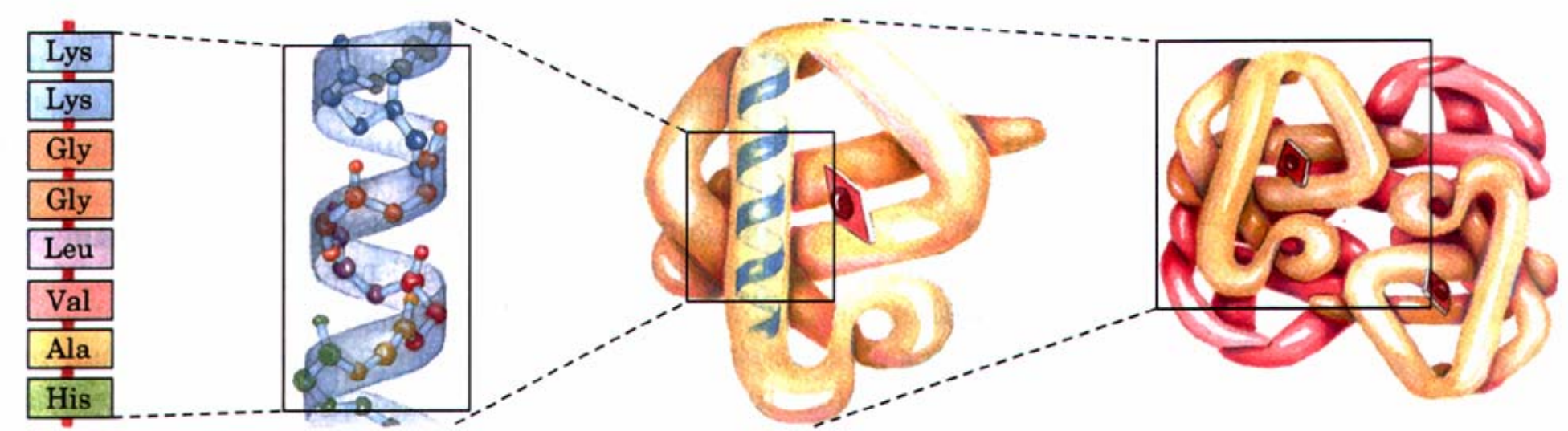
蛋白質的四級構造

胺基酸



一級構造

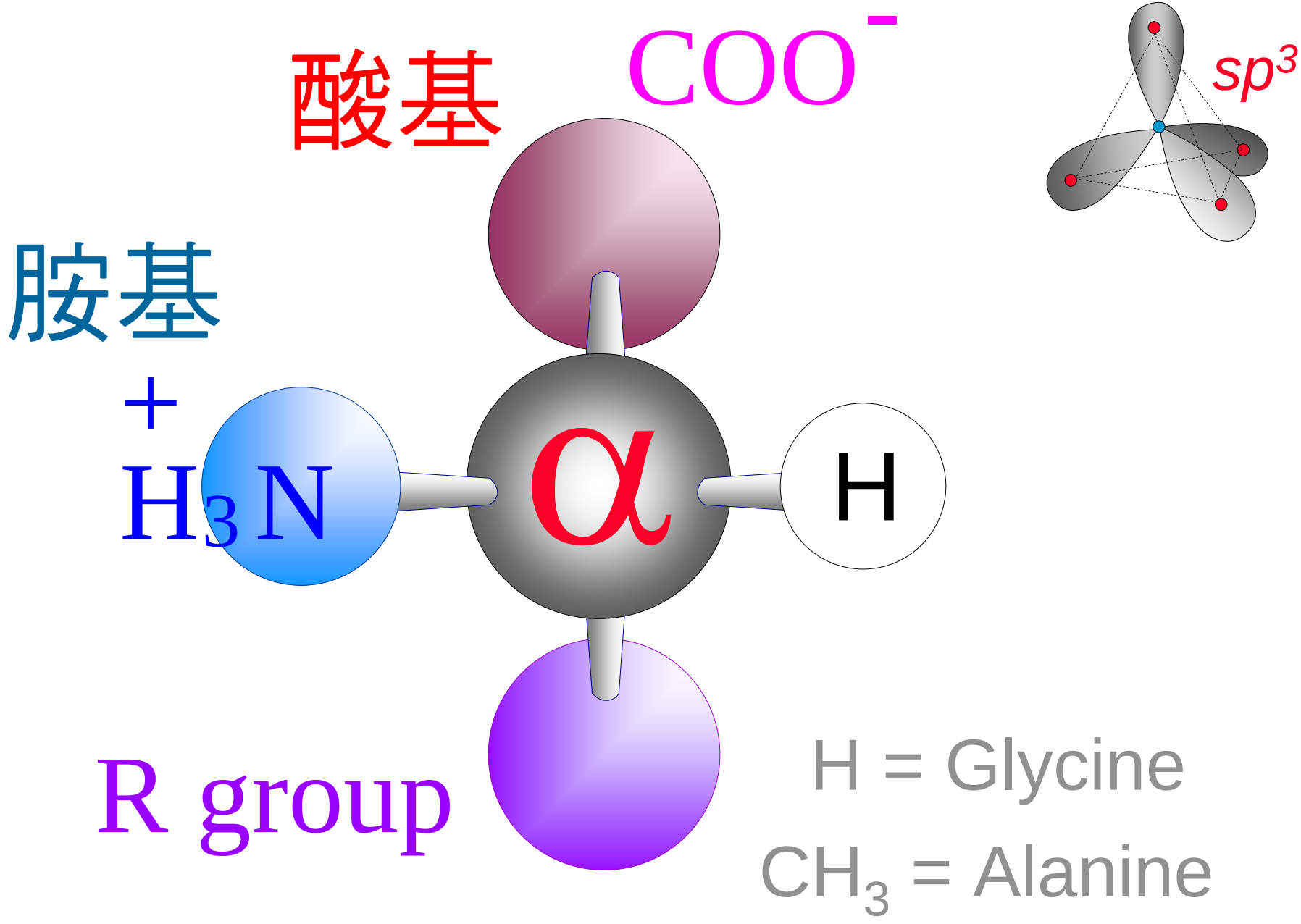
二級構造

三級構造

四級構造

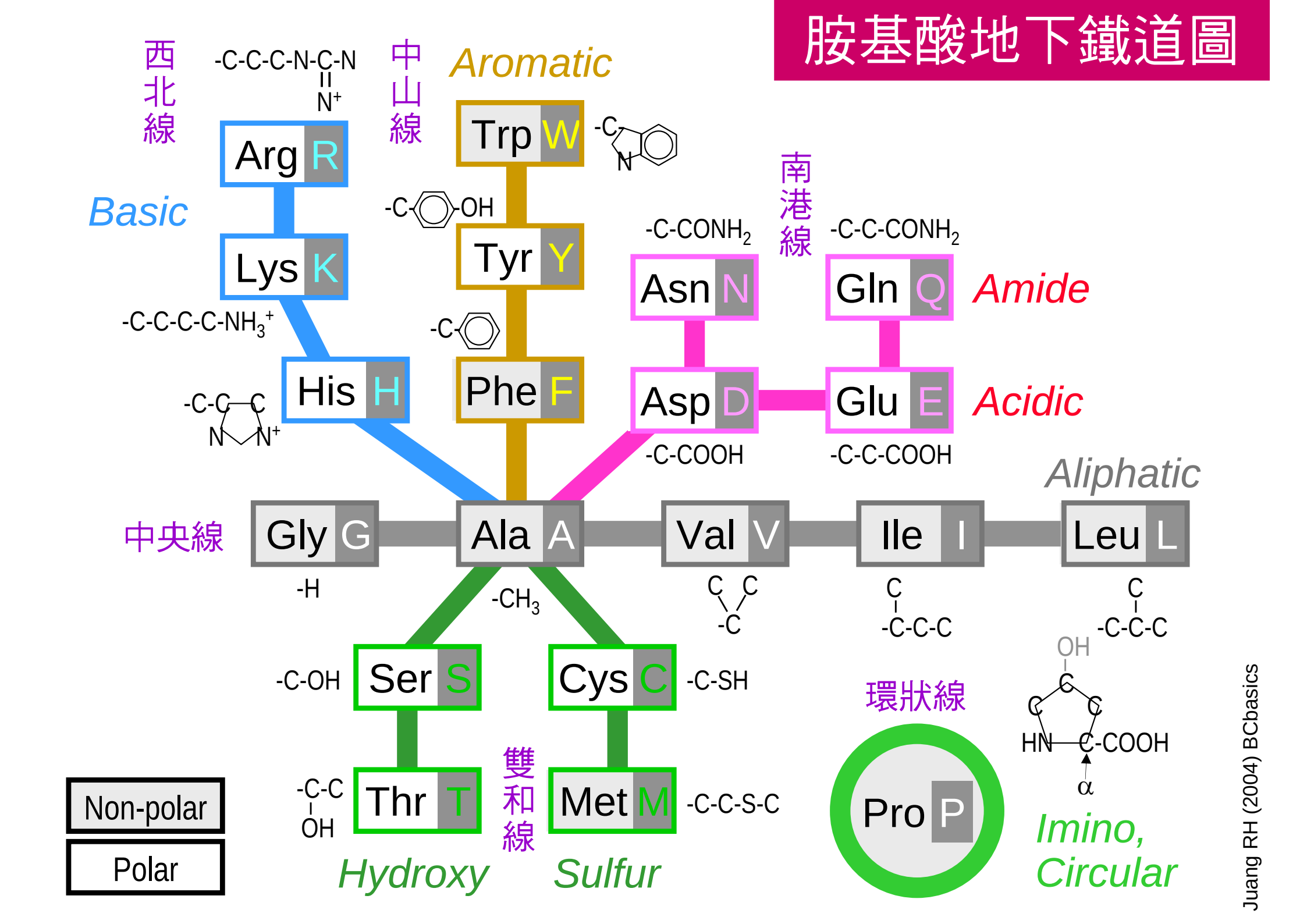
Nelson & Cox (2000) Lehninger Principles of Biochemistry (3e) p.129

L-Form Amino Acid



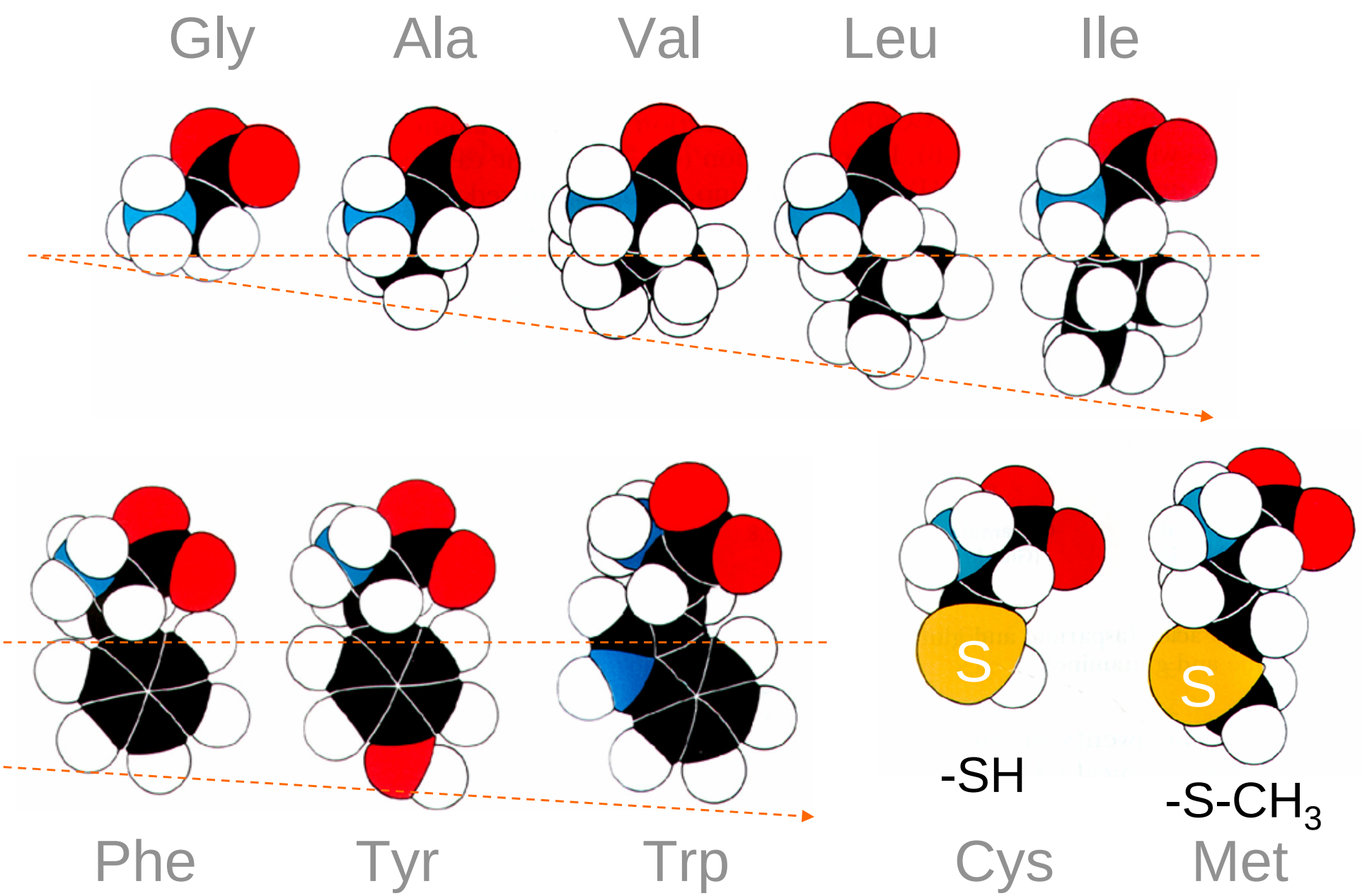
Juang RH (2005) BCbasics

胺基酸地下鐵道圖



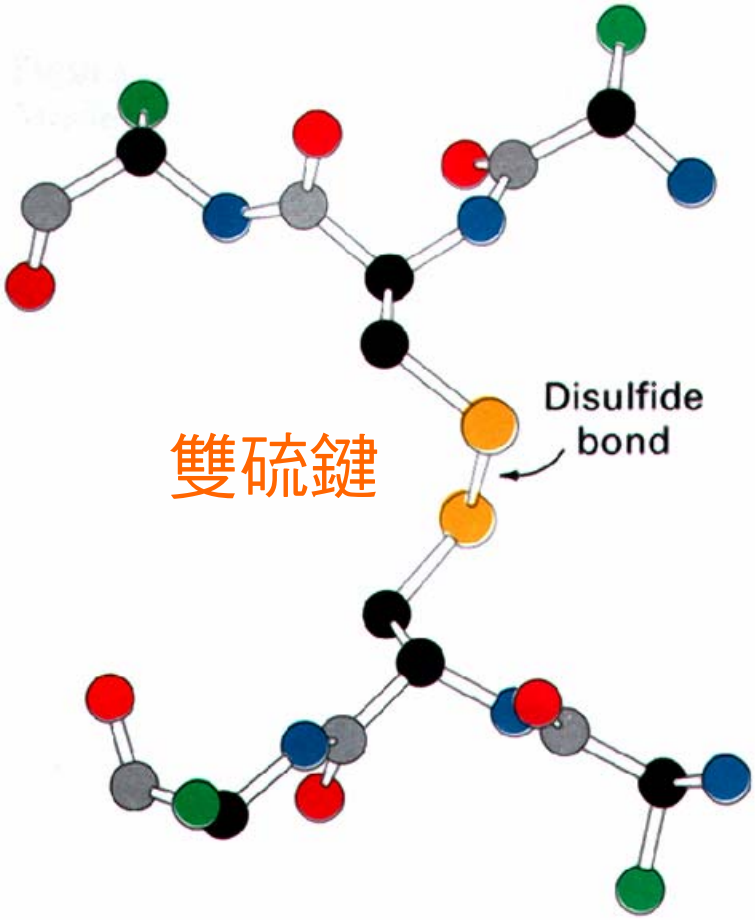
Juang RH (2004) BCbasics

各式胺基酸的大小樣式齊全

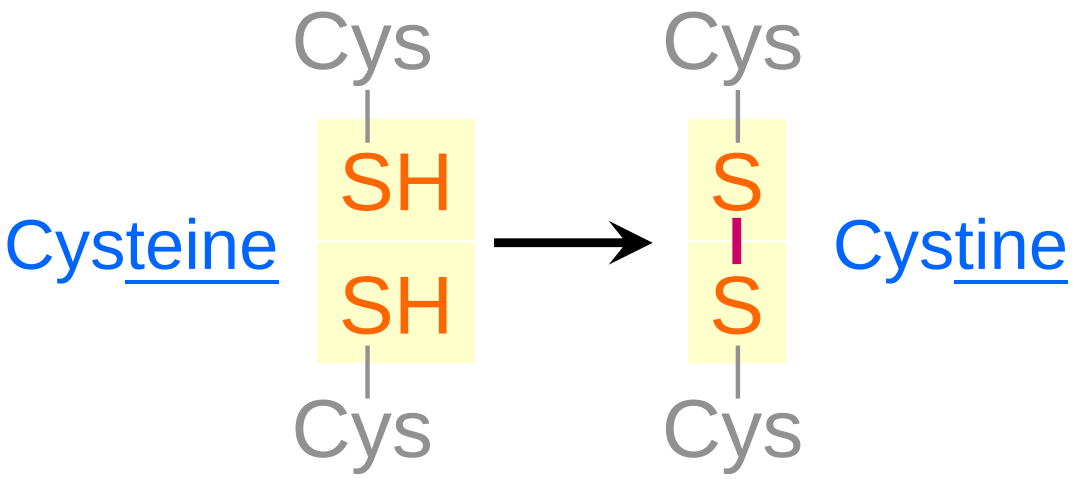


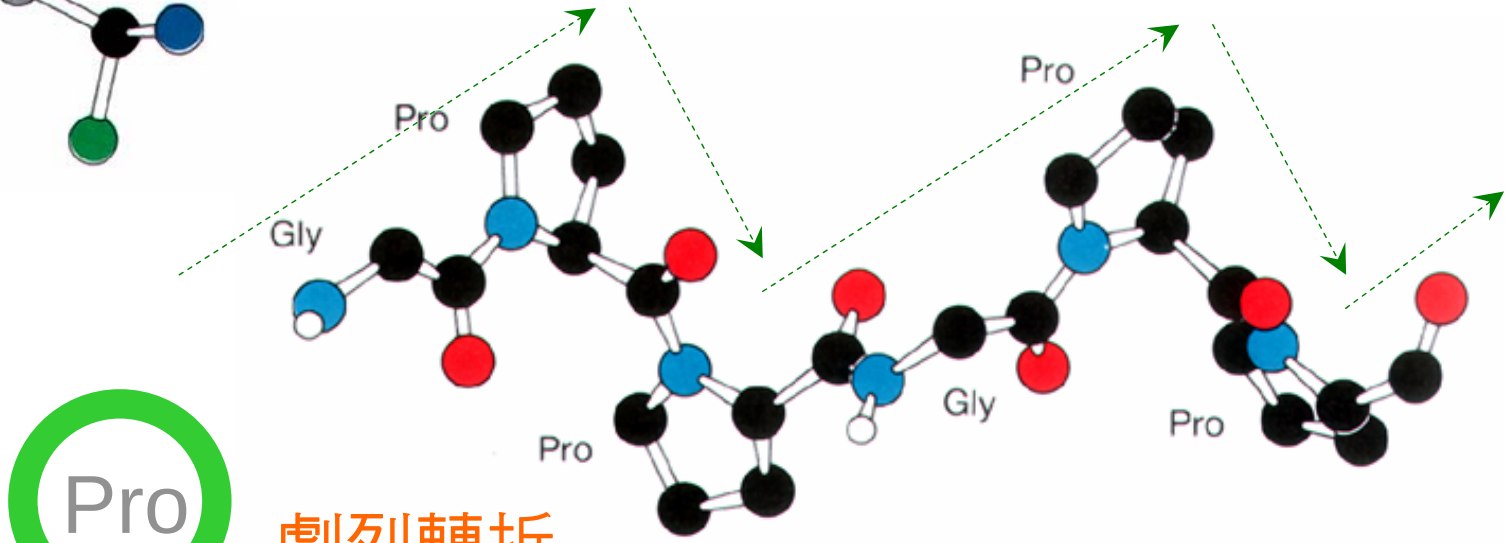
Stryer (1995) Biochemistry (4e) p.20

兩種胺基酸對蛋白質構造影響很大



雙硫鍵

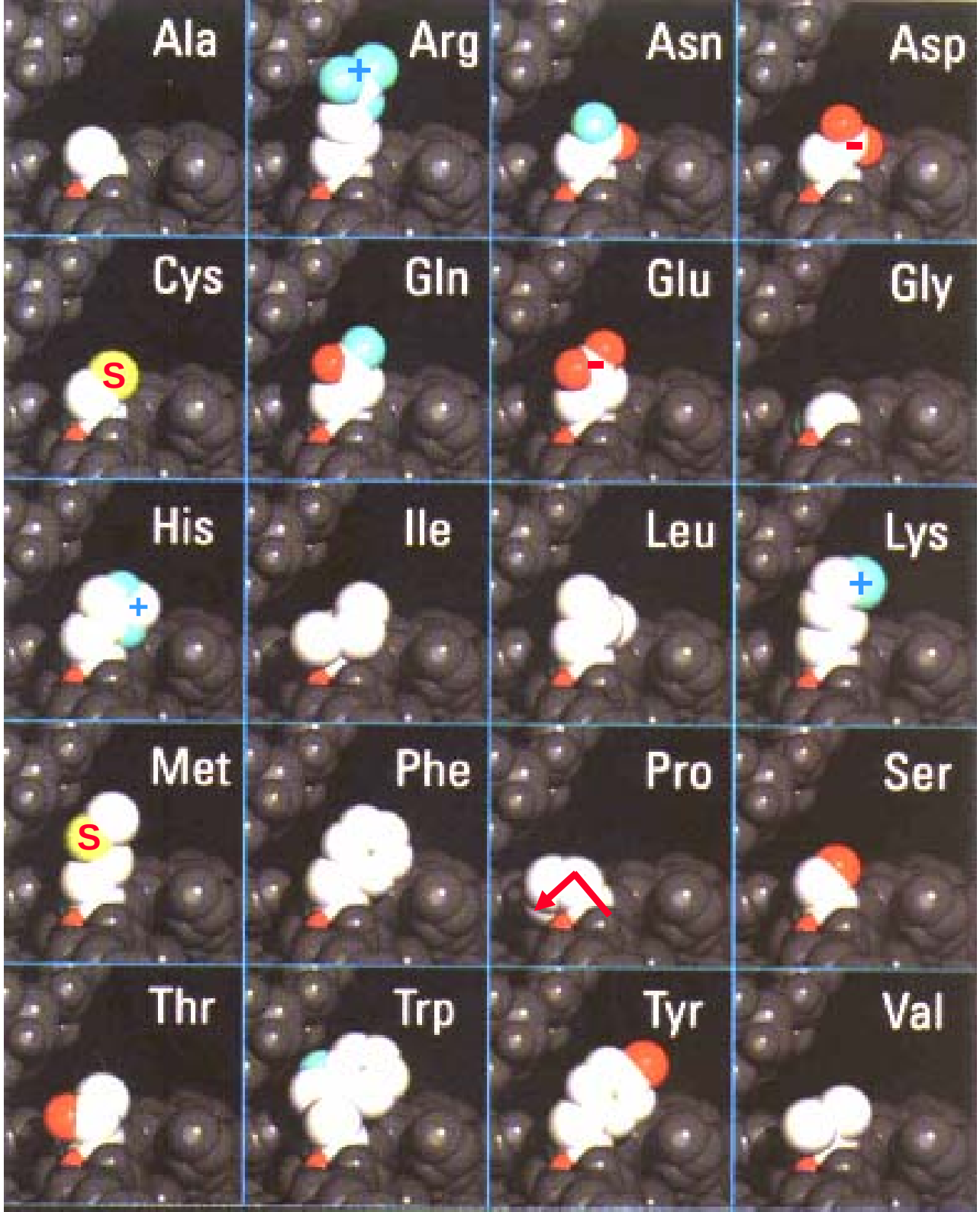




劇烈轉折

Stryer (1995) Biochemistry (4e) p.25, 32

形形色色的胺基酸側基



有大有小

有正有負

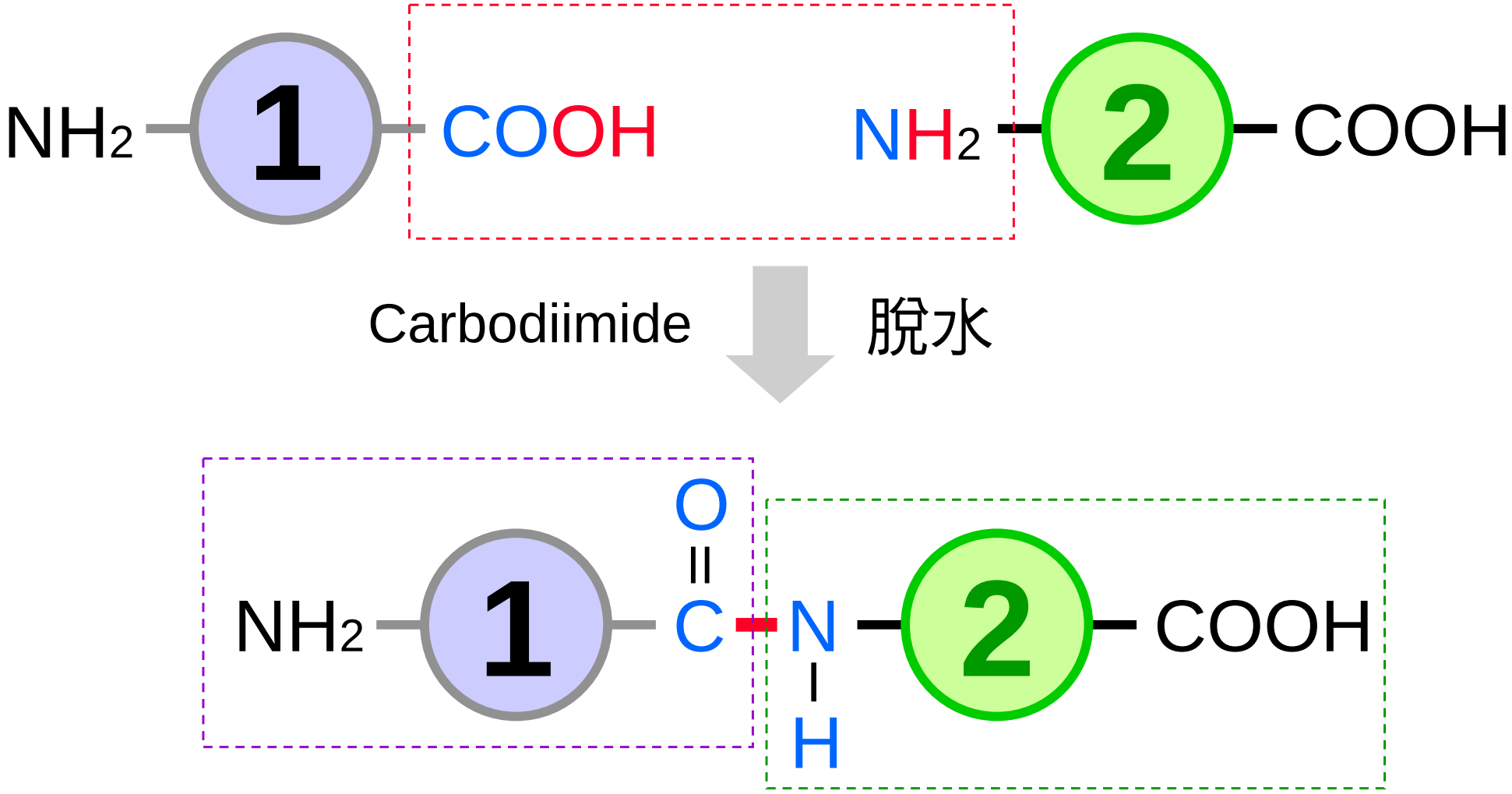
有極性

非極性

Bio-Lab 廣告 Cell 83 (4), 1995

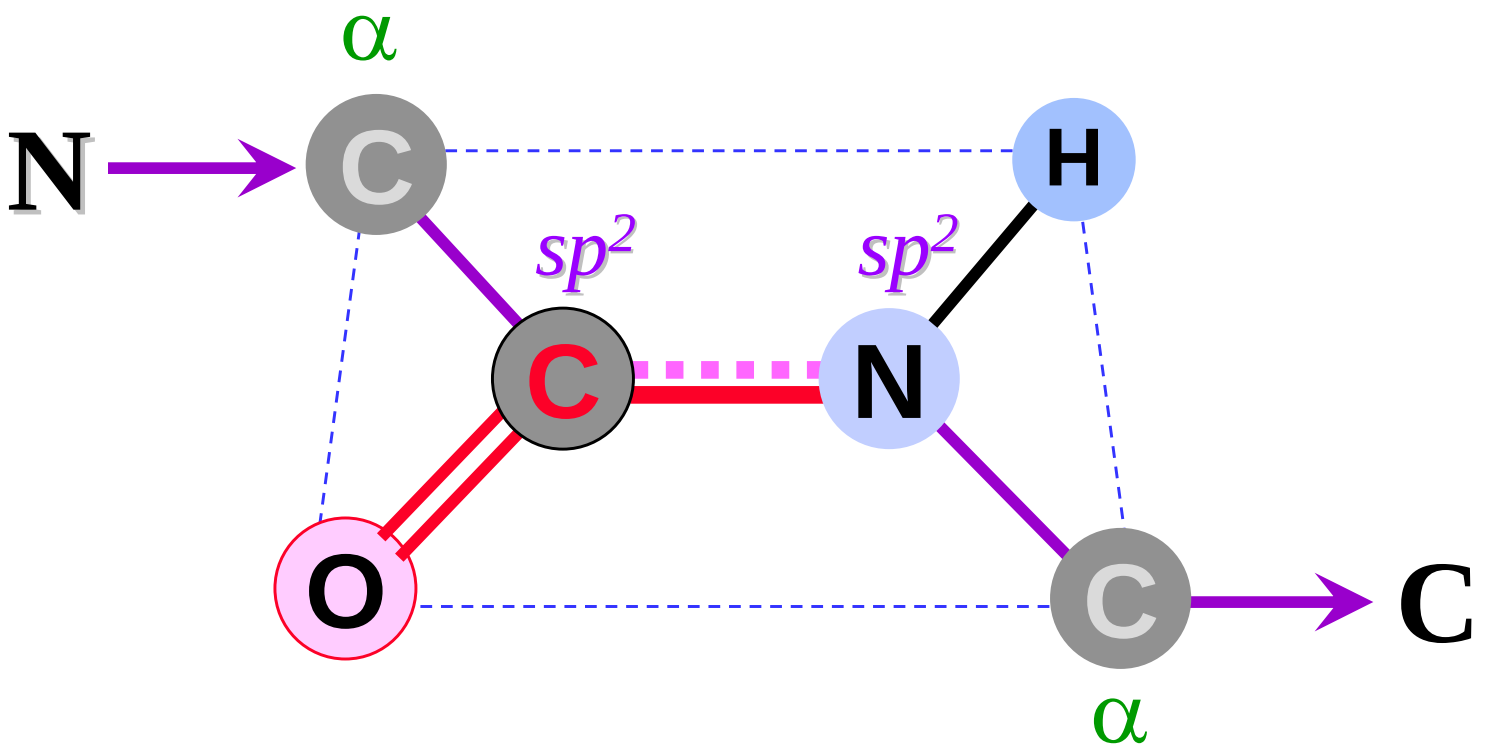
胜肽鍵的形成

兩個胺基酸分子頭尾連接起來

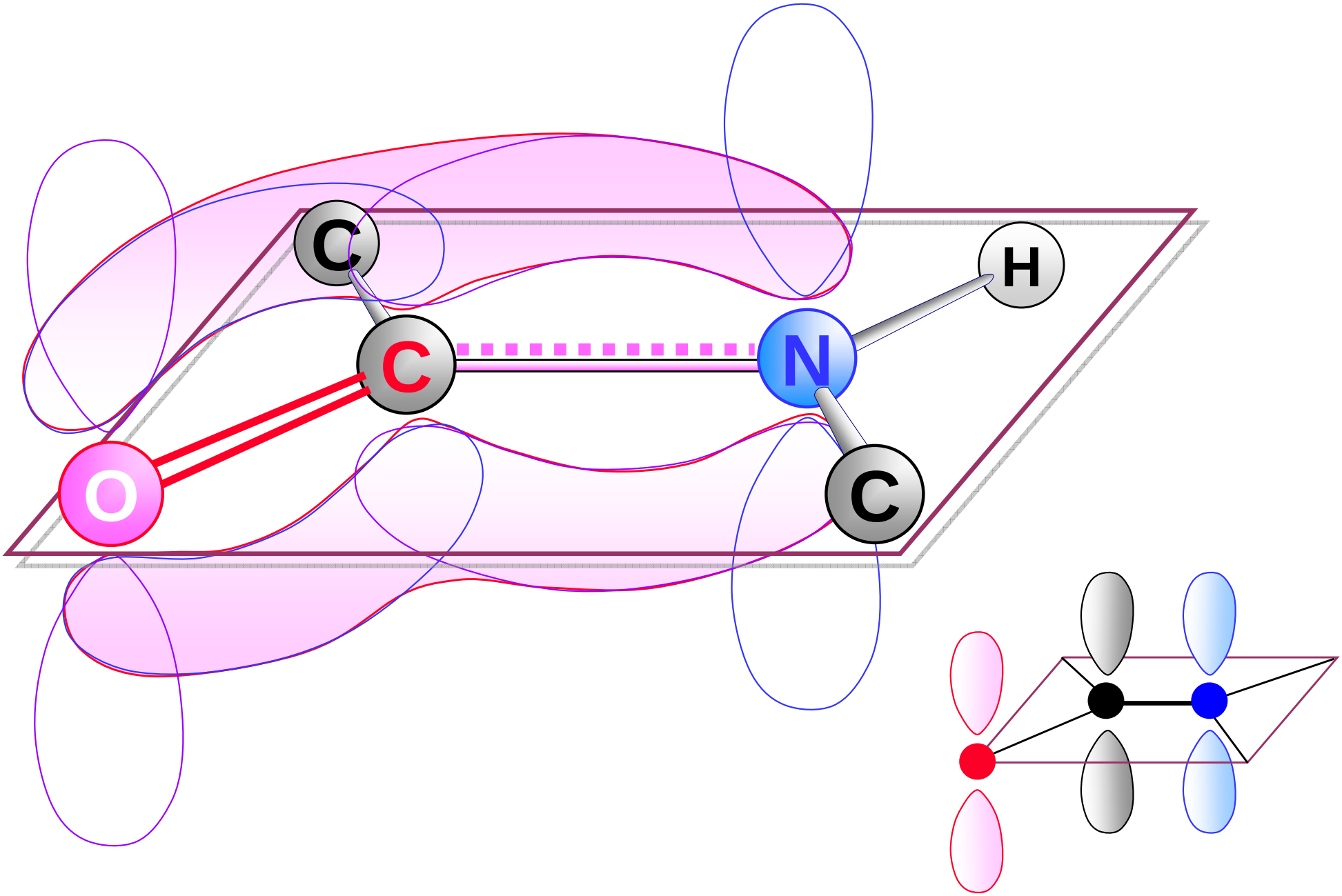


胜肽鍵的特性

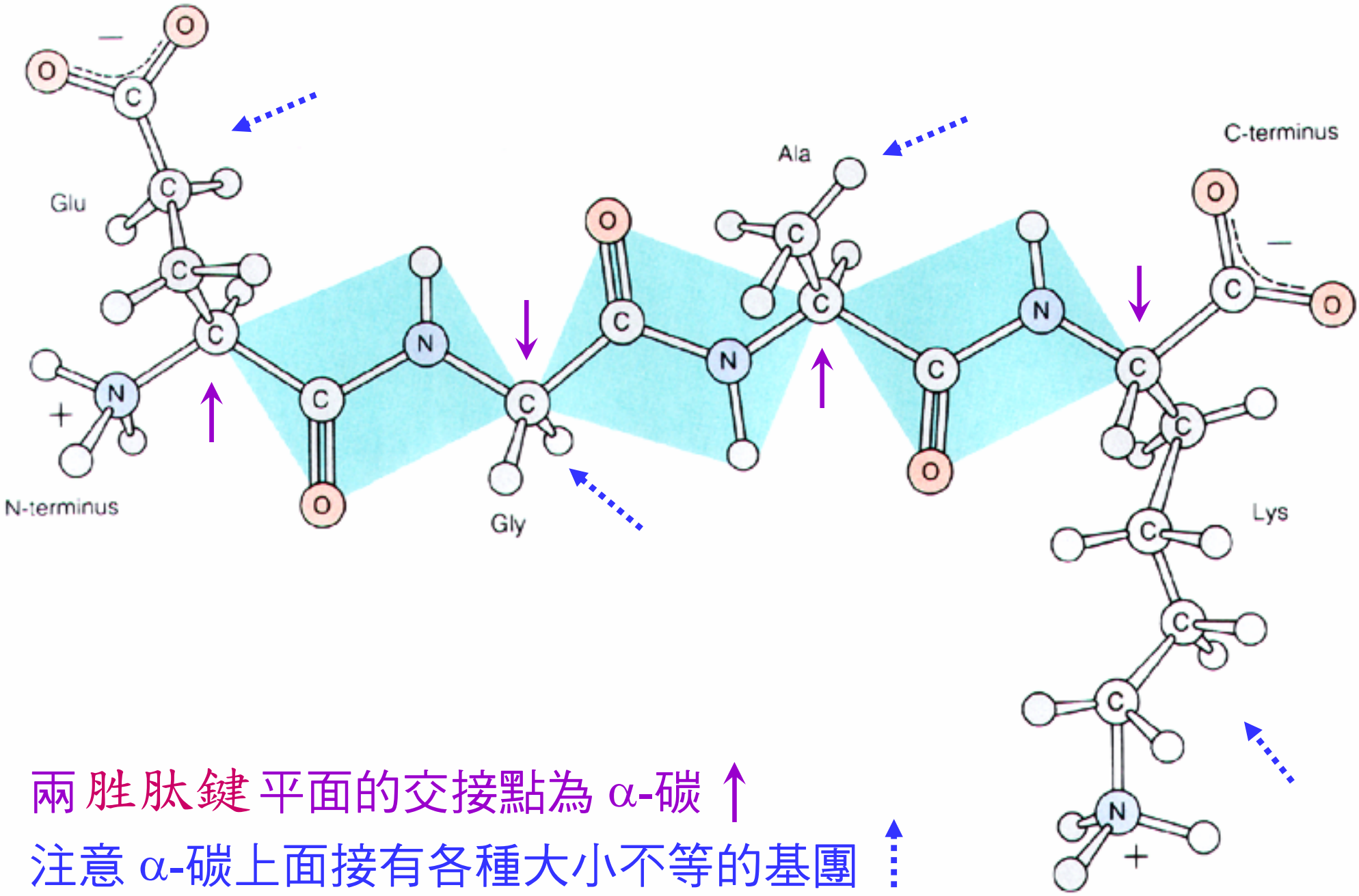
- 胜肽鍵 雖是單鍵卻有雙鍵性質
- 胜肽鍵 周邊六個原子在同一平面上
- 前後兩個胺基酸的 α-carbon 在對角 (trans)



p 軌道電子共振使胜肽鍵具雙鍵特性



以胜肽鍵平面連接成多肽長鏈



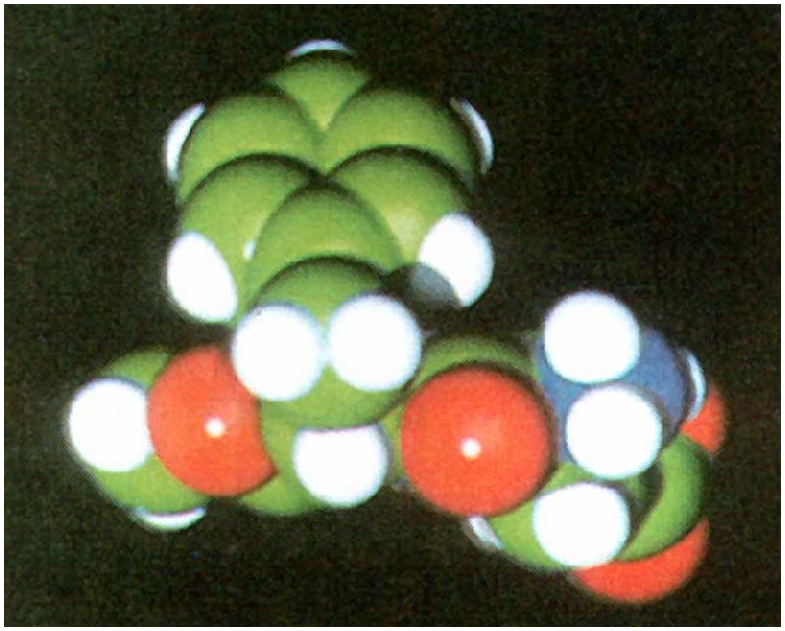
兩胜肽鍵平面的交接點為 α-碳

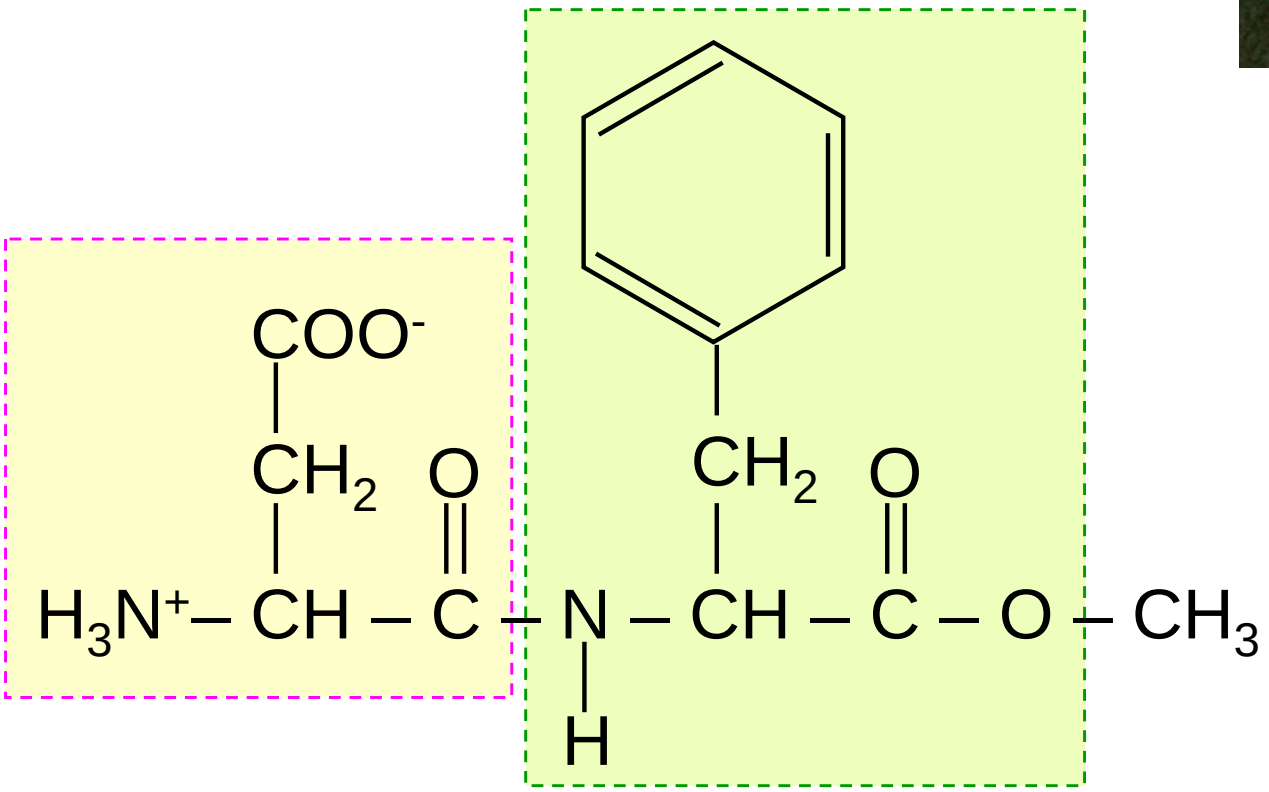
注意 α-碳上面接有各種大小不等的基團

Mathews et al (2000) Biochemistry (3e) p.136

阿斯巴甜

Aspartame





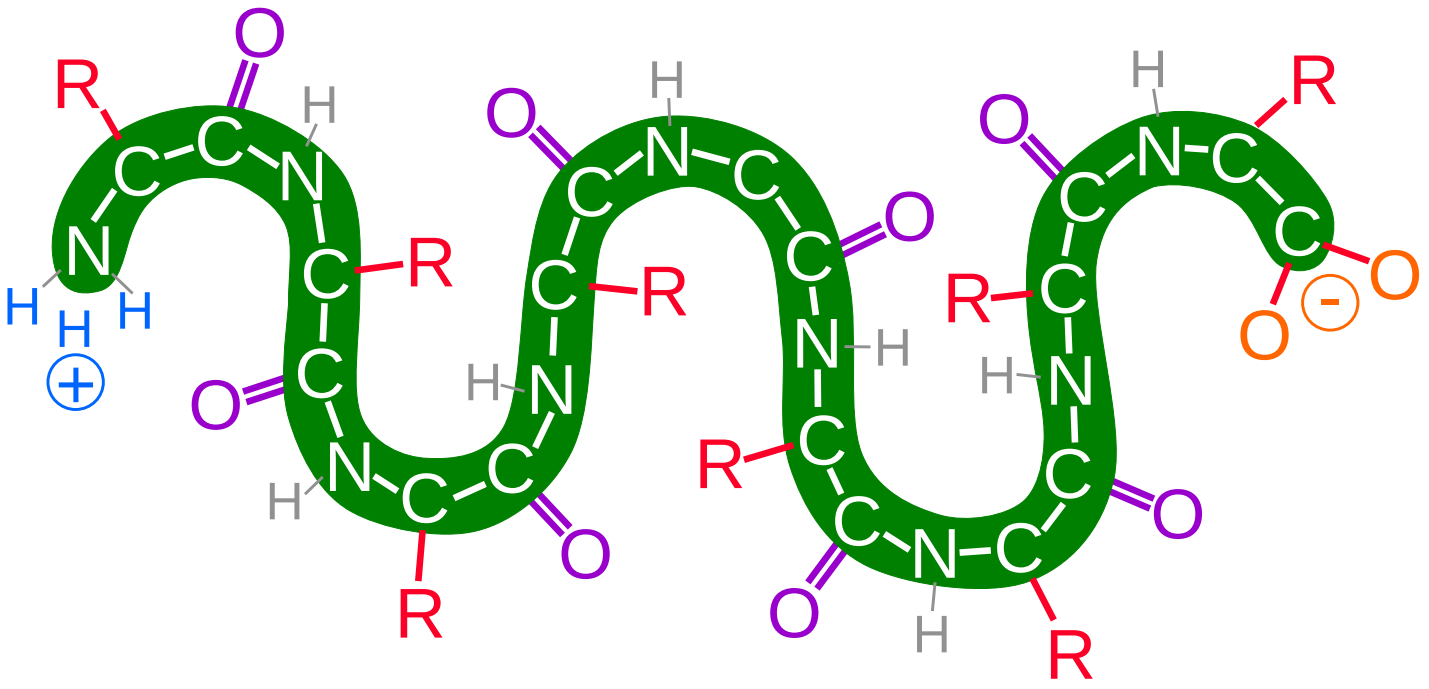
L-Aspartyl-L-phenylalanine methyl ester

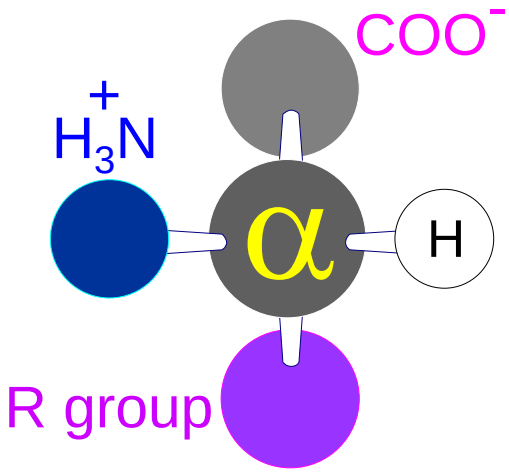
Campbell (1999) Biochemistry (3e) p.95

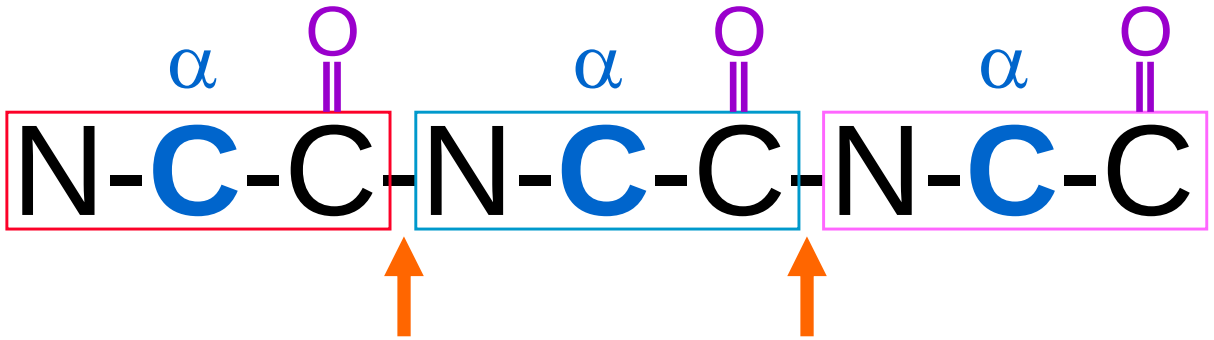
蛋白質的骨架 (Backbone)

Constant

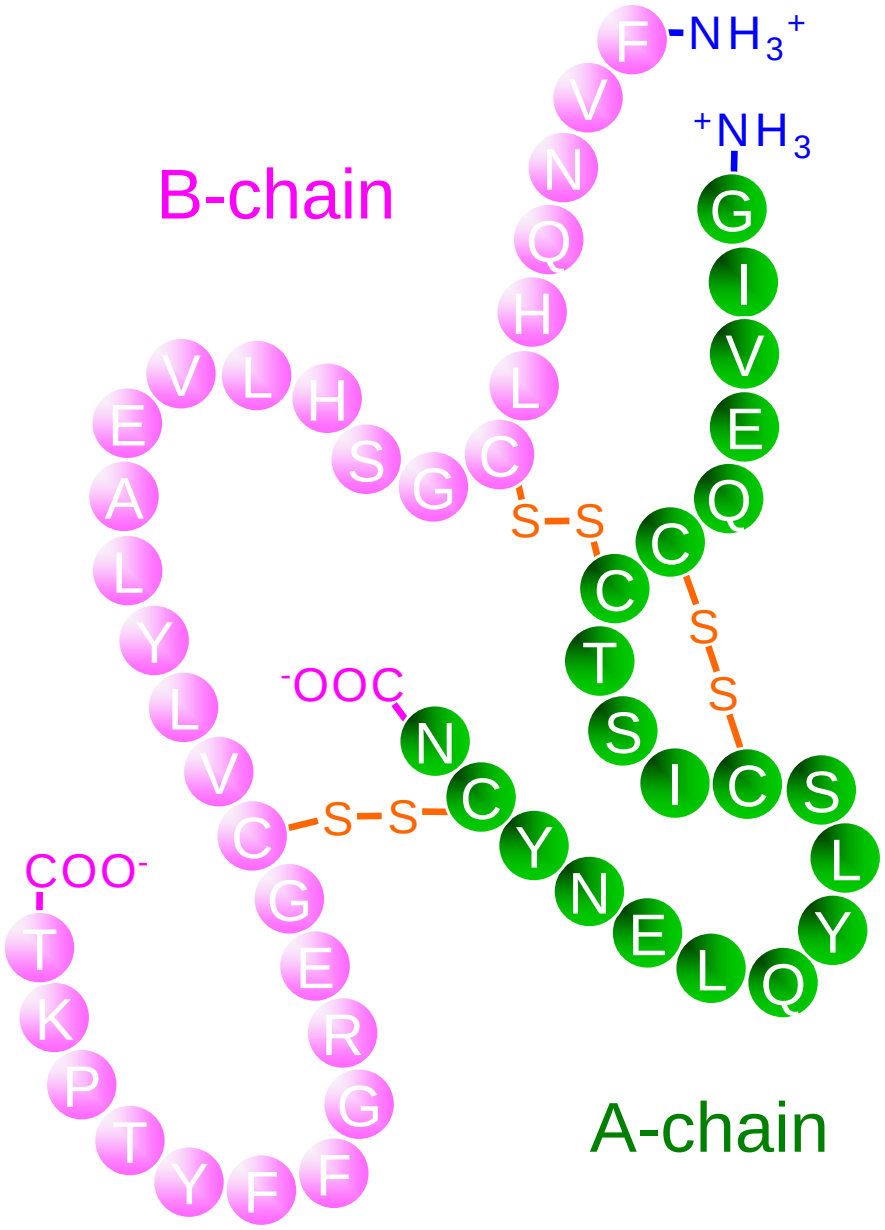
Variable







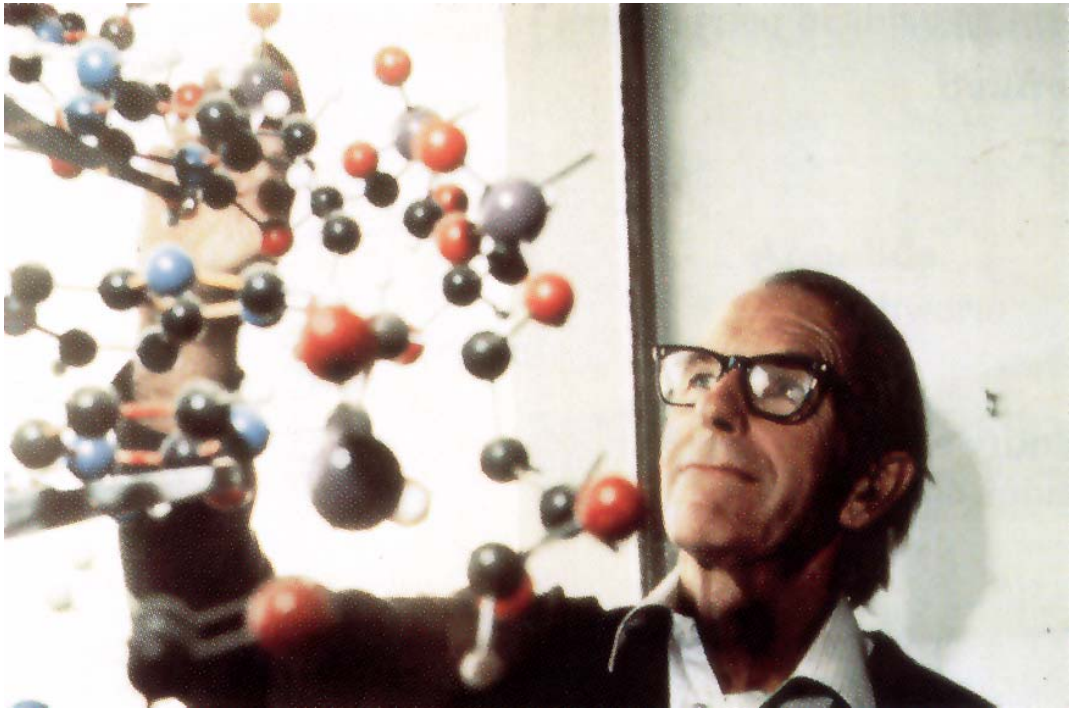
以傳統胺基酸定序法決定蛋白質序列



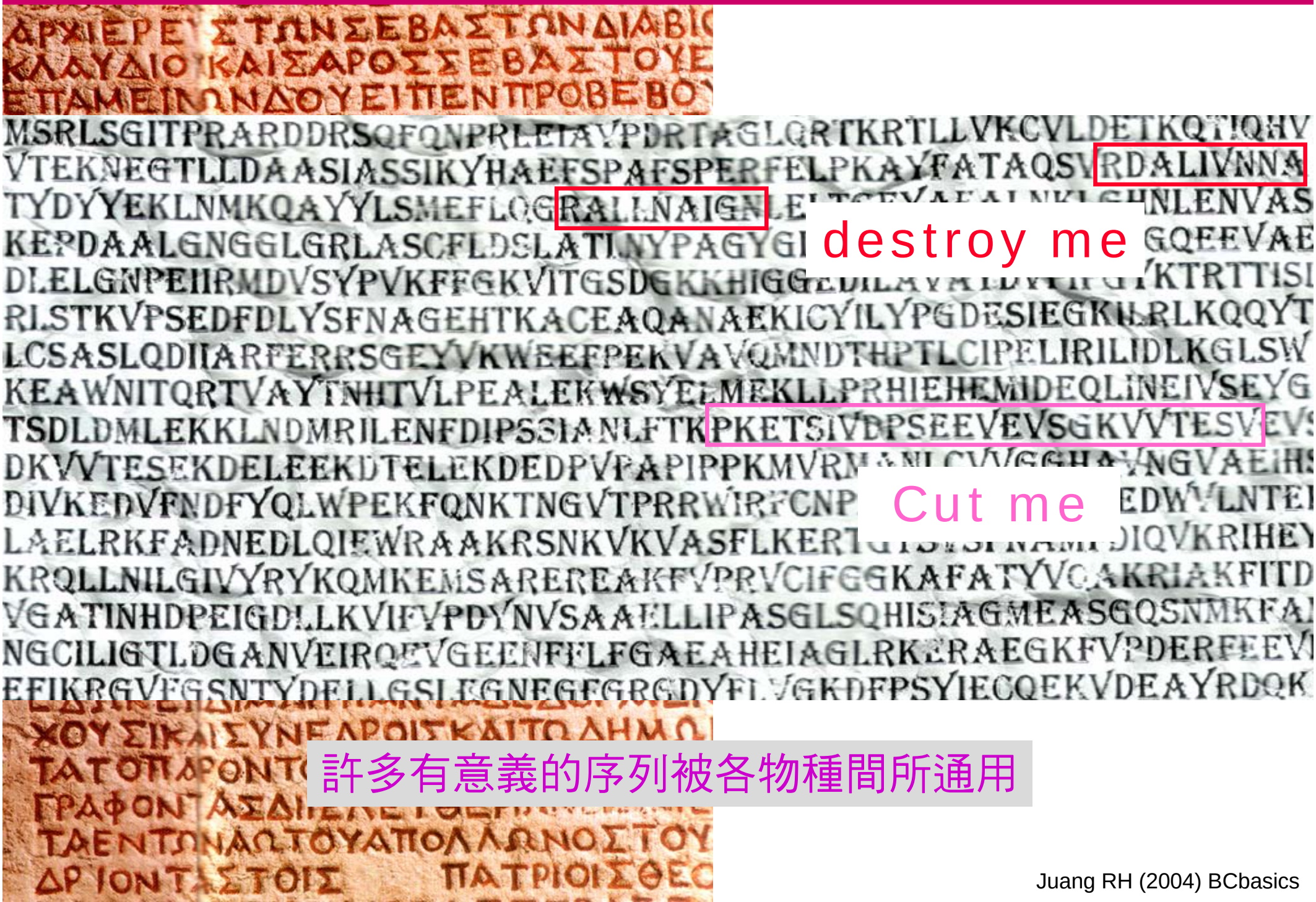
F. Sanger

Cambridge U

Insulin 胰島素 (A, B chains)



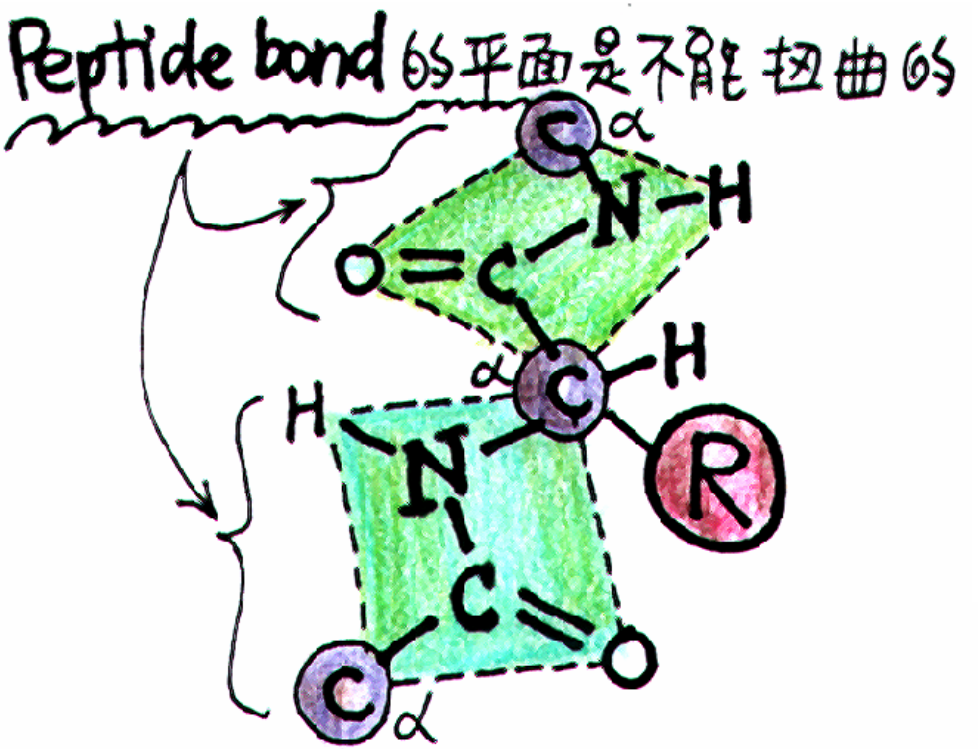
蛋白質的胺基酸序列



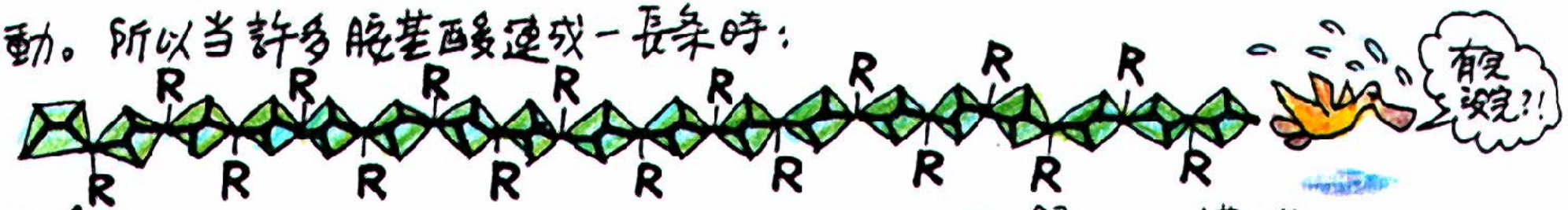
許多有意義的序列被各物種間所通用

Juang RH (2004) BCbasics

胜肽平面連成蛋白質但不會展開成一直線



这兩個平面又因為R group的
関係，只能在一定範圍的角度内
活動。所以当許多胺基酸連成一長条時：



因為↑的関係，会自動捲曲成一定的構造(Secondary structure)，
二級 構造

大略說来有：Helix 或 Sheet
兩种形式

Juang RH (2004) BCbasics

二級構造的成因

α Helix, β Sheet

(1) Peptide bond 不能轉動 → Peptide bond 平面

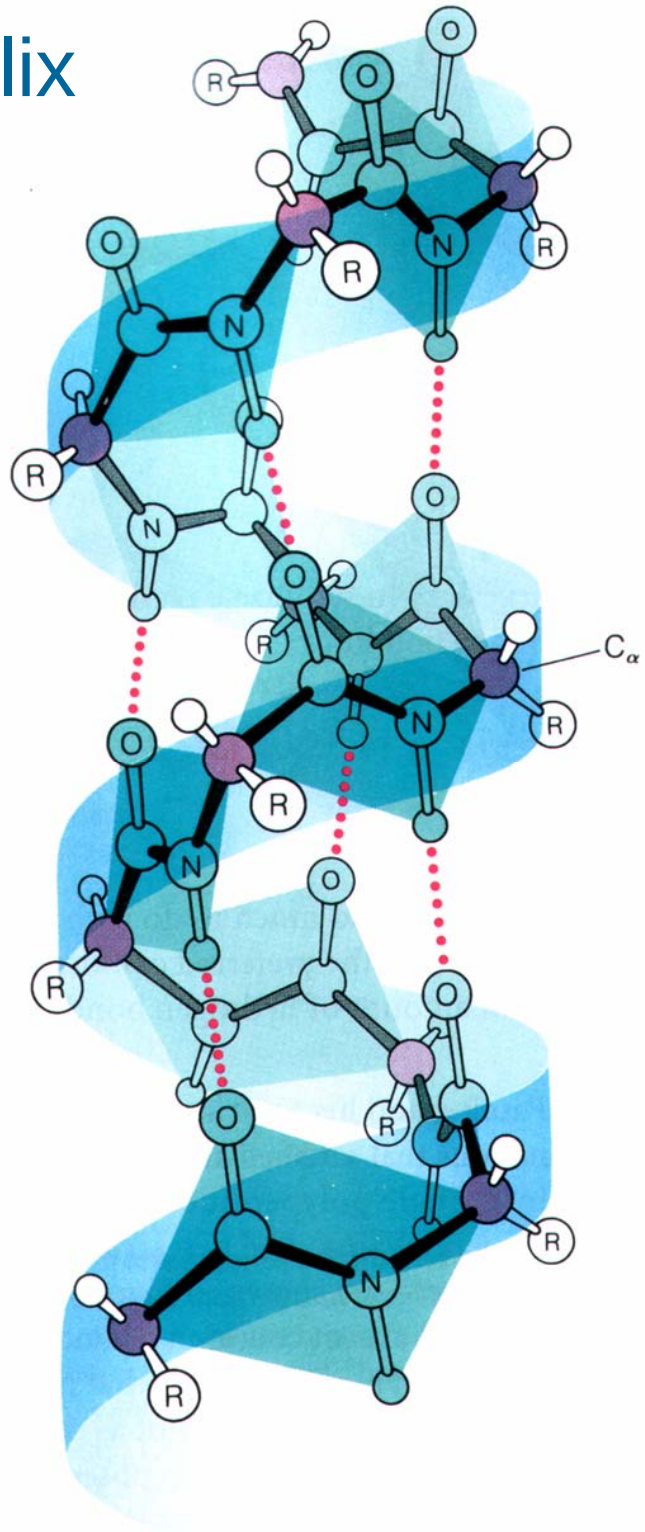
(2) 一個胺基酸 R 基團 與前後 R 基團的限制 →
Peptide bond 平面不能任意轉動 →

(3) R 基團的大小、電荷限制 → 只做 規律摺疊
→ α Helix, β Sheet　Ramachandron plot

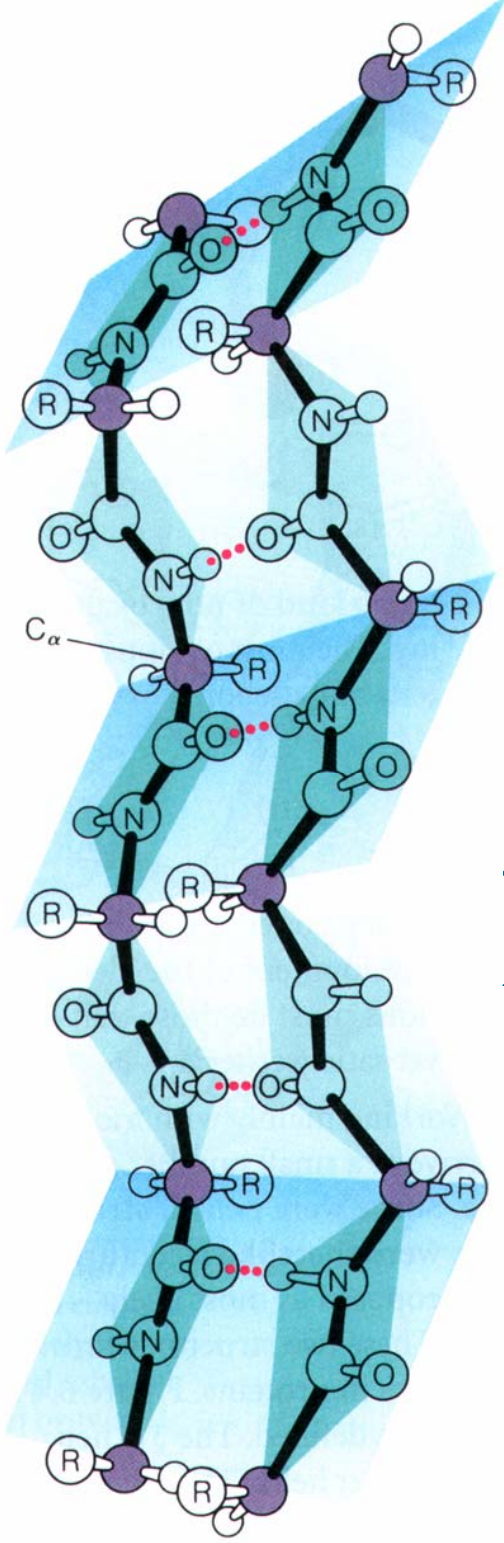
(4) 穩定二級構造的力量： 氫 鍵

蛋白質二級構造

α helix



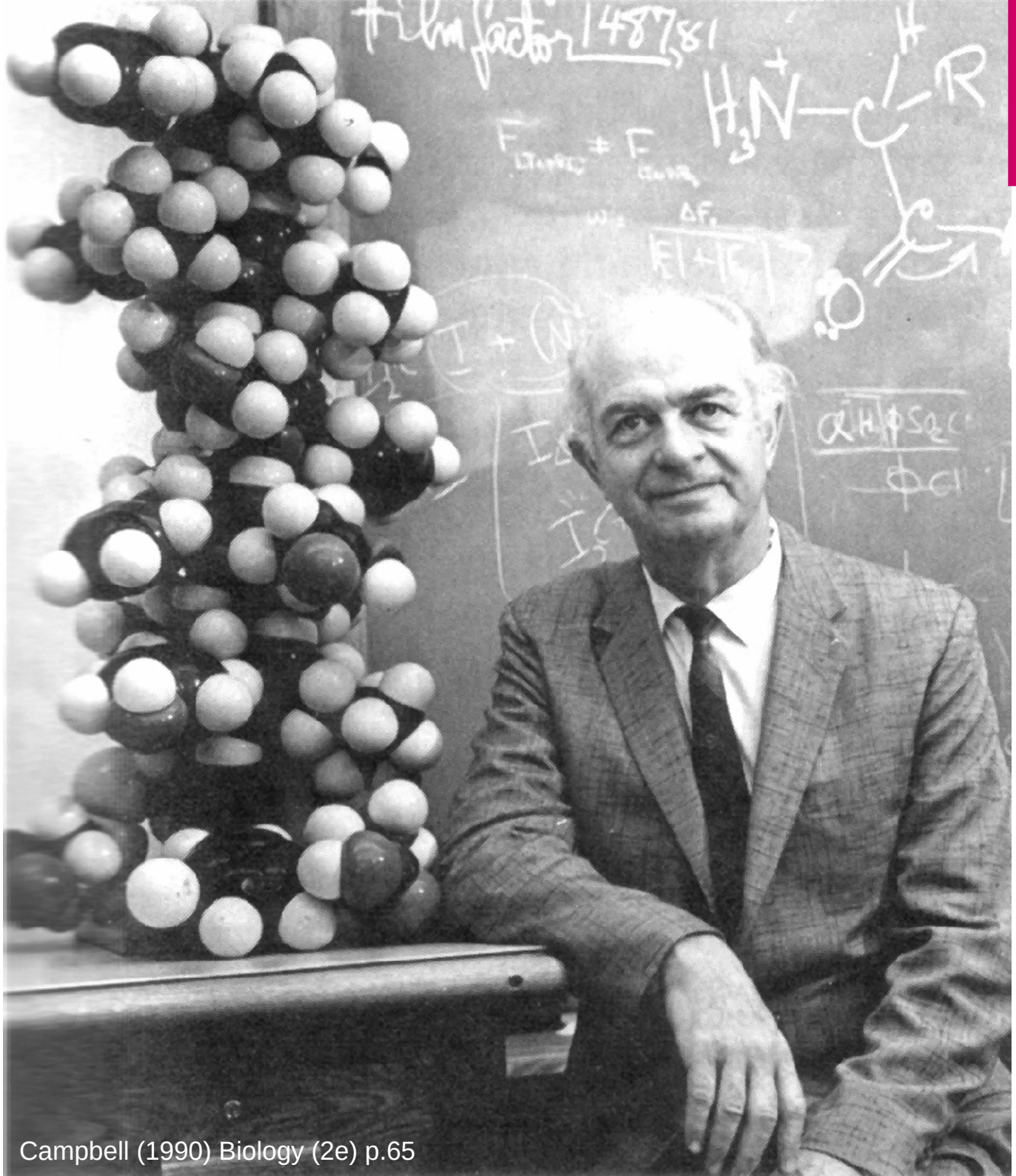
β sheet



兩者都由
氫鍵組成

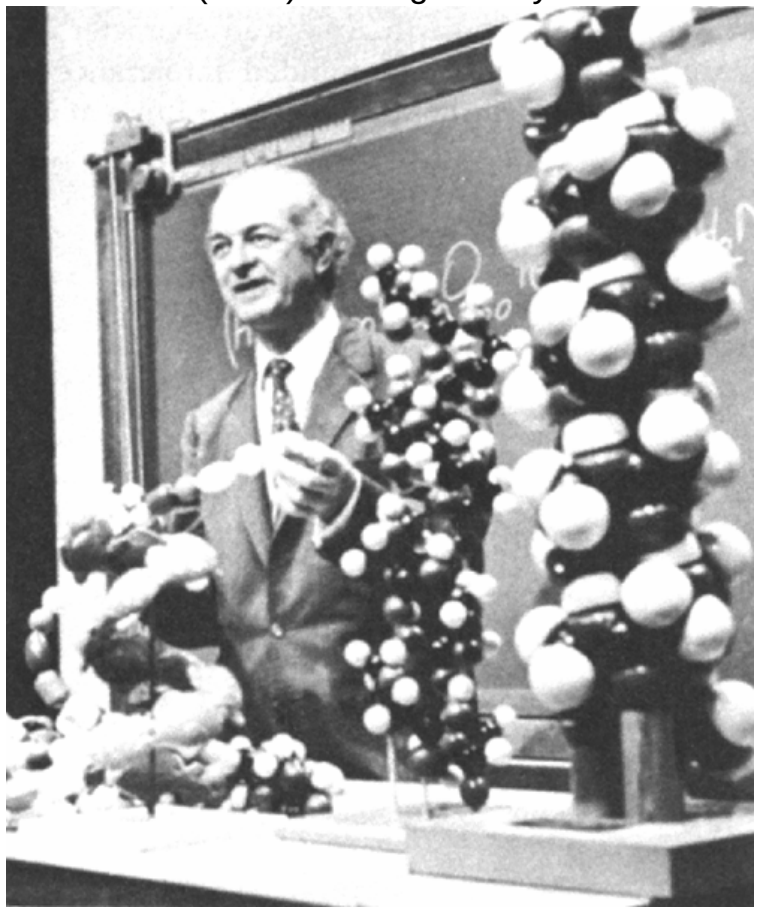
Mathews et al (2000) Biochemistry (3e) p.164

Linus Pauline & α helix

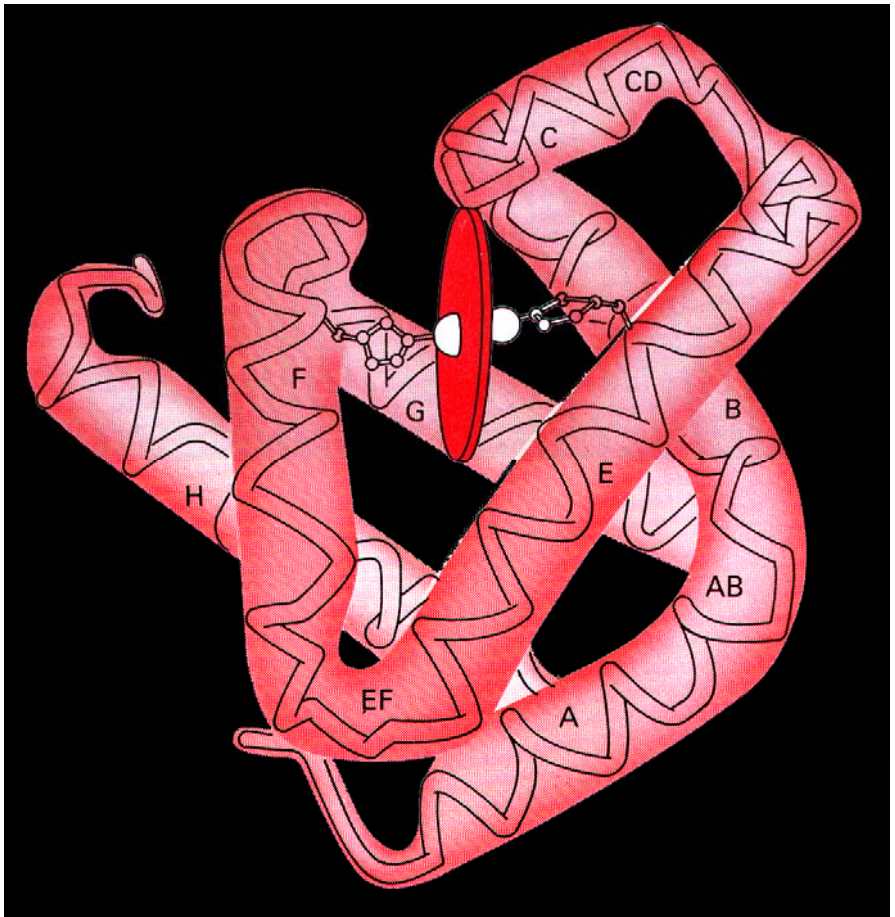


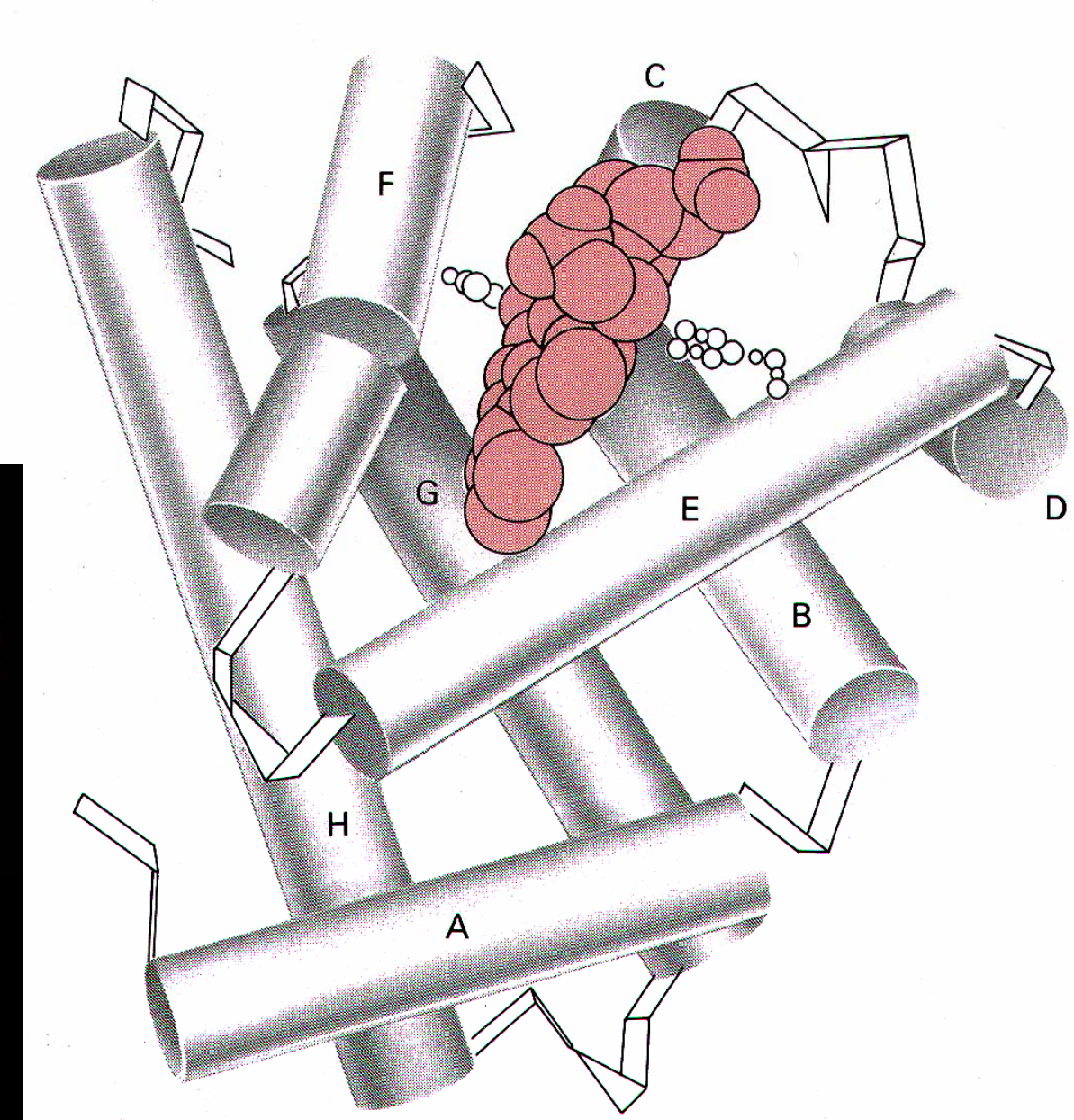
Campbell (1990) Biology (2e) p.65

Judson (1996) The Eighth Day of Creation



肌紅蛋白 myoglobin

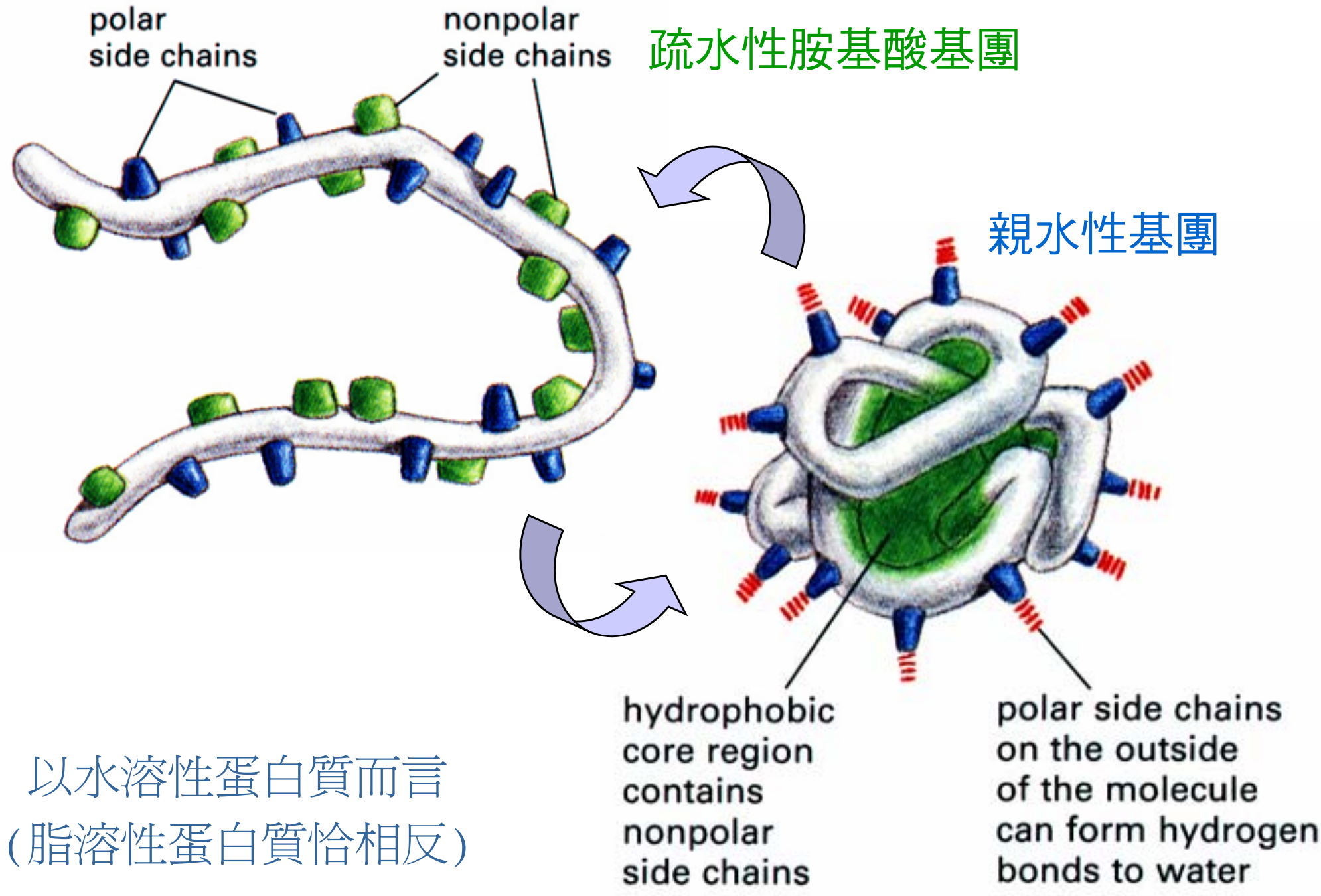




用 α helix 組成堅固的立體構造

Zubay (1988) Biochemistry (2e) p.64

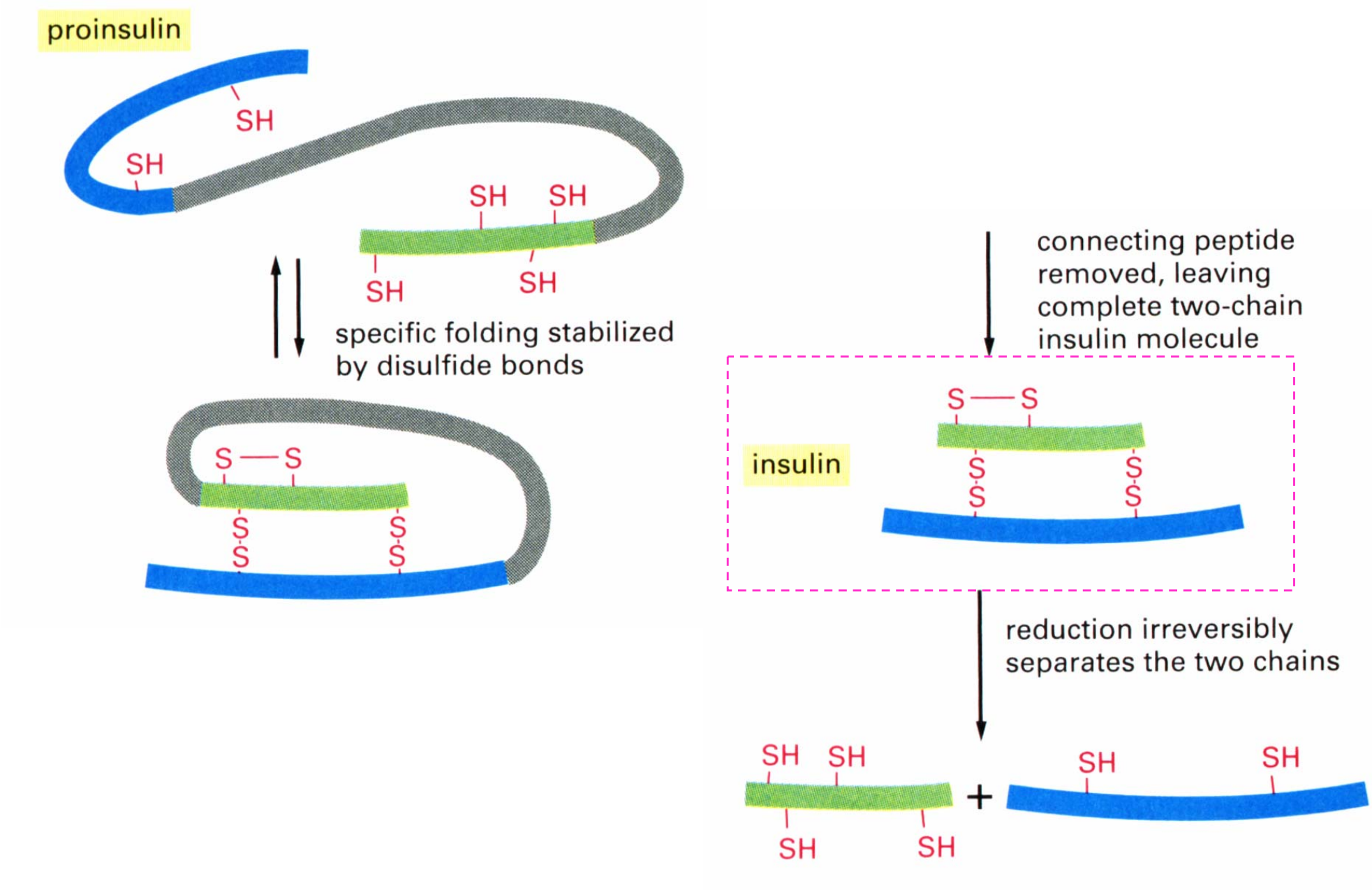
三級構造中的疏水性作用力



以水溶性蛋白質而言
(脂溶性蛋白質恰相反)

Alberts et al (2002) Molecular Biology of the Cell (4e) p.135

裂解是調節蛋白質功能的手段之一

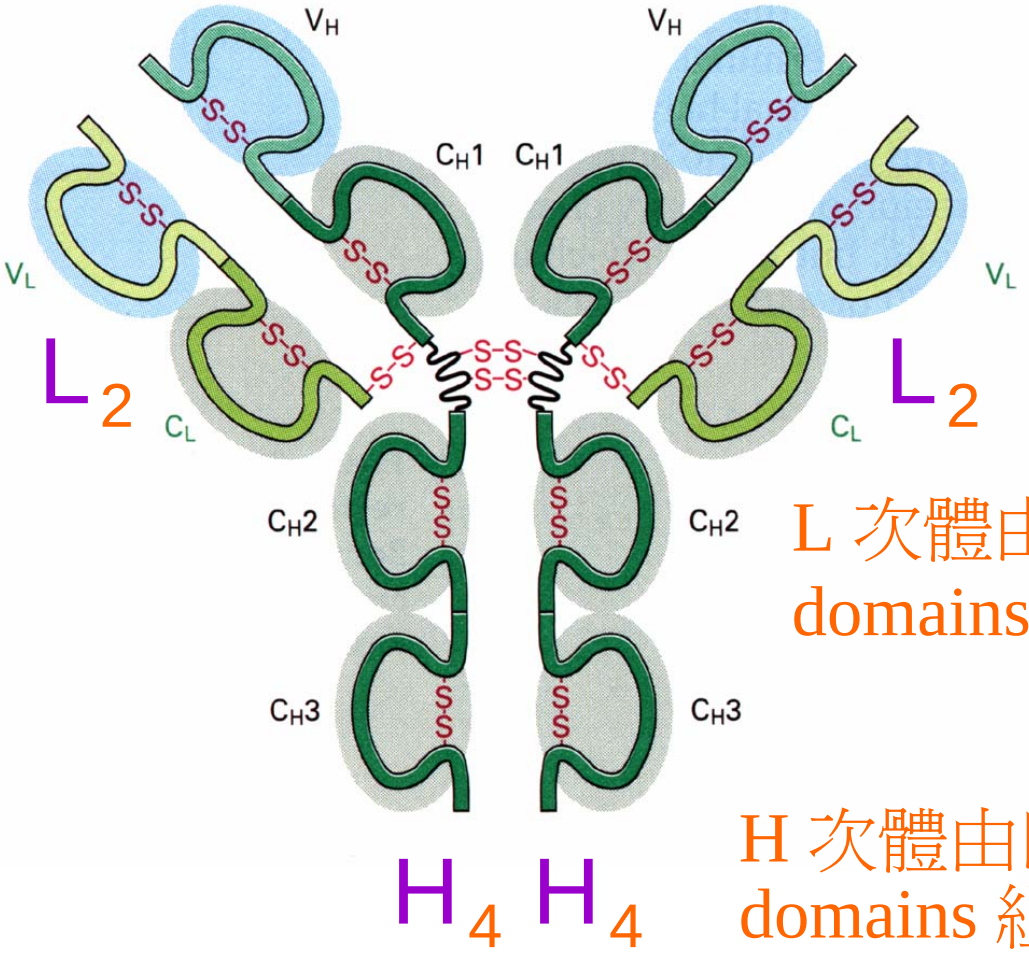


Alberts et al (2002) Molecular Biology of the Cell (4e) p.156

抗體具有十二個以上功能區塊

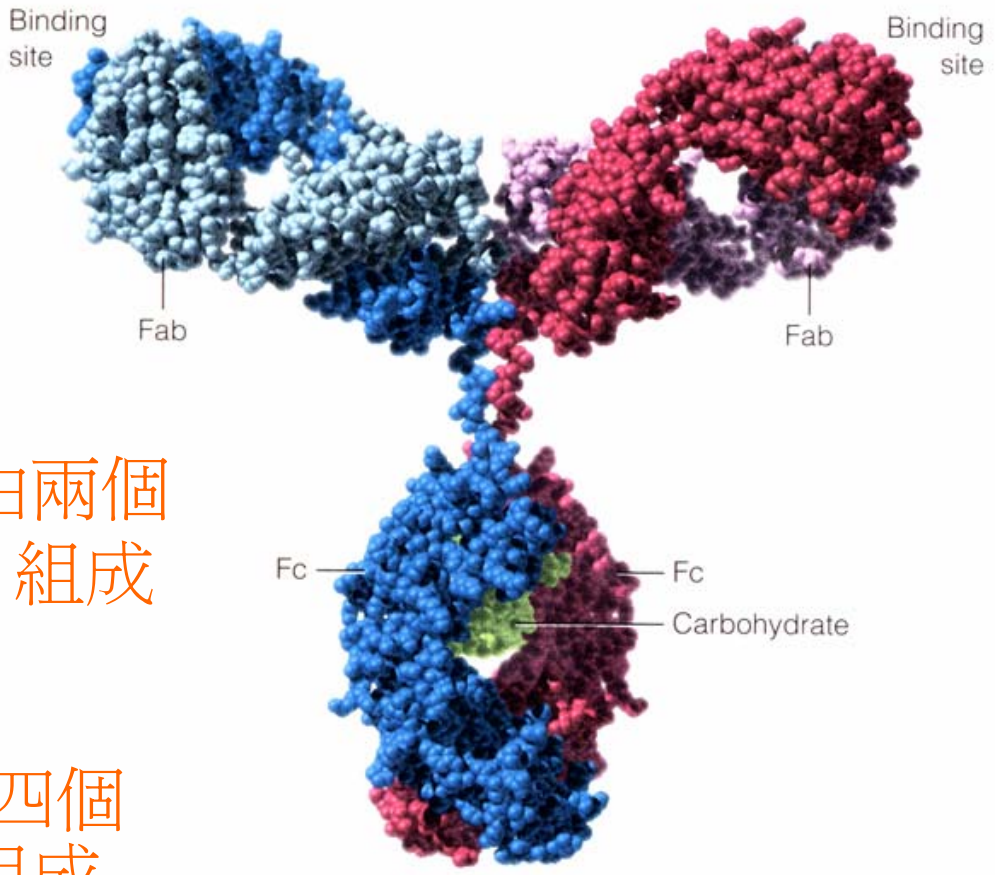
Edelman, Porter (1972)

每一抗體分子有四條次體 (subunits) = 2H (heavy) + 2L (light)



L 次體由兩個 domains 組成

H 次體由四個 domains 組成



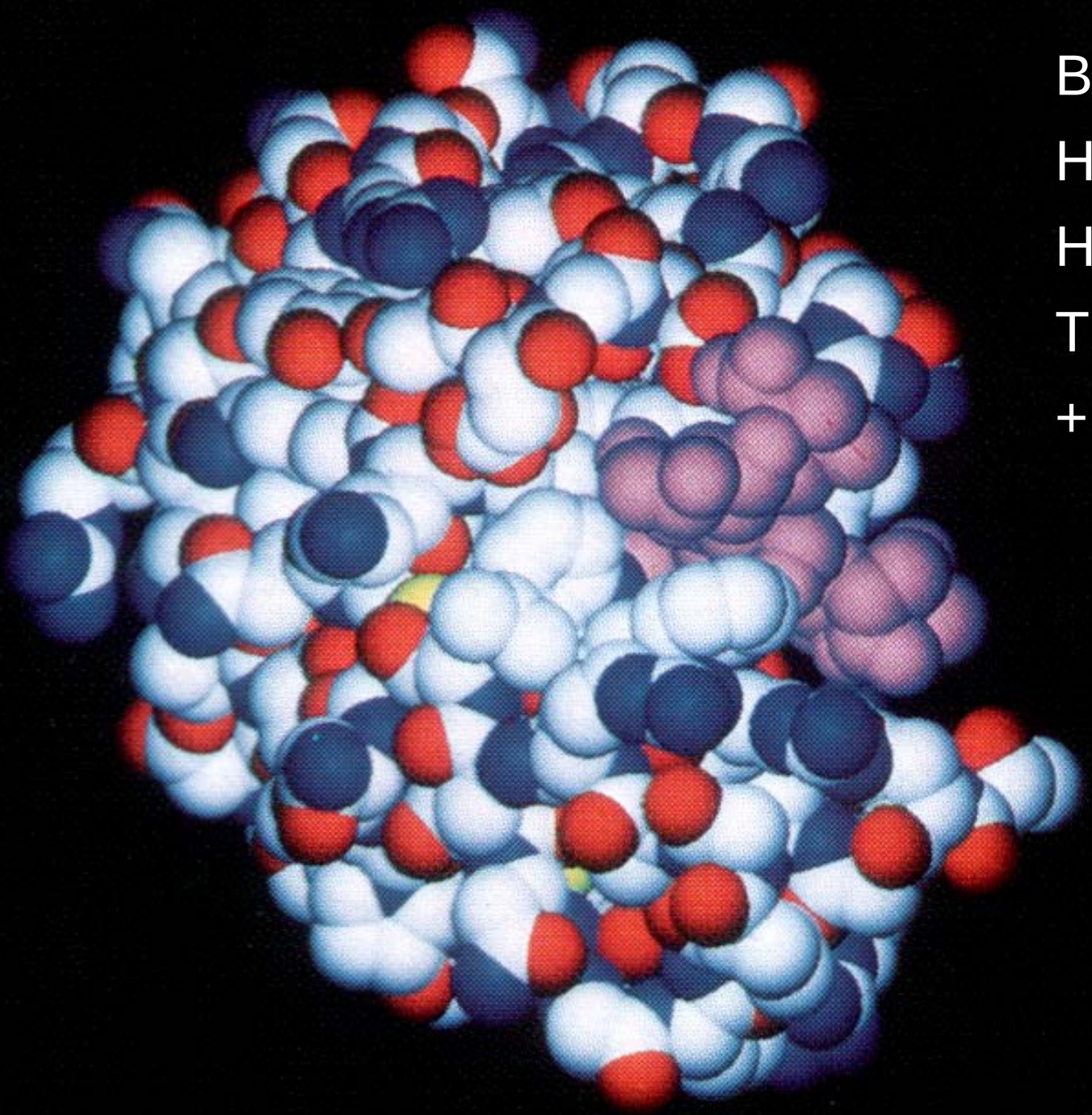
各個 domain 可能由同一原始基因所演化

Gene duplication

Alberts et al (2002) Molecular Biology of the Cell (4e) p.1382

Mathews et al (2000) Biochemistry (3e) p.246

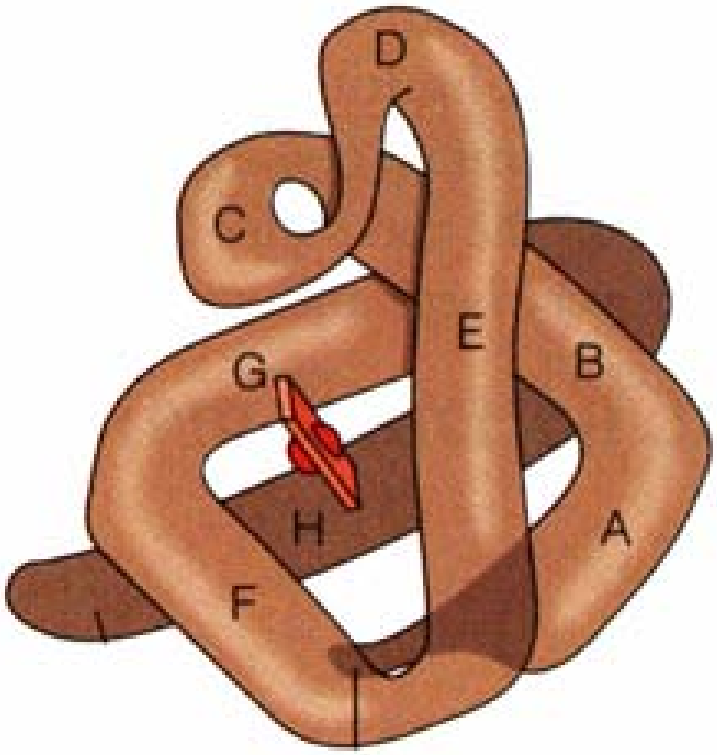
Lysozyme

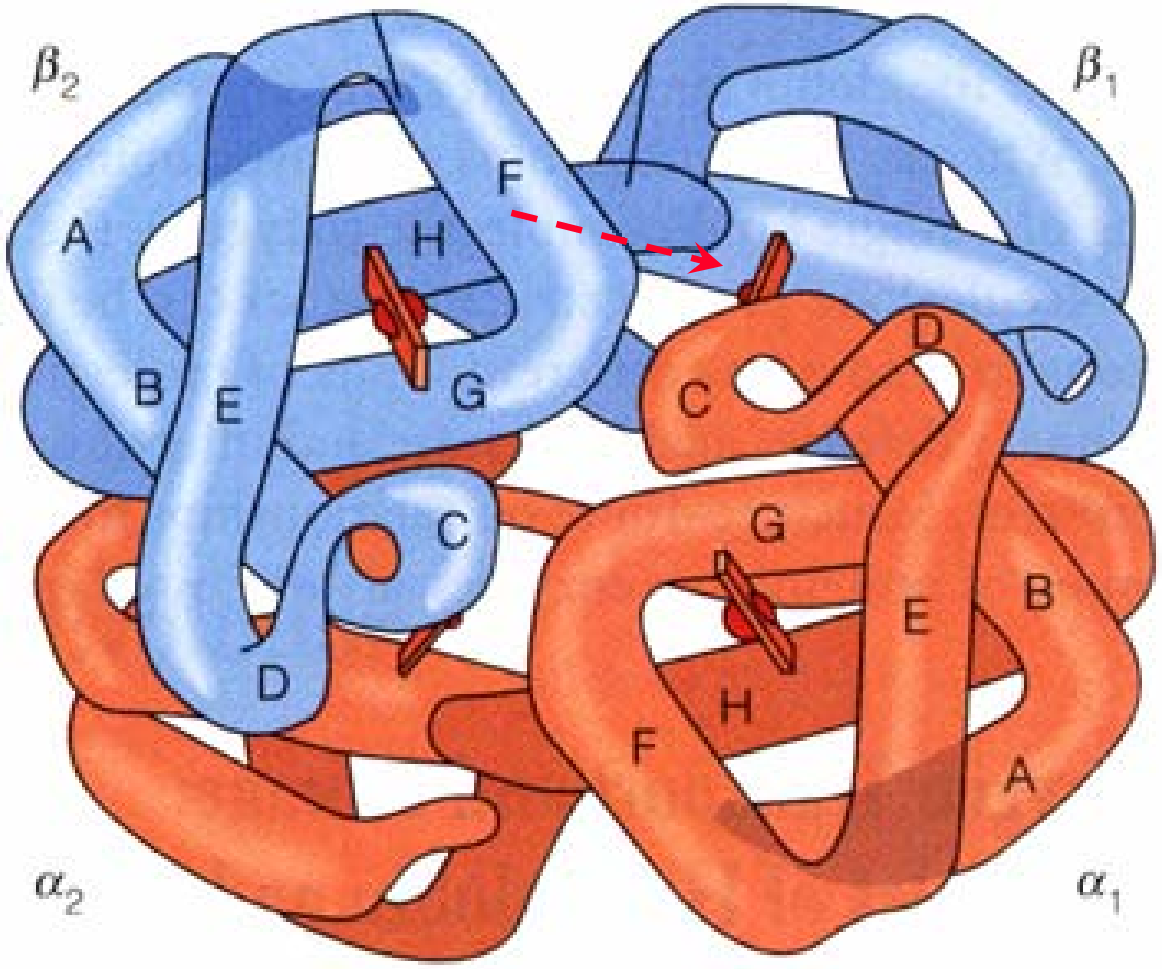


Backbone
Hydrophobic
Hydrophilic
Total
+ substrate

Watson et al. (1987) Mol Biol Gene, Plate 3

四級構造 (Quaternary structure)



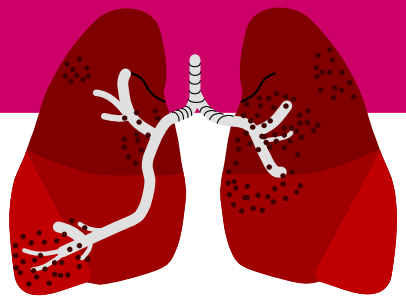


Myoglobin

Hemoglobin

Mathews et al (2000) Biochemistry (3e) p.214

血中氧分子的運送



任何一個次体接受氧分子後，會增進其它次体吸附氧分子的能力

氧分子

Lung

(R)
relaxed state

動 脈

環境氧濃度低時
Hb 迅速釋出氧分子

Muscle

靜 脈

(T)
tense state

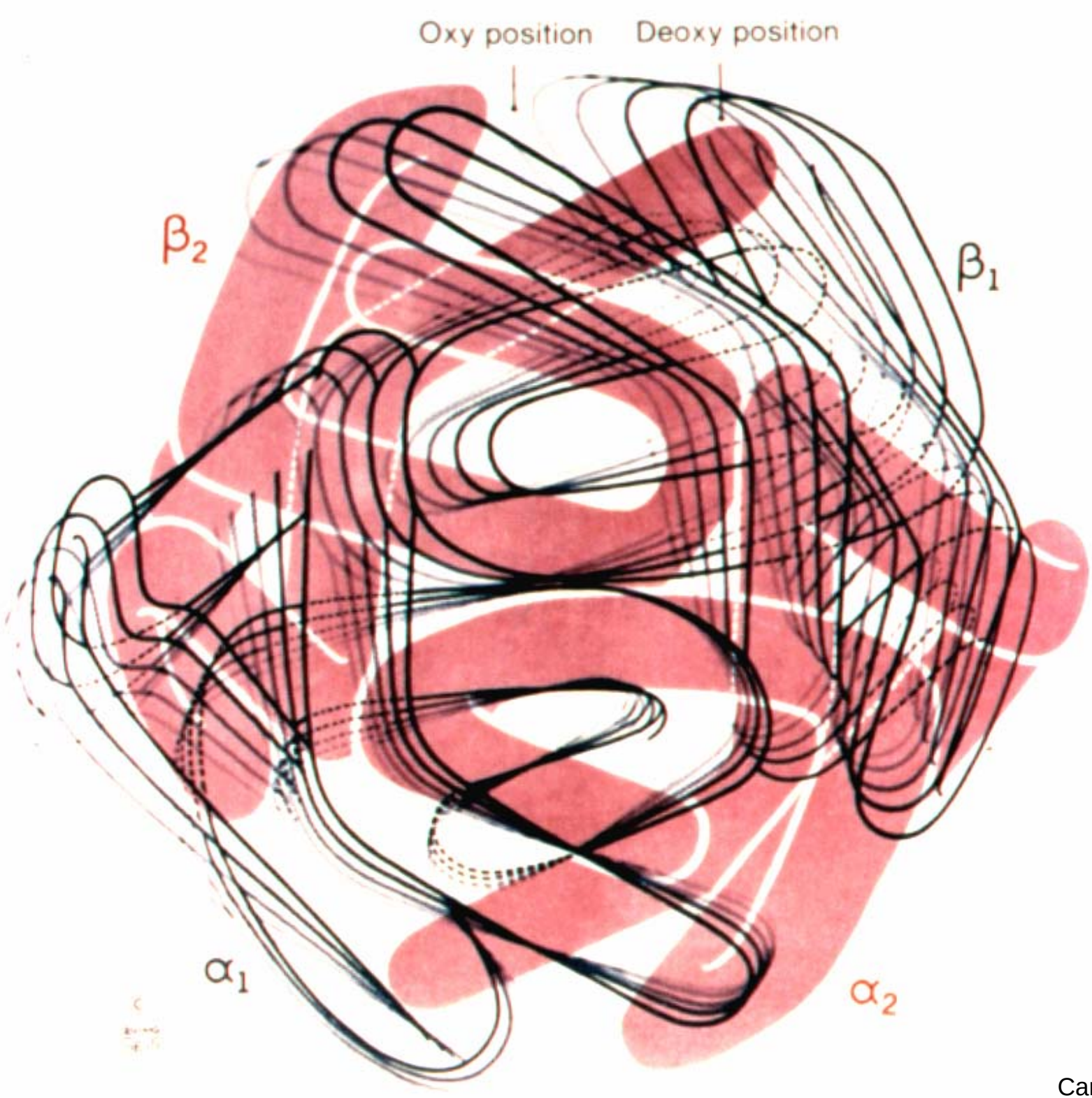
Hemoglobin

Myoglobin

環境氧濃度高時
Hb 快速吸收氧分子

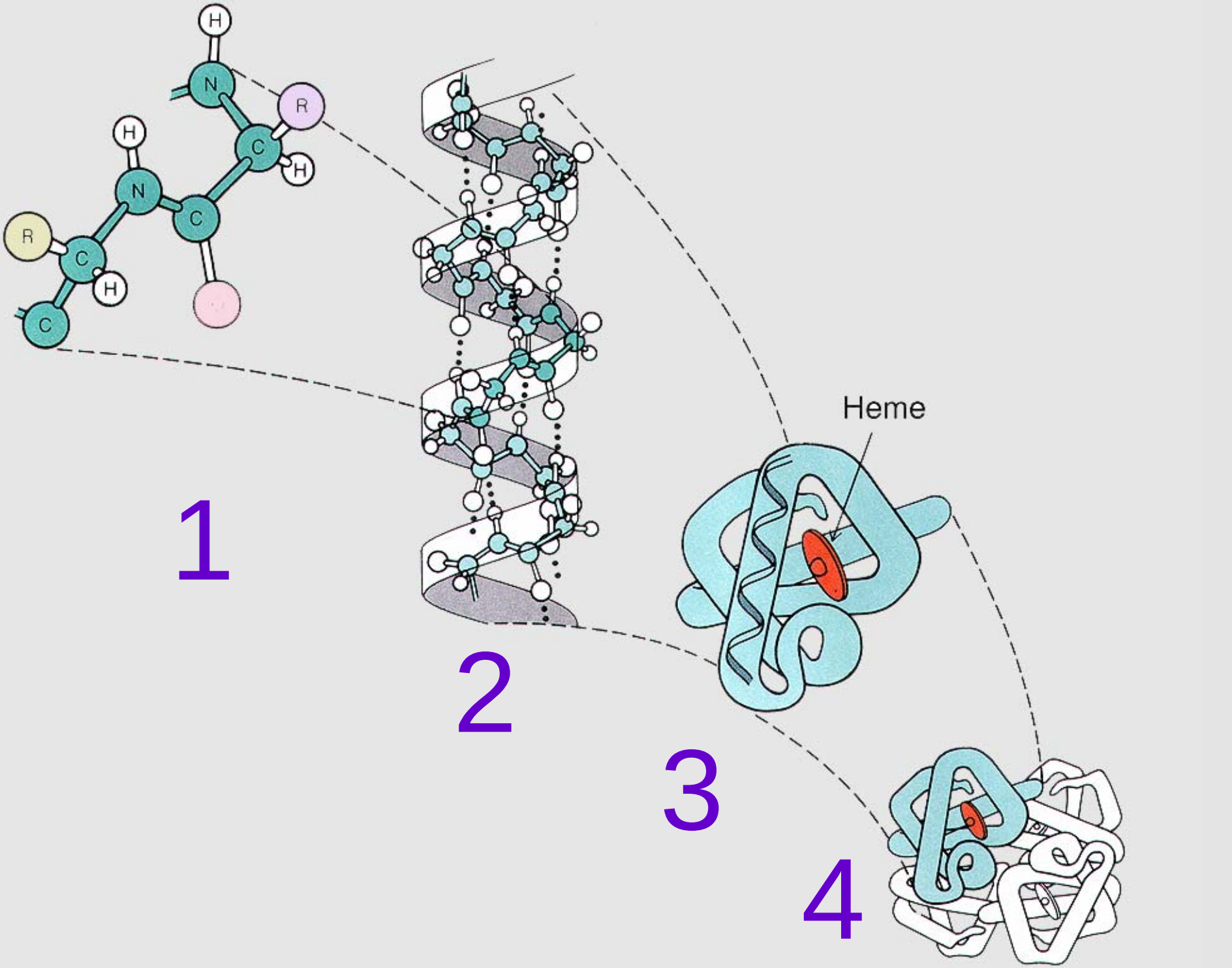
Juang RH (2004) BCbasics

牽一髮動全身 所有次體均受影響



Cartoon by I. Geis

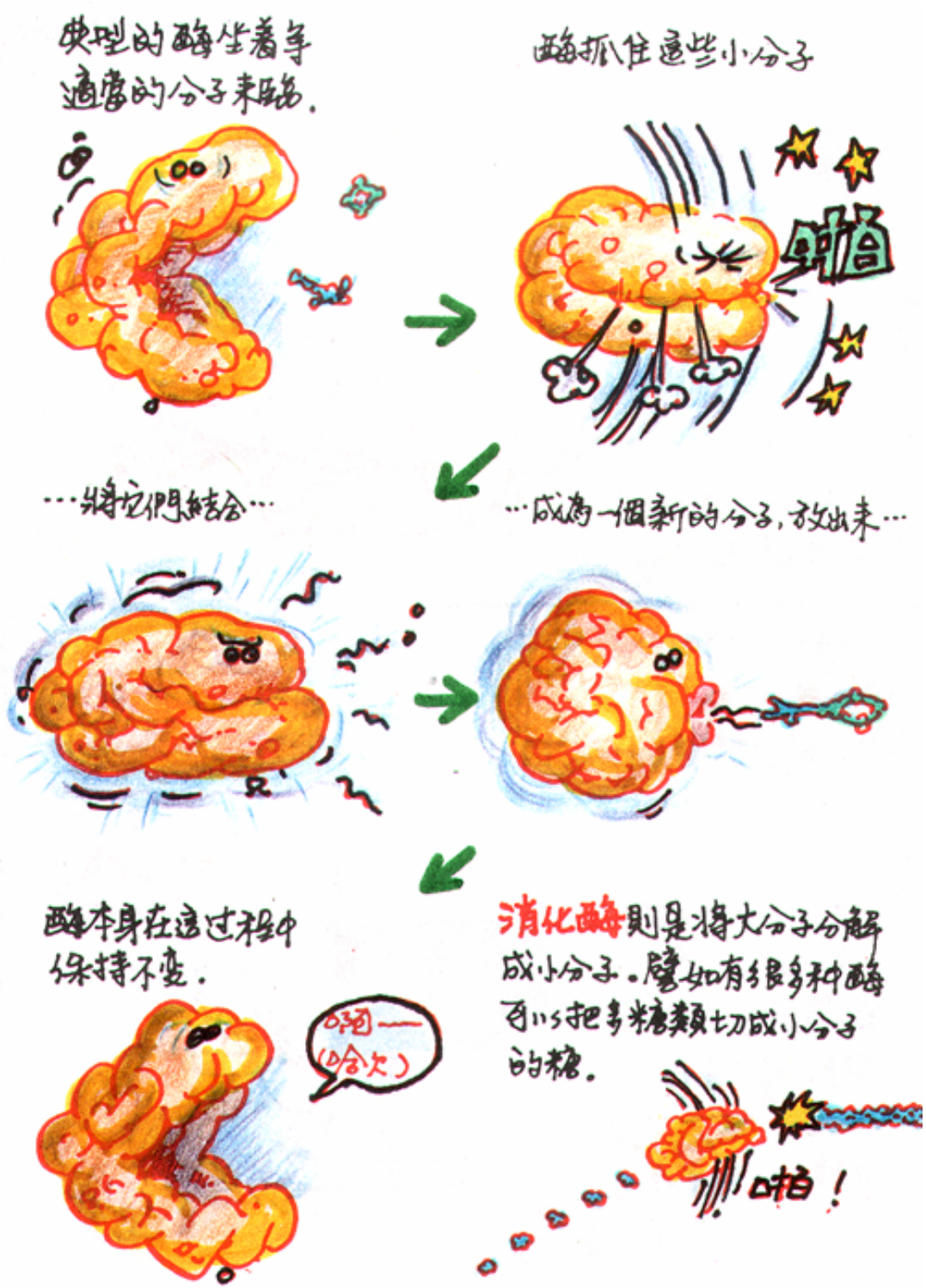
蛋白質的四級構造



Mathews et al (2000) Biochemistry (3e) p.195

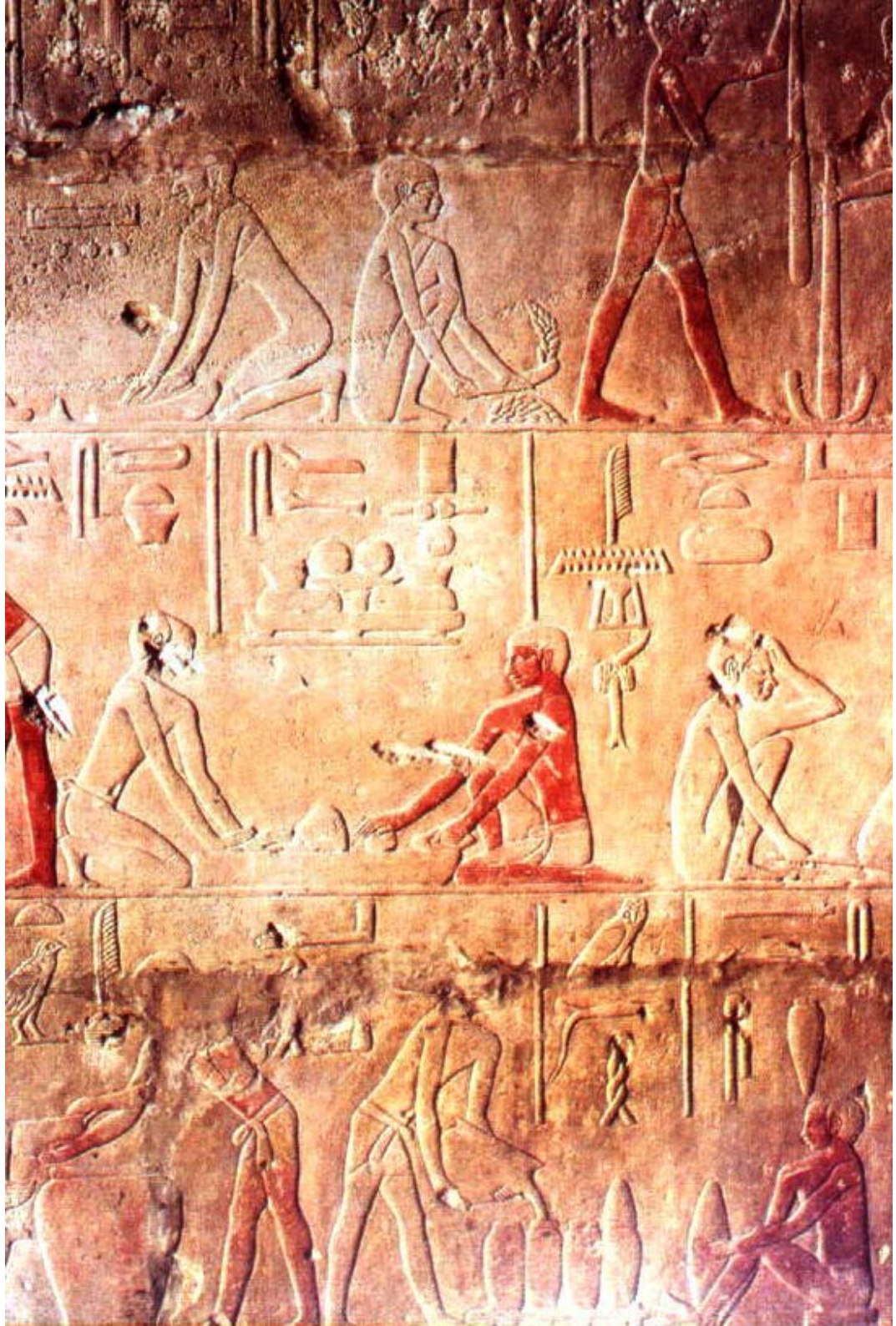
蛋白質的構形不是固定的

Hexokinase



看漫畫學遺傳 (1987) p.112

古埃及人用麥粉釀酵製造啤酒



磨粉 去糠 打碎

麥芽 萌發 浸潤

成酒 釀酵 裝瓶

Discovering Enzyme (1991) p.22

酵素很早就為人類所利用

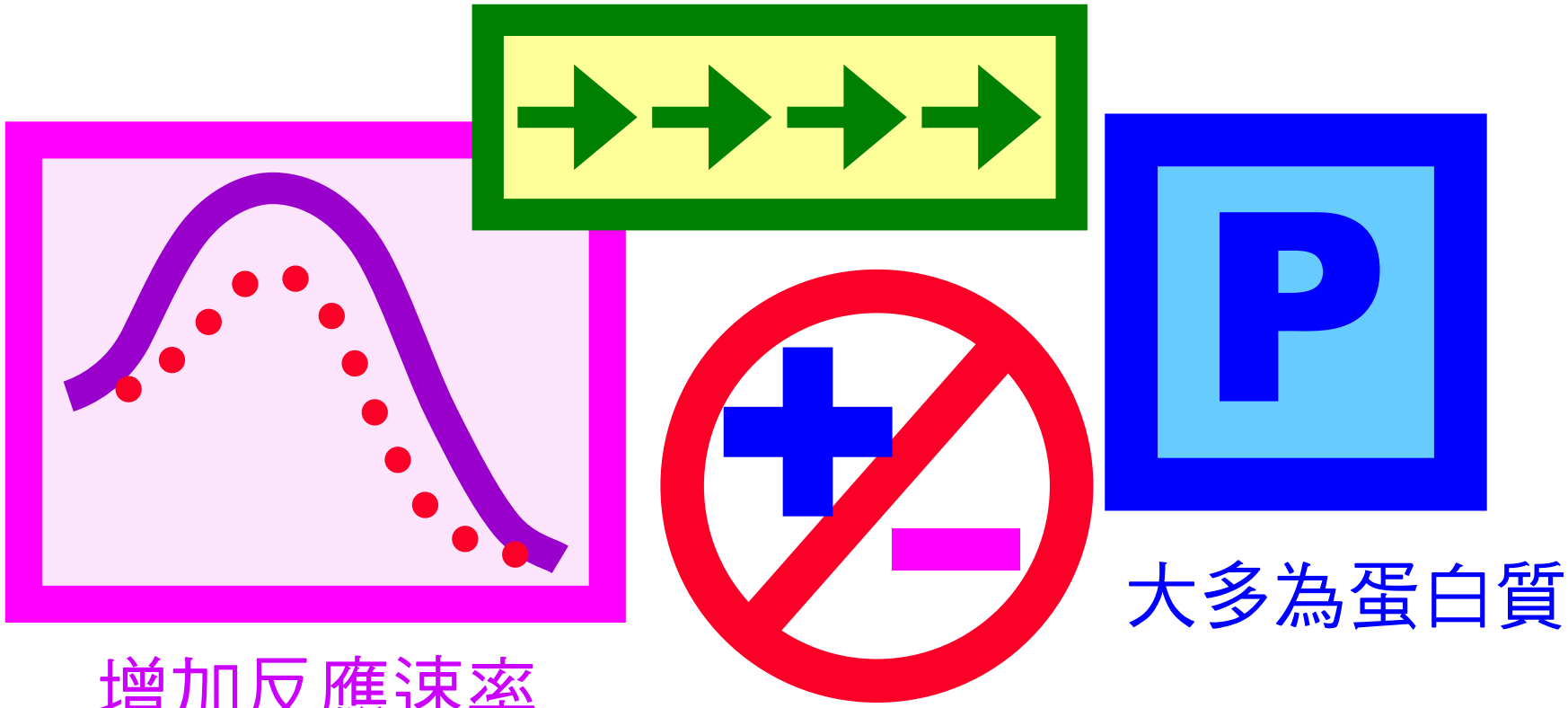
埃及壁畫

神奇轉化力量？ ⇩ 醣解作用產生酒精

■ 1926 *Sumner* 結晶出 urease 可分解尿素

酵素是一種蛋白質

酵素印象



酵素的催化效果

$$2H_2O_2 \longrightarrow 2H_2O + O_2$$ ①

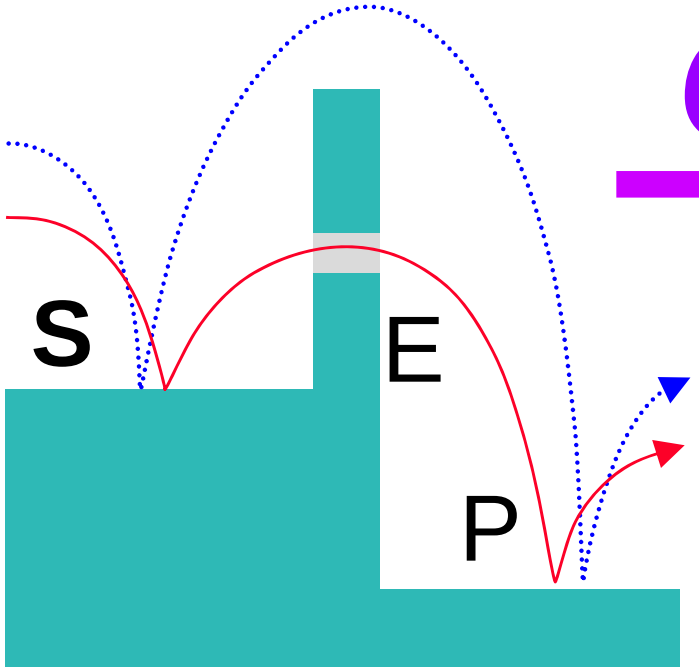
雙氧水裂解

$FeCl_3$ → 1,000

Hemoglobin → 1,000,000

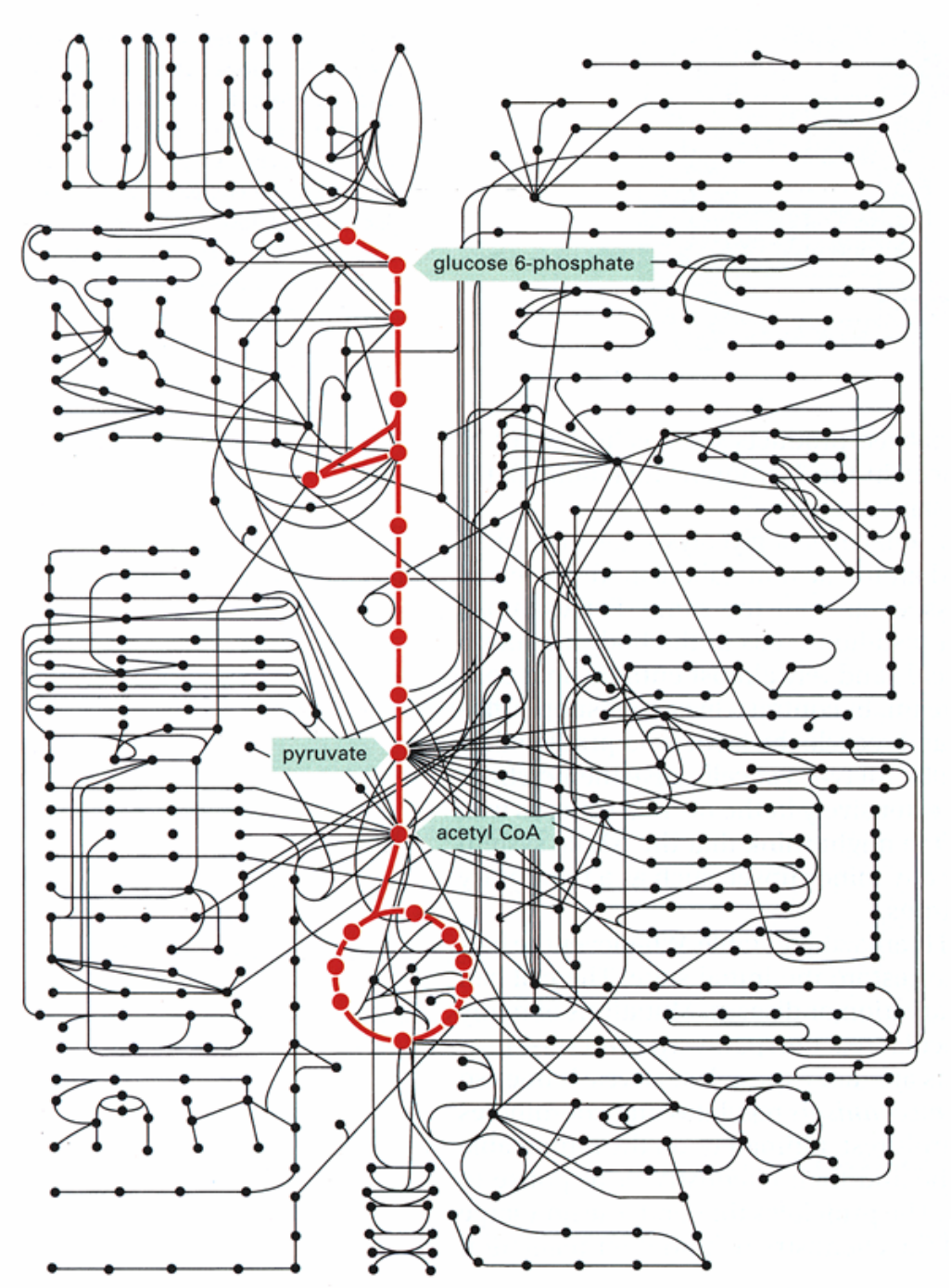
Catalase → 1,000,000,000

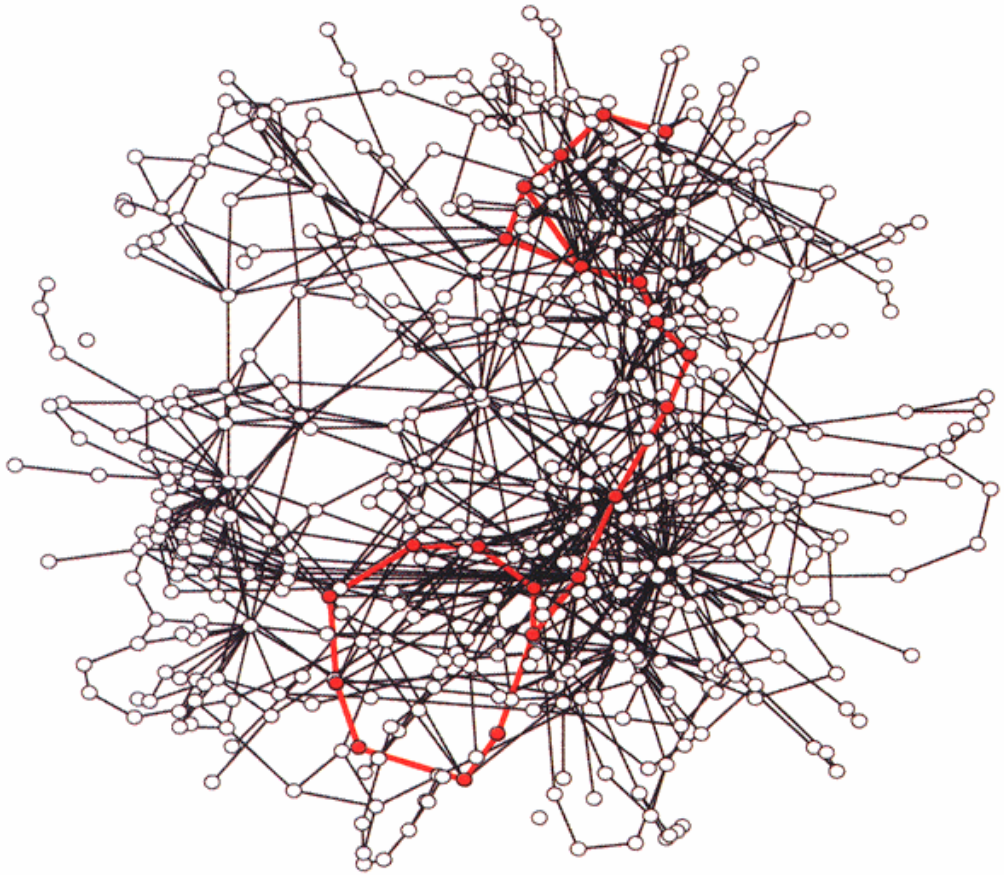
反應速率



Juang RH (2004) BCbasics

酵素參與細胞所有代謝路徑

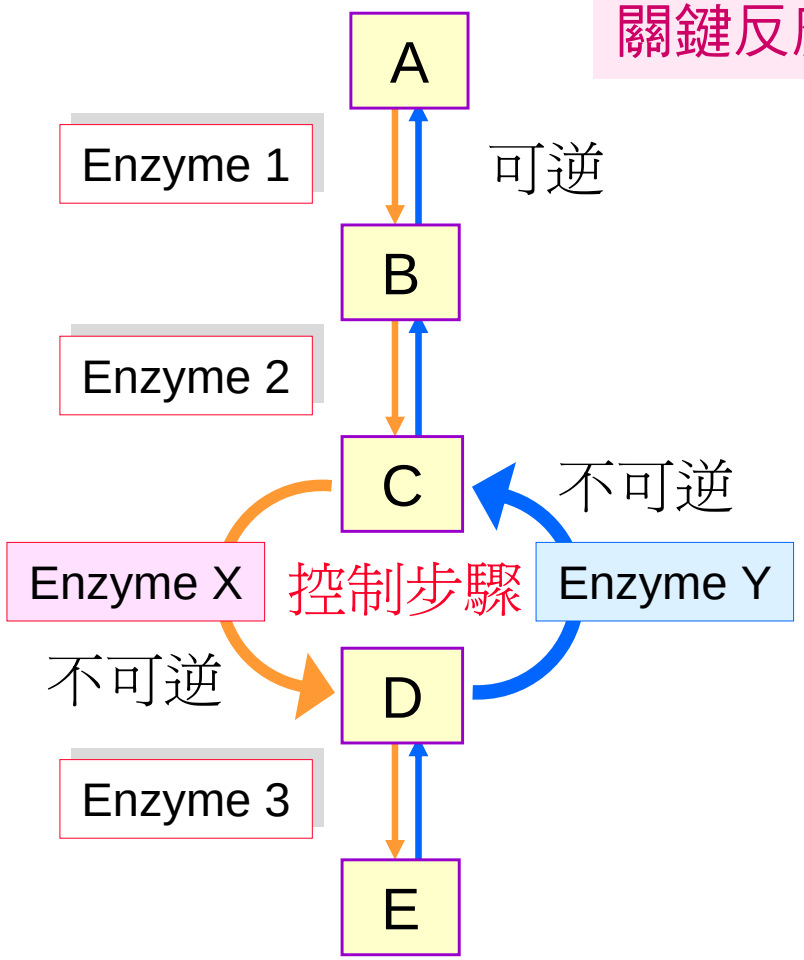




Alberts et al (2002) Molecular Biology of the Cell (4e) p.107

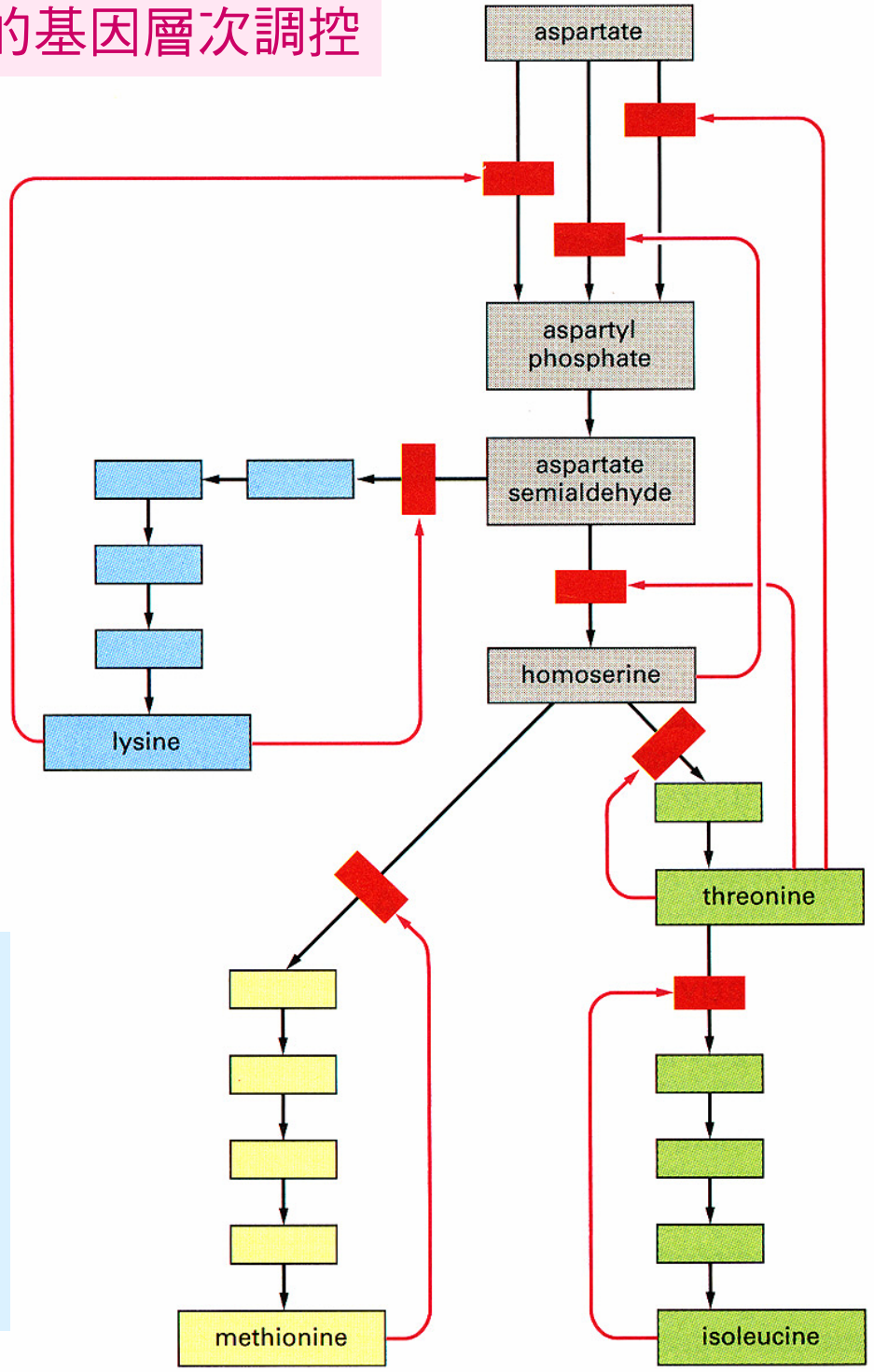
代謝路徑調控原則

關鍵反應的基因層次調控



(1) 每一步反應均有酵素催化
(2) 代謝路徑有速率決定步驟
(3) 反應可能為可逆或不可逆
(4) 各條代謝路徑之間可互通

Yang Cycle (楊祥發發現植物乙烯合成路徑)



Alberts et al (2002) Molecular Biology of the Cell (4e) p.173

蛋白質四級構造的意義

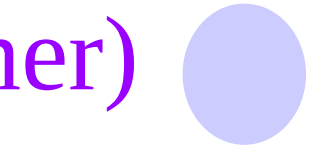
一級構造 (胺基酸序列)

↓

二級構造 (α helix, β sheet)

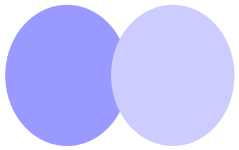
↓ *Domain* (區塊 ααββ)

三級構造 (monomer)



↓

四級構造 (dimer)



構 形

序列

↓

有形体？ → 構形

↓

活性

↓

有生命？ → 活性

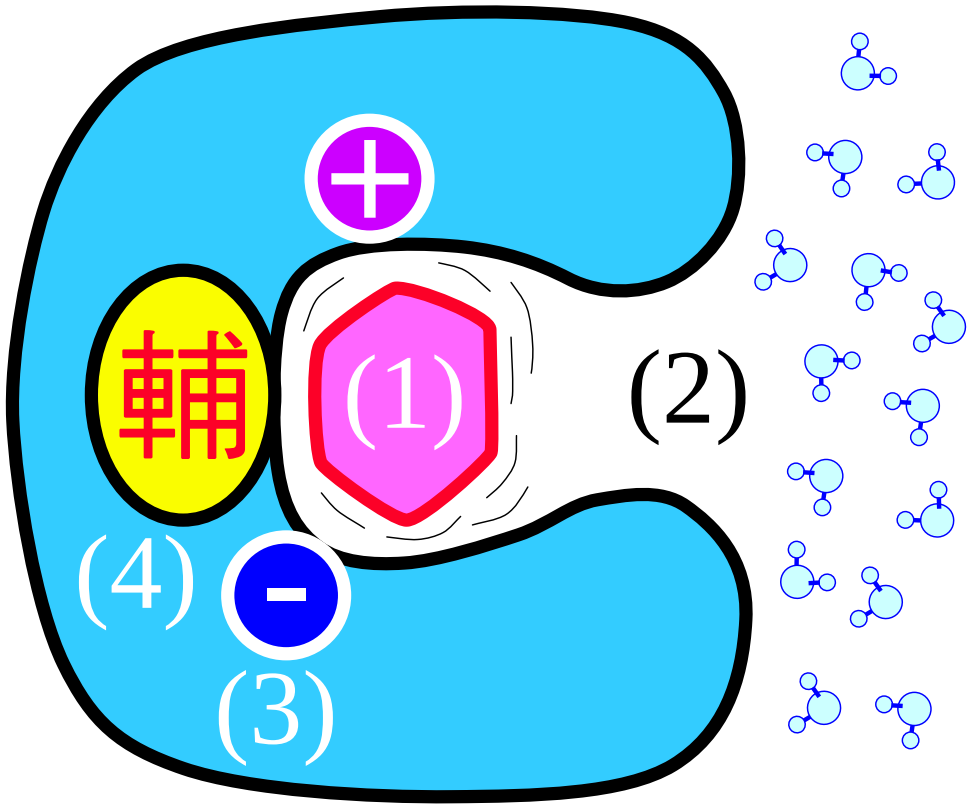
↓

有智慧？ → 調節

Juang RH (2004) BCbasics

酵素活性區是一個凹陷的口袋

酵素活性區為何可降低活化能？



是一個魔術口袋

(1) 可穩定過渡狀態

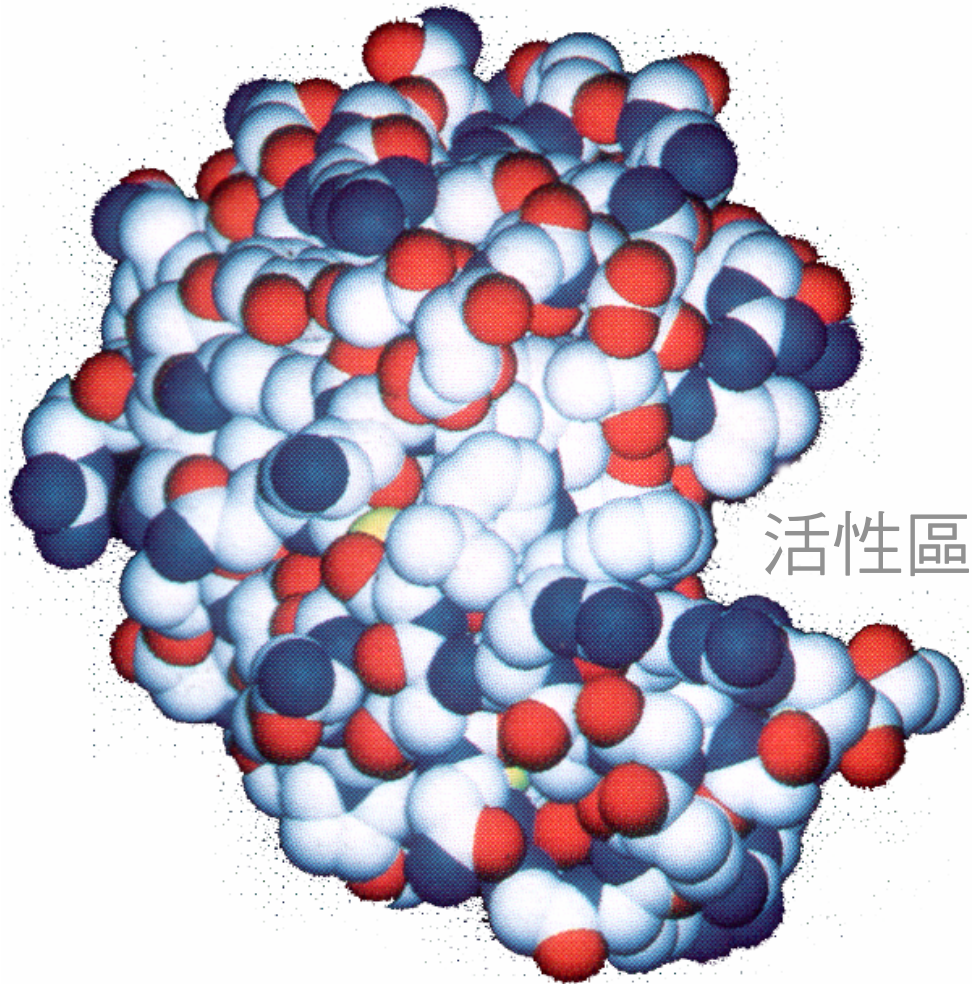
(2) 防止水分子干擾

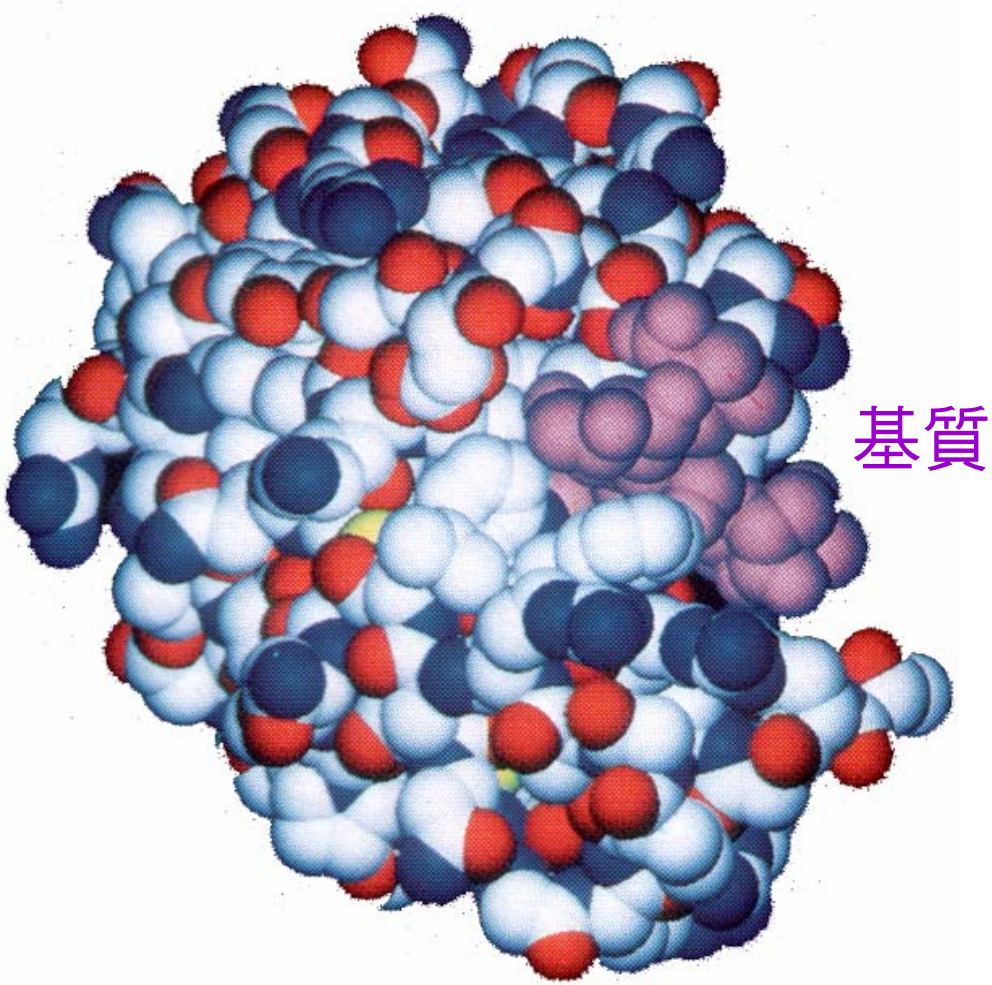
(3) 具高反應性基團

(4) 有輔脢幫助反應

Juang RH (2004) BCbasics

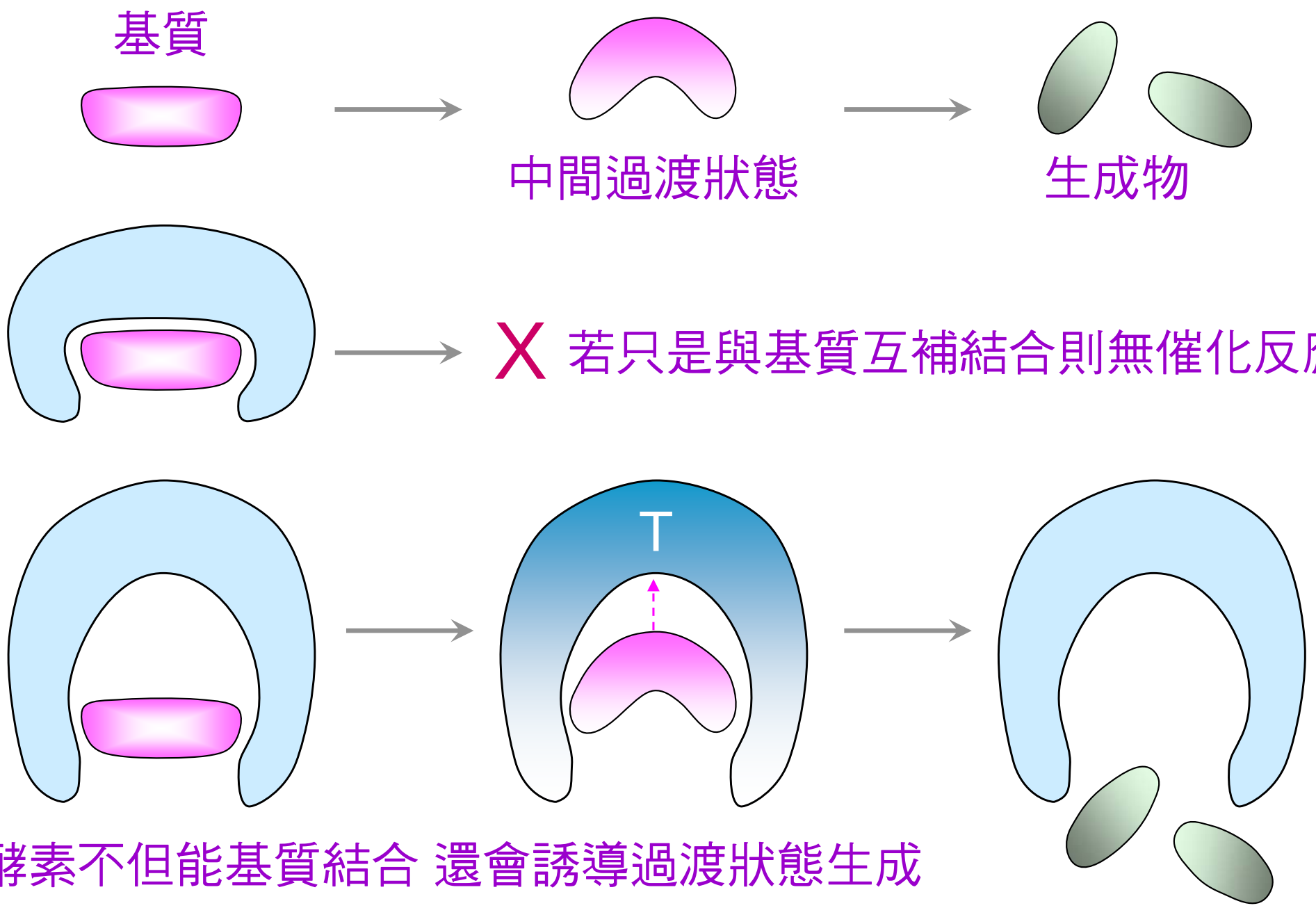
Lysozyme 活性區的口袋





Watson et al. (1987) Mol Biol Gene, Plate 3

棒棒腸 Stickase

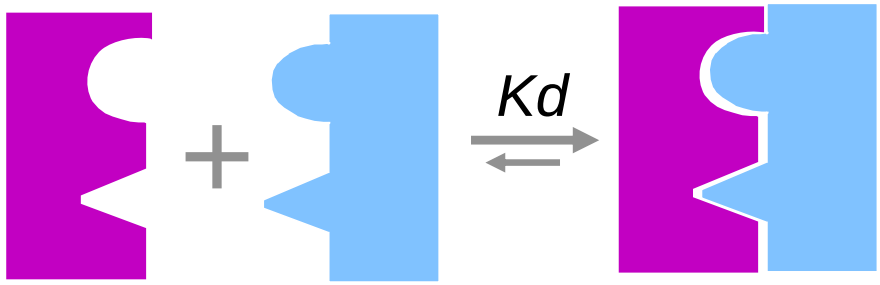


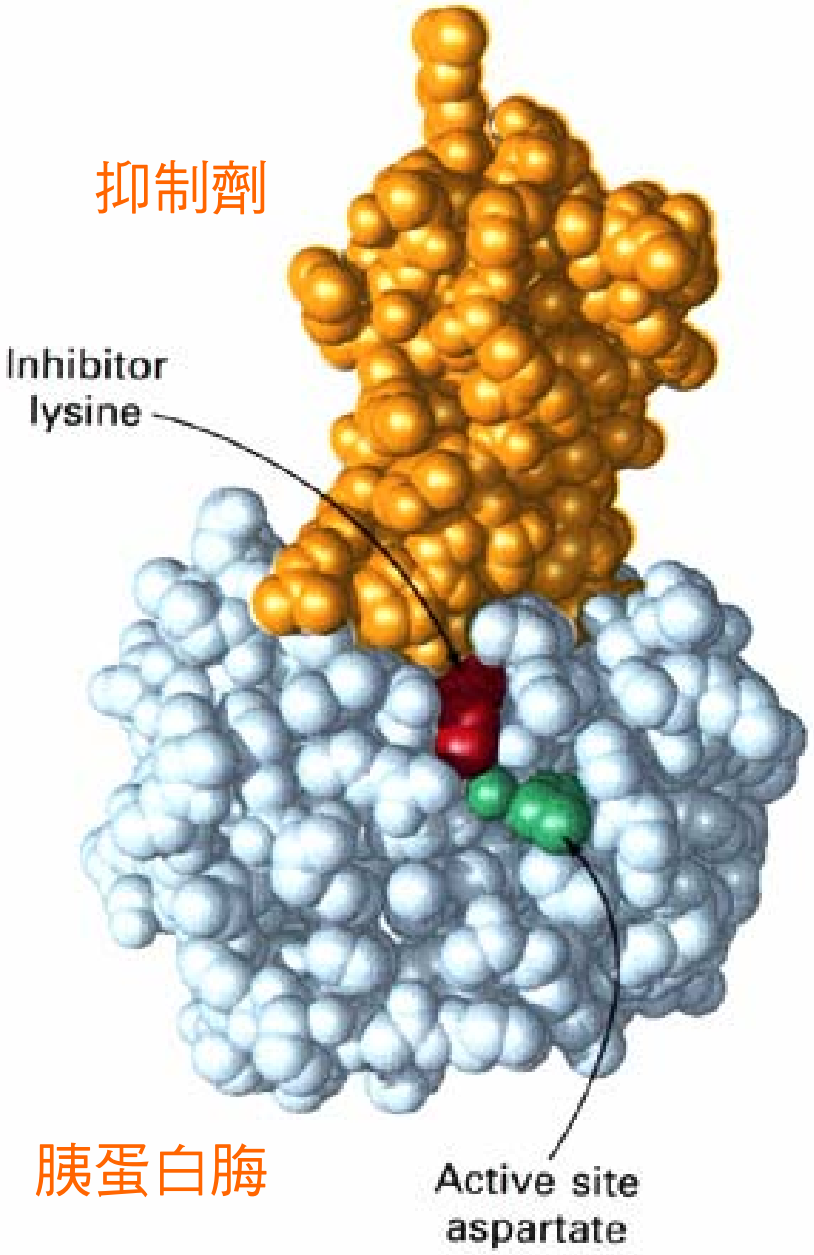
Adapted from Nelson & Cox (2000) Lehninger Principles of Biochemistry (3e) p.252

蛋白質間專一性的形成

I. Conformational Match:

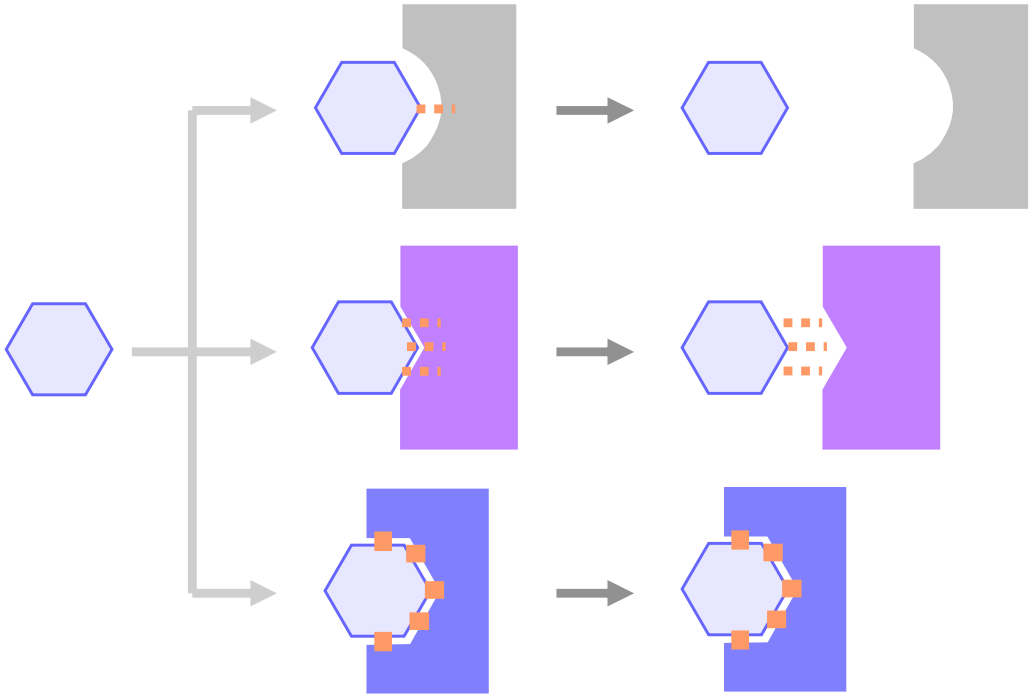
Van der waals interaction





II. Interaction Forces:

(1) Hydrogen bond
(2) Hydrophobic interaction
(3) Electrostatic interaction
(4) Van der waals interaction



Stryer (1995) Biochemistry (4e) p.252

Juang RH (2004) BCbasics

Diabetes Mellitus (1980) Eli Lilly and Company (8e), p.20-21