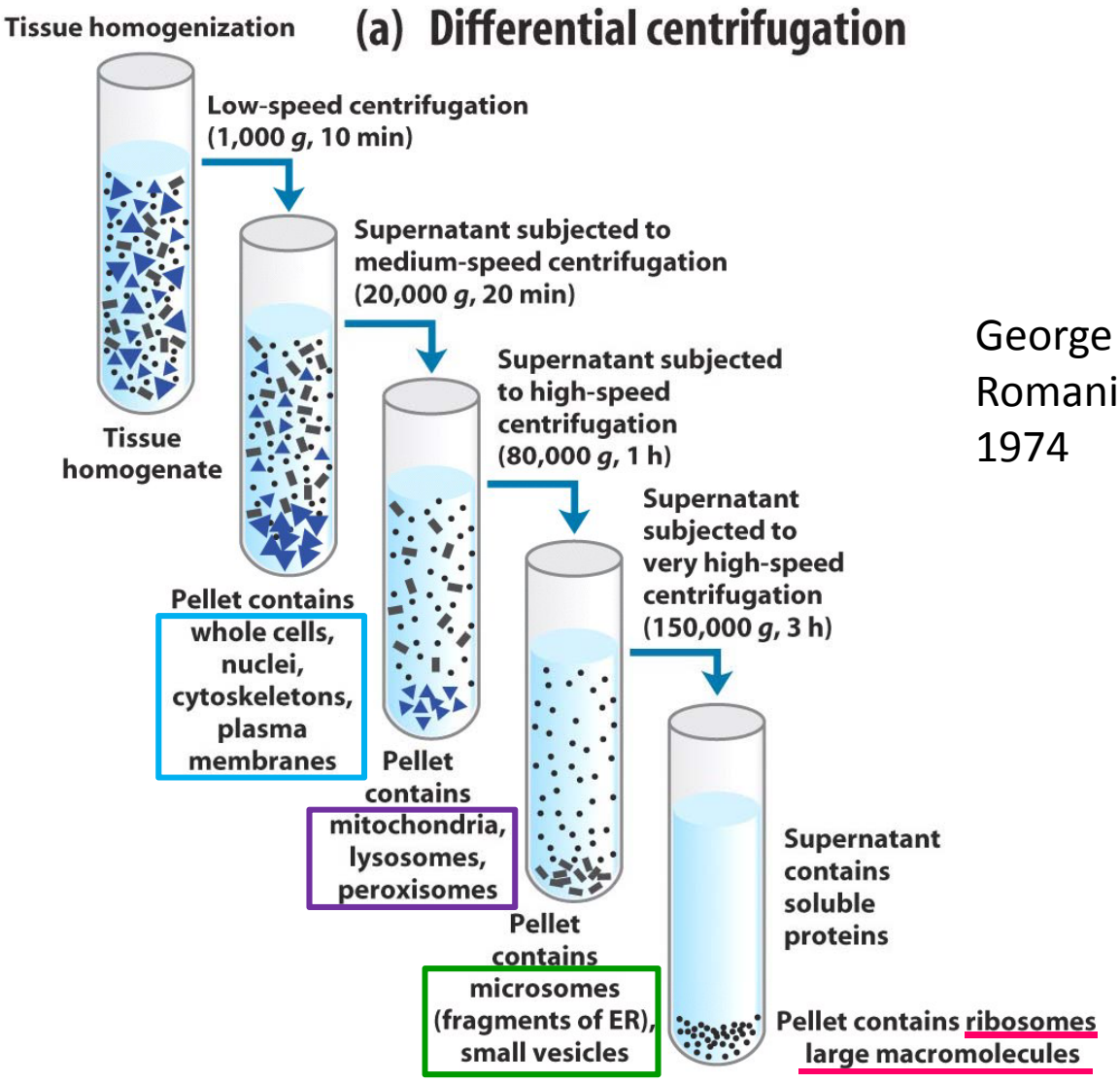
centrifuge at 150,000 *g*

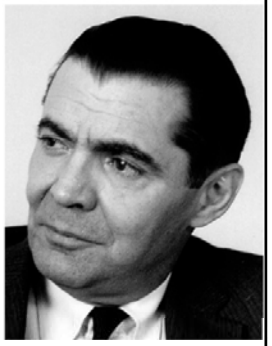
For 1 hour

Supernatant: cytosol
Concentrated solution of enzymes, RNA, monomeric subunits, metabolites, inorganic ions.

Pellet: particles and organelles
Ribosomes, storage granules, mitochondria, chloroplasts, lysosomes, endoplasmic reticulum.

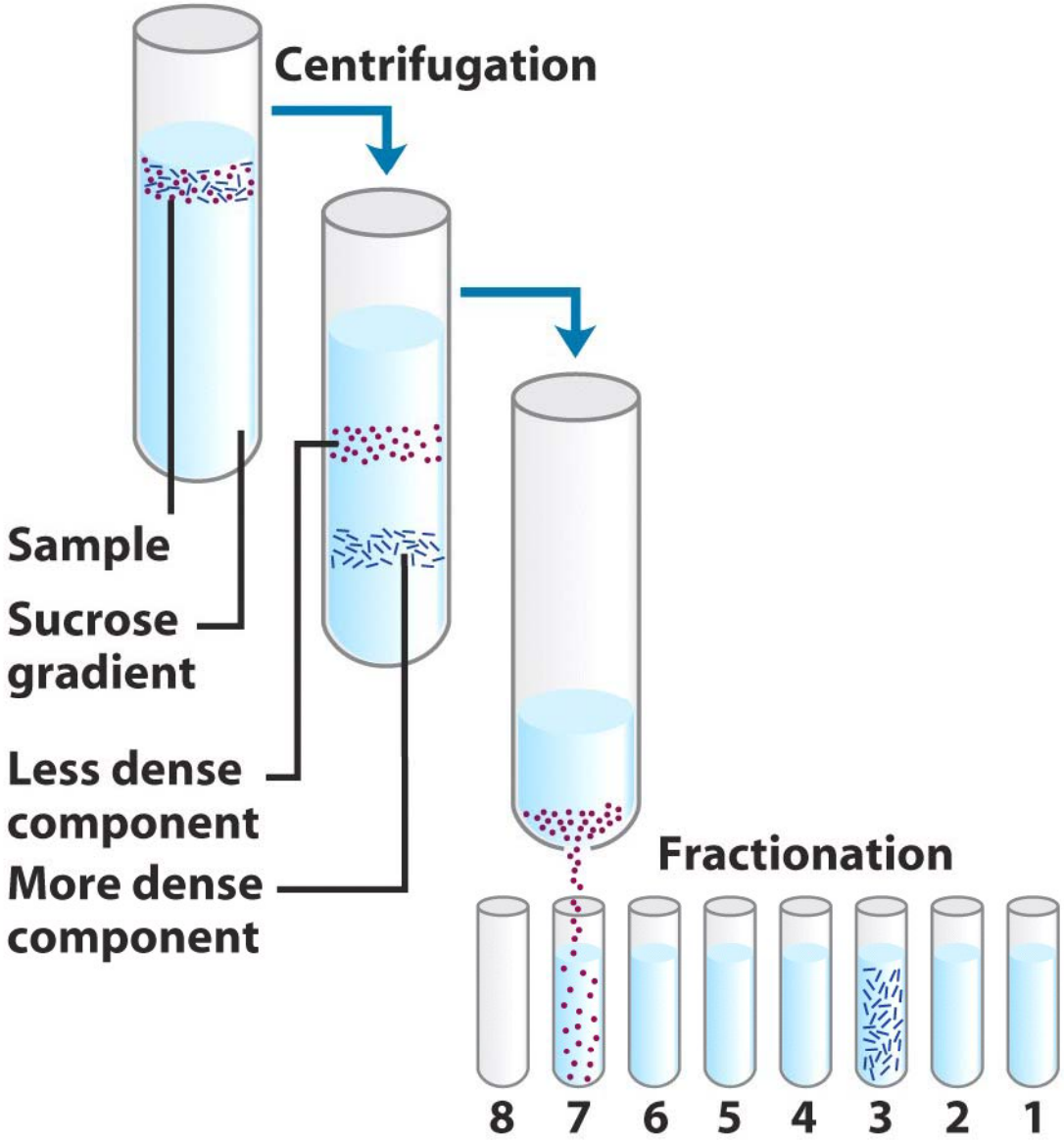
Subcellular fractionation





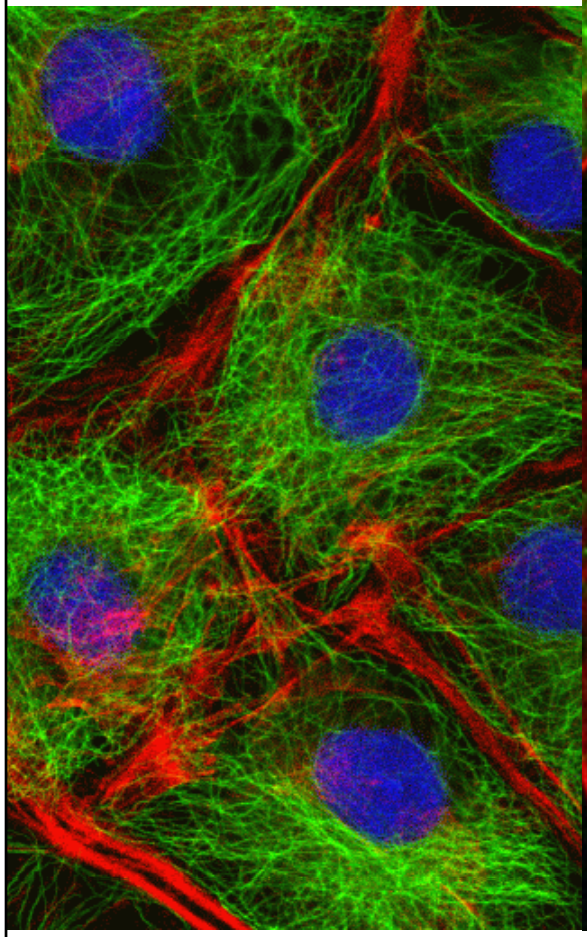
George Emil Palade, Romanian-American cell biologist, 1974

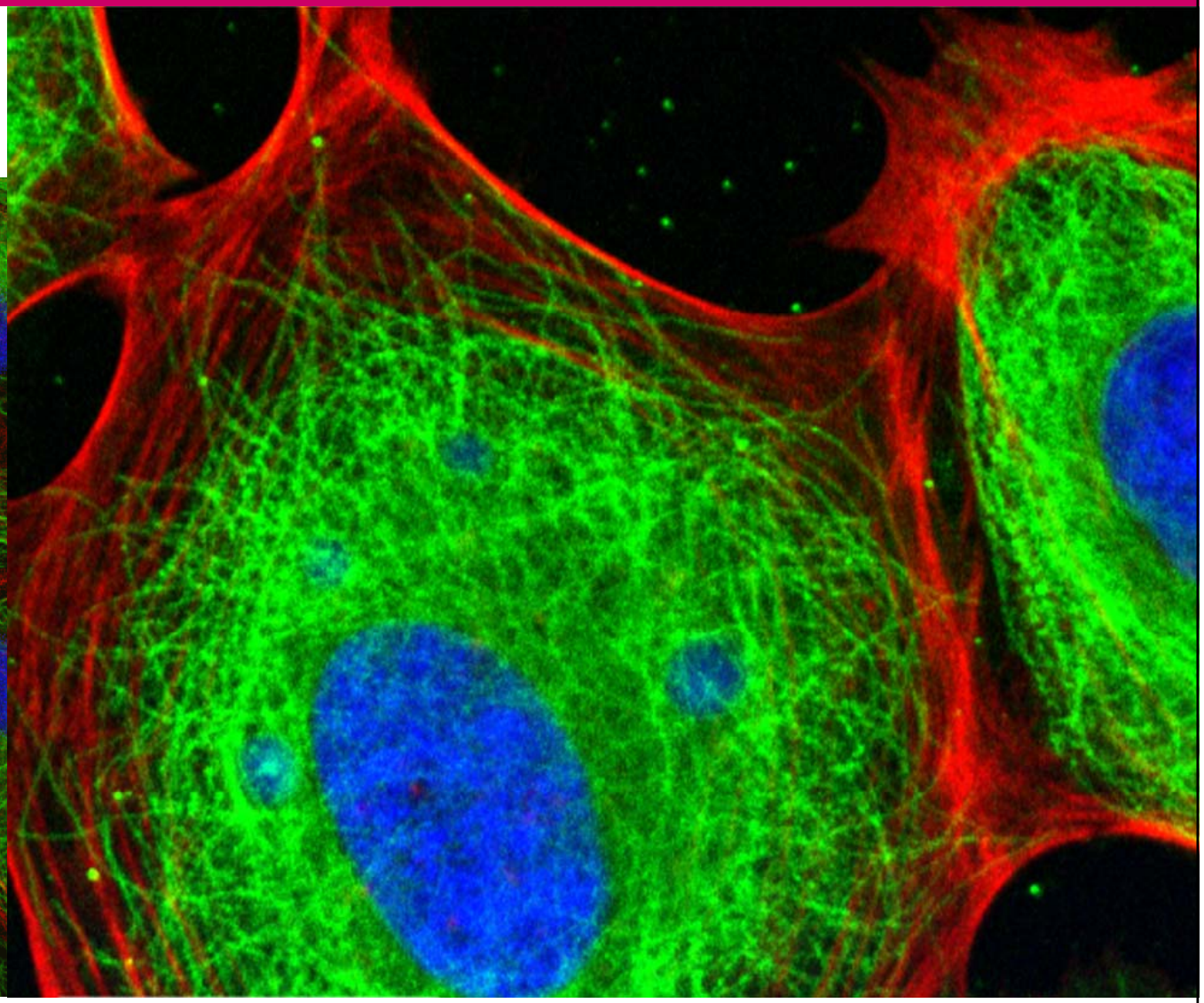
(b) Isopycnic (sucrose-density) centrifugation



Cytoskeleton-SHAPE&TRAFFIC

Microtubules (green)
Actin filaments (red)
Nucleus (blue)





Mark Shipman, James Blyth and Louise Cramer, University College London, UK

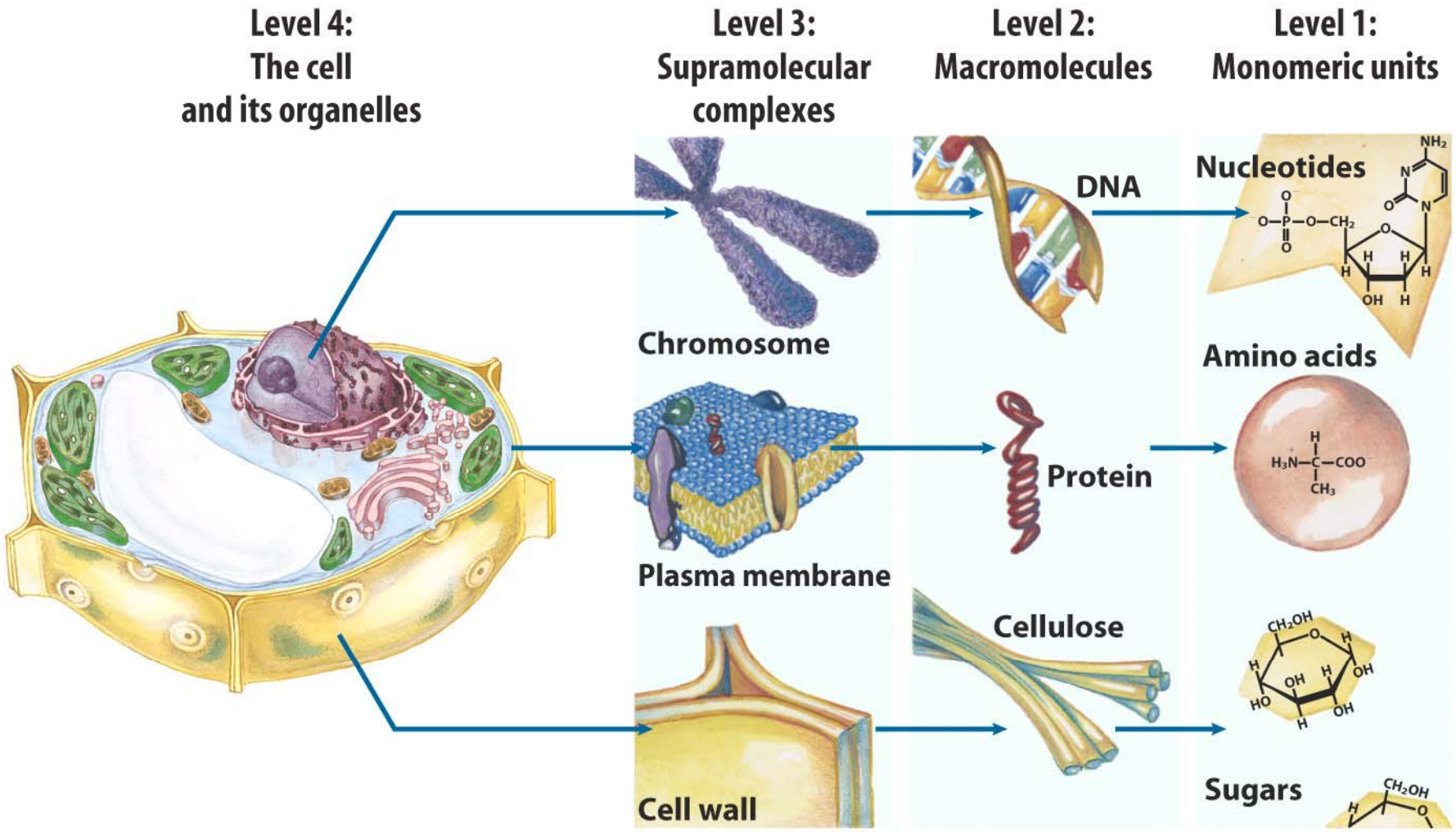
Traffic_The International Journal of Intracellular Transport

Comparison of prokaryotic and eukaryotic cells

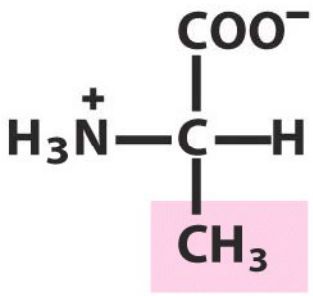
Characteristic	*Prokaryotic cell*	*Eukaryotic cell*
Size	Generally small (1–10 μm)	Generally large (5–100 μm)
Genome	DNA with nonhistone protein; genome in nucleoid, not surrounded by membrane	DNA complexed with histone and nonhistone proteins in chromosomes; chromosomes in nucleus with membranous envelope
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

Assembly of life

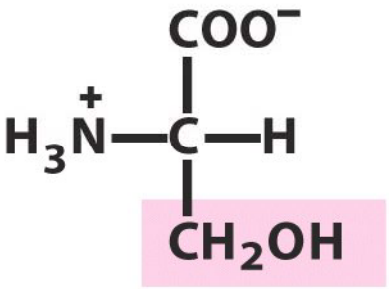
Structural hierarchy in the molecular organization of cells



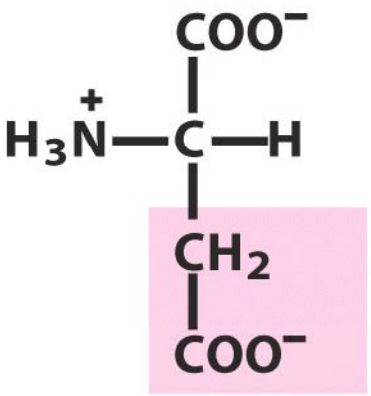
(a) Some of the amino acids of proteins



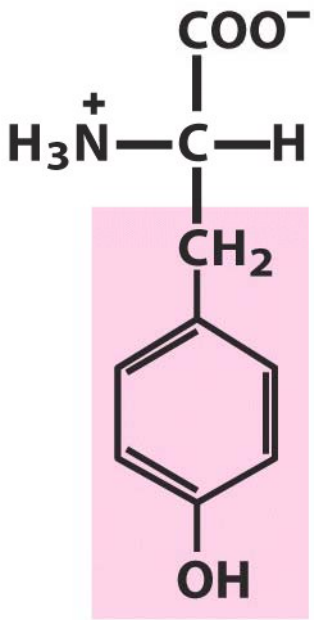
Alanine



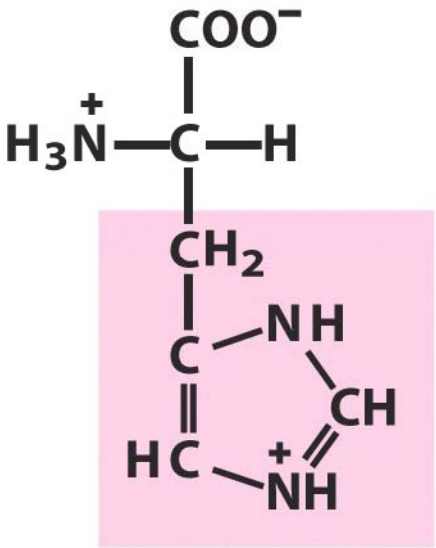
Serine



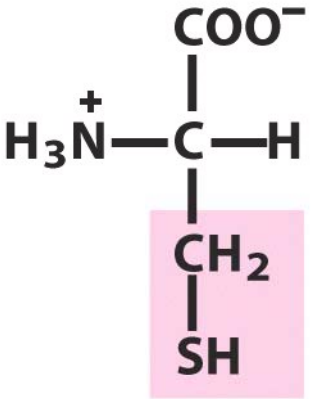
Aspartate



Tyrosine

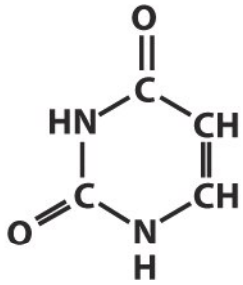


Histidine

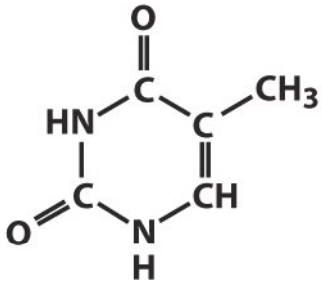


Cysteine

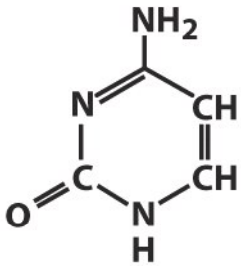
The components of nucleic acids



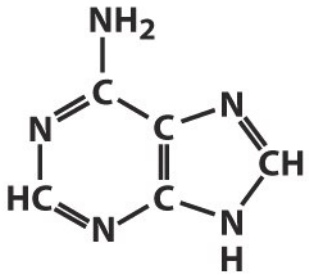
Uracil



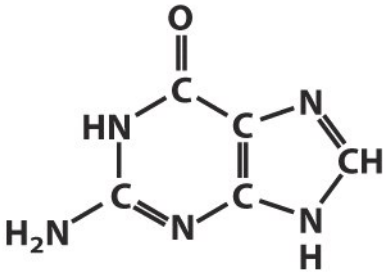
Thymine



Cytosine

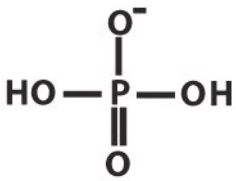


Adenine

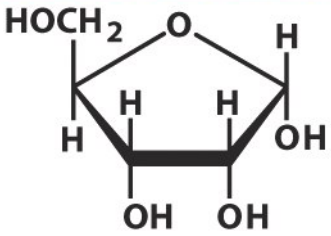


Guanine

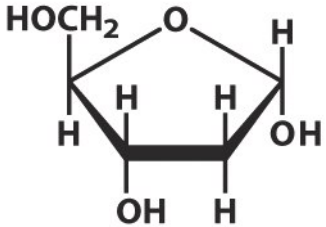
Nitrogenous bases



Phosphoric acid



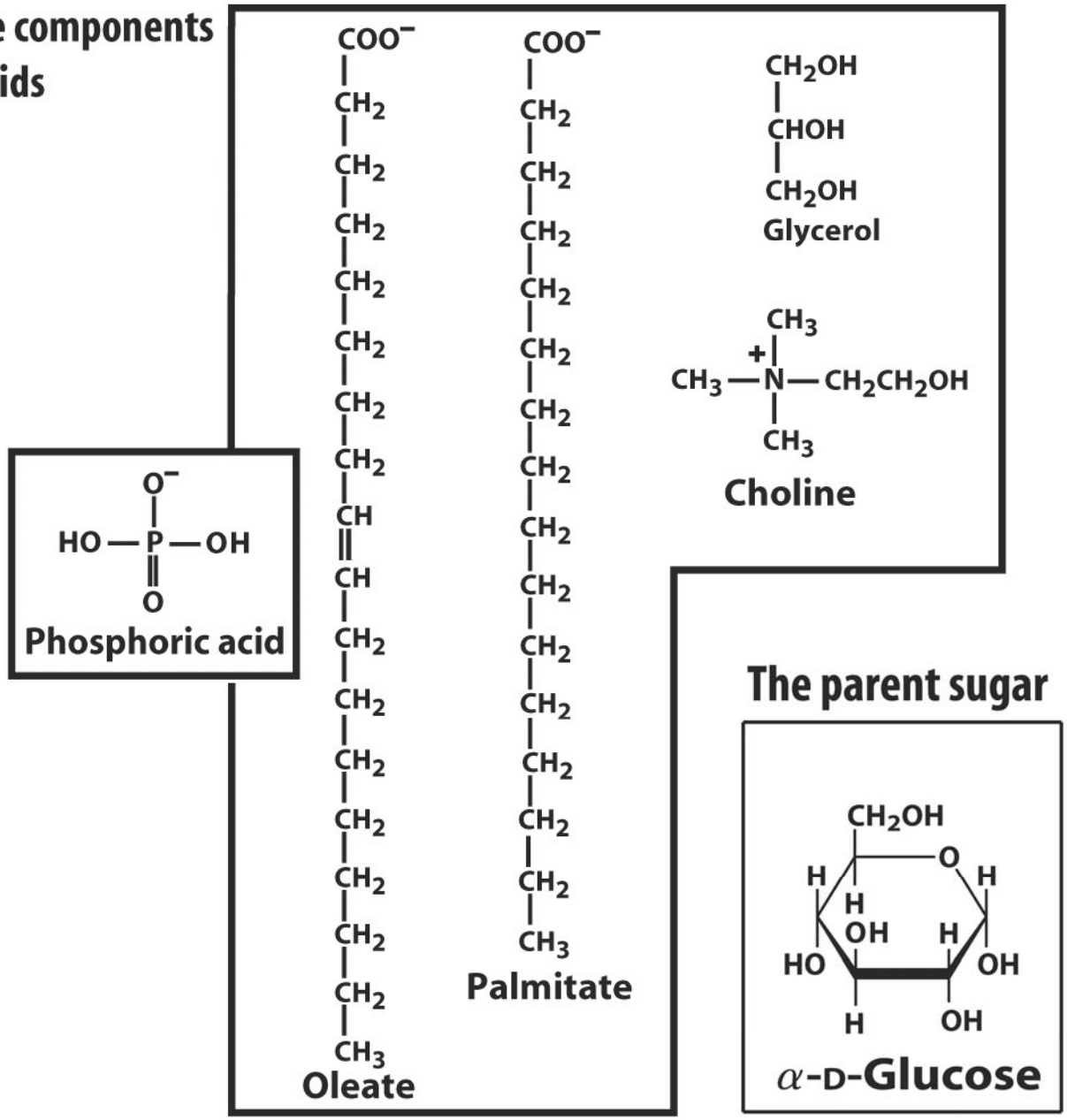
α-D-Ribose



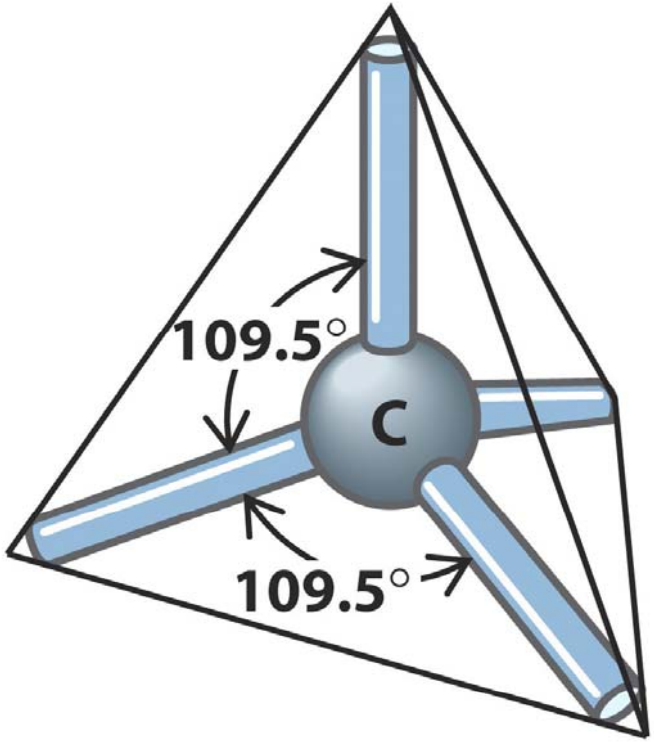
2-Deoxy-α-D-ribose

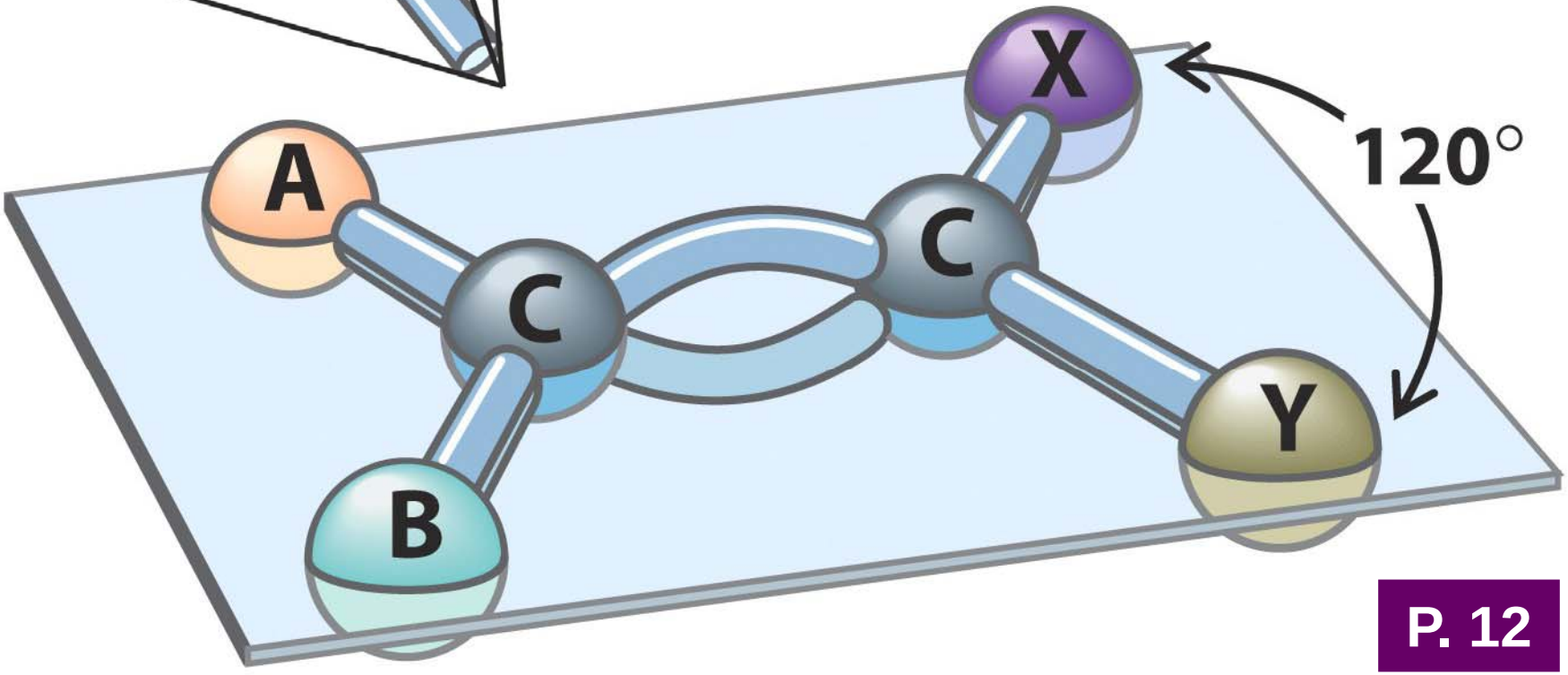
Five-Carbon sugars

Some components of lipids



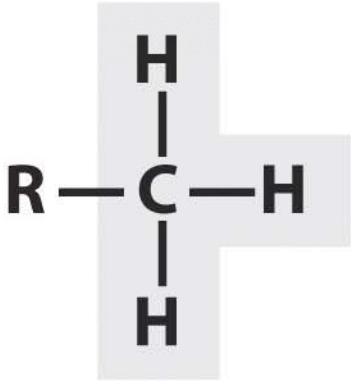
GEOMETRY OF CARBON BONDING



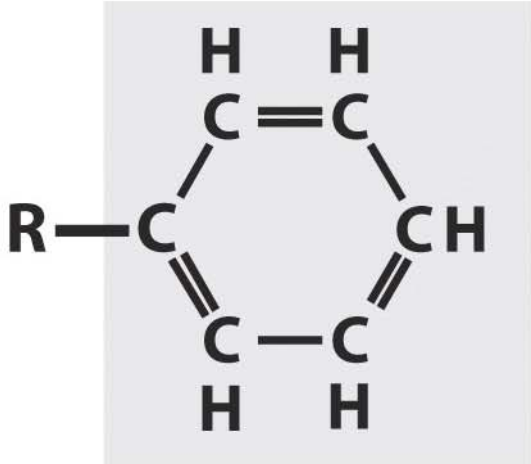


Some common functional groups of biomolecules

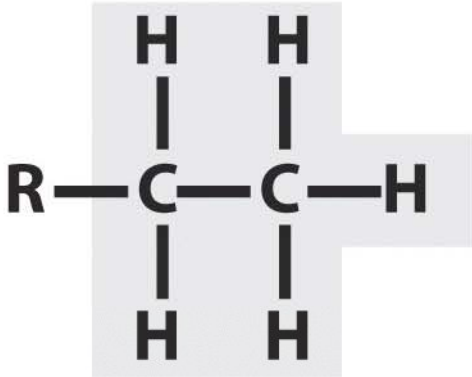
Methyl



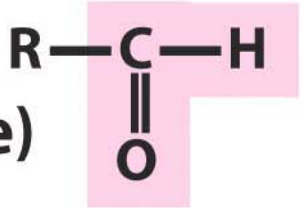
Phenyl



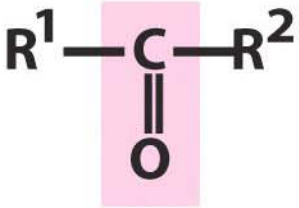
Ethyl



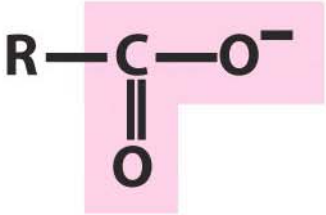
Carbonyl (aldehyde)



Carbonyl (ketone)

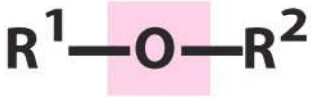


Carboxyl

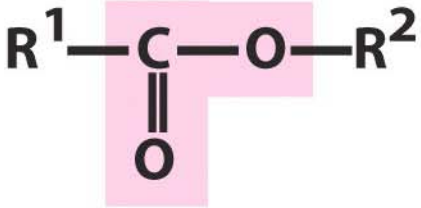


Hydroxyl (alcohol)

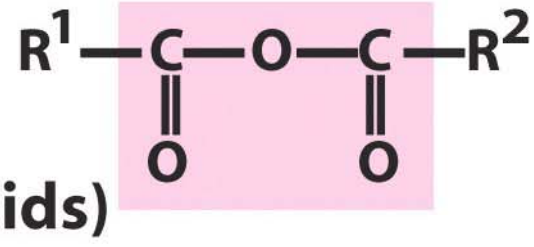
Ether



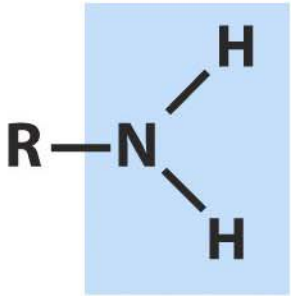
Ester



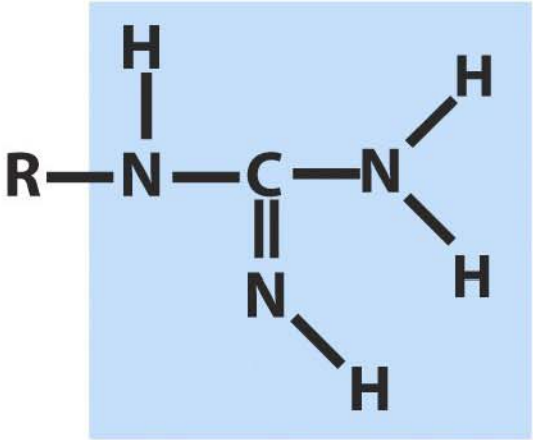
Anhydride (two carboxylic acids)



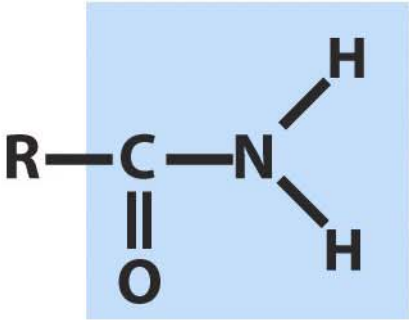
Amino



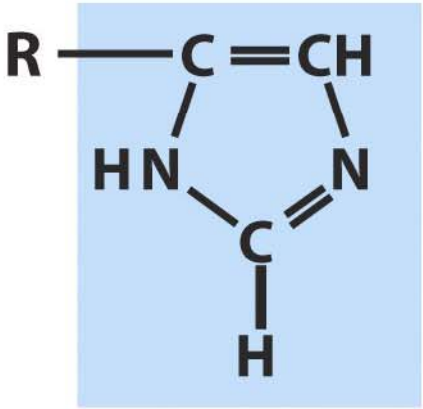
Guanidino



Amido



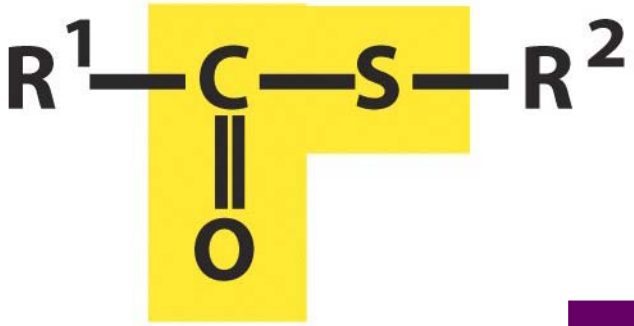
Imidazole



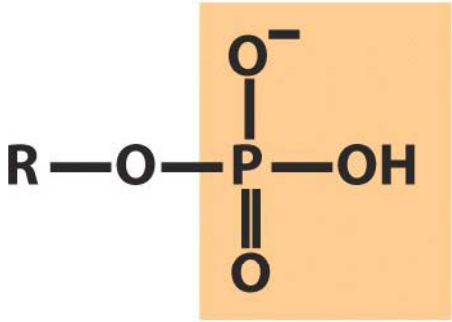
Sulfhydryl

Disulfide

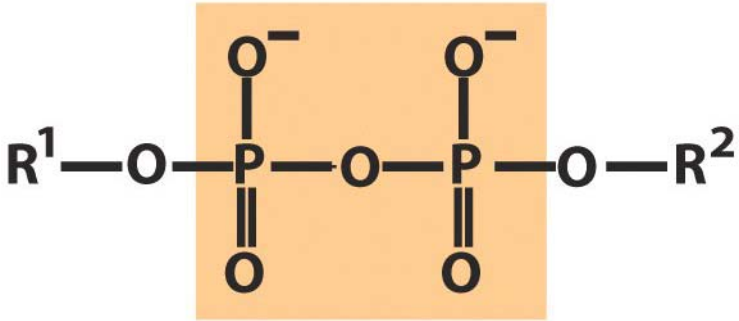
Thioester



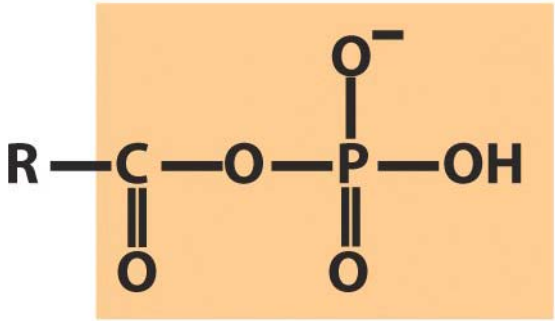
Phosphoryl



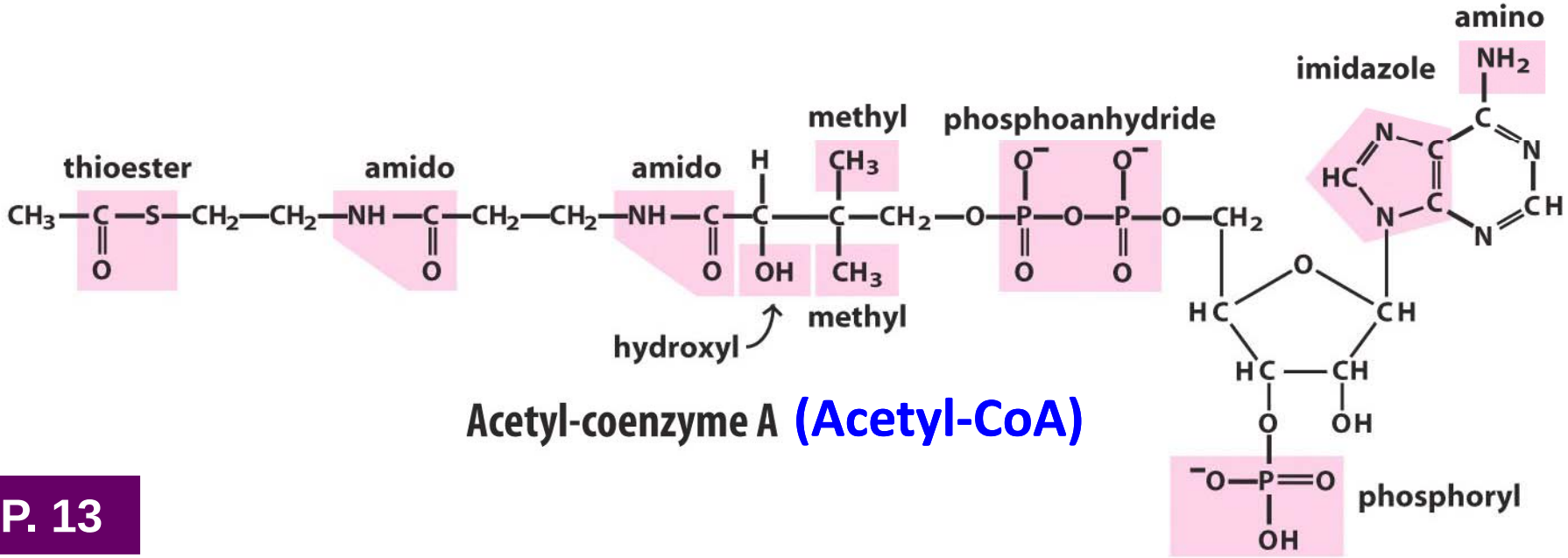
Phosphoanhydride



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

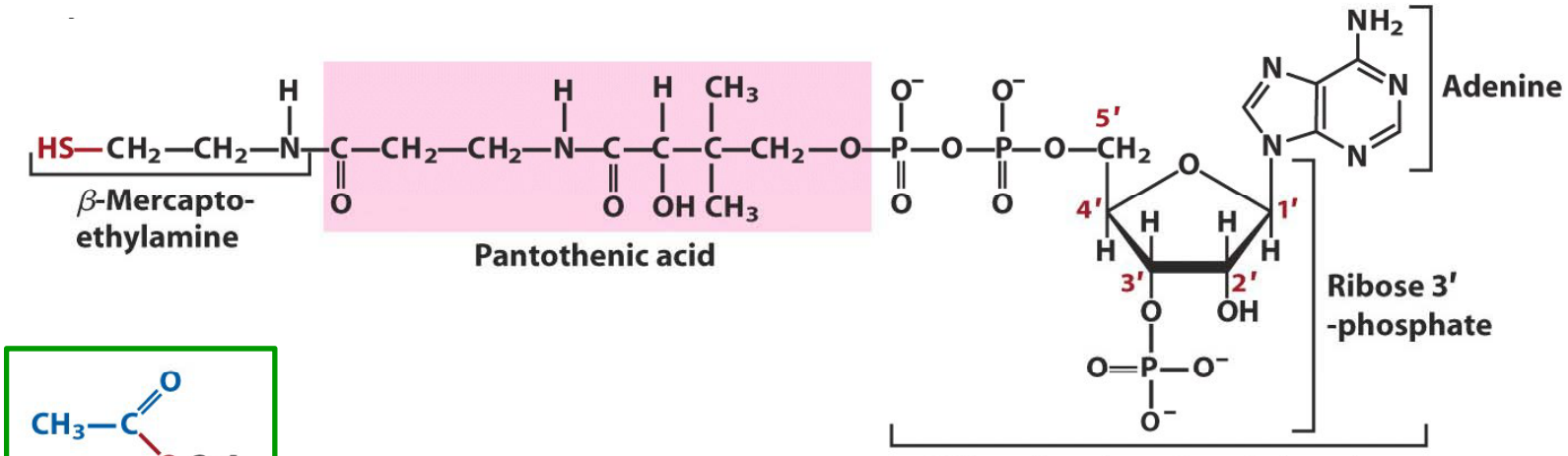


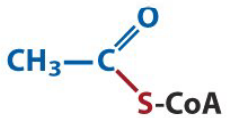
Several common functional groups in a single biomolecule



Acetyl-coenzyme A (Acetyl-CoA)

P. 13



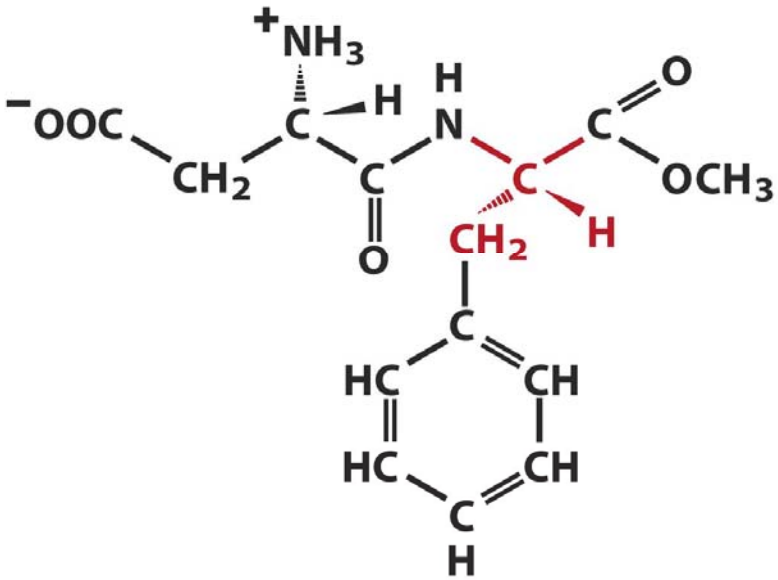


Acetyl-CoA

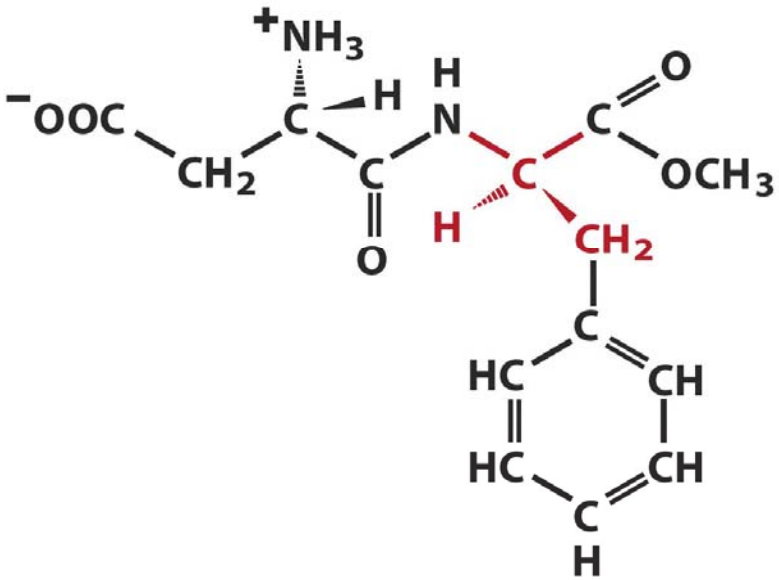
Coenzyme A

P. 617

For life, a simple difference may lead to an opposite consequence



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



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

Aspartame PKU 患者不可過量食用！

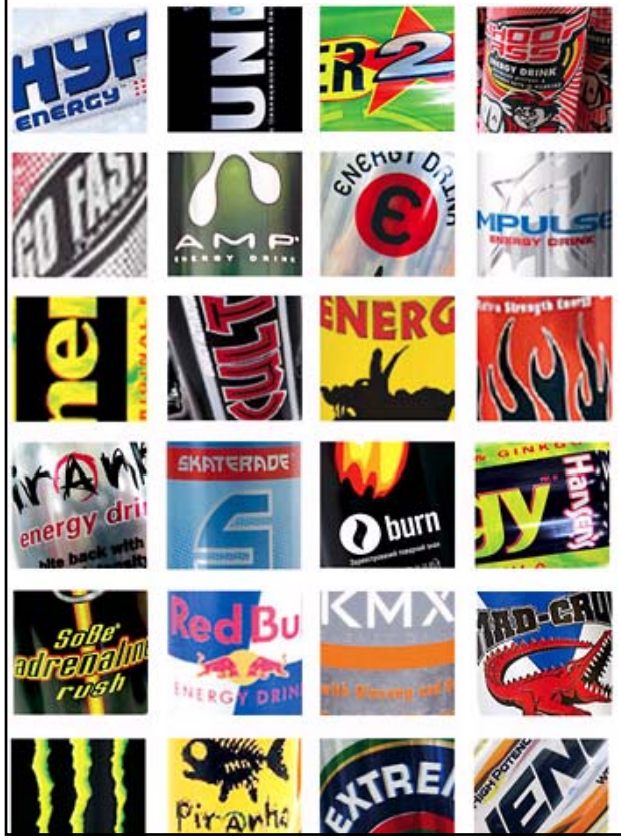
Asp-Phe 的甜度比蔗糖高兩百倍，阿斯巴甜則更高

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.

ENERGY DRINK
blast
STEVEN SEAGAL
LIGHTNING BOLT
HOOAH!
SOLDIER FUEL
MONSTER
ENERGY

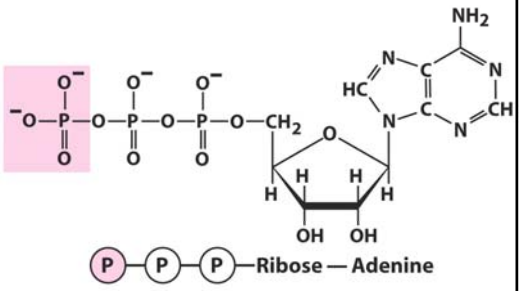

HYP
ENERGY
GO FAST
AMP
ENERGY DRINK
MPULSE
ENERGY DRINK
SKATERADE
burn
Red Bu
KMX
Pir@nha

ENERGY DRINK

DOMOOOO!
ATTACK
energy drink

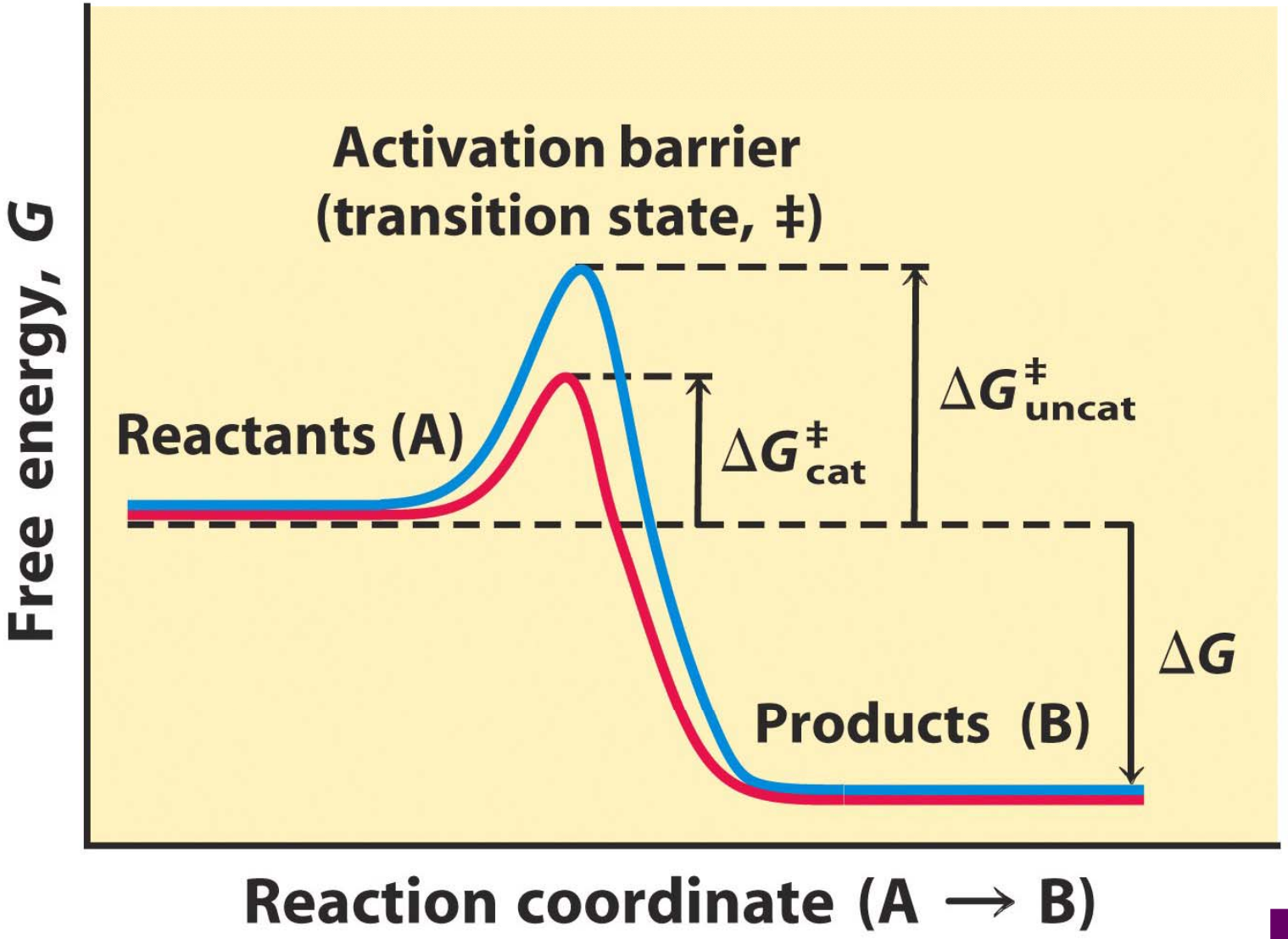
Cocaine
MACE
TOXIC WASTE

PAC-MAN
POWER UP
ENERGY DRINK
NETWEIGHT 8.4 FL.OZ.(250ML)

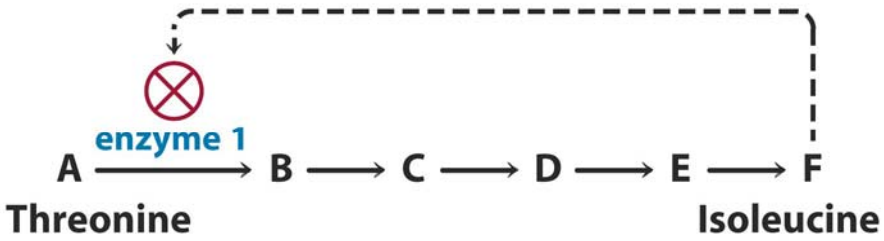

NH2
CH2
OH OH
Ribose — Adenine

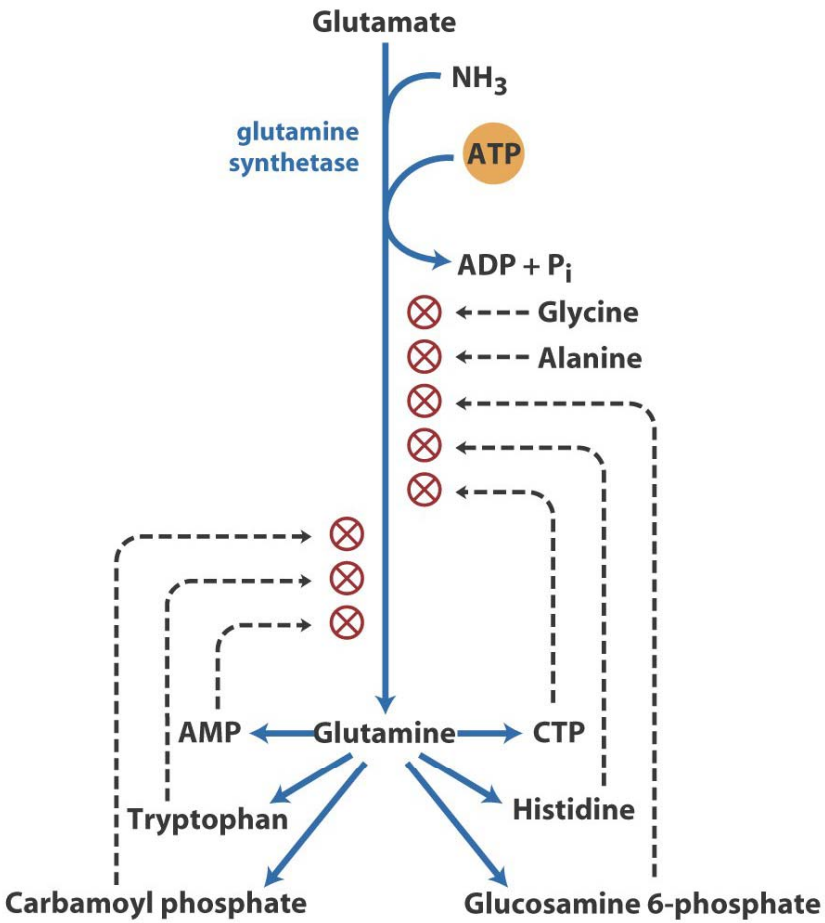
ATP

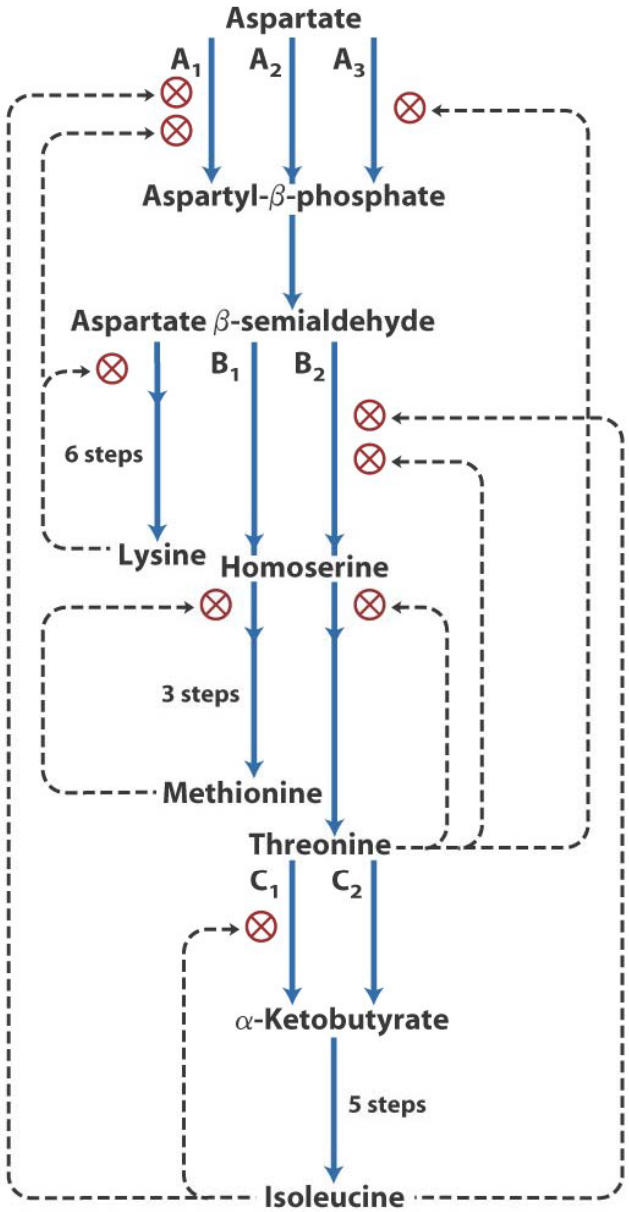
Energy changes during a chemical reaction



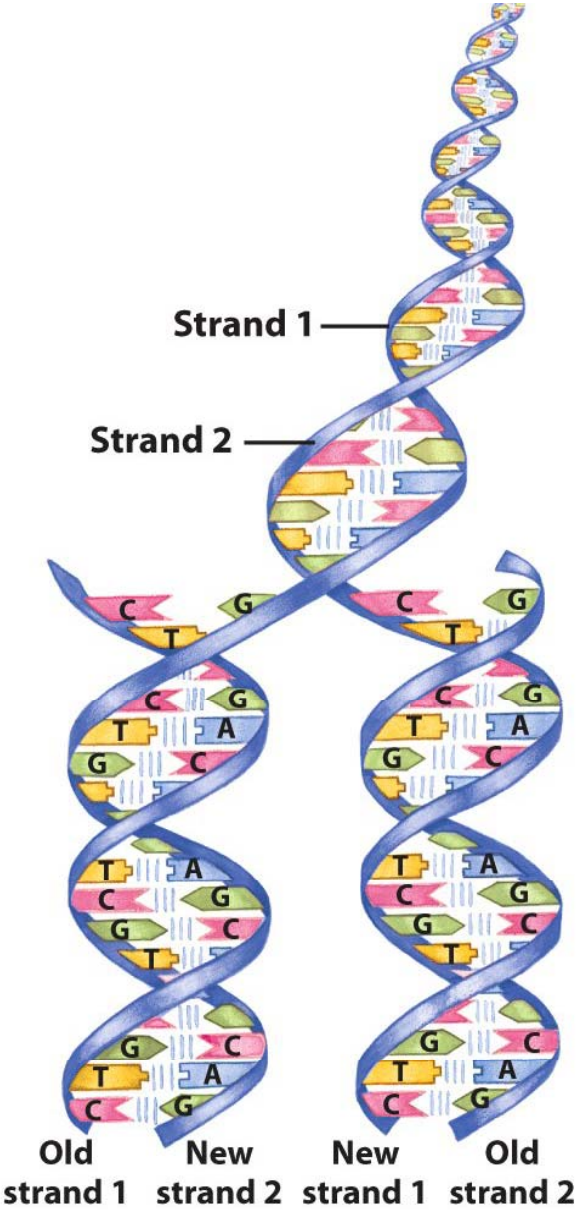
Life is highly regulated

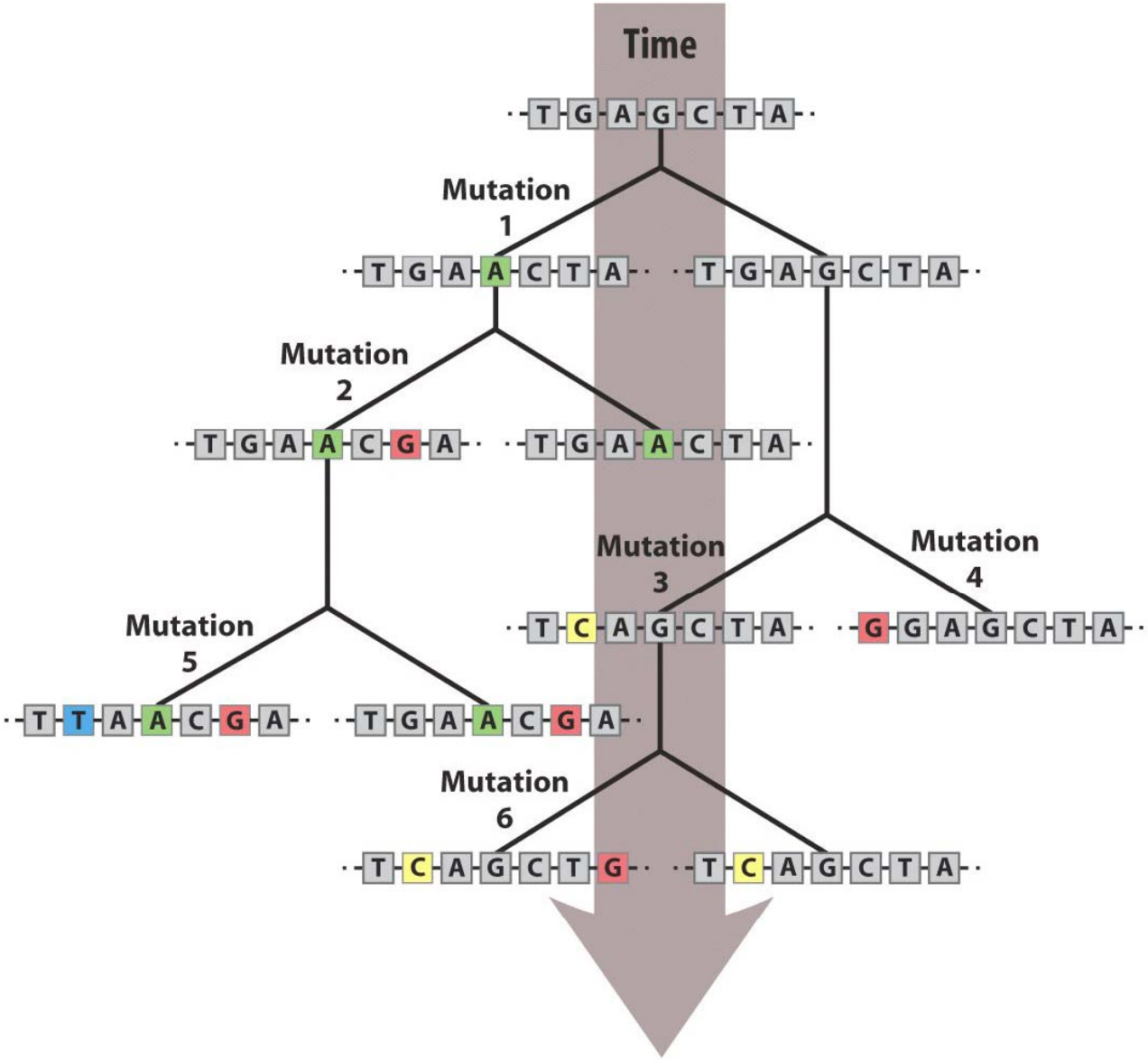






Fidelity vs Mutation





A possible "RNA world" scenario

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

↓

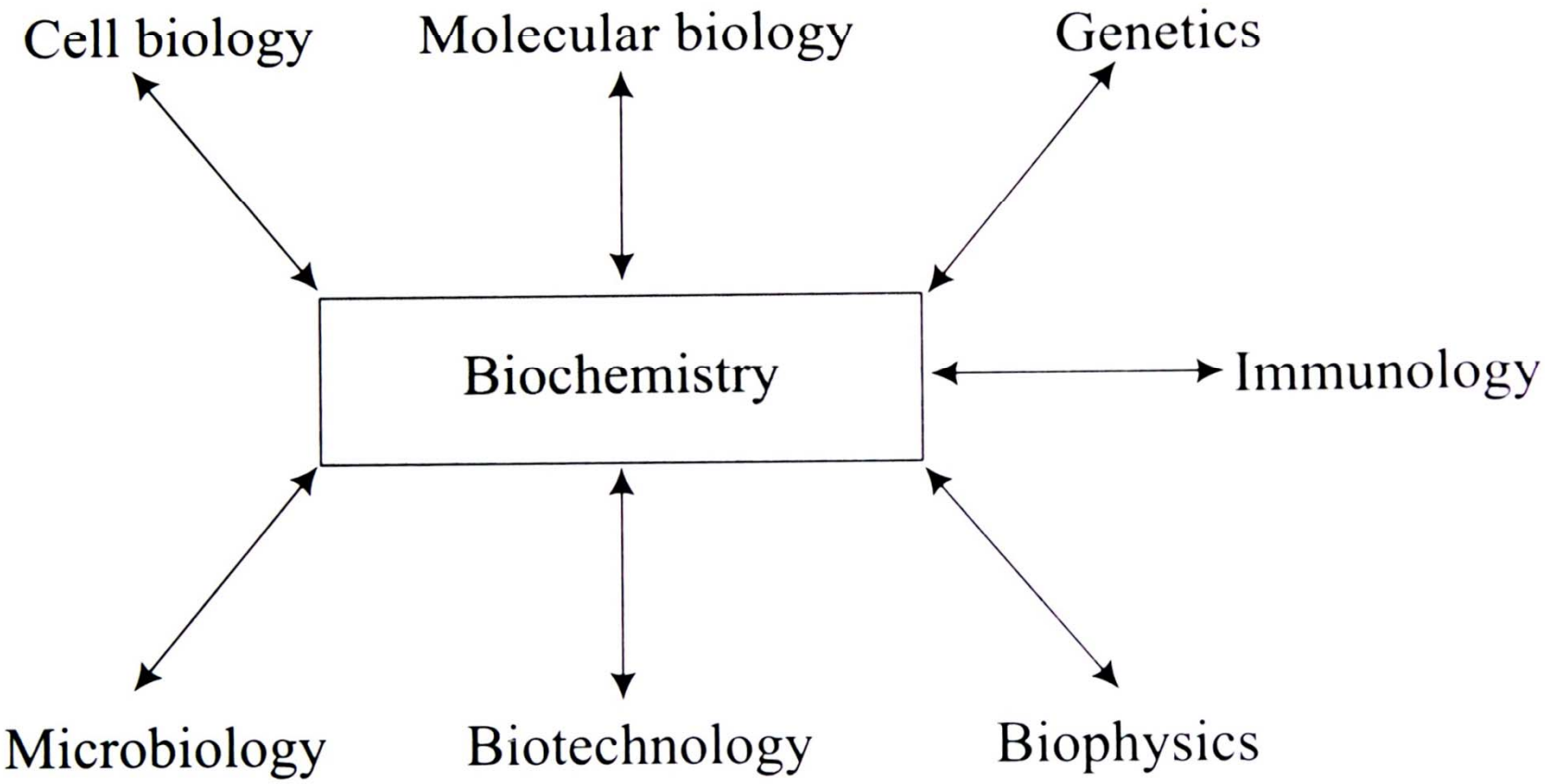
Genomic RNA begins to be copied into DNA

↓

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

Some historical events in biochemistry

Year	*Scientist*	*Event*
1780	Scheele	Isolation of organic compounds from natural resources.
1828	F. Wohler	Synthesis of urea
1878	F.W. Kuhne	Coined the term enzyme
1898	Fischer	Lock and key concept of enzyme action
1903	Carl Neuberg	The term biochemistry **(FEBS Journal)**
1914	Kendell	Isolation of thyroxine
1926	Sumner	Isolation of enzyme urease
1935	Stanley	Isolation of tobacco mosaic virus (TMV)
1937	Krebs	Citric Acid cycle
1948	Calvin and Bensen	Calvin cycle in photosynthesis
1953	Watson and Crick	Double helical model of DNA
1975	Mitstein	Hybridoma cells
1986	Rita-Levi Montalcini Stanley Cohen	Neural growth factor
2006	A.Z. Fire, C.C. Mellow	Role of RNA interference in gene expression

Biochemistry (2010) by Dushyant Kumar Sharma

Biochemistry: An inter disciplinary science