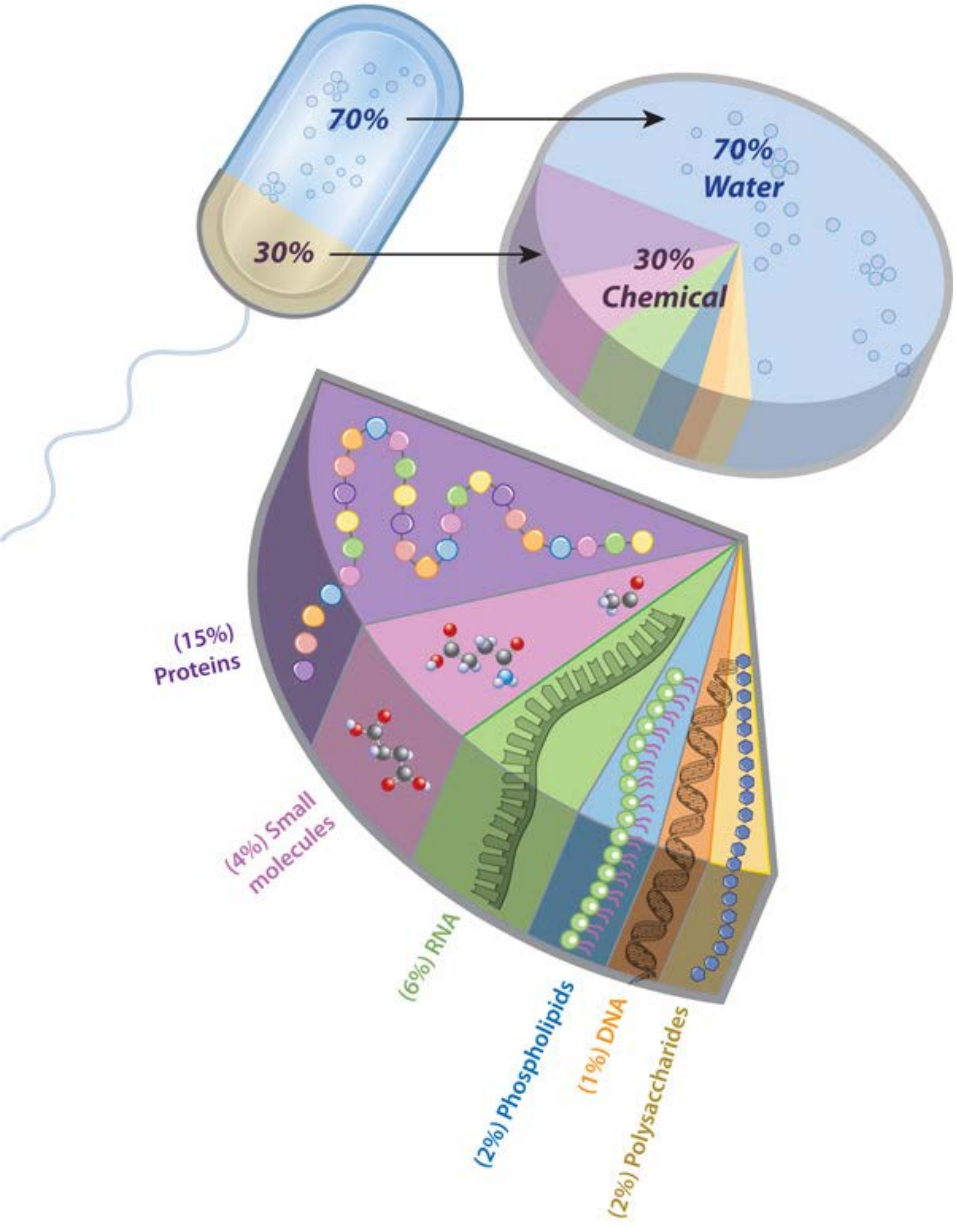
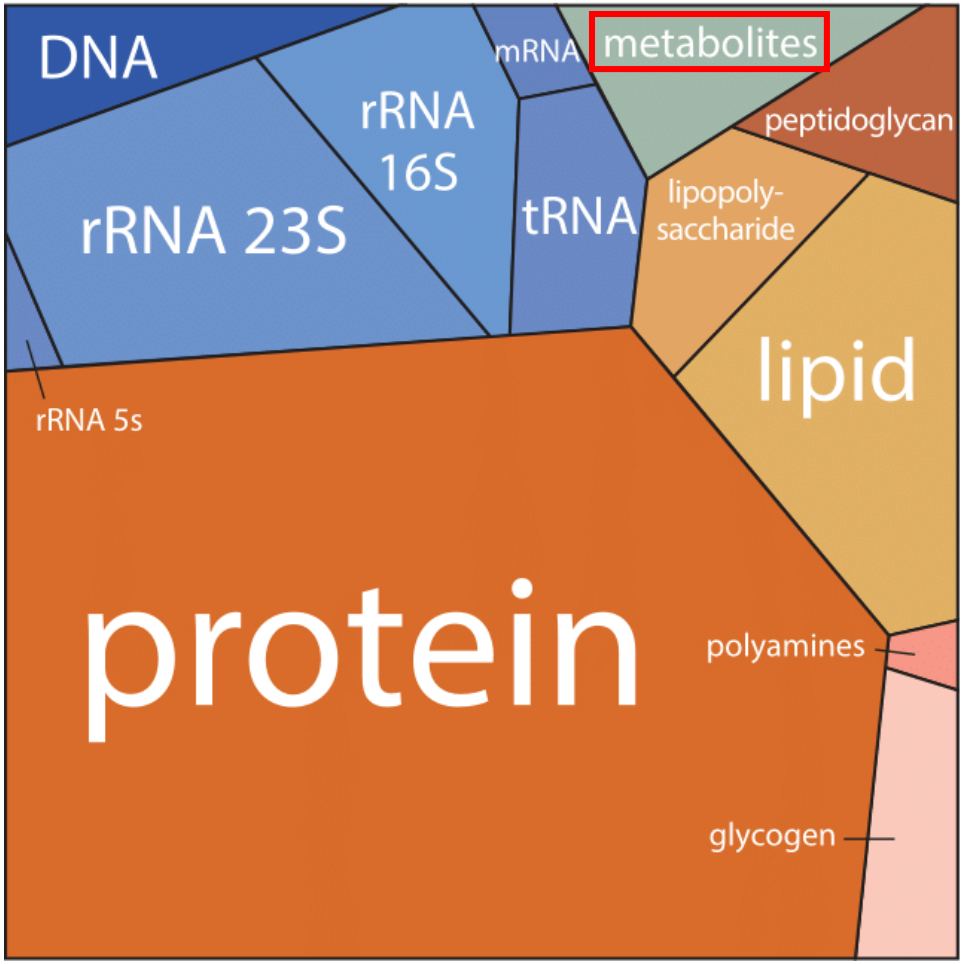
生物大分子簡介

細胞中的大分子組成：以大腸桿菌為例





http://book.bionumbers.org/what-is-the-macromolecular-composition-of-the-cell/
https://www.nature.com/scitable/topicpage/what-is-a-cell-14023083/

醣類

- 單醣
- 醣苷鍵
- 結構與種類
- 生物功能

核酸

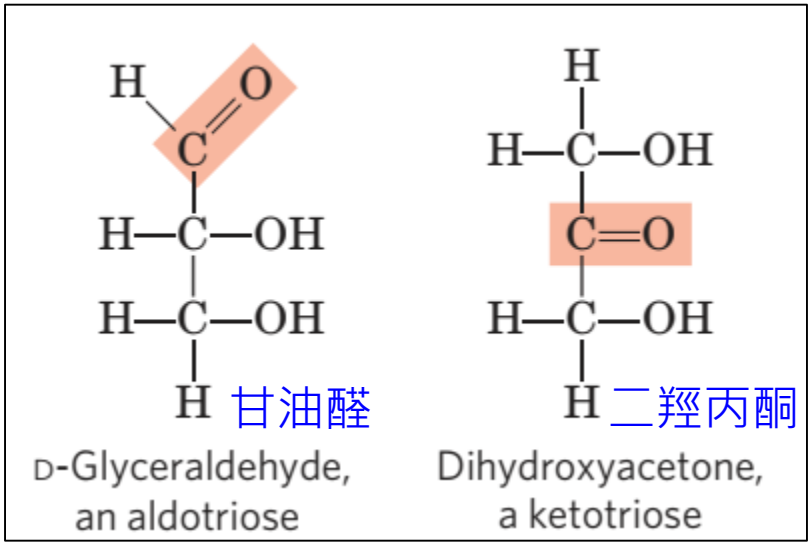
- 核苷酸
- 磷酸二酯鍵
- 結構與種類
- 生物功能

脂質

- 溶於非極性
- 分為八大類
- 結構與種類
- 生物功能

醣類

- 醣類又稱碳水化合物(carbohydrate)。
- 大部分的醣類具有分子式 $(C{\cdot}H_2O)_n$，$n \geq 3$。
- 醣類為含有多羥基的醛類〔醛醣(aldose)〕或酮類〔酮醣(ketose)〕及其衍生物。



醛丙醣　　酮丙醣

醣類的分類

單醣(monosaccharide) 可分為醛醣(aldose)或酮醣(ketose)

以醣苷鍵(glycosidic bond)結合

雙醣(disaccharide) 2個單醣組成

醣苷鍵

寡醣(oligosaccharide) 3-9個單醣組成

醣苷鍵

多醣(polysaccharide) >9個單醣組成

「醣」或「糖」？

主要膳食碳水化合物（醣類）*

類（單醣個數）	亞類	舉例
糖 (1-2) Sugar	單醣	葡萄糖、半乳糖、甘露糖
	雙醣	蔗糖、乳糖、麥芽糖、海藻糖
	多元醇/醣醇	山梨糖醇、甘露醇
寡醣 (3-9)	麥芽寡醣	麥芽糊精
	其他寡醣	棉子糖、水蘇糖、果寡糖
多醣 (>9)	澱粉	直鏈澱粉、支鏈澱粉
	非澱粉多醣	肝醣**、纖維素、果膠

*依據聯合國糧食及農業組織定義　**肝醣亦稱「肝糖」、「糖原」

https://en.wikipedia.org/wiki/Carbohydrate

醣類的生物功能

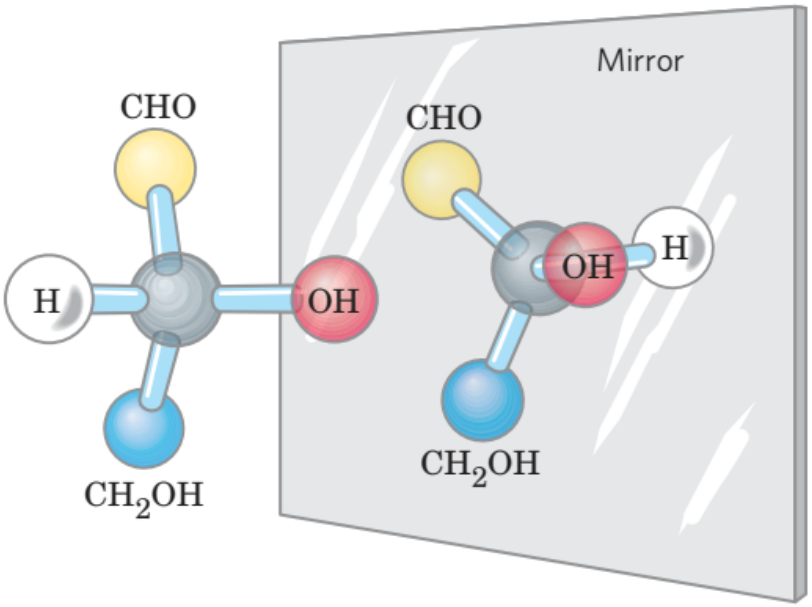
生物功能	舉例
經由氧化提供能量	葡萄糖
合成其他細胞成份的碳原子來源	
作為化學能的主要儲存形式	澱粉與肝醣
作為細胞及組織的結構要素	纖維素
細胞辨識	醣蛋白

單醣

1. 單醣的分類
   - 依所含的官能基可分為醛醣(aldose)或酮醣(ketose)。
   - 依所含的碳原子數目可分為
     - 三碳醣 / 丙醣 (triose)
     - 四碳醣 / 丁醣 (tetraose)
     - 五碳醣 / 戊醣 (pentose)
     - 六碳醣 / 己醣 (hexose)
     - 七碳醣 / 庚醣 (heptose)
     - 八碳醣 / 辛醣 (octose)等。
2. 常見的單醣
   - 六碳醣：葡萄糖、半乳糖、果糖、甘露糖。
     →分子式一樣，差異在哪裡？
   - 五碳糖：核糖、去氧核糖。

單醣具有不對稱碳原子

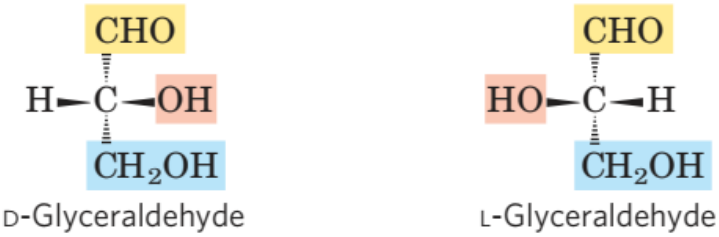
- 除了二羥丙酮外，各種單醣至少含有一個不對稱碳原子→對掌中心(chiral center)。
- 單醣中如有N個不對稱碳原子，則會有2^N個立體異構物(stereoisomer)。
- 依據距離羰基(C=O)碳*最遠的*不對稱碳原子分為D或L系。
- 自然界中大部份醣類化合物為D系。



Ball-and-stick models

甘油醛

Fischer projection formulas

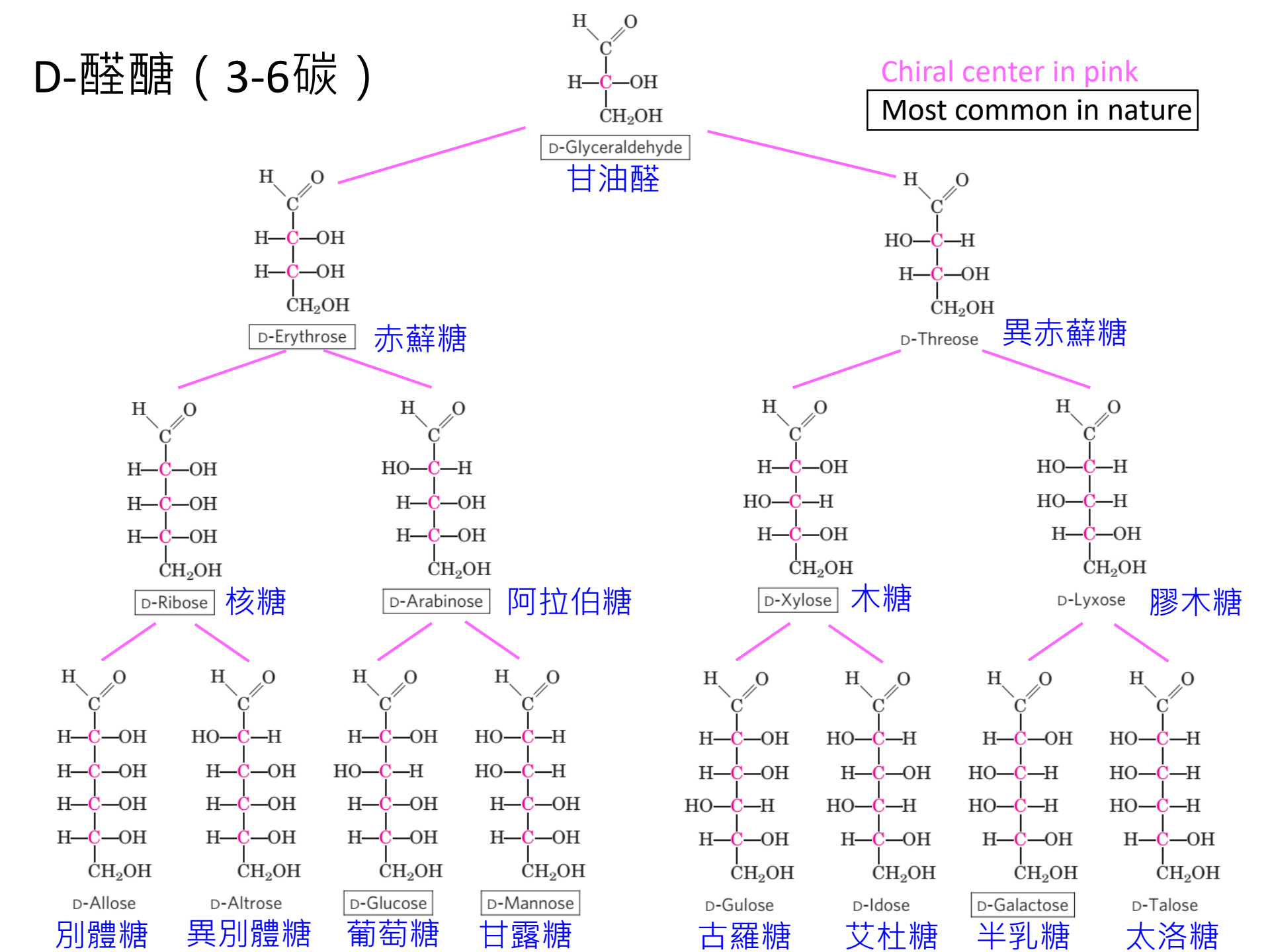


Perspective formulas

D-醛醣（3-6碳）

Chiral center in pink

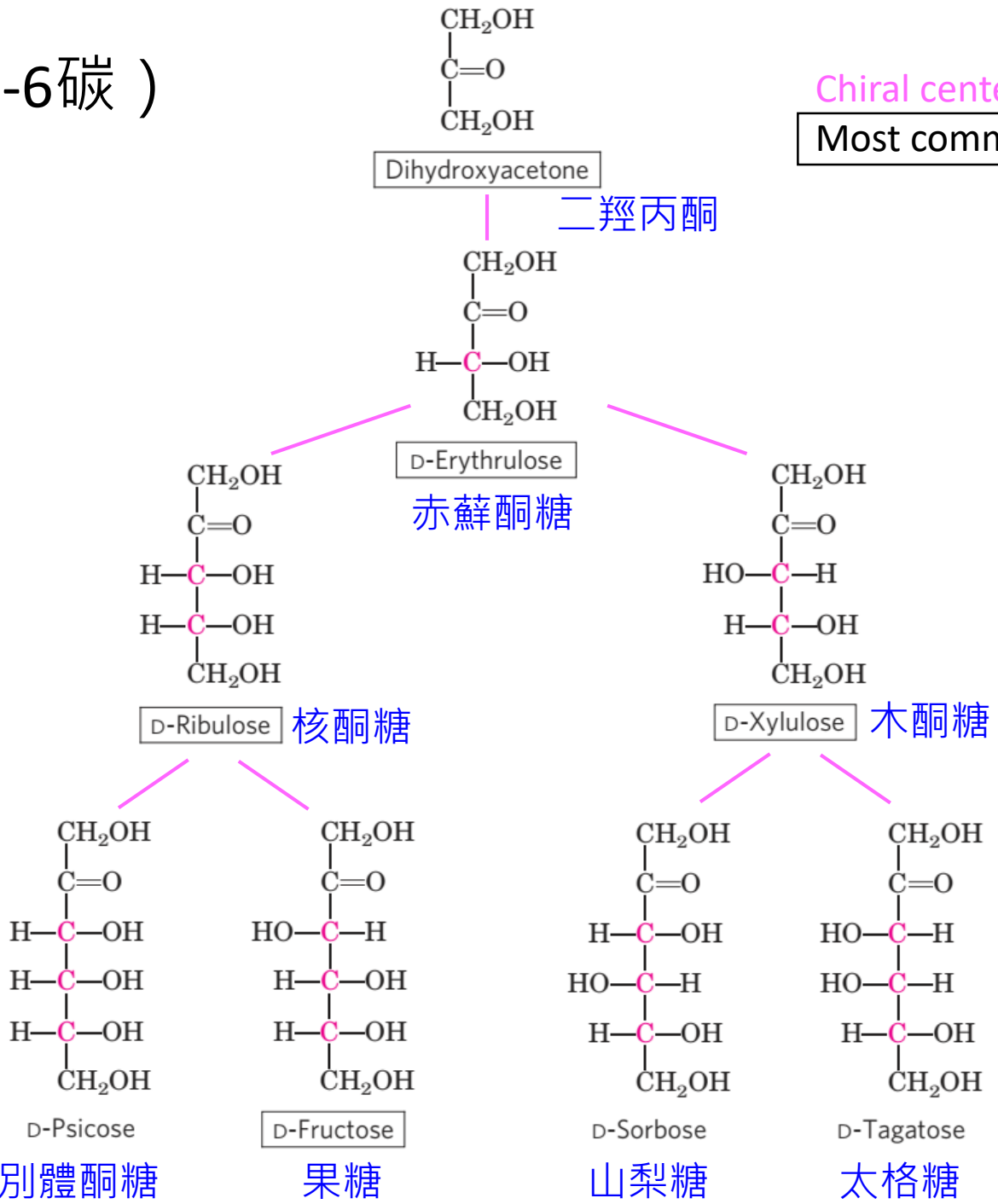
Most common in nature



D-酮醣（3-6碳）

Chiral center in pink

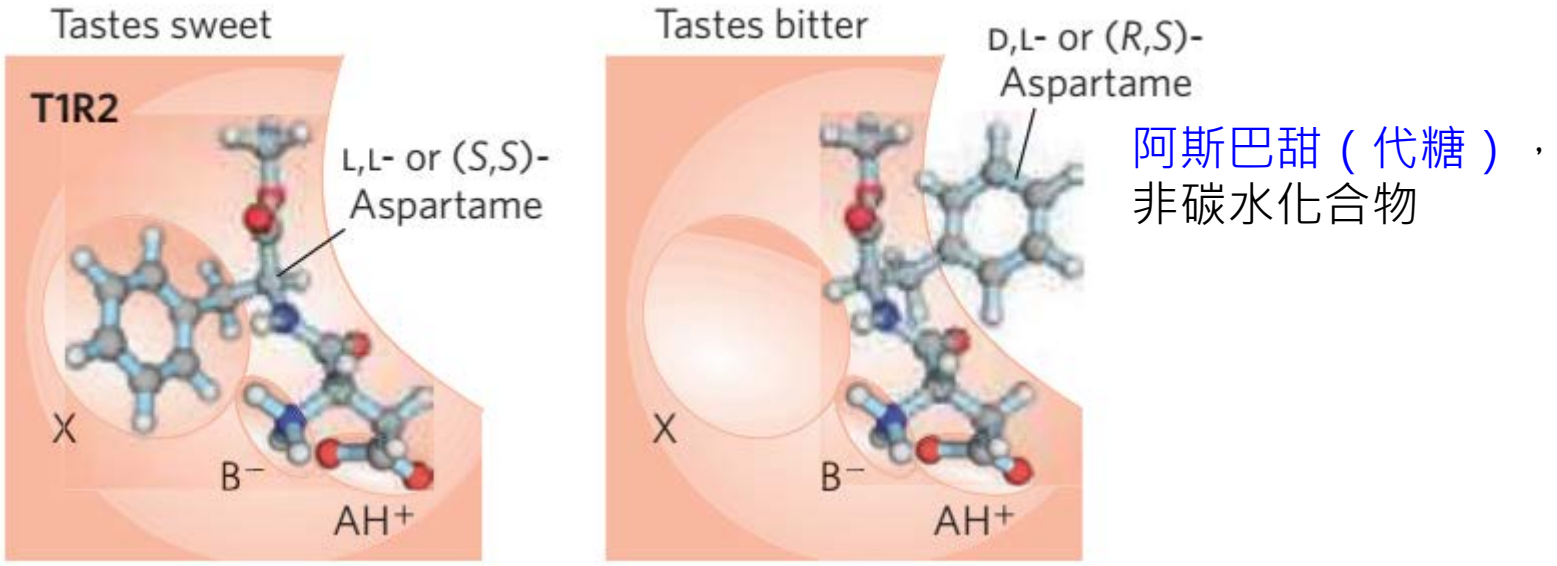
Most common in nature



"-ul-"

不同立體異構物對生物的意義

- 不同單醣異構物與酵素的反應（親和力、反應速率等）差異很大。
- 以甜味劑作例子：

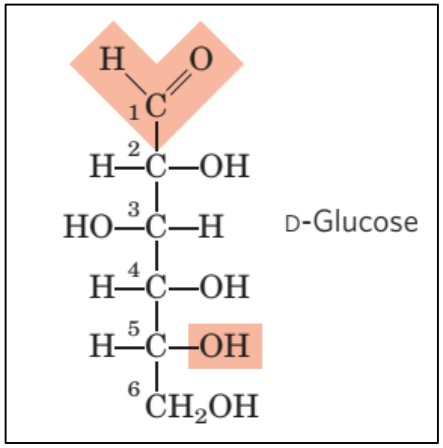


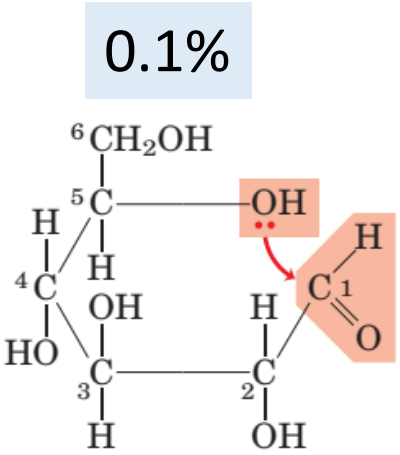
阿斯巴甜（代糖），非碳水化合物

When the steric match is correct, the sweet receptor is stimulated and the signal “sweet” is conducted to the brain. When the match is not correct, the sweet receptor is not stimulated; in fact, in this case, another receptor (for bitterness) is stimulated by the “wrong” stereoisomer of aspartame.

單醣在水溶液中多為環狀結構

- 以D-葡萄糖為例，可在開鏈式與六元環的環式結構之間快速互變。
- 異位體(anomer)：單醣異購物中只有羰基(C=O)碳原子的組態不同稱之。



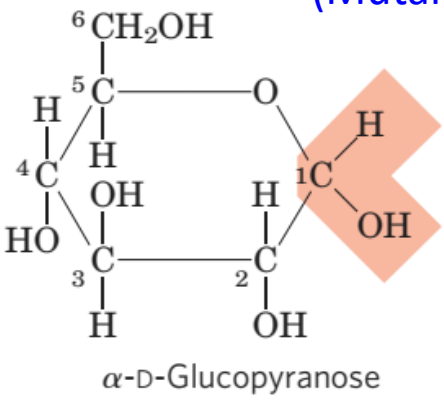


在水中比例

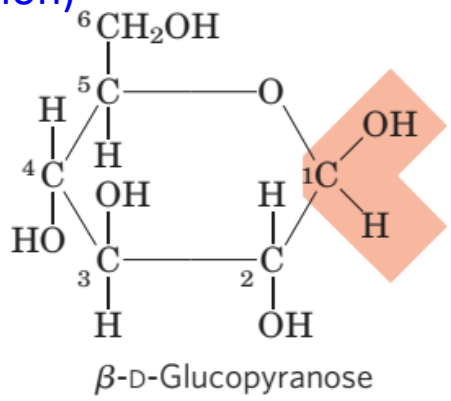
36%

變旋
(Mutarotation)

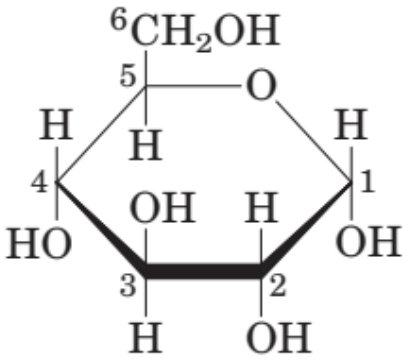
64%



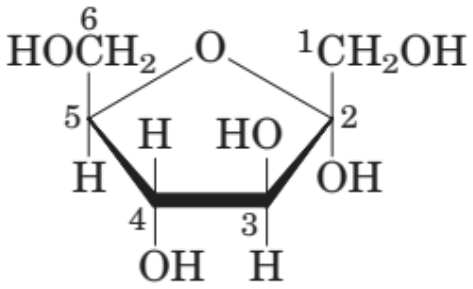
α-D-吡喃葡萄糖



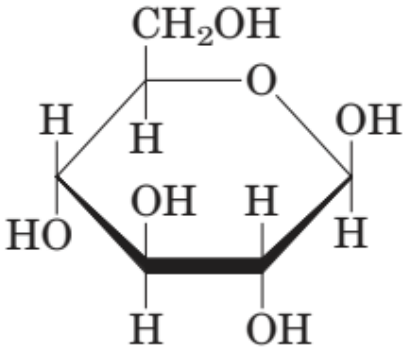
β-D-吡喃葡萄糖



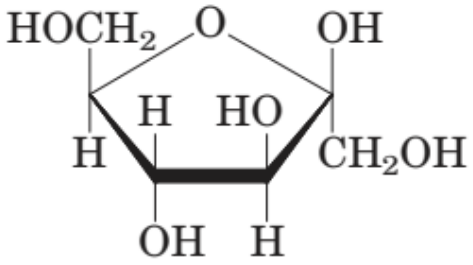
α-D-Glucopyranose



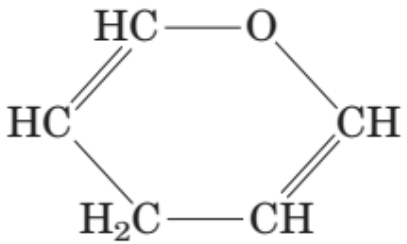
α-D-Fructofuranose



β-D-Glucopyranose

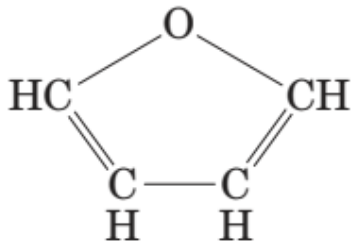


β-D-Fructofuranose



Pyran

吡喃糖

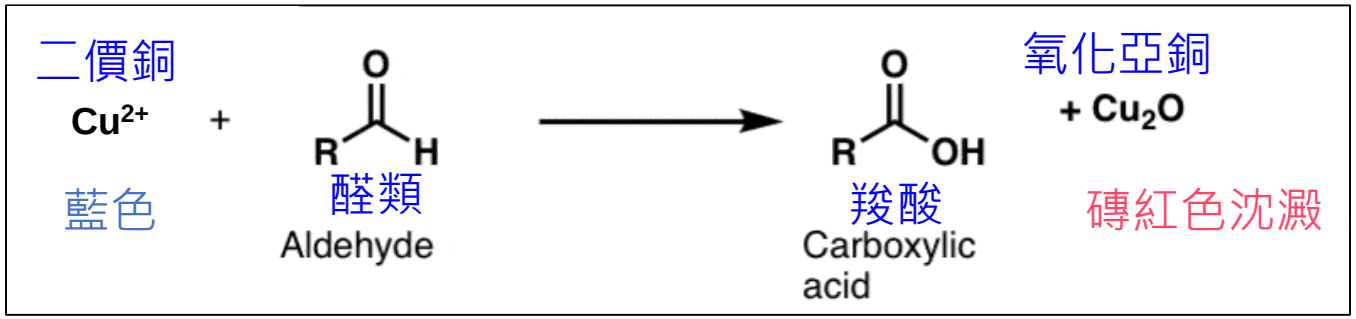


Furan

呋喃糖

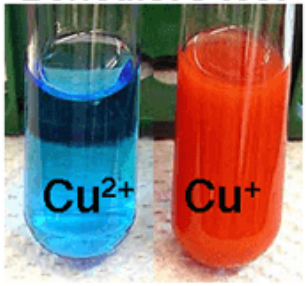
單醣具有還原能力

- 還原糖(reducing sugar) 為俱有還原能力的醣類，在鹼性的溶液中可以將Cu^{2+}還原成Cu^{+}。



Three Common Tests for Aldehydes

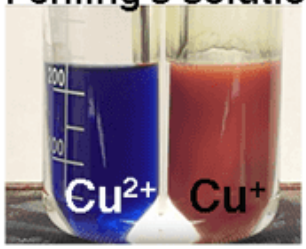
Benedict's test



Control (blue) | Positive test (red)

本氏液

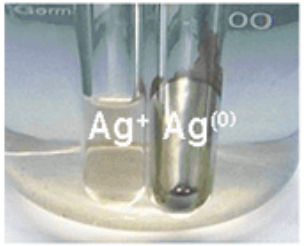
Fehling's solution



Control (blue) | Positive test (red)

菲林氏液

Tollens Test



Control (clear) | Positive test (silver mirror)

多倫試劑

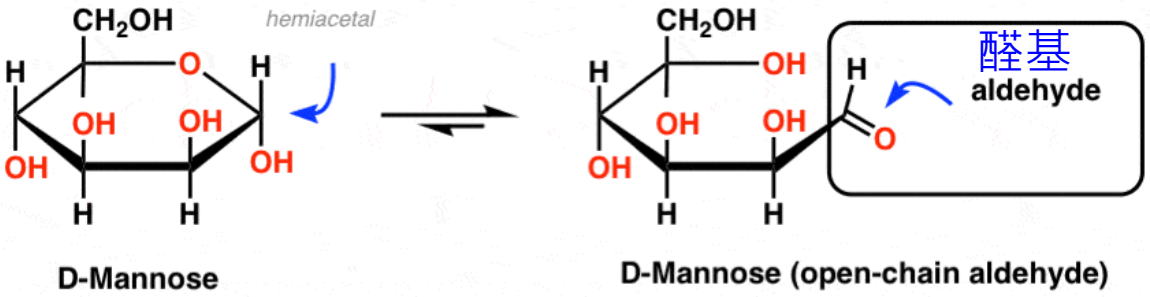
In each case the aldehyde has been oxidized to a carboxylic acid and the metal salt (Cu^{2+} or Ag^{+}) has been reduced.

https://www.masterorganicchemistry.com/2017/09/12/reducing-sugars/

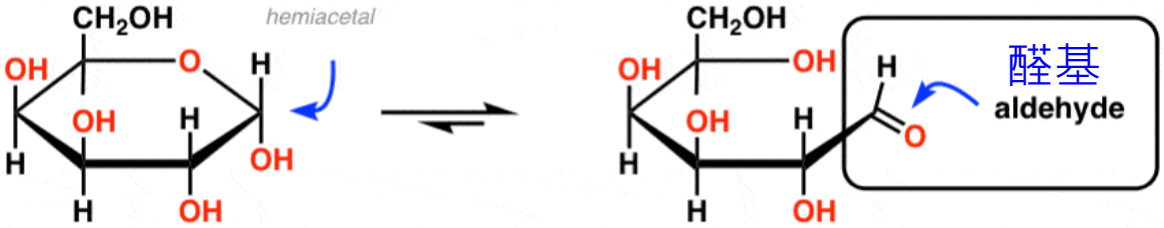
含有醛基與酮基的單醣皆有還原能力

半縮醛

Monosaccharides with a hemiacetal are also "reducing sugars" since their open-chain form contains an aldehyde (or alpha-hydroxy ketone)

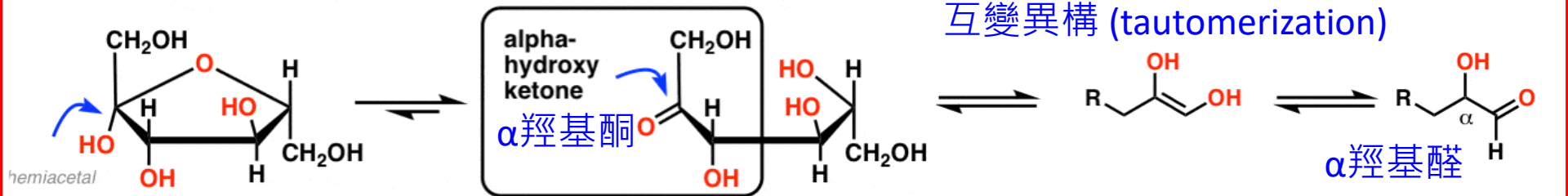


D-Mannose　　D-Mannose (open-chain aldehyde)



D-Galactose　　D-Galactose (open-chain aldehyde)

互變異構 (tautomerization)



D-Fructose　　D-Fructose (keto form)

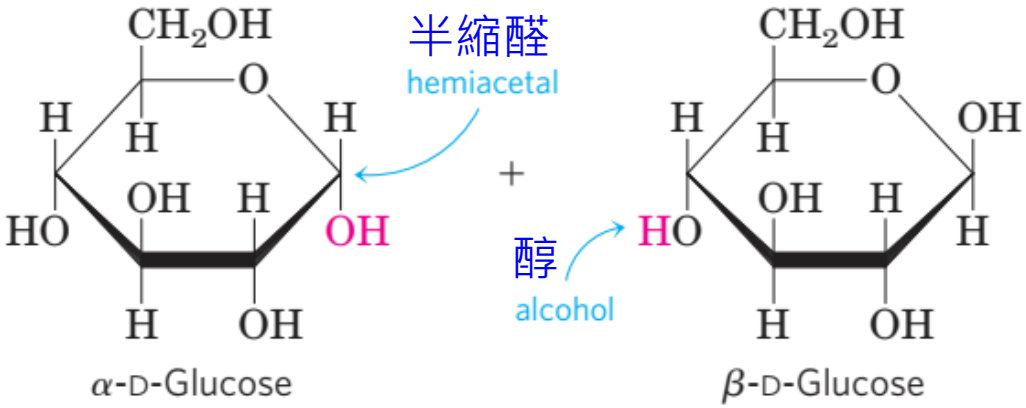
gives positive Tollens, Benedict, Fehlings' test

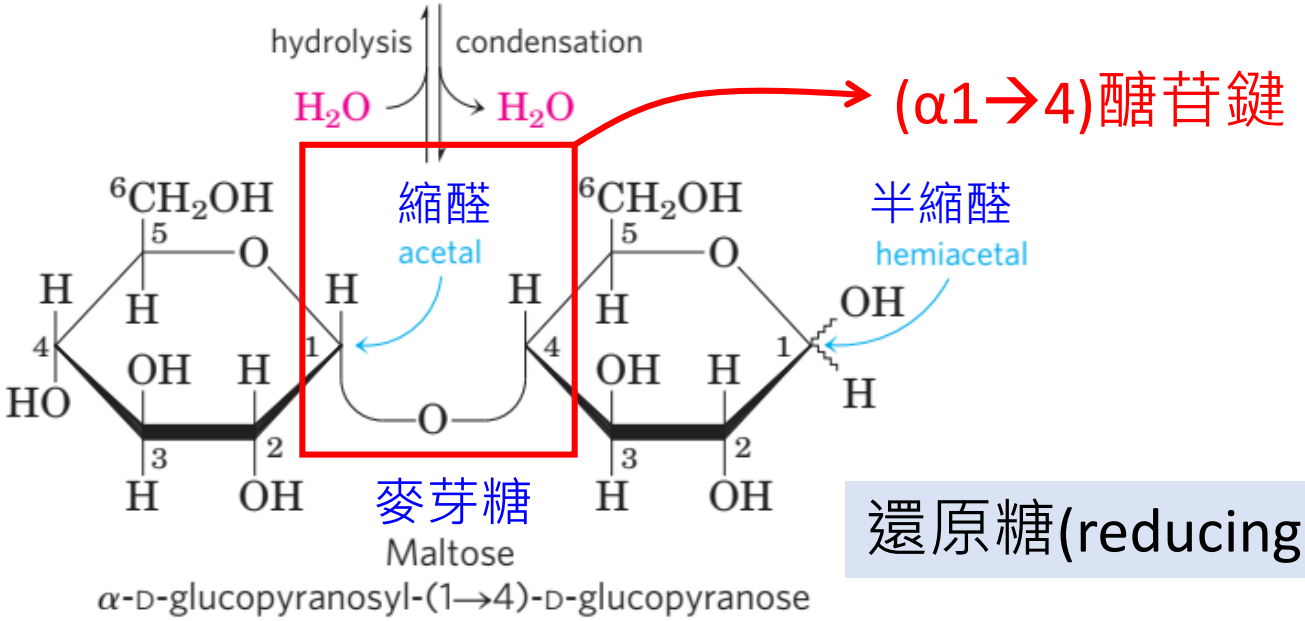
果糖，一種酮醣

https://www.masterorganicchemistry.com/2017/09/12/reducing-sugars/

雙醣

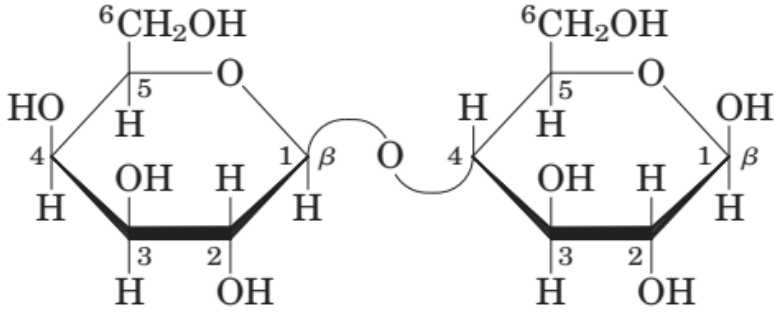
- 雙醣是由合兩個單醣分子以醣苷鍵結合而成。





還原糖(reducing sugar)

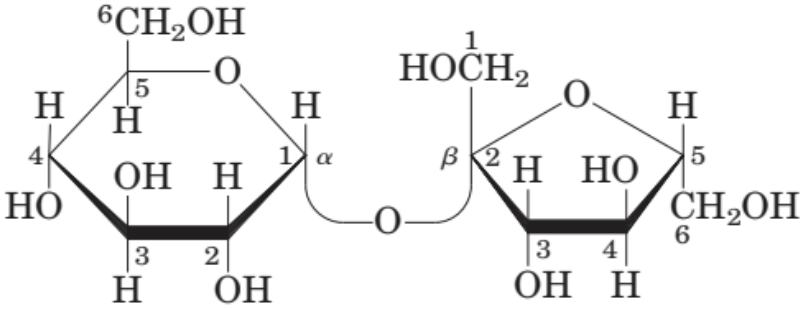
其他常見的雙醣



Lactose (β form)
β-D-galactopyranosyl-(1→4)-β-D-glucopyranose
Gal(β1→4)Glc

(β1→4)醣苷鍵

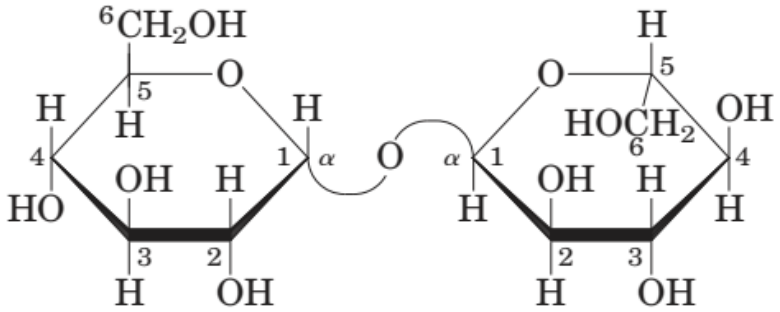
乳糖　　半乳糖+葡萄糖



Sucrose
β-D-fructofuranosyl α-D-glucopyranoside
Fru(2β↔α1)Glc ≡ Glc(α1↔2β)Fru

何者為還原糖？
何者為非還原糖？

蔗糖　　果糖+葡萄糖



Trehalose
α-D-glucopyranosyl α-D-glucopyranoside
Glc(α1↔1α)Glc

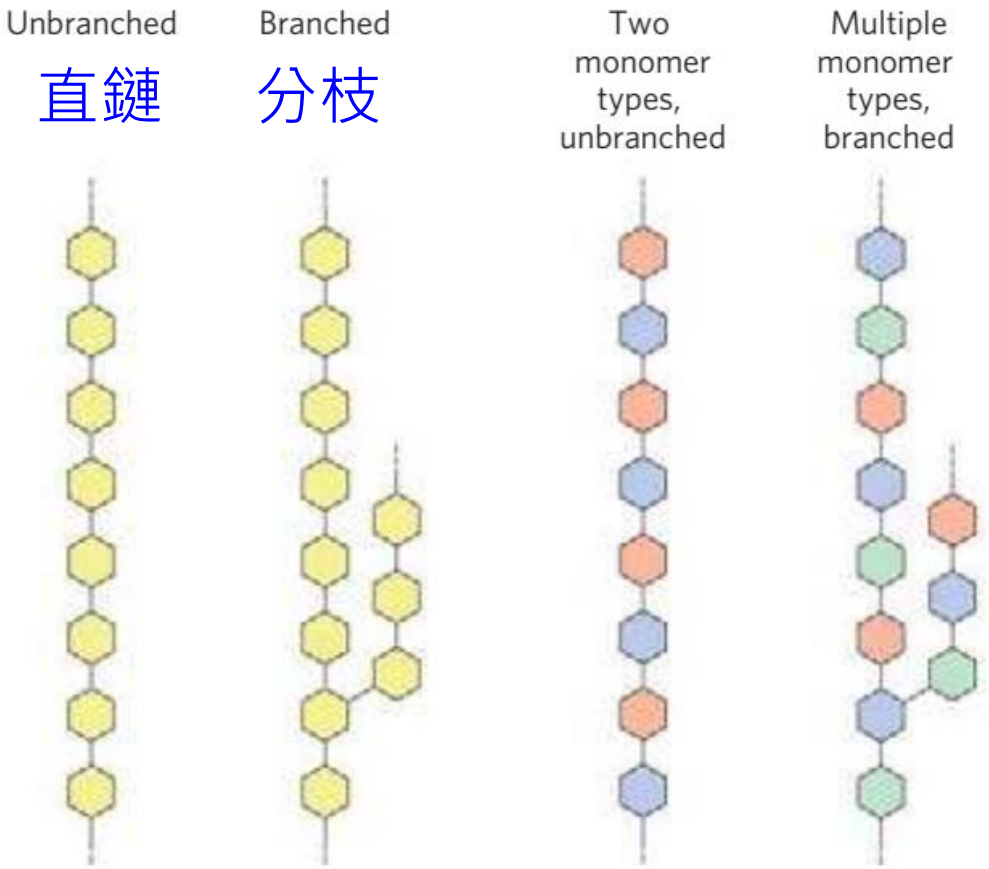
海藻糖　　葡萄糖+葡萄糖

多醣

- 多醣依照單醣組成與結構可分為：

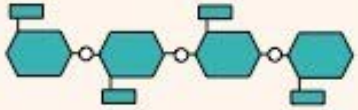
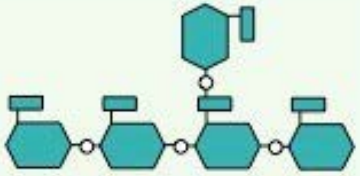
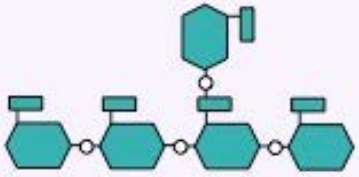
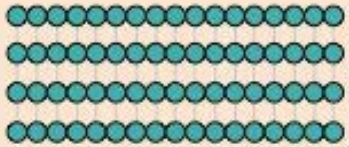
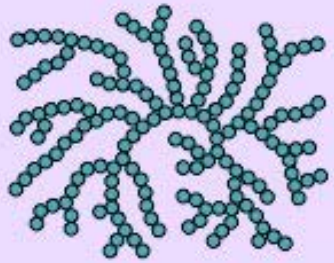
同元多醣 **Homopolysaccharides**

異元多醣 **Heteropolysaccharides**



- 依照其功能可以分為儲存性多醣與結構性多醣。

結構性多醣　　澱粉　　儲存性多醣

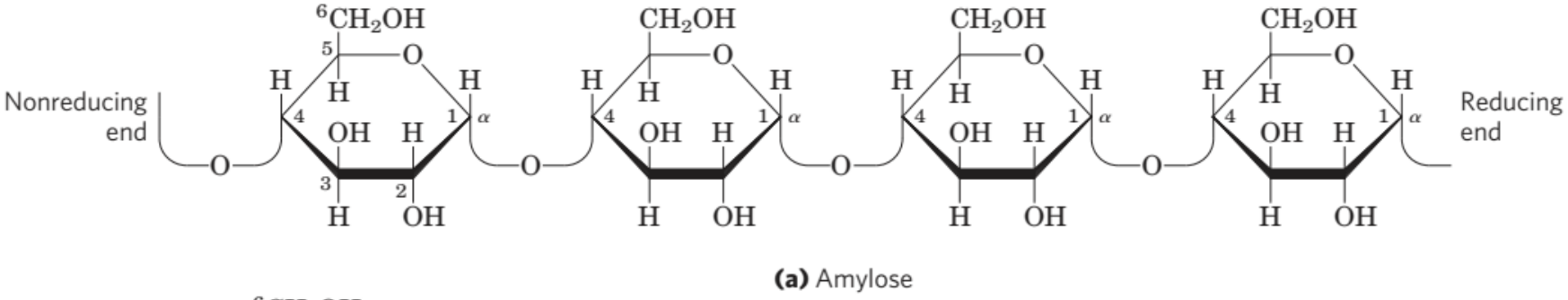
	Cellulose 纖維素	Starch 直鏈澱粉 Amylose	Starch 支鏈澱粉 Amylopectin	Glycogen 肝醣
Source	植物	植物	植物	動物、細菌
Subunit	β-glucose	α-glucose	α-glucose	α-glucose
Bonds	1-4	1-4	1-4 *and* 1-6	1-4 *and* 1-6
Branches	No	No	Yes (~per 20 subunits)	Yes (~per 10 subunits)
Diagram				
Shape				

https://ib.bioninja.com.au/standard-level/topic-2-molecular-biology/23-carbohydrates-and-lipids/sugar-polymers.html

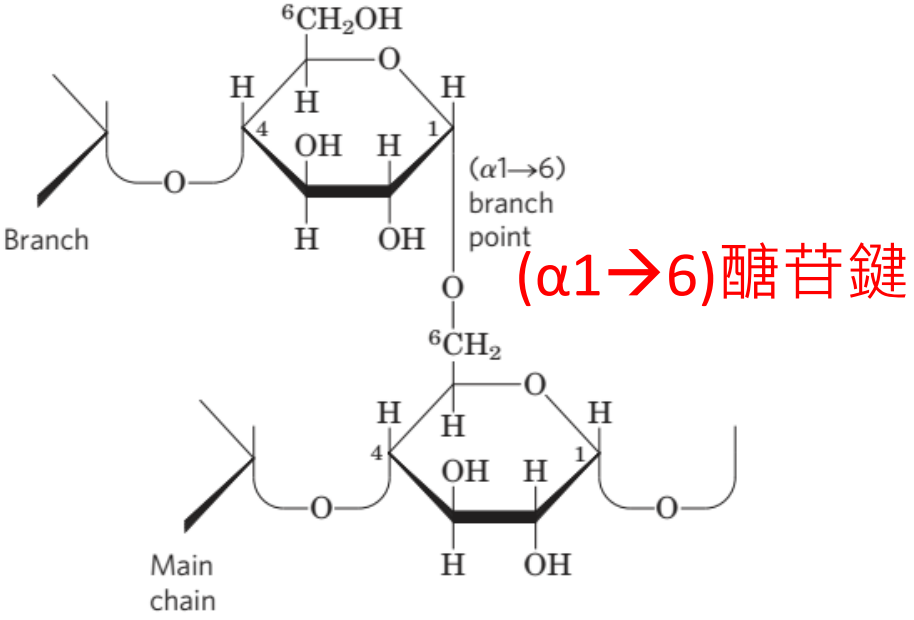
儲存性多醣

- 肝醣(glycogen)與澱粉(starch)

直鏈：直鏈澱粉(amylose)　(α1→4)醣苷鍵

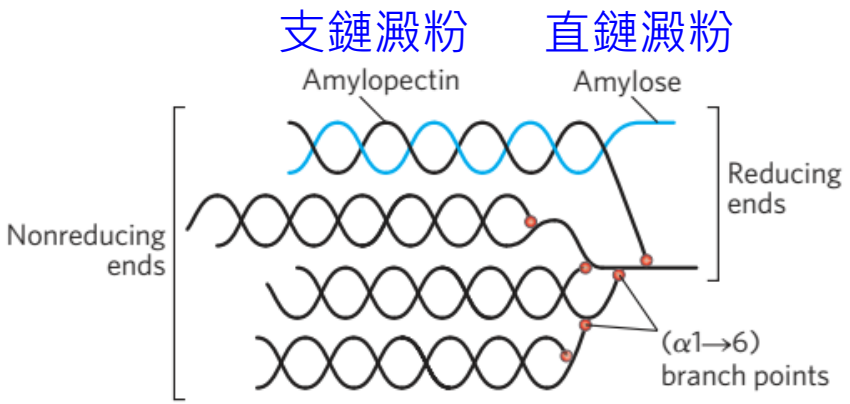


(a) Amylose



(α1→6)醣苷鍵

(b)

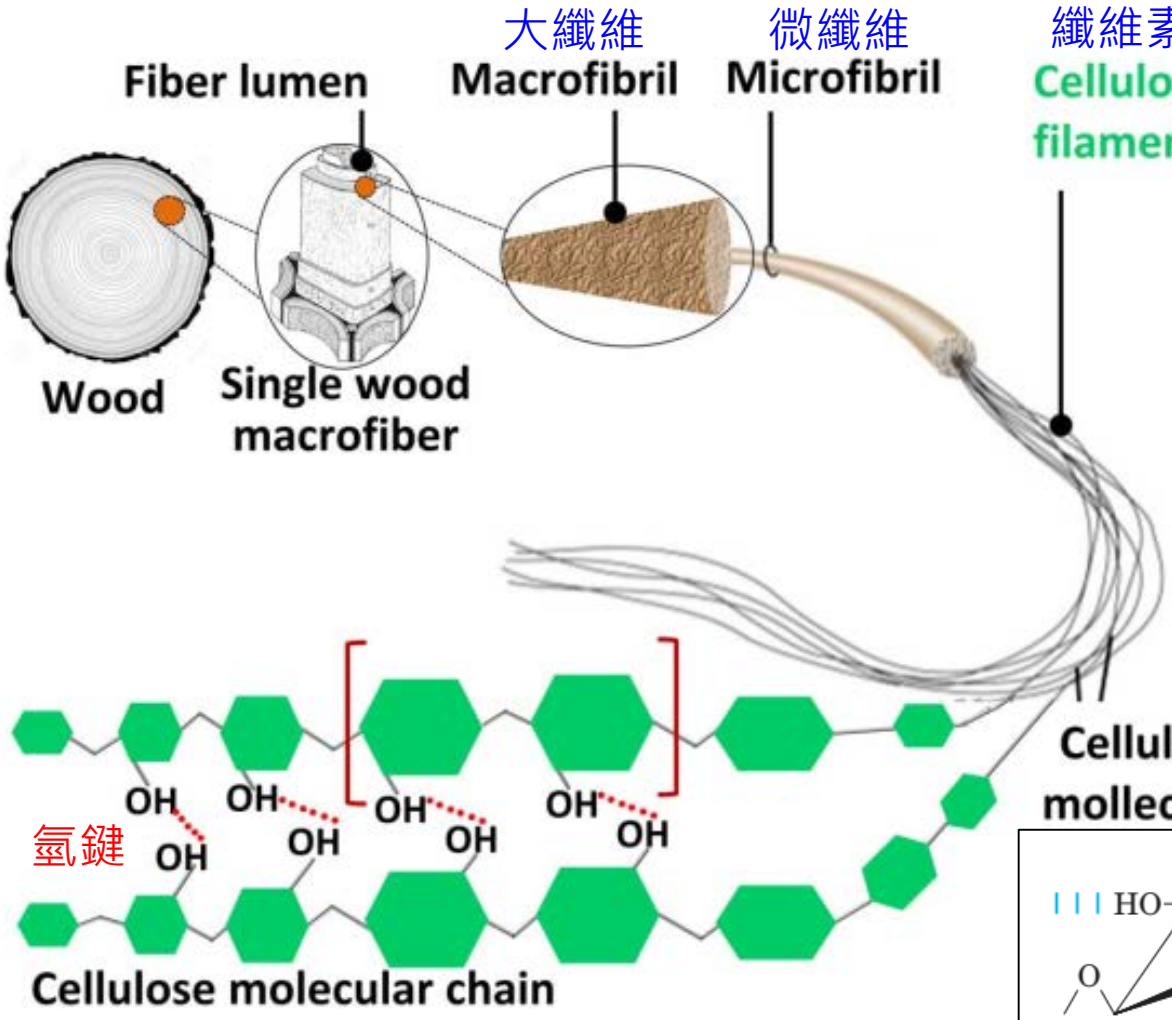


(c)

支鏈：支鏈澱粉(amylopectin)或肝醣

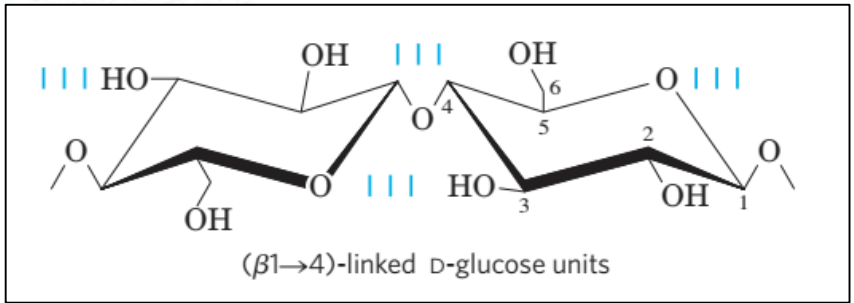
結構性多醣

纖維素(cellulose)



- 植物細胞壁的主要成份，也是自然界含量最多的化合物。
- 結構較為展延，適合擔任結構支撐與保護的角色。
- 人體無法消化利用。(Why?)

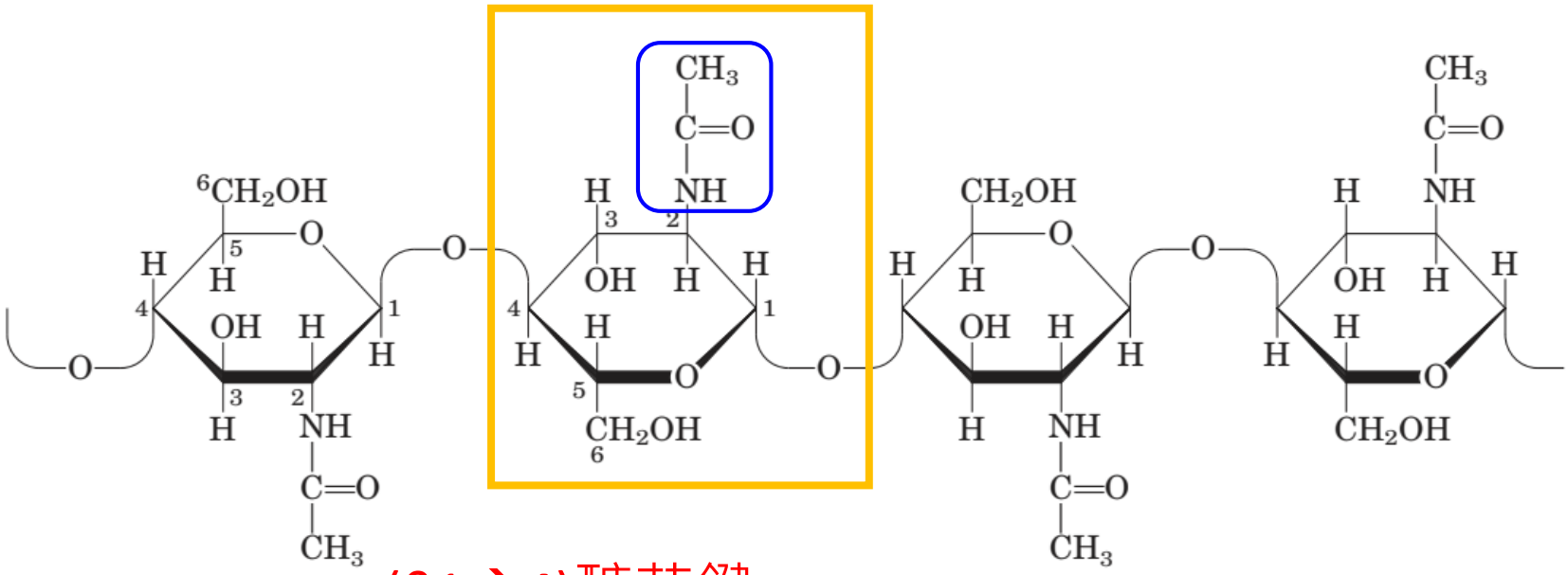
(β1→4)醣苷鍵



Hisseine, O. A. et al. (2018). Journal of materials in civil engineering, 30(6), 04018109.

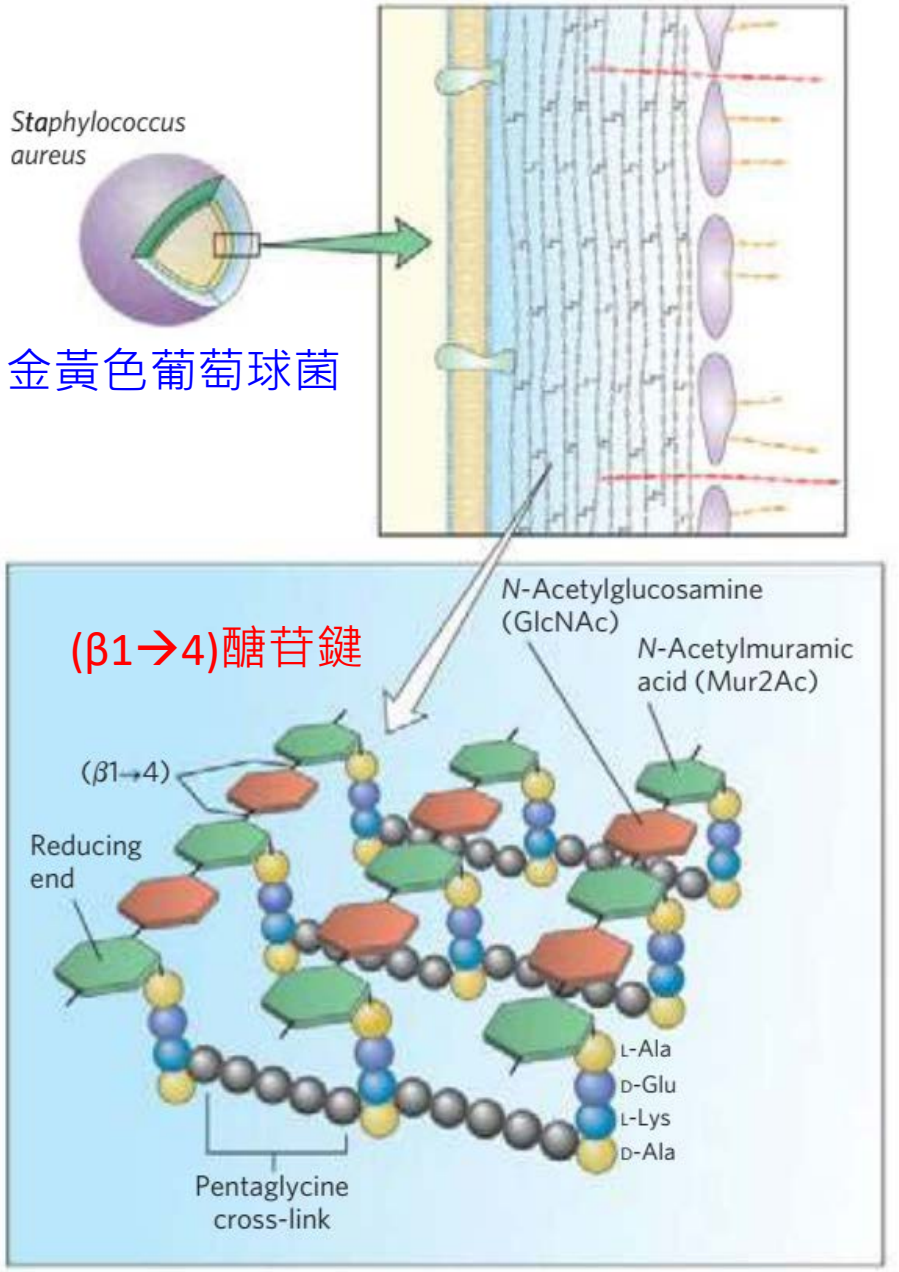
幾丁質(chitin)

- 甲殼動物外骨骼的幾丁質是由單醣衍生物N-乙醯葡糖胺形成的結構性多醣。



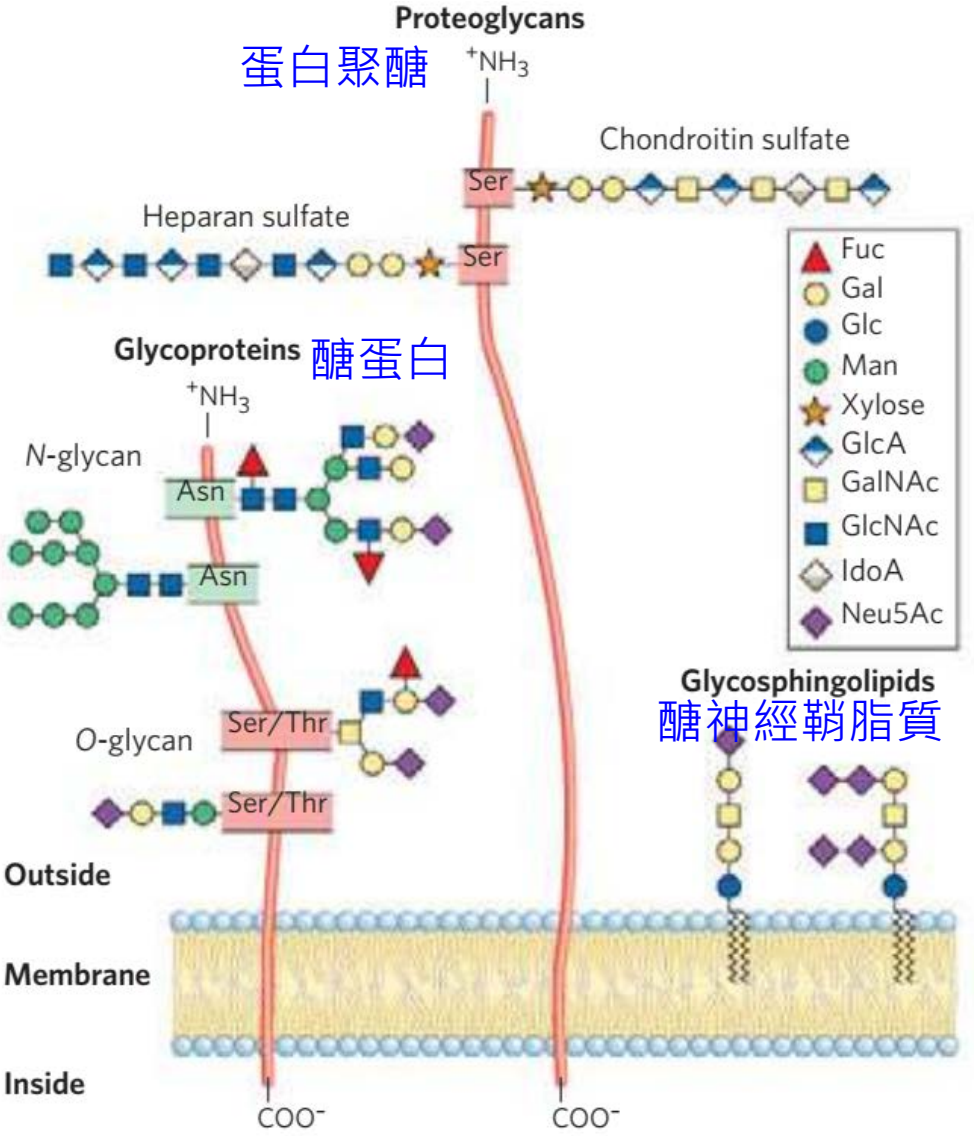
肽聚糖(peptidoglycan)

- 細菌細胞壁的主要成份。
- 由N-乙醯葡糖胺與N-乙醯胞壁酸連結而成的異元多醣，並以短鏈肽交叉鏈接。



醣綴合物(glycoconjugates)

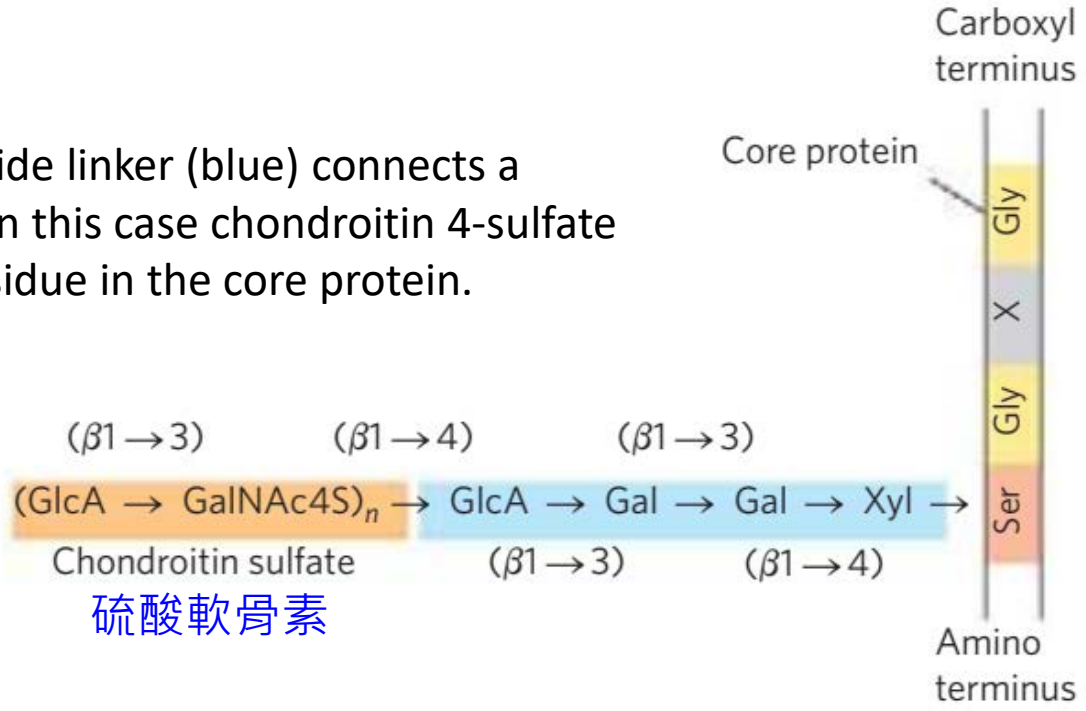
- 除了結構性儲存性多醣與結構性多醣外，醣類分子也可以以寡糖或多醣形式以共價鍵連接在蛋白質或脂質上。
- 醣綴合物上的醣分子可作為訊息辨識功能。



蛋白聚醣(proteoglycan)

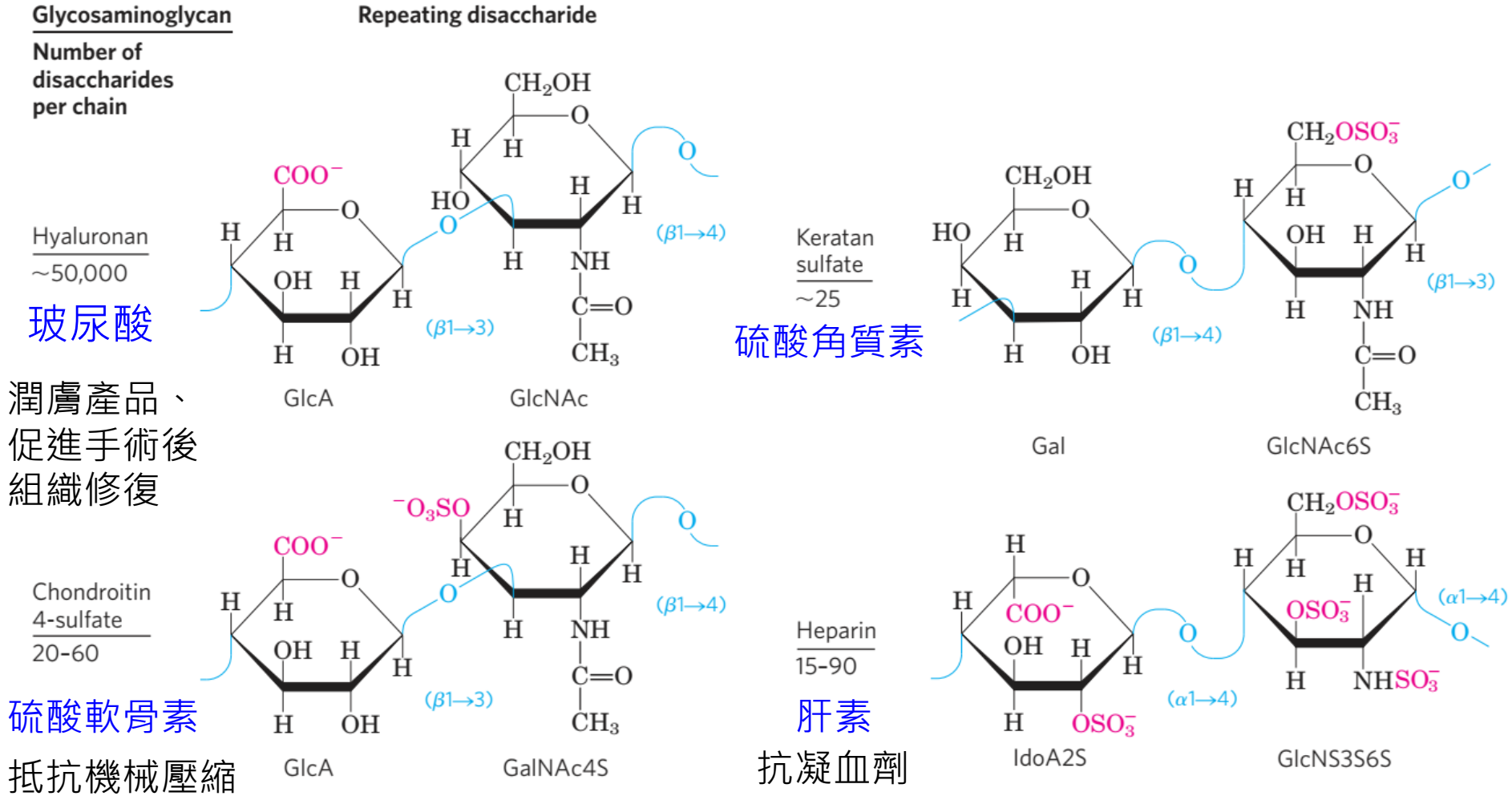
- 位於動物組織中細胞表面與細胞外空隙。
- 細胞外基質的主要成份。
- 蛋白醣可鑲嵌在細胞膜上或者分泌到細胞外基質。

A typical tetrasaccharide linker (blue) connects a glycosaminoglycan—in this case chondroitin 4-sulfate (orange)—to a Ser residue in the core protein.



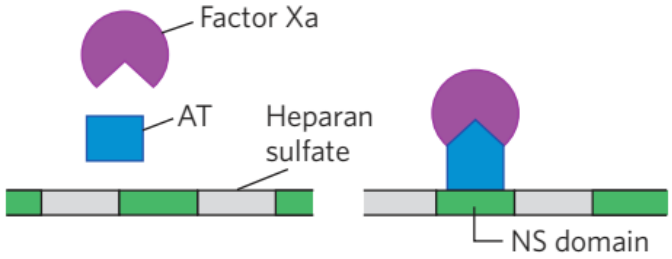
醣胺聚醣(glycosaminoglycan)

- 蛋白醣中醣類部份總稱。



蛋白聚醣中醣類扮演的功能：以肝素為例

(a) Conformational activation

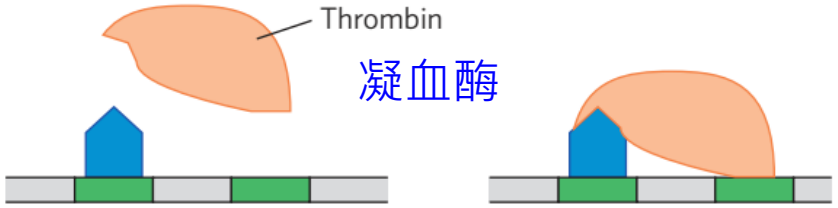


NS: highly sulfated

A conformational change induced in the protein antithrombin (AT) on binding a specific pentasaccharide NS domain allows its interaction with blood clotting factor Xa, preventing clotting.

避免凝血

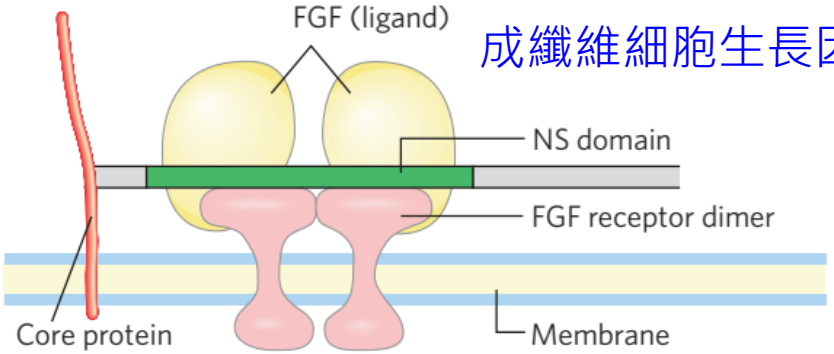
(b) Enhanced protein-protein interaction



Binding of AT and thrombin to two adjacent NS domains brings the two proteins into close proximity, favoring their interaction, which inhibits blood clotting.

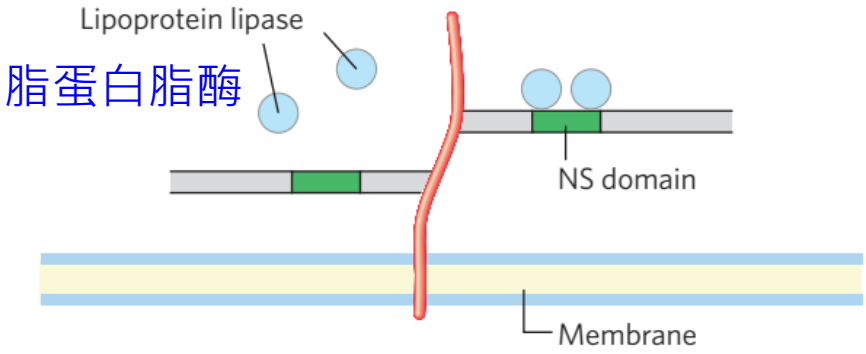
抑制凝血

(c) Coreceptor for extracellular ligands



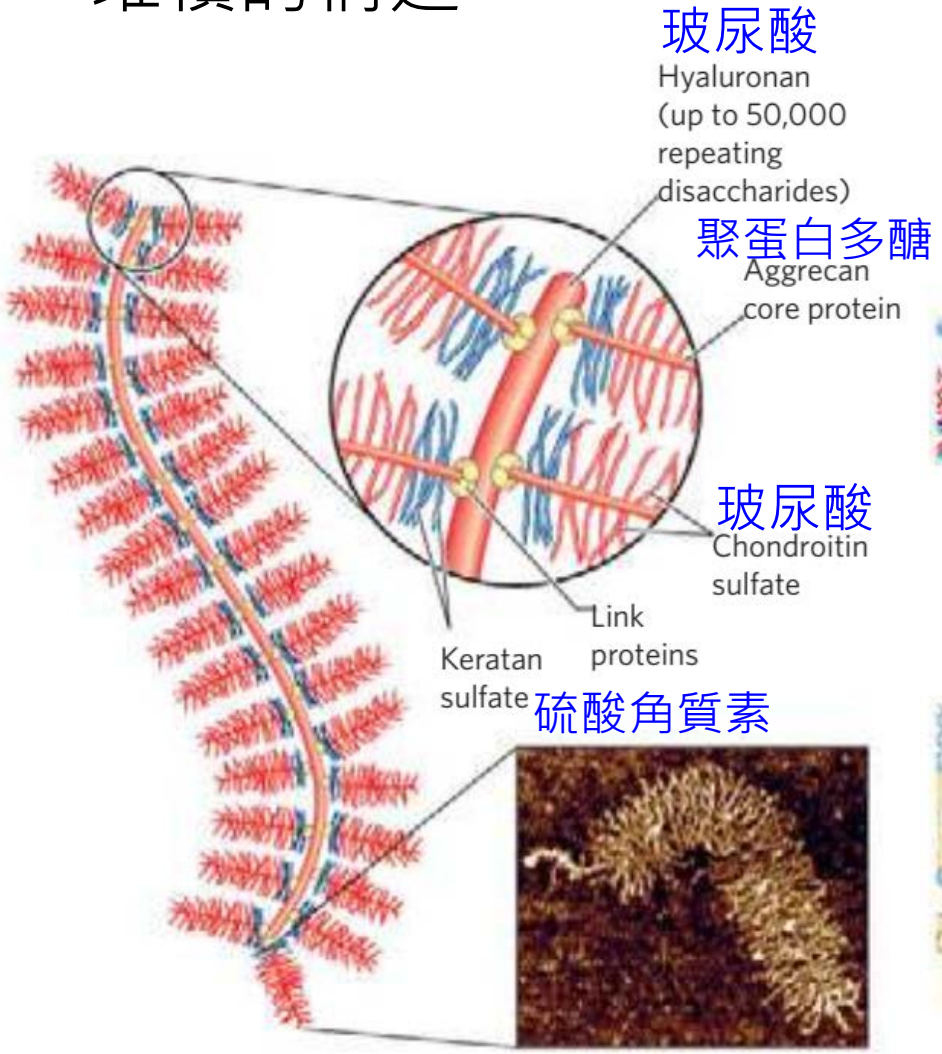
NS domains interact with both the fibroblast growth factor (FGF) and its receptor, bringing the oligomeric complex together and increasing the effectiveness of a low concentration of FGF.

(d) Cell surface localization/concentration

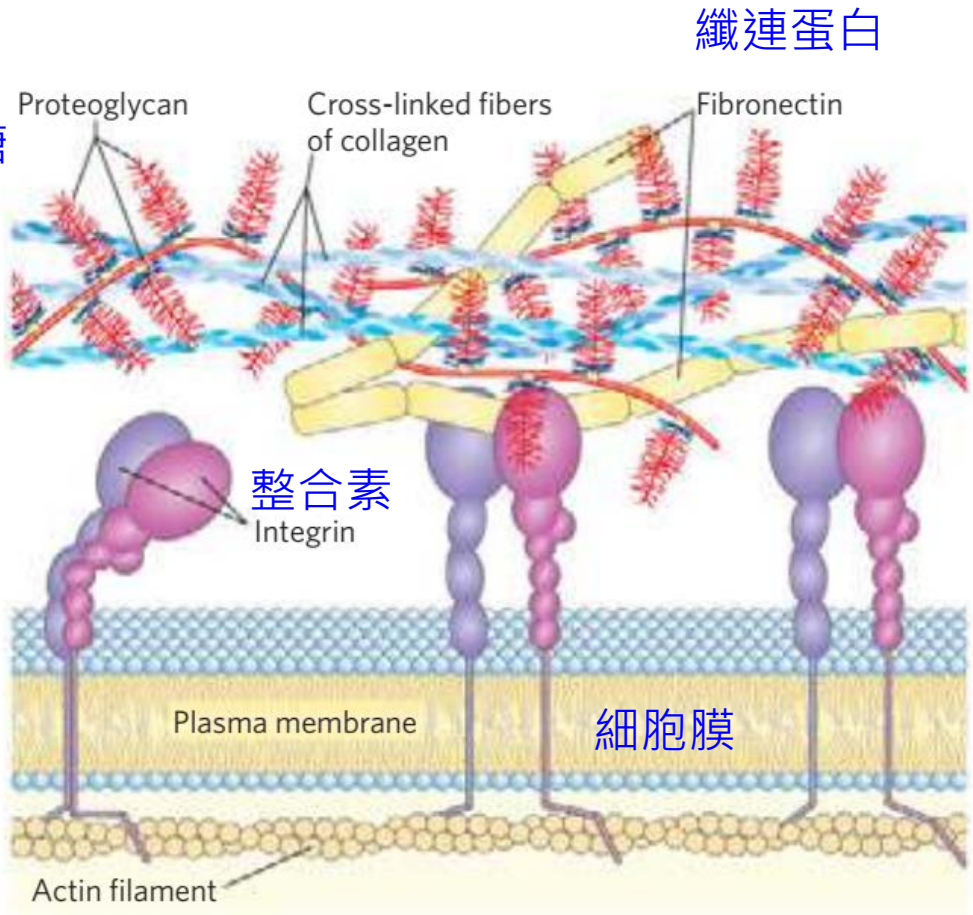


The high density of negative charges in heparan sulfate attracts positively charged lipoprotein lipase molecules and holds them by electrostatic and sequence-specific interactions with NS domains.

蛋白聚醣在細胞外基質堆積的構造

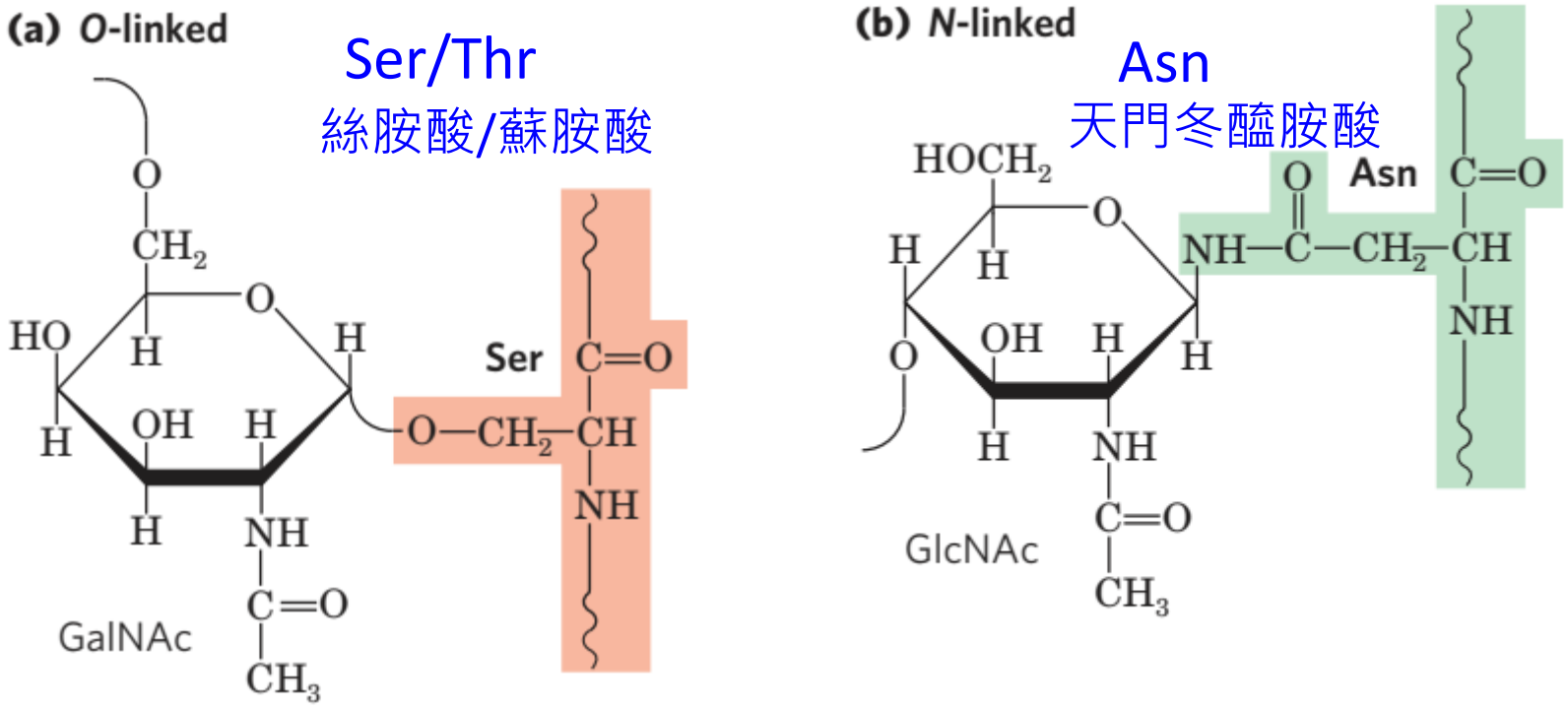


細胞外基質中的蛋白聚醣與細胞膜上蛋白質的交互作用

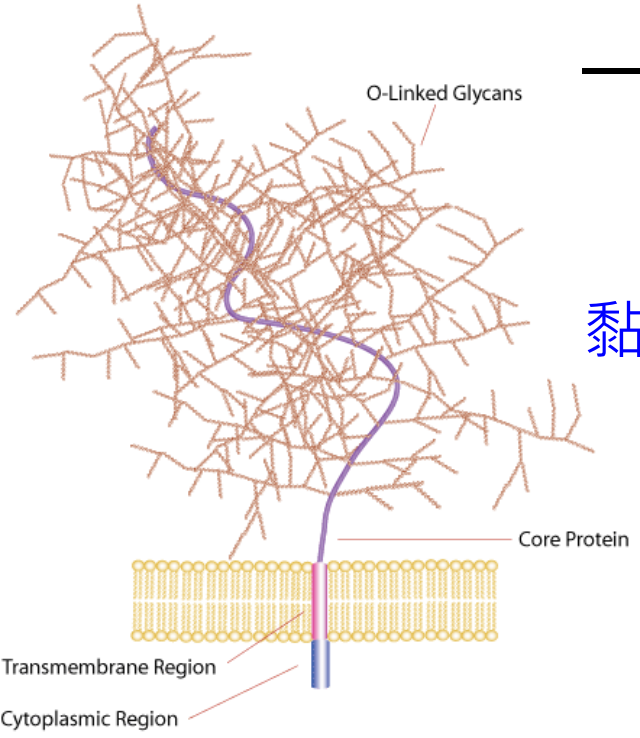


醣蛋白(glycoprotein)

- 寡醣以複雜的組成與排列方式連接在蛋白質上。
- 經常出現在細胞膜外側。
- 寡醣部份依照結合在胺基酸的種類分為兩類：

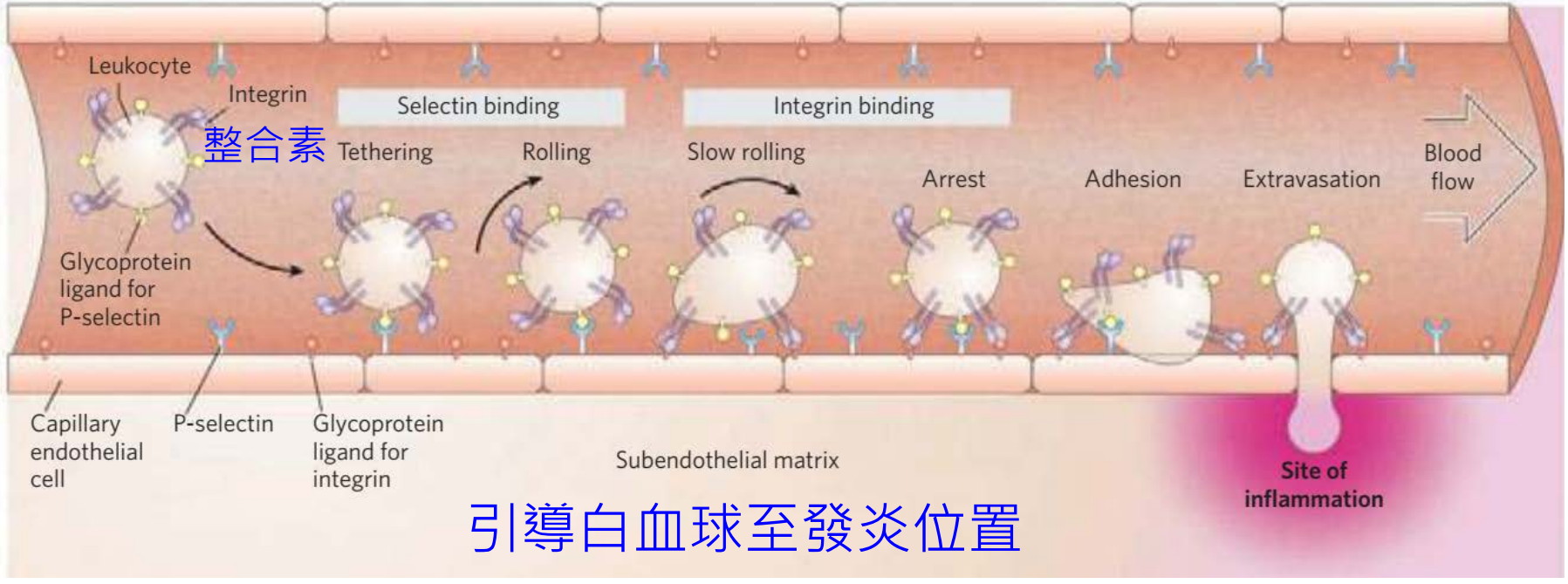


一些醣蛋白的功能



黏液素：潤滑、構築化學屏障...

https://www.sigmaaldrich.com/life-science/metabolomics/enzyme-explorer/learning-center/structural-proteins/mucin.html



引導白血球至發炎位置

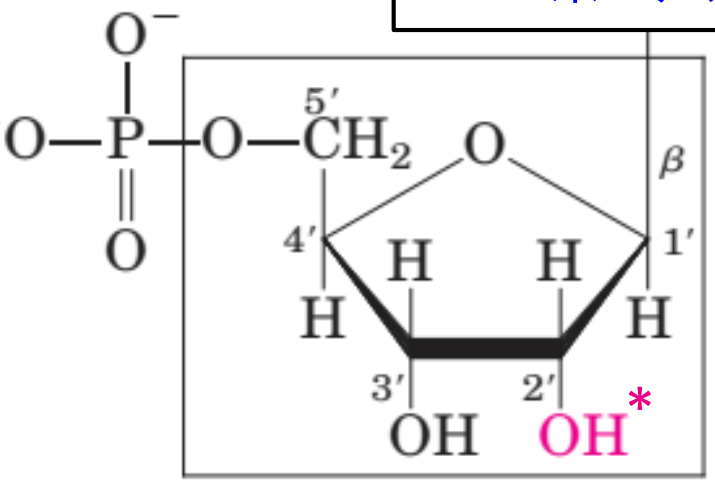
核酸

- 核酸(nucleic acid)為生物中遺傳物質儲存形式。
- 核苷酸(nucleotide)為核酸的基本組成單位，可分為三個部份：

2.（含氮）鹼基：嘌呤或嘧啶

3.磷酸

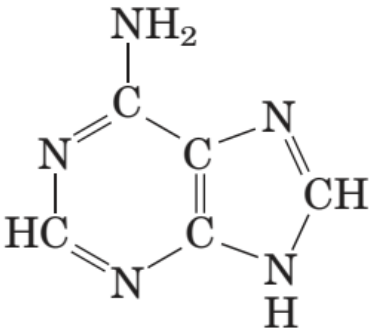
負電荷



1. 五碳醣（核糖）

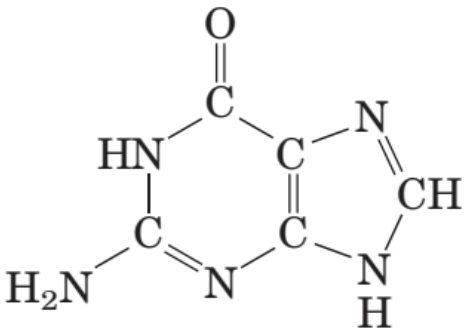
*OH→H 2’-去氧[核糖]核苷酸

含氮鹼基種類



Adenine

腺嘌呤

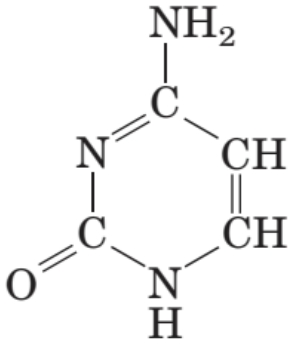


Guanine

鳥嘌呤

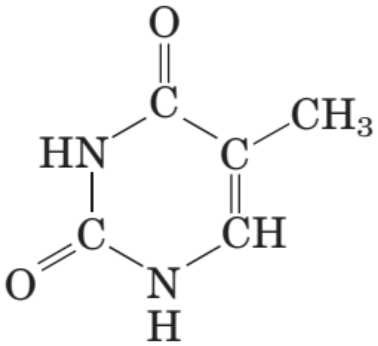
Purines

嘌呤



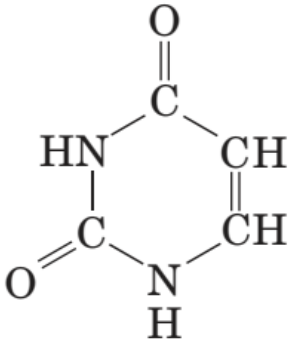
Cytosine

胞嘧啶



Thymine (DNA)

胸腺嘧啶



Uracil (RNA)

脲嘧啶

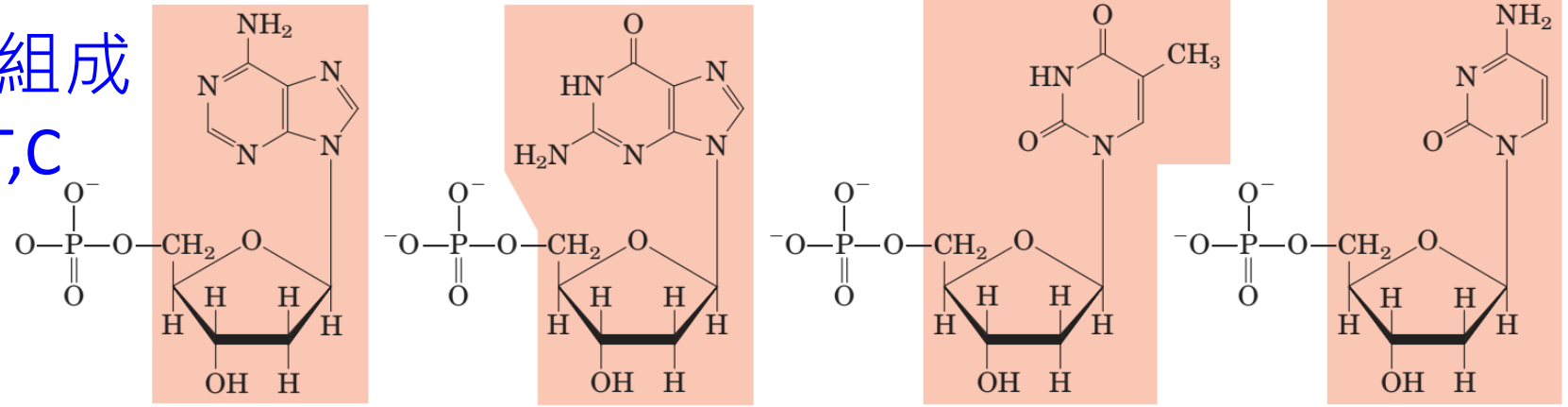
Pyrimidines

嘧啶

為什麼DNA裡沒有U(Uracil)?

https://pansci.asia/archives/65666

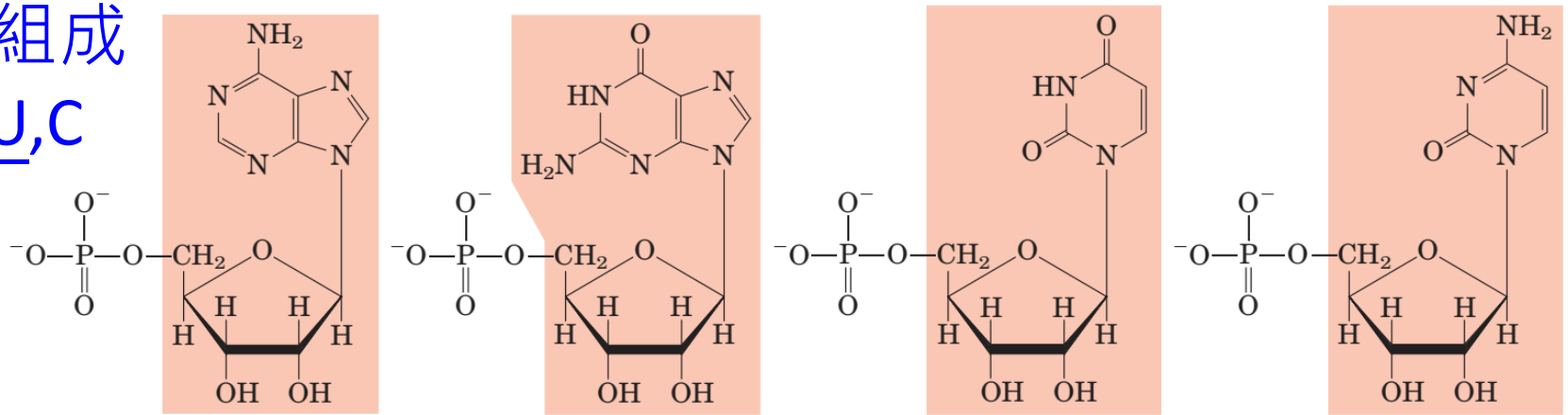
DNA組成
A,G,T,C



	Deoxyadenylate (deoxyadenosine 5′-monophosphate)	Deoxyguanylate (deoxyguanosine 5′-monophosphate)	Deoxythymidylate (deoxythymidine 5′-monophosphate)	Deoxycytidylate (deoxycytidine 5′-monophosphate)
Nucleotide: 核苷酸				
Symbols:	A, dA, dAMP	G, dG, dGMP	T, dT, dTMP	C, dC, dCMP
Nucleoside: 核苷	Deoxyadenosine	Deoxyguanosine	Deoxythymidine	Deoxycytidine

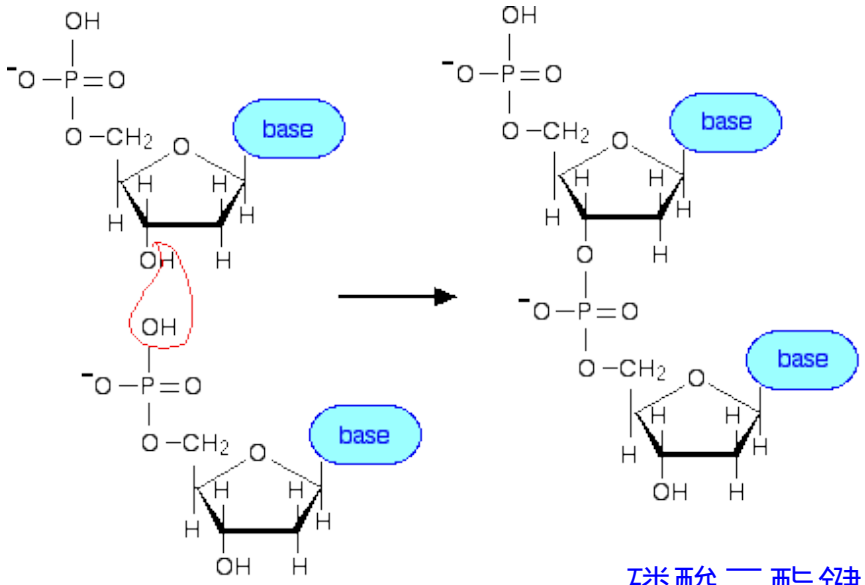
(a) Deoxyribonucleotides

RNA組成
A,G,U,C

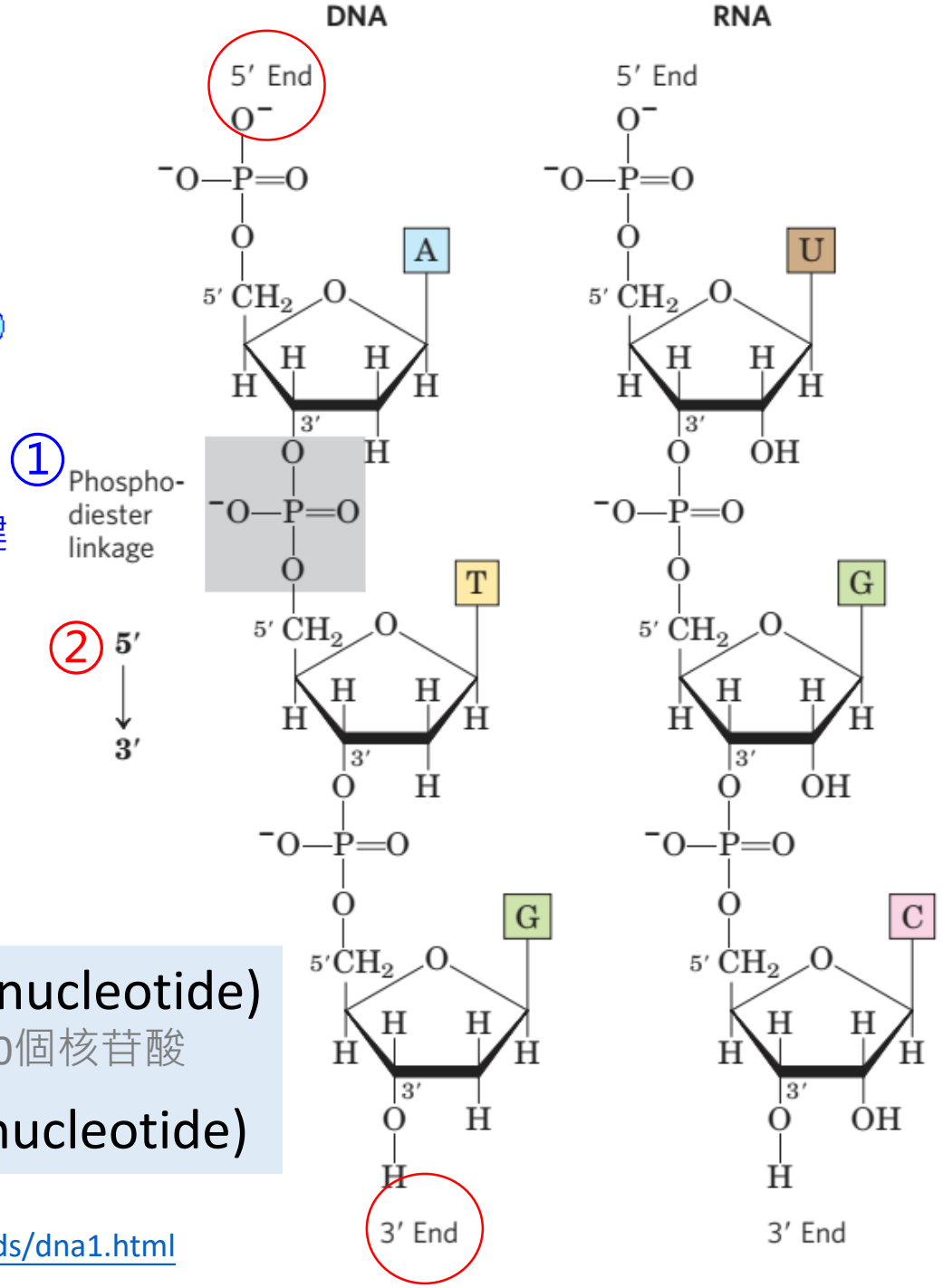


	Adenylate (adenosine 5′-monophosphate)	Guanylate (guanosine 5′-monophosphate)	Uridylate (uridine 5′-monophosphate)	Cytidylate (cytidine 5′-monophosphate)
Nucleotide:				
Symbols:	A, AMP	G, GMP	U, UMP	C, CMP
Nucleoside:	Adenosine	Guanosine	Uridine	Cytidine

(b) Ribonucleotides



磷酸二酯鍵



寡核苷酸 (oligonucleotide)

一般來說<50個核苷酸

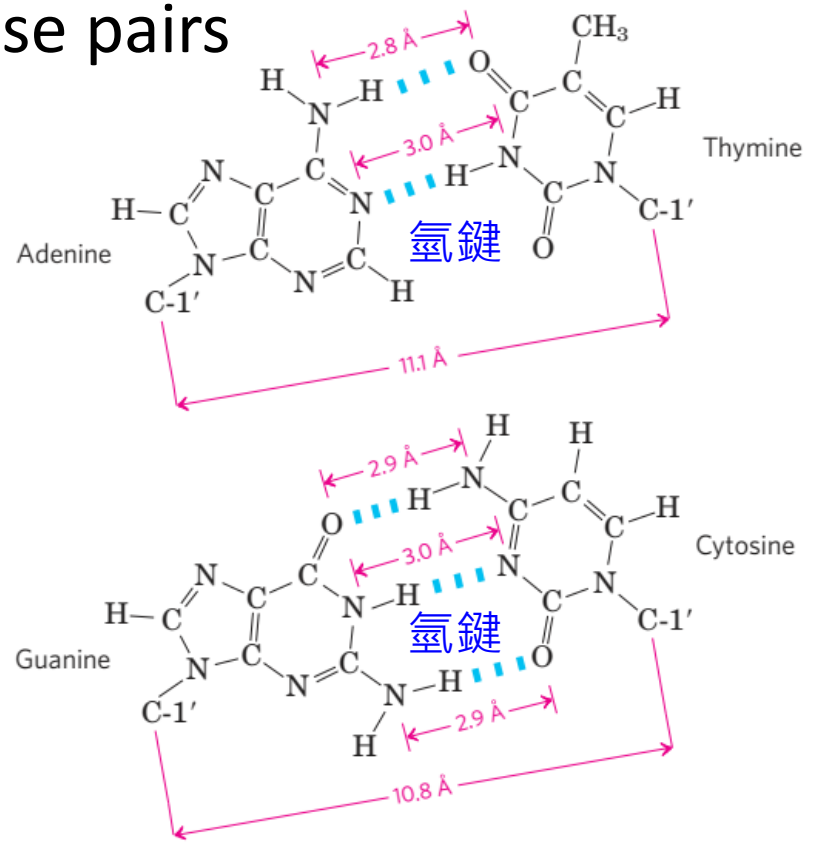
多核苷酸 (polynucleotide)

https://www.chemguide.co.uk/organicprops/aminoacids/dna1.html

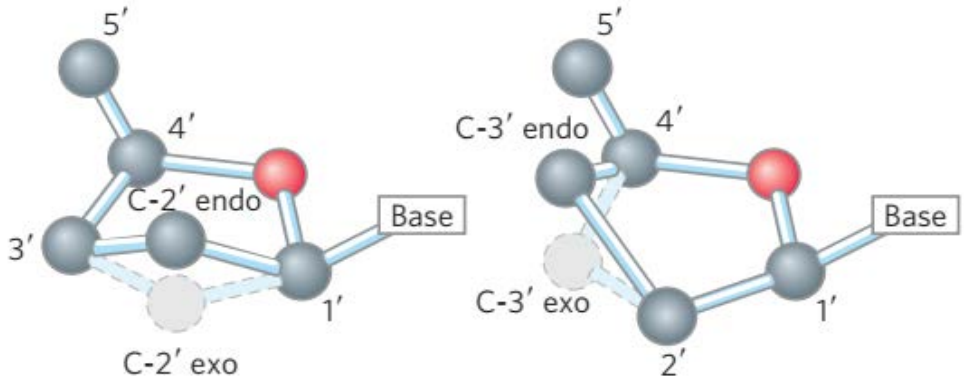
核苷酸的結構

- https://molview.org search “nucleotide”

- Hydrogen-bonding patterns in the base pairs



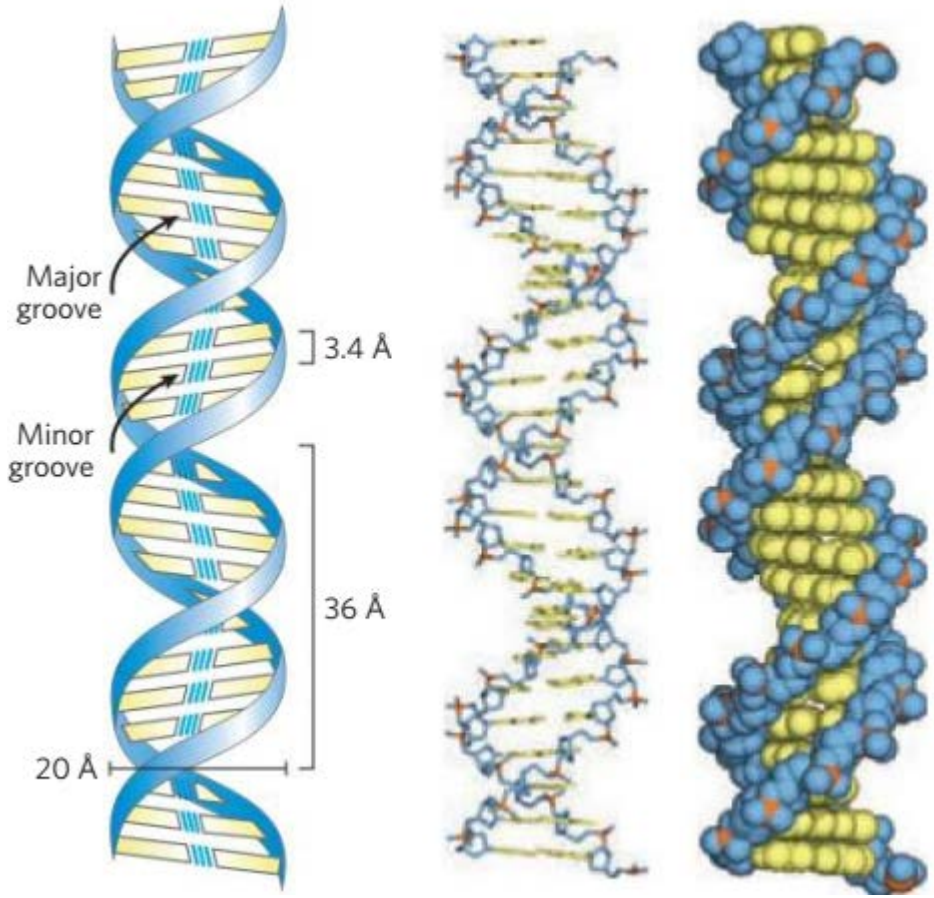
- Conformations of ribose

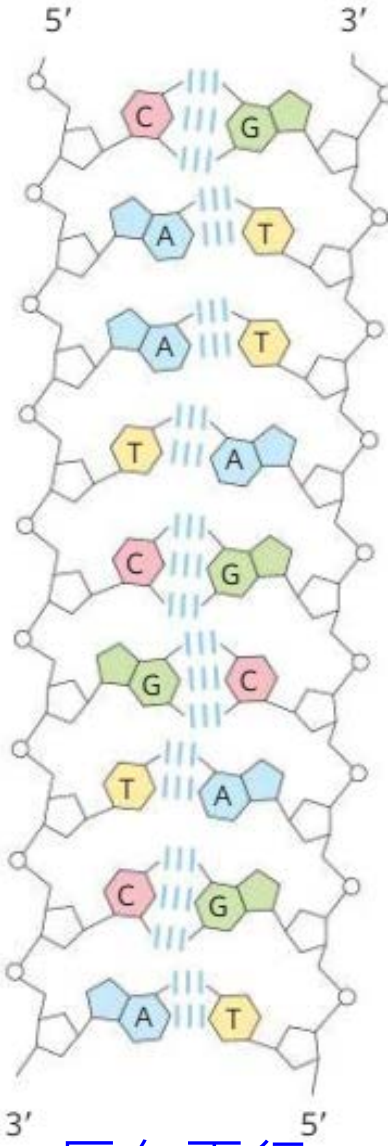


Ribofuranose rings in nucleotides can exist in four different puckered conformations.

核酸的結構

- （由華生與克里克提出的）DNA雙股螺旋模型





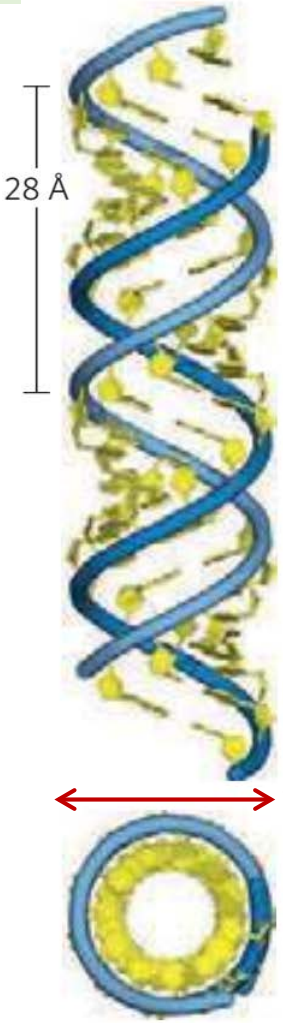
反向平行

https://en.wikipedia.org/wiki/James_Watson

核酸的雙股螺旋結構

Base pairs per helical turn

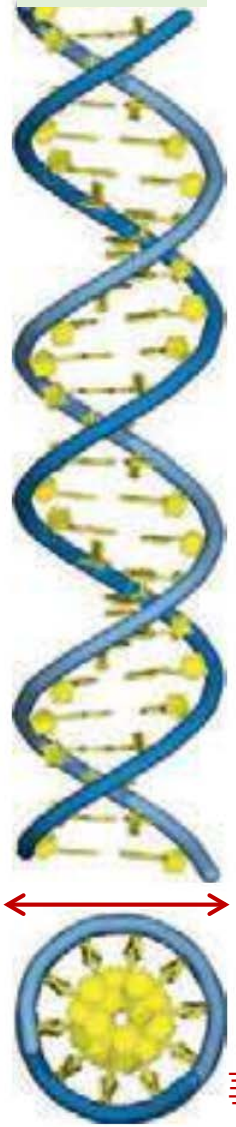
11



右旋

A form

10.5



右旋

B form

華生與克里克所提出的

12

左旋

Z form

DNA迴文序列與其結構

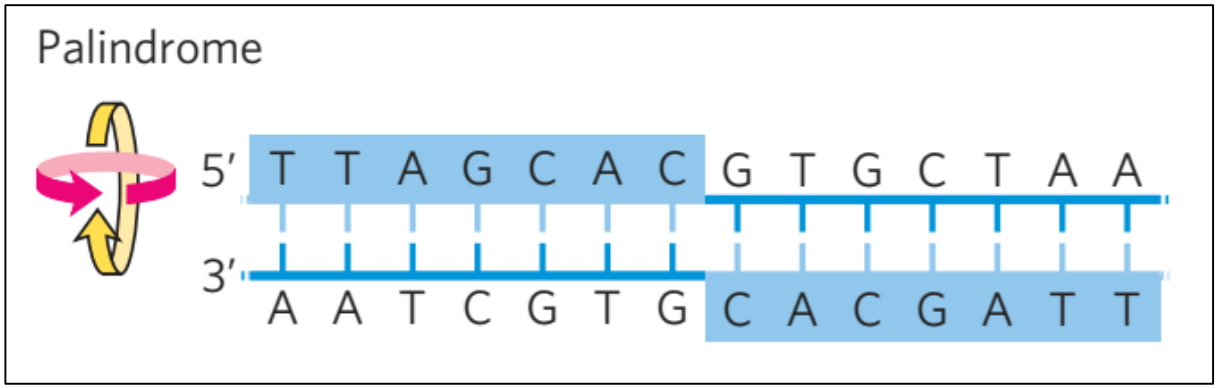
- 迴文
  - 「我為人人，人人為我」
  - 蘇東坡《菩薩蠻·回文》

    嶠南江淺紅梅小，小梅紅淺江南嶠。

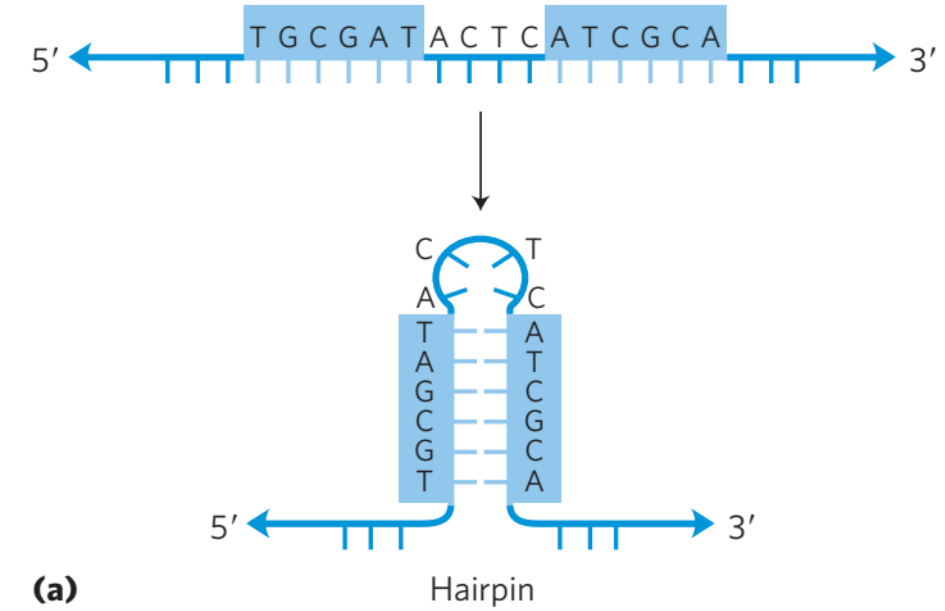
    窺我向疏籬，籬疏向我窺。

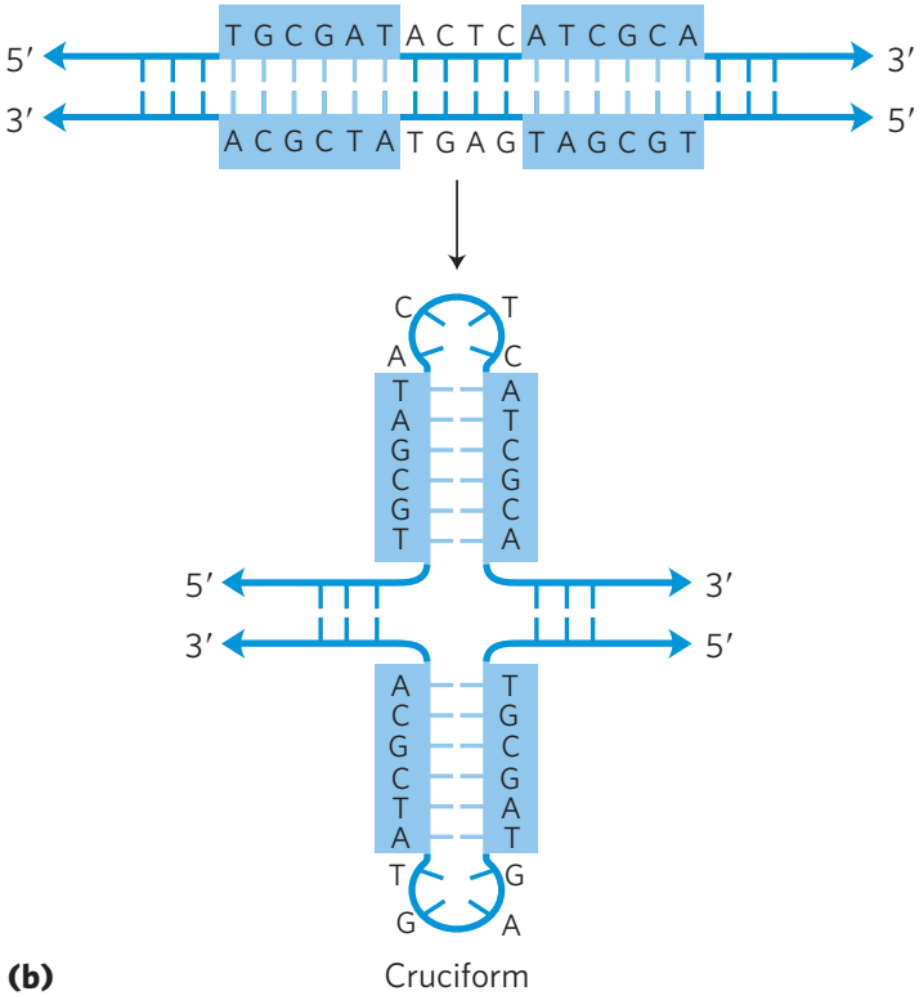
    老人行即到，到即行人老。

    離別惜殘枝，枝殘惜別離。
  - ROTATOR、NURSE RUN。
- DNA迴文序列

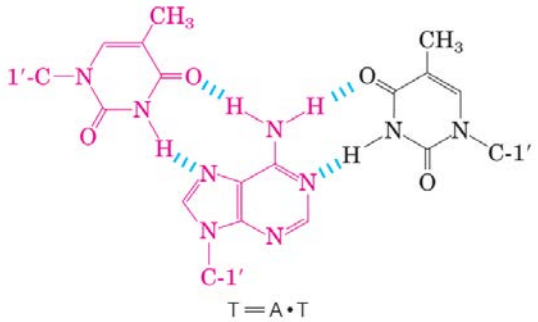


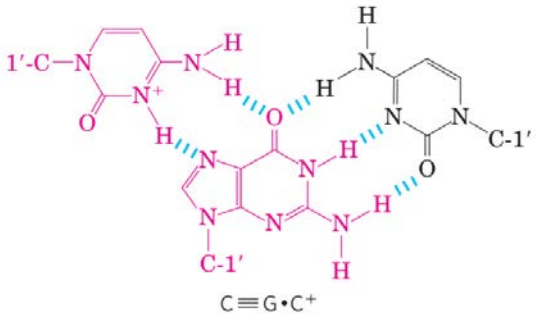
- DNA的迴文序列可以產生(a)「髮夾」與(b)「十字形」結構。



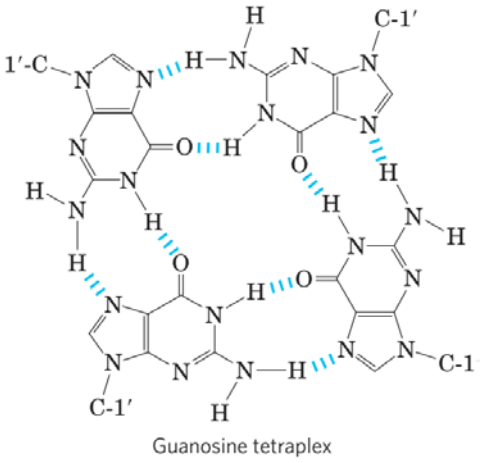


DNA的三股與四股結構

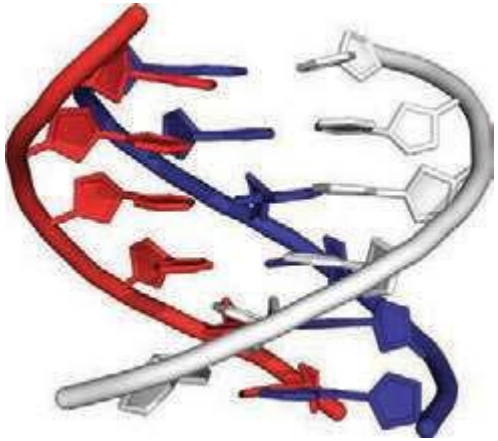


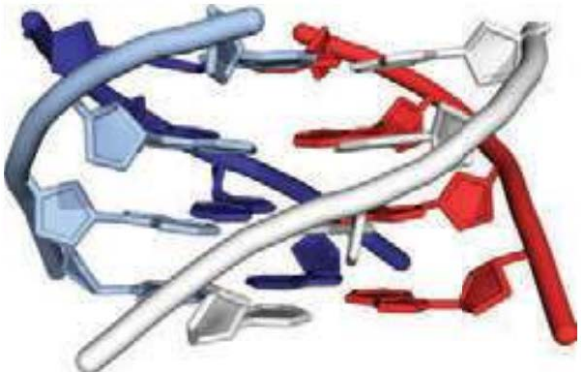


兩股多嘧啶+一股多嘌呤



四股多嘌呤



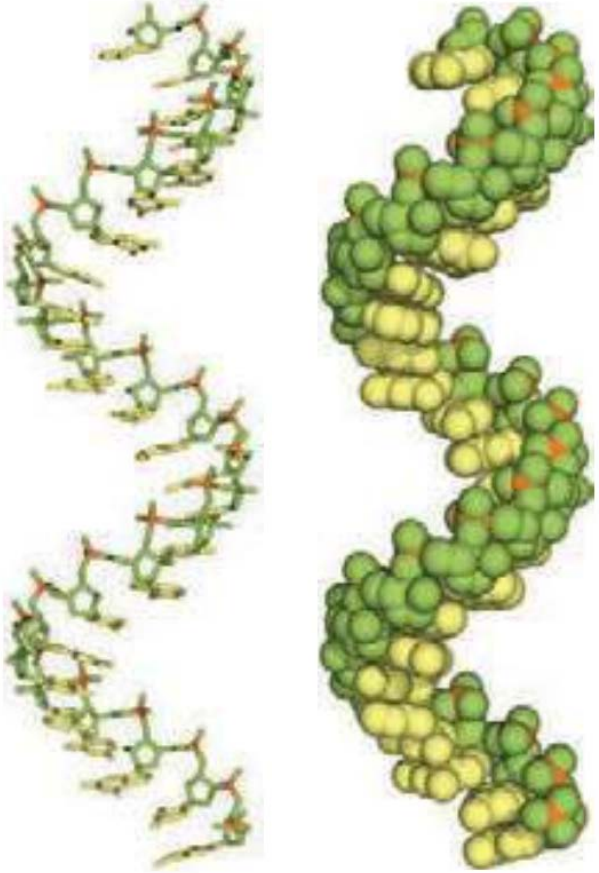


- DNA的迴文、多嘧啶或多嘌呤序列所形成的特殊結構與某些真核生物的基因調節有關。

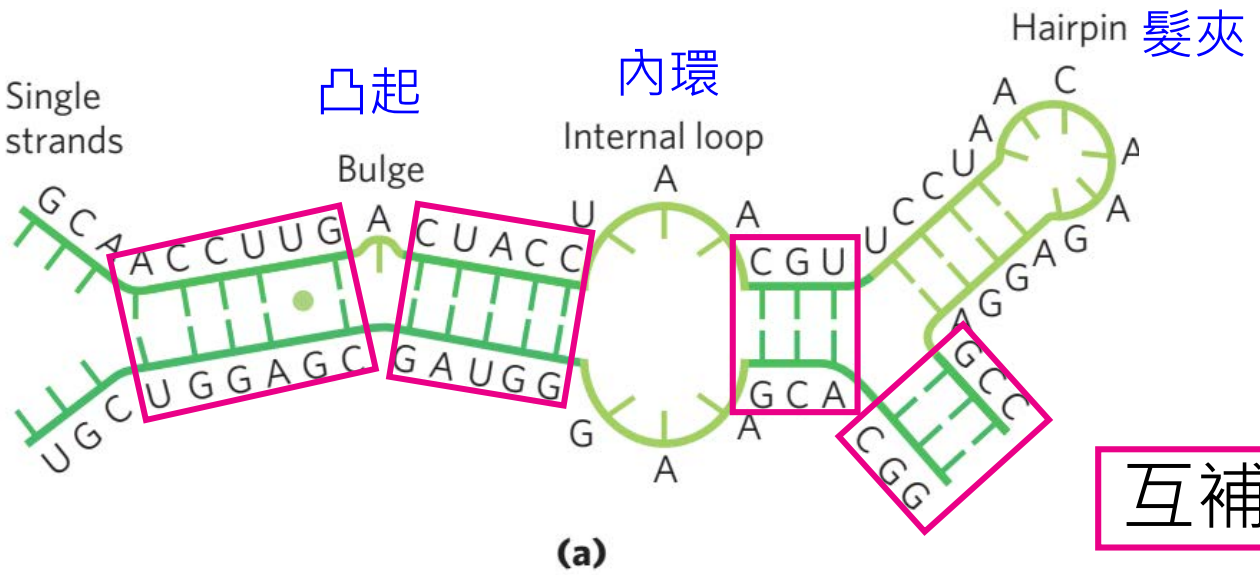
RNA的結構

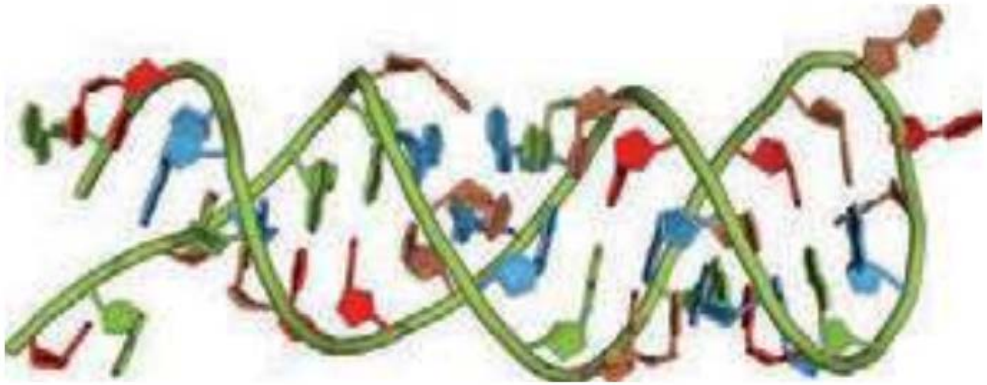
以信使RNA為例

右旋單股結構



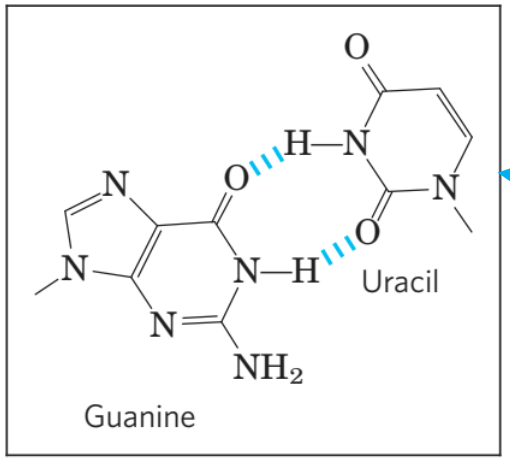
信使RNA的二級結構

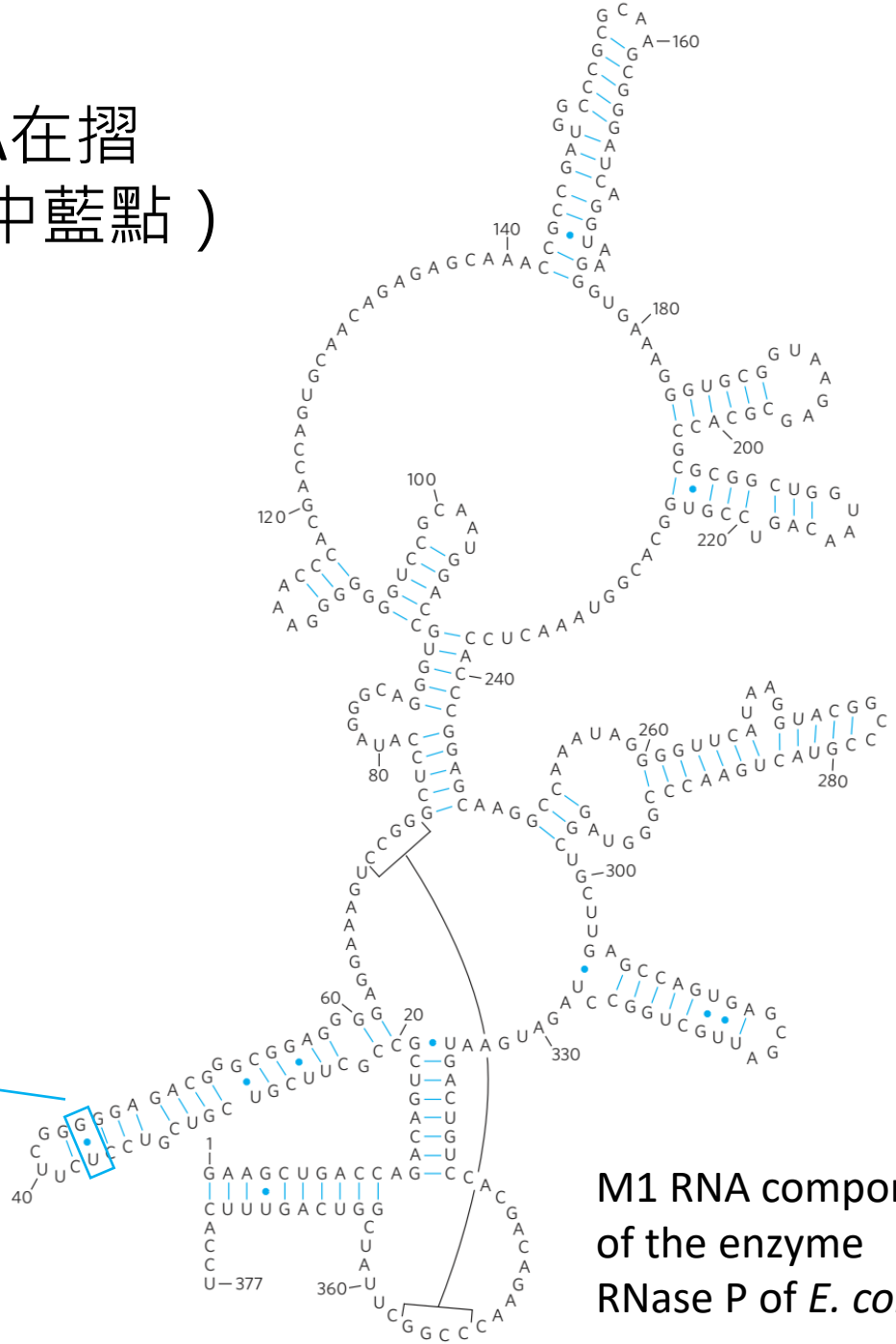

Single strands
凸起
Bulge
內環
Internal loop
Hairpin 髮夾
互補序列
(a)


Hairpin double helix
(b)
An A-form helix

儘管未完全互補，如果RNA在摺疊與黏合中遇到GU（如圖中藍點）也可以利用氫鍵結合配對。

RNA摺疊結構預測：
RNAfold web server,
ViennaRNA web services…





M1 RNA component of the enzyme RNase P of *E. coli*.

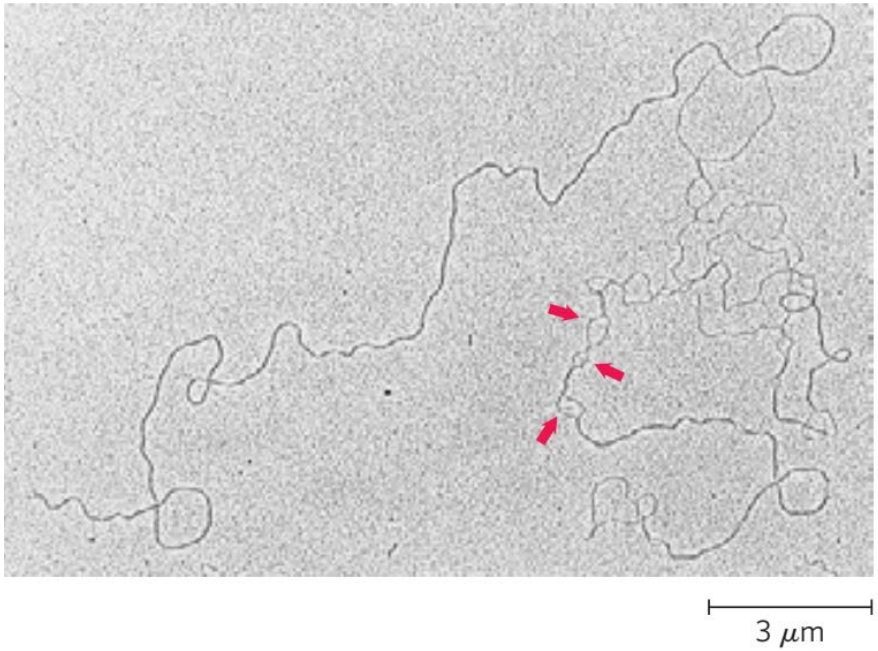
核酸結構的化學變化

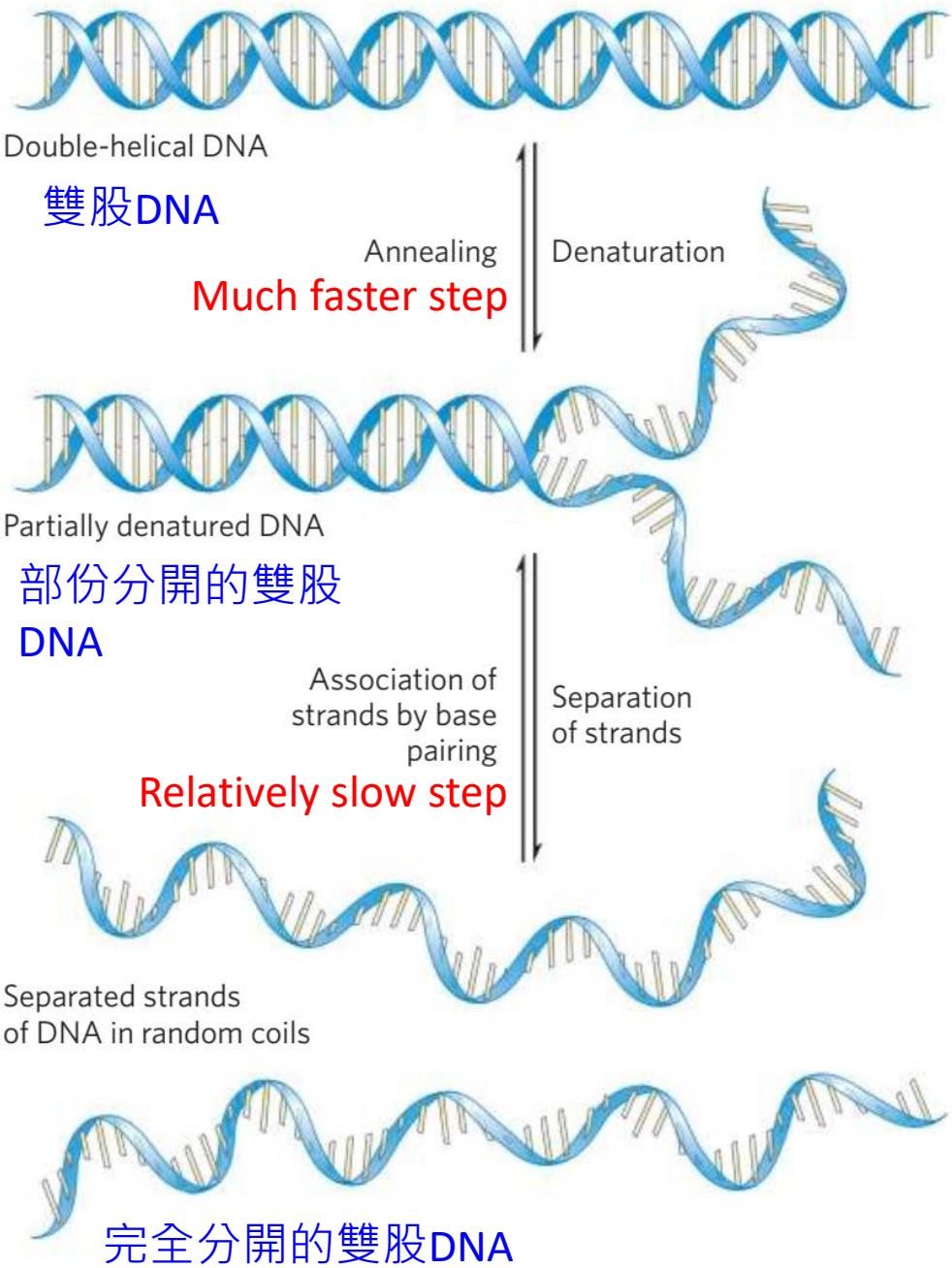
- 核酸（主要為DNA）為生物中遺傳物質儲存形式，因此結構需要保持穩定。
- 一般說來核酸會受到下列因子影響造成可逆或者不可逆的變化：
  - 溫度：變性與復性（黏合）
  - 紫外(UV)光：雙嘧啶鍵結
  - 非酵素性化學反應：去胺基、去嘌呤、烷化

雙股螺旋核酸的變性

- 加熱會造成雙股螺旋間的氫鍵斷裂。
- 在低溫下完全分開的雙股螺旋會先進行序列互補配對，再進行黏合。

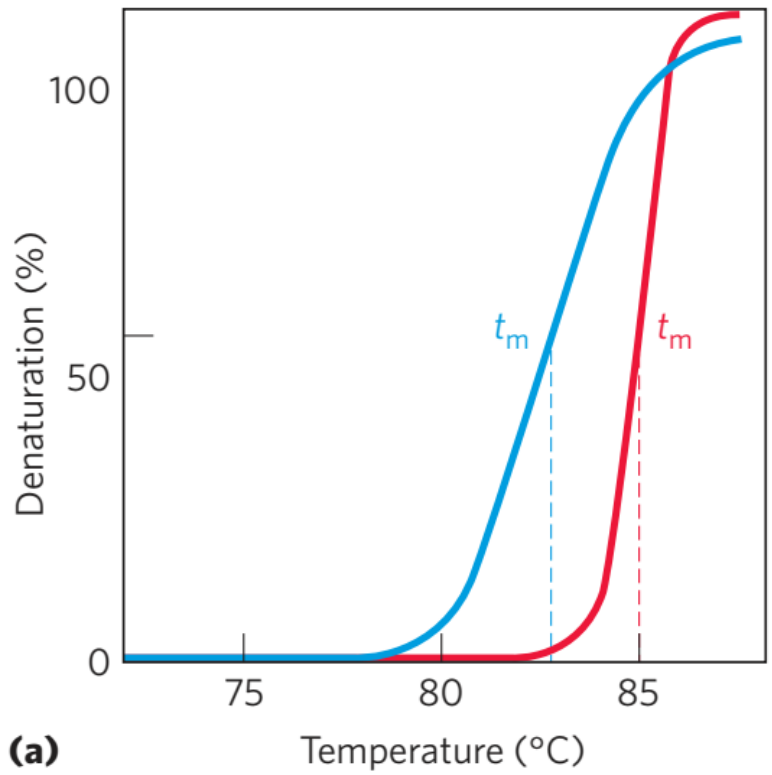
Partially denatured DNA



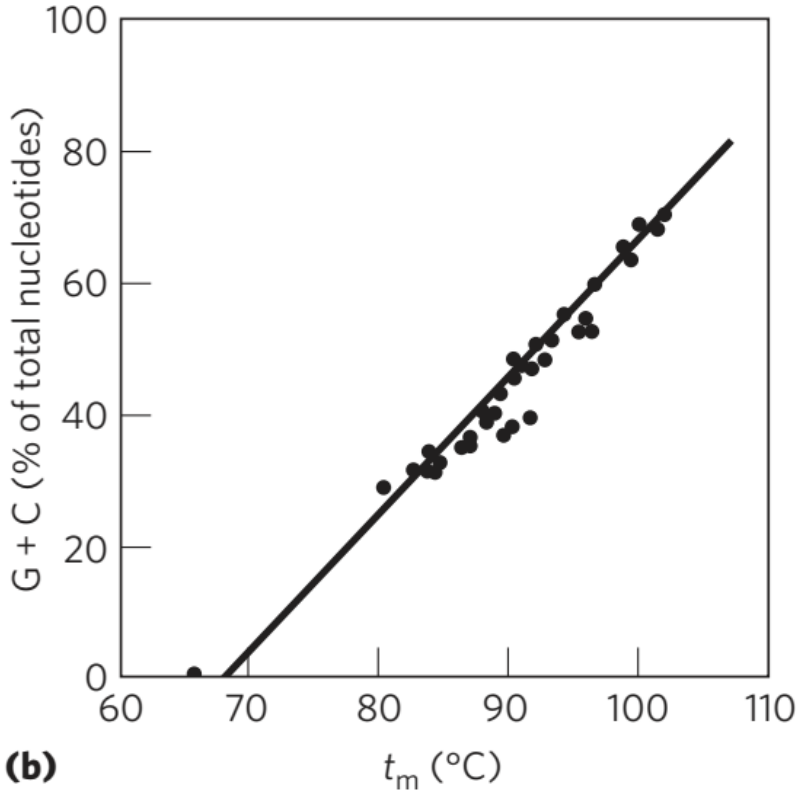


- 核酸分子的變性溫度（熔點）與鹼基配對種類含量（GC含量）、pH值、離子強度有關。

兩個DNA分子的變性溫度曲線

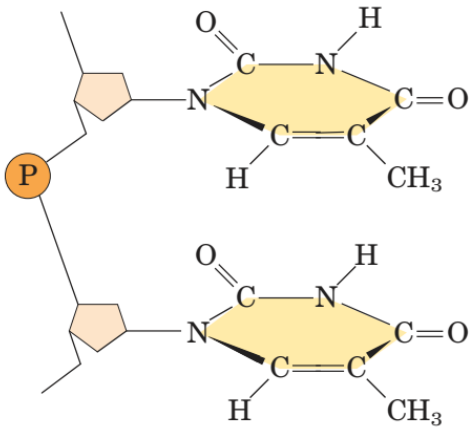


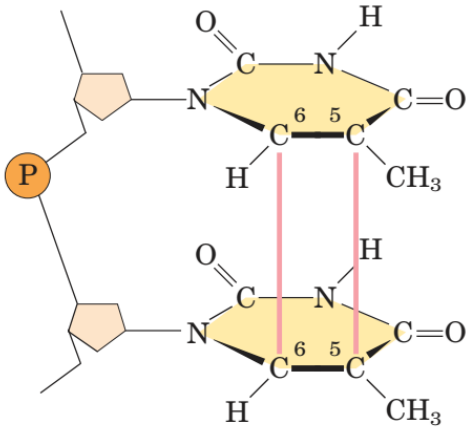
DNA中GC含量與t_m（熔點）關係

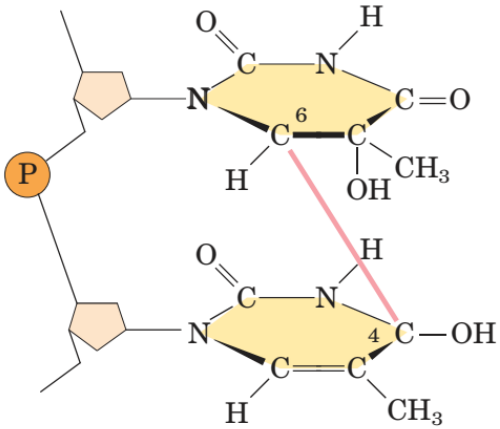


搜尋 “DNA melting temperature calculation”

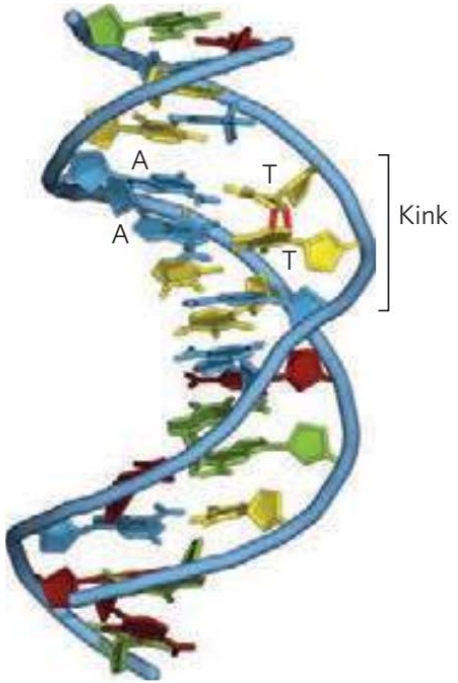
紫外光造成核酸損害





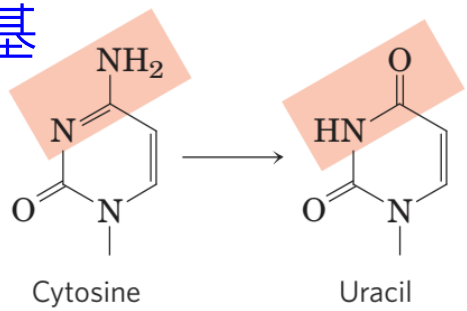


- 如果未修補，可能造成鹼基突變。

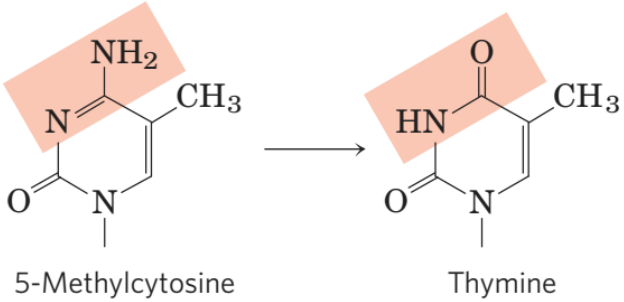


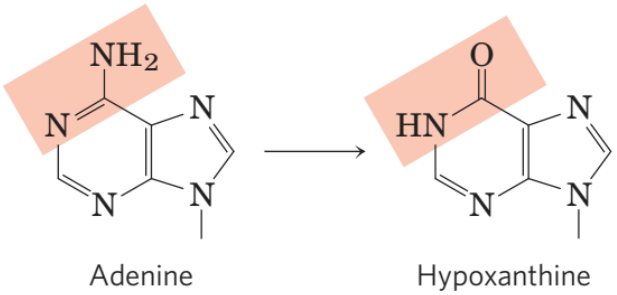
非酵素性化學反應

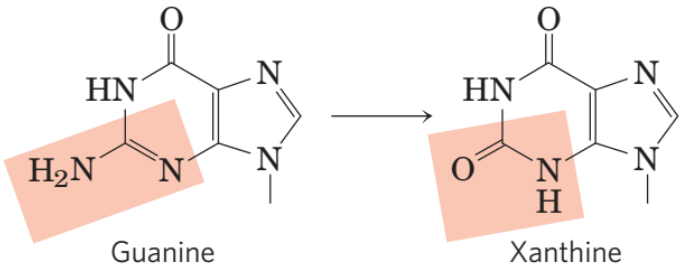
去胺基



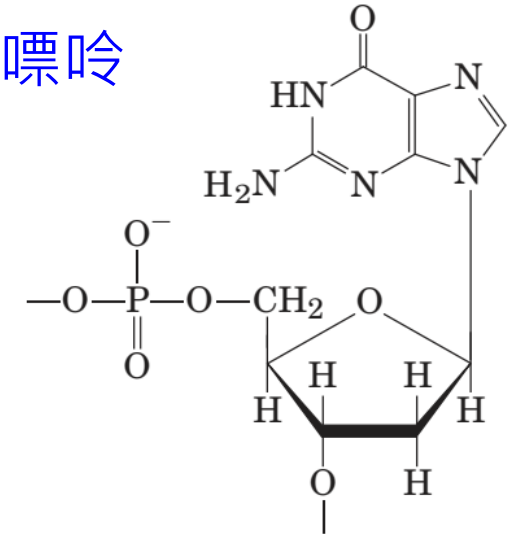
C→U



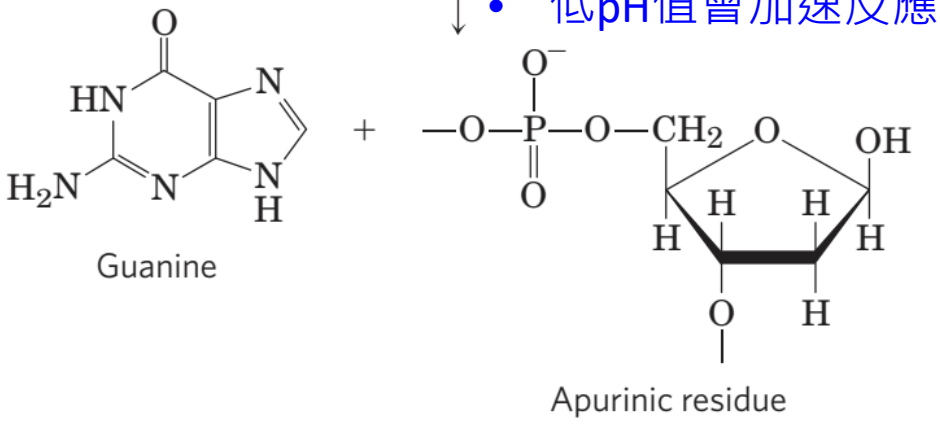




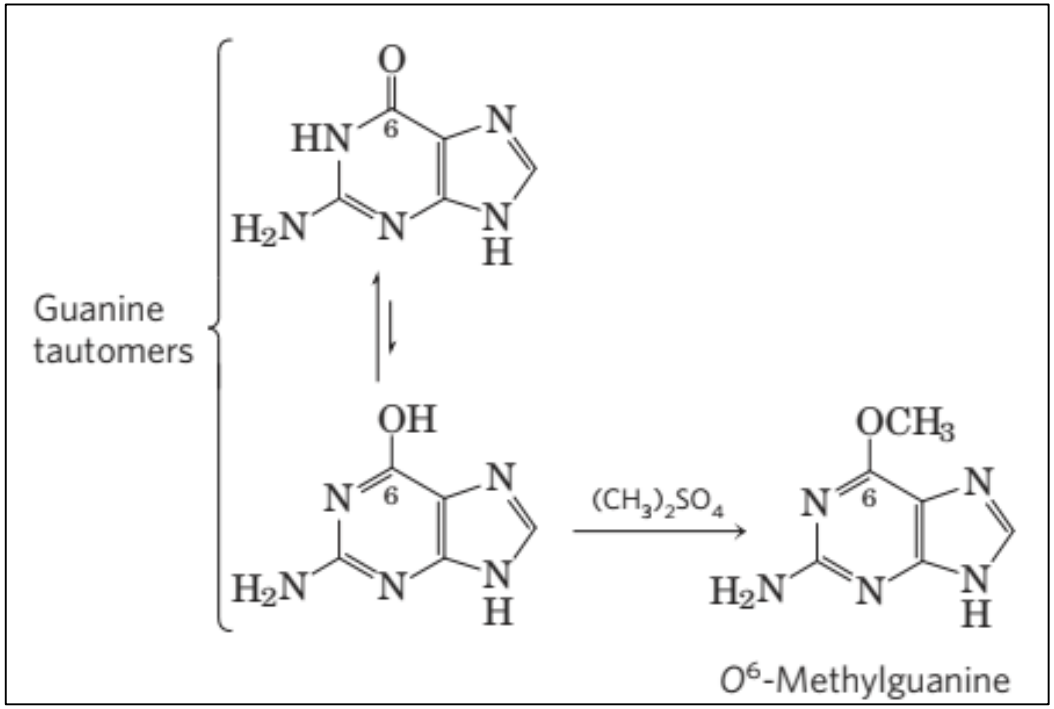
去嘌呤



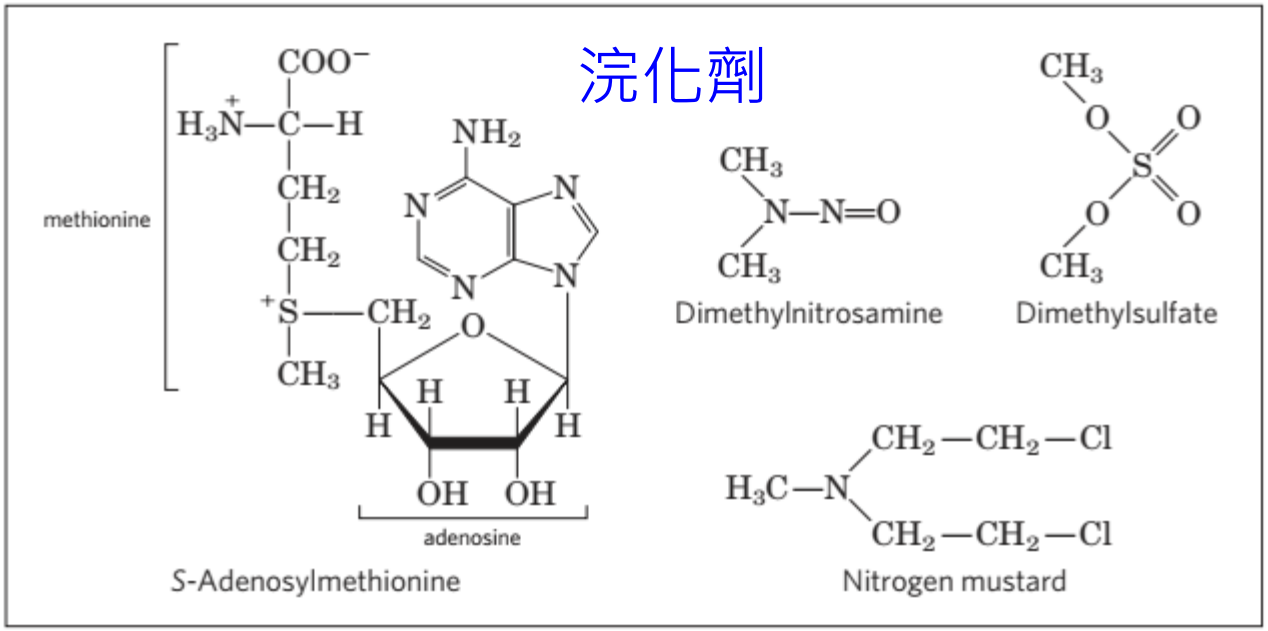
- 自發
- 低pH值會加速反應



浣化反應


Guanine tautomers
O
HN
6
N
H_2N
N
N
H
OH
N
6
N
H_2N
N
N
H
$(CH_3)_2SO_4$
OCH_3
N
6
N
H_2N
N
N
H
O^6-Methylguanine

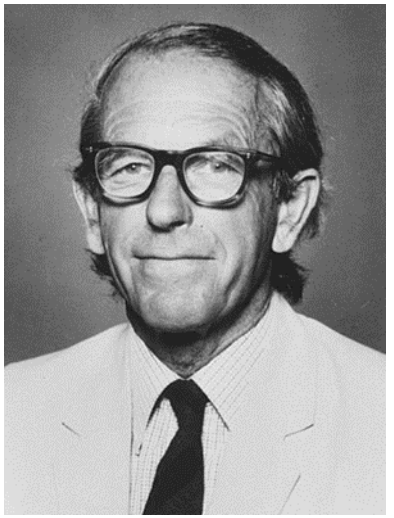
浣化劑


methionine
COO^-
$H_3\overset{+}{N}$—C—H
CH_2
CH_2
^+S—CH_2
CH_3
NH_2
N
N
N
N
O
H
H
H
H
OH
OH
adenosine
S-Adenosylmethionine
CH_3
N—N=O
CH_3
Dimethylnitrosamine
CH_3
O
O
S
O
O
CH_3
Dimethylsulfate
CH_2—CH_2—Cl
H_3C—N
CH_2—CH_2—Cl
Nitrogen mustard

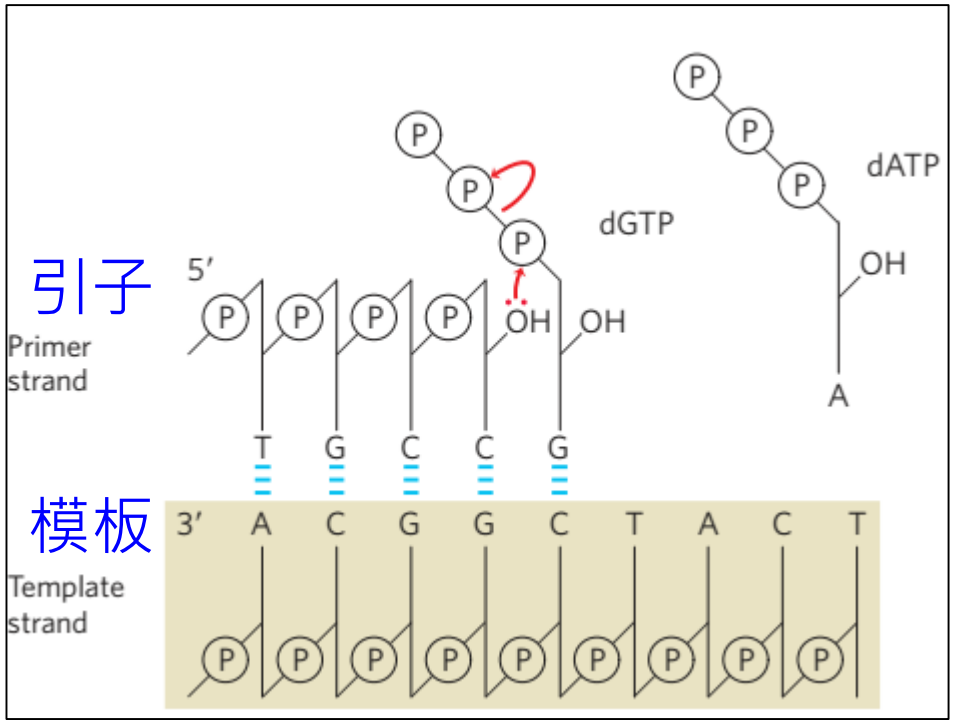
DNA互補配對的技術應用：DNA定序

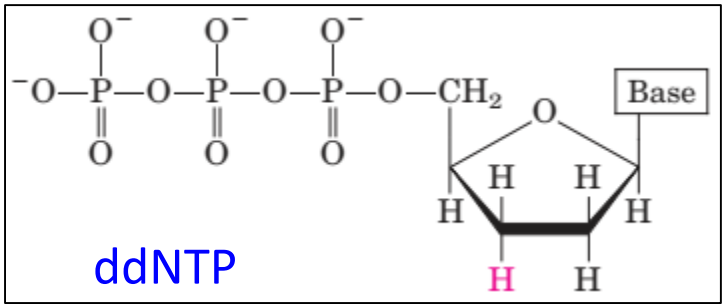
1. Sanger定序法(1977)

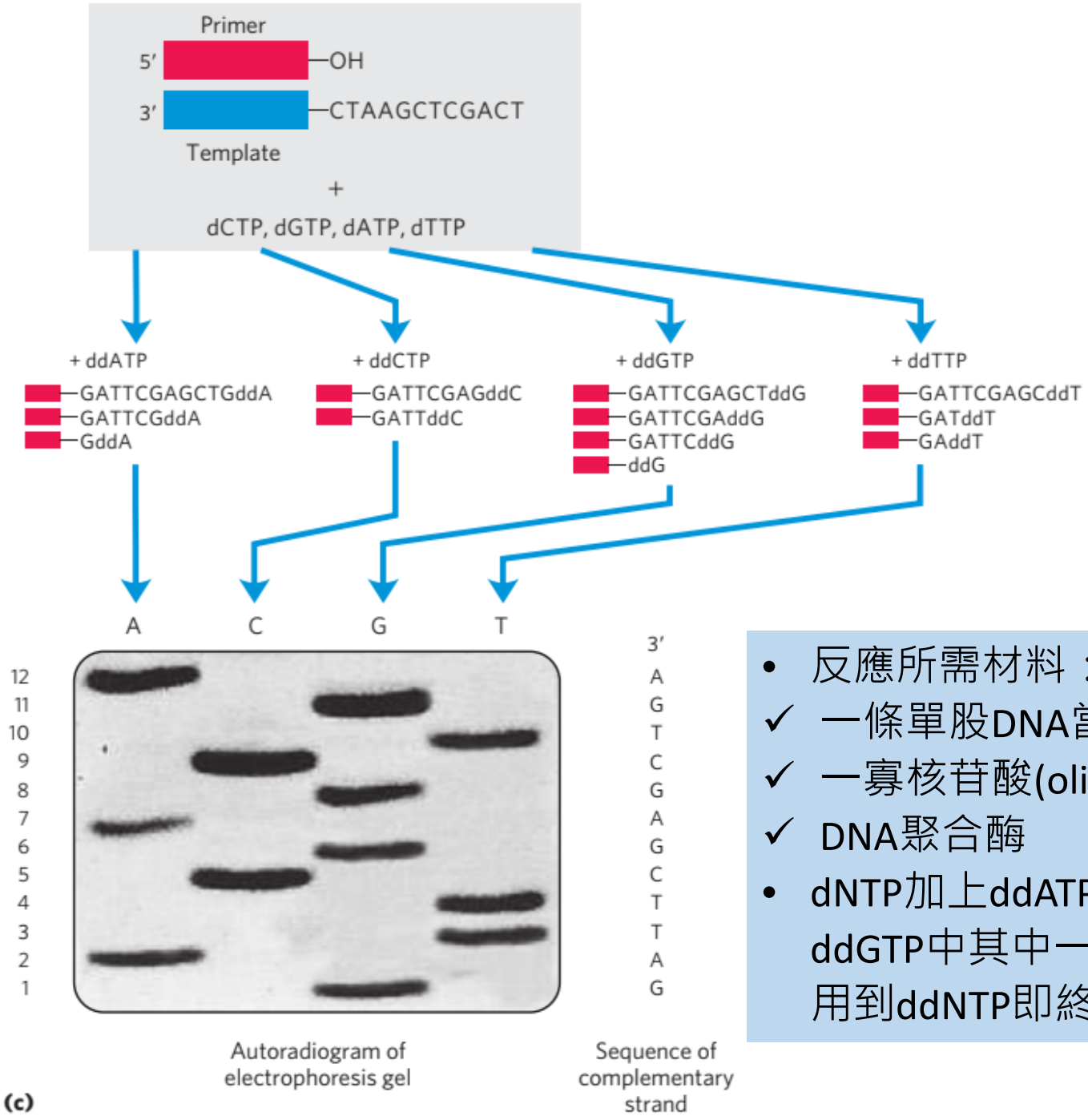
- 又稱鏈中止法。
- 使用雙去氧核苷酸(ddNTP)讓DNA的合成停在特定的位置。



Frederick Sanger

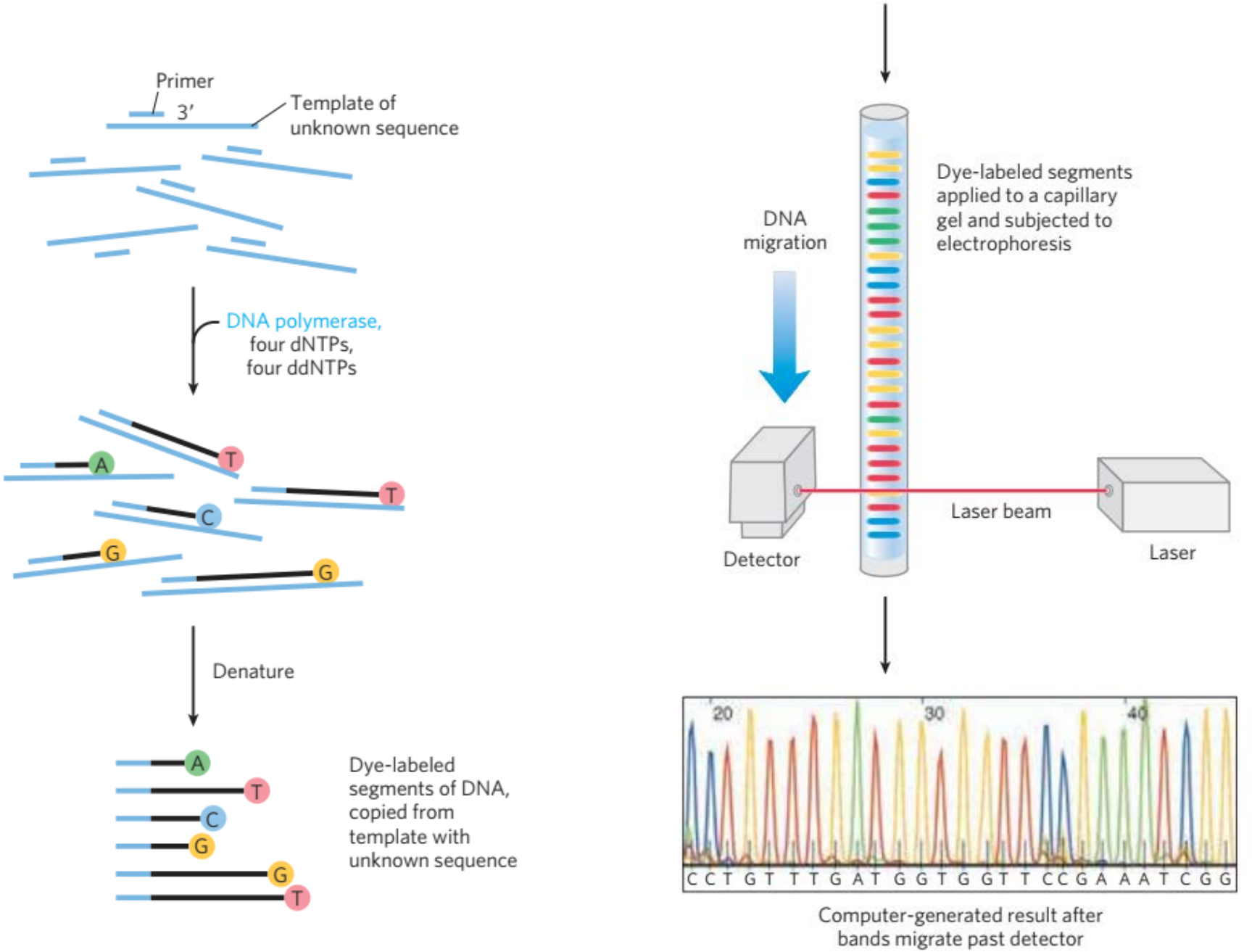






- 反應所需材料：
- ✓ 一條單股DNA當作模板
- ✓ 一寡核苷酸(oligonucleotide)當作引子
- ✓ DNA聚合酶
- dNTP加上ddATP、ddTTP、ddCTP、ddGTP中其中一個，當DNA合成酶使用到ddNTP即終止合成反應。

2. 自動DNA定序法（Sanger定序法的變形）



脂質

- 為一類化學結構變化多樣的天然化合物，其共通的特性為不溶於水。
- 生物產生出的脂質可分為八類：
  - 脂肪醯、甘油脂、（甘油）磷脂、神經鞘脂、醣脂、聚酮、固醇脂、烯醇脂。
- 脂質在生物體的主要功能為儲存能量、細胞膜系的組成、訊息分子、輔因子、色素等。

https://en.wikipedia.org/wiki/Lipid

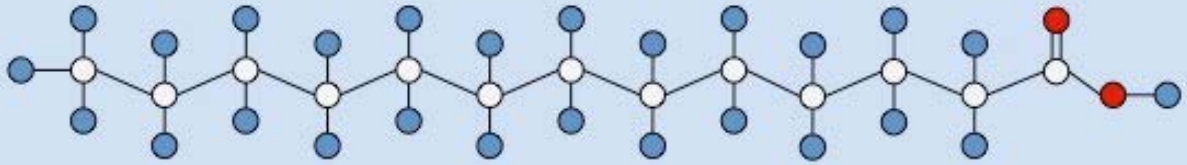
脂肪酸：儲存能量

- 脂肪酸(fatty acid)為具有4-36碳長碳氫鏈之羧酸。
- 生物體內僅有微量的游離脂肪酸。
- 脂肪酸可以依照所含碳鏈長短與雙鍵的數目及位質來作分類。

飽和、不飽和（反式、順式）脂肪酸之結構

飽和脂肪酸
Saturated fatty acid

(***no*** double bonds)

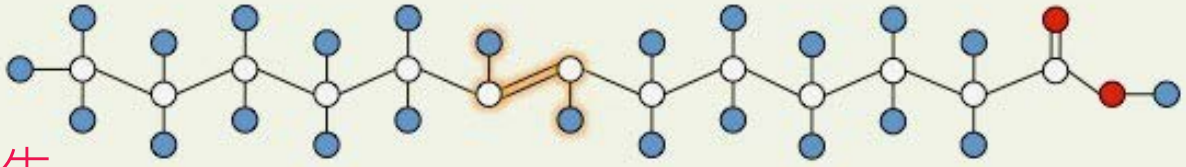


不飽和脂肪酸 反式

Unsaturated – ***trans***

(H atoms opposite)

大部分為食品加工後產生



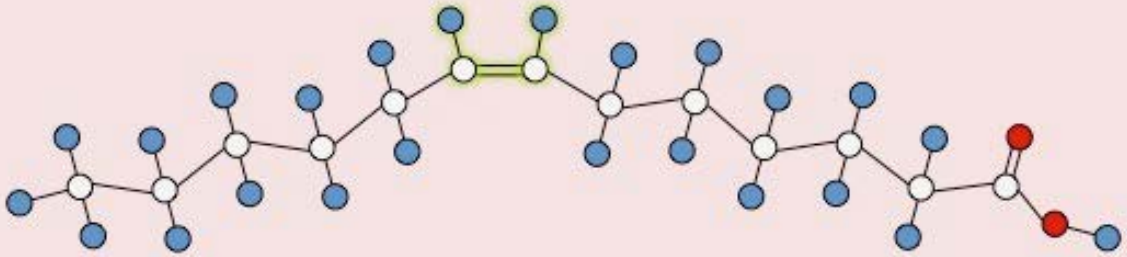
不飽和脂肪酸 順式

Unsaturated – ***cis***

(H atoms same side)

⟹ *bent configuration*

自然中主要存在



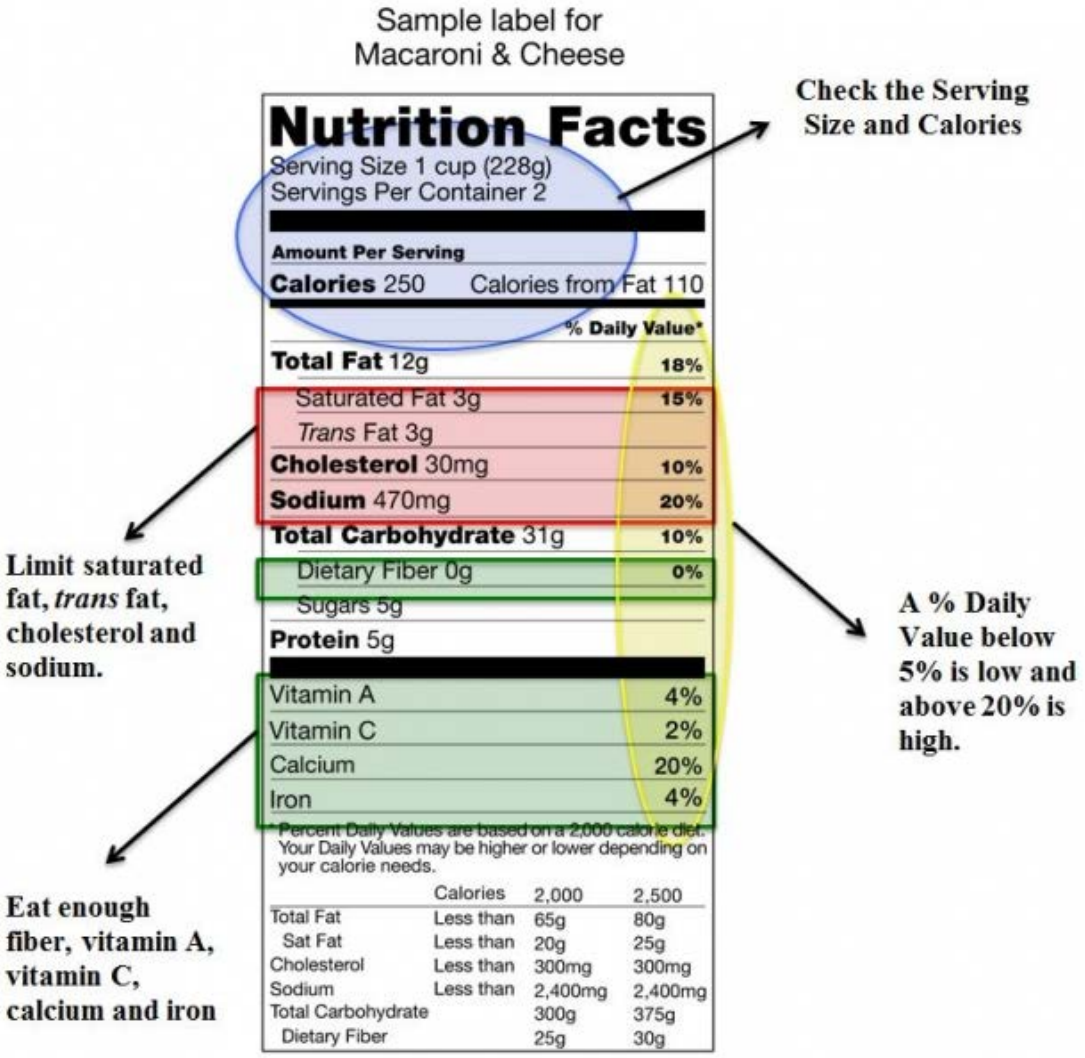
○ = C ● = O ● = H

https://ib.bioninja.com.au/standard-level/topic-2-molecular-biology/23-carbohydrates-and-lipids/types-of-fatty-acids.html

營養標示		
每一份量310毫升 本包裝含3份		
	每份	每100毫升
熱量	138大卡	44.6大卡
蛋白質	9.9公克	3.2公克
脂肪	4.3公克	1.4公克
飽和脂肪	3.1公克	1.0公克
反式脂肪	0公克	0公克
碳水化合物	14.9公克	4.8公克
糖	14.9公克	4.8公克
鈉	130毫克	42毫克
鈣	341毫克	110毫克

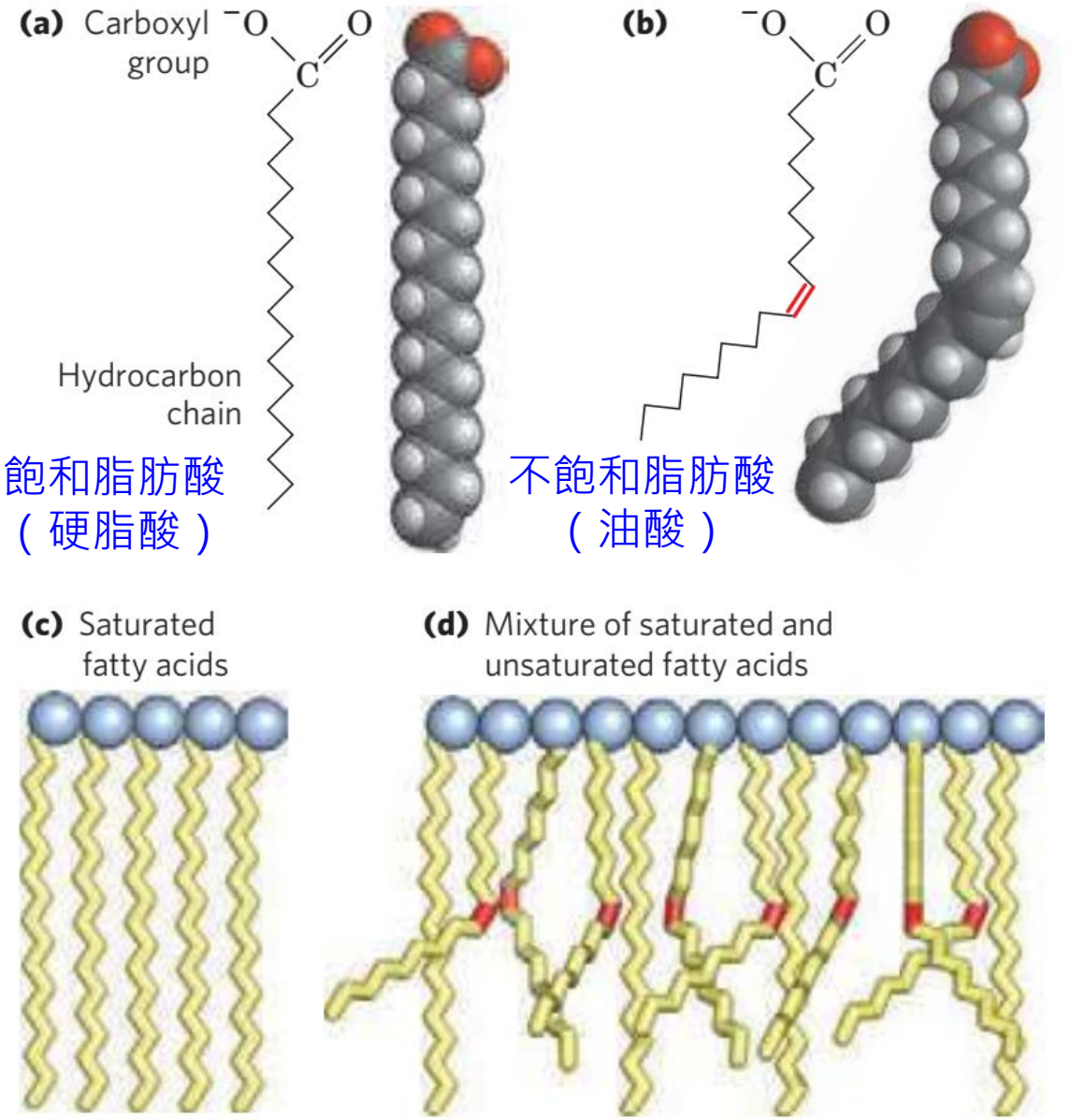
https://www.thenewslens.com/article/86586

脂肪中飽和脂肪酸、
反式不飽和脂肪酸、
順式不飽和脂肪酸所占比例？



https://zfcphp.arizona.edu/your-health/basics/reading-nutrition-facts-labels

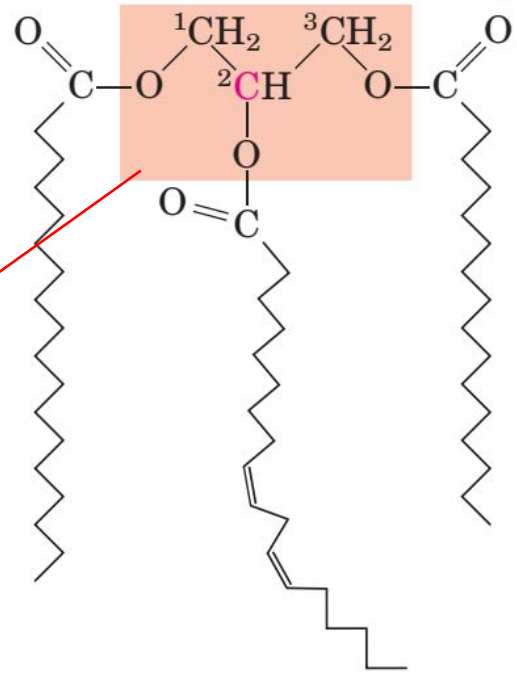
脂肪酸碳鏈長度與雙鍵數目決定其物理特性



- 羧基具有微極性，其他部份為非極性。
- 越長的碳鏈與越少的雙鍵數，其水溶性越差。
- 同樣碳鏈長度的脂肪酸，雙鍵數目越多，熔點越低。

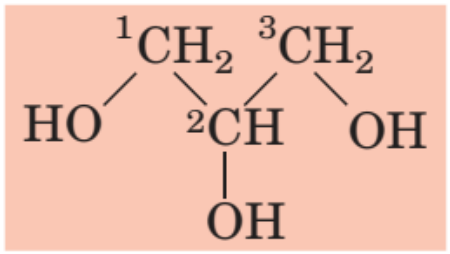
甘油脂：儲存能量

- 甘油+脂肪酸連結而成的酯類。
- 甘油脂為中性脂的一種，為動植物體儲存脂質的主要形式，也是自然界中含量最多的脂質。
- 甘油脂在室溫下為固態者俗稱為脂肪(fat)，為液態者俗稱為油(oil)。



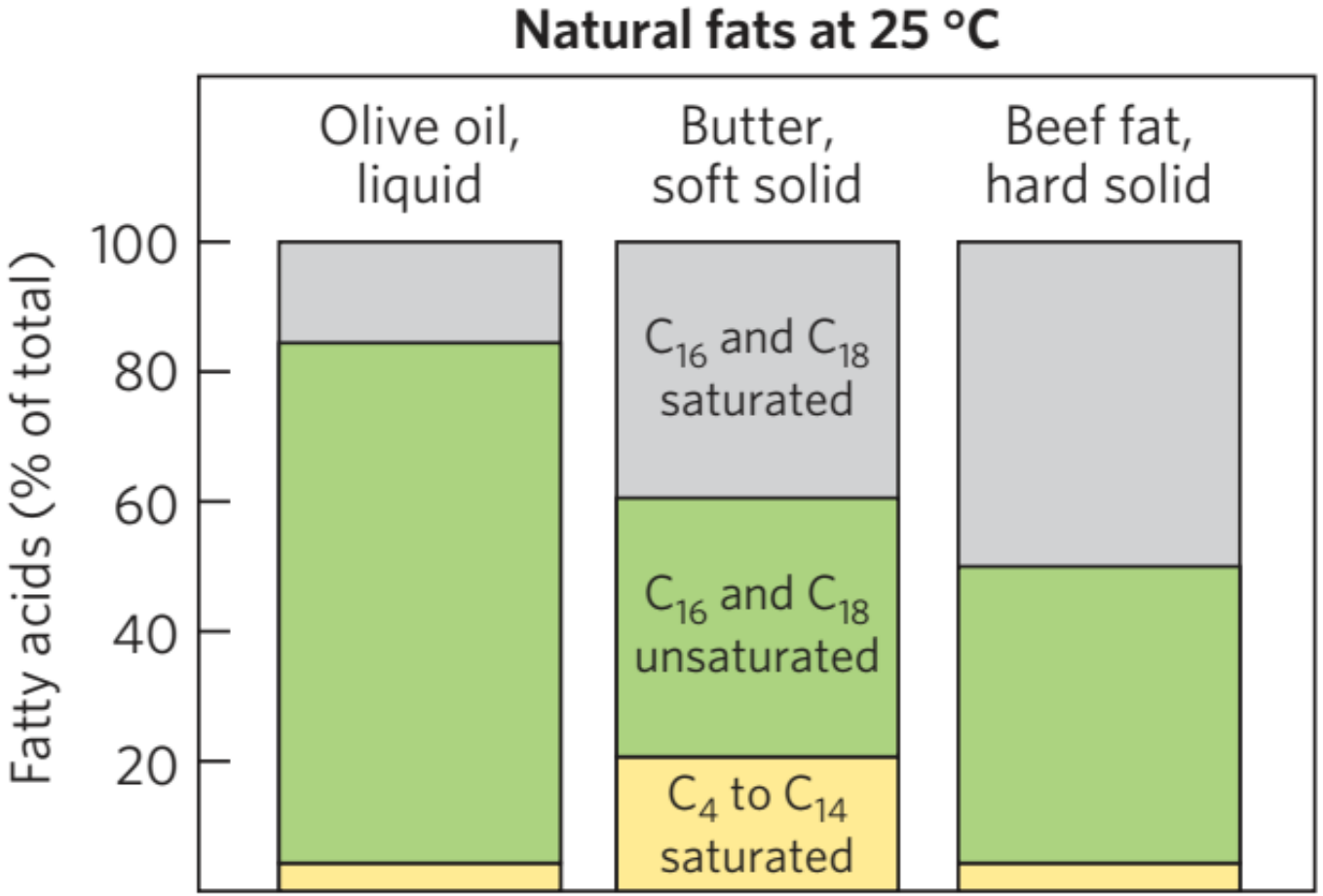
1-Stearoyl, 2-linoleoyl, 3-palmitoyl glycerol, a mixed triacylglycerol

甘油脂（混合脂）



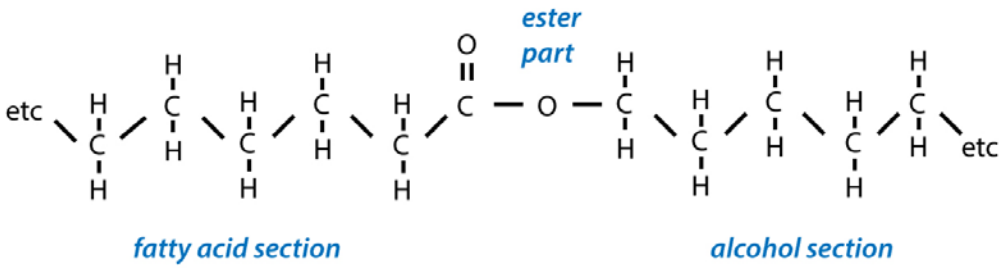
Glycerol

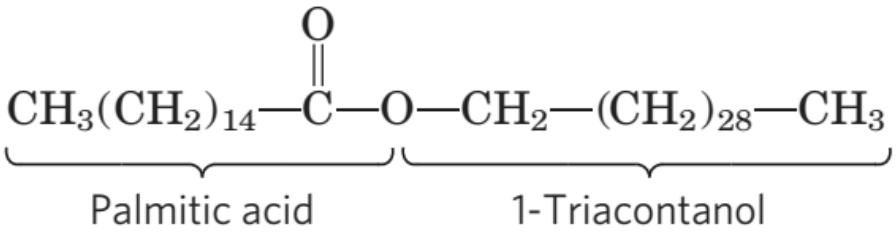
甘油


Natural fats at 25 °C
Olive oil, liquid
Butter, soft solid
Beef fat, hard solid
Fatty acids (% of total)
100
80
60
40
20
C_{16} and C_{18} saturated
C_{16} and C_{18} unsaturated
C_4 to C_{14} saturated

蠟：儲存能量與防水劑

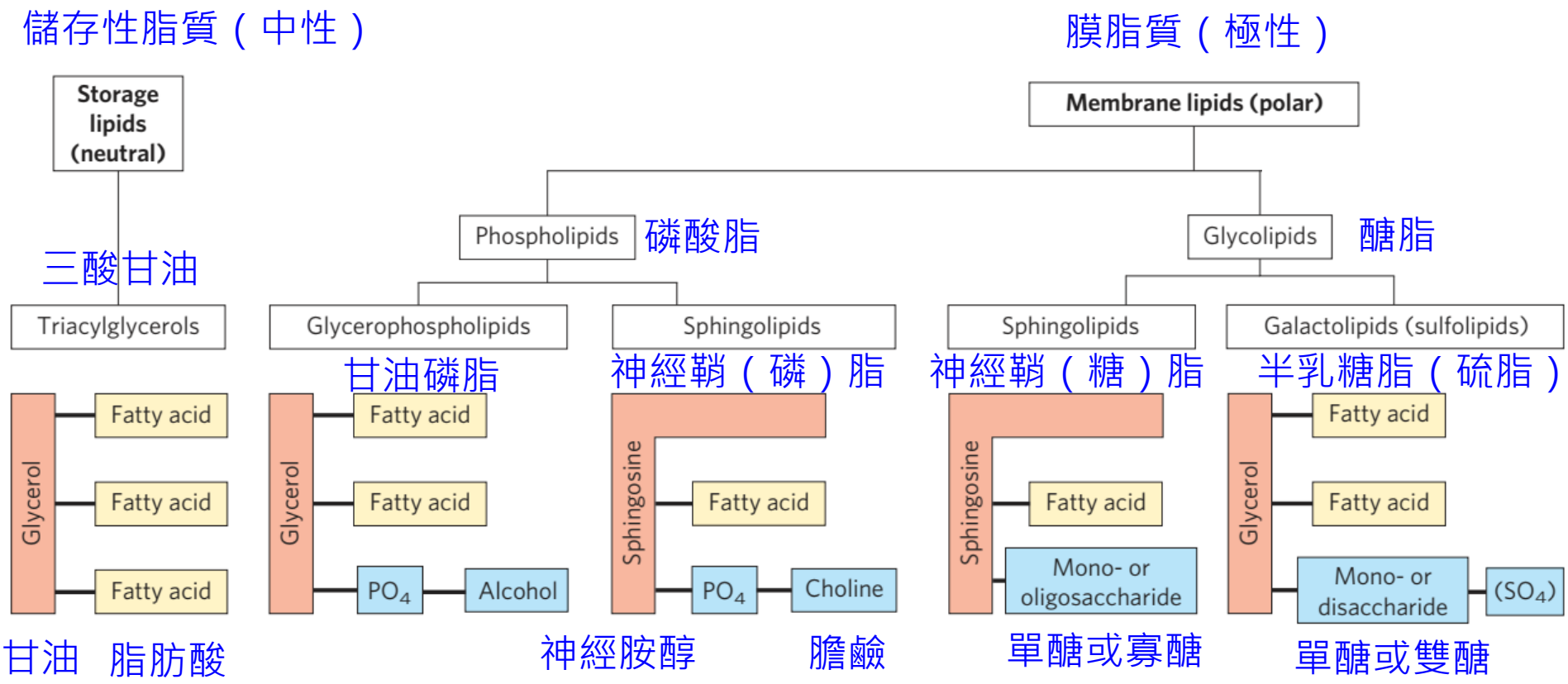
- 由脂肪酸(C_{14}-C_{36})與長鏈醇(C_{16}-C_{30})連結而成的酯類。
- 為中性脂的一種，熔點比甘油酸高（60-100°C）。
- 可在植物表皮外層、蜂巢、水鳥潤羽腺分泌物等地方發現蠟。





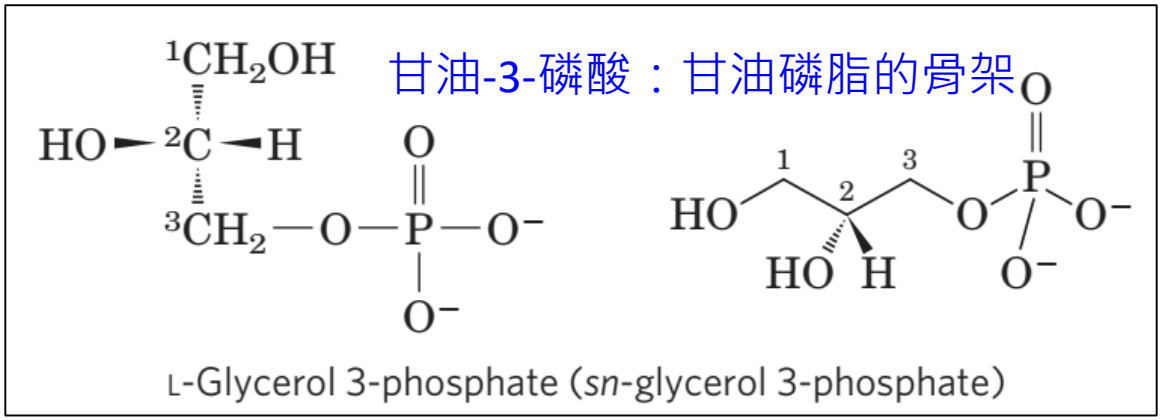
蜂蠟：棕櫚酸+三十烷醇

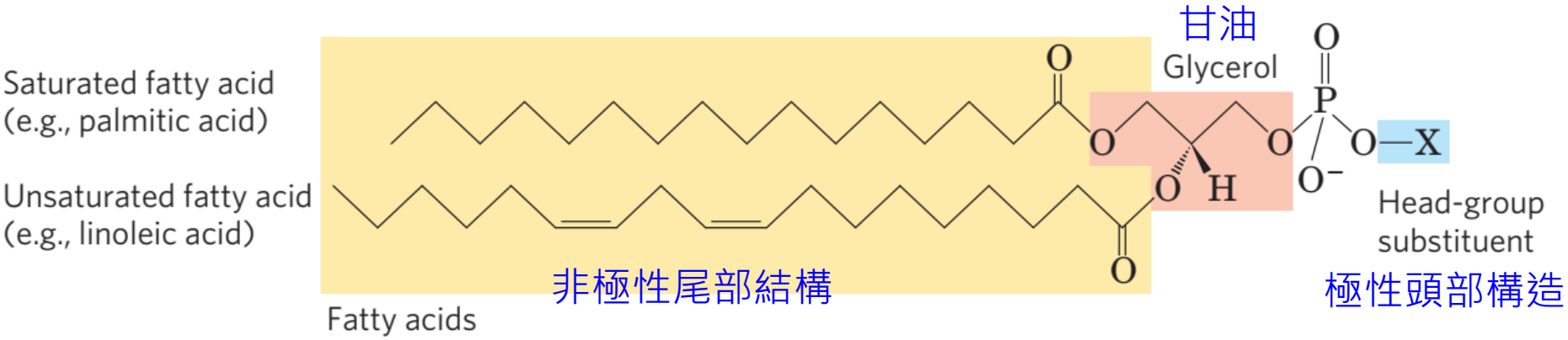
常見的儲存性脂質與膜脂質



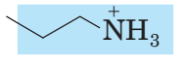
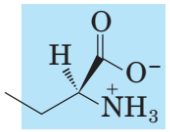
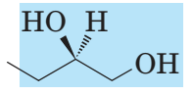
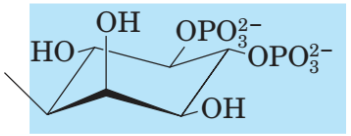
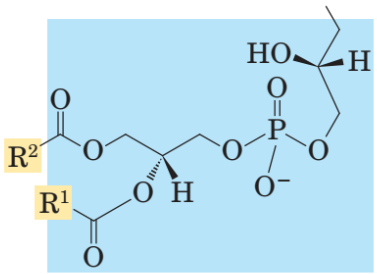
甘油磷脂：細胞膜系的主要脂質

- 甘油磷脂為兩性脂質或雙性脂質。
  - 甘油磷脂分子具有碳氫鏈組成的非極性尾部結構及連接於磷酸基的極性頭部構造。
  - 此雙性特徵是甘油磷脂形成脂雙層結構的分子基礎。

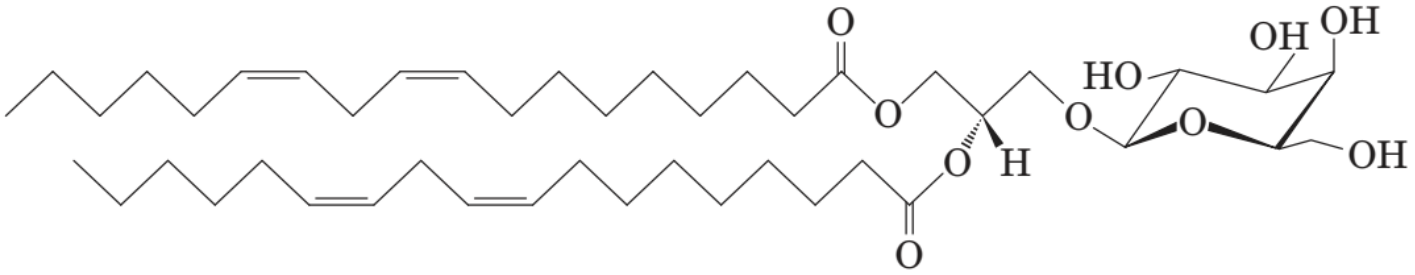




各類甘油磷脂

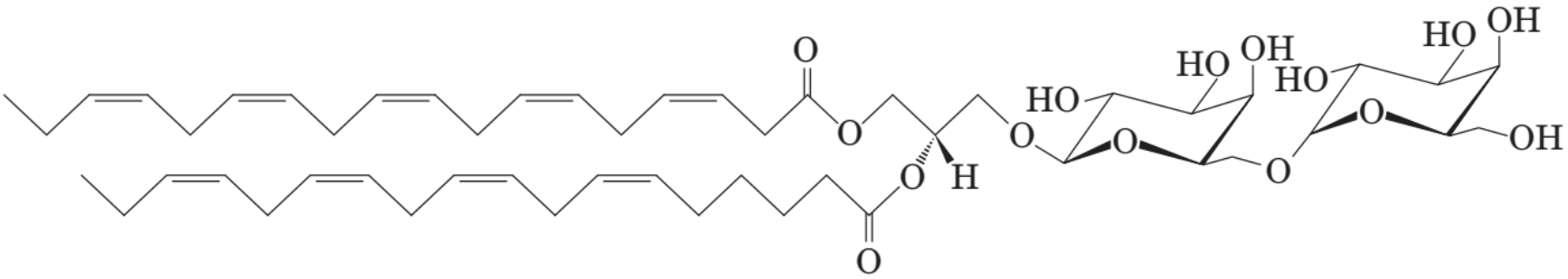
Name of glycerophospholipid	Name of X—O	Formula of X	Net charge (at pH 7)
Phosphatidic acid 磷脂酸	—	—H	−2
Phosphatidylethanolamine 磷脂醯乙醇胺	Ethanolamine		0
Phosphatidylcholine 磷脂醯膽鹼	Choline		0
Phosphatidylserine 磷脂絲胺酸	Serine		−1
Phosphatidylglycerol 磷脂醯甘油	Glycerol		−1
Phosphatidylinositol 4,5-bisphosphate 磷脂酸肌醇4,5-雙磷酸 膜分子、訊息因子	*myo*-Inositol 4,5-bisphosphate		−4*
Cardiolipin 心磷脂 粒線體內膜分子	Phosphatidyl-glycerol		−2

半乳糖脂：葉綠體類囊膜主要脂質分子



Monogalactosyldiacylglycerol (MGDG)

單半乳糖雙醯甘油脂

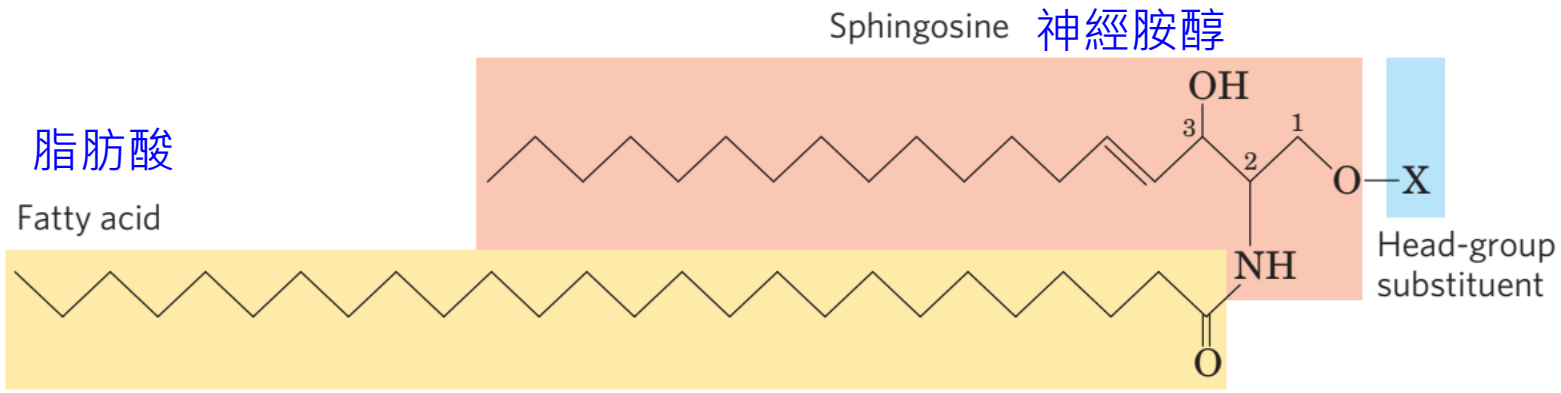


Digalactosyldiacylglycerol (DGDG)

雙半乳糖雙醯甘油脂

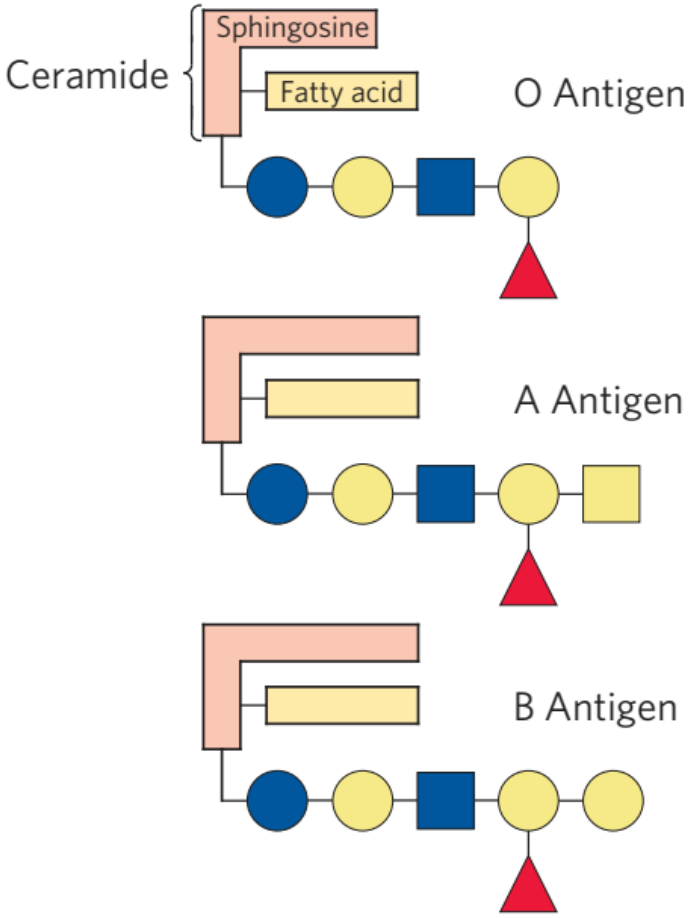
神經鞘脂：細胞膜系分子

- 神經鞘脂由神經胺醇衍生而來。
- 很多神經鞘脂廣泛出現在神經細胞膜當中，其中有一些作為細胞辨識位點。



Name of sphingolipid	Name of X—O	Formula of X
Ceramide 神經醯胺	—	—H
Sphingomyelin 神經磷脂	Phosphocholine 磷脂醯膽鹼	—P(=O)(O⁻)—O—CH₂—CH₂—N⁺(CH₃)₃

神經鞘糖脂作為血型系統辨認分子

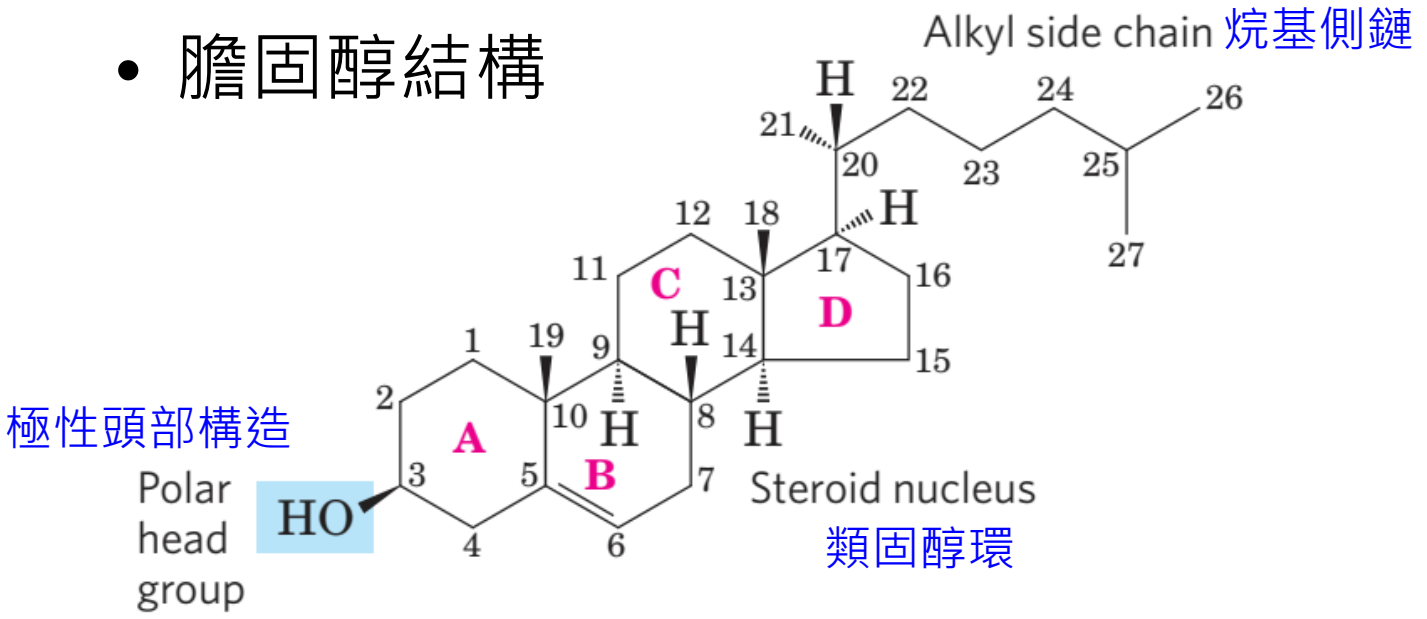


	A 組	B 組	AB 組	O 組
紅血球細胞型態	A	B	AB	O
抗體存在	B 抗體	A 抗體	無	A 與 B 抗體
抗原存在	A 抗原	B 抗原	A 與 B 抗原	無

https://zh.wikipedia.org/wiki/%E8%A1%80%E5%9E%8B

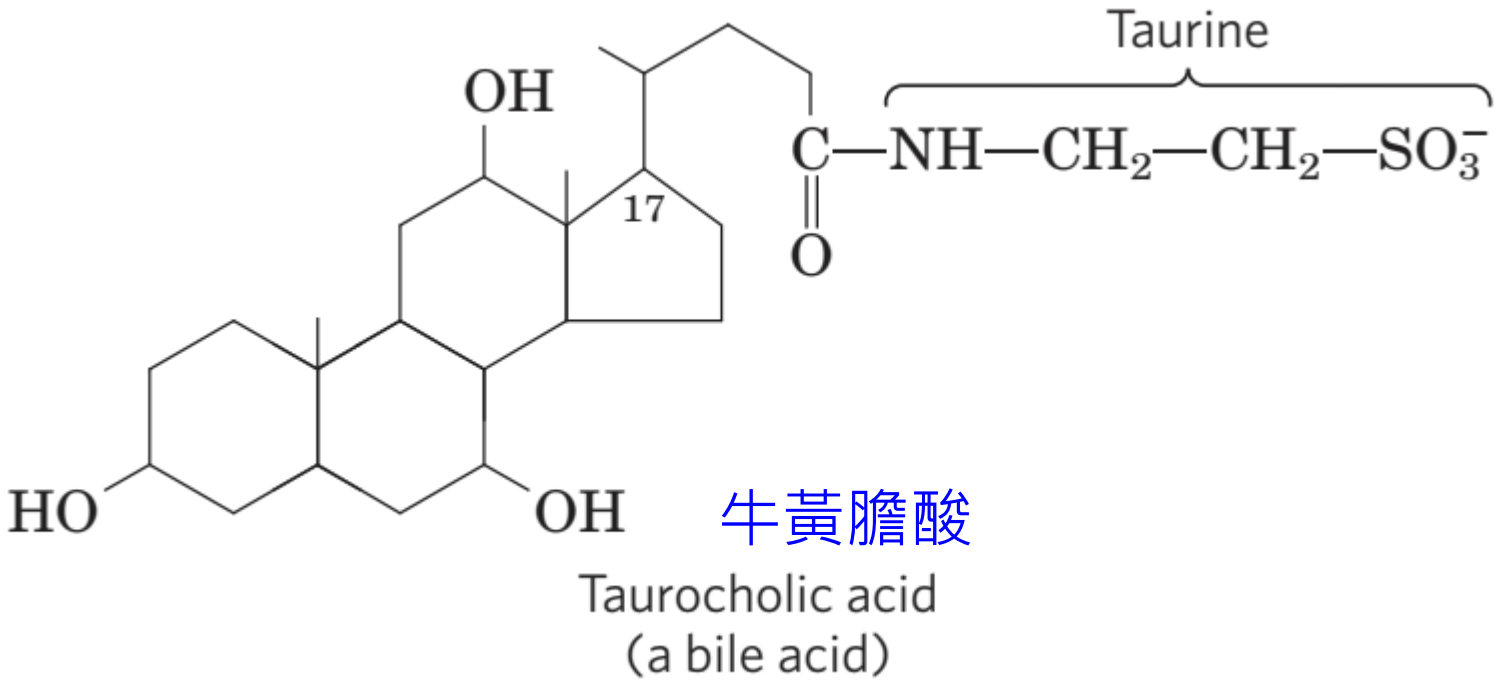
固醇：細胞膜系分子

- 不含有脂肪酸的脂類。
- 動物的主要固醇為膽固醇。
  - 在細胞膜中可以調節細胞膜的流動性。
  - 人血中的膽固醇濃度與動脈硬化等心血管疾病有關。
- 植物則有豆固醇等植物固醇類。
  - 膽固醇結構



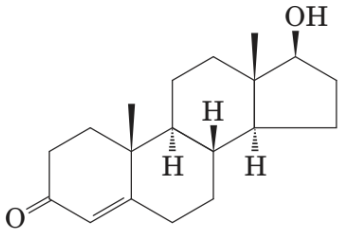
- 膽固醇的代謝產物或衍生物具有重要的生理功能。

例如：膽汁中的膽酸即是由膽固醇代謝而來，具有脂肪乳化與促進吸收等功能。



類固醇：賀爾蒙分子

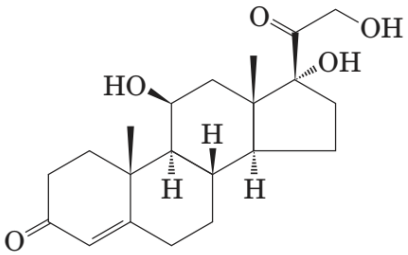
- 類固醇為固醇的氧化衍生物。



Testosterone

睪固酮

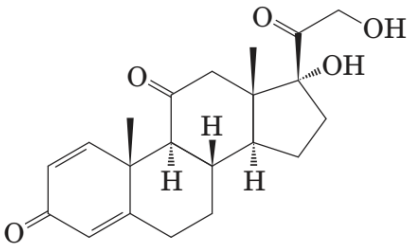
雄性賀爾蒙



Cortisol

皮質醇

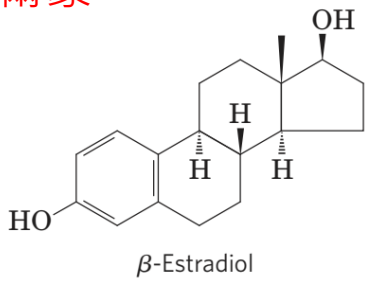
腎上腺皮質



Prednisone

強的松

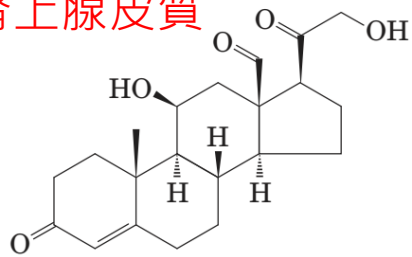
合成、抗發炎



β-Estradiol

雌二醇

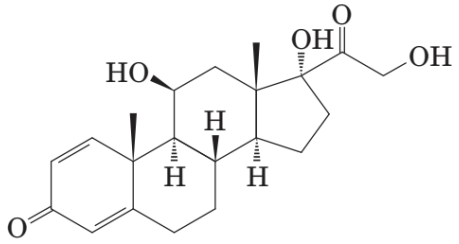
雌性賀爾蒙



Aldosterone

醛固酮

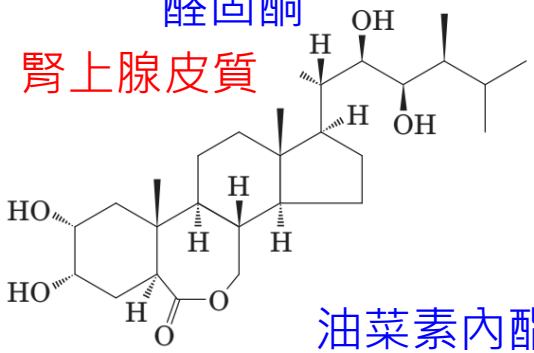
腎上腺皮質



Prednisolone

腎上腺皮質酮

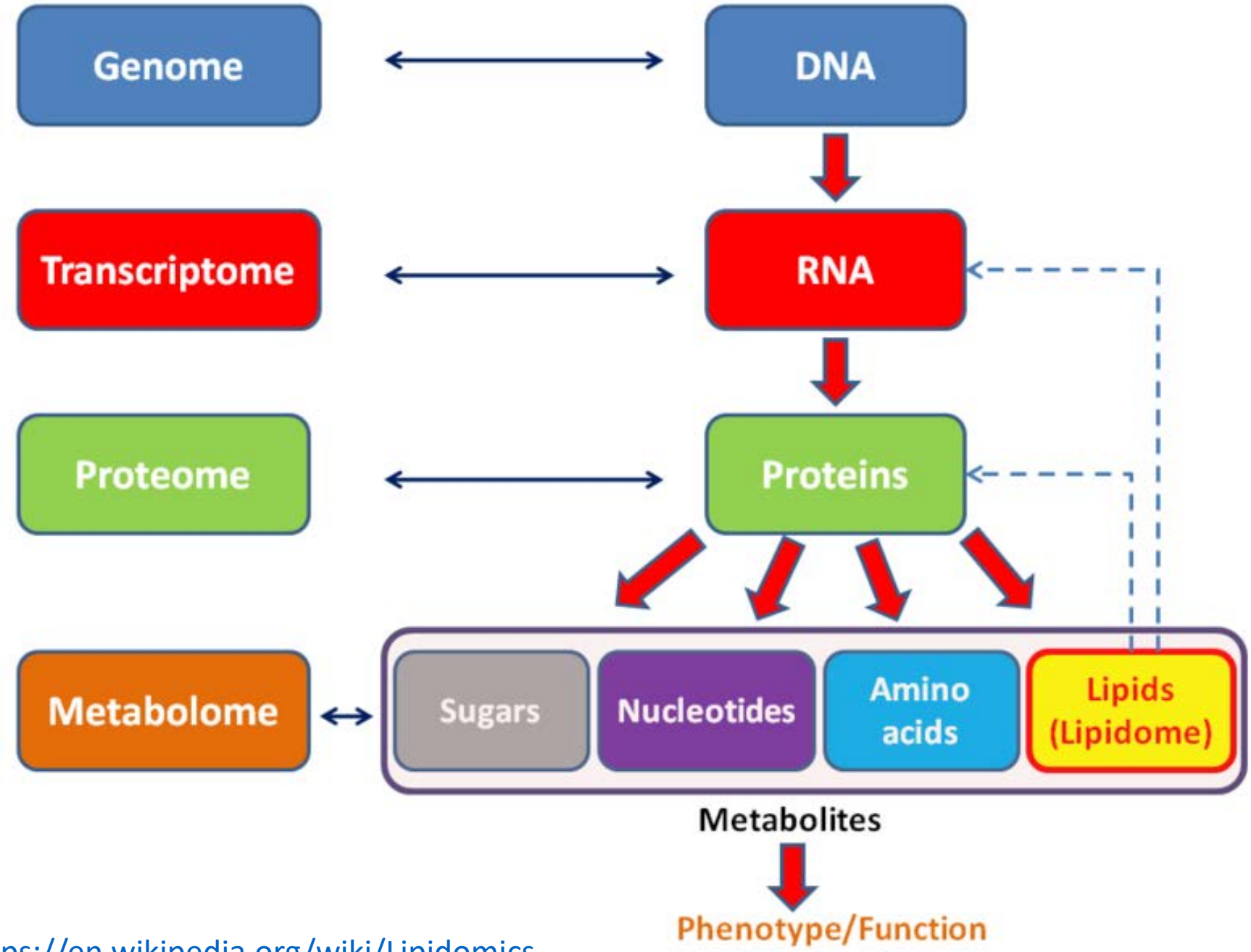
合成、抗發炎



Brassinolide
(a brassinosteroid)

油菜素內酯（油菜素類固醇）

植物生長調節劑



https://en.wikipedia.org/wiki/Lipidomics