Chapter 1: Biochemistry: An evolving science

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1. Biochemical Unity underlines Biological Diversity

強調

異中求同

異: Animal diversity (insect → elephant) whale
plant " (algae 洋菜膠 → sequoias) 紅美洲杉
bacteria, yeast
hot spring

Biological divesity

Vital Force: compounds found in living organisms could not be produced in the laboratory

Wöhler, 1828

NH4OCN → NH_2–C=O–NH_2

Amonia cyanate → urea

同: proteins: 相同的 20 種 ~~DNA~~ Amino Acids 構成

Biochemical unity

DNA, RNA } Nucleic Acid: ATGCU

從細菌到人類的 TATA Box Binding protein 结構都一樣
(Transcription factor. DNA replication 时)

從 metabolics 來看 Glucose + O_2 → CO_2 + H_2O + Energy
細菌到人都一樣

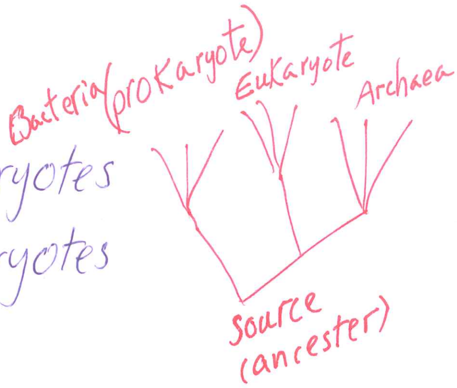
Have a common ancestor!

Timeline (billion yrs):

- 4.5 盤古開天 (Earth Formed)
- 3.5 微生物 (Mico-oganism)
- 2.2 Eukaryacell
- 1.5 O_2 atmosphere forming
- 0.25 恐龍 (Dinosaurs)
- 0 人類 (Human Being)

3 domains: Bacteria (proKarya)
Eukarya
Archaea (hot spring)

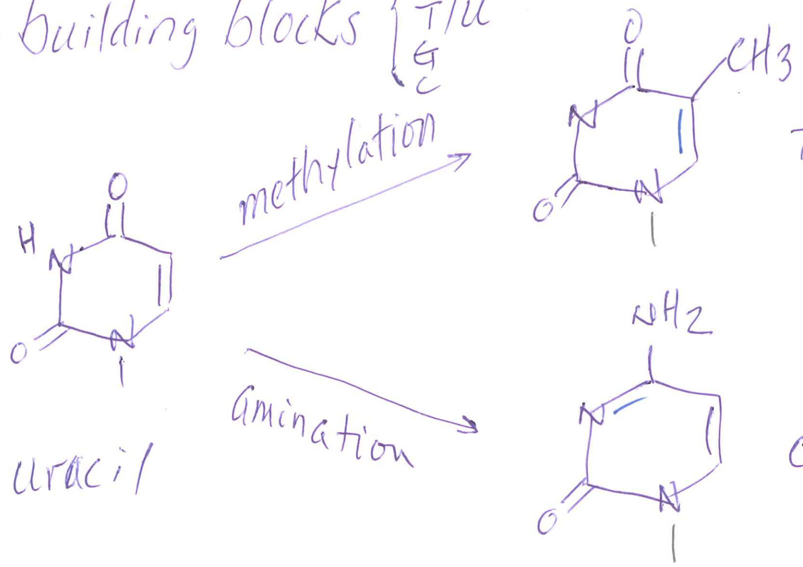
prokaryotes
Eukaryotes



DNA illustrates the interplay between form & function

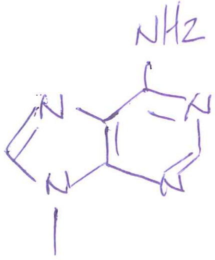
1953: Watson & Crick for DNA Helix

4 building blocks { A, T/U, G, C }

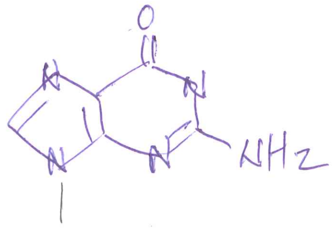


Thymine

cytosine



Adenine



Guanine

Chicago (19岁)
purdue Univ (22)
萨尔瓦多 Ruria
DenmarK (Kalckar)
Oxford, F. crick
Rosy Franklin
pickture 51
two pages Nature, 1953 (25)

Watson
Crick } 1962
Wilkins

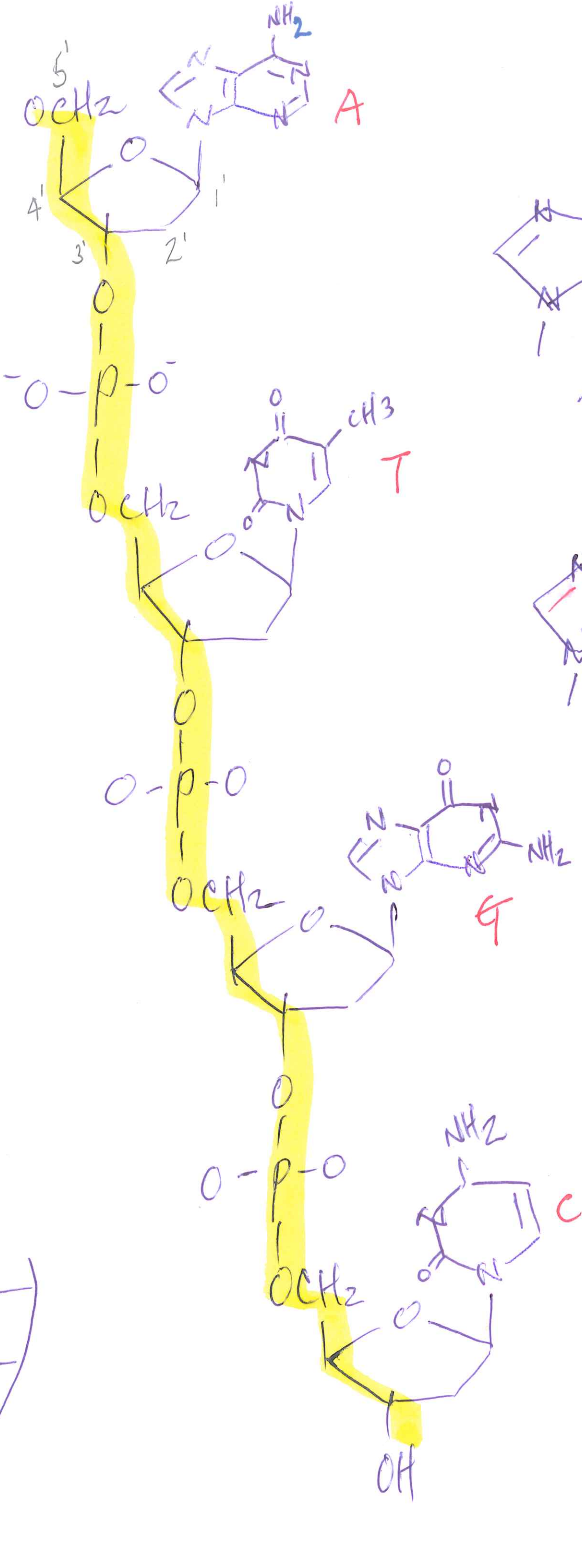
D.H. { 我是 Jim. 我很聪明
Francis 在大部分时候也很聪明
其他人都是笨蛋 }

文筆直接而神經質缺乏耐心
寫作技巧高超

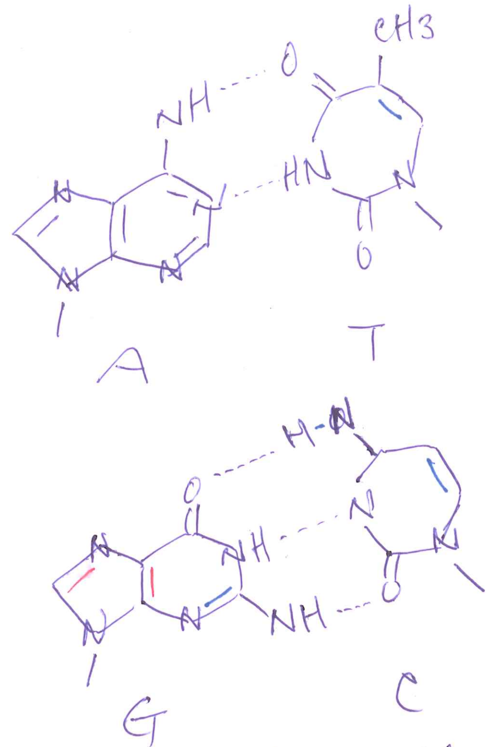
Watson:
1. Have a good mentor
2. Don't spend too much time with dumb people

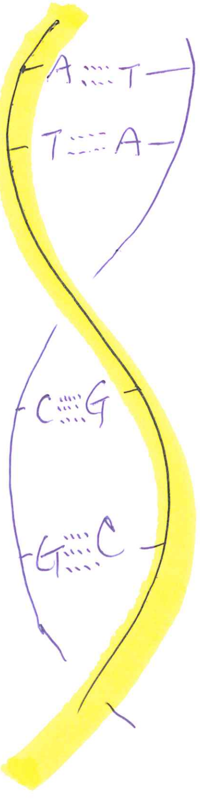
李遠哲
Manhan
问什麼都不知道
遠哲, 我如果知道答案, 就不会讓您来做

Covalent structure of DNA



H-bond { weak for revesible
strong to form a structure (double helix)



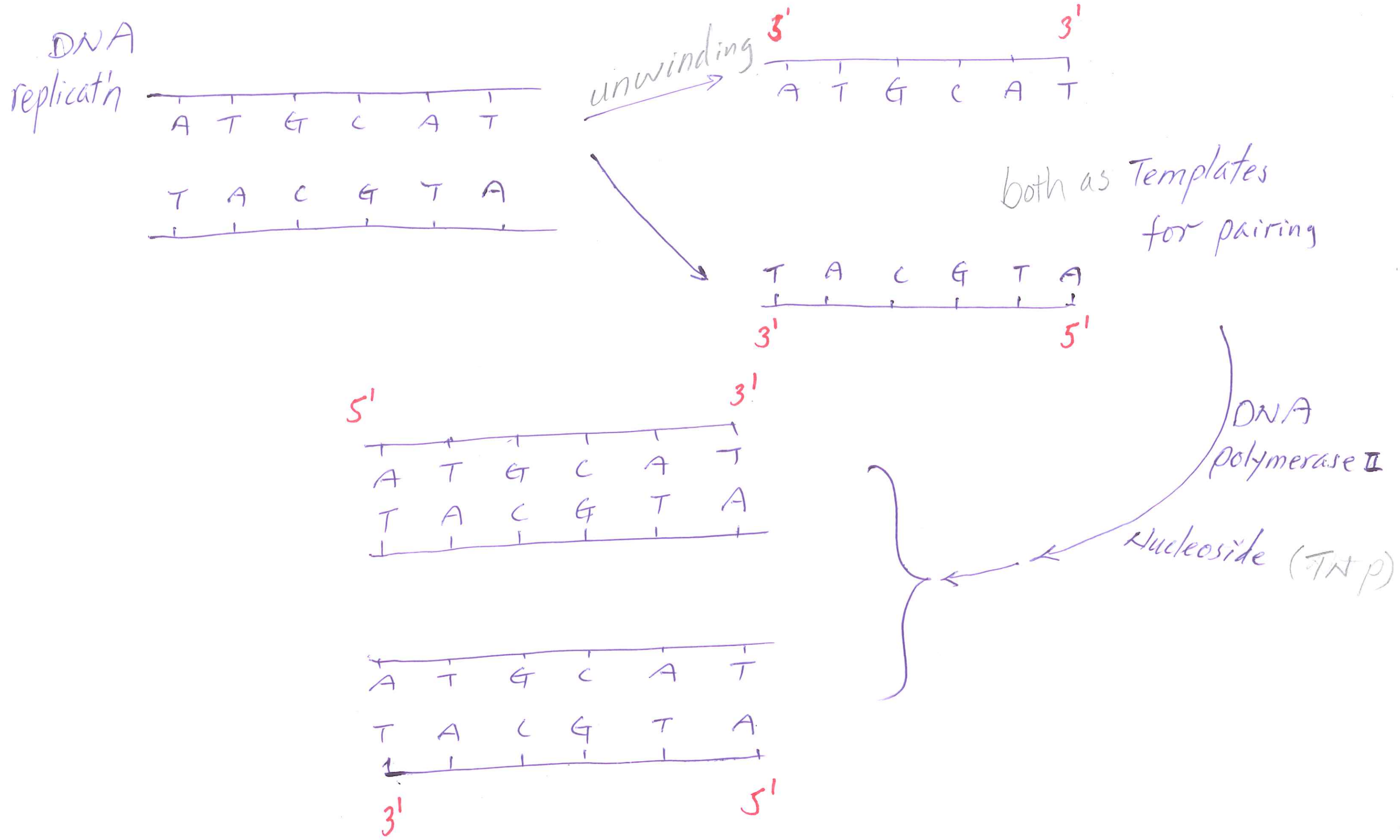


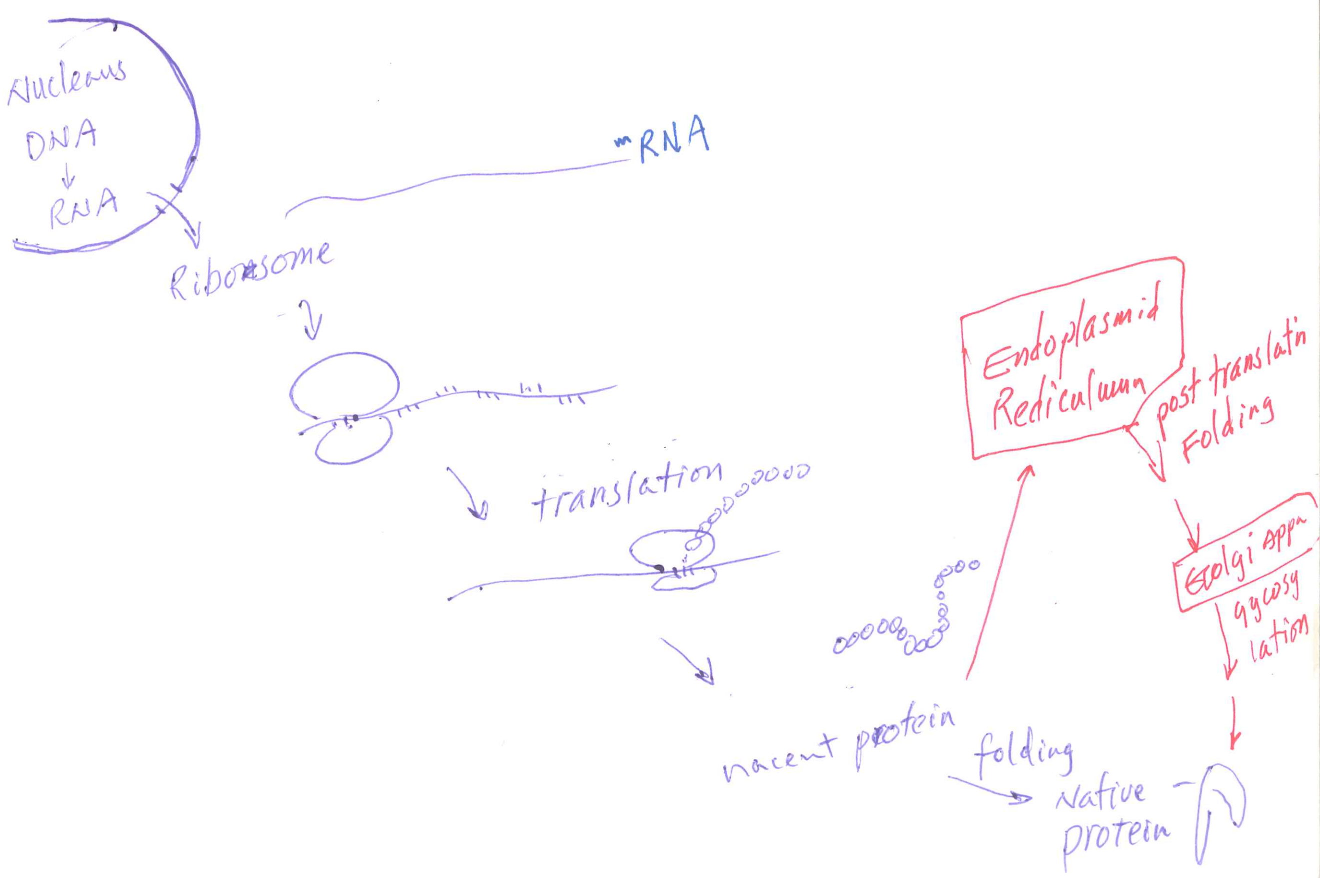
Hydrogen bond stabilizing double helix

{ * sugar phosphate bond (back) on the outside
* bases on inside
成 A:::T . G:::C pair

Heredity

DNA —决定 sequence of→ RNA —决定 a.a sequence of→ protein → Funct'n





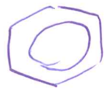
Covalent bond

C−C bond length : 1.54 Å

" bond energy : 85 Kcal/mole

C=O " : 175 Kcal/mole

C=C bond length 1.34 Å , energy = 148 Kcal/mole

 " 1.40 Å

Non-Covalent bond interactions {
- electrostatic interaction
- Hydrogen bond
- van der waals interation
- hydrophobic interaction

① electrostatics :

$q_1 \xleftrightarrow{\ r\ } q_2$ $E = \frac{k q_1 q_2}{D r^2}$

在 H_2O 中 :

$$E = \frac{332 (1)(-1)}{80 \cdot (3Å)^2} = -1.4 \text{ Kcal/mole}$$

在 hexane

$$E = \frac{332(1)(-1)}{2 (3Å)} = -55 \text{ Kcal/mole}$$

② H-bond

δ^+ δ^-

NH ········ N

NH ········ O

OH ········ N

OH ········ O

|← 1.5-2.6 →|

|← 2.4 − 3.5 →|

bond length : 1.5 − 2.6 Å

" energy : 1 − 5 Kcal/mole

N — H ·········· O

|← 0.9 →|← 2.0 →|

Å Å

③ van der Waals (0.5 ~ 1 Kcal/mole)

Source: 分子的 electronic charge distribution 是 fluctuate 状態, 当呈不对称时, 会有静电吸引力

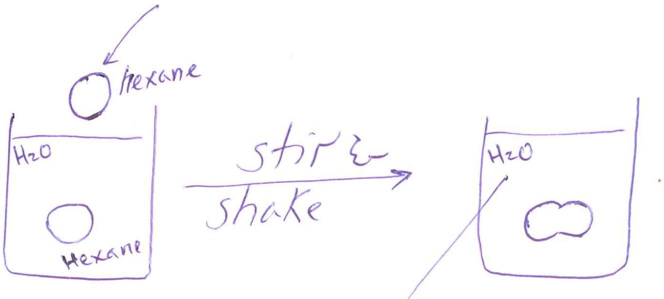
④ hydrophobic interaction

補充 { ① protein folding
② hydrophobic amino acids: G, A, L, I, V, P

property of H_2O

① H_2O 為 polar molecular

② H_2O 為 Highly cohesive: 有H-bond, 相互间作用力强
可溶解 polar 之 charged compound



在 cell enviroment 中, 有70%為 H_2O content.

Double helix formation: rules of chemistry

1. electro-static interaction (repulsion) of phosphate backbone
   minimizing by Mg^{2+} ions & H_2O
2. base-pairing H-bond favor double helix
3. Helix/Double 使 non-polar surface come together
   使 van der waals interaction maximize 而
   minimize non-polar surface (base) 與 H_2O 的接觸

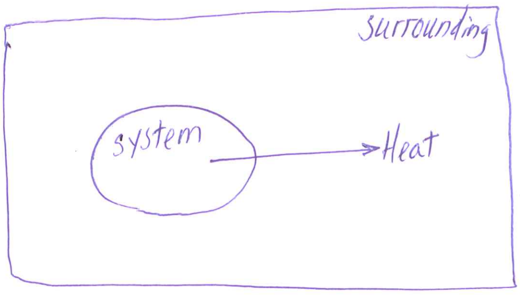
The Laws of Thermodynamics & Double Helix

Total = Universe = System + Surrounding

For a chemical rxns

1st Law: $E_{sys} + E_{sur} = \text{const}$

2nd 〃 : $S_{sys} + S_{sur}$ always increase



$\Delta S_{sur} \propto$ the amount of Heat transfer from system

&

$\Delta S_{sur} \propto \frac{1}{\text{temperature}}$

$\Delta S_{sur} = -\Delta H_{sys} / T$

$\Delta S_{total} = \Delta S_{sys} + \Delta S_{sur}$

$= \Delta S_{sys} - \frac{\Delta H_{sys}}{T}$

$-T\Delta S_{total} = \Delta H_{sys} - T\Delta S_{sys}$

Gibbs free energy $= -T\Delta S = \Delta G$

$\Delta G = \Delta H_{sys} - T\Delta S_{sys}$

2nd Law, ΔS_{total} (the entropy of Universe) must increase

$\Delta S_{total} > 0$

$\Delta S_{total} = \Delta S_{sys} - \Delta H_{sys}/T > 0$

$\Delta S_{sys} > \Delta H_{sys}/T$

$\Delta G = \Delta S - T\Delta S$

$T\Delta S_{sys} > \Delta H_{sys}$

Entropy will increase if & only if $\Delta G = \Delta H_{sys} - T\Delta S_{sys} < 0$

$\Delta G < 0$ 时, rxn occur spontaneously (自然發生)

$\Delta G = 0$ " " reach equilibrium

ΔG 0 ", 逆反应自然發生

$\Delta G = \Delta H - T\Delta S < 0$ 时 spontaneously occurs

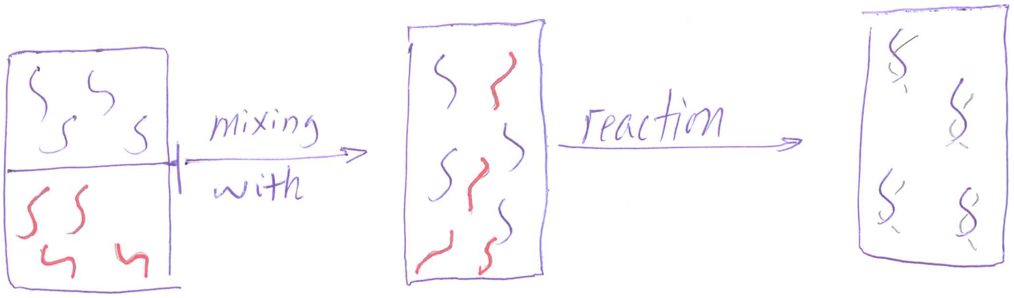
$T\Delta S$ 為負

ΔH 应為負, 故 Heat 為 release

(放熱反应)

· Heat is release when DH is form

entropy ↘



entropy ↗

decrease in order

Heat must release

$\Delta H = -60$ Kcal/mole (25°C, pH=7, [NaCl]=1M)

$\Delta G = \Delta H - T\Delta S < 0$, rxn spontaneously occur (Left to right)

$T\Delta S$: positive (T), negative (ΔS)

$T\Delta S$ → positive

↓

ΔH must be negative (= −60 Kcal/mole)

Acid-Base RxNs

$pH = -\log[H^+]$

$K_w = [H^+][OH^-] = 10^{-14}$

$H_2O \rightleftharpoons H^+ + OH^-$

$K = 1.8 \times 10^{-16} = \frac{[H^+][OH^-]}{[H_2O]} = \frac{[H^+][OH^-]}{55.5}$

$[H^+][OH^-] = K_w = \frac{(1.8 \times 10^{-16})(55.5)}{1}$

$= 10^{-14}$

The Human genome

10^6 : million
10^9 : billion (10億)
10^12 : trillion (兆)

包丢了 3×10^9 bp (~~3兆~~ 30億 个) 鹼基对

500,000 (50萬页 text book page)

Human disease : sickle-cell anemia AGT

Human species originated in Africa

從 bacteria 的 gene 發現同在 Human 中有 (Brian, Nerve) (Mitochondria)

讓 unethical problems 在 Human 实験变得可能

DNA 與 protein

1. DNA 僅 4个 building blocks ; protein 有 20个
2. DNA 僅為 DH, while protein 3D structure 有多种 (double Helix)

Human gene

1. 25,000 个 gene
2. splicing enable a gene encode more than one protein
3. post-translational modification
4. 3% of DNA are genes
5. person-to-person difference ≒ 0.1% in DNA