# 生物化學基礎

細胞與分子 → 胺基酸

蛋白質 → 酵素

核酸

1

2

生物技術

構造 → 性質

研究技術

- 1 生命源起
- 2 細胞的生物化學：
  - 2.1 原核細胞
  - 2.2 古生菌
  - 2.3 真核細胞
- 3 細胞分子：
  - 3.1 水與 pH
  - 3.2 細胞的組成分子
  - 3.3 分子間的作用力： 二級鍵

大 霹 靂

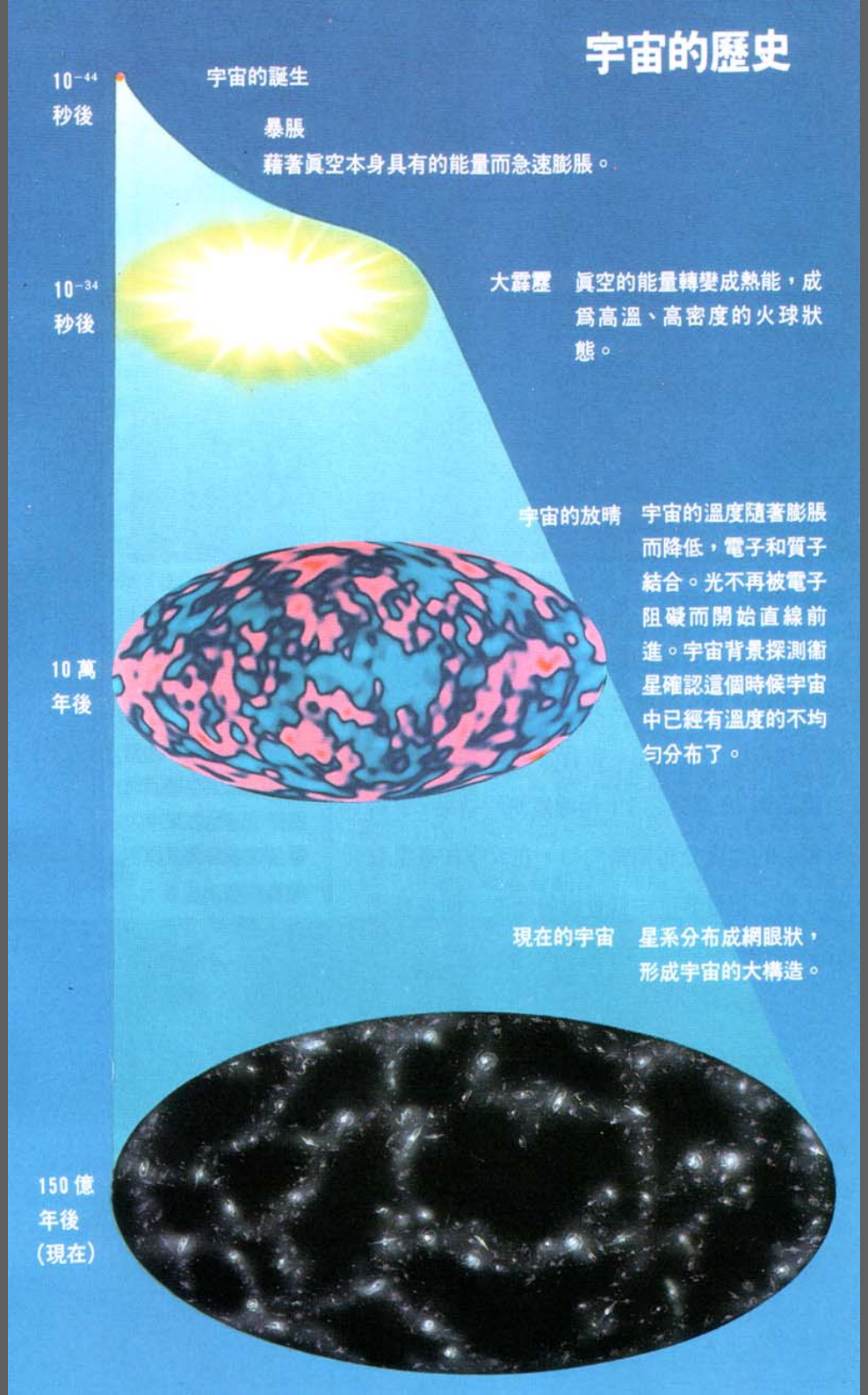
牛頓雜誌 (1994) 第 132 期, p.20

$10^{-44}$ sec

$10^{-34}$ sec

10 萬年

135 億年




大霹靂

大渾沌

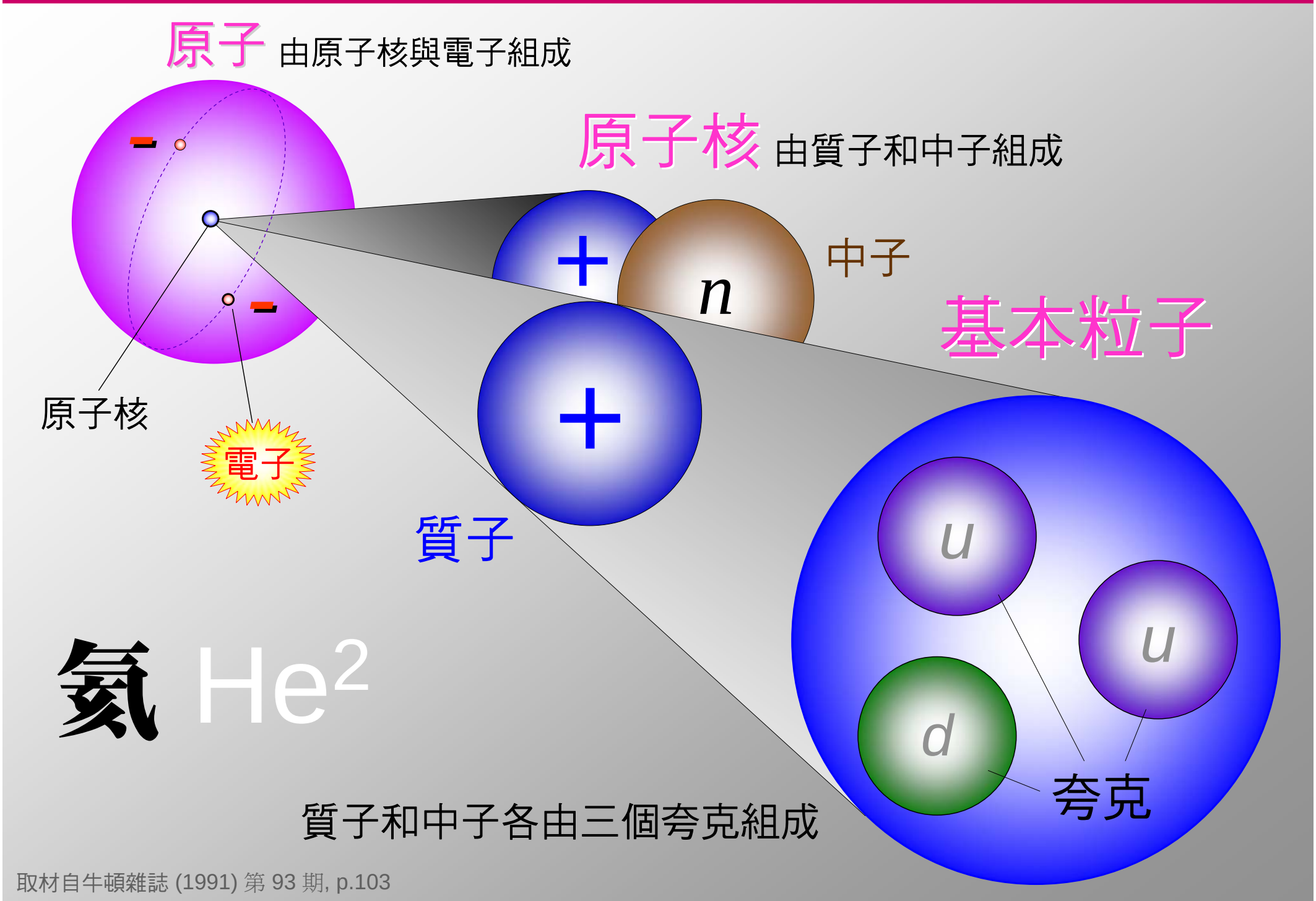
宇宙放晴

現在的宇宙

肥皂泡模型

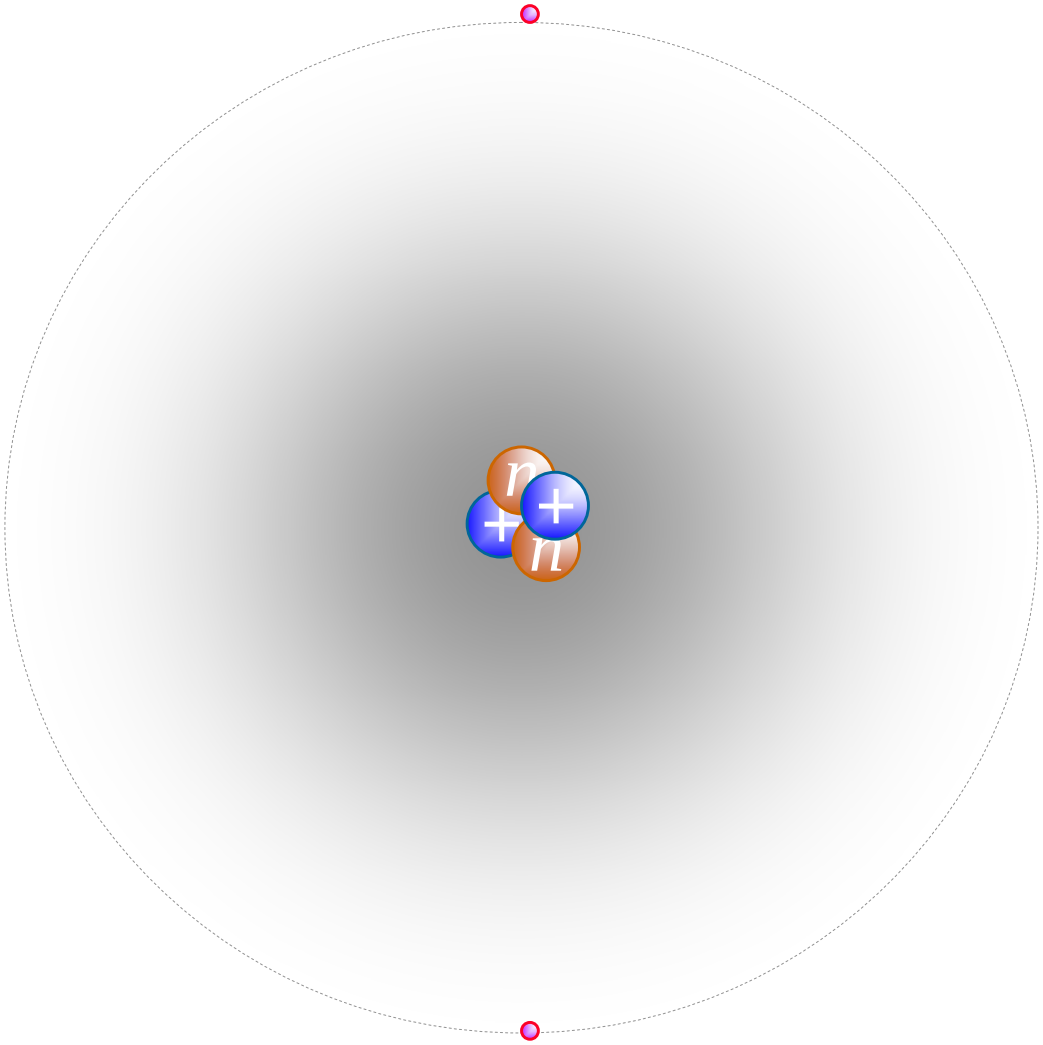
牛頓雜誌 (1994) 第 129 期, p.116

# 由基本粒子到原子




取材自牛頓雜誌 (1991) 第 93 期, p.103

氦 $He^2$




氫 $H^1$

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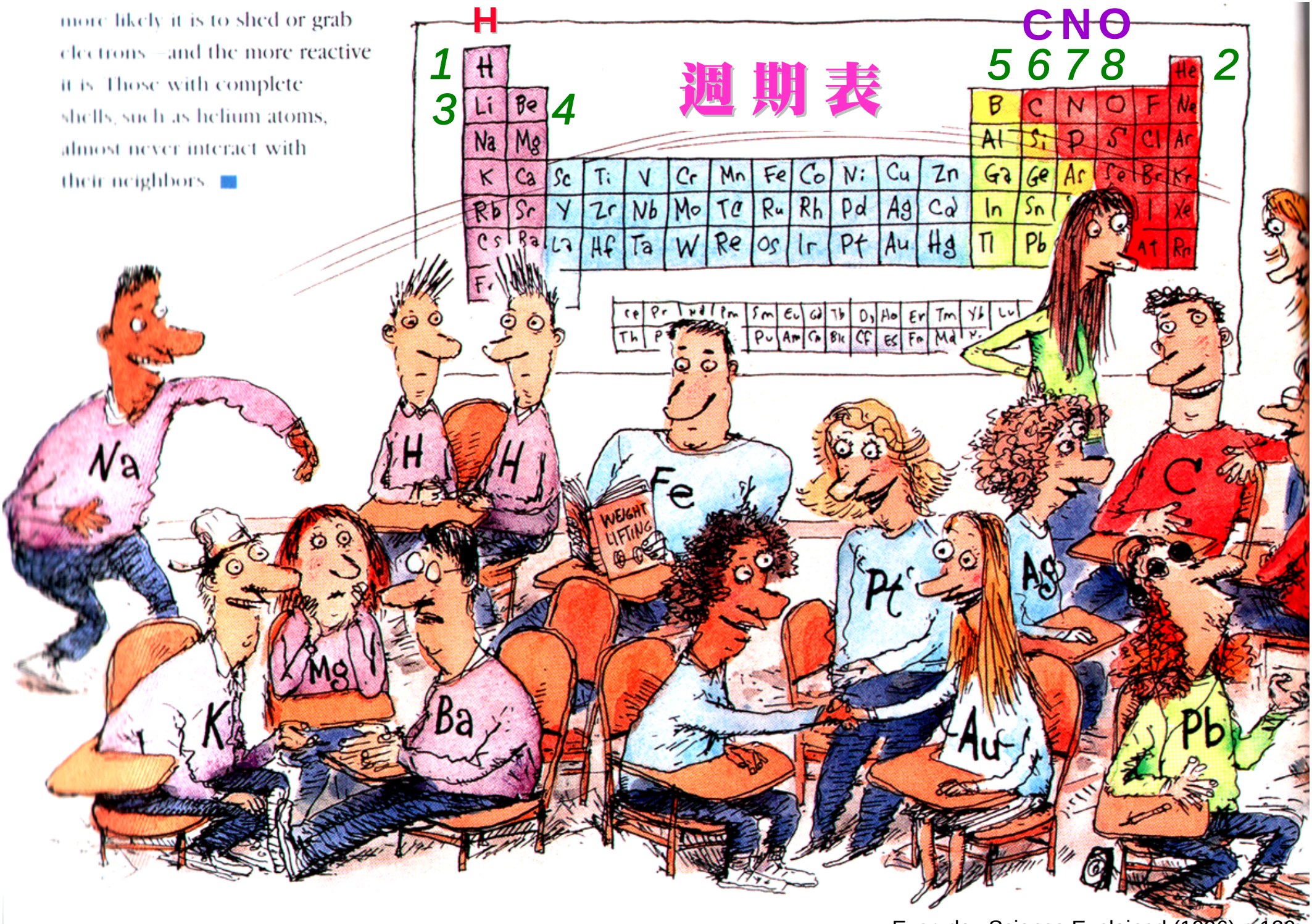
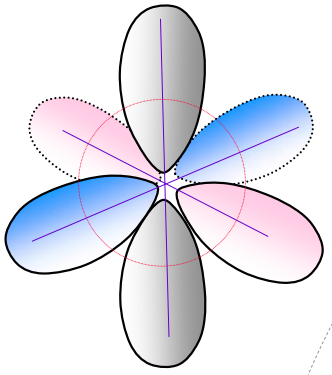
more likely it is to shed or grab electrons—and the more reactive it is. Those with complete shells, such as helium atoms, almost never interact with their neighbors. ■

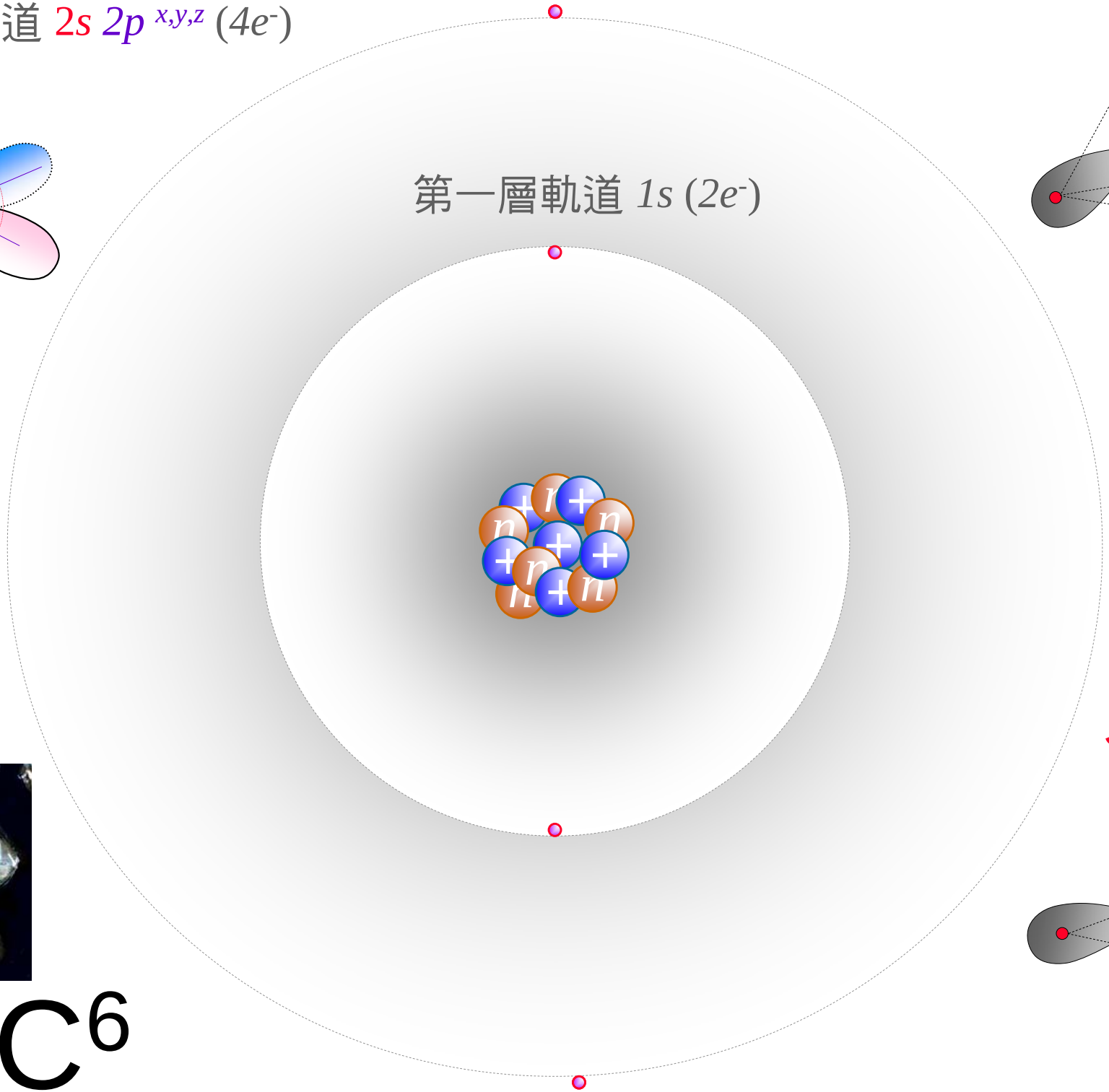



Everyday Science Explained (1996) p.130

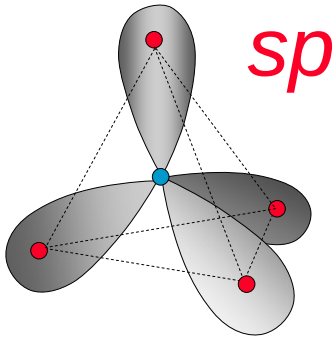
第二層軌道 $2s\ 2p^{x,y,z}$ ($4e^-$)



第一層軌道 $1s$ ($2e^-$)

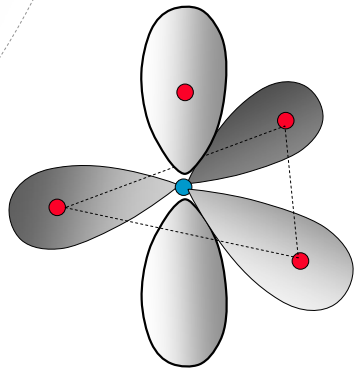


$sp^3$



混成軌道

$sp^2 + p$



Wikipedia

碳 $C^6$

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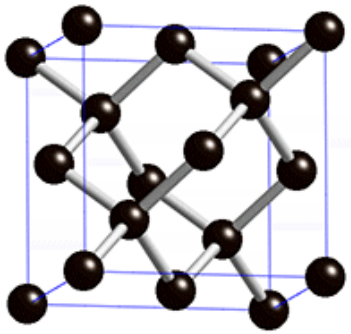
# 混成軌道 (4 個外層電子)

$sp^3$

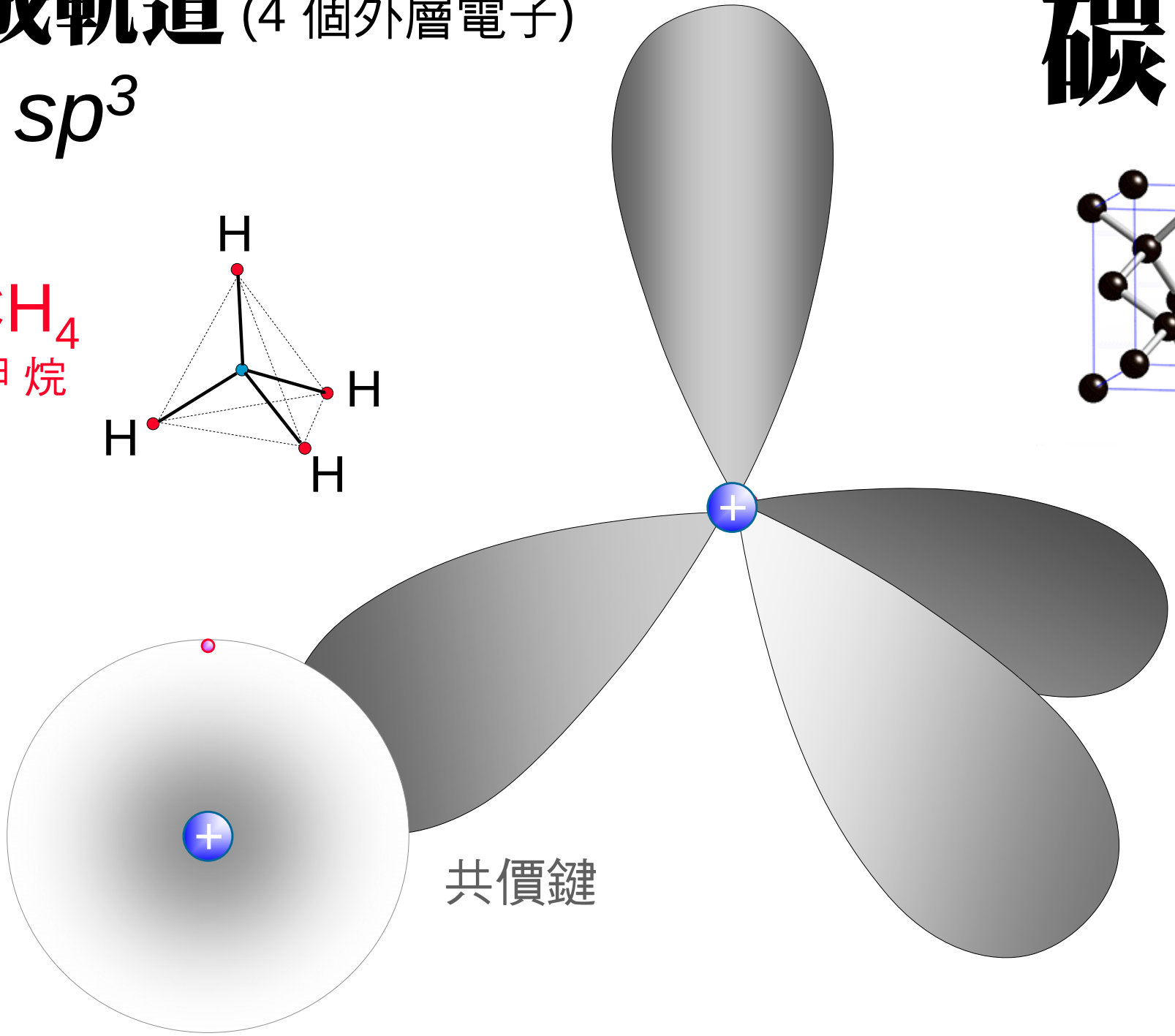
# 碳 $C^6$

$CH_4$
甲 烷



Wikipedia

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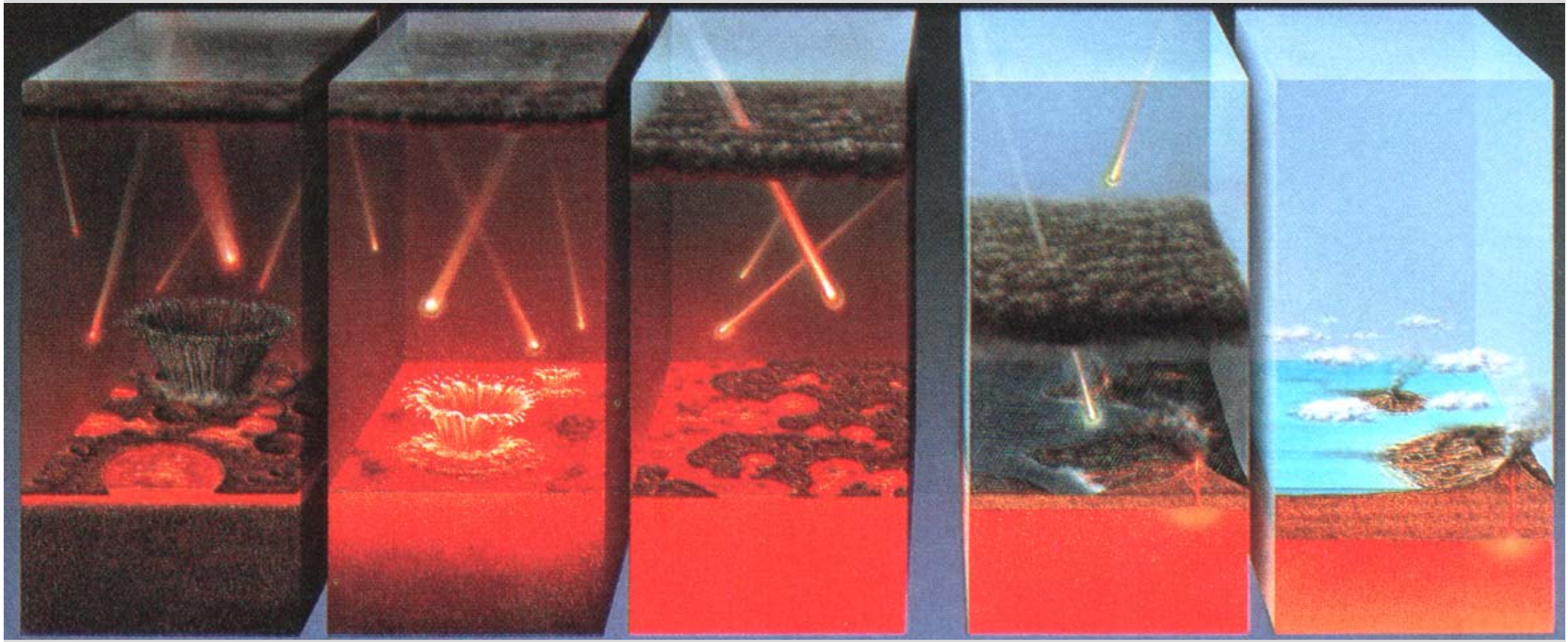
# 地球早期演進的重要關鍵

地球只有薄薄一層地殼是冷的

小行星碰撞　岩漿海　地殼形成　第一場大雨　天空放晴

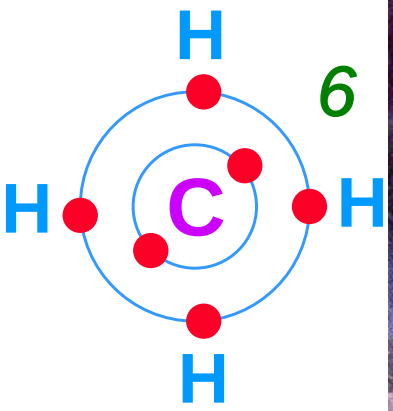


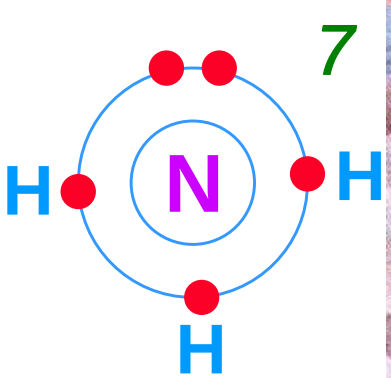
46 億年前　38 億年前

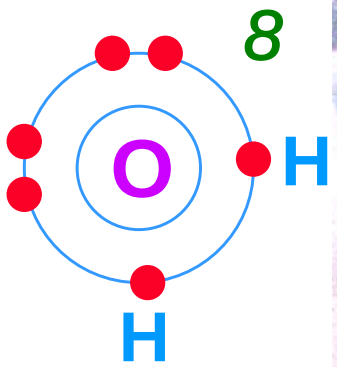
地球上的水分是由殞石帶來的

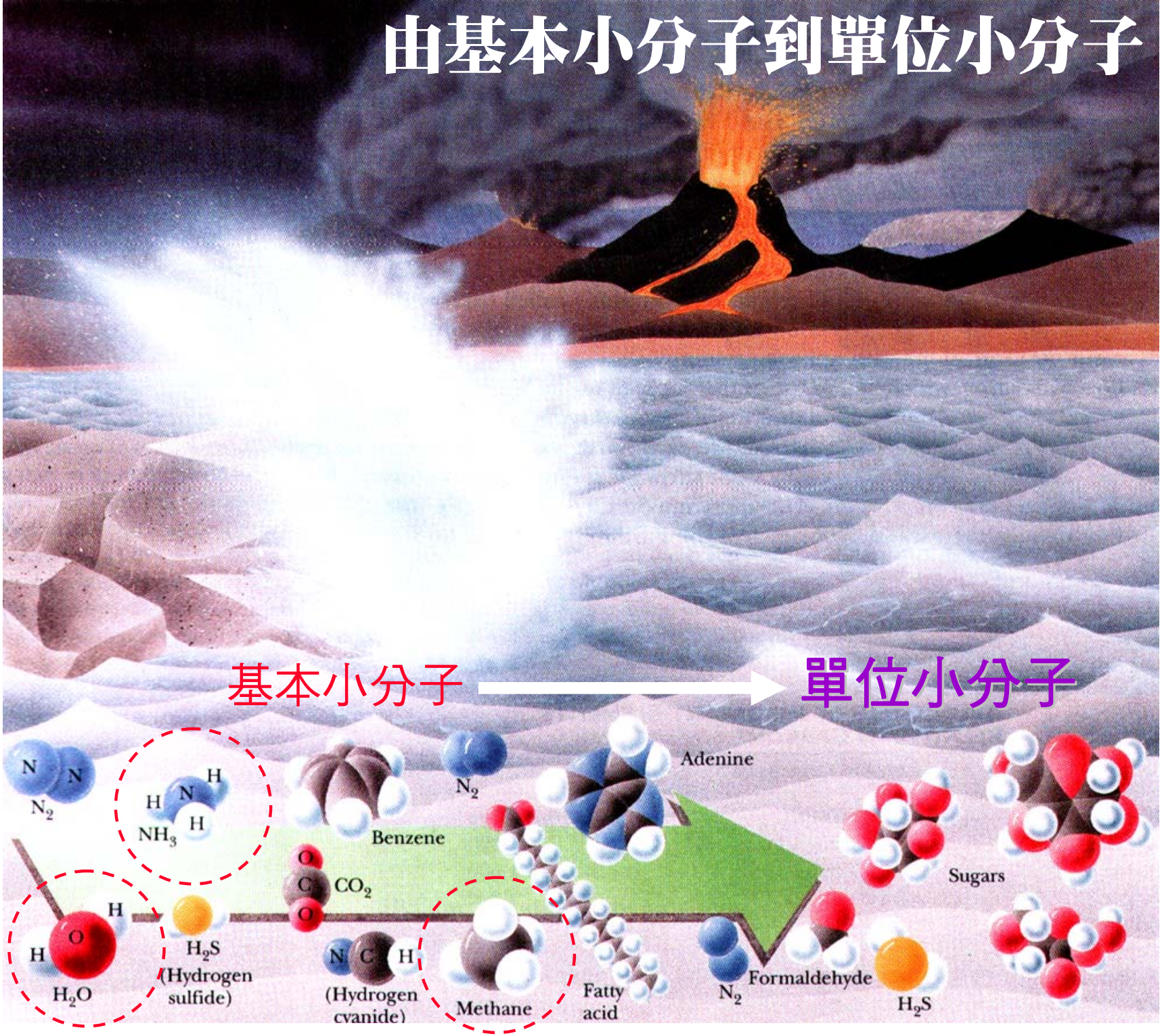
牛頓雜誌 (1994) 第 132 期, p.37

# 由基本小分子到單位小分子



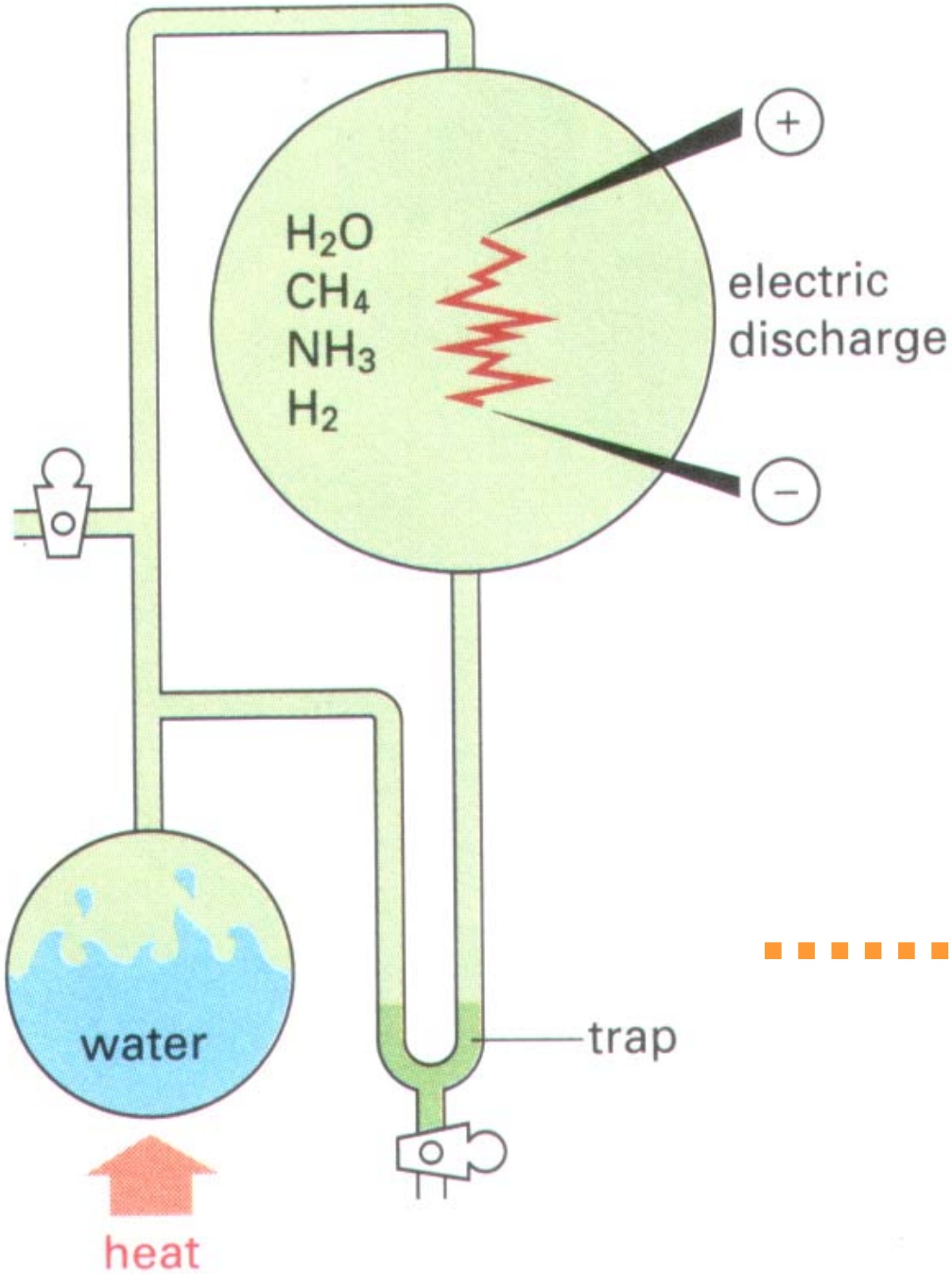



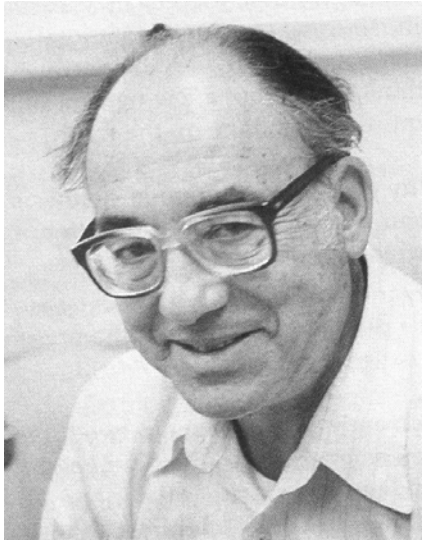




Campbell (1999) Biochemistry (3e) p.16

# 可以在試管中模擬地球初始狀態

Alberts et al (1994) Molecular Biology of the Cell (3e) p.4

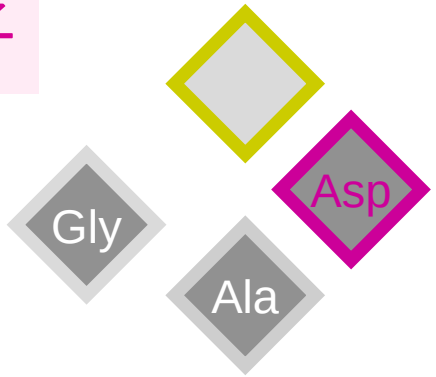


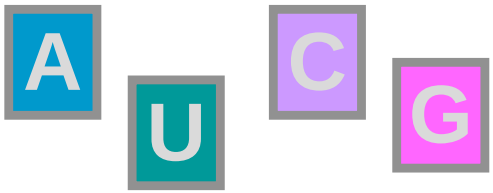
S Miller

單位小分子

胺基酸

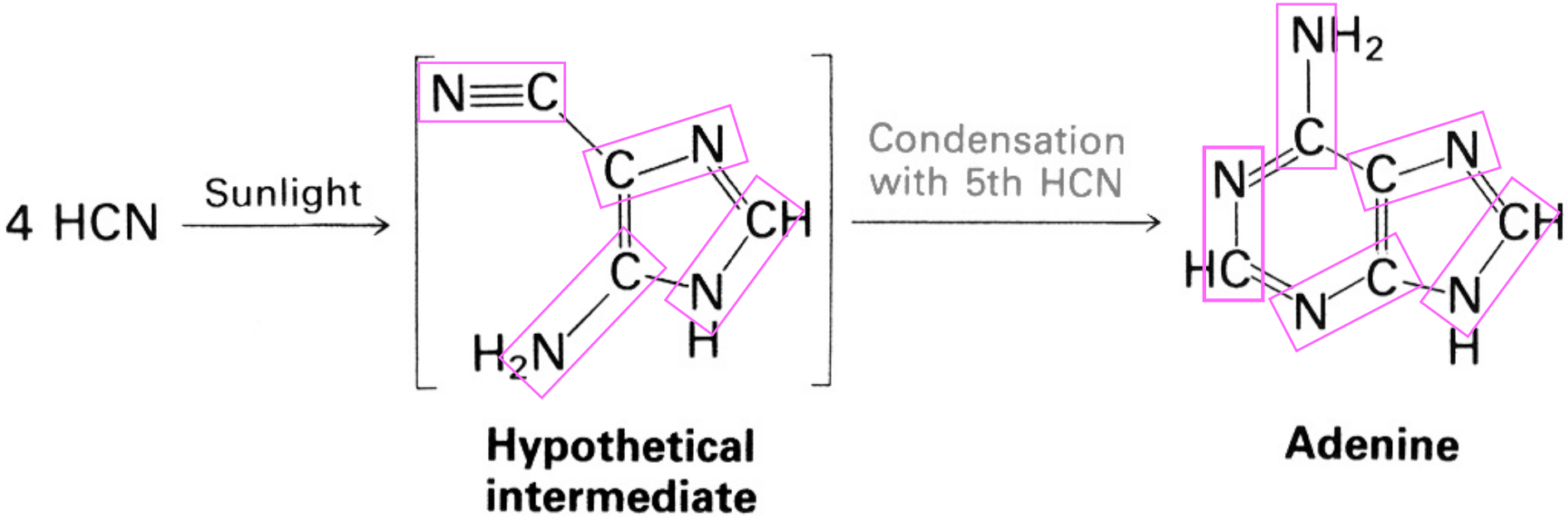



核酸鹼基




Campbell (1990) Biology p.17

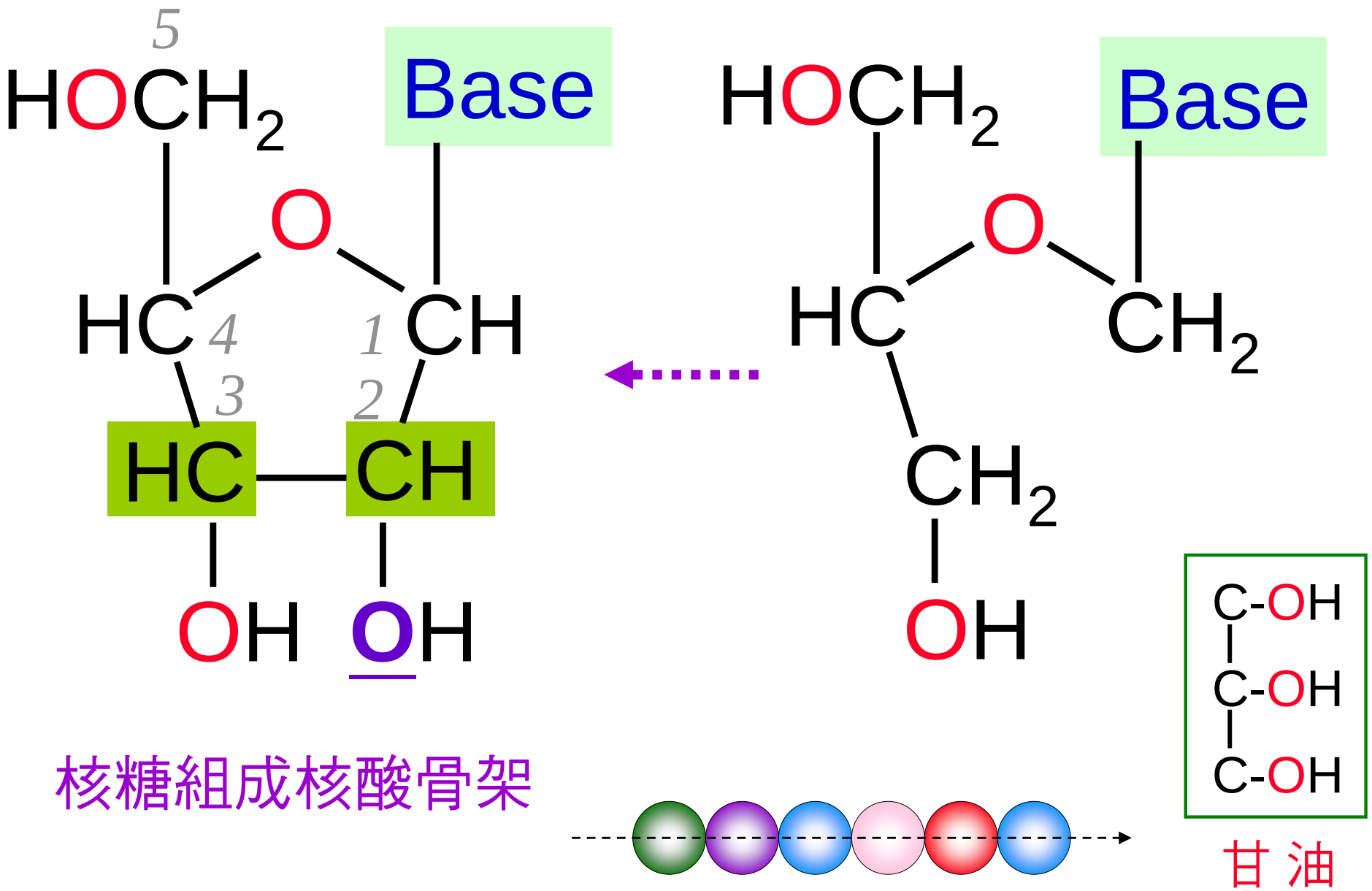
# 鹼基可能由數個 HCN 組成




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

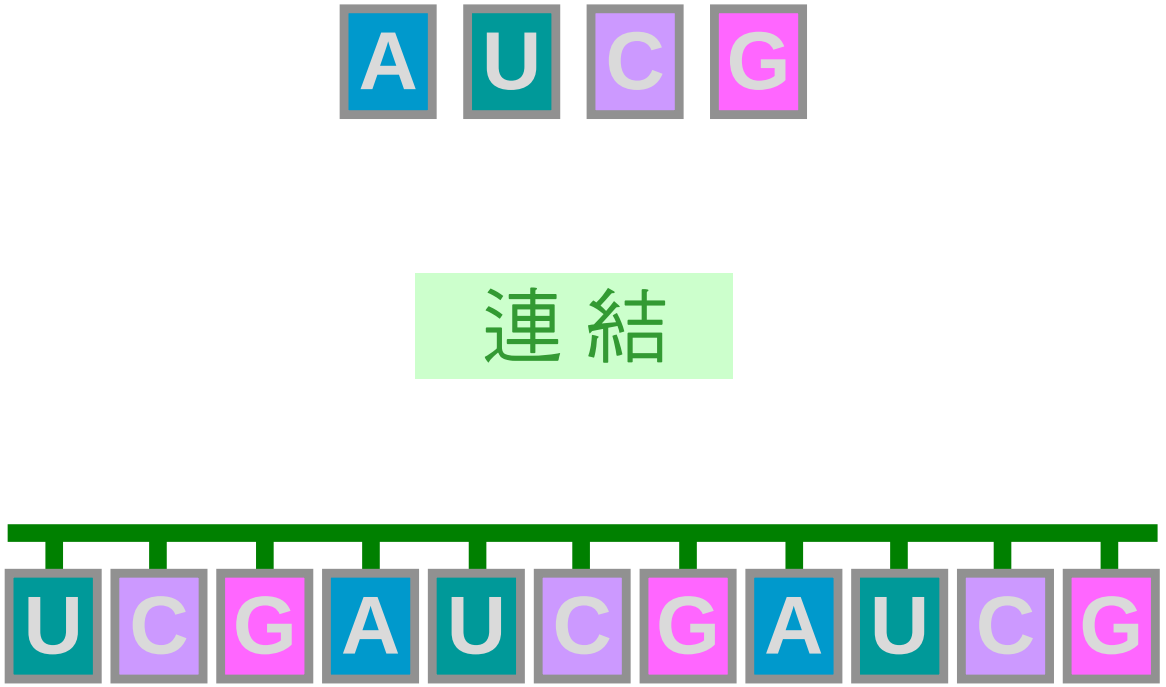
Darnell et al (1990) Molecular Cell Biology (2e) p.1053

# 甘油可能形成最早的核酸骨架




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

# 巨分子的自我複製機制




*Trick*

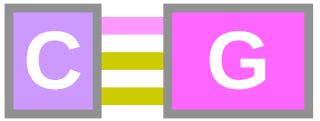
*1*

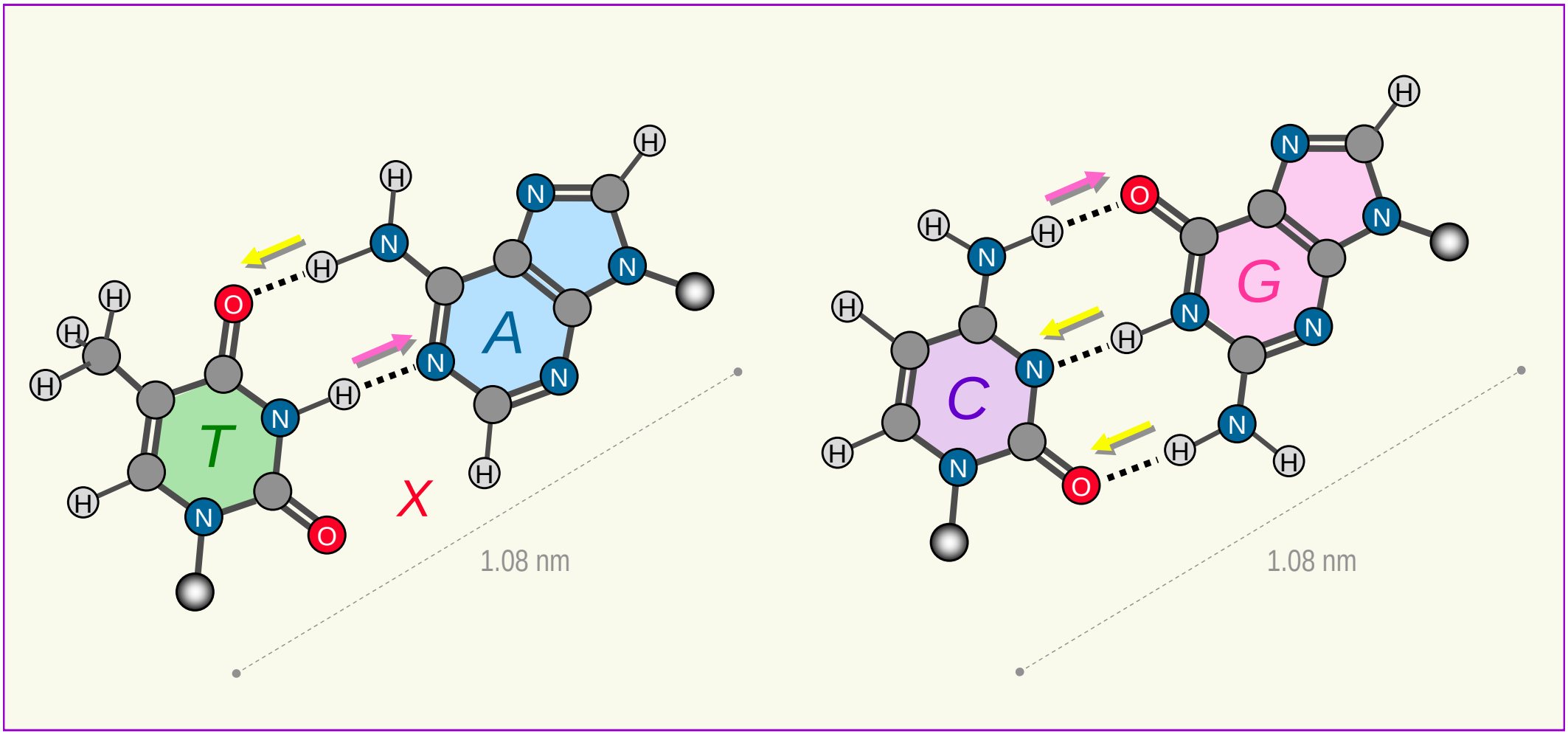
Trick

2

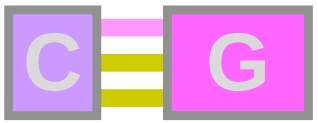
# 配 對

DNA



RNA

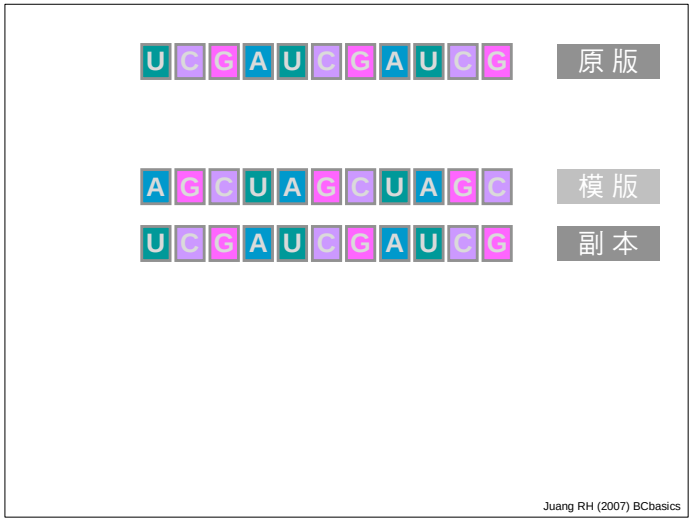


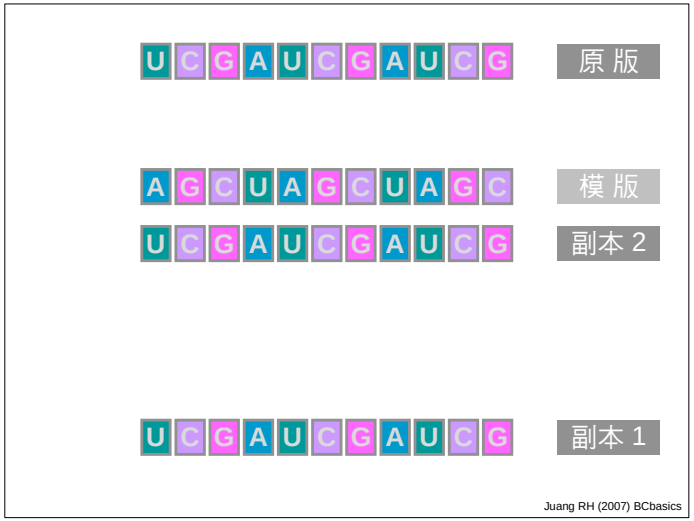

Juang RH (2007) BCbasics

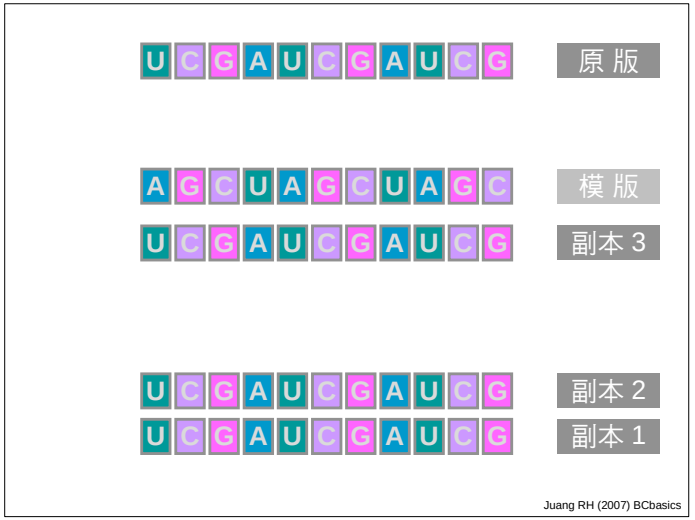
# Trick

1 U C G A U C G A U C G 原 版

2 A G C U A G C U A G C 配 對

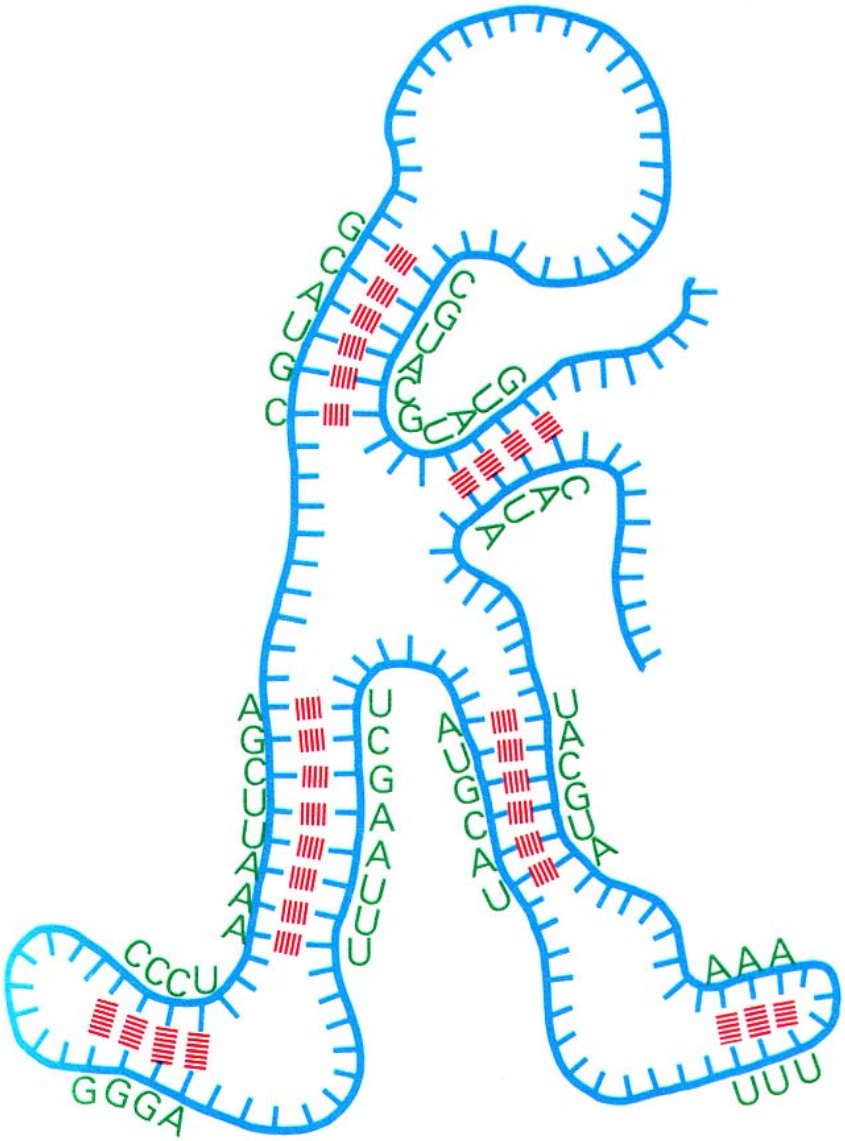


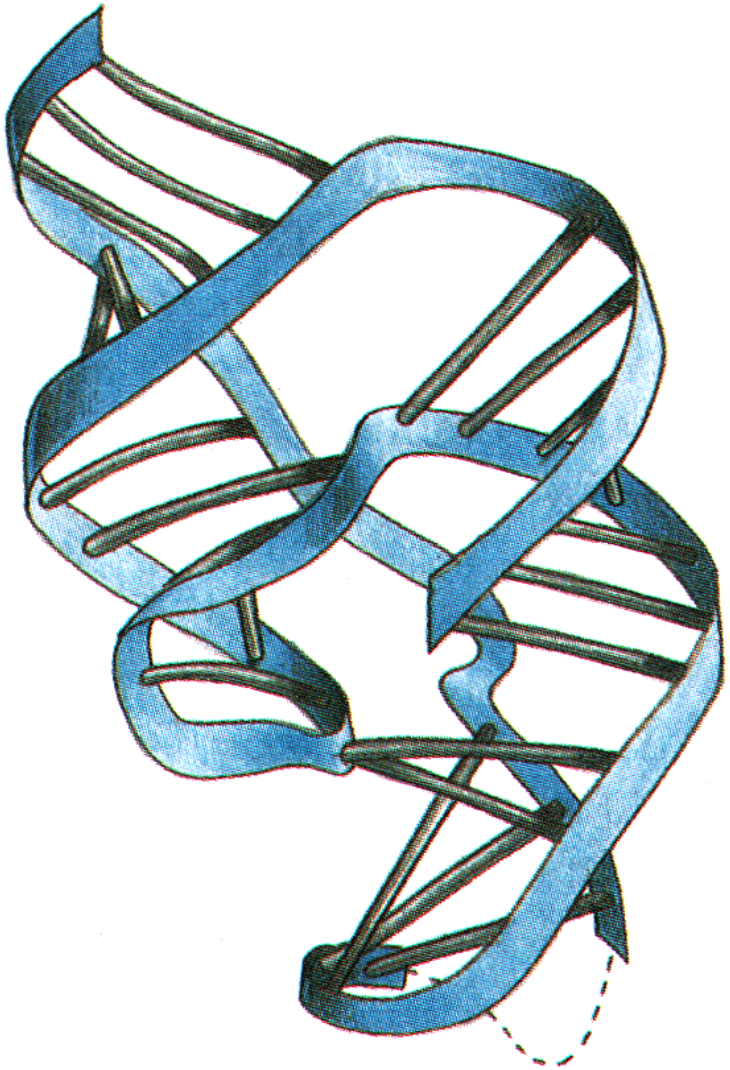




Juang RH (2007) BCbasics

# 同時具有遺傳訊息及構形的 RNA 分子

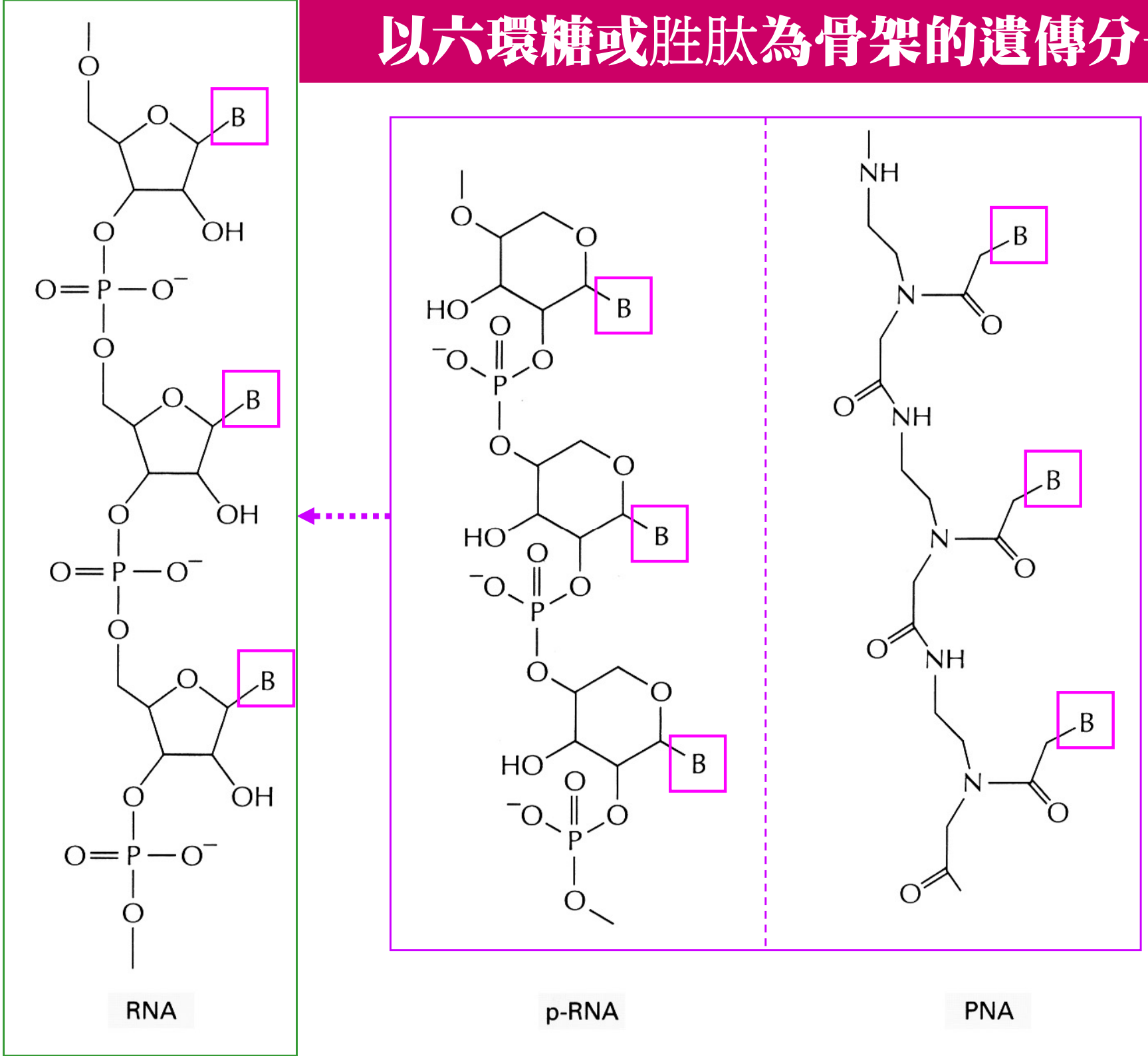


Hepatitis delta RNA

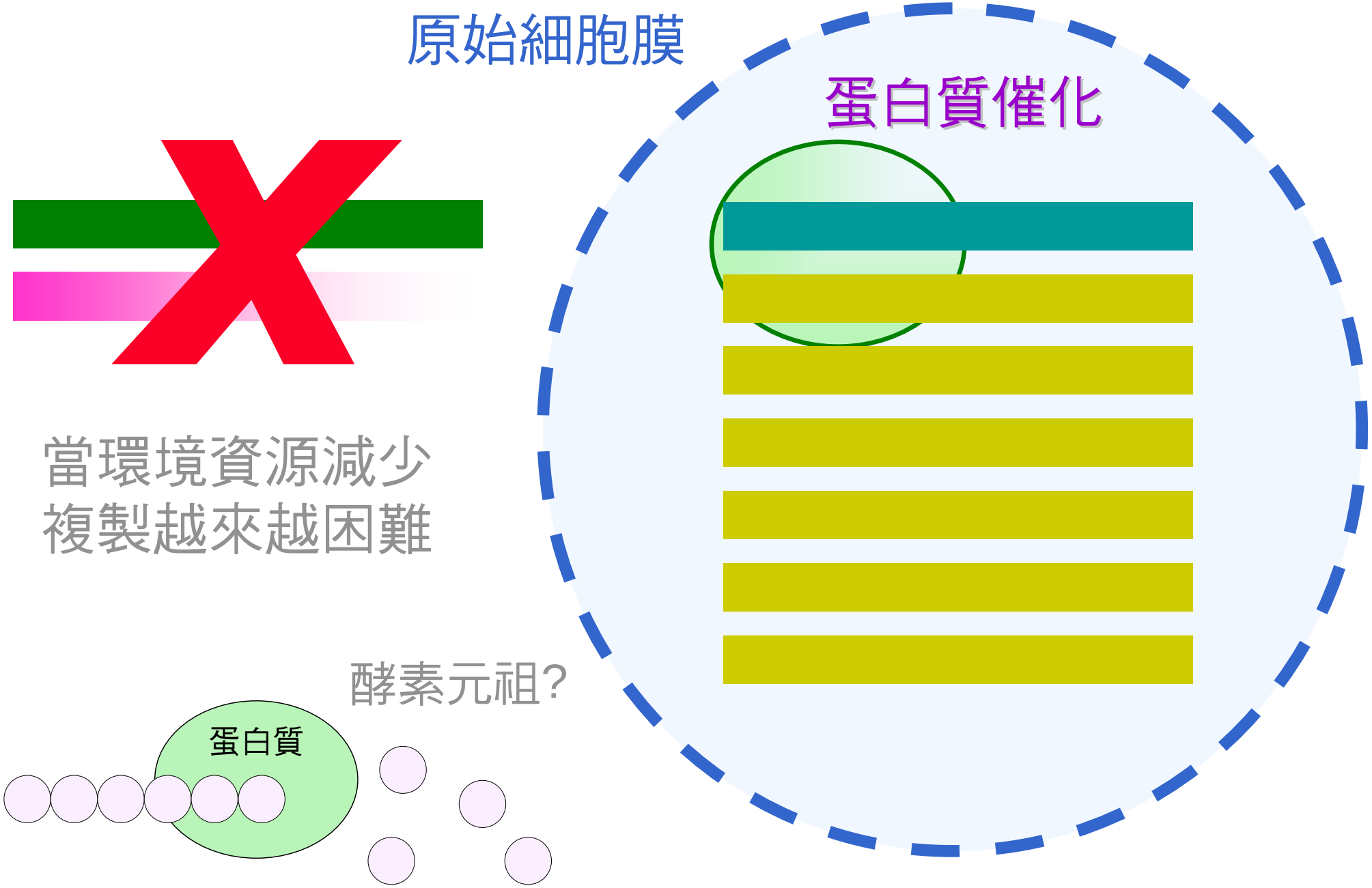
Alberts et al (2002) Molecular Biology of the Cell (4e) p.7

# 以六環糖或胜肽為骨架的遺傳分子




Alberts et al (2002) Molecular Biology of the Cell (4e) p.367

# 催化性蛋白質及細胞膜的出現



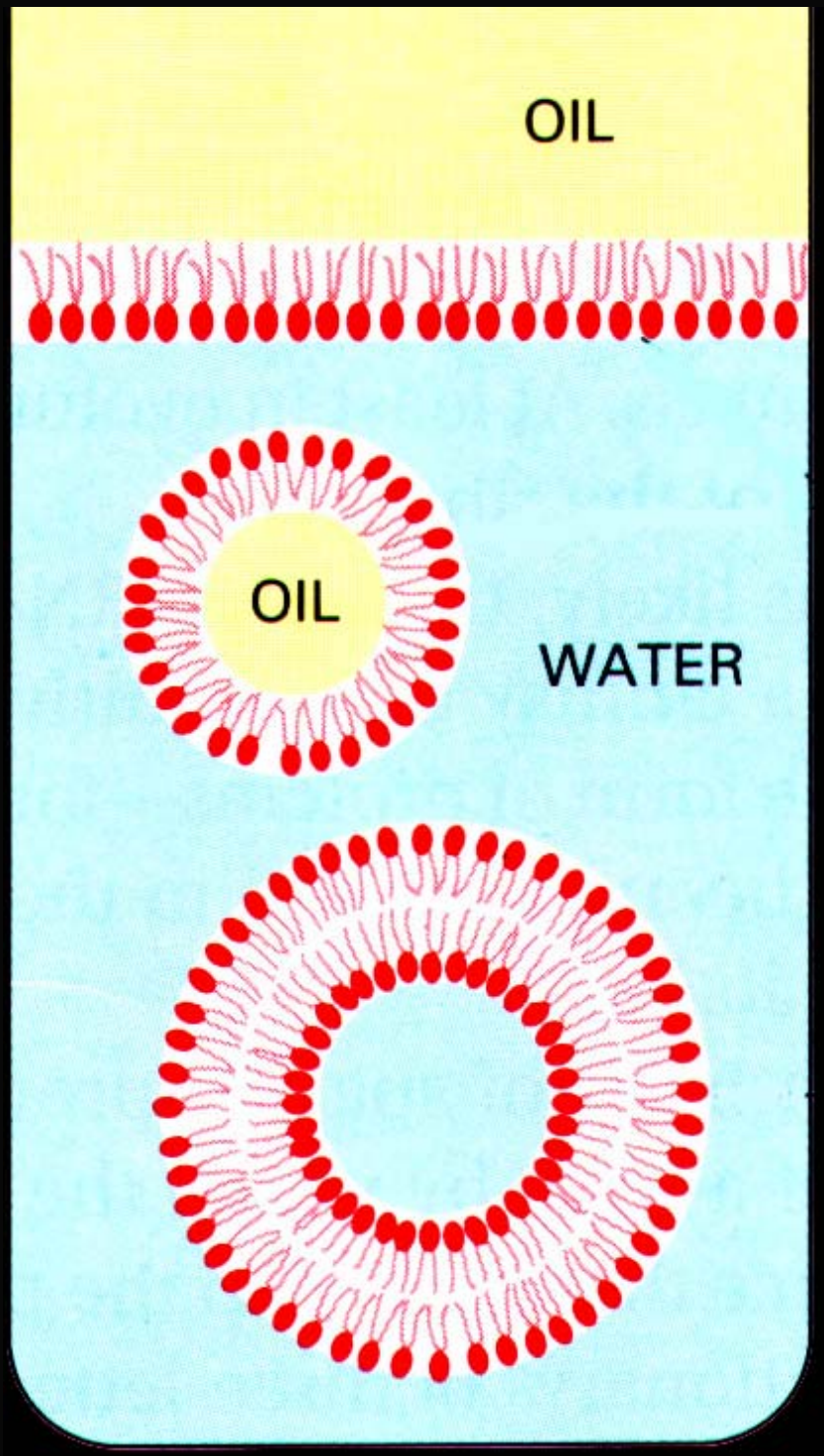

Juang RH (2007) BCbasics

# 細胞膜的形成並不困難

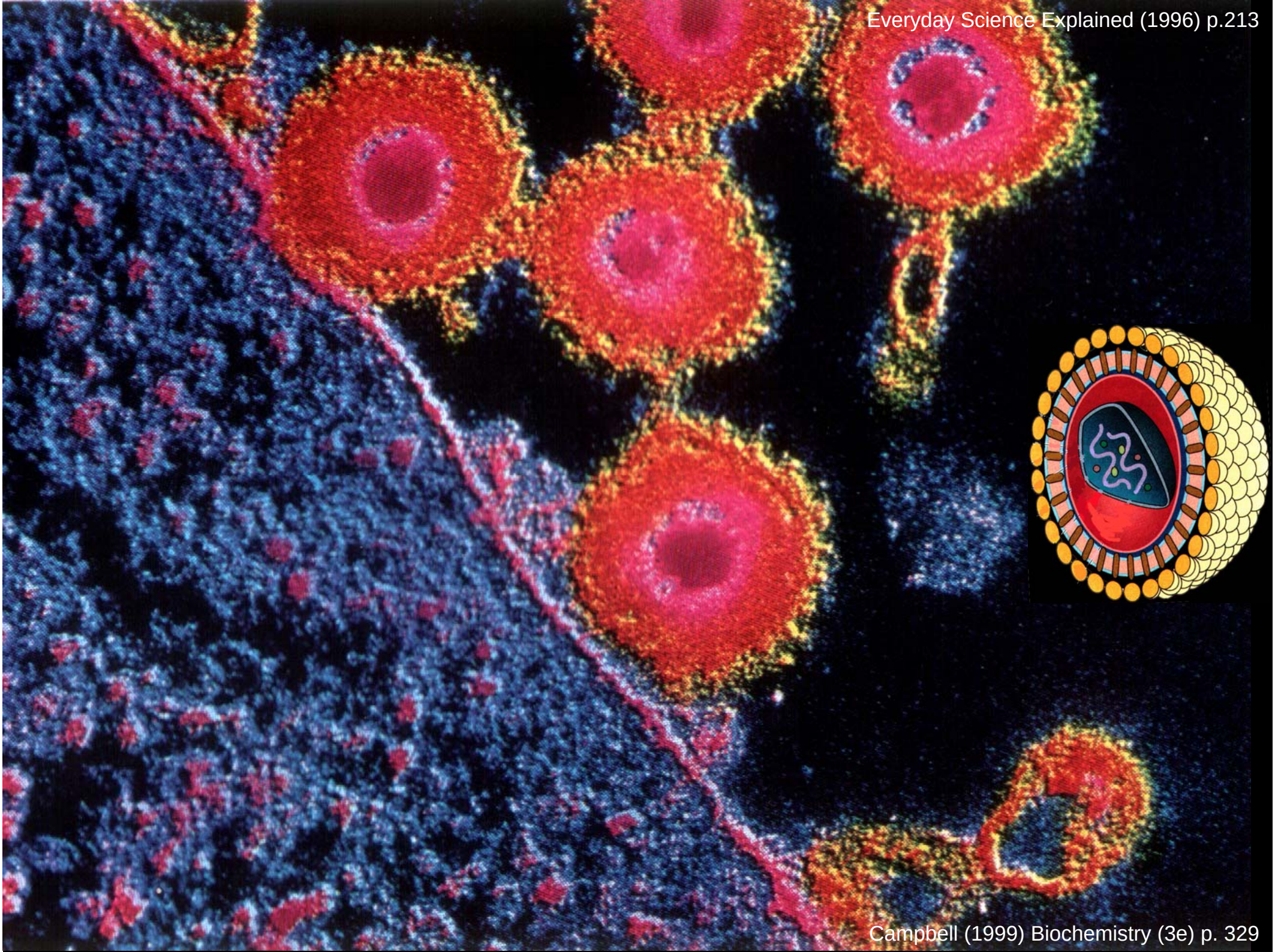
單層脂肪膜

單層脂肪球

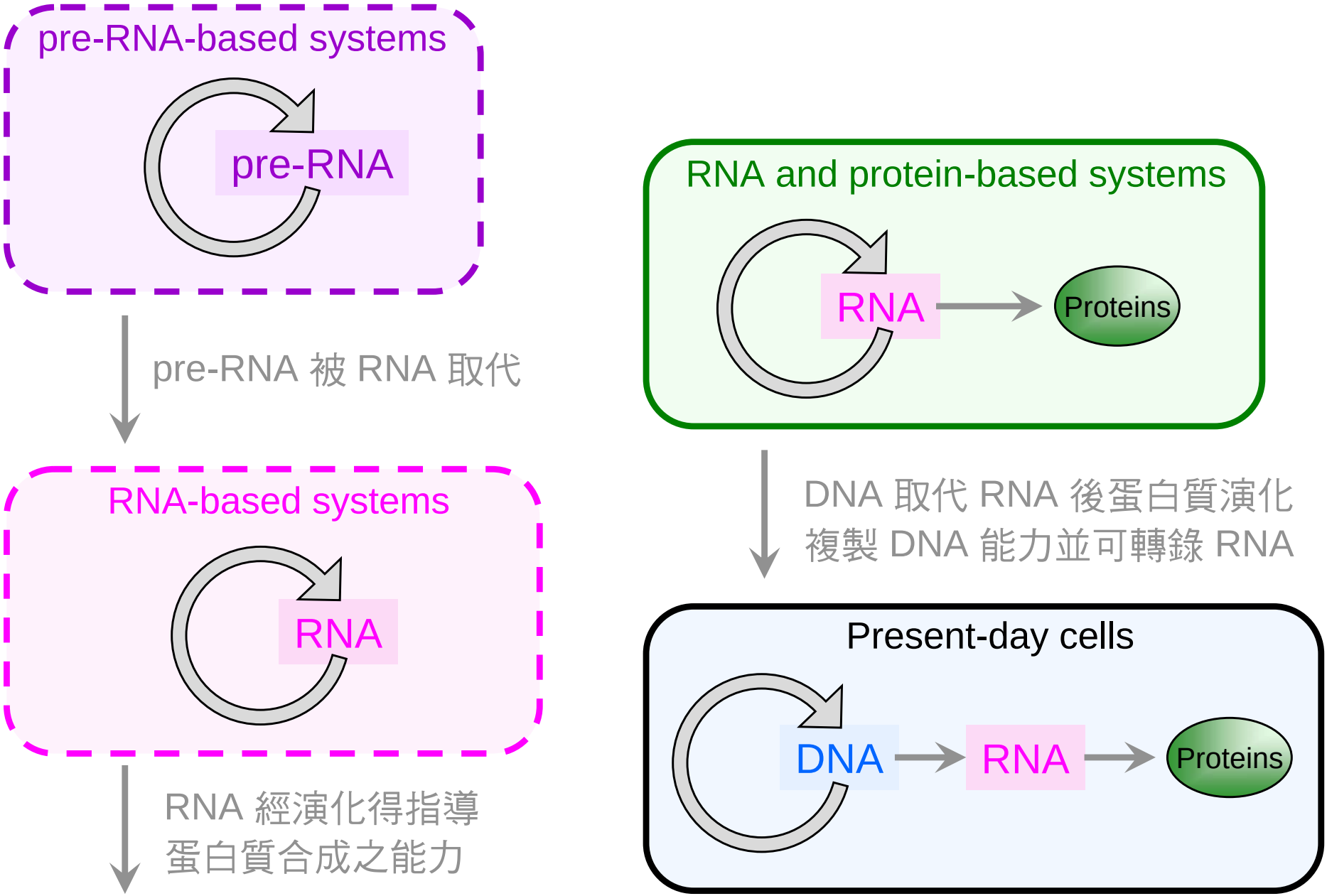
雙層脂肪球
(liposome)



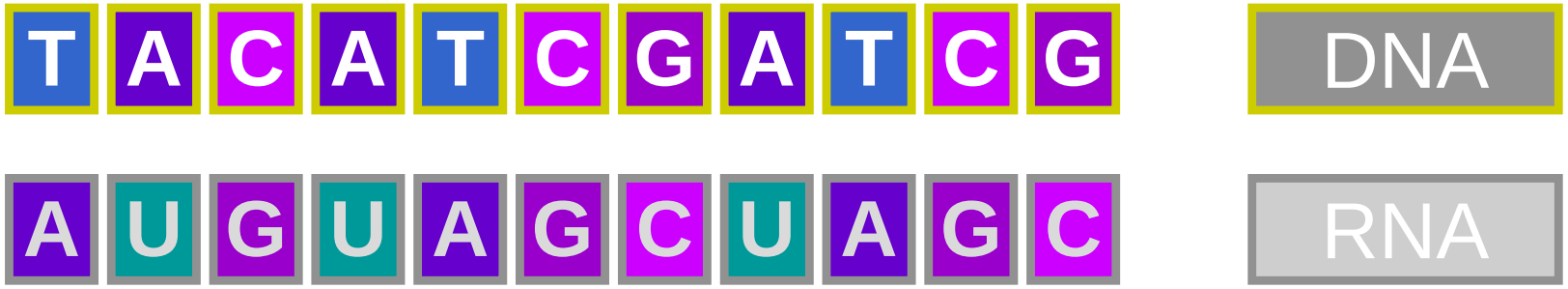

Alberts et al (1994) Molecular Biology of the Cell (3e) p.10


Everyday Science Explained (1996) p.213
Campbell (1999) Biochemistry (3e) p. 329

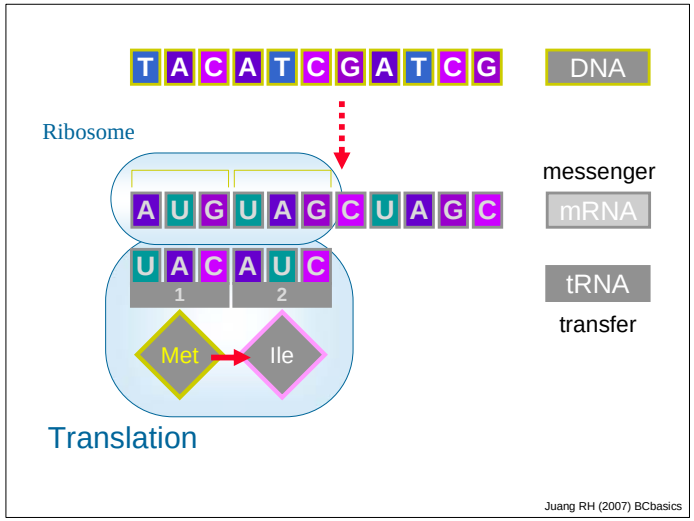
# Central Dogma 的演化進程

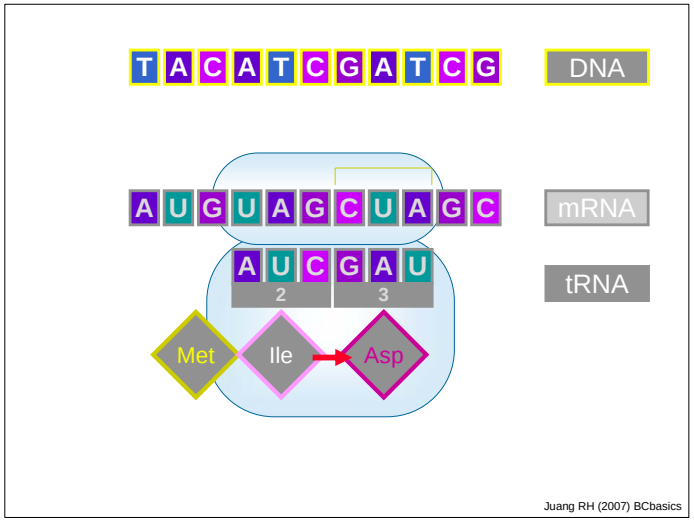


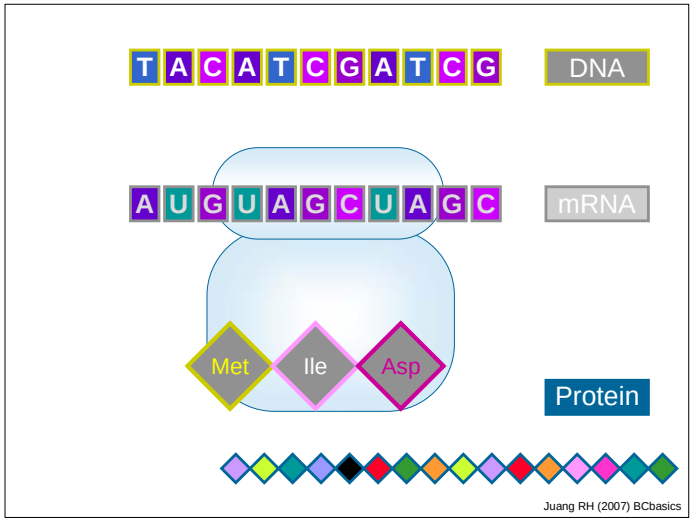

Adapted from Alberts et al (2002) Molecular Biology of the Cell (4e) p.372




# Transcription

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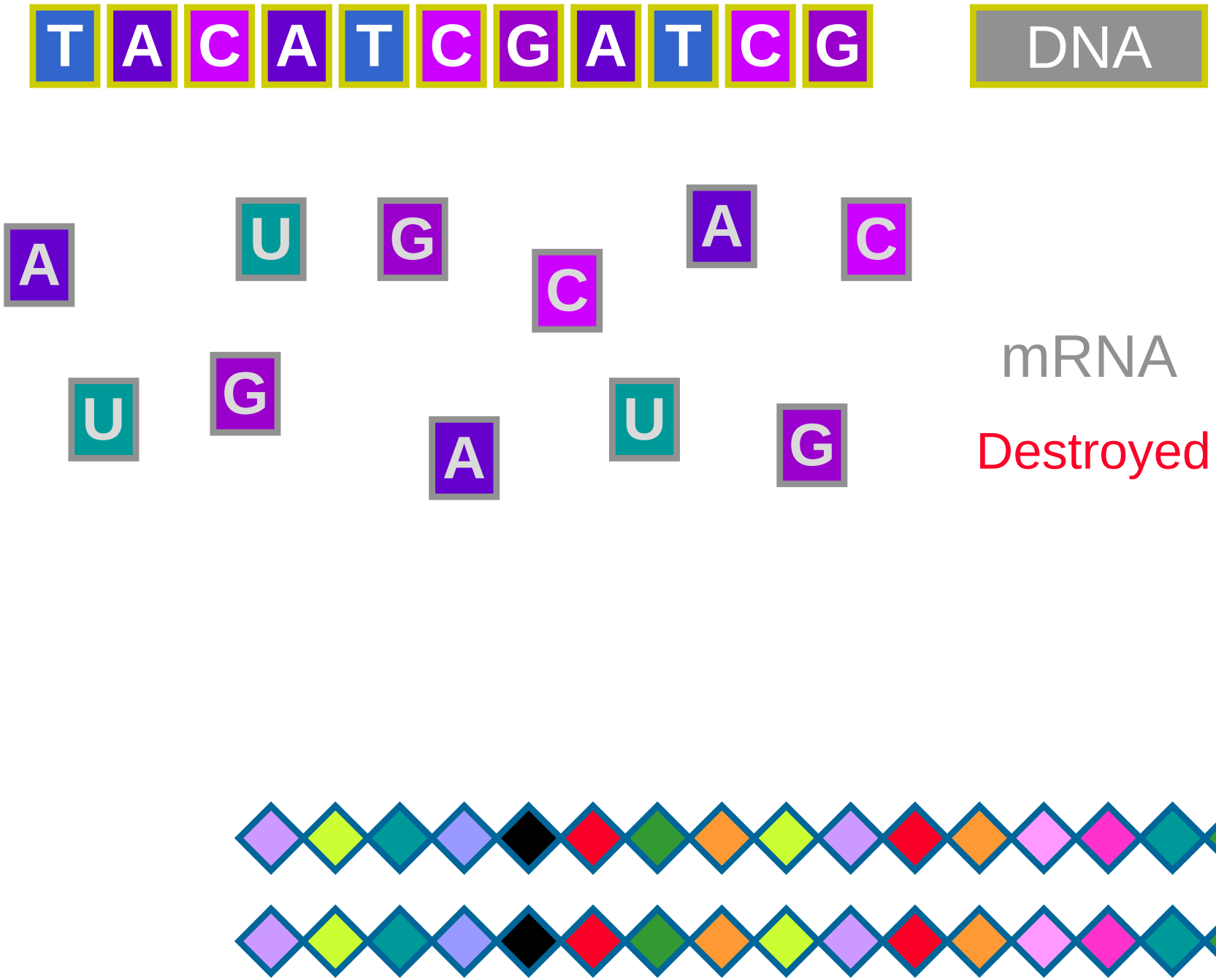


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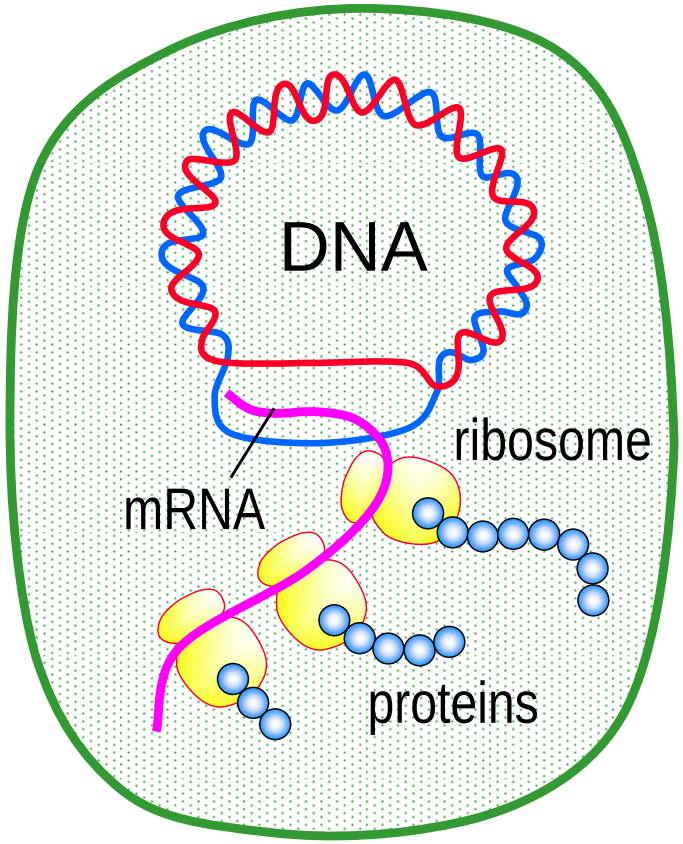
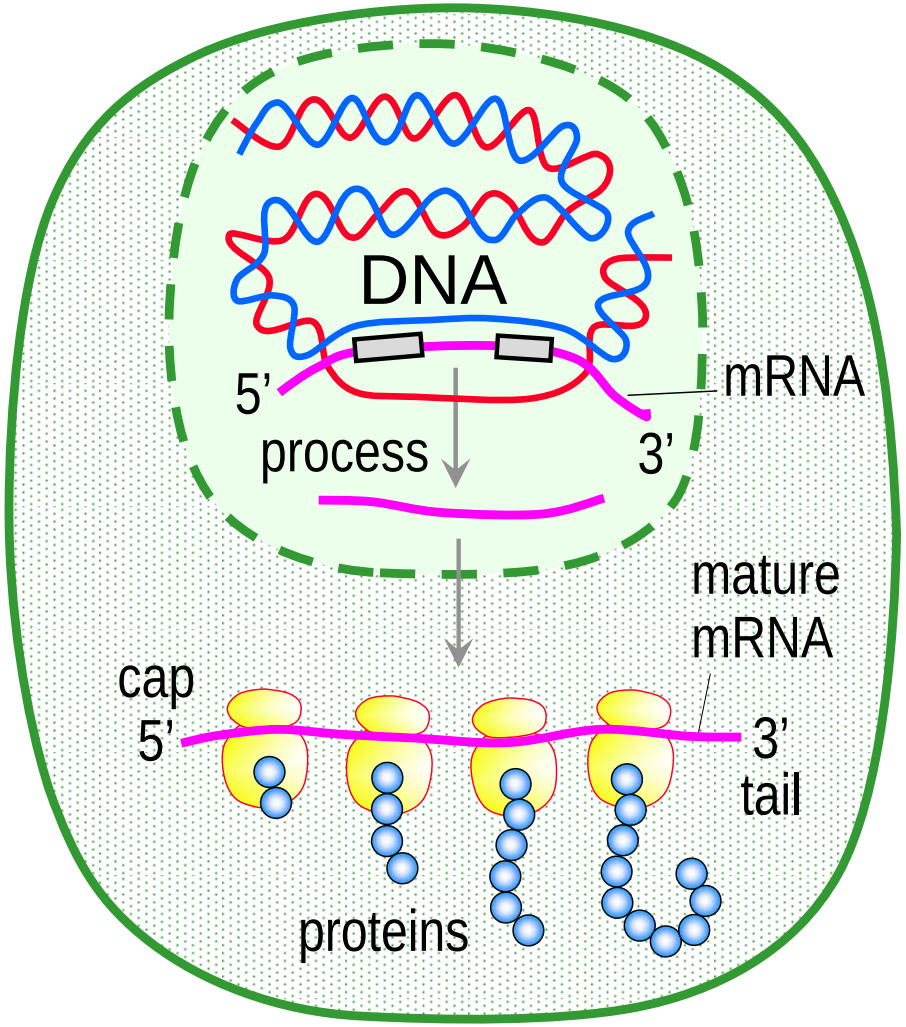
# 最後形成目前的細胞模式

DNA 取代 RNA 成為遺傳物質

RNA 專司蛋白質的合成




原核細胞

單身宿舍

真核細胞

三房兩廳

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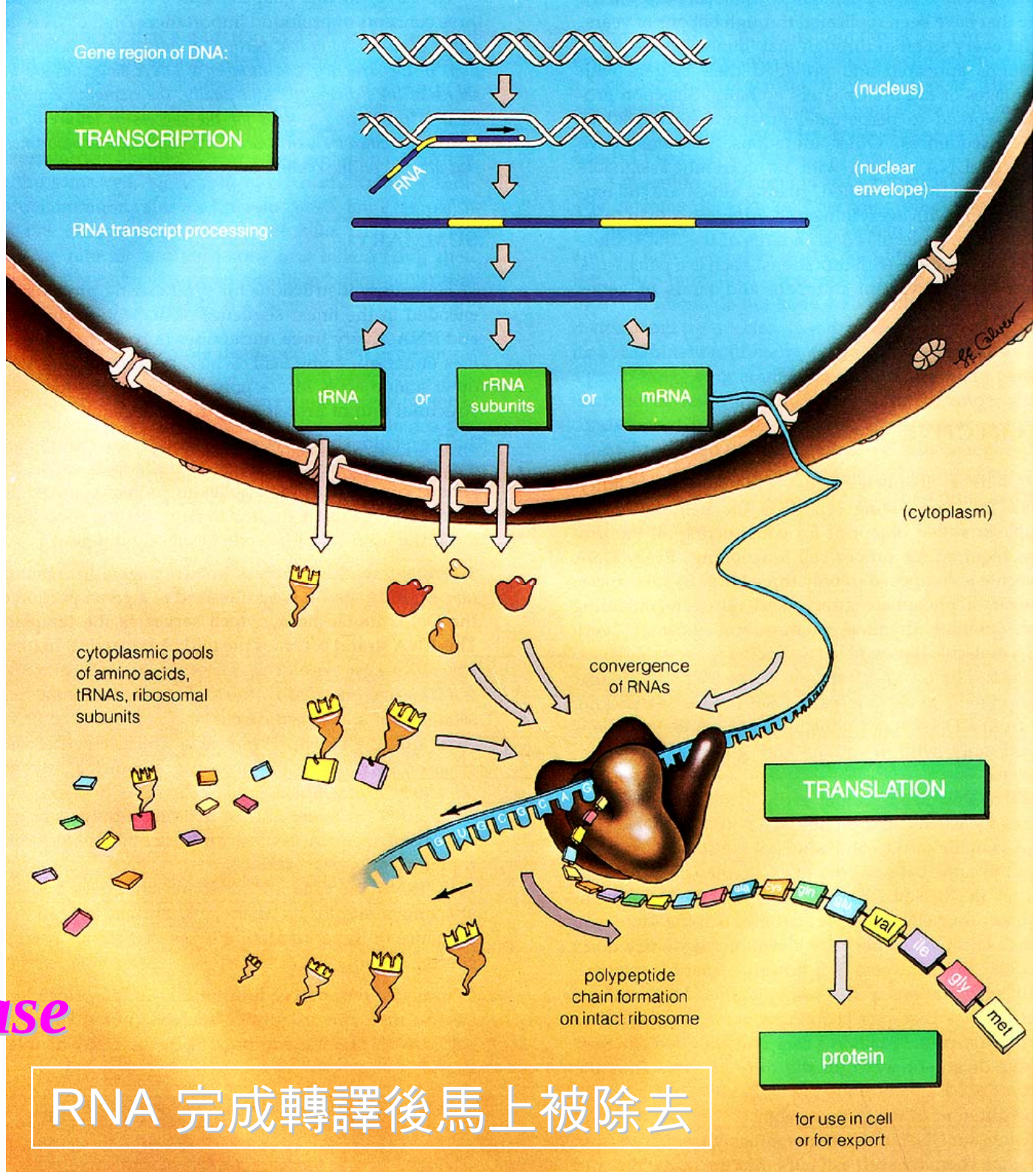
# 細胞內基因表現的故事




DNA

↓

mRNA

↓

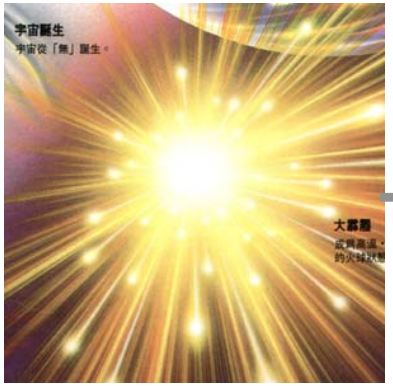
Protein

***RNase***

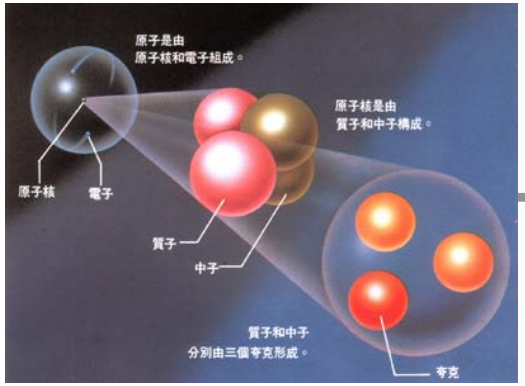
RNA 完成轉譯後馬上被除去

Starr & Taggart (1987) Biology (4e) p.216

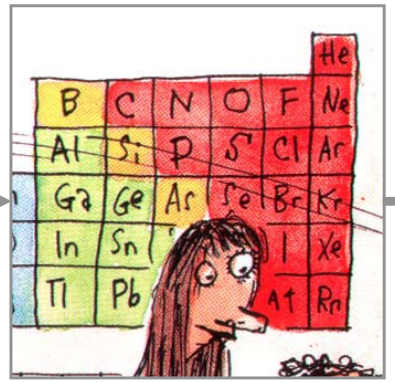
大霹靂



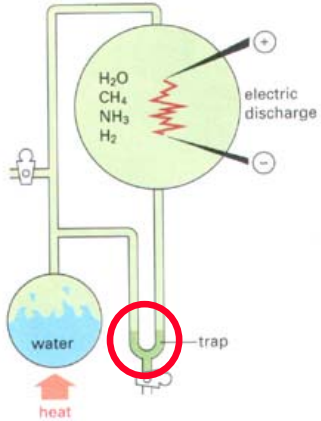

基本粒子



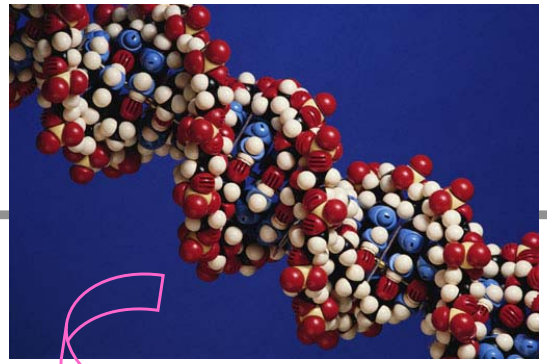

原子

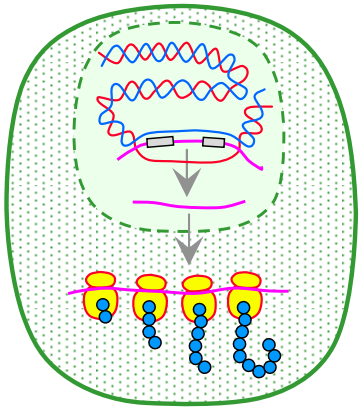



基本小分子




核酸
複製 信息

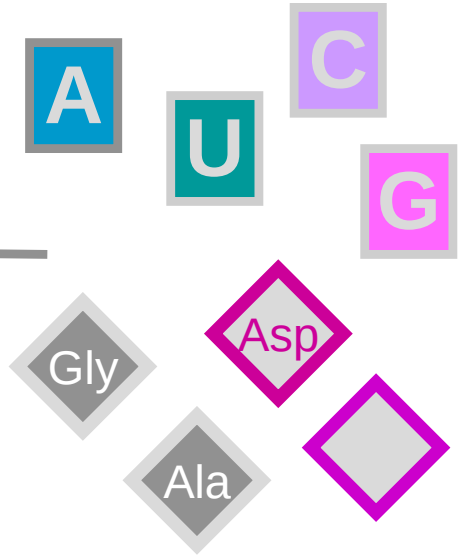




Central
Dogma

蛋白質
催化 功能

巨分子




單位小分子

**組合**

# 細胞與分子

- 1 生命源起
- 2 細胞的生物化學：
  - 2.1 原核細胞
  - 2.2 古生菌
  - 2.3 真核細胞
- 3 細胞分子：
  - 3.1 水與 pH
  - 3.2 細胞的組成分子
  - 3.3 分子間的作用力： 二級鍵

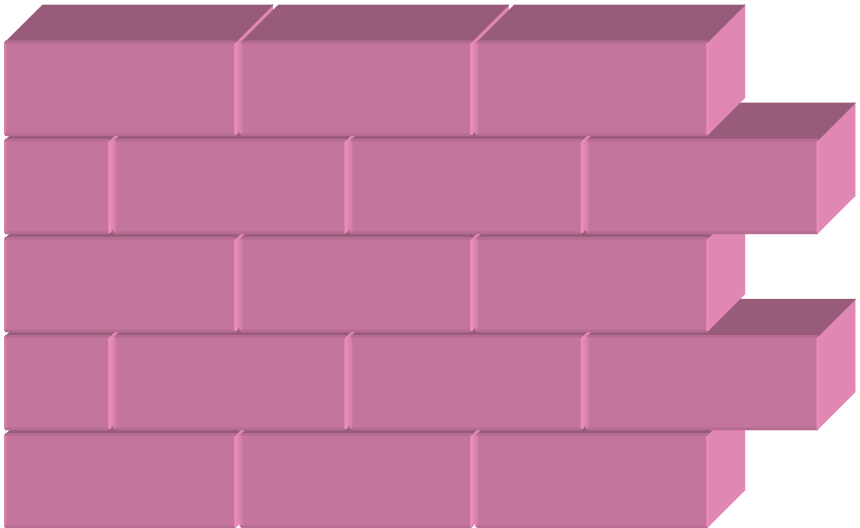
巨分子的序列

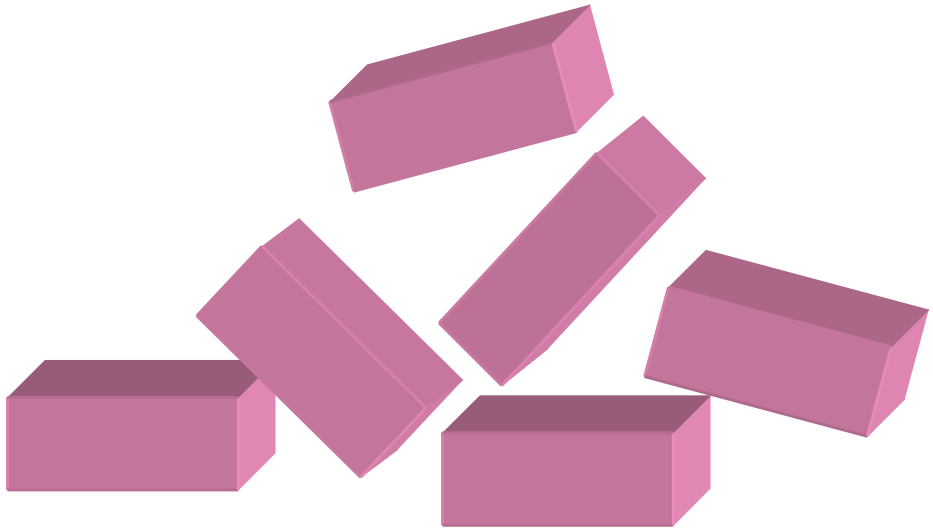
# 有規則的序列

一堆凌亂磚塊 不能組成一間房屋 (建築)

一堆散亂字母 無法組成有意義的文章 (文法)

串起一堆胺基酸 不能成為一個有用的蛋白質





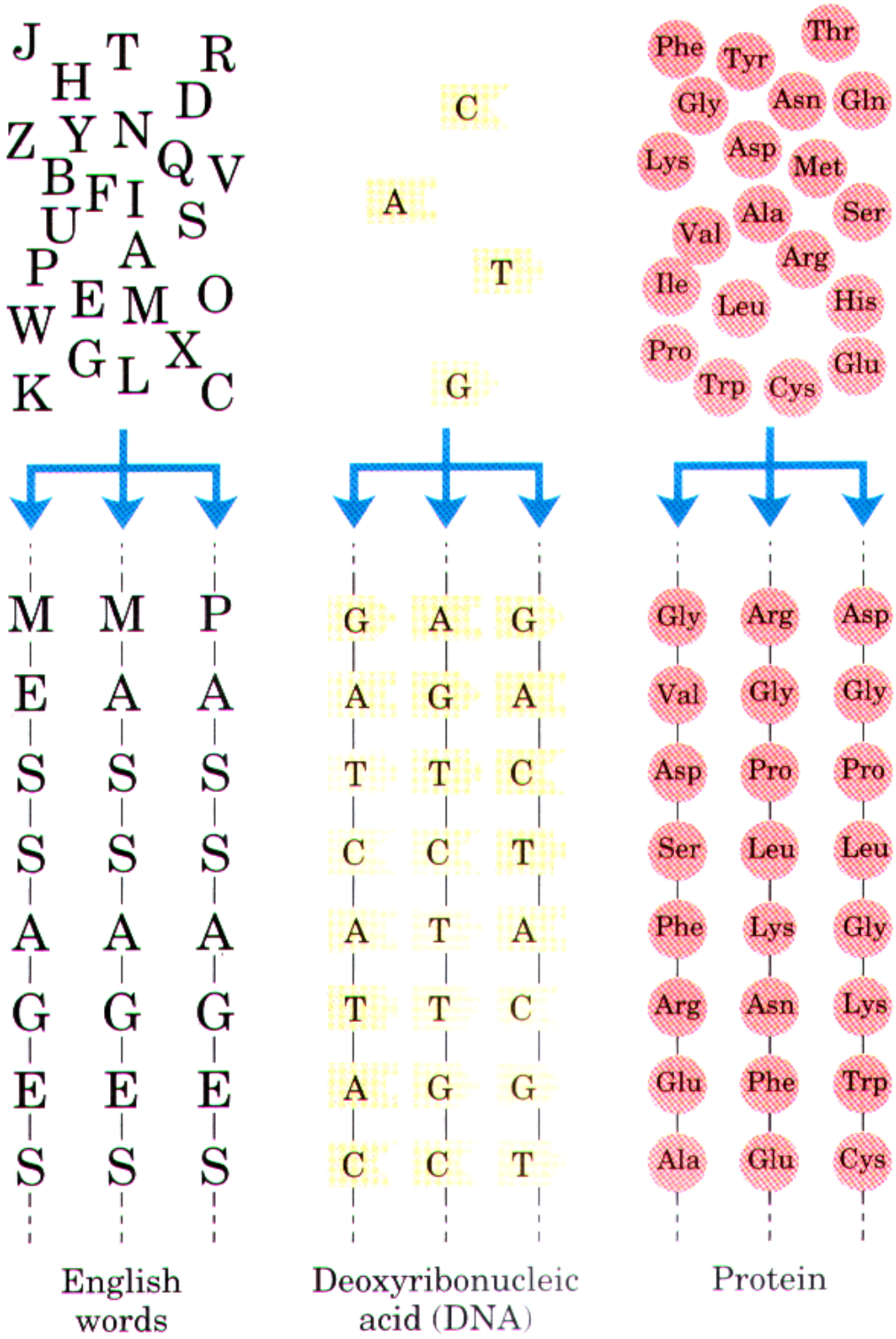
Juang RH (2007) BCbasics

# 細胞內的三種巨分子

| | | |
|---|---|---|
| **核　酸** | 遺傳信息傳遞<br>蛋白質合成 | DNA<br>RNA |
| **蛋白質** | 細胞構造<br>生理功能 | 肌肉<br>酵素 |
| **醣　類** | 細胞構造<br>能量 | 細胞壁<br>葡聚糖 |

Juang RH (2007) BCbasics

# 細胞內巨分子的特性

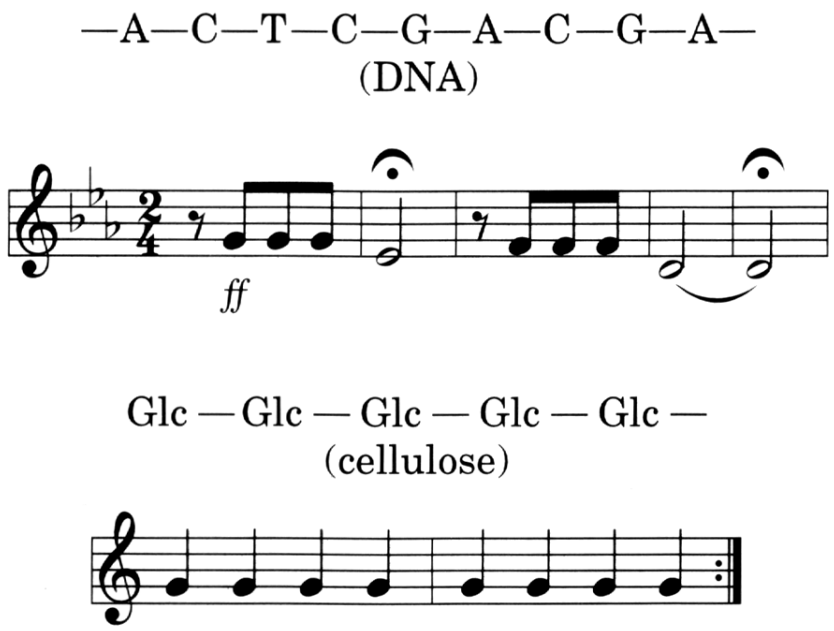



(1) 巨分子由單位小分子聚合成

(2) 單位小分子的序列有其意義

(3) 每一層次組合都有新的機能

(4) 越後來的組合其複雜性越高

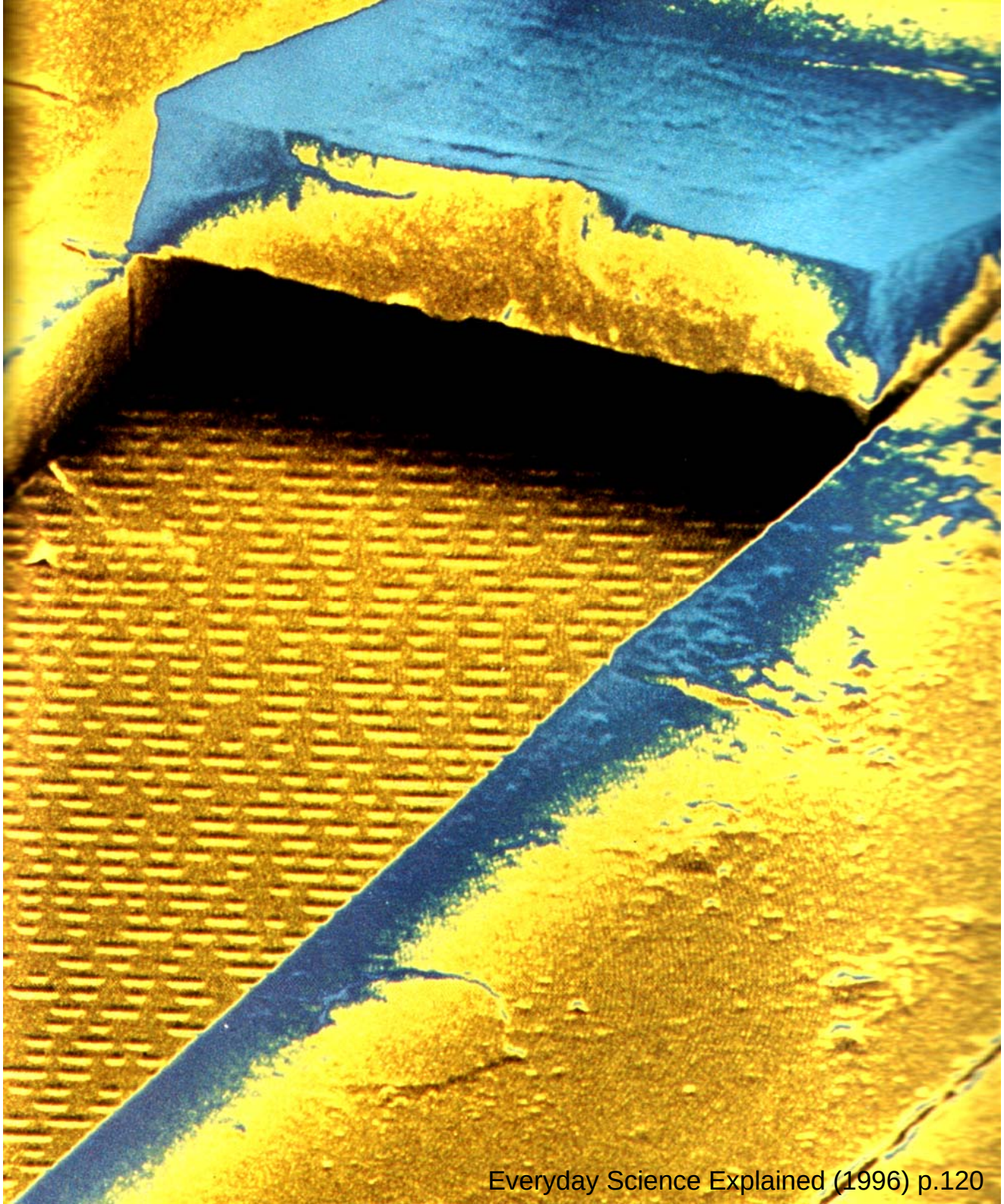



Nelson & Cox (2000)
Lehninger Principles of Biochemistry (3e) p.5, 70

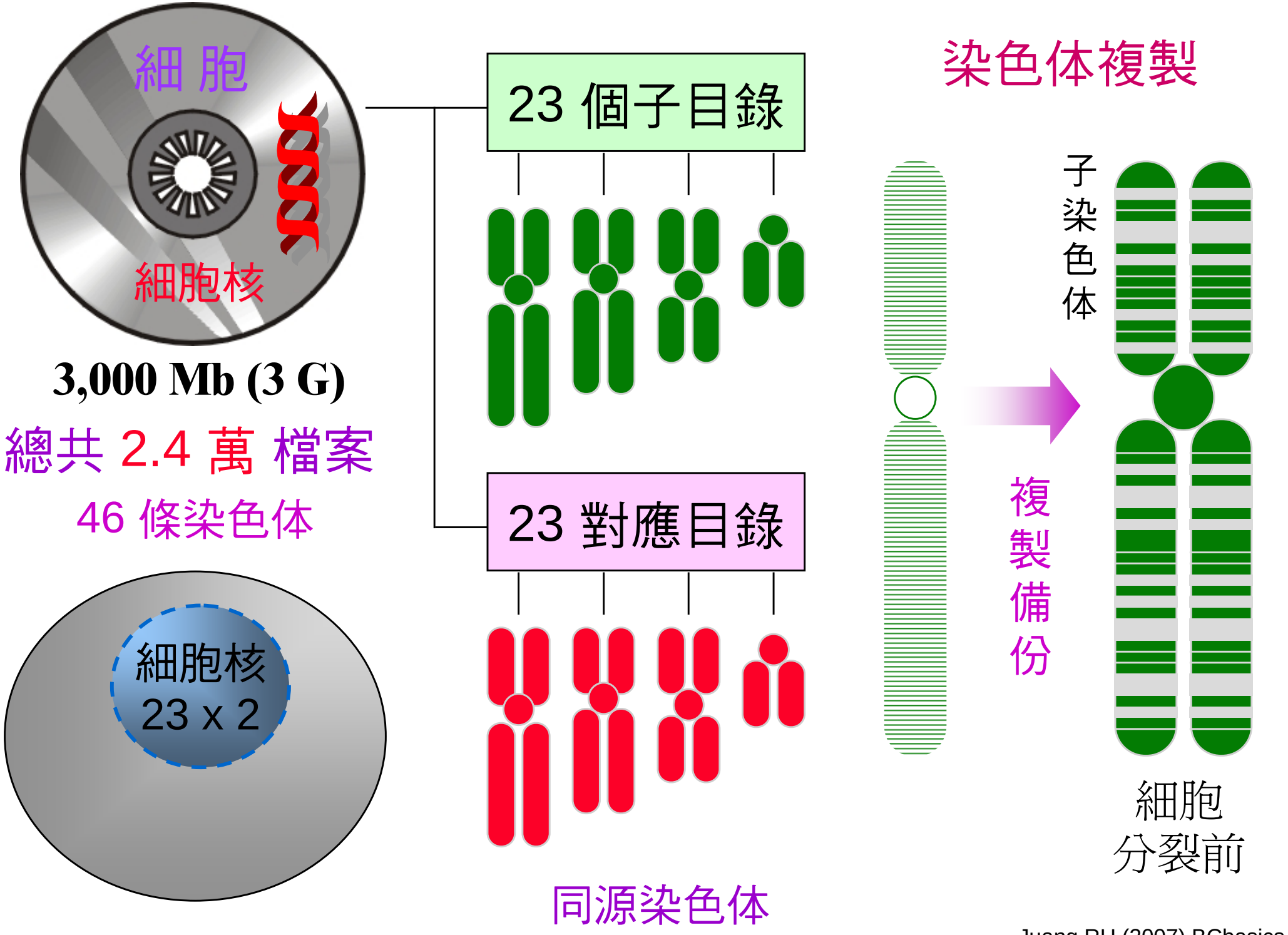
生物資訊學已成形

Bioinformatics

Nature 阿拉伯芥基因體紀念光碟

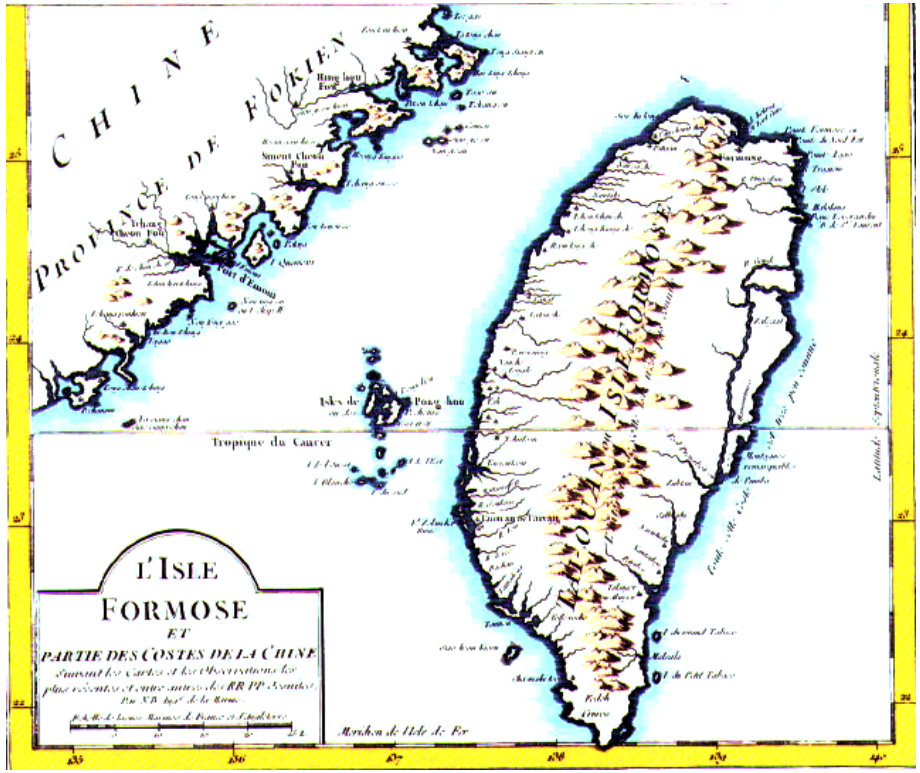


Everyday Science Explained (1996) p.120




Juang RH (2007) BCbasics

# 大多生物基因體的解碼只完成草圖




台灣古代地圖

台灣空照地圖

功能地圖

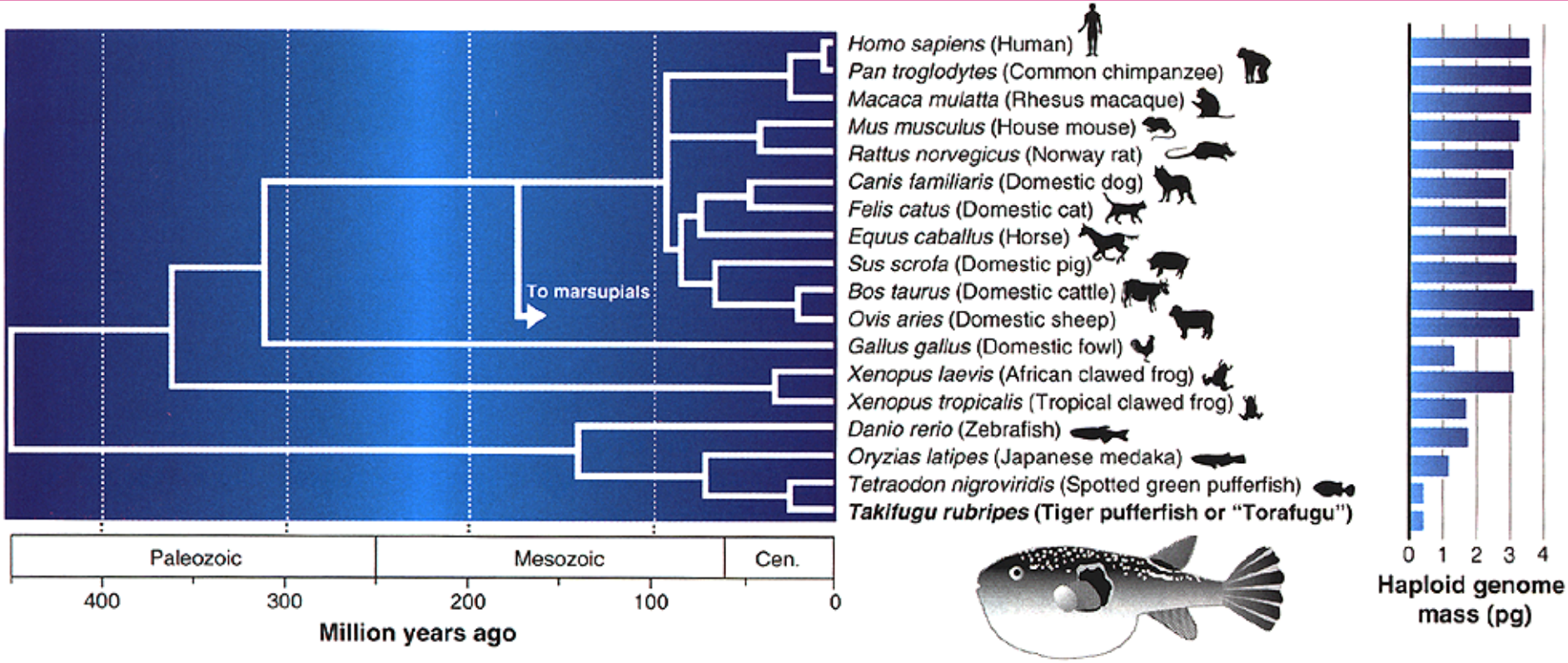
核酸序列 必須加以定義註解 (annotation) 才能得到有用的資訊

生物資訊學 (bioinformatics) 就是對這些資訊的解讀與應用

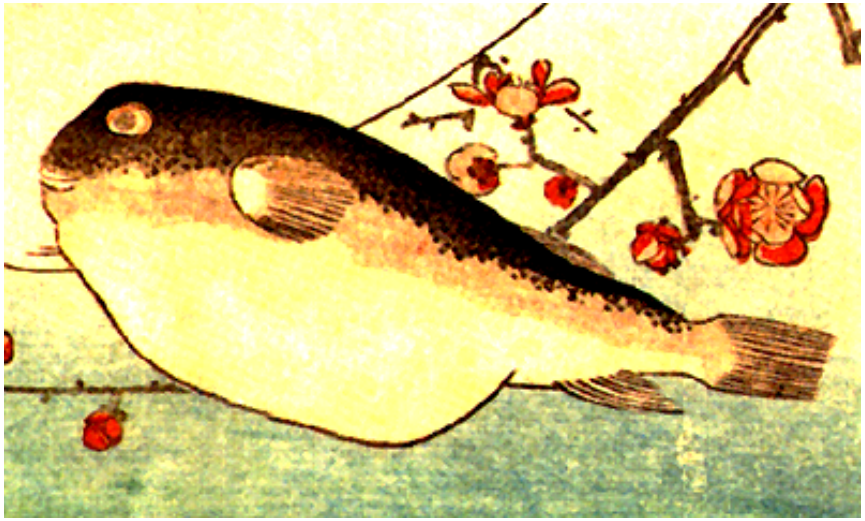
Juang RH (2007) BCbasics

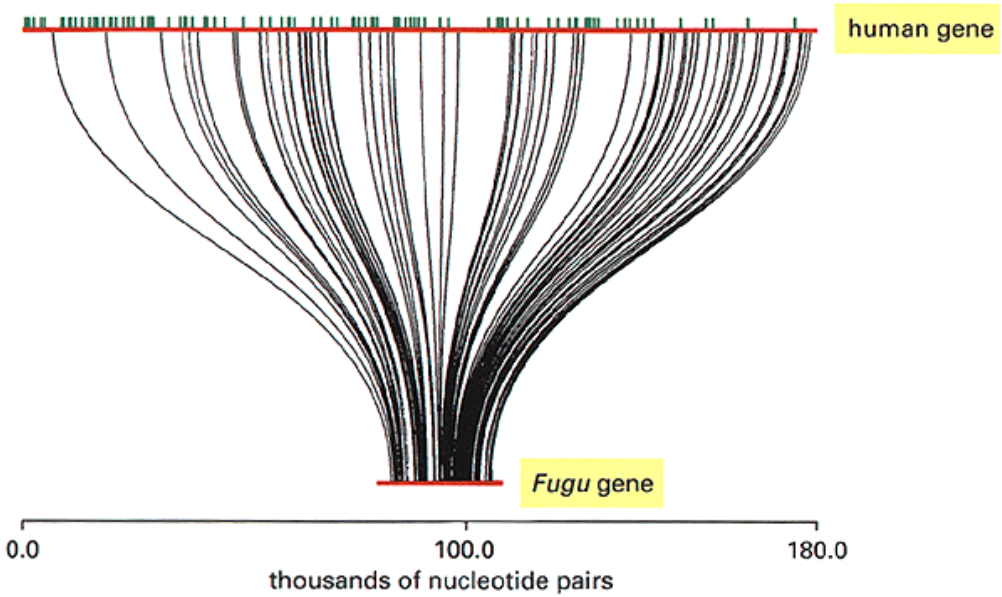
# 不同生物的基因體大小相差很大

Hedges & Kumar (2002) Science (297) p.1284



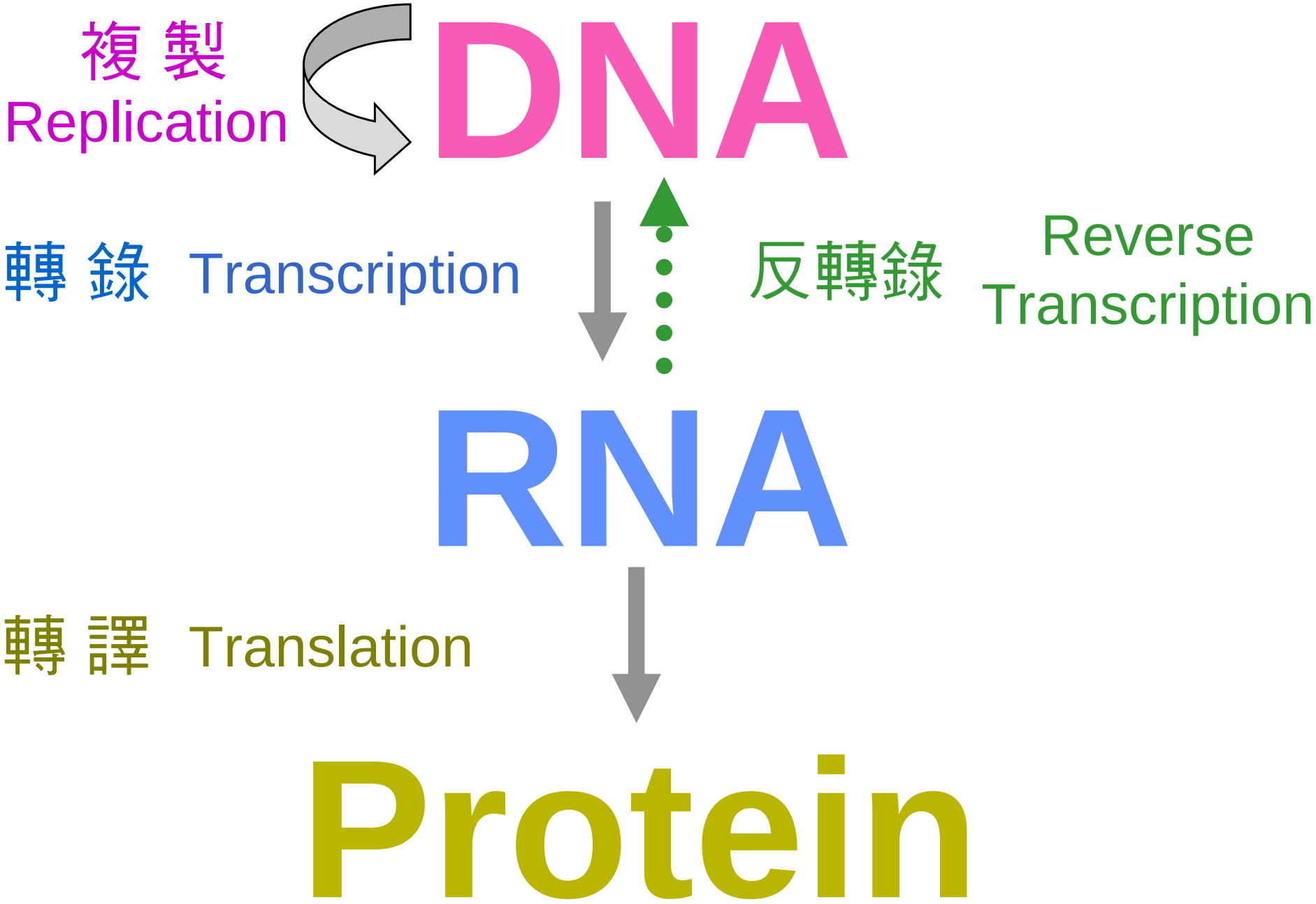

把基因擠到十分之一大小之內





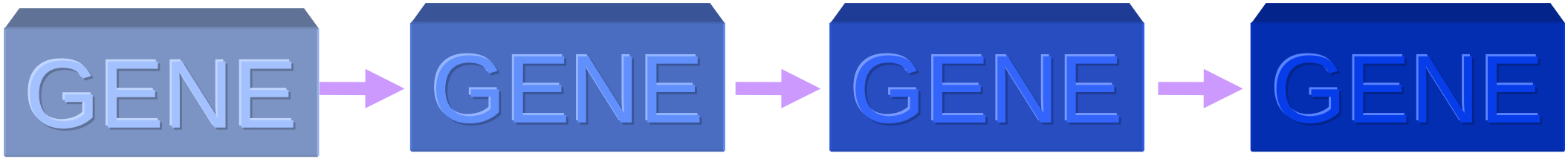

Alberts et al (2002) Molecular Biology of the Cell (4e) p.33, 459

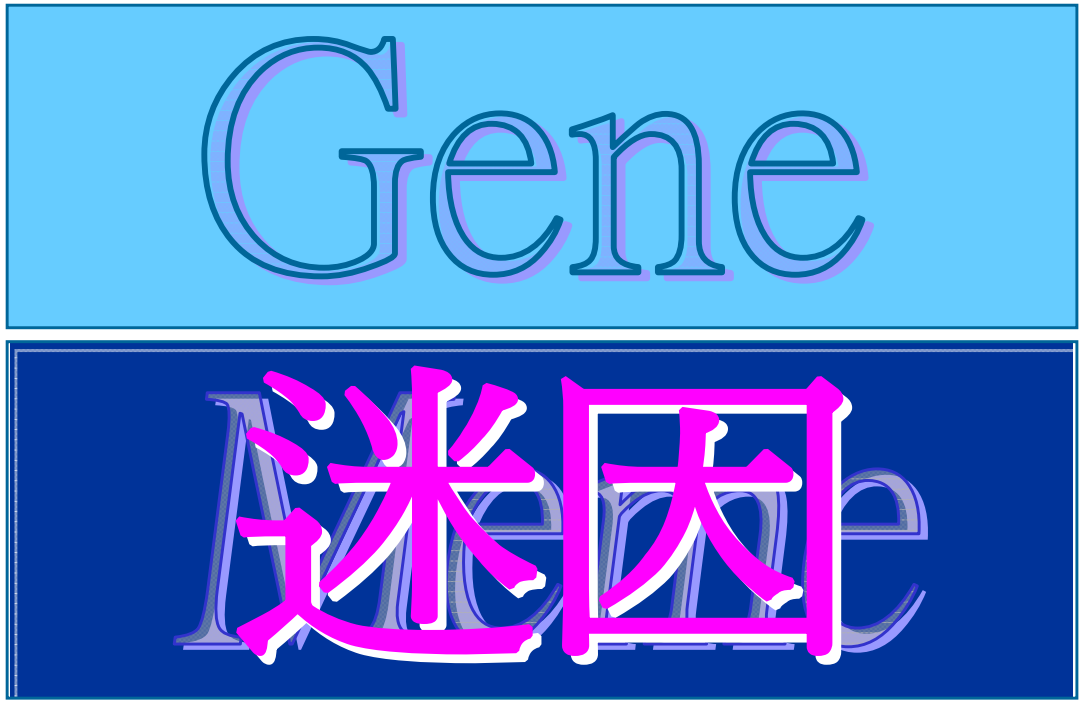
# Central Dogma




Juang RH (2007) BCbasics

# 自私 Selfish Gene 基因




Juang RH (2007) BCbasics

# ATCG

包括動物、植物、微生物之所有生物，以及病毒等，都是使用這四種遺傳密碼單位；這是天地萬物合一，以及眾生皆平等的最佳說明。

胺基酸也是一樣

ACDEFGHIKLMNPQRSTVWY

Juang RH (2007) BCbasics

- 1 生命源起
- 2 細胞的生物化學：
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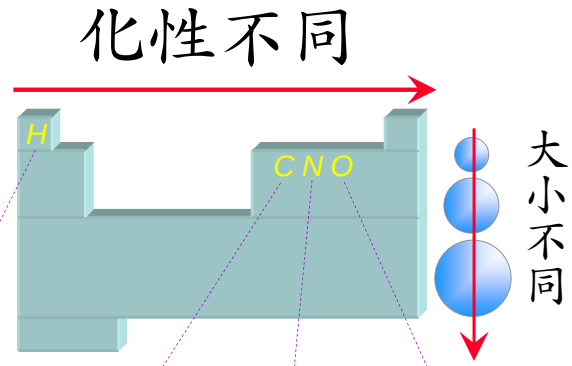
  - 2.2 古生菌
  - 2.3 真核細胞
- 3 細胞分子：
  - 3.1 水與 pH
  - 3.2 細胞的組成分子
  - 3.3 分子間的作用力： 二級鍵

# 由原子到生物分子

**週期表**

生物偏好較輕原子

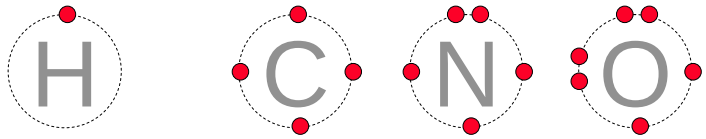
地球上存量較多
且原子間鍵結較強




$^{1}H$ $^{6}C$ $^{7}N$ $^{8}O$

*1s* *2s 2p*

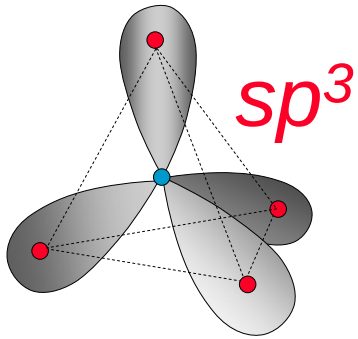
外層電子




$sp^3$

地球早期的大氣成分： $H_2$ $CH_4$ $NH_3$ $H_2O$

組成生物分子的
原子成分種類
比無生物複雜許多




碳原子的四面體構造
有很強的立體限制性
是蛋白質構形的根本

Juang RH (2007) BCbasics

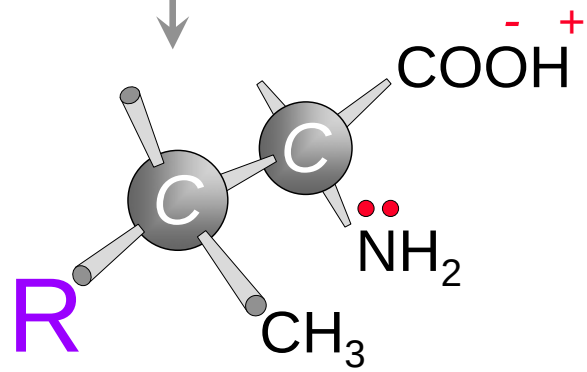
# 陰電性對化學性質有重大影響

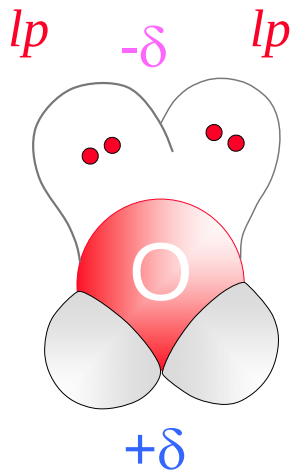
地球早期的大氣成分： $H_2$ $CH_4$ $NH_3$ $H_2O$

C-C

重新看水分子構造

## 有機化合物




永久的偶極性

| 陰電性 | |
|---|---|
| *O* | 3.5 |
| *N* | 3.0 |
| C | 2.5 |
| H | 2.1 |

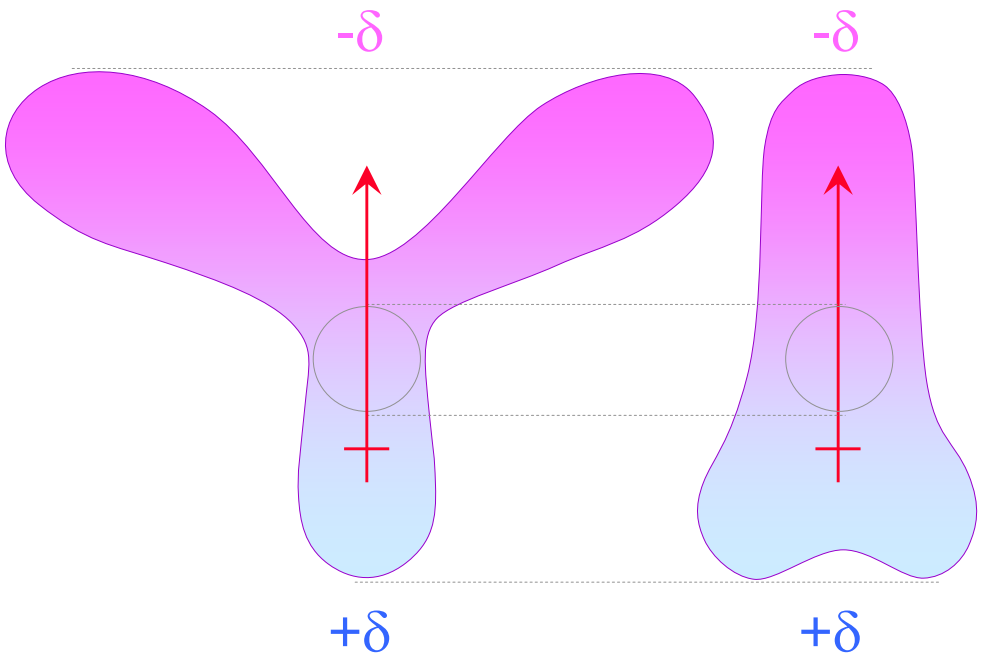
## 官能基

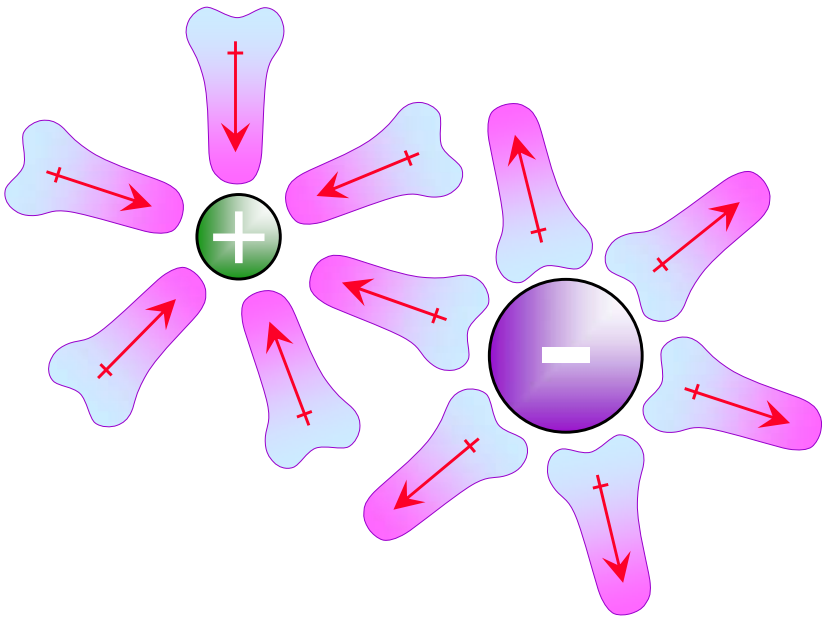
由各種原子所組合成的官能基，因為原子間陰電性的不同，造成官能基的極性大小不同，反應性也有所差異。

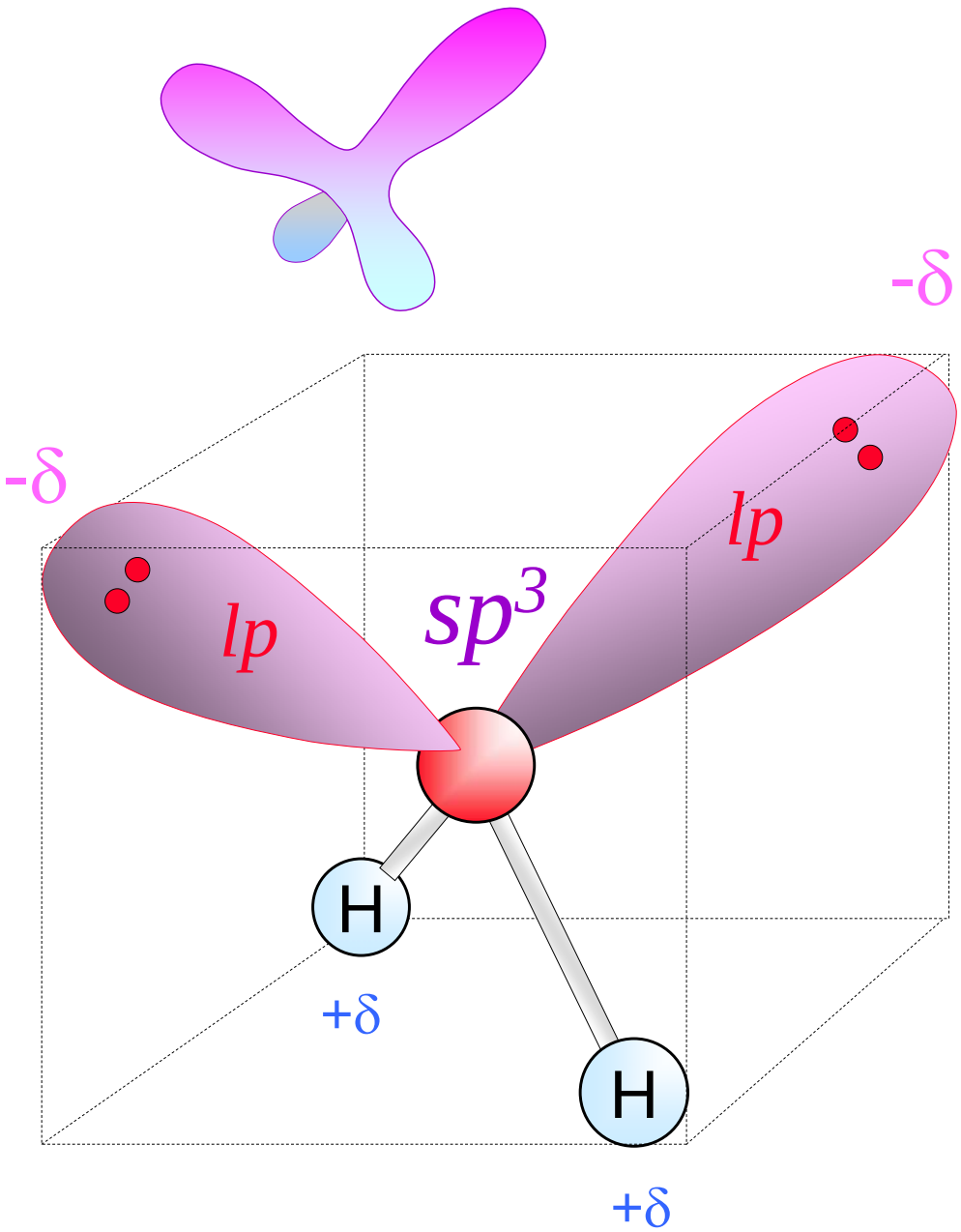
- 水分子的極性
- 水的介電常數
- 水分子間的氫鍵
- 水與 pH 的關係

Juang RH (2007) BCbasics

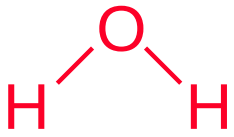
# 誇張但較正確的水分子模型

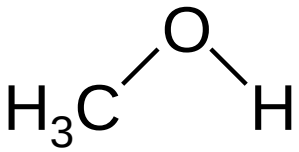


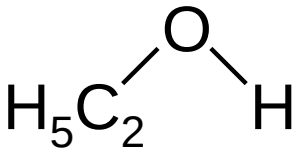



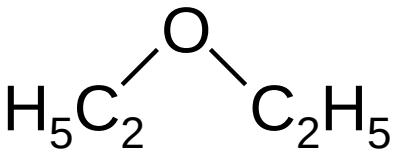



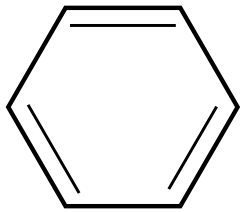

Adapted from Zubay (1988) Biochemistry (2e) p.57







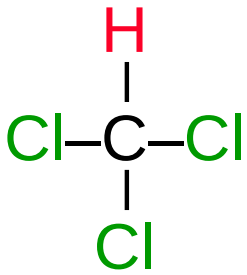


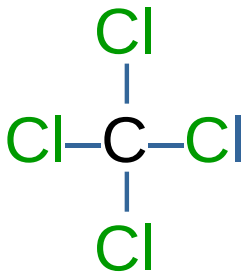


# 各種分子的介電常數

| | |
|---|---|
| Water | 80.4 |
| Methanol | 33.6 |
| Ethanol | 24.3 |
| Ammonia | 17.3 |
| Acetic acid | 6.15 |
| Chloroform | 4.81 |
| Ethyl ether | 4.43 |
| Benzene | 2.28 |
| Carbon tetrachloride | 2.24 |

*DMSO*



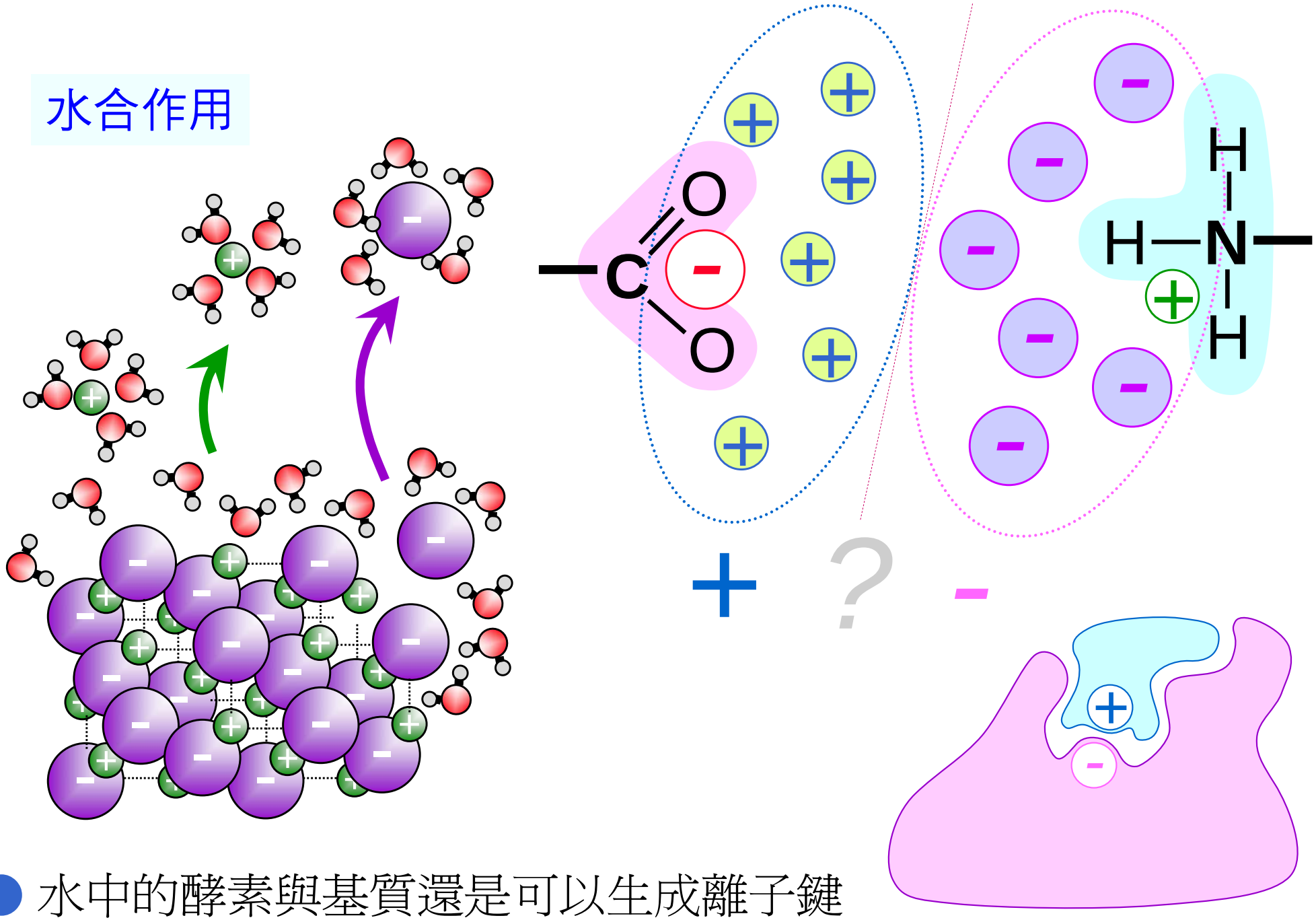


越對稱的分子極性越小

Adapted from Bohinski (1987) Modern Concepts in Biochemistry (5e) p.37

# 離子鍵在鹽溶液中不易形成

Adapted from Nelson & Cox (2004) Lehninger Principles of Biochemistry (4e) p.51




Adapted from Alberts et al (2002) Molecular Biology of the Cell (4e) p.115

- 水中的酵素與基質還是可以生成離子鍵

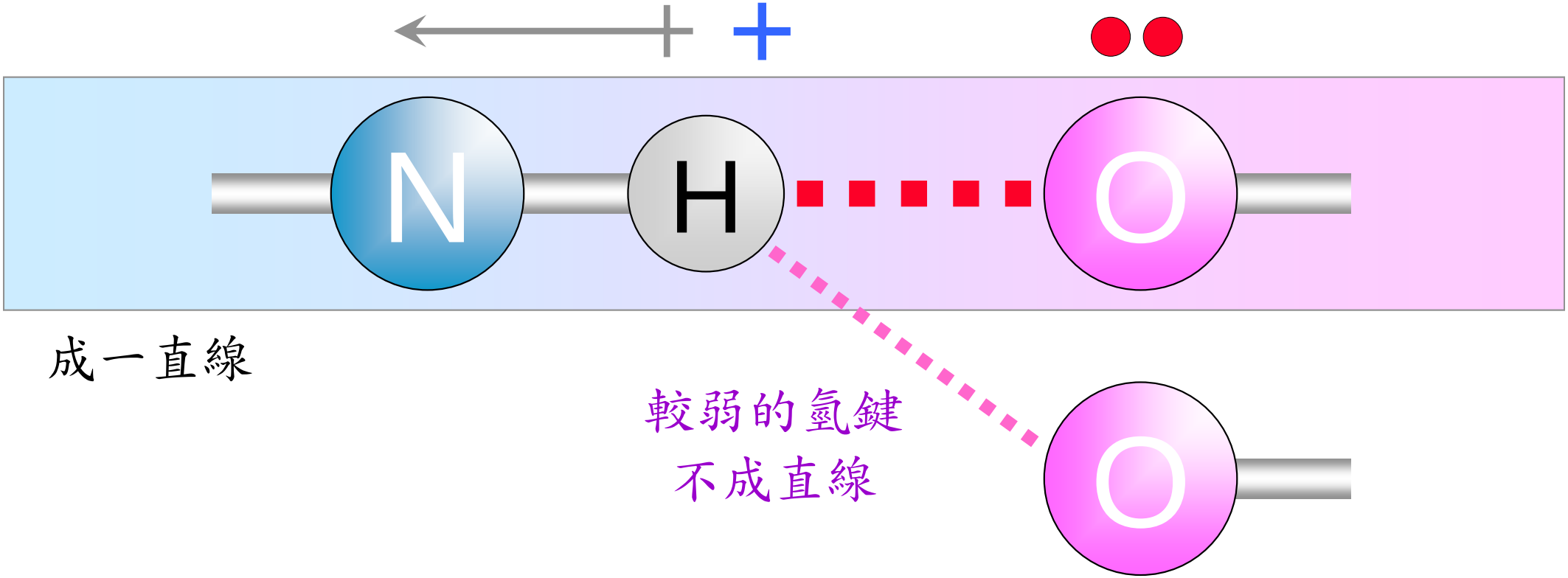
# 共價鍵或非共價鍵的鍵能

| | 鍵 長 | 真空中 | 水溶液 |
|---|---|---|---|
| 共價鍵 | 0.15 nm | 90 | 90 |
| 離子鍵 | 0.25 nm | 80 | *3* |
| 氫 鍵 | 0.30 nm | 4 | *1* |
| 凡得瓦爾力 | 0.35 nm | 0.1 | 0.1 |

kcal/mole

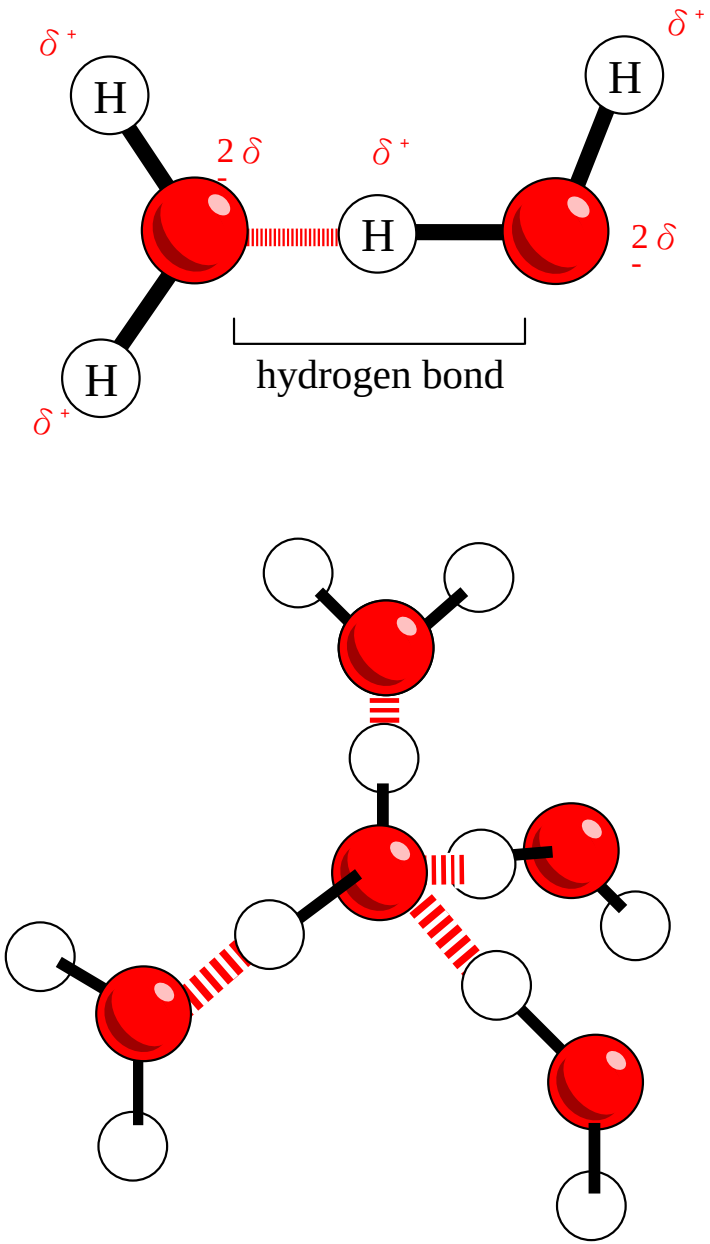
Adapted from Alberts et al (2002) Molecular Biology of the Cell (4e) p.57

# 氫 鍵 Hydrogen Bond

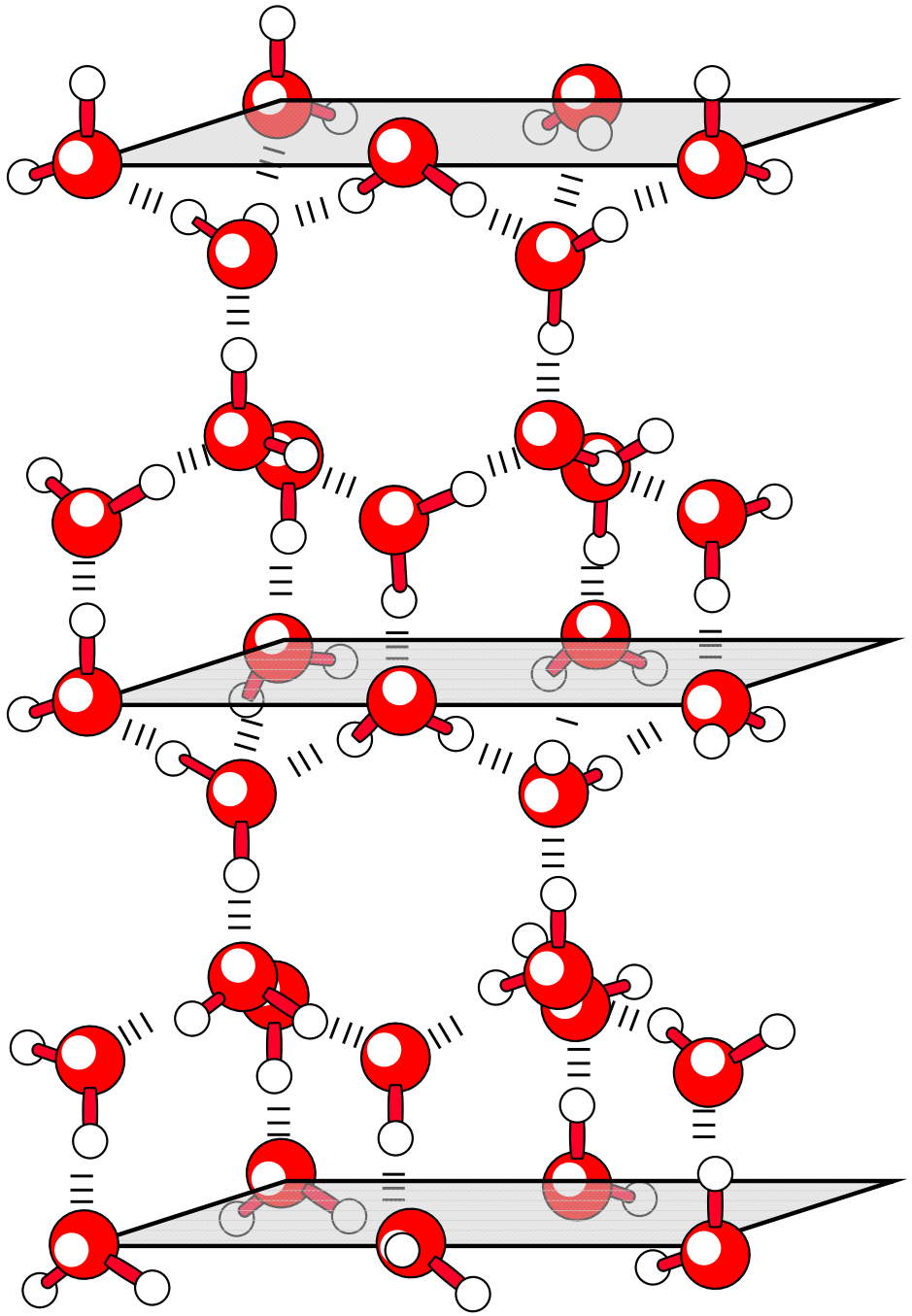



Adapted from Alberts et al (2002) Molecular Biology of the Cell (4e) p.58

# 水分子間藏有龐大的氫鍵系統

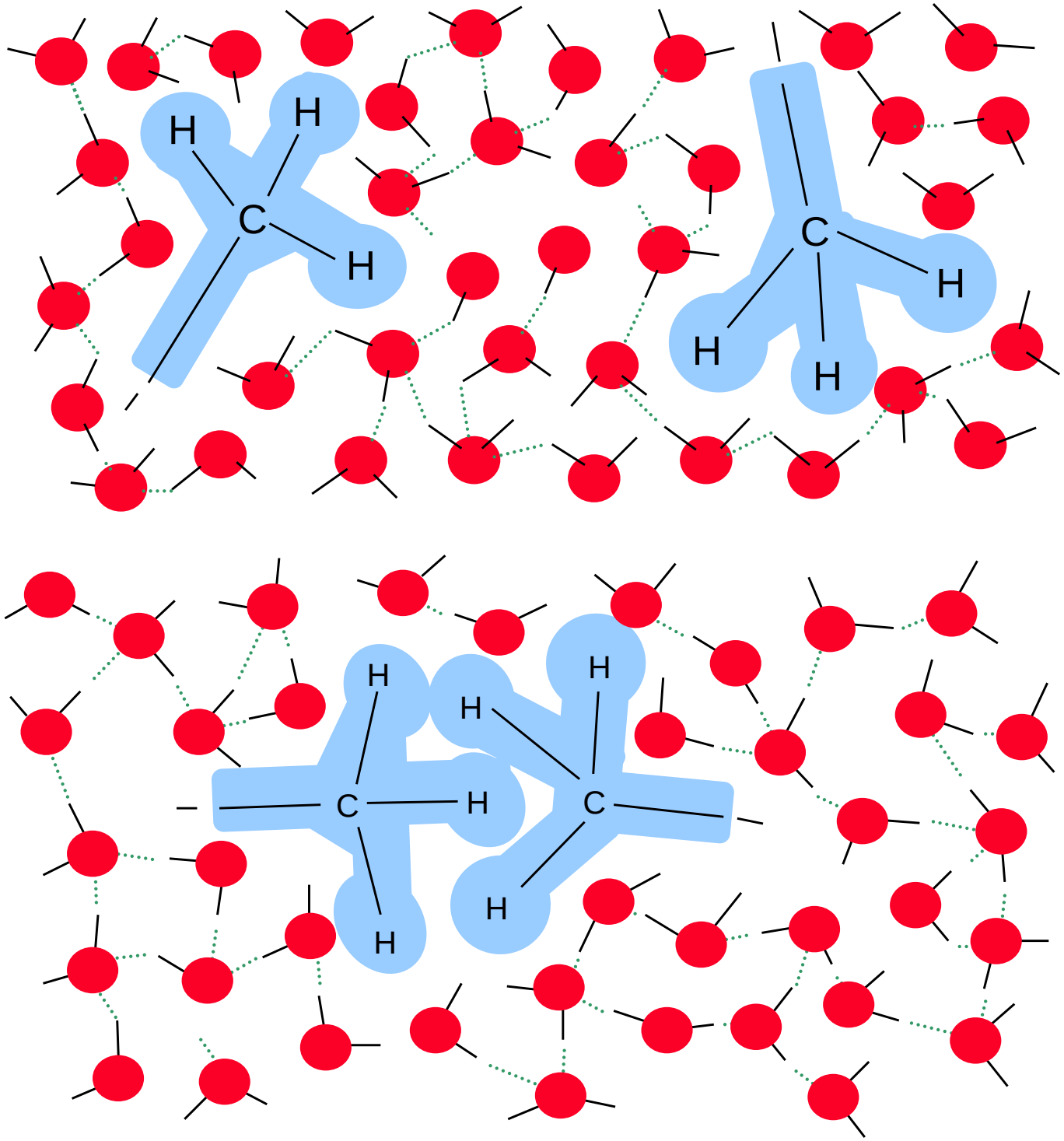



Adapted from Alberts et al (2002) Molecular Biology of the Cell (4e) p.112



Adapted from Nelson & Cox (2000) Lehninger Principles of Biochemistry (3e) p.84

# 疏水鍵的形成

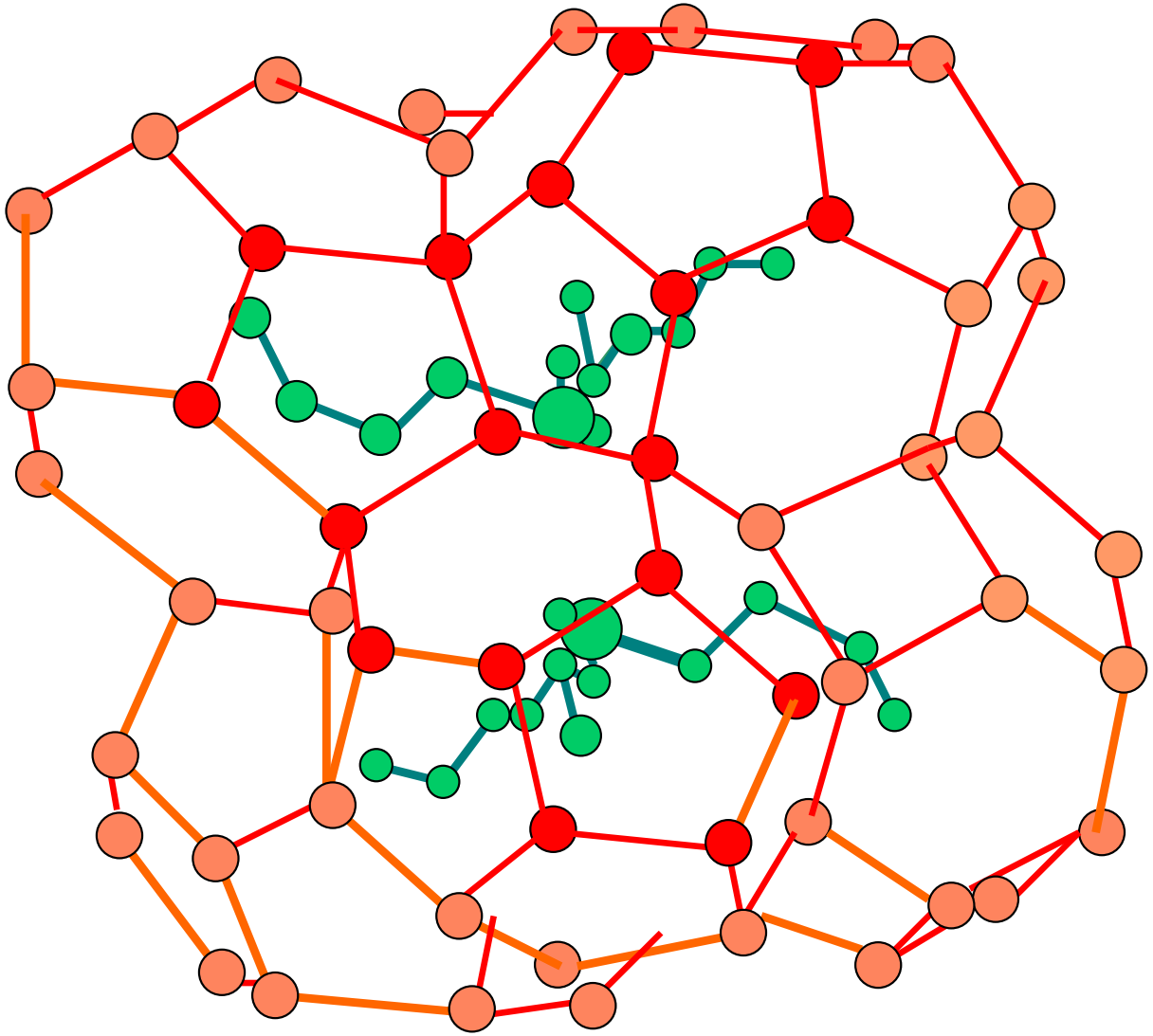



水分子與氫鍵
強迫非極性
分子之間
產生吸引力
即爲疏水鍵

疏水鍵多爲
凡得瓦爾力
所貢獻

Adapted from Alberts et al (2002) Molecular Biology of the Cell (4e) p.115

# 非極性物質間的親和力： 疏水性引力



## 水籠 Clathrate

- 水分子會包圍在非極性分子四周，形成類似竹籠的構造，隔離非極性分子，水分子本身的流動性因此而降低。

Adapted from Alberts et al (1994) Molecular Biology of the Cell (3e) p.49

# 極性相近者互相吸引

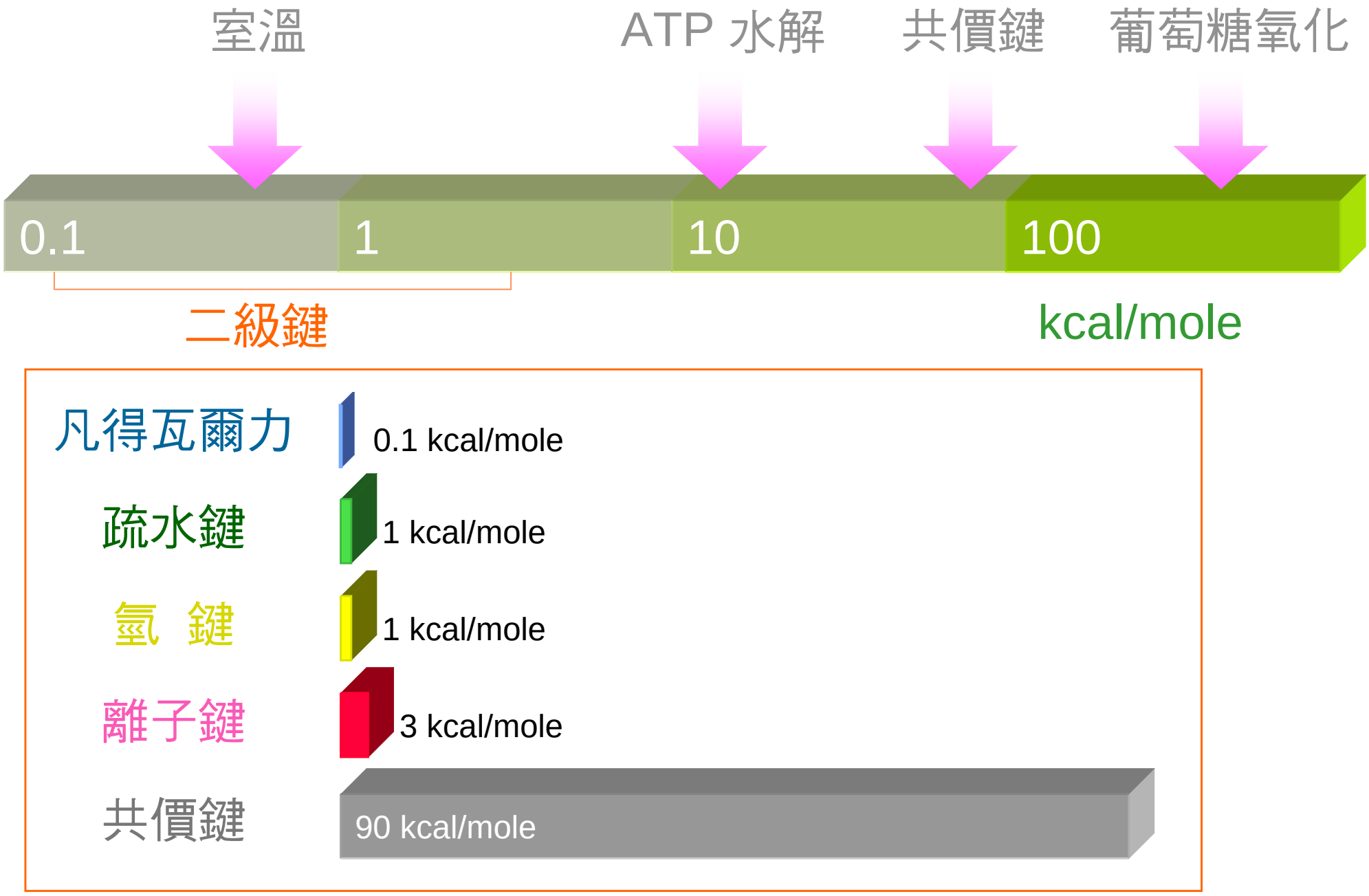
***Like***
***Dissolves***
***Like***

- 極性相似的兩分子間，其親和力較強。

極性 → 極性
非極性 → 非極性

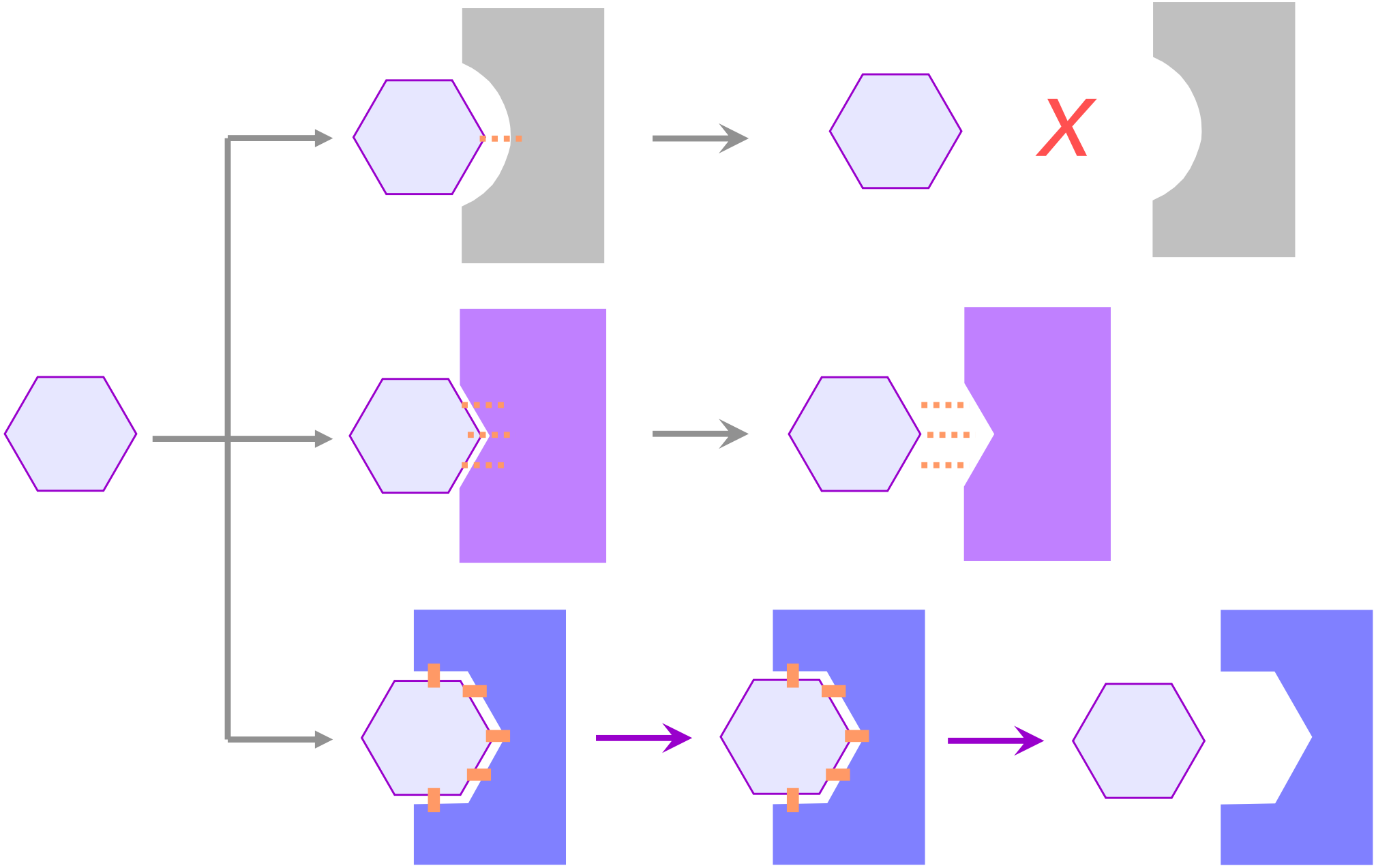
# 細胞內各種鍵結能量大小

Adapted from Alberts et al (2002) Molecular Biology of the Cell (4e) p.53




Juang RH (2007) BCbasics

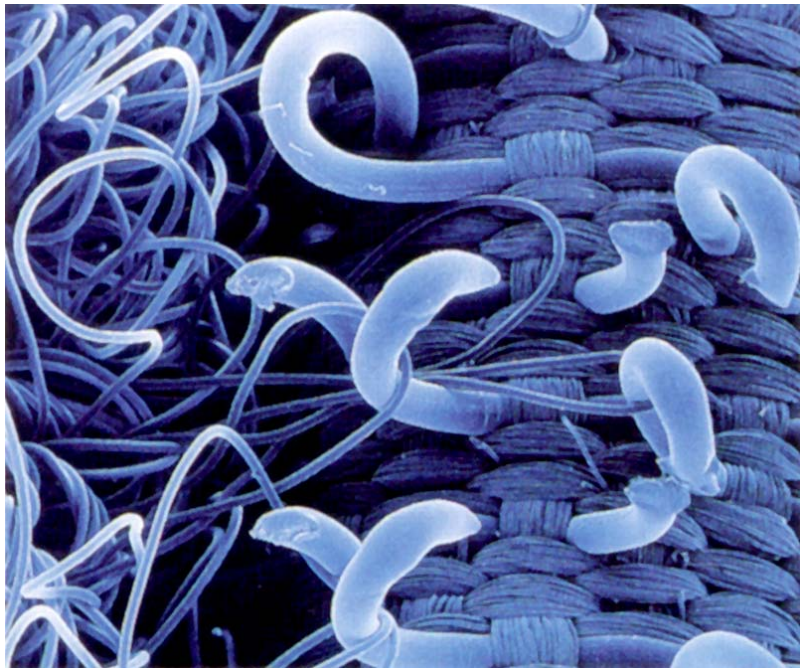
# 二級鍵是巨分子間的專一性結合力量



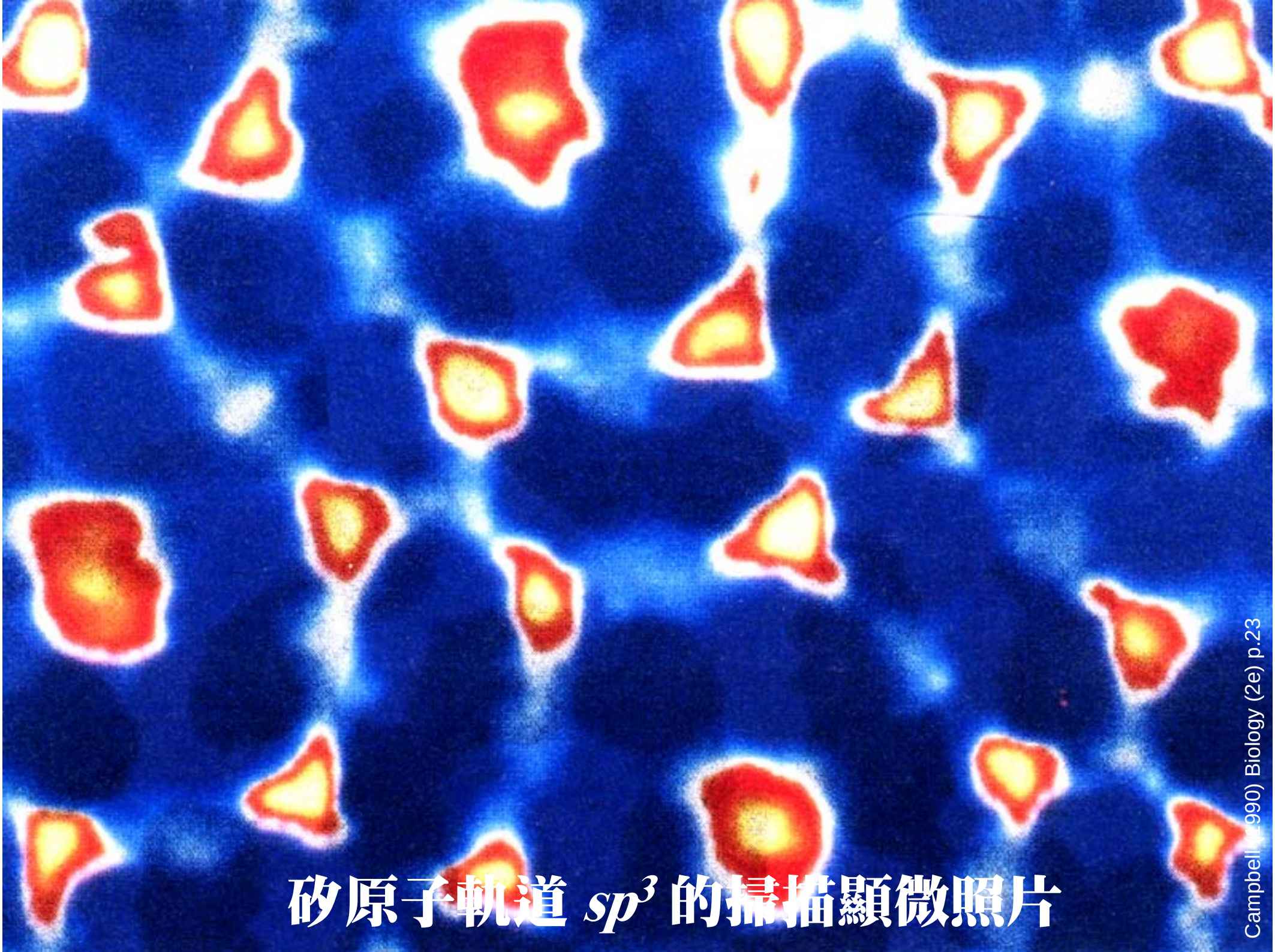
可逆性的非共價結合

Adapted from Alberts et al (2002) Molecular Biology of the Cell (4e) p.161

# 魔鬼氈也是由微弱作用力所組合



Everyday Science Explained (1996) p.41



# 矽原子軌道 $sp^3$ 的掃描顯微照片

Campbell (1990) Biology (2e) p.23