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Fundamentals of Biochemistry Second Edition

Chapter 1: Introduction to the Chemistry of Life

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Biochemistry: the study of the chemistry of life

What are the chemical and 3D structures of biomolecules
How do bimolecules interact with each other
How does the cell synthesize and degrade biomolecules
How is energy conserved and used by the cell
What are the mechanisms for organizing biomolecules

and coordinating their activities

How is genetic information stored, transmitted, and expressed

Evolution

The origin of the universe and the chemical elements from simple elements to biochemically important elements The origin of the solar system and the earth

Chemical evolution: Abiotic synthesis of biomolecules

functional groups condensation complementary

Cellular evolution

compartmentation: the rise of protocells primitive catalysts energy

Organismal evolution



Chapter 1 Opener Fundamentals of Biochemistry, 2/e

The earth, 4.6 billion yrs old

Table 1-1 Most Abundant Elements in theHuman Body^a

Element	Dry Weight
	(70)
С	61.7
Ν	11.0
Ο	9.3
Н	5.7
Са	5.0
Р	3.3
K	1.3
S	1.0
Cl	0.7
Na	0.7
Mg	0.3

^{*a*}Calculated from Frieden, E., *Sci. Am.* 227(1), 54–55 (1972).

Table 1-1 Fundamentals of Biochemistry, 2/e © 2006 John Wiley & Sons



How old is life on earth?



Stromatolite, 3.5 billion yrs old



Figure 1-1 Fundamentals of Biochemistry, 2/e

Chemical evolution



http://en.wikipedia.org/wiki/Abiogenesis

Origin of chemical evolution

simple compounds to biochemically significant molecules 1903s, Oparin & Haldane 1953, Miller & Urey





Life from the sea?



Figure 1-2 Fundamentals of Biochemistry, 2/e

The Essential Role of Water

Water is the key to understanding the behavior of macromolecules the solvent of life all living transformations occur in an aqueous media

Water-insoluble compounds (lipid membranes) derive their nature and function by their interactions with water

Common Functional Groups

Arise from simple organic compounds

Compound Name	Structure ^a	Functional Group or Linkage
Amine ^b	RNH ₂ or $R\overset{+}{N}H_3$ R ₂ NH or $R_2\overset{+}{N}H_2$ R ₂ N or $R_2\overset{+}{N}H$	-N < or $-N = (amino group)$
Alcohol	ROH	-OH (hydroxyl group)
Thiol	RSH	—SH (sulfhydryl group)
Ether	ROR	-O- (ether linkage)
Aldehyde	О Ш R—С—Н	O
V.		
Ketone	K - C - K	-C- (carbonyl group)
Carboxylic acid ^b	$R - C - OH \text{ or } R - C - O^{-}$	$ \begin{array}{c} O \\ \parallel \\ -C - OH (carboxyl group) \text{ or } \\ O \\ \parallel \\ -C - O^{-} (carboxylate group) \end{array} $
	0	
Ester	R—C—OR	$ \begin{array}{c} \\ \parallel \\ \\ -C \\ -O \\ \end{array} (ester linkage) R \\ -C \\ -C \\ (acyl group)^c \end{array} $
	0	
Thioester	R-C-SR	$-\ddot{C}$ - S - (thioester linkage) R - \ddot{C} - (acyl group) ^c

Table 1-2	Key to Structure.	Common Functional	Groups and	Linkages in	Biochemistry
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^aR represents any carbon-containing group. In a molecule with more than one R group, the groups may be the same or different.

^bUnder physiological conditions, these groups are ionized and hence bear a positive or negative charge.

^cIf attached to an atom other than carbon.

Table 1-2 part 1 Fundamentals of Biochemistry, 2/e © 2006 John Wiley & Sons

Compound Name	Structure ^a	Functional Group or Linkage
Amide	$ \begin{array}{c} O \\ R \\ -C \\ -NH_2 \\ O \\ R \\ -C \\ -NHR \\ O \\ R \\ -C \\ -NR_2 \end{array} $	$ \begin{array}{c} O \\ \parallel \\ -C - N \\ \end{array} (amido group) R - C \\ -C - N \\ \end{array} (acyl group)^c $
Imine (Schiff base) ^{b}	$R=NH$ or $R=NH_2$	>C=N- or $>C=N<$ (imino group)
Disulfide	R=NR or R=NHR R-S-S-R O	—S—S— (disulfide linkage) O
Phosphate ester ^b	$\begin{array}{c} R - O - P - O^{-} \\ 0 H \end{array}$	│ ─P──O [−] (phosphoryl group) │ OH
Diphosphate ester ^b	$\begin{array}{ccc} O & O \\ \parallel & \parallel \\ R - O - P - O - P - O^{-} \\ O^{-} & OH \end{array}$	$ \begin{array}{cccc} O & O \\ \parallel & \parallel \\ -P - O - P - O^{-} & (phosphoanhydride group) \\ \downarrow & \downarrow \\ O^{-} & OH \end{array} $
Phosphate diester ^b	$ \begin{array}{c} O \\ \parallel \\ R - O - P - O - R \\ O \\ O \\ \end{array} $	-O - P - O - (phosphodiester linkage)

Table 1-2 Key to Structure. Common Functional Groups and Linkages in Biochemistry

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Table 1-2 part 2 Fundamentals of Biochemistry, 2/e © 2006 John Wiley & Sons

Condensation reactions

Chemical Evolution, simple molecules condense to form more complex forms (polymers)



Replication through complementarity



Figure 1-5 Fundamentals of Biochemistry, 2/e © 2006 John Wiley & Sons

Self-perpetuation & natural selection

- More complex molecules increases chemical versatility
- Specific pairing of functional groups gives rise to complementarity
- Complementarity makes it possible for macromolecules to replicate
- Over time natural selection favored molecules that made accurate copies of themselves

Double origin hypothesis: DNA & protein

RNA world hypothesis



Figure 1-6 Fundamentals of Biochemistry, 2/e © 2006 John Wiley & Sons

Cell compartmentation: independent life Required Biosynthesis & Energy

Fermentation as a source of energy

Development of photosynthesis

Evolution of aerobic metabolism

Replicate & propagate

differentiated & became multicellular



Figure 1-7 Fundamentals of Biochemistry, 2/e © 2006 John Wiley & Sons

Physical Units of Space, Time, and Energy.

LENGTH You must know this and be comfortable using them.

Length is very important!! •C - C bond is 1.54 Å •Hemoglobin 65Å •Ribosomes 300Å •Viruses 100 - 1000Å •Cells 7 μ m or 7 x 10⁴ Å

 $1 \text{ Å} = 10^{-10} \text{ m}$

Limit of a light microscope $= 2000 \text{ Å or } 0.2 \mu \text{m}$

1 Å \Rightarrow 10⁴ Å knowledge comes from X-ray crystallography, electron microscope or atomic force microscope

Life is in constant flux

Enzyme catalyzed reactions- Substrates \Rightarrow Products 10⁻³ sec - milli sec Unwinding of DNA 10⁻⁶ sec - micro sec

10 ⁻¹⁵ s femto	10 ⁻¹² s pico	10 ⁻⁹ s nano	10 ⁻⁸ s	10 ⁻⁶ s micro	10 ⁻³ s milli	10 s sec	10 ³ s
	•femto fs		excita	ation of ch	lorophyl	1	
	•pico ps	char	ge separat	ion in pho	tosynthe	sis	
	•nano ns	hing	ge protein a	action			
	•10 ⁻⁸ 10 ns		fluore	escence lif	etime		
	•micro µs		DNA	unwind			
	•milli ms		enzyr	natic react	tions		
	•10 ³ sec		gener	ation of b	acteria		
	•2.3 x 10 ⁹ sec		avera	ge human	life spar	ı	



Figure 1-8 Fundamentals of Biochemistry, 2/e



Living organisms operate within the same physical laws that apply to physics and chemistry

Thermodynamics:

Allows a prediction as to the spontaneous nature of a chemical reaction:

Will this reaction proceed in a forward direction as the reaction is written:

 $A + B \longrightarrow C$

Will A react with B to form C or not?

Definitions:

System:a defined part of the universe
a chemical reaction
a bacteria
a reaction vessel
a metabolic pathway

Surroundings: the rest of the universe

Open system: allows exchange of energy and matter

<u>Closed system</u>: no exchange of matter or energy.

The 1st Law of Thermodynamics: Energy is Conserved

Energy (U) is neither created or destroyed. $\Delta U = U_{\text{final}} - U_{\text{initial}} = q - w$ heat absorbed by the system from the surroundings

- work done by the system on the surroundings

change in internal energy



Enthalpy $(\mathbf{H}) = \mathbf{U} + \mathbf{PV}$

Enthalpy is the sum of the internal energy of matter and the product of its volume and pressure.

Most biological processes take place at constant pressure ($\Delta P=0$)

 $\Delta H = H(\text{products}) - H(\text{reactants})$ $= \Delta U + P\Delta V$ $= q_p - w + P\Delta V$ $= q_p - P\Delta V + P\Delta V$ $= q_p \text{ (heat at constant pressure)}$

therefore, $\Delta H = \Delta U$ in biochemical reactions where volume changes are insignificant

It is impossible to measure H, but possible to measure ΔH $\Delta H = H(\text{products}) - H(\text{reactants}) = q(+ \text{ or } -; \text{ age tes})$

Thermodynamics is useful for indicating the spontaneity of a process However, ΔH is not suitable for the purpose

Enthalpy shows heat change but not the direction $\Delta H < 0$ exothermic (enthalpically favored) $\Delta H > 0$ endothermic (enthalpically disfavored) The 2nd law of thermodynamics

Systems tend to proceed from a state of low probability (ordered) to a state of high probability (disordered)

Entropy (S): measure the degree of randomness Entropy tends to increase: consider both system & env

$S = k_b LnW$

k_b: Boltzman's constant
W: all the equivalent arrangements of its components
It is difficult or (impossible) to count the number of arrangements or the most probable state!

There is another expression for entropy at constant pressure conditions

1

$$\Delta S \ge \frac{q}{T}$$

Free energy

At constant pressure we have changes in q_p (Enthalpy) and changes in order A spontaneous process gives up energy and becomes more disordered

$$\begin{split} \Delta S \geq q_p/T &= \Delta H/T \\ \Delta H \text{ - } T\Delta S \leq 0 \\ G &= H \text{ - } TS \end{split}$$

If ΔG is negative, the process is spontaneous

 $\Delta G = \Delta H - T \Delta S < 0 \text{ exergonic}$ $\Delta G = \Delta H - T \Delta S > 0 \text{ endergonic}$ $\Delta G = \Delta H - T \Delta S = 0 \text{ equilibrium}$

Table 1-3Variation of Reaction Spontaneity (Sign of ΔG) with
the Signs of ΔH and ΔS

ΔH	ΔS	$\Delta G = \Delta H - T \Delta S$
_	+	The reaction is both enthalpically favored
		(exothermic) and entropically favored. It is
		spontaneous (exergonic) at all temperatures.
—	—	The reaction is enthalpically favored but entropically
		opposed. It is spontaneous only at temperatures
		below $T = \Delta H / \Delta S$.
+	+	The reaction is enthalpically opposed (endothermic)
		but entropically favored. It is spontaneous only at
		temperatures above $T = \Delta H / \Delta S$.
+	—	The reaction is both enthalpically and entropically
		opposed. It is unspontaneous (endergonic) at all
		temperatures.

Table 1-3 Fundamentals of Biochemistry, 2/e © 2006 John Wiley & Sons

Chemical equilibria & Standard state Standard Temperature and Pressure and at 1M concentration.

We calculate ΔG 's under these conditions.

 $aA + bB \iff cC + dD$



If we are at equilibrium (or $\Delta G = 0$)

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

$$\Delta G^{\circ} = -RTln \frac{[C]^{c}[D]^{d}}{[A]^{a}[B]^{b}} \quad OR \quad \Delta G^{\circ} = -RTlnK_{eq}$$

What does ΔG^{o} really mean?

If $K_{eq} = 1$, then $\Delta G^o = 0$

 K_{eq} can vary from 10⁶ to 10⁻⁶ or more!!!

$$\operatorname{Keq} = \frac{\left[C\right]_{eq}^{c}\left[D\right]_{eq}^{d}}{\left[A\right]_{eq}^{a}\left[B\right]_{eq}^{b}} = e^{\frac{-\Delta G^{\circ}}{RT}}$$

The Variation of K_{eq} with ΔG^{o} at 25 °C	
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K _{eq}	ΔG^{O}
106	-34.3
104	-22.8
10 ²	-11.4
101	-5.7
100	0.0
10-1	5.7
10-2	11.4
10-4	22.8
10-6	34.3

K depends on temperature

$$\ln K_{eq} = \frac{-\Delta H^{o}}{R} \left(\frac{1}{T}\right) + \frac{\Delta S^{o}}{R}$$

R = gas constant for a 1 M solutionPlot lnKeq vs. 1/T (remember T is in absolute degrees Kelvin)



Standard State for Biochemistry

1 M, 1 atm, 25 °C pH = 7.0 (not 0, as used in chemistry) [H₂O] is taken as 1



Life obeys the Laws of Thermodynamics

Living organisms are open systems Living things maintain a steady state not equilibrium Enzymes catalyze biological reactions



Figure 1-11 Fundamentals of Biochemistry, 2/e © 2006 John Wiley & Sons