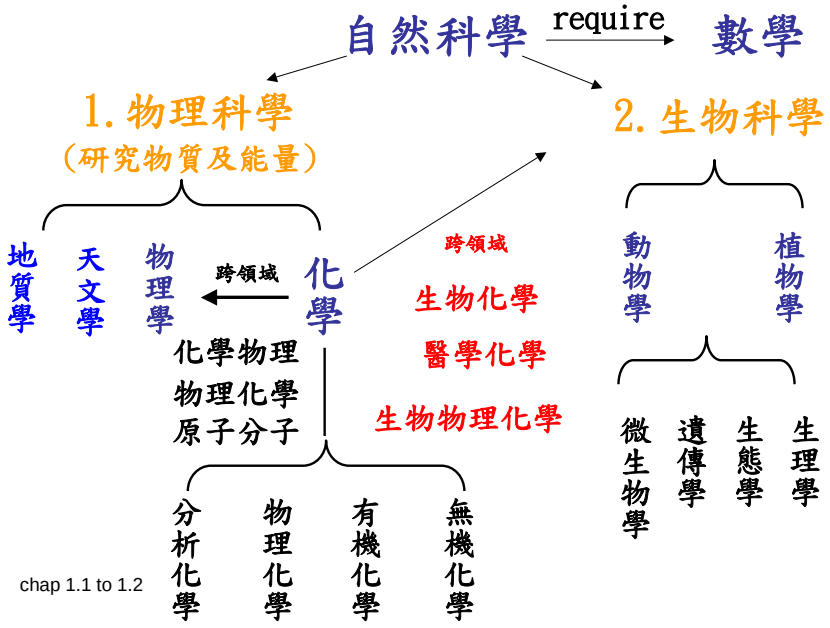
科學的範疇



化學與物理

量子力學(quantum mechanics)

本世紀初，量子力學肇始並宣稱已解決
所有的化學問題及一半的物理問題

Schrodinger Equation： $H\Psi = E\Psi$

H：Hamiltonian operator
Ψ：wavefunction
E：energy

所有的分子性質、化學反應皆可由此
Schrodinger Equation推測

然而現今只能成功地推測小分子！！

化學與應用化學

- 材料科學：金屬材料
  高分子材料

電子工程：電子材料

化學工程：將化學實驗室的製程放大

食品：食品添加物

生化及藥化產業：製藥、生物科技

Chapter 1
Foundations of Biochemistry

What is Chemistry？

This science that tries to understand：

(A)The properties of substances

(B)The changes that substances undergo

The realm of substances：

(A)Natural substances：

e.g.water, air, element, salt...

(B)New compounds created by chemists

e.g.polymer ,nylon...

(C)Chemicals found in living creatures：

e.g.DNAs, proterins, carbohydrates...

Biochemistry tries to understand：

(A)The properties of biomolecules

(B)The changes that biomolecules undergo

The molecular logic of life

- **Consider the properties of living organisms**
- **Describe a set of principles that characterize all living organism**

Diverse living organisms share common chemical features

The differences between livings and inanimate objects

1. **Chemicail complexity & organization**
2. **Living organism extract, transform,and use "energy" from their environments, usually in the form of chemical nutrients or sunlight.**
3. **Living organisms are capable of "self-assemby" and self-replication**
4. **Mechanisms for sensing and responding to alterations in their surrounding**
5. **Defined functions for each of their components and regulated interaction among them.**
6. **A history of evolutionary change**

Biochemistry explains diverse forms of life in unifying chemical terms：

異(巨觀)	同(微觀)
Living organisms are enormously diverse：animals、plants	**Living organisms are remarkably alike at the cellular and chemical levels**

Biochemistry describes：

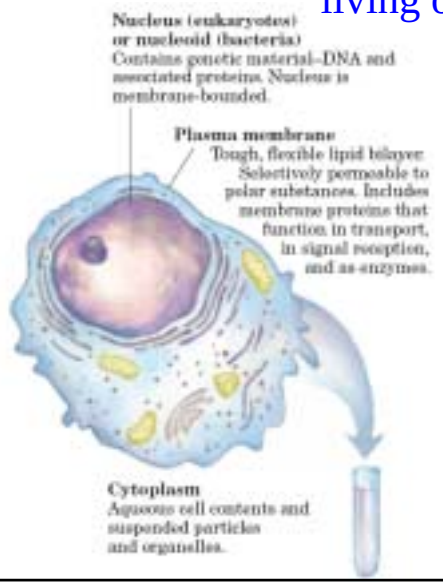
1.The structures, mechanisms, and chemical processes shared by all organisms in "molecular terms"

2.Provides organization principles that underlie life

The molecular logic of life

1.1 Cellular Foundations

Cells are the structural and functional units of all living organisms

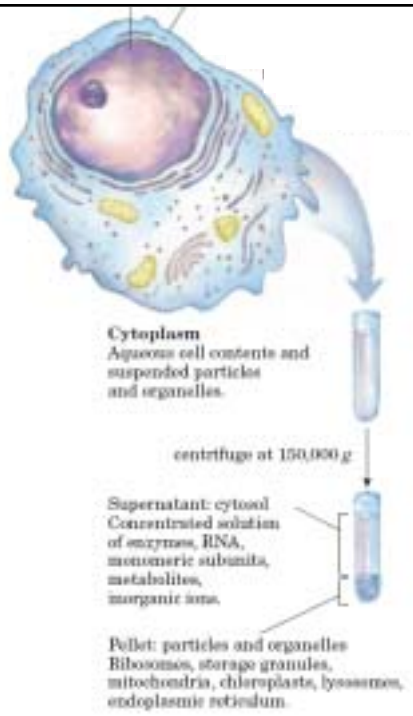


Cells:

1. Plasma membrane：

defines the periphery of the cell, separating its contents from the surroundings.

It is composed of lipid and protein molecules that form a thin, tough, pliable, hydrophobic barrier around the cell.



2. Cytoplasm：

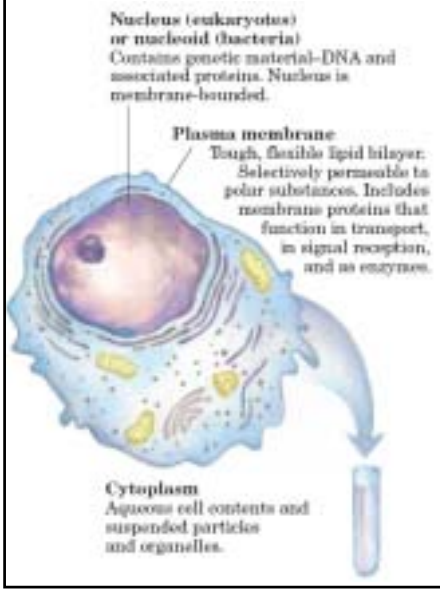
composed of cytosol and suspended particles

Cytosols：

enzymes, RNA molecules, monomeric subunits(amino acids and nucleotides), metabolites(small organic molecules), coenzymes.

suspended particles：

Supramolecular,organelles(like ribosomes) specialized metabolic mechinery



3. Nucleus or Nucleoid：

Complete set of genes (genome)

Eukaryotes (真核生物)：

Cells with nuclear envelopes

Prokaryotes (原核生物)：

without nuclear envelopes

Cellular Dimensions Are Limited by Oxygen Diffusion

- **Animal and plant cells are 5 to 100 μm in diameter**
- **many bacteria are only 1 to 2 μm long**
- **the smallest cells：mycoplasmas (黴漿菌), ~300nm in diameter, and ~10^{-14} ml in volume**
- **Upper limit of cell size：defined by the rate of diffusion of solute molecules in aquaous systems**
- **Lower limit of cell size：Set by the minimum number of each type of biomolecule (supramolecules and organelles) required by the cell (e.g. ribosome，~20nm long)**

There Are Three Distinct Domains of Life

1. Eubacteria (真細菌)

inhabits soils, surface waters, tissues.

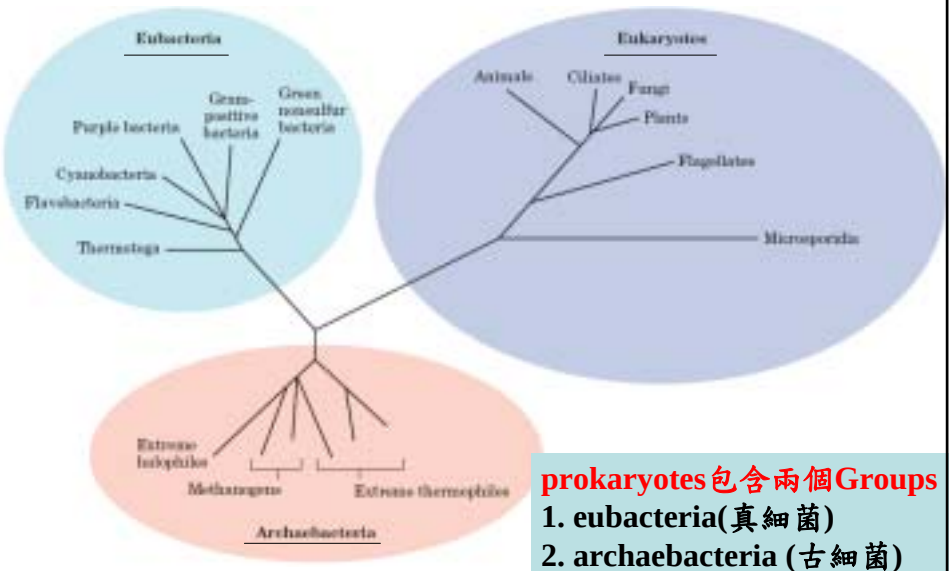
e.g. E. Coli

2. Archaebacteria (古細菌)

inhabits more extreme environments (salt lakes, hot springs…) e.g. methanococcus jannasch

3.Eukaryotes (真核生物)

There Are Three Distinct Domains of Life



prokaryotes包含兩個Groups

1. eubacteria(真細菌)

2. archaebacteria (古細菌)

Organisms can be classified according to their energy source (sunlight or oxidizable chemicals)

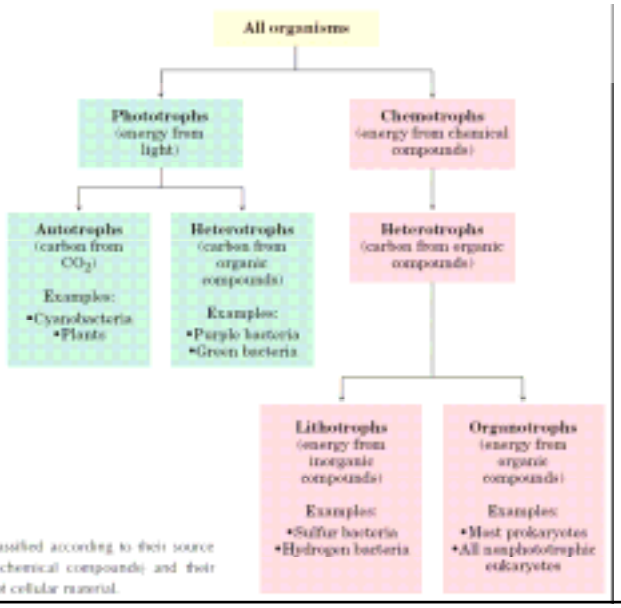
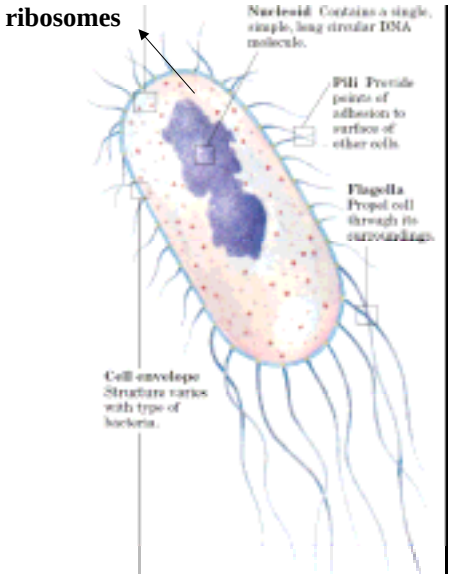


FIGURE 1-5 Organisms can be classified according to their source of energy (sunlight or oxidizable chemical compounds) and their source of carbon for the synthesis of cellular material.

Escherichia coli (大腸桿菌) is the most-studied prokaryotic cell ： 5 μm in length; 2 μm in diameter



Escherichia coli is the most-studied prokaryotic cell

***E Coli* 由 membrane 伸出：Pili, flagella**

- **cytoplasm：Ribosomes (15,000個), enzymes (1000種), metabolites, and cofactors**
- **Nucleoid：A single, circular molecule of DNA. 1000x length(*v.s.* cell)，packed 成1 μm左右大小**
- **Plasmid：Few smaller, circular molecule of DNA Resistance to toxins and antibiotics.Amenable to manipulation for molecular genetic study**

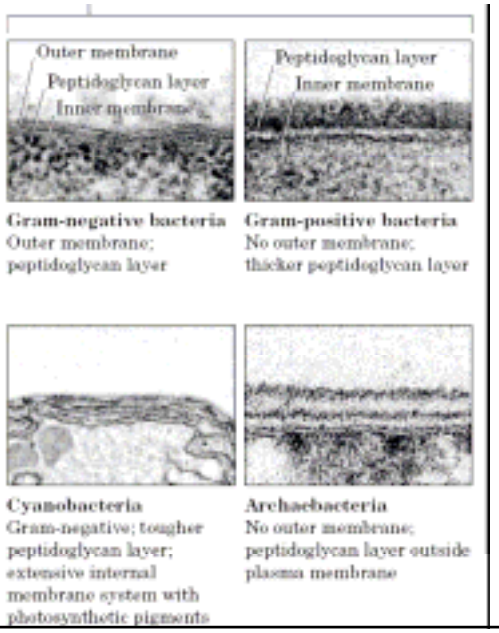
Escherichia coli is the most-studied prokaryotic cell

Cell envelopes：

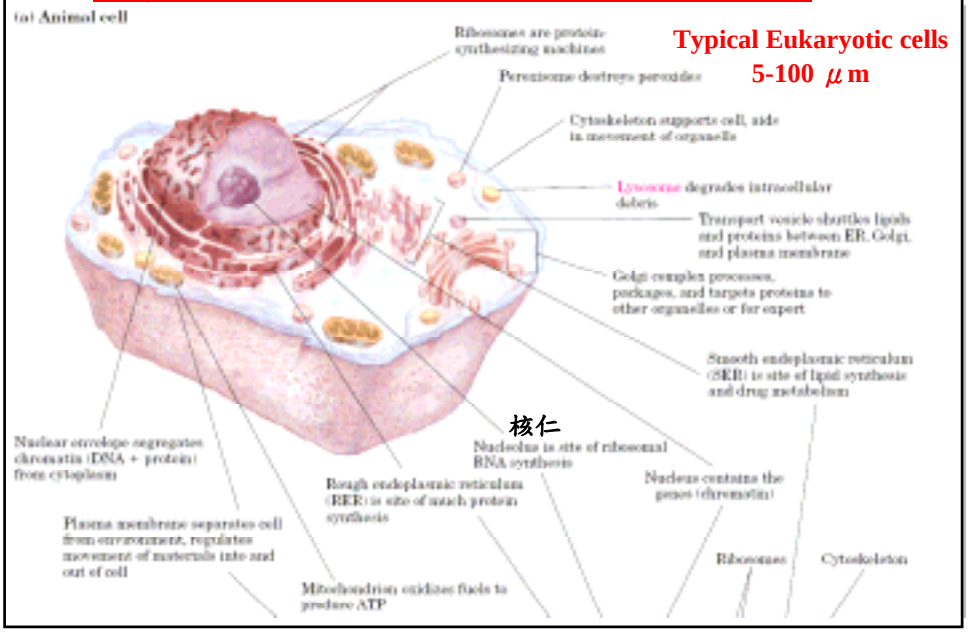
- Gram-negative bacteria (e.g. *E. Coli*, cyanobacteria 氰菌, etc)
  - with outer membrane
  - peptidoglycan layer
  - extemsive inner membrane system
- Gram-postive bacteria (e.g. Bacillus subbtilis 桿菌, staphylococcus aureus 葡萄球菌, archaebacteria, etc.)
  - without outer membrane
  - peptidoglycan layer thicker
  - inner membrane

Cell envelopes

Gram negative and positive bacteria



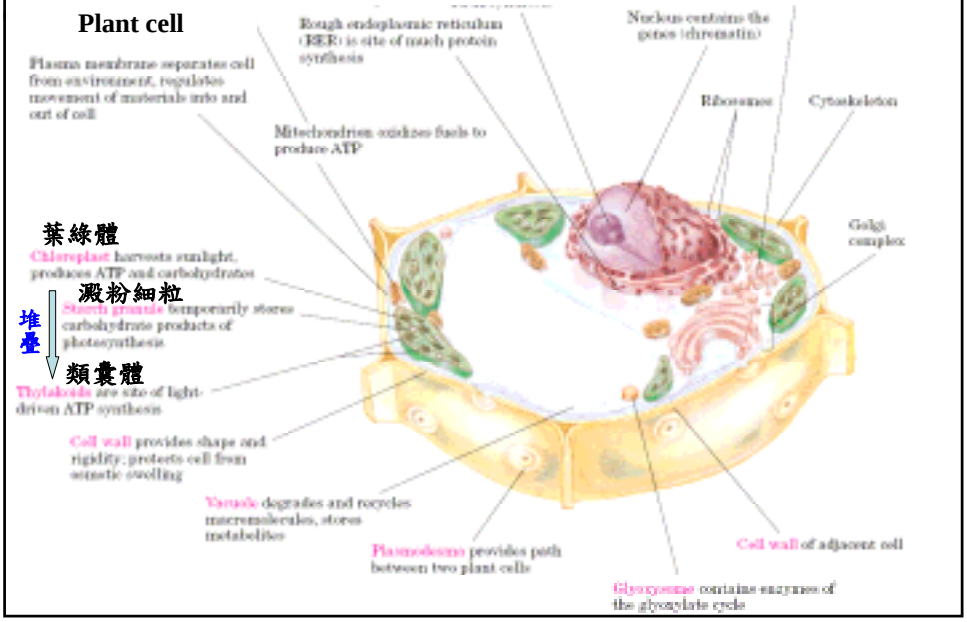
Eukaryotic Cells Have a Variety of Membranous Organelles, Which Can Be Isolated for Study



Typical Eukaryotic cells

5-100 μm

Eukaryotic Cells Have a Variety of Membranous Organelles, Which Can Be Isolated for Study



Eukaryotic Cells Have a Variety of Membranous Organelles, Which Can Be Isolated for Study

Plasma membrane：

Lipid bilayer, contains transporter and receptors

1.Transporters：proteins that span the membrane and carry nutrients into the cell and products out

2.Signal receptors：bind with extra-cellular signaling molecules (ligands)

receptors recognize ligands (can be small molecules or macromolecules).

e.g. drugs – receptor

virus/bacteria/protein – receptors

(antigens) (antibody)

- **Higher plants have cell wall(rigid, protective shell) formed by cellulose & carbohydrate polymers outside the plasma membrane**

Endocytosis and Exocytosis carry traffic across the plasma membrane

Endocytosis(胞飲)：

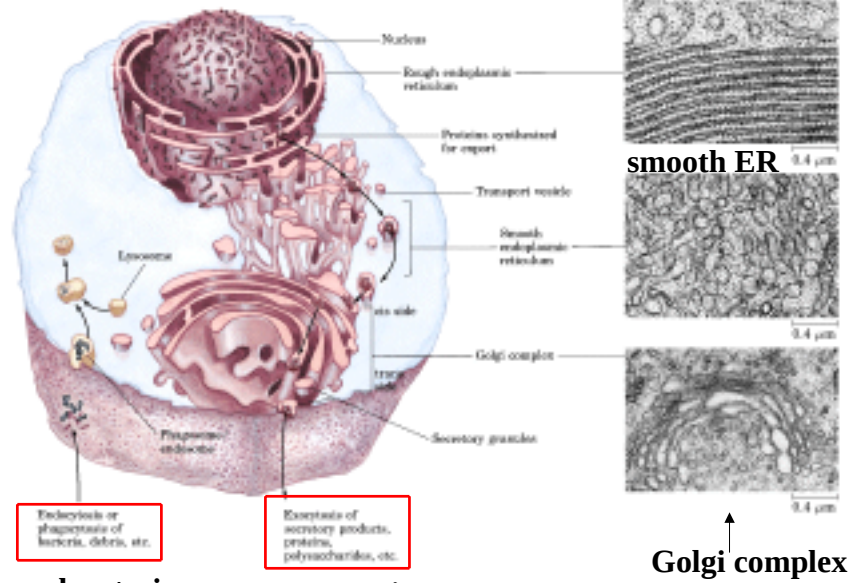
A mechanism for transporting components of the surrounding medium deep into the cytoplasm

Phagocytosis(吞噬)：

One kind of endocytosis，but carry cell fragment or other smaller cells

Exocytosis (胞吐) ：

A vesicle in the cytoplasm moves to the inside surface of the plasm membrane fuses with it, then release the contents outside the membrane



Cellular Components of Eukaryotic Cells

Endoplasmic reticulum(ER)：

Highly convoluted, three-dimensional network of membrane-enclosed spaces throughout the cytoplasm and enclosing a subcellular compartment(the lumen of the ER)

Rough ER：

Granular appearance (because ribosomes attached)

Smooth ER：

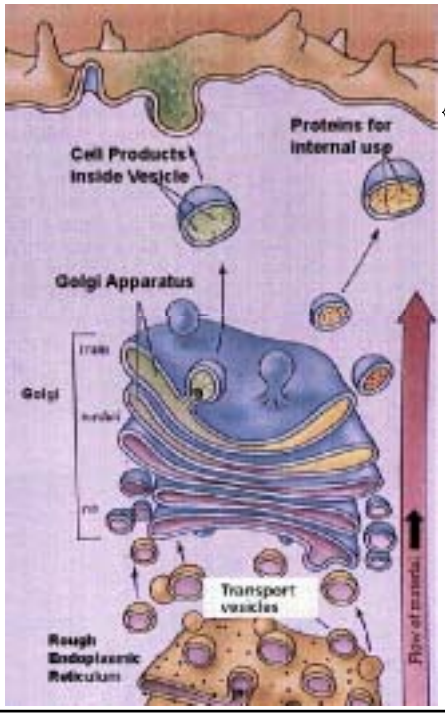
1. the site for lipid synthesis

2. metabolism of certain drugs and toxic compound

3. In some tissues(e.g skeletal muscle), storage and release Ca^{+2}

Golgi complex：

- **Cis side：face rough ER**
- **Medial element**
- **Trans side：face plasma membrane**
- **Proteins will be modified (e.g. adding sulfate, lipid, carbohydrate groups)**



1.Targeted for intracellular organelles(e.g. lysosomes)
2.Released from the cell by exocytosis
3.Incorporate into plasma membrane

⇧

Move to the Golgi complex (Proteins will be modified e.g. adding sulfate, lipid, carbohydrate groups)

⇧

Bud

⇧

Small membrane vesicles (Transport vesicles)

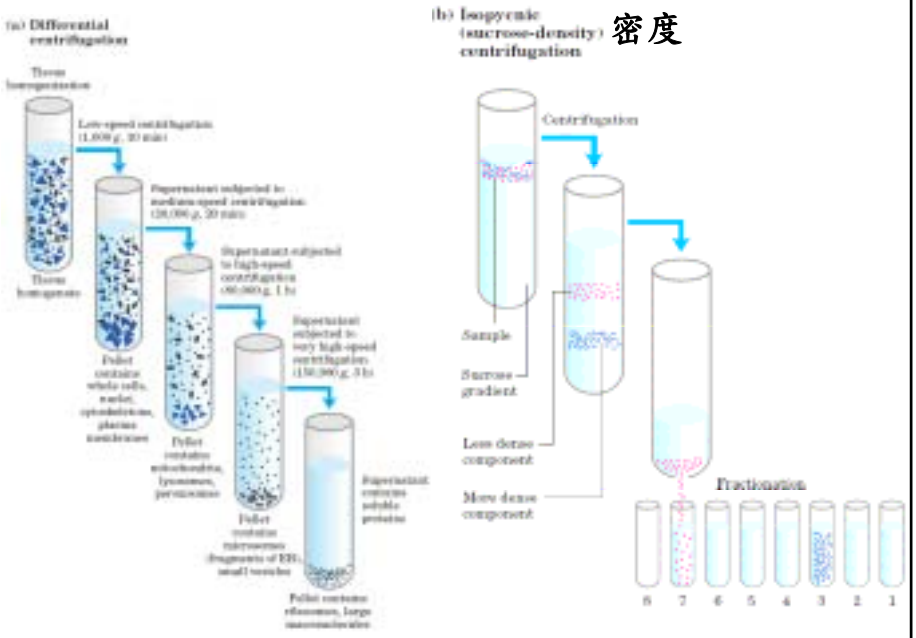
⇧

Inserted into rough ER lumen

⇧

Proteins(during the synthesis on ribosomes on rough ER)

Study of Cellular Components



Eukaryotic Cells Have a Variety of Membranous Organelles, Which Can Be Isolated for Study

Ribosome：

- **Synthesis of proteins**
- **Ribosomes attached ER synthesis protein that will be：**

1.Released from the cell(secretory proteins)
2.Targeted for intracellular organelle(e.g. lysosome)
3.Inserted into nuclear or plasma membranes

- **Cytoplasmic ribosomes synthesize proteins that will remain and function in cytosol**

Lysosomes(溶酶體)：(Only in animal cells)

- **contain enzymes, capable of digesting proteins, polysaccharides, nucleic acids, and lipids.**

- **act as recycling centers**

  分解：complex molecules carried from endocytosis
  foreign cell fragment carried from phagocytosis
  organelles carried from cell's cytoplasm

  分解成 a.a, monosaccharides, fatty acids.

- **pH of lysosomal compartment $\leq$ 5**
  enzymes inside are more active in acidic pH

Peroxisomes(過氧化氫酶體)： contain catalase

$$2H_2O_2 \xrightarrow[\text{catalase}]{} 2H_2O + O_2$$

Glyoxysomes(乙醛酸循環體)：

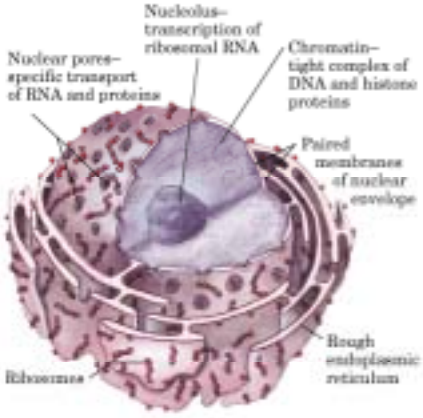
- **specialized peroxisomes in certain plant cells**
- **contain high conc. of enzymes of glyoxylate cycle**

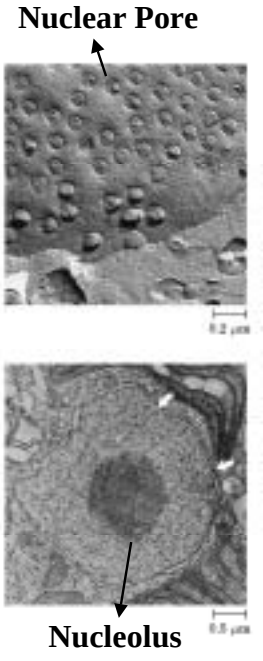
$$\text{fats} \xrightarrow[\text{enzymes}]{} \text{Carbohydrates}$$

Lysosomes, peroxisomes, and glyoxysomes
稱為 microbodies

Vacuoles of plant cells

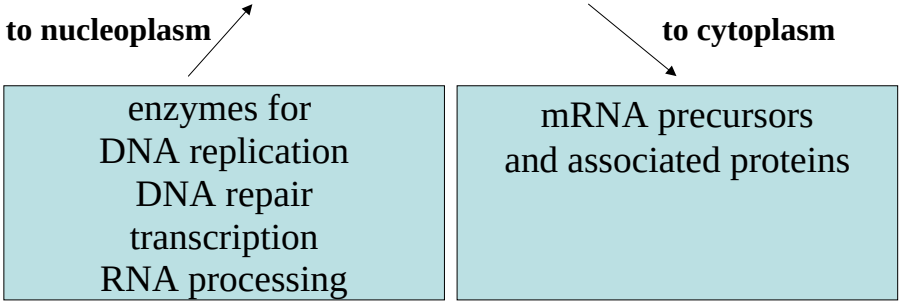
- **plant cells have no lysosomes.**
- **vacuoles carry similar “degradative” rx**
- **Tonoplast (the membrane surrounding the vacuole): regulate the entry of ions, metabolites etc. for degradation.**
- **Vacuole (at acidic pH) : degrade and recycle biomolecules 的enzymes**
- **Vacuoles also provide physical support to the plant cell.(因salt含量比cytosol高，產生osmotic pressure or call turgor pressure 將cell撐起)**
- **Vacuoles 含染料，會使花果有顏色**





Nucleus：**contains the genome**

•Nuclear pores(～90 nm in diameter) associated with nuclear pore complexes specific transporters

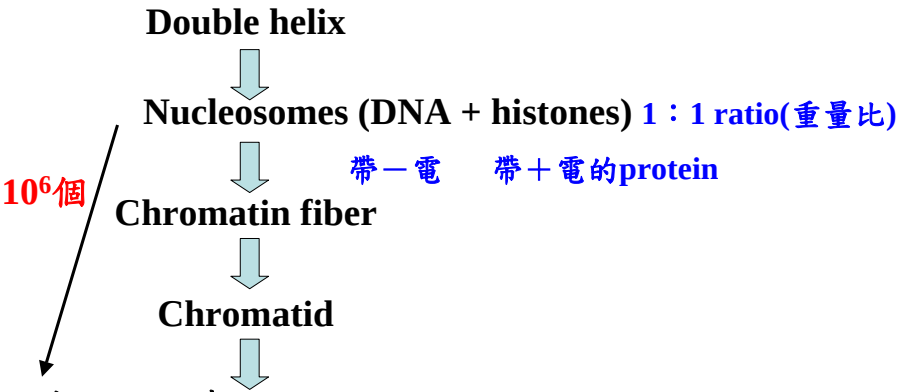


Chromatin(染色質)：contain DNA and proteins (histones) bound tightly together

Nucleolus：在nucleus中，含many copies of the genes coding ribosomal RNAs (有效地transcribe into ribosomal RNA！)以備有效產生許多ribosomes！

Mitosis：**Nuclear division 有絲分裂**

Cytokinesis：細胞分裂, 胞質分裂(cell division)



Somatic cells(體細胞)：
have two copies of each chromosome (diploid,雙倍的)

Gametes(配子) (egg, sperm 生殖細胞):
•have only one copy of each chromosome (haploid, 單倍的)
•有性生殖時與不同性的配子合成 zygate (合子)

DNA of a single diploid human cell
拉長時：～2m
packed時：～200 μm } **10^4差別**

Mitochondria are the power plants of Aerobic Eukaryotic cells

- **1 μm in size**
- **數百～1000個 mitochondria / eukaryotic cell**
- **含two membrane：**
  - **outer membrane**
  - **inner membrane (called cristae)：**
    內含物(matrix)：enzymes involving in the energy-yielding metabolism.

利用oxidation of organic nutrients

↓ **產生能量**

製造ATP

Mitochondria are the power plants of Aerobic Eukaryotic cells

- **mitochondria are produced only by division of previously existing mitochondria.**
- **mitochondria contains its own DNA, RNA, and ribosomes.**
- **mitochondria DNA codes for certain proteins specific the mitochondria inner membrane.**

Chloroplast(葉綠體)：power plants of plant cells

Pigment molecules (chlorophyll,葉綠素)

⇓ **在chloroplast的inner membranes (thylakoid類粒體)**

adsorb solar light

⇓

make ATP

⇓

reduce CO_2 to carbohydrates：

Mitochondria and chloroplast probably evolved from endosymbiotic bateria (內共生菌).

The Cytoplasm is organized by the cytoskeleton and is highly dynamic

Cytoskeleton：

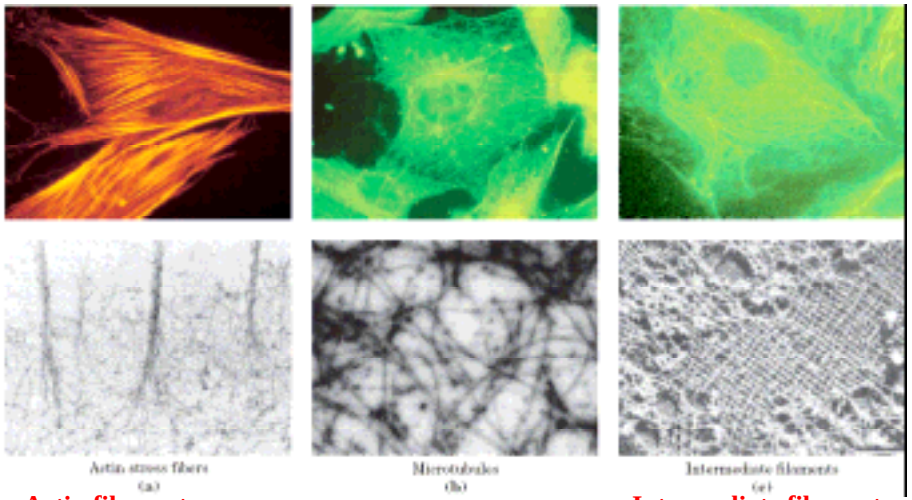
1. actin filaments 6nm
   (又叫microfilament 肌動蛋白絲)
2. microtubules 22nm
   (微管)
3. intermediate filaments 6-22nm

Cytoskeletal components

↓↑ constantly disassemble & reassemble

Simple protein subunits that polymerize

(location in cells, not rigidly fixed, change during mitosis, cytokinesis….)



Actin filaments bundled together to form 'stress fibers'

Microtubules radiating from the cell centers

Intermediate filaments Extended throught the cytoplasm

(1) Actin(肌動蛋白) filament (or microfilament): 6-7nm

Actin sununits

↓

actin thin filament

↓ ＋filamin ＋Fordin

parallelly-linked(by fordin)
cross-linked(by filamin) } actin filament

Actin filament
+
Myosin
+ ATP ↓

{ head(binds to actin filament)
tail(binds to the membrane of a cytoplasmic organelle)

move cytoplasmic organelle or vesicle along the actin filament (called cytoplasmic streaming)

*muscle contraction 亦相似

Actin filament
+
Myosin
+
ATP
↓
muscle contraction
(See figure 5-33)

(2)microtubles (22nm)

subunits：α- & β- tubulin
(throughout the cell, but concentrated around nucleus)
mitosis時, microtubules 會 highly organized & help the separation of chromosomes (可能provide motive force)

Microtubules
+
kinesin
dynesin
+
ATP
↓

e.g. cilia
flagella } **beating motion**

move organelle along microtubules (以1 μm/s移動)

e.g.
•contraction of muscle propelling action of cilia and flagella
• intracellular transport of organelles

reason：
myosin, kinesin,dynesin
↓
splitting "ATP"
↓
driving sliding motion along microtubules and microfilaments

(3)Intermediate filaments (8-10nm)：

provide internal mechanical support for the cell and to position its organelles

subunit： vimentin, keratin,desmin等

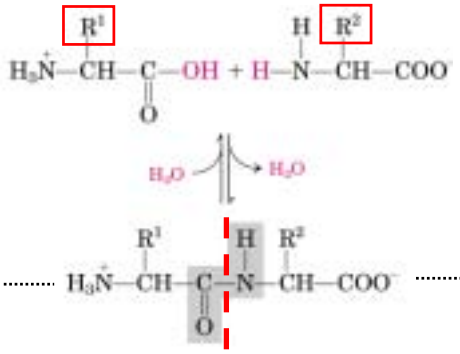
e.g. 在endothelial cells(內皮細胞), vimentin fibers anchor nucleus and fat droplets in the specific location

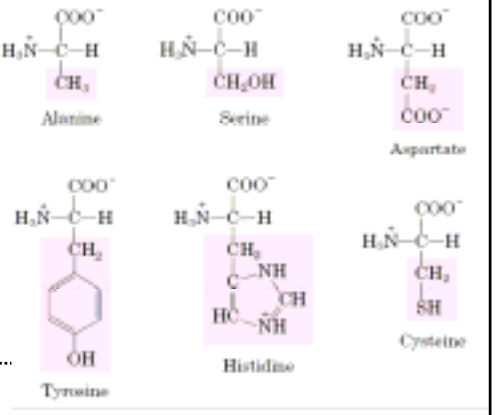
• The cytoplasm is crowded, highly organize and dynamic!!
• Cytoplasm：
meshwork of structural fibers (protein fibers)
membrane-bound organelles locate在其中

Cells Build Supramolecular Structures

(A)Protein：

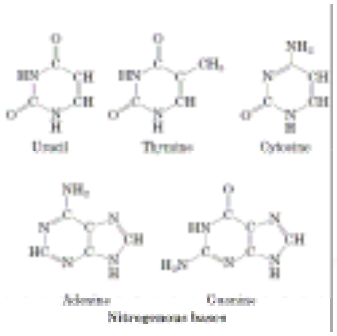
20種amino acids as building blocks

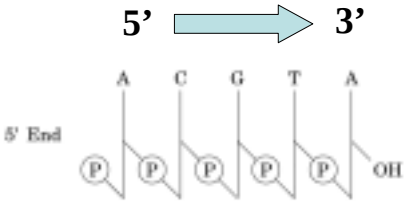


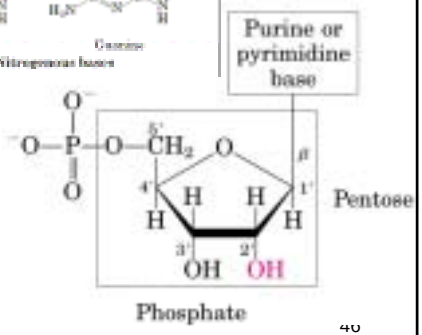


Cells Build Supramolecular Structures

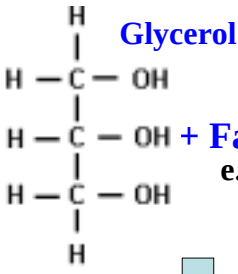
(B)DNA：4 possibilities







(C)Lipids

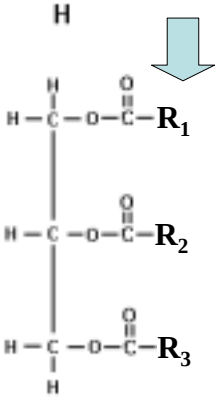


Glycerol

+ Fatty acids

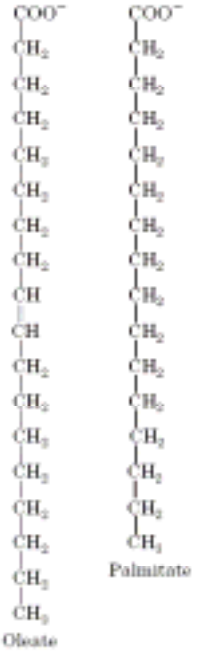
e.g. Oleate

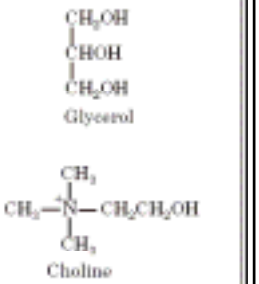
palmitate

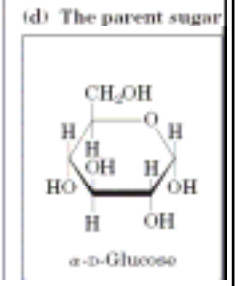


可形成

Lipid bilayer





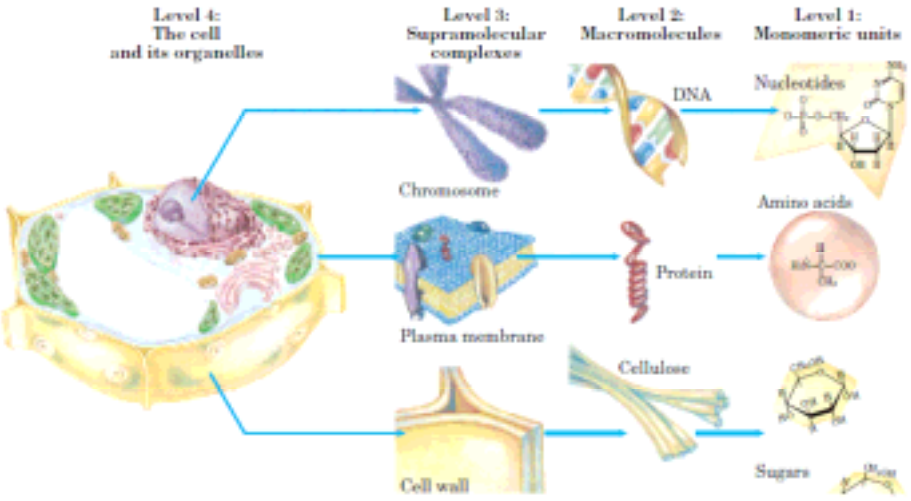


(D)Polysaccharides

Most abundant polysaccharides：starches, glycogen and cellulose

Monomeric subunit：主要為glucose

Structural hierarchy in the molecular organization of cells



Structural hierarchy in the molecular organization of cells

Cell

Organelles
- Nucleus
- Mitochondria
- Golgi body
- E.R

Supramolecular assemblies
- Membranes
- Ribosomes
- Chromatin
- Microtubules

Non-covalent interactions
- Hydrogen bond
- Ionic interaction
- Hydrophobic interaction
- Van der Waals forces

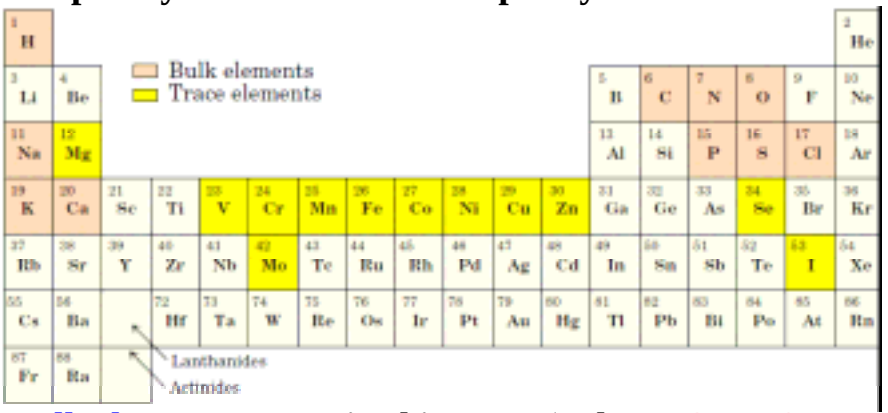
Macromolecules
- Proteins
- DNA
- RNA
- Polysaccharides

Covalent bonds

Building blocks
- Amino acids
- Nucleotides
- Sugars

1.2 Chemical Foundations

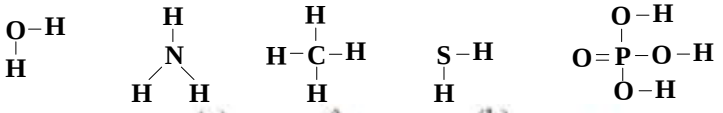
Complexity of life ⟷ Simplicity of "element"world



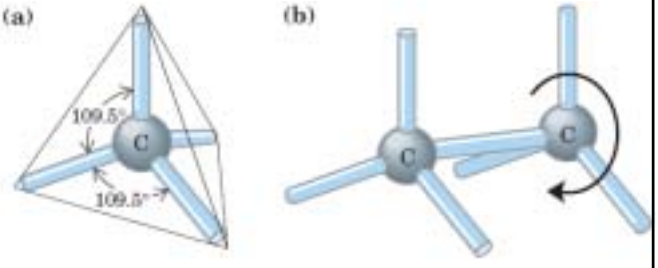
Bulk elements：required in gram(only H, C, N, O, Na, P, S, Cl, K, Ca) 佔99%

Trace elements：required much less (colored in yellow)
如Mg, V, Cr, Mn, Fe, Co, Ni, Cu, Zn, Se, Mo, I

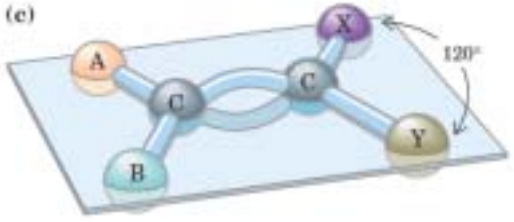
Covalent bonding ⟷ 組成biomolecule的骨架



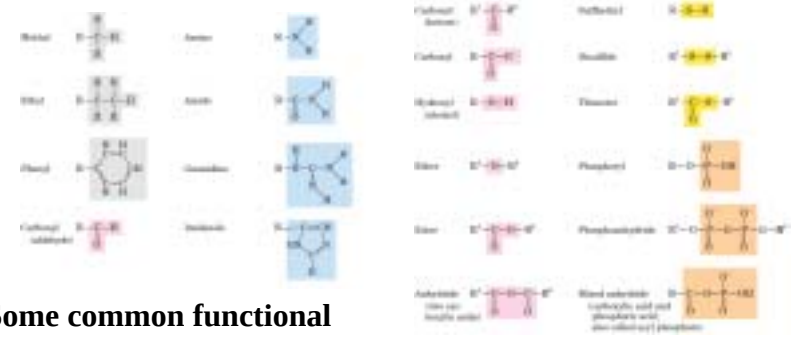
Geometry of Carbon Bonding



C—C Bond length 1.54A



Biomolecules Are Compounds of Carbon with a Variety of Functional Groups

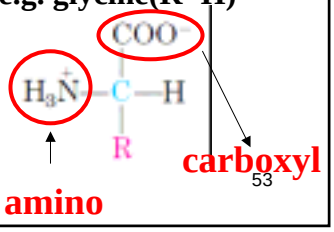


Some common functional groups of biomolecules

Many biomolecules ⇨ Multi-functional

"reactivity (chemical properties) of biomolecules determined by: (1) functional groups, (2) 3-dimensional structure

e.g. glycine(R=H)



Macromolecules Are the Major Constituents of Cells

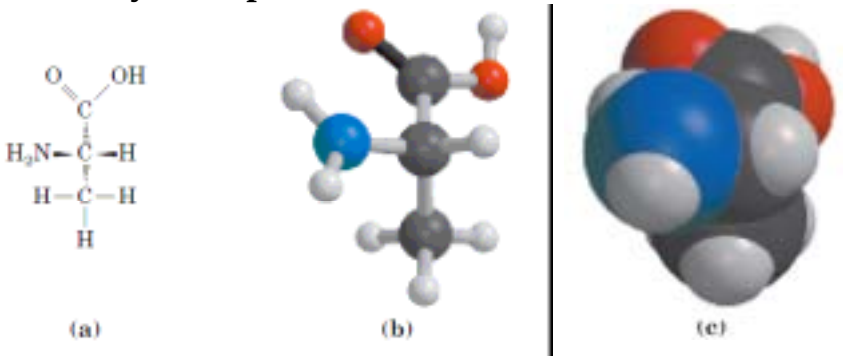
TABLE 1-2 Molecular Components of an *E. coli* Cell

	Percentage of total weight of cell	Approximate number of different molecular species
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

Proteins and nucleic acids are informational macromolecules

Three-Dimensional Structure Is Described by Configuration and Conformation

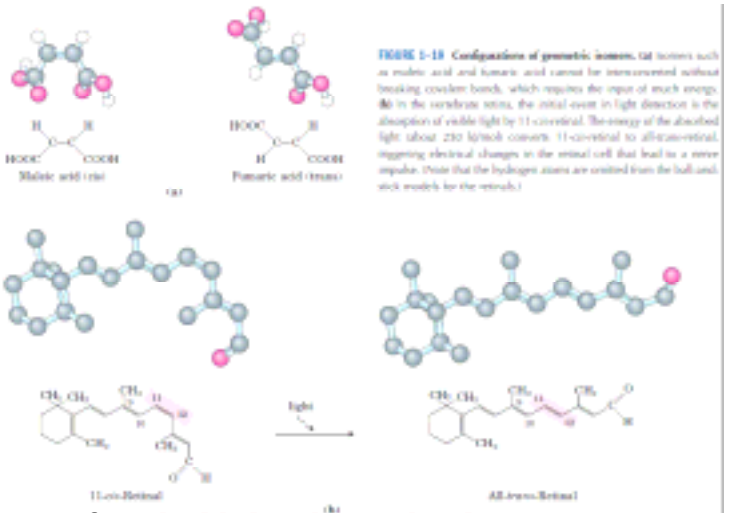
Three ways to represent the structure of Biomolecules：



(a) Structure Formula
(b) Ball-and-stick model (shows relative bond length and bond angles
(c) Space-filling model (shows correct 電子密度的bond length)

Configuration －changed only by bond-breaking

Configuration ：fixed spatial arrangement of atoms in a molecule



In the presence of (1) double bonds (2) chiral center

→ **configurational isomers**

respected to

double bond ⇨ { geometric isomers / or cis-trans }

chiral centers ⇨ stereoisomers { R/S form / D/L form }

{ enantiomers (mirror images) / diastereomers (non-mirror images) }

n 個 Chiral carbons ⇨ 2^n個 stereoisomers

Configurational isomers can be isolated (if use proper separating methods)

有chiral center，表四個不同的atom，C的四周圍電子密度不均勻，使電磁波偏移

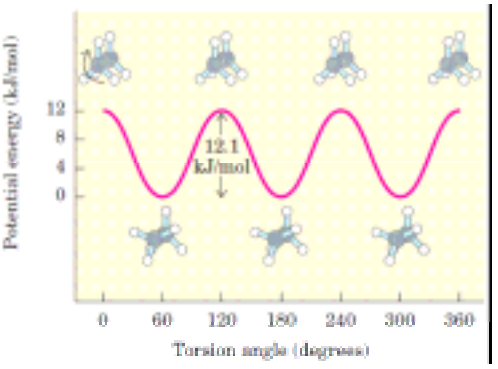
- Enantiomers will notate the plane of plane-polarized light
- Racemic mixtures(equimolar mixture of two enantiomers) will not rotate the plane-polarized light

Molecular Conformation is Changed by Rotation about Single Bonds

Molecular conformation

⇩

The spatial arrangement of substituent groups can be changed by "free rotation"(w/o any bond breaking)



See figure 1-21

Potential energy differences of many conformations of ethane

⇩

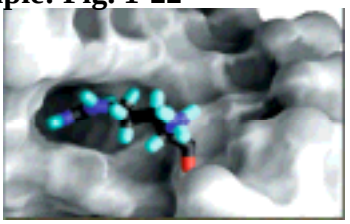
Energy differences are two small conformational isomers can be interconverted ⇦ Cannot be separated

Configuration and conformation define biomolecular Structures

Molecular recognition：related to their three-dimensional structures (結構上的互補性, complementarity)

e.g.	Hormone molecule	with	receptor
	Antigen	with	a specific antibody
	Substrate	with	the catalytic site of an enzyme

Example: Fig. 1-22



TAR region of HIV genome w/arginine

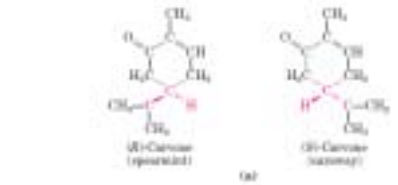
Interactions between Biomolecules are stereospecific

In vivo, biomolecules are usually present in only one of their chiral forms.

e.g. Amino acids ⇨ Only L isomers

Glucose ⇨ Only D form

Enzymes have the ability to distinguish between isomers. (Enzymes are stereospecific！)
Example: Fig. 1-23

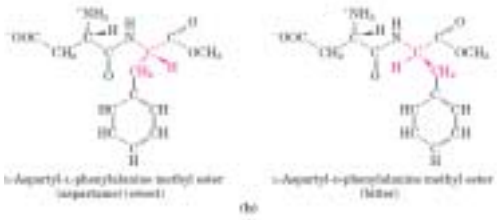


(a)Carvone：

Smell as spearmint (R form)

caraway香菜 (S form)

Smell sensory receptor can distinguish！



(b) aspartame：

Taste sweet ⇨ aspartame

taste receptor can distinguish！