1.3 Physical Foundations

Living cells and organisms must perform work to stay alive and to reproduce themselves

Living Organisms Exist in a Dynamic Steady State, Never at Equilibrium with Their Surroundings

Precursors (amino acid) $\xrightarrow[r_1]{}$ Hemoglobin $\xrightarrow[r_2]{}$ Breakdown products (amino acid)

When $r_1 = r_2$

[hemoglobin]=const

在動力學上。稱為 Steady State，但非 Equilibrium !

Organisms Transform Energy and Matter from Their Surroundings

Universe { System; Surroundings }

closed system : the system exchanges energy but not matter

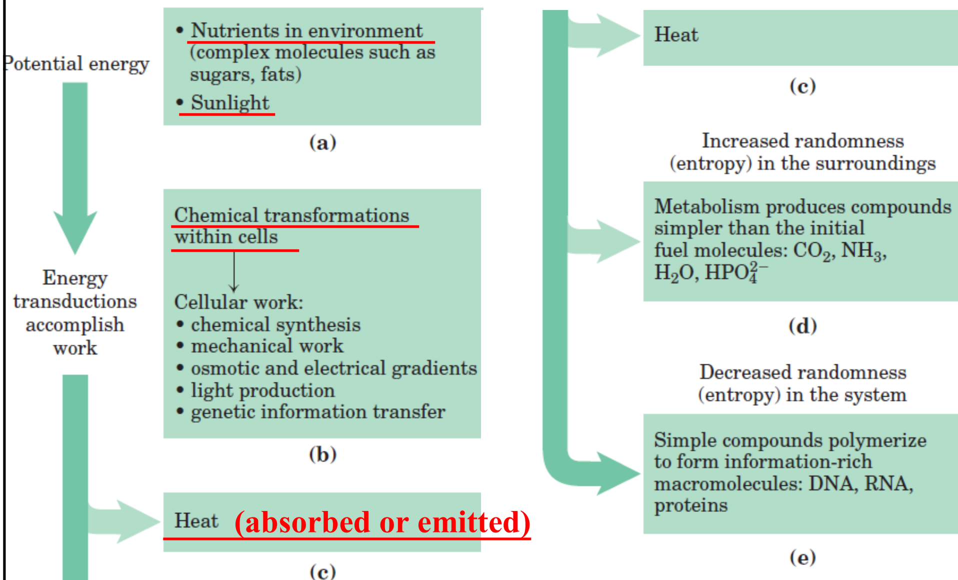
open system： exchanges energy and matter

isolated system： exchanges neither energy nor matter

Living organism is an open system

- Living organisms create and maintain their complex, orderly structure using energy extracted from fuels or sunlight.
- In any physical or chemical change, the total amount of energy in the universe remains const.

The Flow of Electrons Provides Energy for Organisms



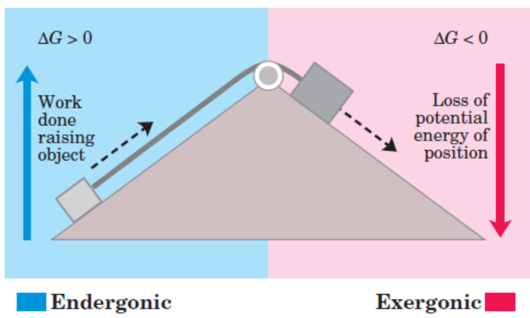
Energy Coupling Links Reactions in Biology

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

Free energy (G) & Free energy change (ΔG)

Exergonic: $\Delta G < 0$ **Endergonic: $\Delta G > 0$**

(a) Mechanical example



Energy Coupling Links Reactions in Biology

(1) Glucose ＋ Pi ⟹ Glucose 6-phosphate

(phosphate)

$\Delta G_1 > 0$

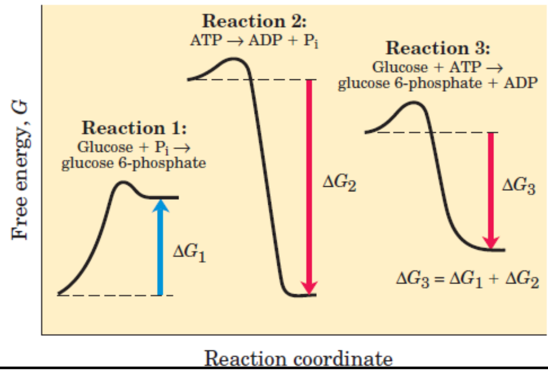
(2) ATP ⟹ ADP＋ Pi

Adenosine triphosphate (major carrier of chemical energy in all cells)

$\Delta G_2 < 0$

(3)Glucose ＋ ATP ⟹ Glucose 6-phosphate ＋ ADP

$\Delta G_3 = \Delta G_1 + \Delta G_2 < 0$



a reaction：

$$aA+bB \longrightarrow cC+dD \qquad K_{eq}=\frac{[C]^c[D]^d}{[A]^a[B]^b}$$

未達平衡時：

$$\Delta G = \Delta G^0 + RT\ln\frac{[C]^c[D]^d}{[A]^a[B]^b}$$

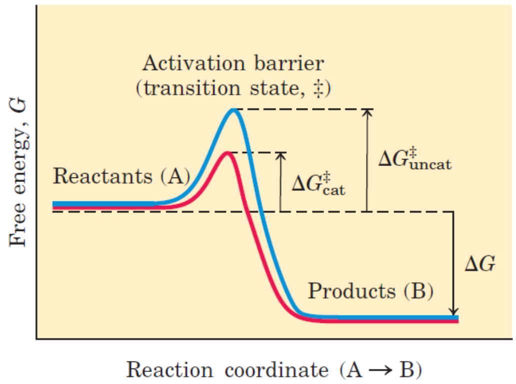
平衡時： $\Delta G=0$

⇓

$$\Delta G^0 = -RT\ln K_{eq}$$

Enzymes Promote Sequences of Chemical Reactions

Enzymes catalyze reactions by lowering the activation energy($\Delta G^{\ddagger}$)



collision frequency

$$k = z p e^{-\frac{\Delta G^{\ddagger}}{RT}}$$

steric factor

rate const.

$e^{-\frac{\Delta G^{\ddagger}}{RT}}$: **fraction of collisions with sufficient energy to produce a reaction**

Each enzyme protein catalyzes a specific reaction, and each reaction in a cell is catalyzed by a different enzyme

- **multiplicity**
- **specificity**
- **susceptibility to regulation**

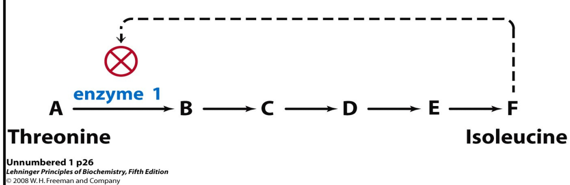
$\}$ **of the enzymes**

⇩

give cells the capacity to lower activation barrier selectivity

⇩

Effective regulation of cellular processes



reaction pathway
每一步驟皆有專司負責的enzyme

Feedback inhibition

Metabolism: Catabolism and Anabolism

Nutrients
Foods
Solar
photons

Cellular works
Complex biomolecules
Mechanical works
Osmotic work

catabolism
(exergonic)

ADP
ATP

ADP
ATP

anabolism
(endergonic)

CO_2
NH_3
H_2O
precursors

Summary of 1.3

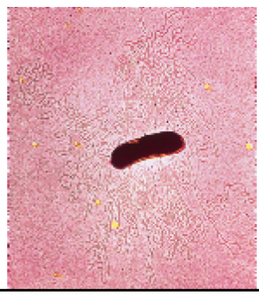
1.4 Genetic Foundations

遺傳物質：DNA (deoxyribonucleic acid)

A. Genetic continuity is vested in DNA molecule

文明的記錄
↓
石頭上的文字

遺傳的記錄
↓
DNA
reproduce themselves with nearly perfect fidelity for countless generations



B. The structure of DNA allows for its repair and replication with near-perfect fidelity

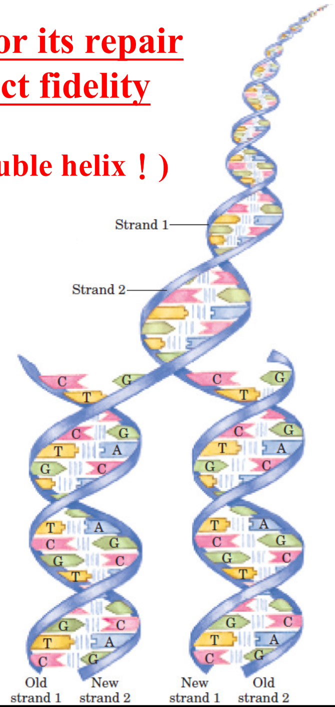
雙股DNA(double helix！)

•Complementarity between the two strands accounts for the accurate replication essentials for genetic continuity

•Genetic information is encoded in the linear sequence of four kinds of subunits of DNA

•The double-helical DNA molecule contains an internal template for its own replication and repair

chap 1.3 to 1.5



The linear sequence in DNA encodes proteins with 3-dimensional structures

DNA

↓ Transcription of DNA sequence into RNA sequence

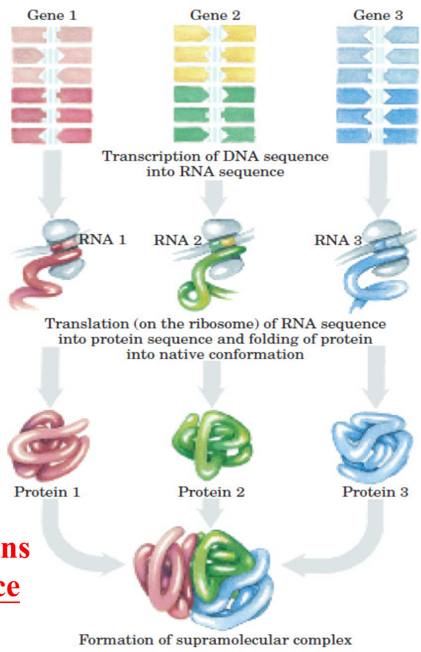
RNA

↓ Translation of RNA sequence into protein sequence

Linear amino acid sequence

↓ Noncovalent interactions

Protein with native conformation



The structure and function of proteins are encoded in its linear a.a. sequence

chap 1.3 to 1.5

Summary of 1.4

1.5 Evolutionary Foundations

Changes in the Hereditary Instructions Allow Evolution

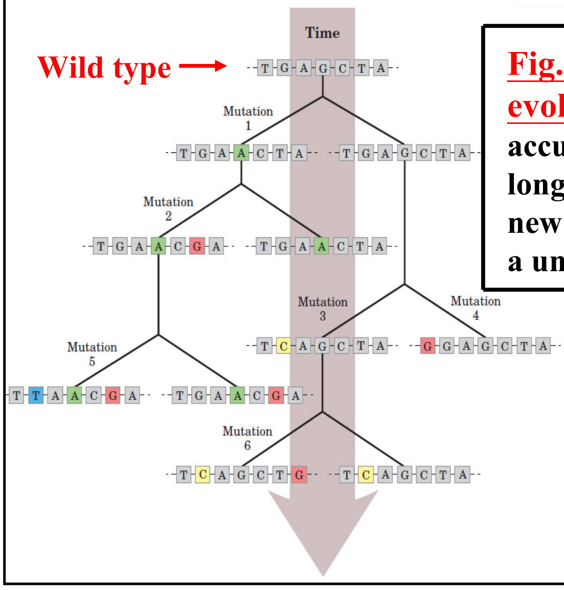


Fig. 1-32 Role of mutation in evolution The gradual accumulation of mutations over long periods of time results in new biological species, each with a unique DNA sequence.

Gene duplication and mutation (I)

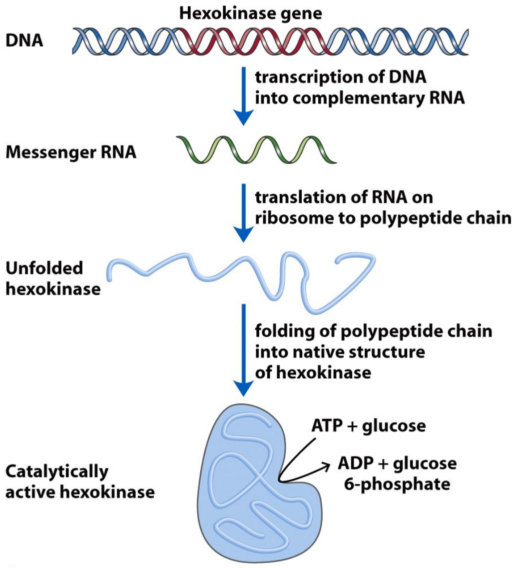


Figure 1-31
Lehninger Principles of Biochemistry, Fifth Edition

Gene duplication and mutation (II)

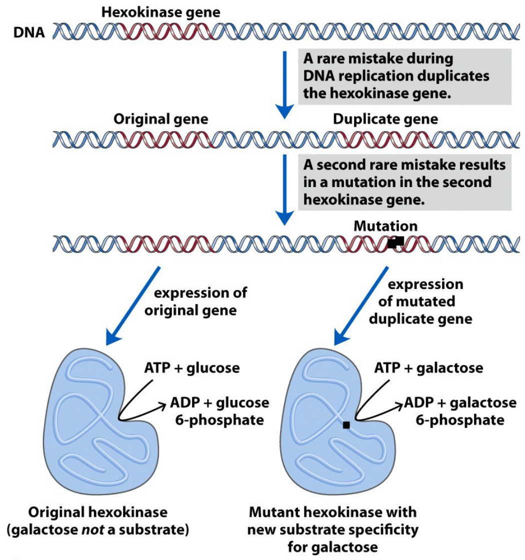


Figure 1-32
Lehninger Principles of Biochemistry, Fifth Edition

One pathway to generate new enzymatic activities

Biomolecules First Arose by Chemical Evolution

In 1922, Oparin proposed ：

early in the history of the earth at a reducing atmosphere(rich in methane, ammonia, and water)

↓

electrical energy (from lightning discharge or heat energy from volcanoes

↓

forming simple organic compounds

↓

dissolved in the ancient seas

↓ millions of years

simple organic molecules associate into larger complexs

↓ millions of years

form membrane and catalysts(enzymes)

Chemical Evolution Can Be Simulated in the Laboratory

In 1953, Stanley Muller's expt'l:

NH_3, CH_4, H_2, and H_2O

⇩

Electrical sparks for a weak or more

⇩

analyzed the contents:

amino acids
hydroxy acids
aldehydes
hydrogen cyanide

} produced

Even, polypeptides and RNA-like molecules!! (later expt'l)

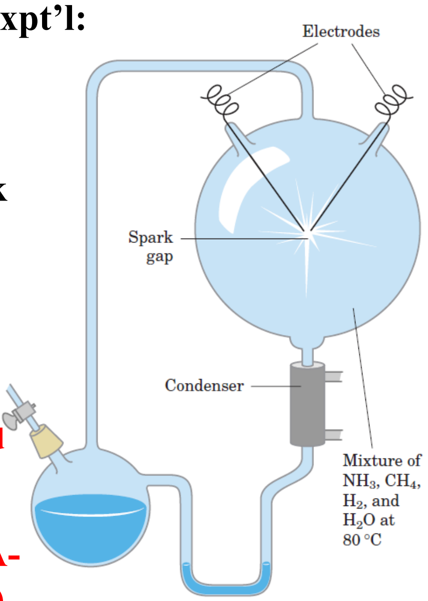


Figure 1-33

In conclusion,
many biomolecules, under prebiotic condition can be formed：including
polypeptides and RNA-like molecules (as catalyst)

↓

Protein

<u>Whether life also arose on the planets of other solar systems?</u>

RNA or Related Precursors May Have Been the First Genes and Catalysts

RNA can act as catalysts on their own formation

↓

RNA may have been the first catalyst and first gene

RNA World

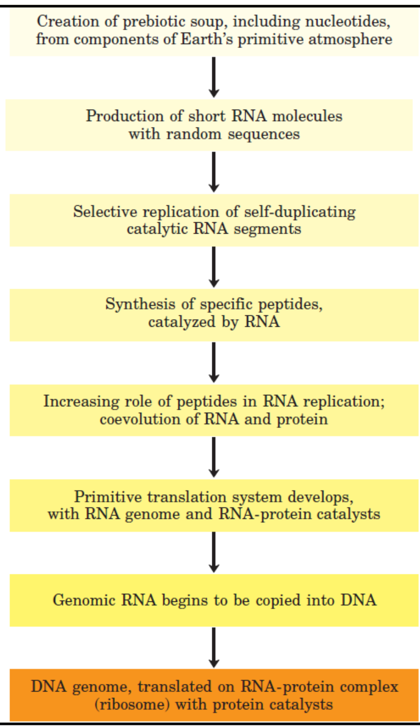


Fig 1-34

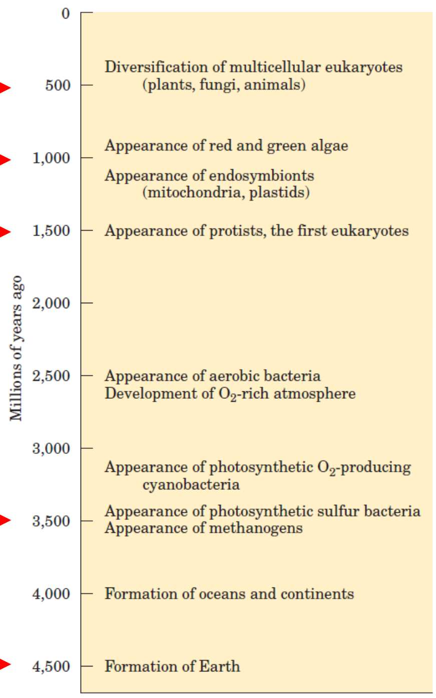
5億年前
Multicellular eukaryotes

10億年前endosymbionts (mitochondria and plastids)

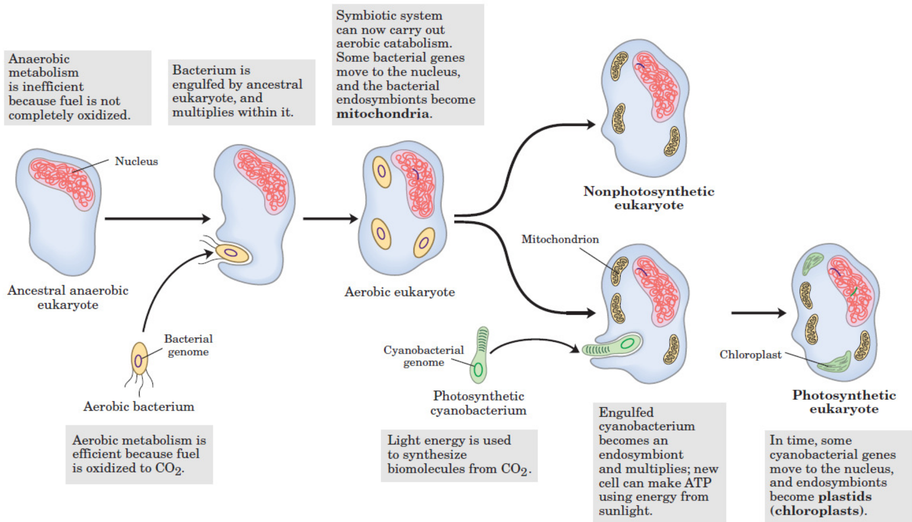
15億年前
first eukaryotes, protists (原生生物)

35億年前
Photosynthetic sulfur bacteria

45億年前
Formation of earth



Evolution of eukaryotes through endosymbiosis



Comparison of prokaryotic and eukaryotic cells

TABLE 1–3 Comparison of Prokaryotic and Eukaryotic Cells

Characteristic	*Prokaryotic cell*	*Eukaryotic cell*
Size	Generally small (1–10 μm)	Generally large (5–100 μm)
Genome	DNA with nonhistone protein; genome in nucleoid, not surrounded by membrane	DNA complexed with histone and nonhistone proteins in chromosomes; chromosomes in nucleus with membranous envelope
Cell division	Fission or budding; no mitosis	Mitosis, including mitotic spindle; centrioles in many species
Membrane-bounded organelles	Absent	Mitochondria, chloroplasts (in plants, some algae), endoplasmic reticulum, Golgi complexes, lysosomes (in animals), etc.
Nutrition	Absorption; some photosynthesis	Absorption, ingestion; photosynthesis in some species
Energy metabolism	No mitochondria; oxidative enzymes bound to plasma membrane; great variation in metabolic pattern	Oxidative enzymes packaged in mitochondria; more unified pattern of oxidative metabolism
Cytoskeleton	None	Complex, with microtubules, intermediate filaments, actin filaments
Intracellular movement	None	Cytoplasmic streaming, endocytosis, phagocytosis, mitosis, vesicle transport

Molecular anatomy reveals evolutionary relationships

- **Relatedness of species:**
  - 18 century, anatomic similarities and differences among organisms (Linnaeus)
  - 19 century, phylogeny of modern organisms (Darwin)
  - 20 century, 'molecular anatomy': sequences and three-dimensional structure of nucleic acids and proteins
- **Genome (the complete endowment of an organism)**
- **Some organisms whose genomes have been completely sequenced: (see table 1.2)**

TABLE 1–2 A Few of the Many Organisms Whose Genomes Have Been Completely Sequenced

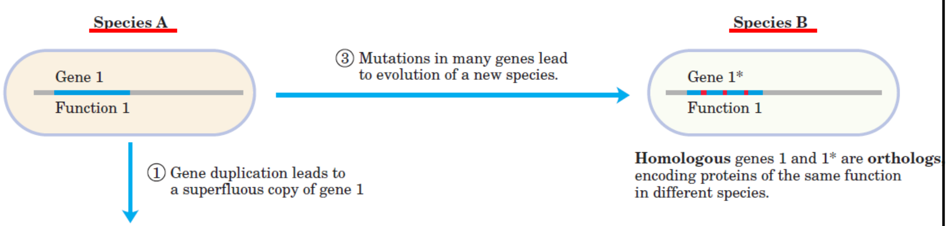
Organism	Genome size (millions of nucleotide pairs)	Number of genes	Biological interest
Mycoplasma genitalium	0.58	483	Smallest true organism
Treponema pallidum	1.1	1,039	Causes syphilis
Borrelia burgdorferi	1.44	1,738	Causes Lyme disease
Helicobacter pylori	1.7	1,589	Causes gastric ulcers
Methanococcus jannaschii	1.7	1,783	Archaean; grows at 85 °C!
Haemophilus influenzae	1.8	1,738	Causes bacterial influenza
*Archaeoglobus fulgidus**	2.2	—	High-temperature methanogen
Synechocystis sp.	3.6	4,003	Cyanobacterium
Bacillus subtilis	4.2	4,779	Common soil bacterium
Escherichia coli	4.6	4,377	Some strains cause toxic shock syndrome
Saccharomyces cerevisiae	12.5	5,770	Unicellular eukaryote
Plasmodium falciparum	23	5,268	Causes human malaria
Caenorhabditis elegans	100	19,400	Multicellular roundworm
Anopheles gambiae	278	13,700	Malaria vector
Arabidopsis thaliana	157	25,500	Model plant
Oryza sativa	390	37,500	Rice
Drosophila melanogaster	140	13,000	Laboratory fly ("fruit fly")
Mus musculus domesticus	2.4×10^3	25,000	Laboratory mouse
Pan troglodytes	2.4×10^3	25,000	Chimpanzee
Homo sapiens	2.9×10^3	25,000	Human

*The number of genes is not yet determined.

Table 1-2
Lehninger Principles of Biochemistry, Fifth Edition

Molecular phylogeny is derived from gene sequences

- When two genes DNA or protein share detectable sequence similarities , their sequences are **'homologous'** and the proteins they encode are **'homologs'.**
- Two homologous genes occur in the same species, they are **'paralogous'** and the proteins are **'paralogs'.**
- Two homologous genes occur in the different species, they are **'orthologous'** and the proteins are **'orthologs'.** **Annotated genome** includes (1) DNA sequence, and (2) a description of the **likely function** of each gene product (deduced from comparisons with other genomic sequences and established protein function).



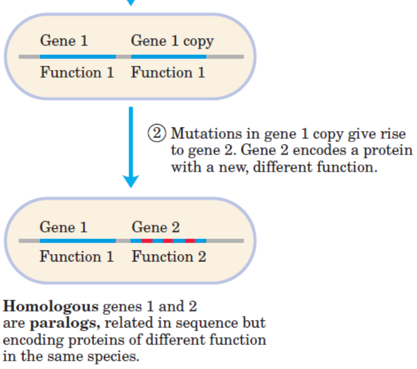


FIGURE 1–37 Generation of genetic diversity by mutation and gene duplication. ① A mistake during replication of the genome of species A results in duplication of a gene (gene 1). The second copy is superfluous; mutations in either copy will not be deleterious as long as one good version of gene 1 is maintained. ② As random mutations occur in one copy, the gene product changes, and in rare cases the product of the "new" gene (now gene 2) acquires a new function. Genes 1 and 2 are *paralogs*. ③ If species A undergoes many mutations in many genes over the course of many generations, its genome may diverge so greatly from that of the original species that it becomes a new species (species B)—that is, species A and species B cannot interbreed. Gene 1 of species A is likely to have undergone some mutations during this evolutionary period (becoming gene 1*), but it may retain enough of the original gene 1 sequence to be recognized as *homologous* with it, and its product may have the same function as (or similar function to) the product of gene 1. Gene 1* is an *ortholog* of gene 1.

Molecular phylogeny is derived from gene sequences

- **The sequence differences between two homologous genes may be taken as a measure of the degree to which the two species have diverged during evolution.**

- **The larger the number of sequence differences, the earlier the divergence in evolutionary history.**

- **Phylogeny (family tree) (see fig. 1-4)**