BIOCH 755: Biochemistry I Fall 2015

1. Biochemistry, and thermodynamics

Jianhan Chen
Office Hour: M 1:30-2:30PM, Chalmers 034
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Overall Course Setup

- **Time & Location:** MWF 12:30-1:20 pm, Burt 114
- **Instructors:**
  - **Section I**: Jianhan Chen, 034 Chalmers, 532-2518, jianhac@ksu.edu
  - **Section II**: Larry Davis, 062 Chalmers, 532-6124, ldavis@ksu.edu
  - **Section III**: Gerald Reek, 203 Burt, 532-6117, reeck@ksu.edu
- **Textbook:** Voet, Voet, & Pratt "Fundamentals of Biochemistry", 4th Ed., Wiley (Note: the same book will be used in BIOCH 765: Biochemistry II in Spring 2016).
- **1-h Exams:** please mark your calendar and plan accordingly
  - Section I: Sep 28 (M) during the class time
  - Section II: Nov 2 (M) during the class time
  - Section III: Dec 16 (Wed) 4:10-6:00 PM (In the finals week)
- **Grading**: 100 points each section; the final letter grades for the entire course will be determined by by adding the scores from all three sections and grading on a curve.

Section I Overview

- Focus: proteins and protein structure
- Aug 24 (M) – Sept 28 (M)
- Mostly cover Chapters 1-2, 4-7
- Redacted PowerPoint slides will be available on KSOL
  - Be prepared to take good notes during lectures
- Office hours: M 1:30 – 2:30 PM, Chalmers 034
  - Or by appointment

- 1 Quiz: 10 points, Sept 4 (Friday)
- 1 Essay assignment: 20 points, due Sept 25
- 1 exam: 70 points, Sept 28 (Monday)
- No make-up: please plan your schedule accordingly

Schedule (tentative):

Aug 24	Review of thermodynamics; water	Book Chapter 1, 2
Aug 26	Acid-base reactions	2
Aug 28	Amino Acids	4
Aug 31	Amino Acids/Peptides	4, 5
Sep 2	Protein Primary Structure	5
Sep 4	**10 min Quiz**, Protein Secondary Structure	6
Sep 7	**UNIVERSITY HOLIDAY (Labor Day)**	
Sep 9	Protein Tertiary and Quaternary Structure	6
Sep 11	Protein Stability and Folding	6
Sep 14	Molecular mechanics	class notes
Sep 16	Molecular modeling and simulation	class notes
Sep 18	Oxygen-binding proteins	7
Sep 21	Muscle Proteins	7
Sep 23	Protein Purification	5
Sep 25	Protein Sequencing	5
Sep 28	**Section I Exam**	

Which of the following fields is biochemistry NOT relevant to?

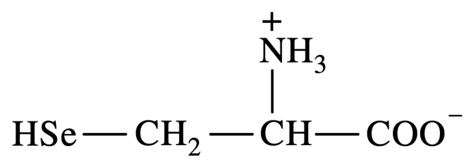
A. Immunology
B. Nutrition
C. Kinesiology
D. Waste management
E. Brewing

Which of the following elements is most abundant (in % weight) in the human body?

A. H
B. O
C. N
D. C
E. Both H and C are equally abundant

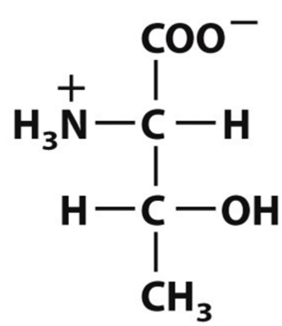
To what class does the following compound belong?

A. Lipid
B. Carbohydrate
C. Amino acid
D. Nucleotide



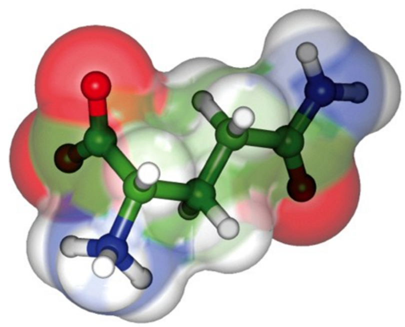
Which of the following functional groups does the compound shown NOT contain?

A. amino
B. carboxyl
C. hydroxyl
D. aldehyde



To what class of molecule does the following belong?

A. Carbohydrate
B. Lipid
C. Amino acid
D. Nucleotide



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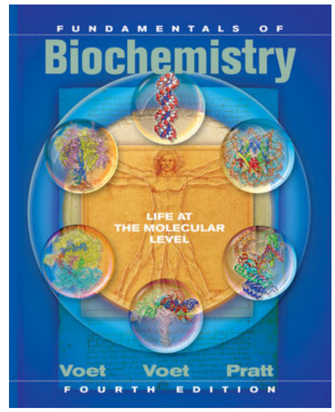
Biochemistry

- Chemistry of life
  - Chemical nature and structure of biological molecules
  - Interaction of biomolecules
  - Synthesis and degradation of biomolecules (metabolism)
  - Energy generation and consumption
  - Regulation of biomolecules
  - Genetic information storage, translation, and propagation
- Highly interdisciplinary
- Direct implication in heath and medicine



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1.1: Introduction to the Chemistry of Life

- **Key Concepts 1.1:**
  - Biological molecules are constructed from a limited number of elements.
  - Certain functional groups and linkages characterize different types of biomolecules.
  - During chemical evolution, simple compounds condensed to form more complex molecules and polymers.
  - Self-replicating molecules would have been subject to natural selection.

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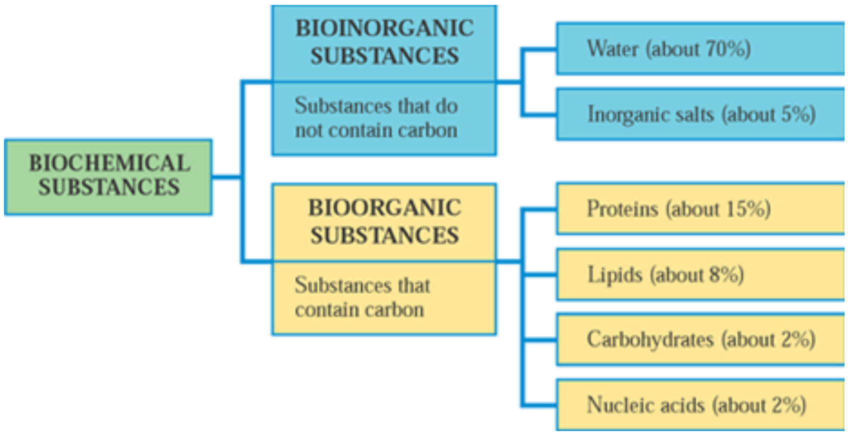
Human Body Mass Composition



Living Matter Consists of Few Elements

TABLE 1-1 Most Abundant Elements in the Human Body[a]

Element	Dry Weight (%)
C	61.7
N	11.0
O	9.3
H	5.7
Ca	5.0
P	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

Organic Chemistry & Biochemistry

TABLE 1-2 Common Functional Groups and Linkages in Biochemistry

Compound Name	Structure[a]	Functional Group or Linkage
Amine[b]	RNH_2 or $R\overset{+}{N}H_3$ R_2NH or $R_2\overset{+}{N}H_2$ R_3N or $R_3\overset{+}{N}H$	—N< or —N⁺(—)— (amino group)
Alcohol	ROH	—OH (hydroxyl group)
Thiol	RSH	—SH (sulfhydryl group)
Ether	ROR	—O— (ether linkage)
Aldehyde	R—C(=O)—H	—C(=O)— (carbonyl group)
Ketone	R—C(=O)—R	—C(=O)— (carbonyl group)
Carboxylic acid[b]	R—C(=O)—OH or R—C(=O)—O^-	—C(=O)—OH (carboxyl group) or —C(=O)—O^- (carboxylate group)
Ester	R—C(=O)—OR	—C(=O)—O— (ester linkage) R—C(=O)— (acyl group)[c]
Thioester	R—C(=O)—SR	—C(=O)—S— (thioester linkage) R—C(=O)— (acyl group)[c]
Amide	R—C(=O)—NH_2 R—C(=O)—NHR R—C(=O)—NR_2	—C(=O)—N< (amido group) R—C(=O)— (acyl group)[c]
Imine (Schiff base)[b]	R=NH or R=$\overset{+}{N}H_2$ R=NR or R=$\overset{+}{N}HR$	>C=N— or >C=$\overset{+}{N}$< (imino group)
Disulfide	R—S—S—R	—S—S— (disulfide linkage)
Phosphate ester[b]	R—O—P(=O)(OH)—O^-	—P(=O)(OH)—O^- (phosphoryl group)
Diphosphate ester[b]	R—O—P(=O)(O^-)—O—P(=O)(OH)—O^-	—P(=O)(O^-)—O—P(=O)(OH)—O^- (phosphoanhydride group)
Phosphate diester[b]	R—O—P(=O)(O^-)—O—R	—O—P(=O)(O^-)—O— (phosphodiester linkage)

[a]R represents any carbon-containing group. In a molecule with more than one R group, the groups may be the same or different.
[b]Under physiological conditions, these groups are ionized and hence bear a positive or negative charge.
[c]If attached to an atom other than carbon.

Table 1-2

Biological Polymers

- Biological macromolecules are polymers: formed through condensation reactions of various monomers
- Two extremely important outcomes:
  - Exponentially increase in the chemical versatility (N^M)
  - Possibility of replication (information storage, propagation & evolution)!

TABLE 1-3 Major Biological Polymers and Their Component Monomers

Polymer	Monomer
Protein (polypeptide)	Amino acid
Nucleic acid (polynucleotide)	Nucleotide
Polysaccharide (complex carbohydrate)	Monosaccharide (simple carbohydrate)

Table 1-3

Condensation and Hydrolysis

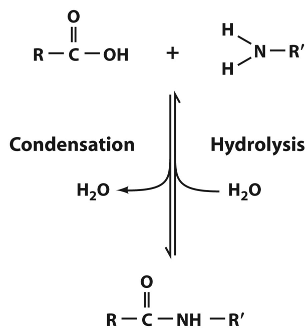


Figure 1-3

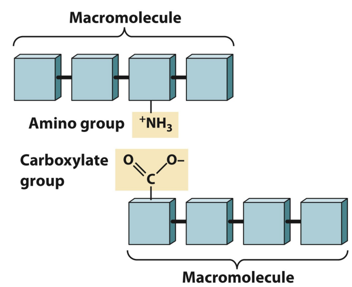
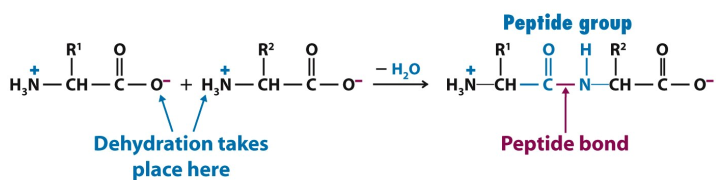


Figure 1-4



Replication: Mutation & Evolution

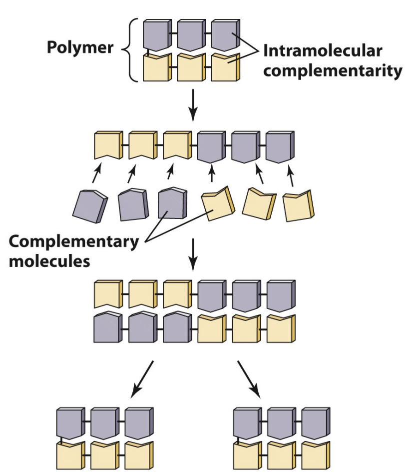
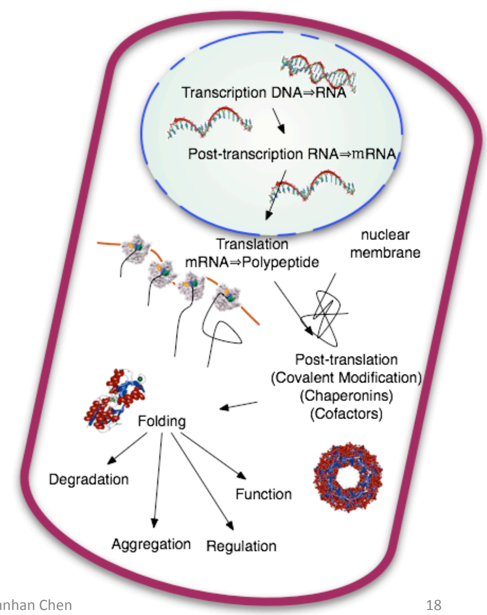


Figure 1-5



Typical Animal Cell

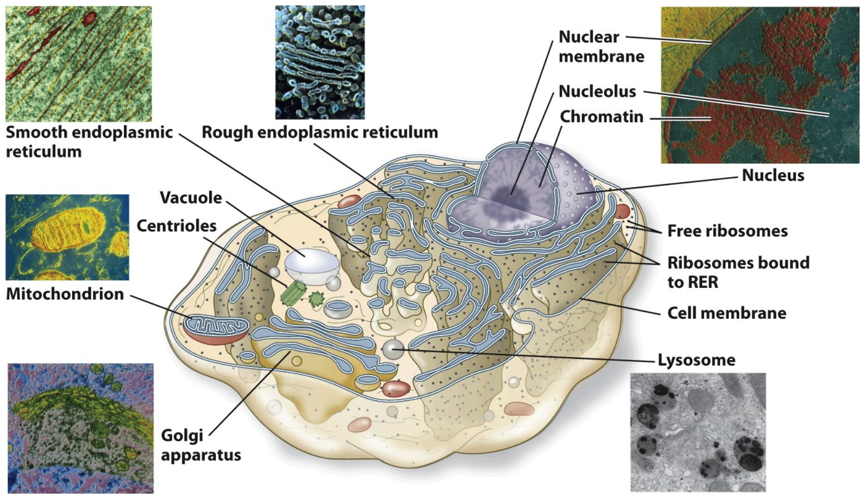


Figure 1-8

Life Obeys Thermodynamics

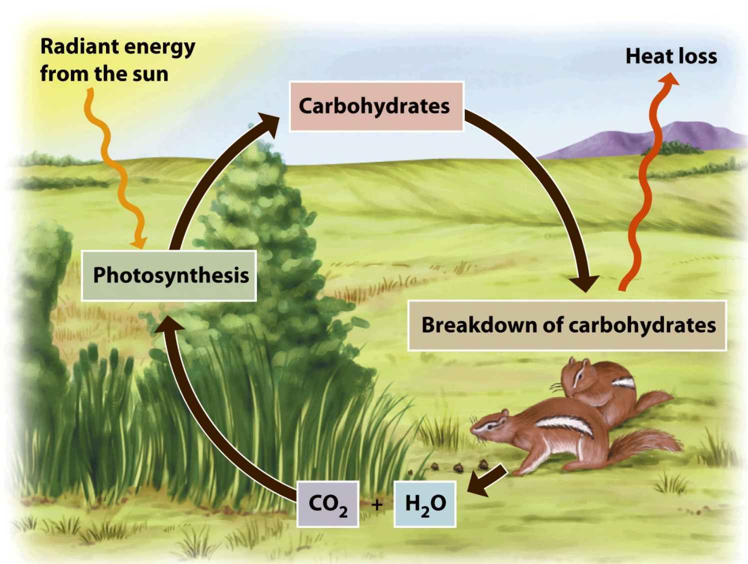


Figure 1-11

1.3. Thermodynamics

- **Key Concepts 1.3:**
  - Energy must be conserved, but it can take different forms.
  - In most biochemical systems, enthalpy is equivalent to heat.
  - Entropy, a measure of a system's disorder, tends to increase.
  - The free energy change for a process is determined by the change in enthalpy and the change in entropy ($\Delta G = \Delta H - T\,\Delta S$).
  - A spontaneous process occurs with a decrease in free energy.
  - The free energy change for a reaction can be calculated from the temperature and the concentrations and stoichiometry of the reactants and products ($\Delta G = -RT \ln K_{eq}$).
  - Biochemists define standard state conditions as a temperature of 25°C, a pressure of 1 atm, and a pH of 7.0.
  - Organisms are nonequilibrium, open systems that constantly exchange matter and energy with their surroundings.
  - Enzymes increase the rates of thermodynamically favorable reactions.

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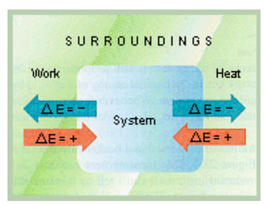
Measuring Internal Energy

- Only changes can be measured

$$\Delta E = q - w$$
$$dE = \delta q - \delta w$$



- If only P dV work (expansion or contraction) done:

$$dE = \delta q - PdV$$
$$= \delta q \qquad \text{if constant } V$$
$$\Delta E = q_v$$

  - Heat exchange measured at constant volume (without other types of work done) is the internal energy change!

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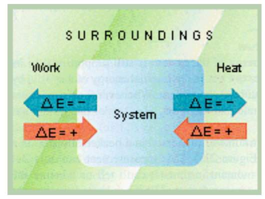
First Law of Thermodynamics

- Conservation of energy: heat (q), work(w), and (internal) energy (E)

$$\Delta E = q - w$$
$$dE = \delta q - \delta w$$



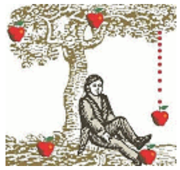
- Internal energy (E)
  - State Function: depends only on the state, regardless of the path of arrival
  - Microscopically: multiple contributions including: kinetic, vibrational, rotational, (chemical) bonding, non-bonded interaction, nuclei (typically not relevant in chemistry/biochemistry) components
  - Macroscopically: only definable on relative scale (see Eq above)

What about heat measured in more "natural" settings with constant pressure?

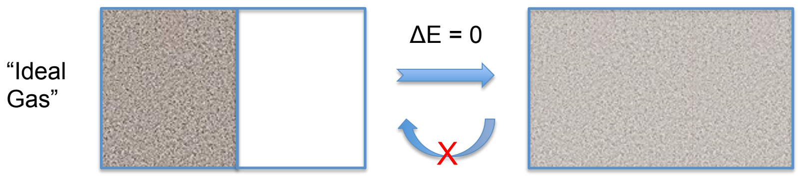
- Most (biochemical) experiments done on open systems with PV work exchange with environment:

$$dE = \delta q - PdV$$

  - Heat exchange no longer measures internal energy change!
- Need to introduce the concept of enthalpy: $H = E + PV$
  - Heat exchange measured at constant pressure (without other types of work done) is the enthalpy change!
- Biochemical reactions in solution (NPT condition)
  - Volume change is minimal ($\Delta V \sim 0$)
  - $dH = dE + P\Delta V \sim dE$
  - That is, enthalpy is more or less equivalent to internal energy



Energy dictates the direction of many processes … but not always



Entropy instead of energy dictates the direction here!

Second and Third Laws of Thermodynamics

- Law of increasing entropy: entropy must increase in an irreversible process
- Many other forms in different contexts
  - "No process is possible whose sole result is the transfer of heat from a body of lower temperature to a body of higher temperature" (Rudolf Clausius)
  - "No process is possible in which the sole result is the absorption of heat from a reservoir and its complete conversion into work". (Lord Kevin"
  - …
- Existence of absolute zero temperature (T = 0 K)
- Third law of thermodynamics: S = 0 at T = 0 for perfect crystals.

Entropy

- A measure of internal heat content, or, the unavailability of a system's energy to do work ($S=q_{rev}/T$).
- The physical meaning of entropy is only provided in the context of statistical mechanics
  - A statistical measure of the probability for a given macro state (left equation)
  - A measure of uncertainty (from information theory) (right equation)

$S = k_B \ln W$

$$S = -k_B \sum_i p_i \ln p_i$$

k_B: Boltzmann's constant
W: number of microscopic state
p_i: probability of a microscope state

Free Energy & Spontaneous Processes

- Both enthalpy and entropy matter (normal/NPT condition)
- Gibbs free energy: $\Delta G = \Delta H - T\,\Delta S$
- Free energy decreases in a spontaneous process.

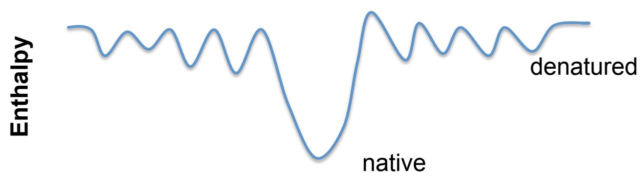
TABLE 1-4 Variation of Reaction Spontaneity (Sign of ΔG) with the Signs of ΔH and ΔS

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 nonspontaneous (endergonic) at all temperatures.

Table 1-4

Enthalpy and Entropy Compensation

- $\Delta G = \Delta H - T\Delta S$
- Consider an example of protein folding:



$\Delta H_f < 0 \quad \Delta S_f < 0$

1. Low temperature, $\Delta G_f = \Delta H_f - T\Delta S_f < 0$ (folding)
   (the favored state is not the more "random" denatured state!)
2. At folding temperature T_m, $\Delta G_f = 0$ ($p_f = p_u = 0.5$)
3. High temperature, $\Delta G_f = \Delta H_f - T\Delta S_f > 0$ (unfolding)

Equilibrium Constant

- Remember that given a reaction:

  A + B = C + D

  the quantity: K = [C][D]/[A][B] is a constant that is commonly referred to as an "equilibrium constant". But why a constant?
- **Proof**:
  - First, needs to define a "standard state" (commonly 298K, 1atm, 1M). Then for a solution with a concentration [A],

    $G = G^0 + RT \ln([A]/[A]^0) = G^0 + RT \ln [A]$
  - Therefore,

    $\Delta G = \Delta G^0 + RT \ln([C][D]/[A][B])$
  - At equilibrium, $\Delta G = 0$. Thus,

    $\Delta G^0 + RT \ln([C][D]/[A][B]) = 0$

    $\Delta G^0 = - RT \ln K$

    $K = [C][D]/[A][B] = \exp(-\Delta G^0/RT)$

Thermochemistry

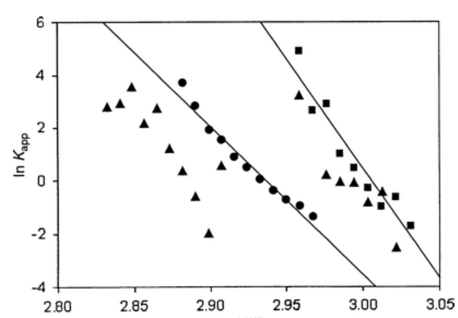
- Experimental determination of the thermodynamic parameters such as ΔG, ΔH and ΔS.
- ΔG can be directly calculated from K_{eq}
  - Often done by fitting to a titration curve
  - Require choosing a measurable that responds to binding or (bio-)chemical reaction
- Determination of ΔH and ΔS
  - Van' t Hoff Relationship
  - Calorimetry
  - Theory and simulation: not reliable at quantitative level

Van' t Hoff Relationship

- The classical approach, require multiple measurements of Keq at different temperatures and certain assumptions

$$\ln K_{eq} = -\frac{\Delta G^0}{RT} = -\frac{\Delta H^0}{RT} + \frac{\Delta S^0}{R}$$

- Assuming that ΔH and ΔS are temperature independent (often a strong assumption in biochemical/biophysical processes
- "safer" to calculate ΔS=(ΔH-ΔG)/R



Biosphere: Energy Flow in an Open System

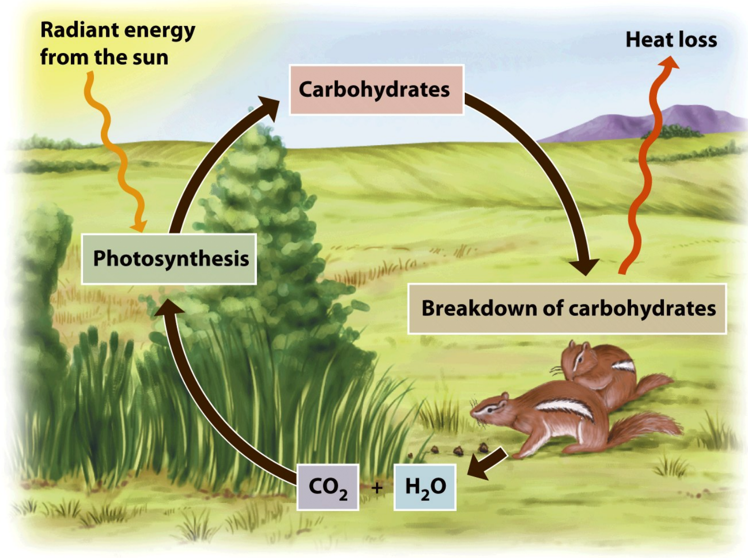


Figure 1-11

Summary

- Biochemistry
- Organic nature of biomolecules
- Biopolymers
- Key concepts of thermodynamics

- Coming up: water and what is special about it

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Which of the following is not true for biochemical standard conditions?

A. The concentrations of reactants and products is 1M.
B. The concentration of hydrogen ions is 1M.
C. Temperature is 25^{o}C/298K.
D. Pressure is 1 atmosphere.