

Molecular Biology (一)



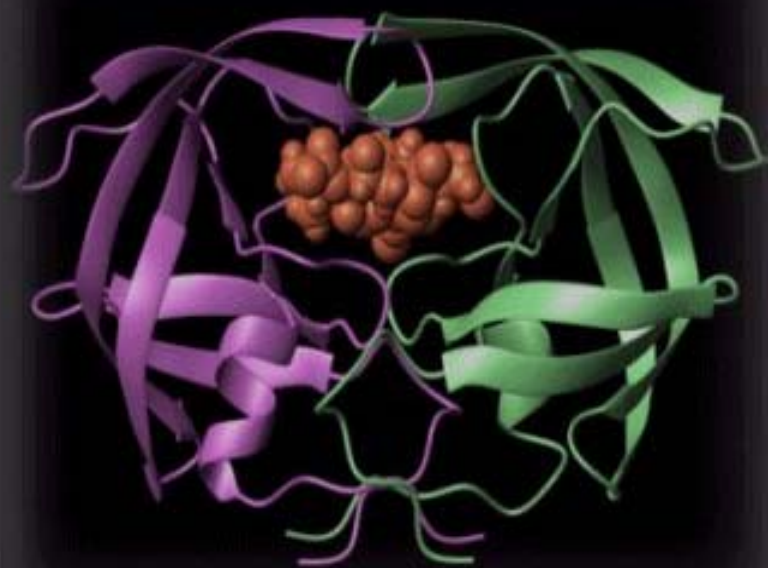
細胞簡介



DNA & RNA的結構



蛋白質的結構與功能



細胞簡介

生物細胞可分兩大類：

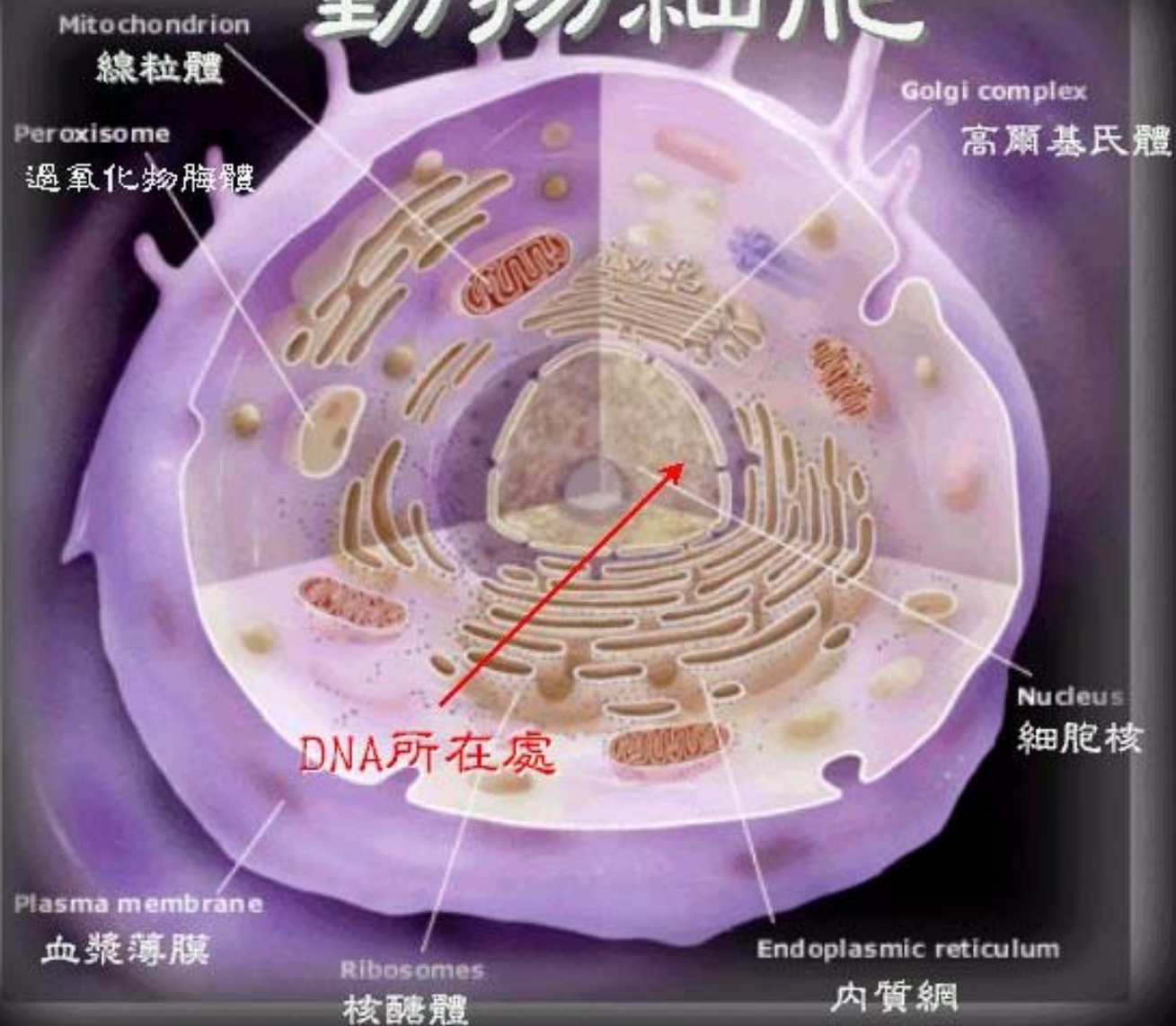
1. 原核細胞 (prokaryotic cell)

- 細胞內不含細胞核(nucleus)
包含所有的細菌 (bacteria)
EX: 大腸桿菌 (Escherichia coli)

2. 真核細胞 (eukaryotic cell)

- 細胞內含細胞核(nucleus)
包含動、植物及真菌 (fungi)
EX: 酵母菌 (yeast)

動物細胞



核酸的基本單位

核甘酸(nucleotide)
由三部份所組成：

S：戊糖
(pentose)

B：鹼基
(nitrogenous base)

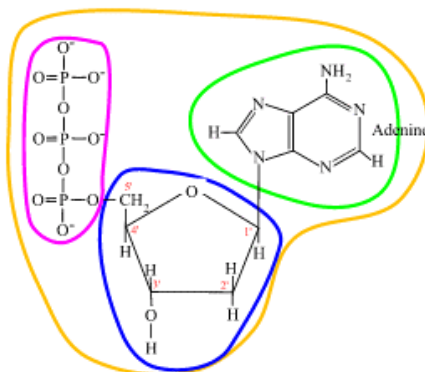
P：磷酸根
(phosphate group)

The components of nucleotides

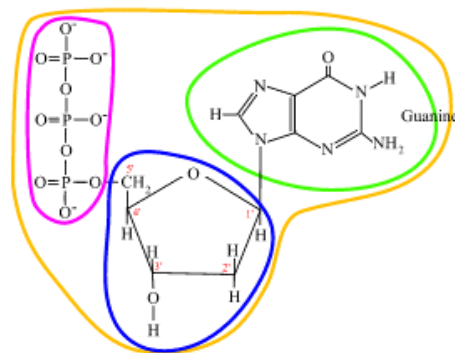
Nucleotide = base + sugar + phosphate

4 different dNTP's (deoxynucleoside triphosphate) :

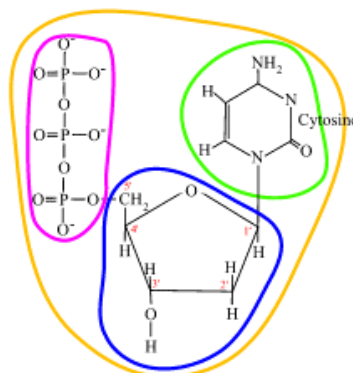
deoxyadenosine triphosphate = dATP



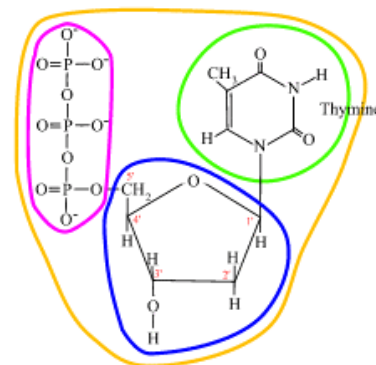
deoxyguanosine triphosphate = dGTP



deoxycytidine triphosphate = dCTP



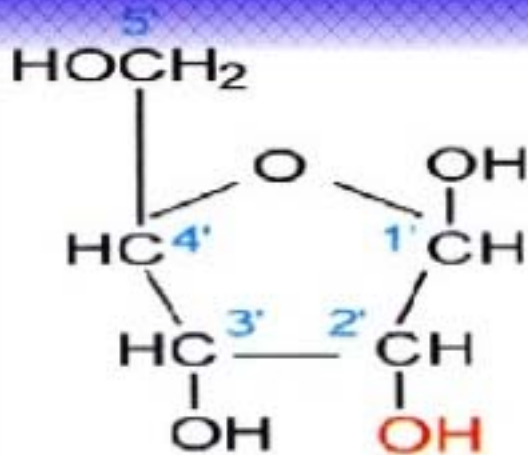
deoxythymidine triphosphate = dTTP



戊糖 (pentose)

1'碳與鹼基連接

5'碳與磷酸根連接

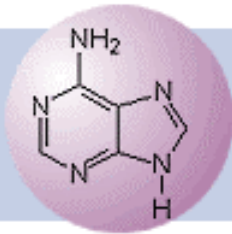


Ribose
(in RNA)

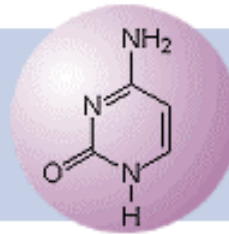


2'-Deoxyribose
(in DNA)

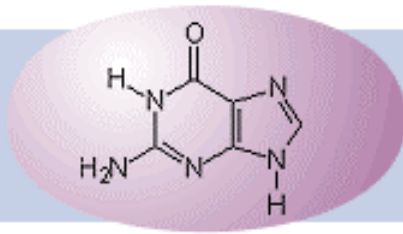
鹼基 (Nitrogenous Base)



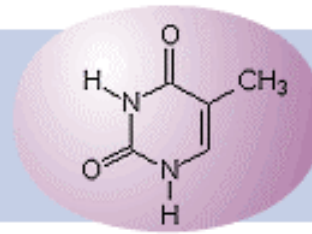
Adenin 腺嘌呤



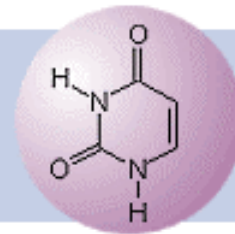
Cytosin 胞嘧啶



Guanin 鳥嘌呤



Thymin 胸腺嘧啶



Uracil 尿嘧啶

Two types of nitrogenous bases :

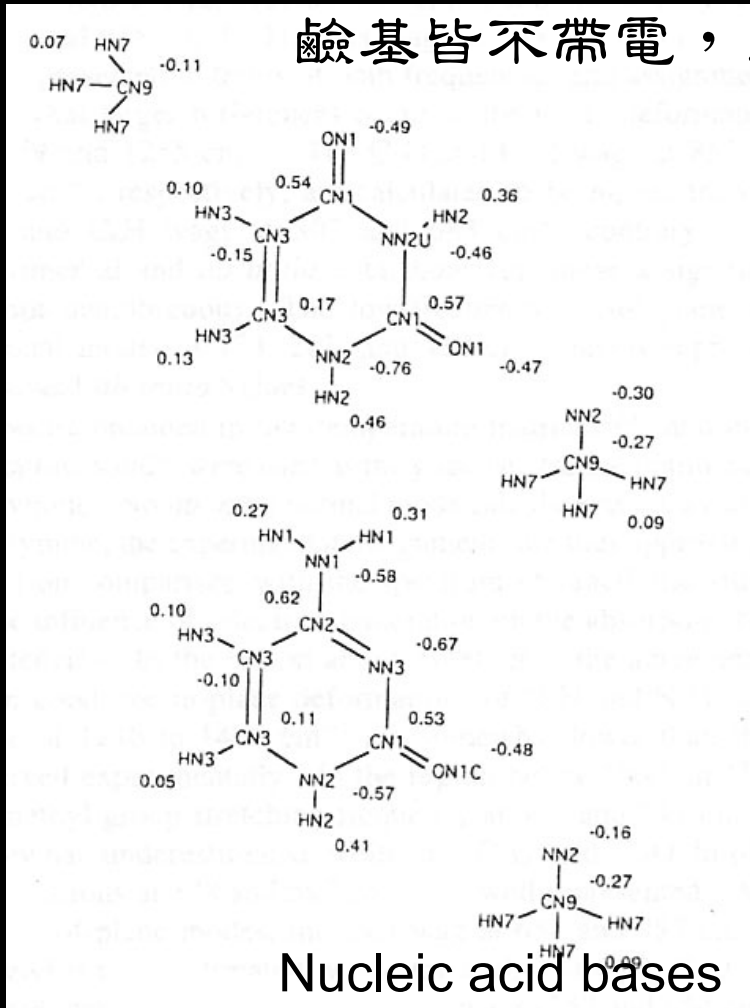
嘌呤 **purine** (fused five and six member rings)

嘧啶 **pyrimidine** (six member ring)

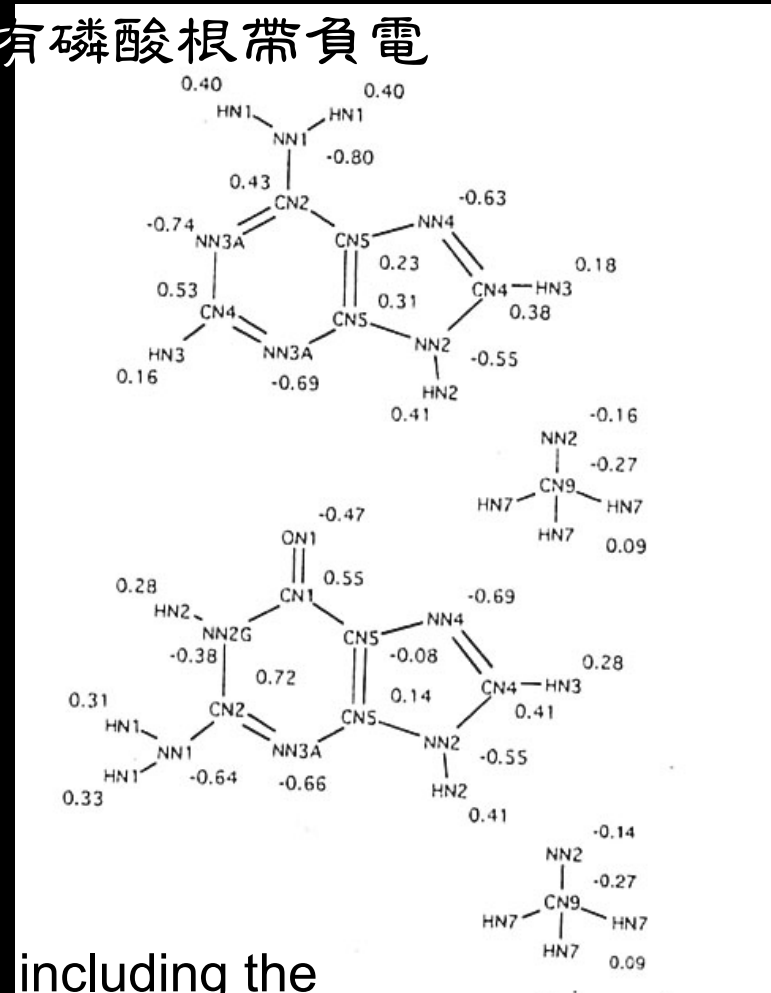
鹼基 (Nitrogenous Base)

在中性溶液中，nucleotide的戊糖和

鹼基皆不帶電，只有磷酸根帶負電



Nucleic acid bases



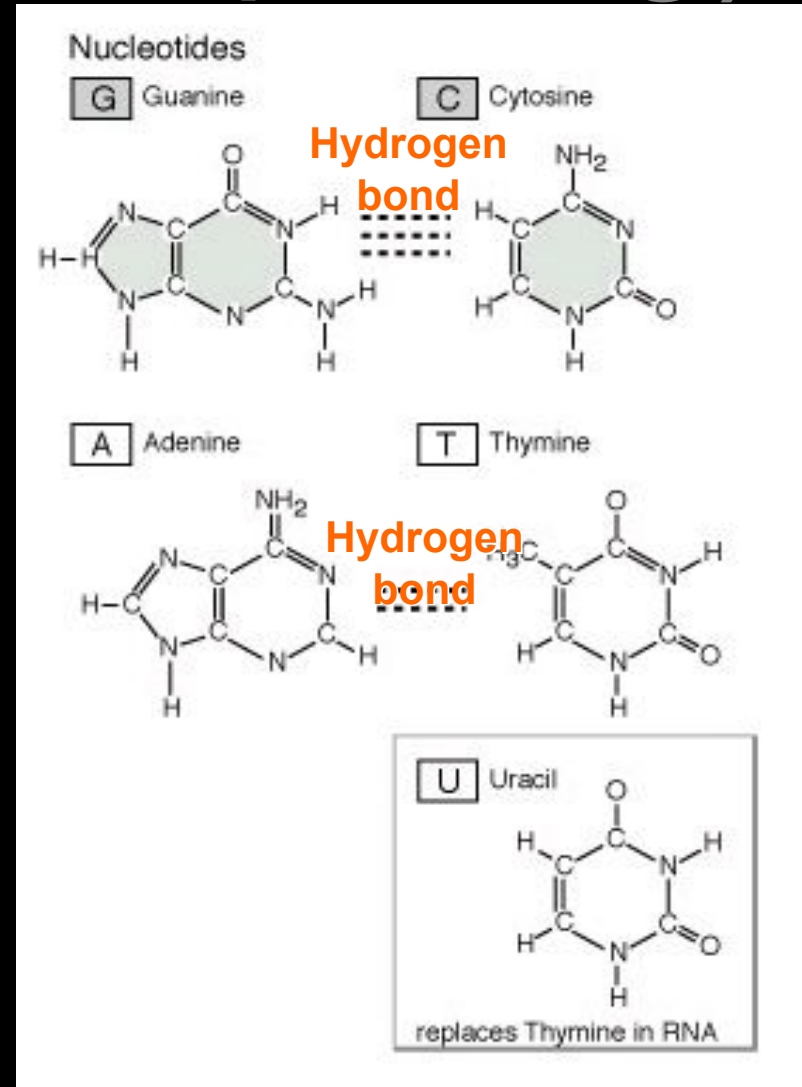
including the

atom types and partial atomic charges.

鹼基配對(base pairing)



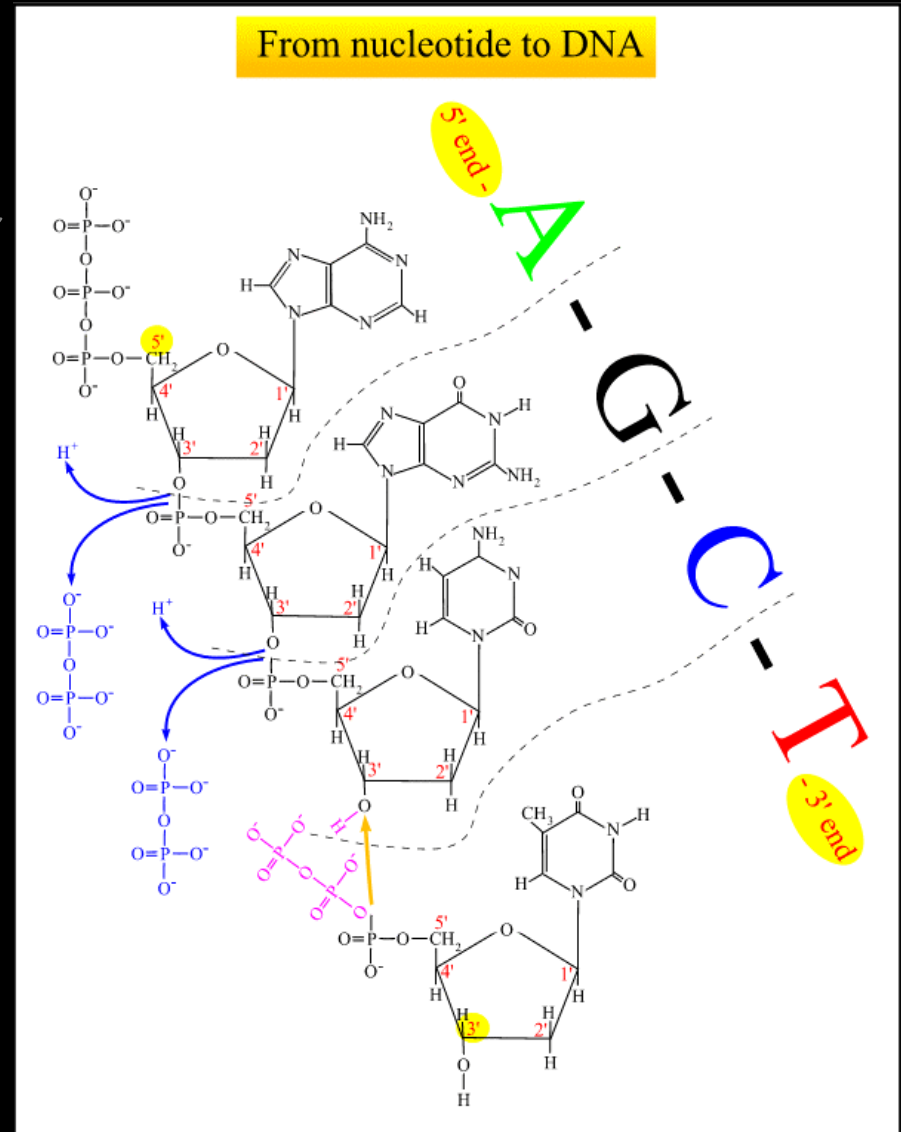
G : T 或 C : T 雖可能
形成氫鍵，但整個結
合力不如上述兩種



核甘酸鏈 (polynucleotide chain)

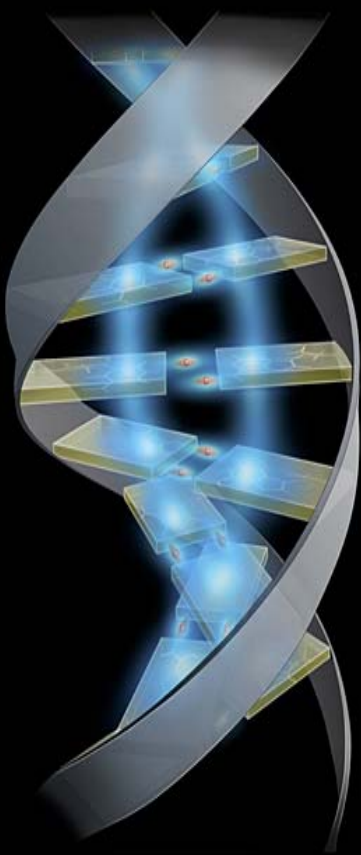
核甘酸鏈是藉由磷酸二酯鍵 (phosphodiester bond) 組成長鏈

核甘酸鏈具有方向性
(5'端至3'端)

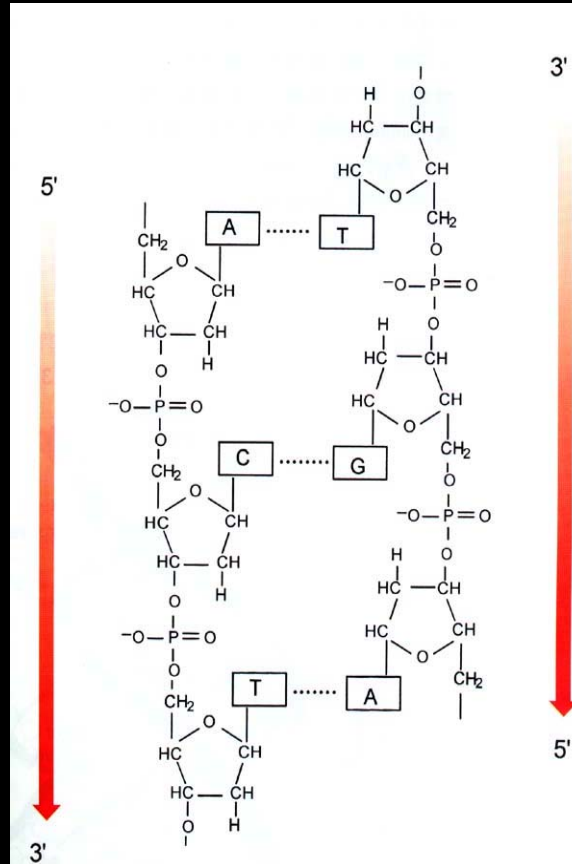


雙股DNA (Double Strands DNA)

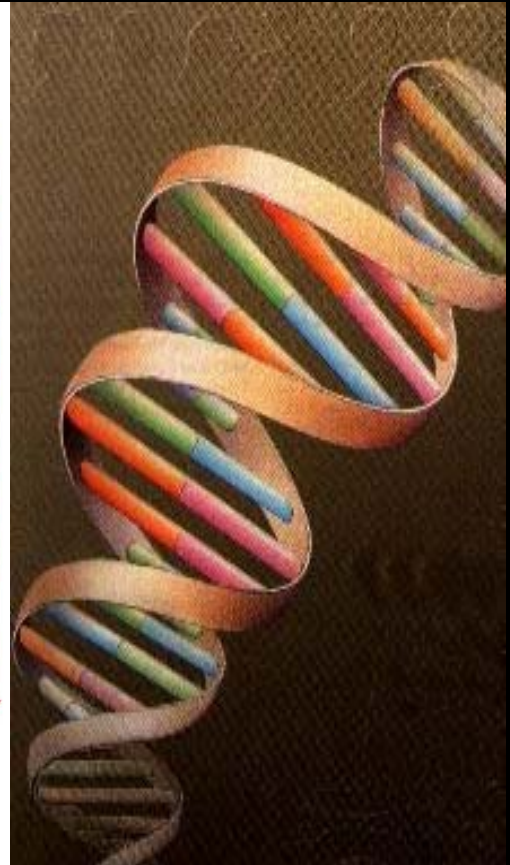
DNA 的雙股方向相反，藉 A : T & C : G 的配對關係互相結合



3D 結構 DNA



以化學形式表示的DNA

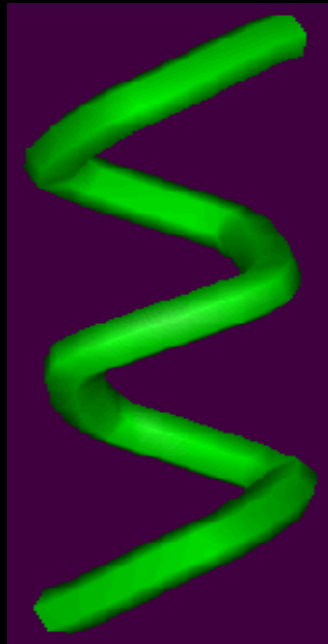


3D 結構 DNA

雙螺旋DNA旋轉的方向性

An α helix can be either right-handed or left-handed, as defined in the following figure.

(a)



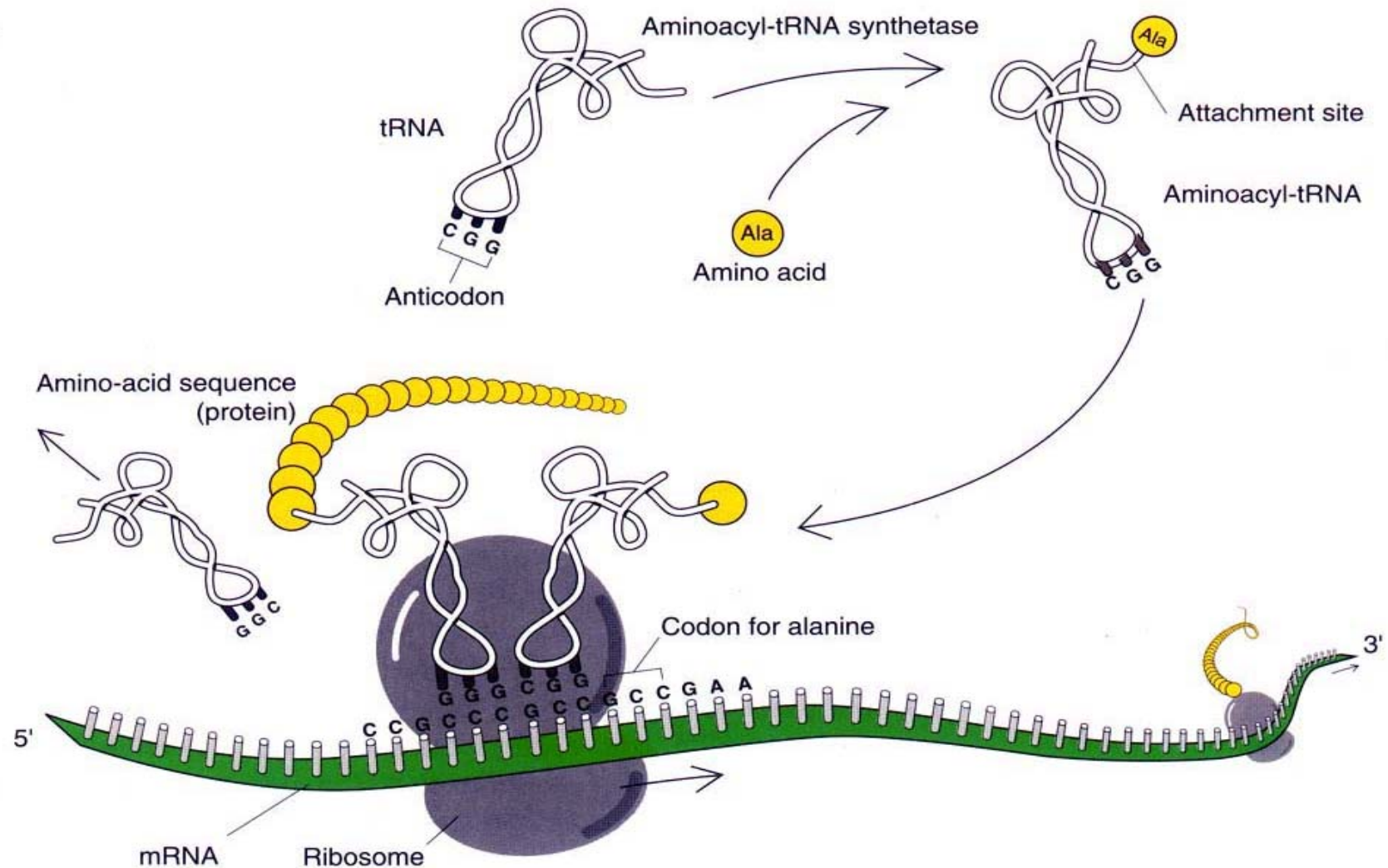
(b)



(a) The right-handed α helix without showing atoms.

(b) the left-handed α helix.

Translation of mRNA to protein



RNA structure

The major role of RNA is to participate in protein synthesis

RNA may be double stranded, but most cellular RNA molecules are single stranded.

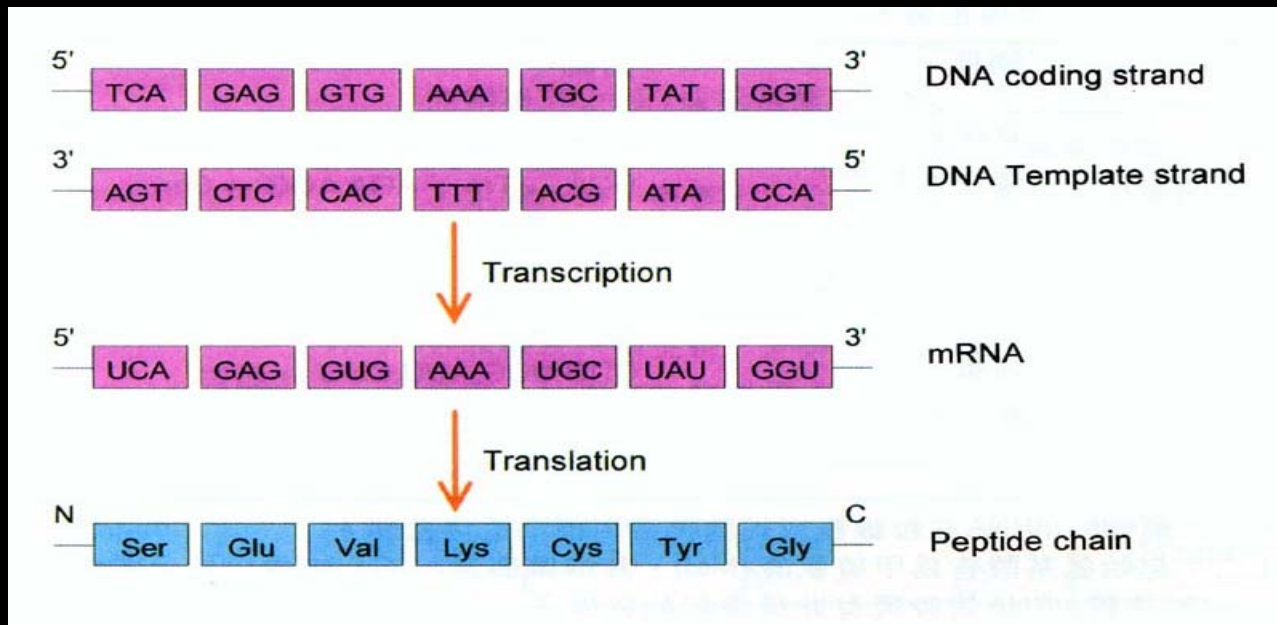
This requires three classes of RNA:

- 1. ribosomal RNA (rRNA)**
- 2. messenger RNA (mRNA)**
- 3. transfer RNA (tRNA)**

Messenger RNA

mRNA is transcribed from DNA, carrying information for protein synthesis. The consecutive trinucleotides is known as a codon

Three consecutive nucleotides in mRNA encode an amino acid or a stop signal for protein synthesis.



Transfer RNA

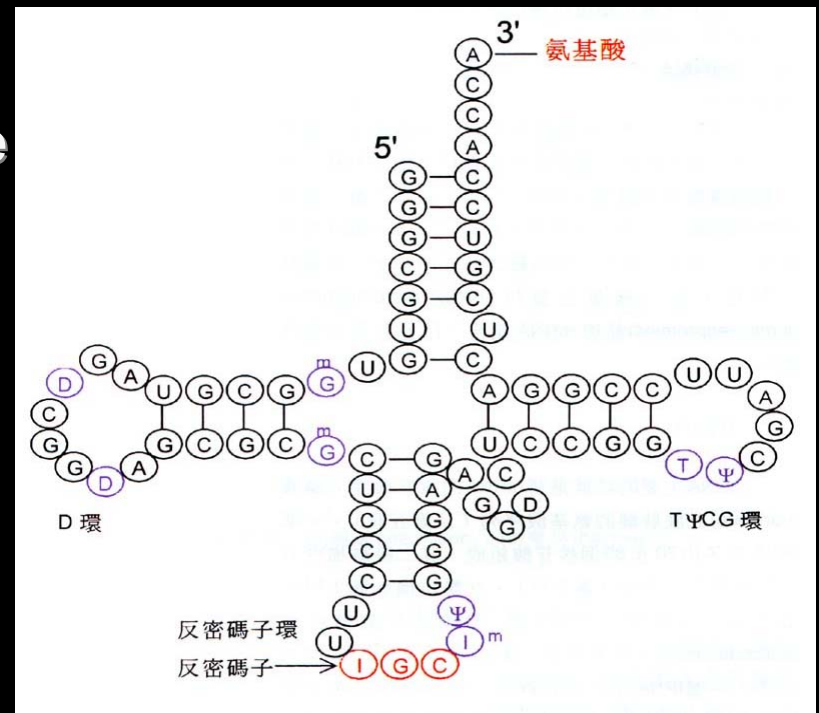
The major role of tRNA is to translate mRNA sequence into amino acid sequence

Some nucleotides in tRNA have been modified, such as :

dihydrouridine (D)

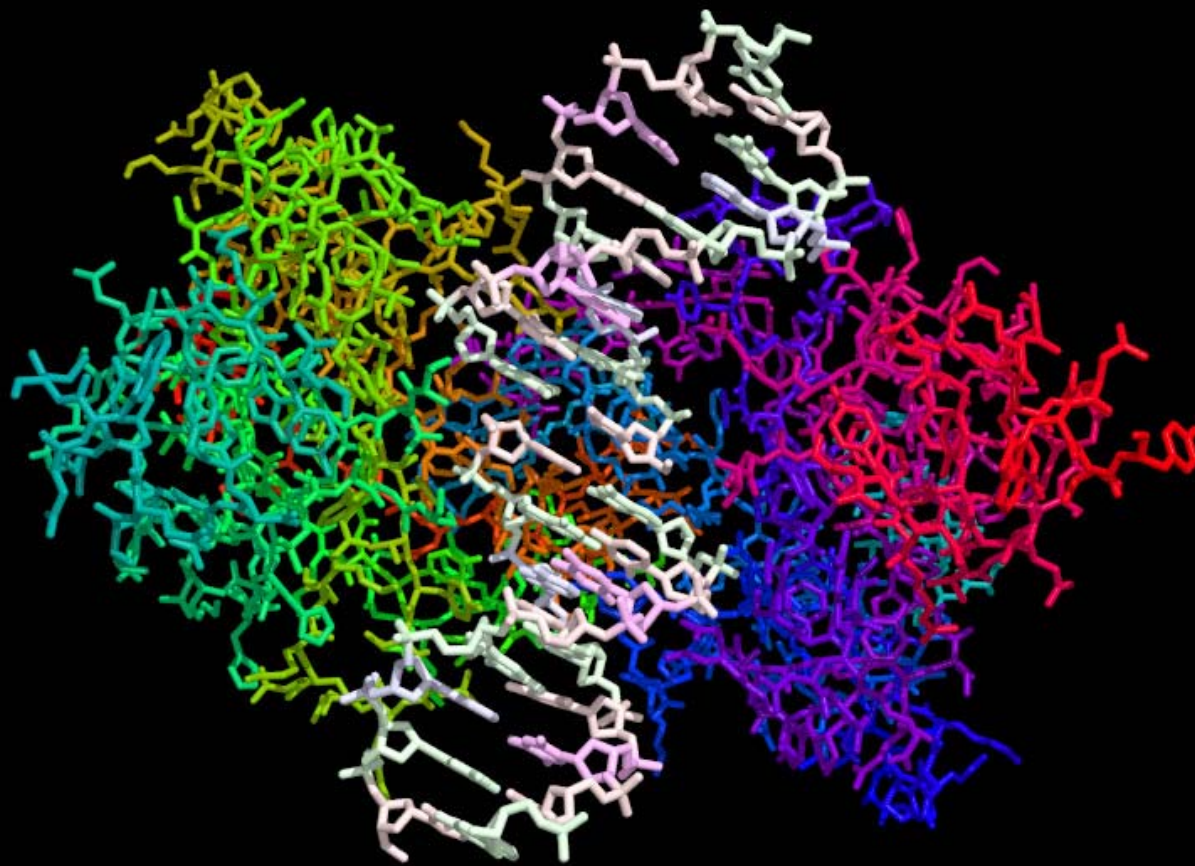
pseudouridine (Y)

inosine (I)



A tRNA molecule consists of 70-80 nucleotides

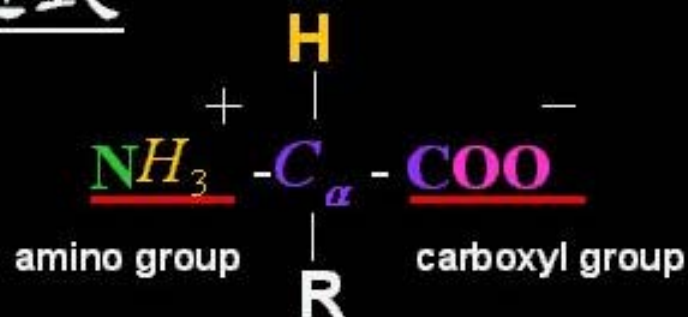
蛋白質的結構與功能



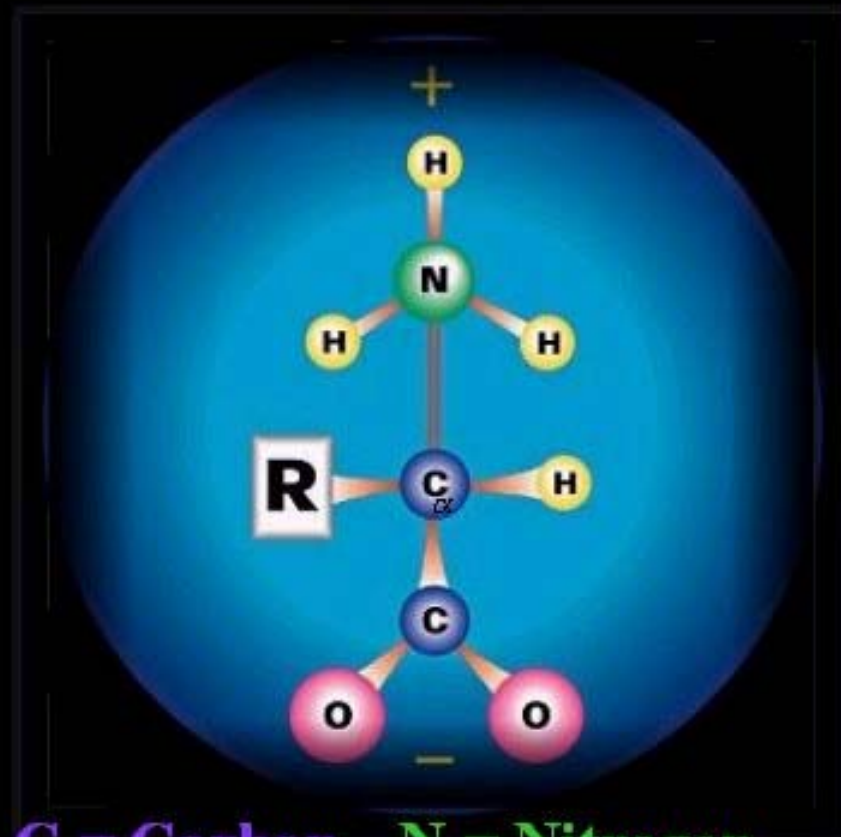
氨基酸(Amino acid)

Anatomy of an Amino Acid

通式

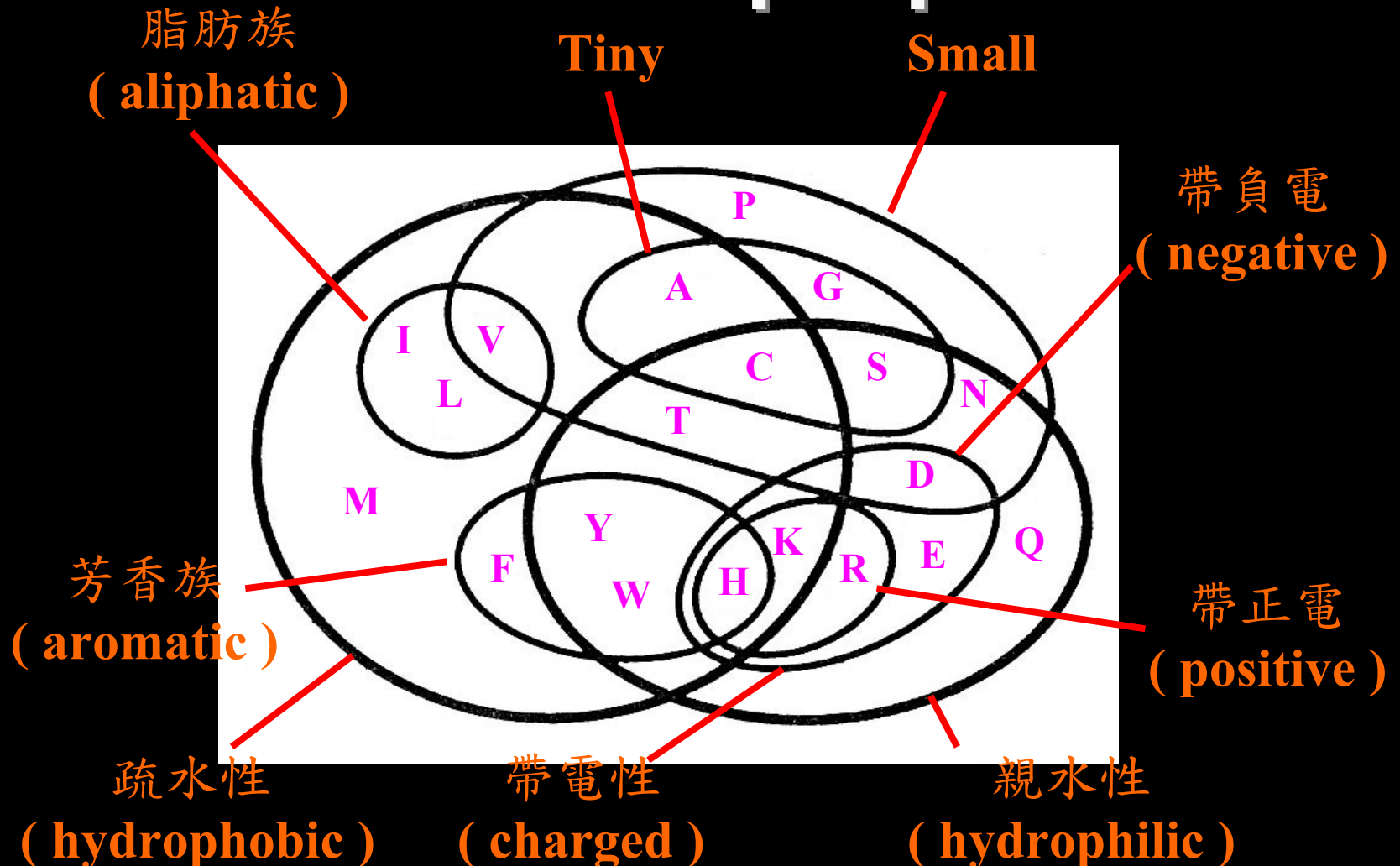


R代表氨基酸之間相異的部分，叫R基，又稱側鏈(sidechain)



C = Carbon N = Nitrogen
O = Oxygen H = Hydrogen

The overlapping range of amino acid properties



20 Amino Acid

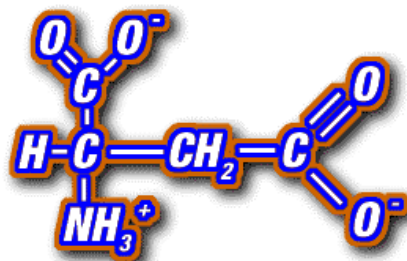
/Formula/Number of atoms/

L-Alanine	$C_3H_7O_2N$	13
L-Arginine	$C_6O_{15}N_4$	27
L-Asparagine	$C_4H_8O_3N_2$	17
L-Aspartic acid	$C_4H_6O_4N$	15
L-Cysteine	$C_3H_7O_2NS$	14
L-Glutamic acid	$C_5H_8O_4N$	18
L-Glutamine	$C_5H_{10}O_3N_2$	20
Glycine	$C_2H_5O_2N$	10
L-Histidine	$C_6H_9O_2N_3$	20
L-Isoleucine	$C_6H_{13}O_2N$	22

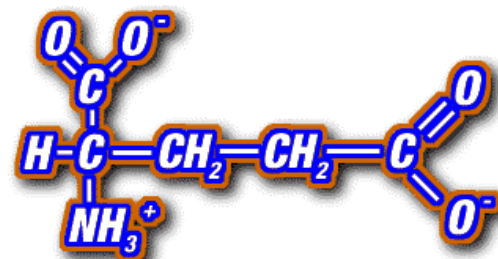
L-Leucine	$C_6H_{13}O_2N$	22
L-Lysine	$C_6H_{15}O_2N_2$	25
L-Methionine	$C_5H_{11}O_2NS$	20
L-Phenylalanine	$C_9H_{11}O_2N$	23
L-Proline	$C_5H_9O_2N$	17
L-Serine	$C_3H_7O_3N$	14
L-Threonine	$C_4H_9O_3N$	17
L-Tryptophan	$C_{11}H_{12}O_2N_2$	27
L-Tyrosine	$C_9H_{11}O_2N$	24
L-Valine	$C_5H_{11}O_2N$	19

酸性(acidic)

R基在中性溶液中失去氫離子而帶負電



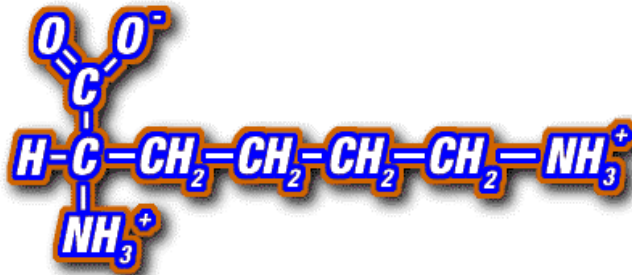
天冬氨酸 Aspartate ; Asp ; D



麩氨酸 Glutamate ; Glu ; E

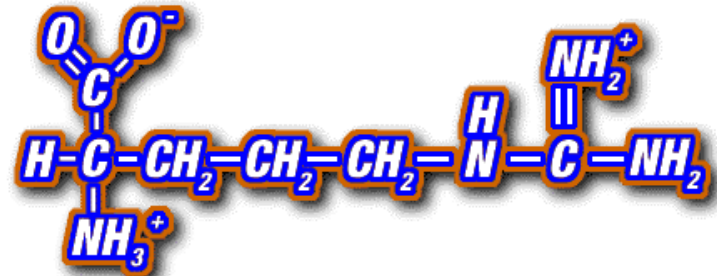
鹼性(basic)

R基在中性溶液中獲得氫離子而帶正電



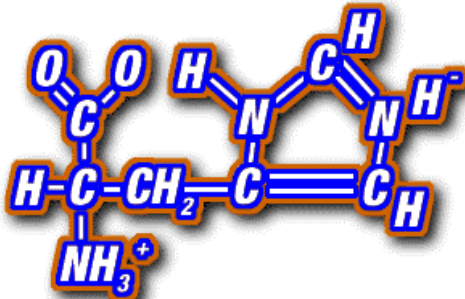
COMMON GROUP ← SIDE GROUP ("R" GROUP)

賴氨酸 Lysine ; Lys ; K



COMMON GROUP ← SIDE GROUP ("R" GROUP)

精氨酸 Arginine ; Arg ; R

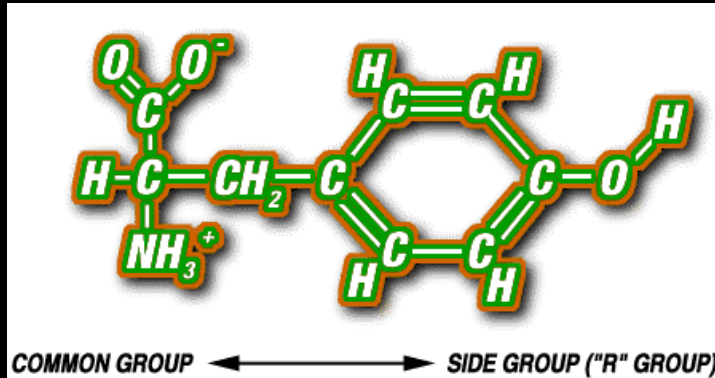


COMMON GROUP ← SIDE GROUP ("R" GROUP)

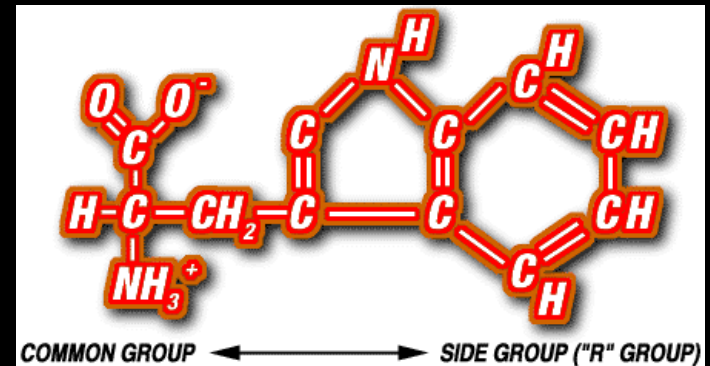
組氨酸 Histidine ; His ; H

芳香族(aromatic)

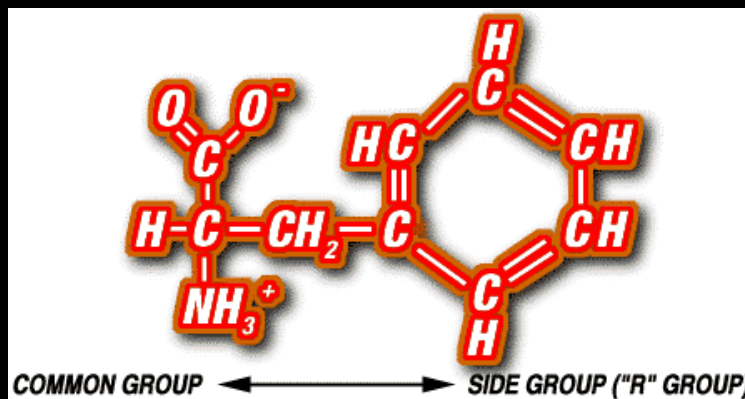
R基含碳環



酪氨酸 Tyrosine ; Tyr ; Y



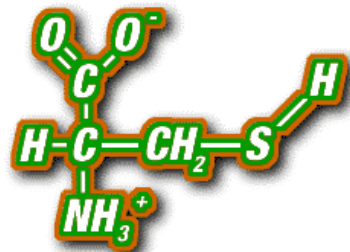
色氨酸 Tryptophan ; Trp ; W



苯丙氨酸 Phenylalanine ; Phe ; F

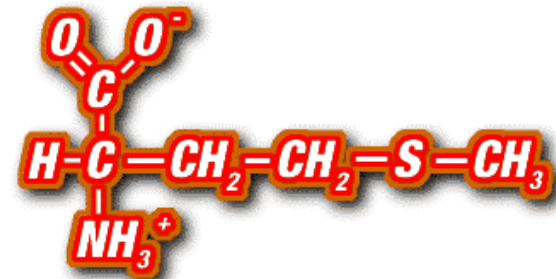
硫族(sulfur)

R基含有硫原子



COMMON GROUP ← SIDE GROUP ("R" GROUP)

胱氨酸 Cysteine ; Cys ; C

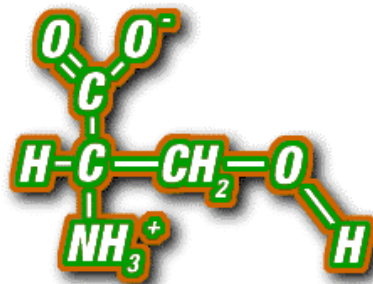


COMMON GROUP ← SIDE GROUP ("R" GROUP)

甲硫氨酸 Methionine ; Met ; M

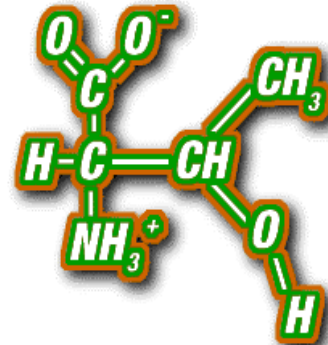
親水性(hydrophilic)

R基為極性基(polar group)



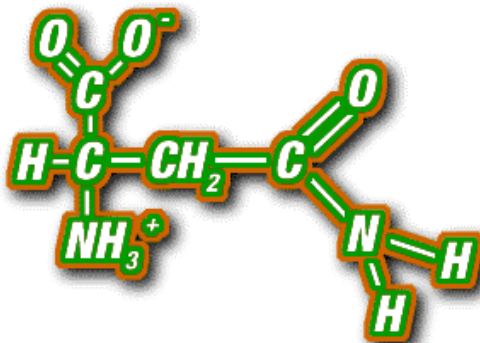
COMMON GROUP ← SIDE GROUP ("R" GROUP)

絲氨酸 Serine ; Ser ; S



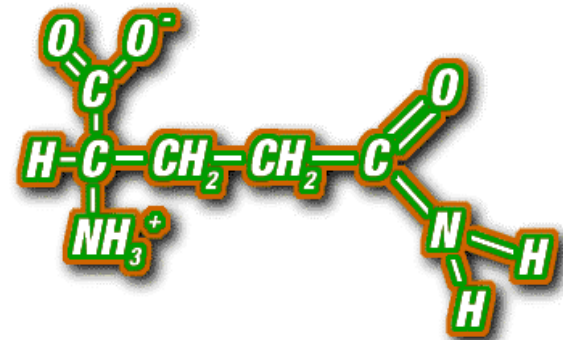
COMMON GROUP ← SIDE GROUP ("R" GROUP)

蘇氨酸 Threonine ; Thr ; T



COMMON GROUP ← SIDE GROUP ("R" GROUP)

天冬醯胺 Asparagine ; Asn ; N

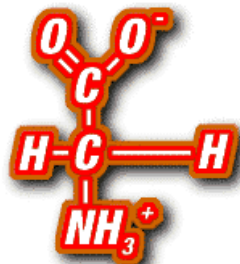


COMMON GROUP ← SIDE GROUP ("R" GROUP)

麩氨醯胺 Glutamine ; Glu ; Q

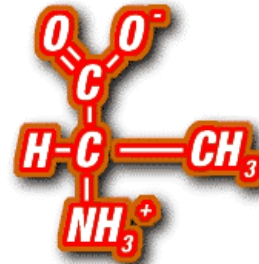
疏水性(hydrophobic)

R基為非極性基(non-polar group)



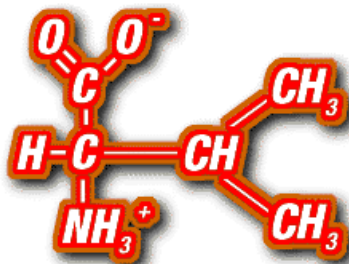
COMMON GROUP ← SIDE GROUP ("R" GROUP)

甘氨酸 Glycine ; Gly ; G



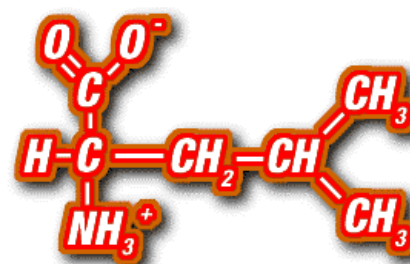
COMMON GROUP ← SIDE GROUP ("R" GROUP)

丙氨酸 Alanine ; Ala ; A



COMMON GROUP ← SIDE GROUP ("R" GROUP)

纈氨酸 Valine ; Val ; V
Aliphatic

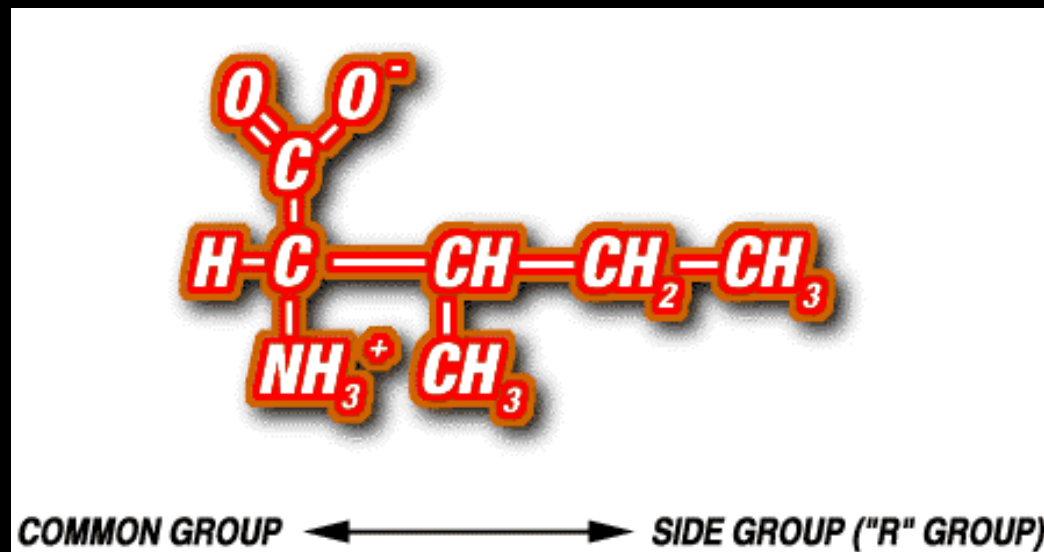


COMMON GROUP ← SIDE GROUP ("R" GROUP)

白氨酸 Leucine ; Leu ; L
Aliphatic

疏水性(hydrophobic)

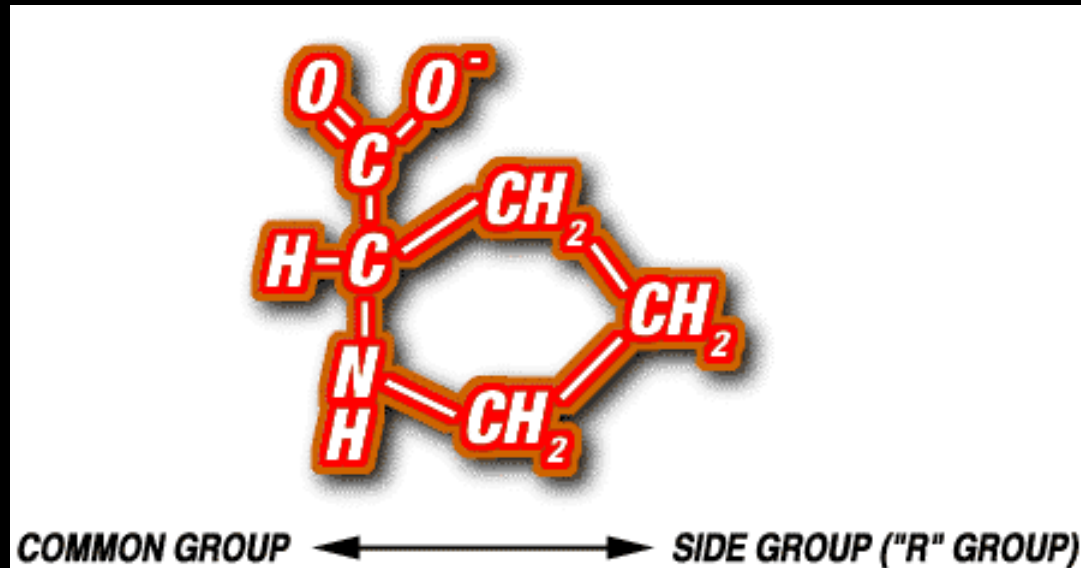
R基為非極性基(non-polar group)



異白氨酸 Isoleucine ; Ile ; I

特殊結構

氨基 (amino group) 與 R 基形成環狀結構



脯氨酸 Proline ; Pro ; P

在蛋白質立體結構中，脯氨酸經常位於 peptide chain 轉彎之處

維持蛋白質結構之力量

- Peptide Bond：連接氨基酸鏈之骨架 (backbone)。
- 鹽鍵(salt bridge)：帶正電之R基與帶負電之R基所形成。
- 雙硫鍵(disulfide bond)：由兩個胱氨酸所形成。
- 氫鍵(hydrogen bond)

Alanine & Leucine利於形成 α helix能增加蛋白質結構之穩定性

親水性(hydrophilic) 疏水性(hydrophobic)

- 親疏水性在蛋白質構形中為最重要之交互作用力

- 由實驗數據得知當疏水性氨基酸互相靠近時能量降低最多，疏水-疏水氨基酸的鄰接數目愈多蛋白質的結構就越穩定。

【 以簡單的晶格模型研究蛋白質結構 】

- 疏水性氨基酸通常聚集在蛋白質的內部形成疏水核心；親水性的蛋白質覆蓋在表面以增加與水接觸的面積。

蛋白質的骨架特色

兩端 $\text{N}-\text{C}-\text{C}-\text{N}-\text{C}-\text{C}-\text{N}-\text{C}-\text{C}-\text{N}-\text{C}-\text{C}-\text{N}-\text{C}-\text{C}$

α 碳 $\text{N}-\overset{\alpha}{\text{C}}-\text{C}-\text{N}-\overset{\alpha}{\text{C}}-\text{C}-\text{N}-\overset{\alpha}{\text{C}}-\text{C}-\text{N}-\overset{\alpha}{\text{C}}-\text{C}-\text{N}-\overset{\alpha}{\text{C}}-\text{C}$

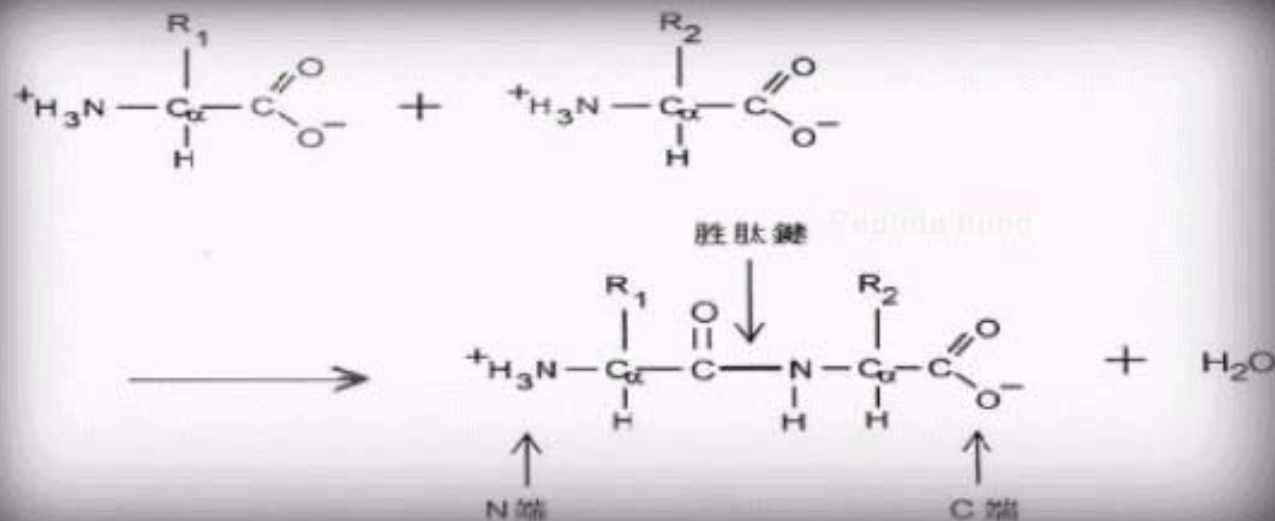
單位 $\text{N}-\text{C}-\text{C}-\text{N}-\text{C}-\text{C}-\text{N}-\text{C}-\text{C}-\text{N}-\text{C}-\text{C}-\text{N}-\text{C}-\text{C}$

Peptide Bond $\text{N}-\text{C}-\text{C}-\text{N}-\text{C}-\text{C}-\text{N}-\text{C}-\text{C}-\text{N}-\text{C}-\text{C}-\text{N}-\text{C}-\text{C}$

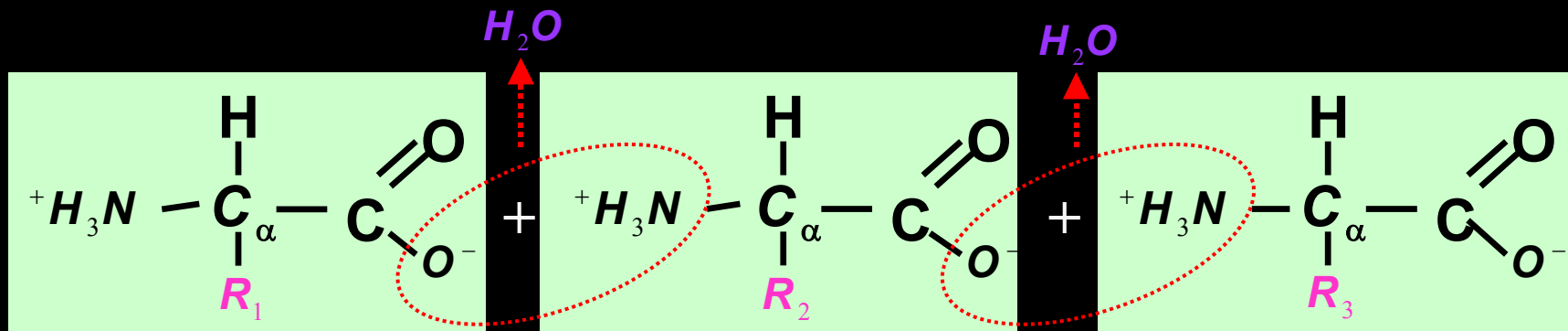
蛋白質的一級結構

Primary Structure

氨基酸序列 e.g. MFCVLIPCTNQQPNQ.....

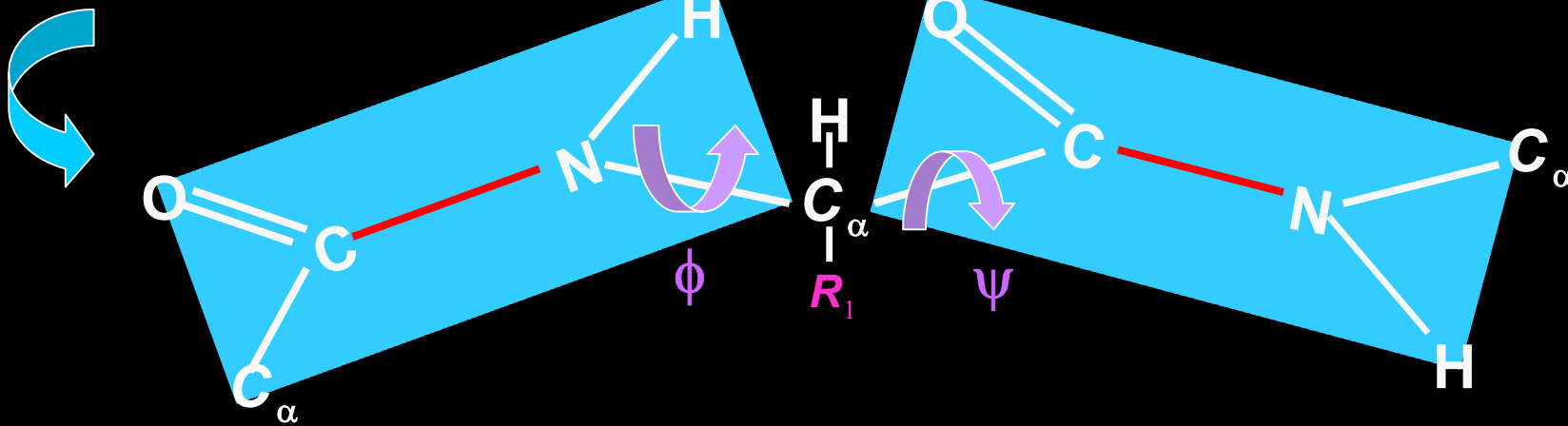
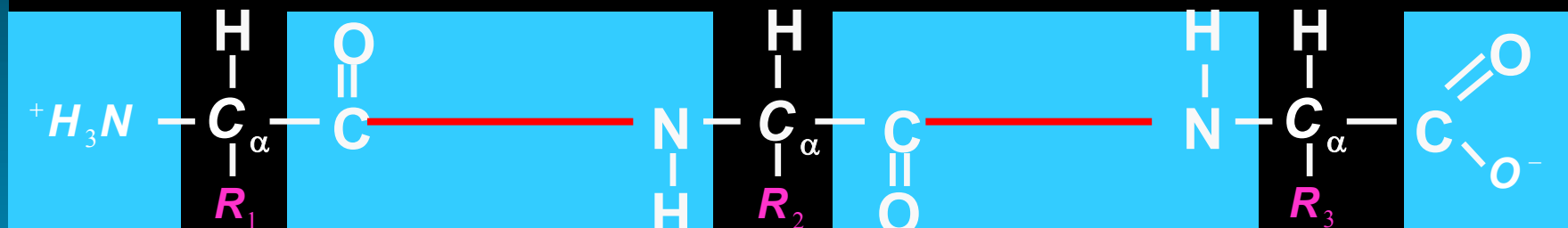


Condensation Reaction

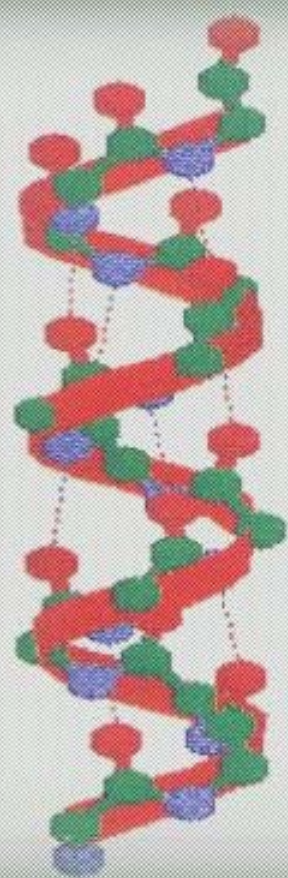


Form peptide bond

Form peptide bond

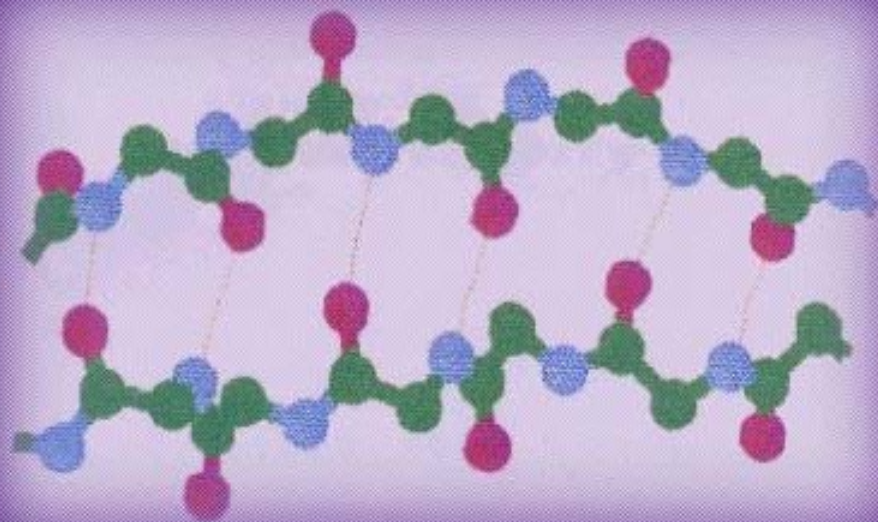


蛋白質的二級結構



5.4Å

α helix



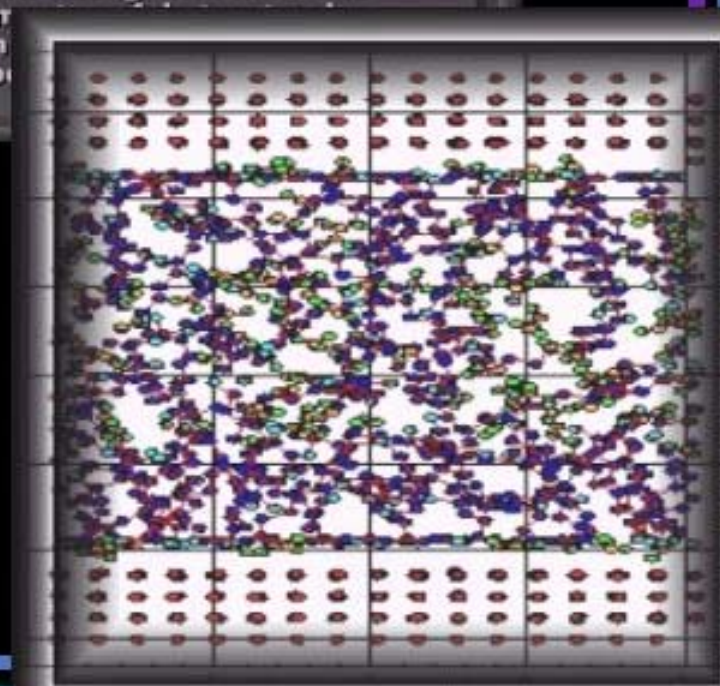
β strand

平行 (parallel)

反平行 (anti-parallel)

決定蛋白質立體結構之方法

1. X光晶體繞射
(x-ray crystallography)
2. 核磁共振
(**N**uclear **M**agnetic
Resonance **NMR**)
3. 理論計算模擬
(simulation of theoretical
calculation)



蛋白質立體結構方法之限度

1. X光晶體繞射：

須先將蛋白質結晶，所得的結構為晶體結構。

2. 核磁共振：

為得到蛋白質在溶液中的結構。

3. 理論計算模擬：

利用 MD method、MC method、molecular Mechanics 等分析方法模擬。

蛋白質立體結構方法之限度：

1. X光晶體繞射只限於能被結晶的蛋白質。

2. 核磁共振只能用於較小的蛋白質，目前大多小於200個氨基酸。

3. 理論計算模擬可用來預測蛋白質的3D立體結構，但受限於電腦的軟硬體設備。

蛋白質分子結構資料

PDB Holdings List : 27-Feb-2001

	Molecular Type				
	Proteins, Peptides, and Viruses	Protein/Nucleic Acid Complexes	Nucleic Acids	Carbohydrates	total
X-ray diffraction and other	10876	520	552	14	11962
NMR	1803	70	354	4	2231
Theoretical Modeling	277	19	21	0	317
	12956	609	927	18	14510

PDB Holdings List : 05-Mar-2002

	Molecular Type				
	Proteins, Peptides, and Viruses	Protein/Nucleic Acid Complexes	Nucleic Acids	Carbohydrates	total
X-ray diffraction and other	13196 2320	635 115	602 50	14 0	14447 2485
NMR	2164 361	82 12	423 69	4 0	2673 442
Theoretical Modeling	321 44	24 5	28 7	0 0	373 56
	15681 2725	741 132	1053 126	18 0	17493 2983