

General Biochemistry; BBT-3001-(Semester III)- 18/08/2022

Unit I: Biomolecules in their Cellular Environment

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Overview

Introduction to Cellular Basis of Life

Cell structures – Prokaryotes and Eukaryotes

Chemical principles in biomolecular structure

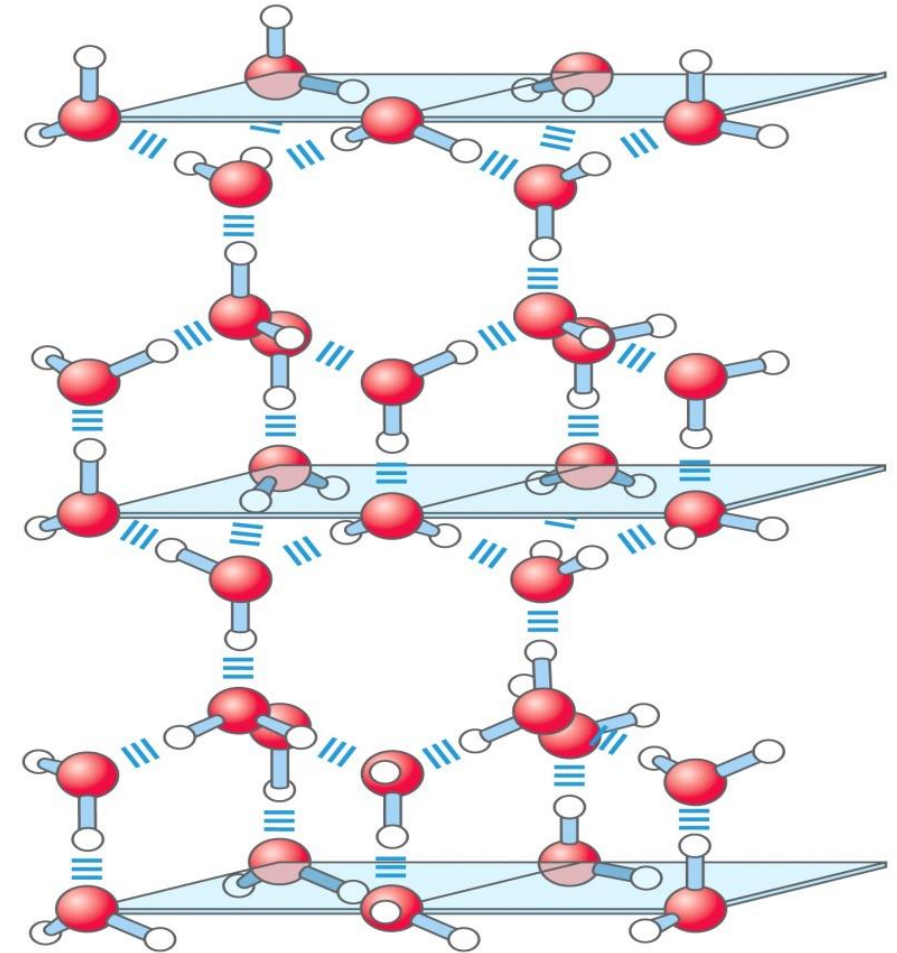
Major Classes of biomolecules

Role of water in design of biomolecules



Hydrogen Bonding in Ice

- ✓ Each water molecule in ice forms four hydrogen bonds to its neighbors, creating a regular tetrahedral crystal lattice.
- ✓ In liquid water each water molecule forms hydrogen bonds with an average of 3.4 other water molecules.
- ✓ Due to the more expanded crystal lattice structure of ice, ice is less dense than liquid water, and ice floats on water. Hydrogen bonds account for the relatively high melting point of ice and boiling point of liquid water.



Noncovalent Interactions and Macromolecular Structure

✓ As summarized above, noncovalent interactions are weak electrical bonds between molecules. The types of noncovalent interactions are

- 1) hydrogen bonds,
- 2) 2) ionic (electrostatic) bonds, and
- 3) 3) van der Waals interactions.

✓ Noncovalent interactions (1-5 kcal/mol) are typically ~100-fold weaker than covalent bonds.

✓ Their stability is only slightly greater than thermal energy in biological systems.

✓ Nonetheless, noncovalent interactions play important roles in protein and nucleic acid stabilization because they are collectively strong.

TABLE 2-5 Four Types of Noncovalent (“Weak”) Interactions among Biomolecules in Aqueous Solvent

Hydrogen bonds

Between neutral groups



Between peptide bonds



Ionic interactions

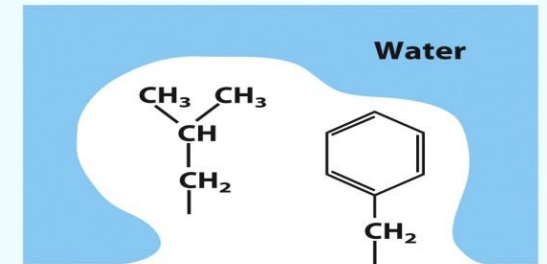
Attraction



Repulsion



Hydrophobic interactions



van der Waals interactions

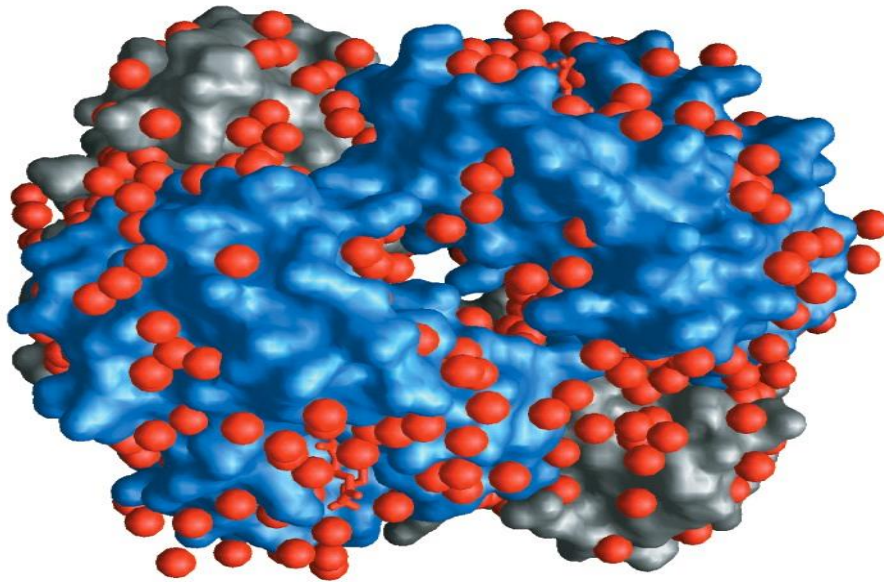
Any two atoms in close proximity

R
E
C
A
P

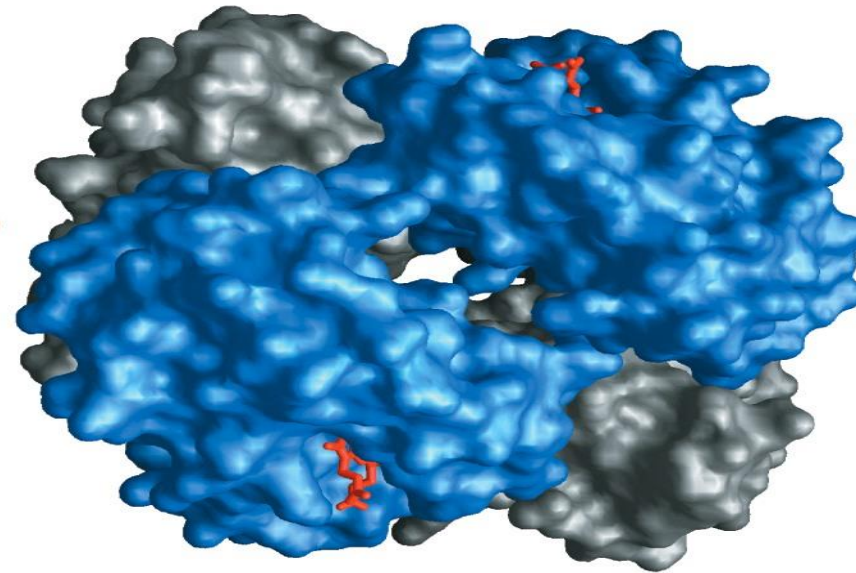


Binding of Water Molecules to Proteins

- ✓ Structural analysis indicates that some water molecules are tightly bound to proteins.
- ✓ These water molecules have different properties from those of the bulk water of the solvent.
- ✓ In certain proteins, tightly bound water molecules play roles in catalysis and roles in ligand binding.



(a)



(b)

ACIDS, BASES, pH, BUFFERS



DEFINITIONS

Acid: A substance, sour in taste, that dissociates in aqueous medium to release H^+ ions and reacts with bases to form salts & water

Alkali: A substance, bitter in taste, that dissociates in aqueous medium to release OH^- ions and reacts with acids to form salts & water

Neutralization reaction: A reaction between an acid and its conjugate base in aqueous to yield salt and water



The nature of the hydrated proton

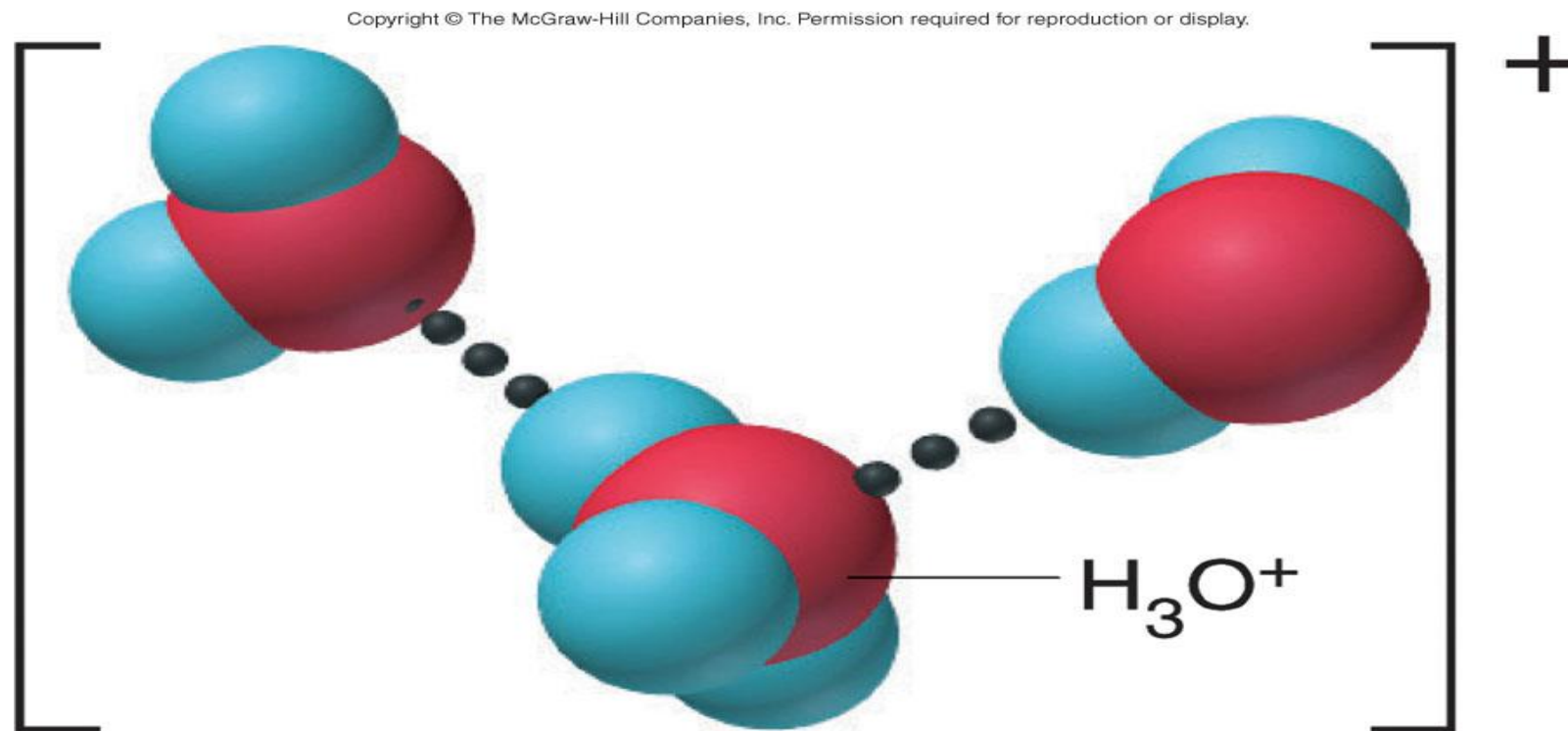


Figure 18.2

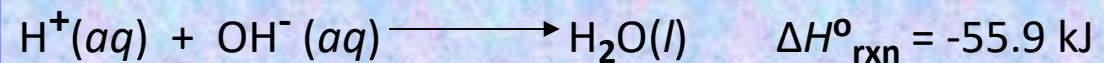
The Classical (Arrhenius) Definition of Acids and Bases

An **acid** is a substance that has H in its formula and dissociates in water to yield H_3O^+ .

A **base** is a substance that has OH in its formula and dissociates in water to yield OH^- .

Arrhenius acids contain **covalently** bonded H atoms that ionize in water.

Neutralization occurs when the H^+ ion from the acid and the OH^- ion from the base combine to form water.



Brønsted-Lowry Acid-Base Definition

An acid is a ***proton donor***, any species that donates an ***H⁺ ion***.

- An acid must contain H in its formula.

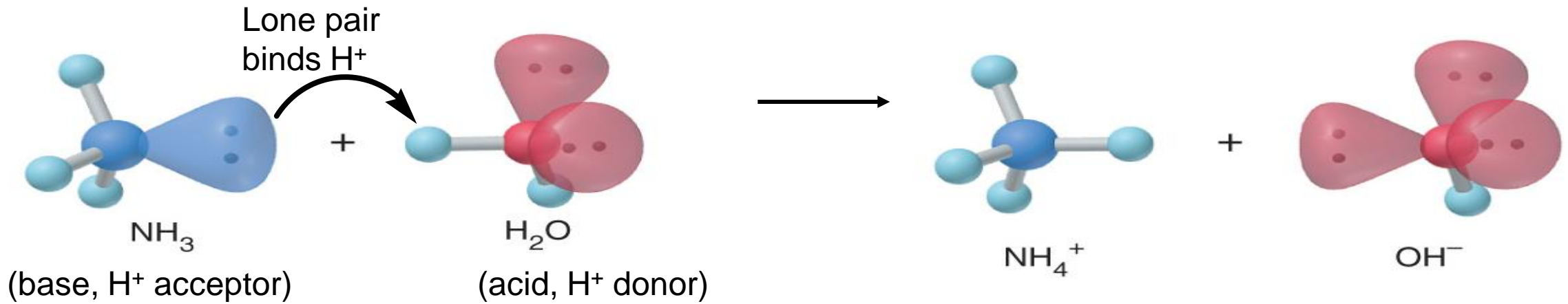
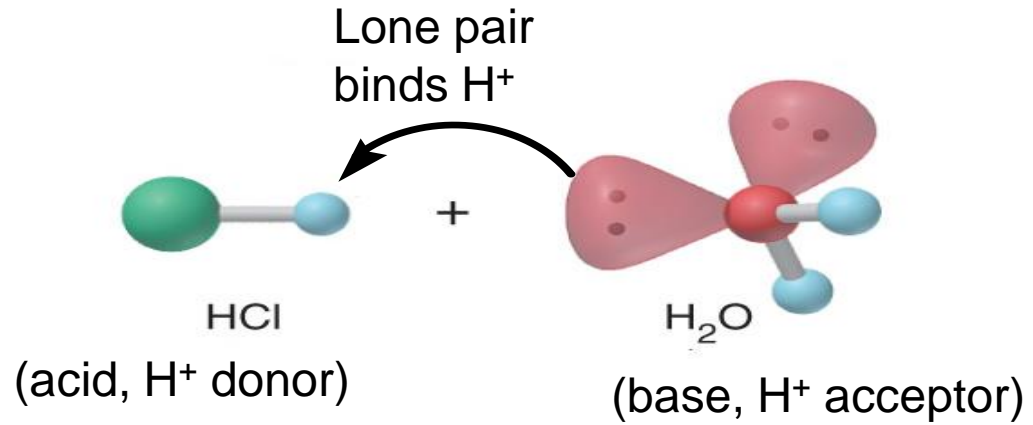
A base is a ***proton acceptor***, any species that accepts an ***H⁺ ion***.

- A base must contain a ***lone pair of electrons*** to bond to H⁺.

An acid-base reaction is a ***proton-transfer process***.



Dissolving of an acid or base in water as a Brønsted-Lowry acid-base reaction.

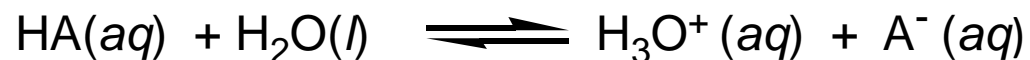


Strong acids dissociate completely into ions in water.



$$K_c \gg 1$$

Weak acids dissociate very slightly into ions in water.



$$K_c \ll 1$$

Defining the acid dissociation constant

$$K_c = \frac{[\text{H}_3\text{O}^+][\text{A}^-]}{[\text{H}_2\text{O}][\text{HA}]}$$

stronger acid, higher $[\text{H}_3\text{O}^+]$,
larger K_a

$$K_c[\text{H}_2\text{O}] = K_a = \frac{[\text{H}_3\text{O}^+][\text{A}^-]}{[\text{HA}]}$$

weaker acid, lower $[\text{H}_3\text{O}^+]$,
smaller K_a

The relationship between $[H_3O^+]$ and $[OH^-]$ and the relative acidity of solutions

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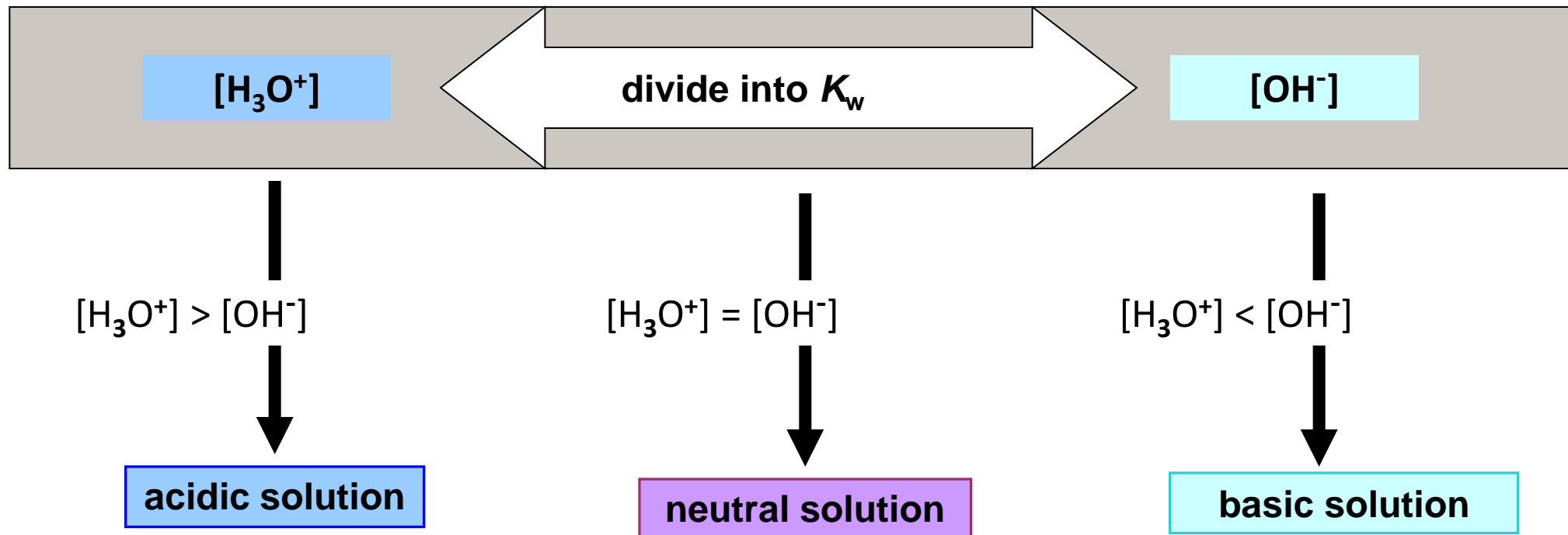


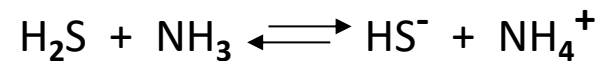
Figure 18.5

Table 18.3 The Relationship Between K_a and pK_a

Acid Name (Formula)	K_a at 25°C	pK_a
Hydrogen sulfate ion (HSO_4^-)	1.02×10^{-2}	1.991
Nitrous acid (HNO_2)	7.1×10^{-4}	3.15
Acetic acid (CH_3COOH)	1.8×10^{-5}	4.74
Hypobromous acid (HBrO)	2.3×10^{-9}	8.64
Phenol ($\text{C}_6\text{H}_5\text{OH}$)	1.0×10^{-10}	10.00

A low pK corresponds to a high K .

The Conjugate Acid-Base Pair



H₂S and HS⁻ are a **conjugate acid-base pair**.
HS⁻ is the conjugate base of the acid H₂S.

NH₃ and NH₄⁺ are a **conjugate acid-base pair**.
NH₄⁺ is the conjugate acid of the base NH₃.

An acid **reactant** produces a base **product** and the two constitute an **acid-base conjugate pair**.

Every acid has a conjugate base, and every base has a conjugate acid.

The conjugate base of the pair has one fewer H and one more negative charge than the acid.

The conjugate acid of the pair has one more H and one less negative charge than the base.

A Bronsted-Lowry acid-base reaction occurs when an acid and a base react to form their conjugate base and conjugate acid, respectively.

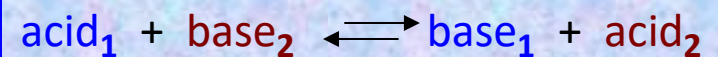
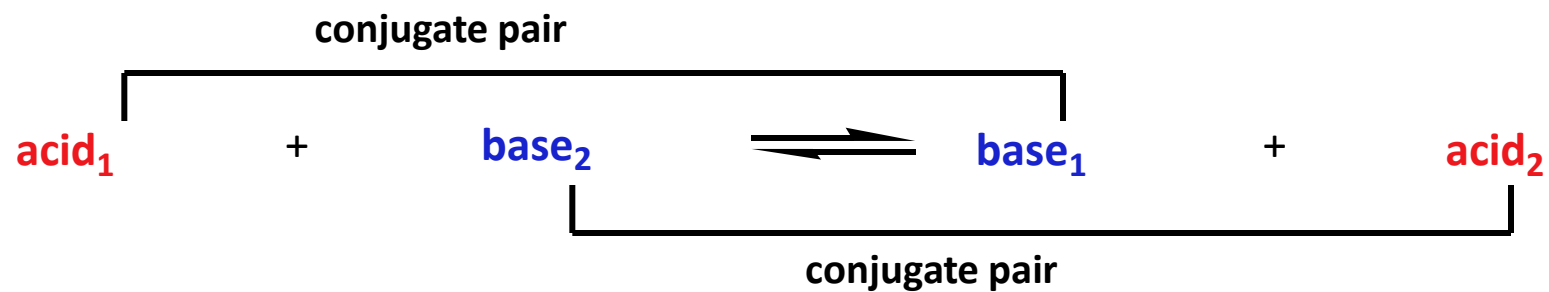


Table 18.4 Conjugate Pairs in Some Acid-Base Reactions



reaction 1	HF	+	H ₂ O	\rightleftharpoons	F ⁻	+	H ₃ O ⁺
reaction 2	HCOOH	+	CN ⁻	\rightleftharpoons	HCOO ⁻	+	HCN
reaction 3	NH ₄ ⁺	+	CO ₃ ²⁻	\rightleftharpoons	NH ₃	+	HCO ₃ ⁻
reaction 4	H ₂ PO ₄ ⁻	+	OH ⁻	\rightleftharpoons	HPO ₄ ²⁻	+	H ₂ O
reaction 5	H ₂ SO ₄	+	N ₂ H ₅ ⁺	\rightleftharpoons	HSO ₄ ⁻	+	N ₂ H ₆ ²⁺
reaction 6	HPO ₄ ²⁻	+	SO ₃ ²⁻	\rightleftharpoons	PO ₄ ³⁻	+	HSO ₃ ⁻

SAMPLE PROBLEM 18.4

Identifying conjugate acid-base pairs

PROBLEM:

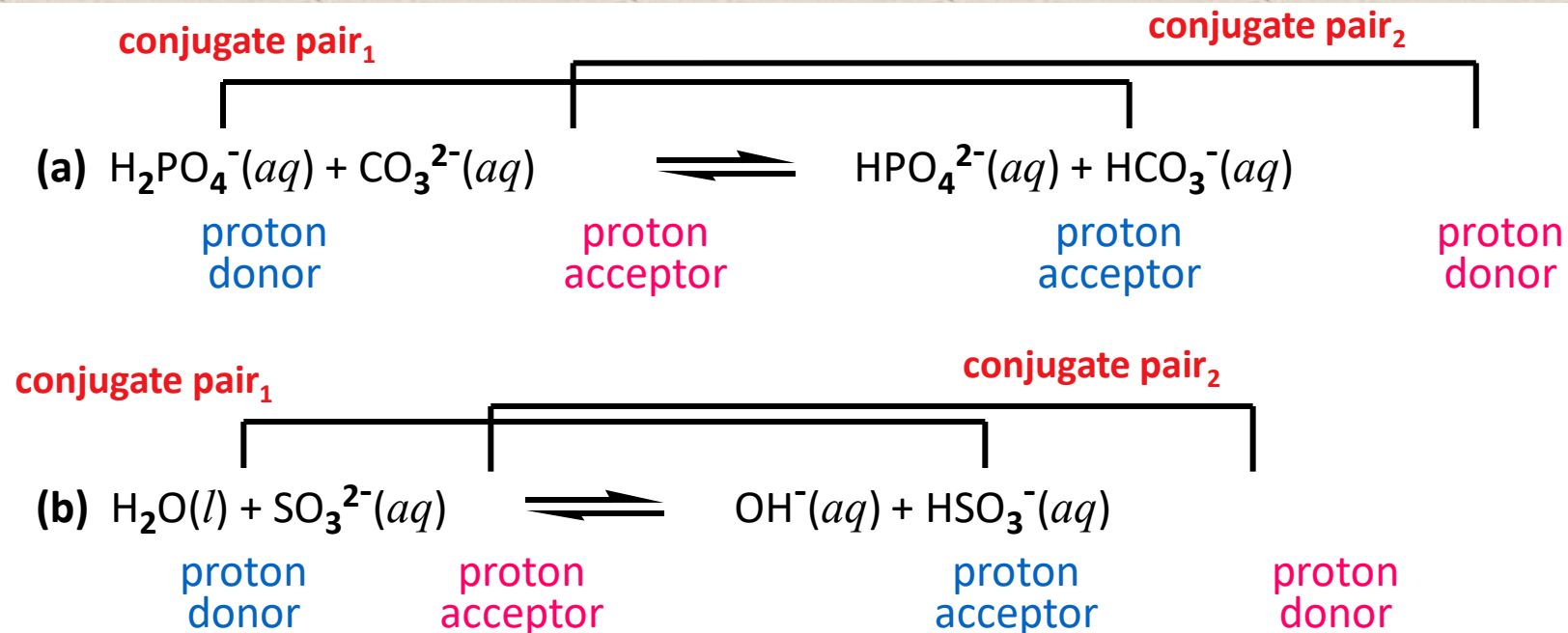
The following reactions are important environmental processes. Identify the conjugate acid-base pairs.



PLAN:

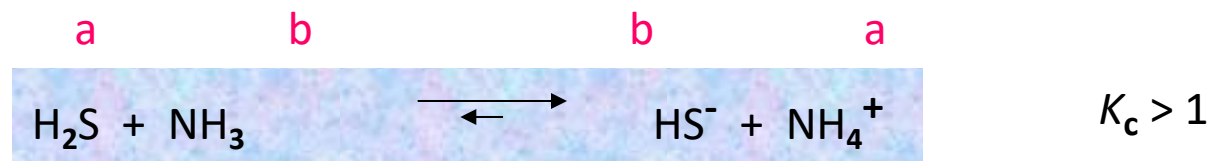
Identify proton donors (acids) and proton acceptors (bases).

SOLUTION:

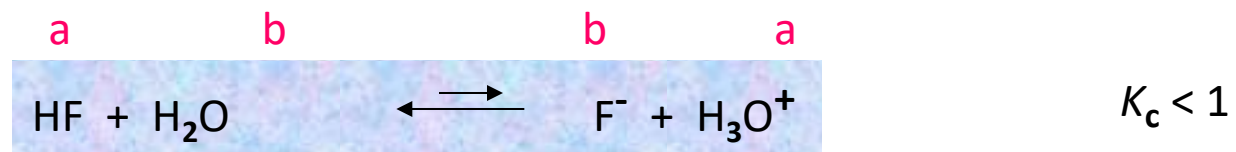


Relative Acid-Base Strength and Reaction Direction

General Rule: An acid-base reaction proceeds to the greater extent in the direction in which a *stronger acid and stronger base form a weaker acid and a weaker base.*



A competition for the proton between the two bases!



Strengths of conjugate acid-base pairs

A weaker acid has a stronger conjugate base.

An acid-base reaction proceeds to the right if the acid reacts with a base that is lower on the list because this combination produces a **weaker** conjugate base and a **weaker** conjugate acid.

ACID STRENGTH ↑	ACID	BASE	BASE STRENGTH ↓
Strong	HCl	Cl ⁻	Negligible
	H ₂ SO ₄	HSO ₄ ⁻	
	HNO ₃	NO ₃ ⁻	
Weak	H ₃ O ⁺	H ₂ O	Weak
	HSO ₄ ⁻	SO ₄ ²⁻	
	H ₂ SO ₃	HSO ₃ ⁻	
	H ₃ PO ₄	H ₂ PO ₄ ⁻	
	HF	F ⁻	
	CH ₃ COOH	CH ₃ COO ⁻	
	H ₂ CO ₃	HCO ₃ ⁻	
	H ₂ S	HS ⁻	
	HSO ₃ ⁻	SO ₃ ²⁻	
	H ₂ PO ₄ ⁻	HPO ₄ ²⁻	
Negligible	HCN	CN ⁻	Strong
	NH ₄ ⁺	NH ₃	
	HCO ₃ ⁻	CO ₃ ²⁻	
	HPO ₄ ²⁻	PO ₄ ³⁻	
	H ₂ O	OH ⁻	
	HS ⁻	S ²⁻	
	OH ⁻	O ²⁻	

Figure 18.10

DEFINITIONS

pH: *Negative logarithm of H^+ ion concentration.*

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

Buffer: *Aqueous systems that resist changes in the pH. All weak acids or bases, in the presence of their salts with strong base or strong acid respectively, form buffer systems, e.g. carbonic acid/bicarbonate, dihydrogen phosphate/monohydrogen phosphate, proteins/proteinate*



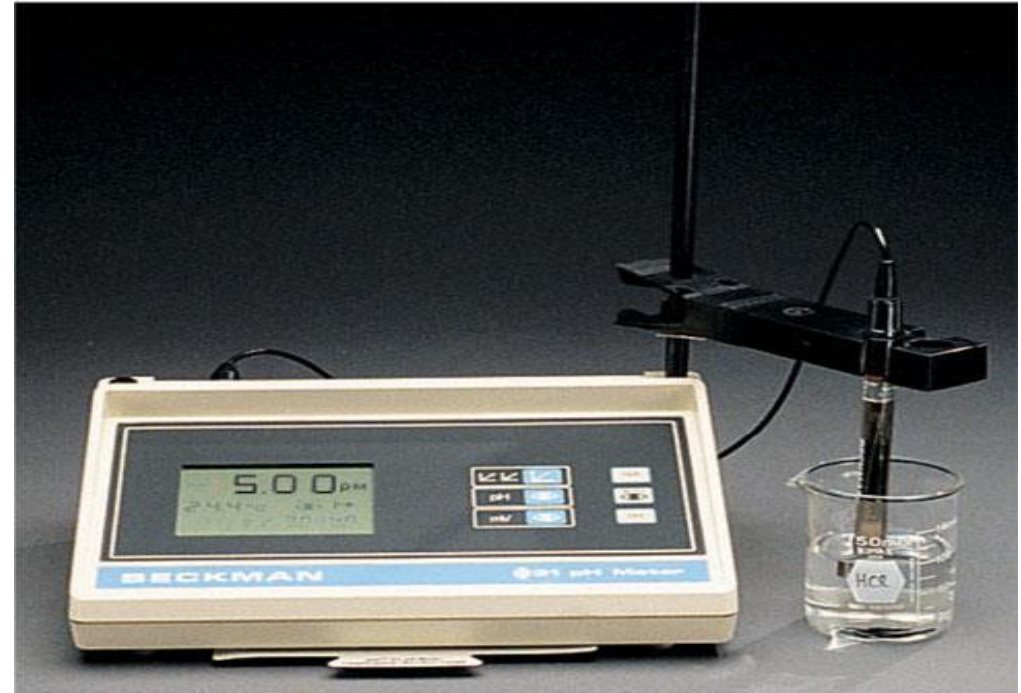
SIGNIFICANCE OF pH

- All biochemical reactions in the body take place in an aqueous environment and enzymes catalyze most of these reactions
- Enzymes optimally active at a particular H⁺ ion concentration
- Extremes of pH can cause protein precipitation leading to loss of activity
- pH range: 0-14

Methods for measuring the pH of an aqueous solution.

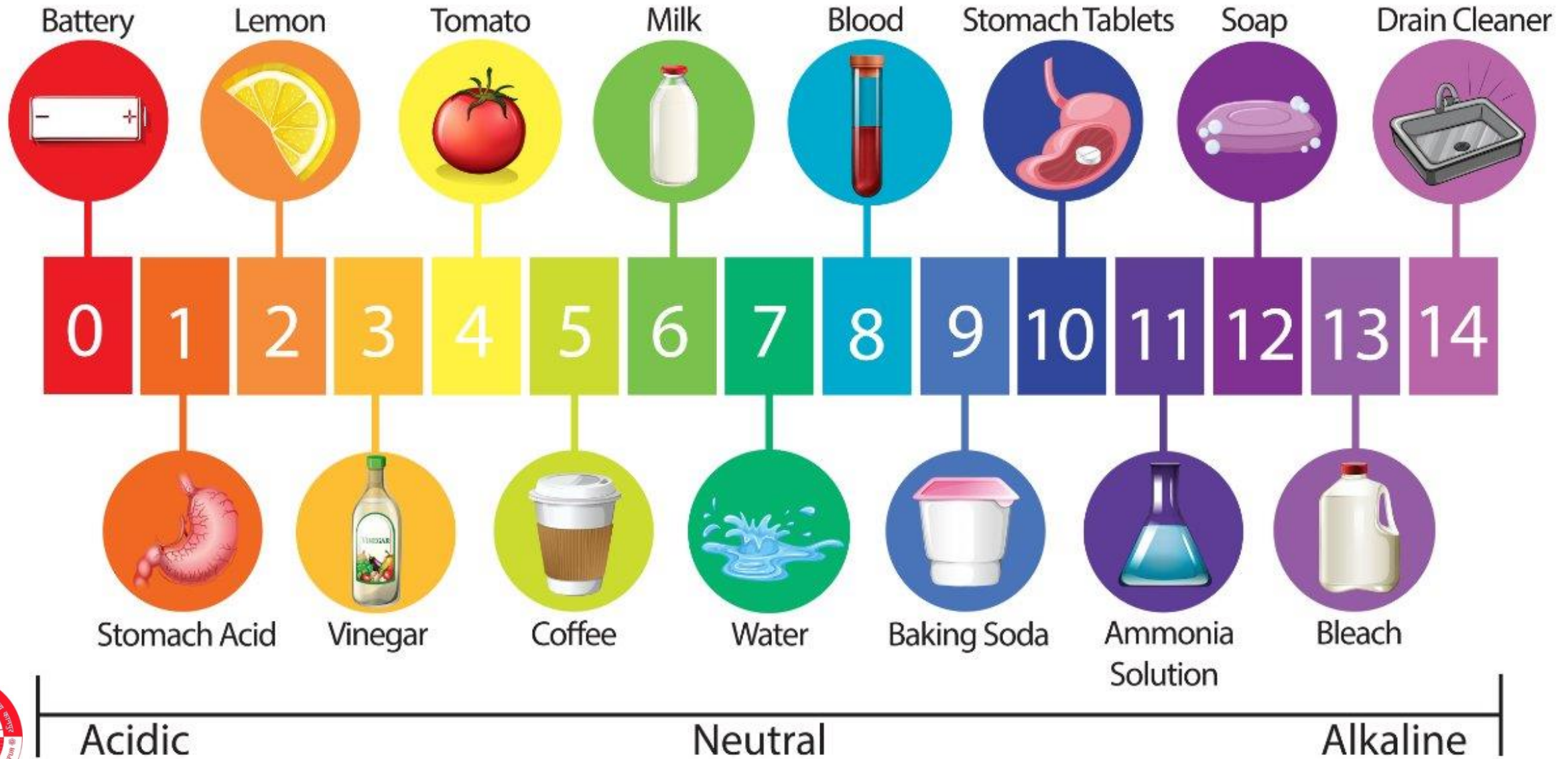


pH paper

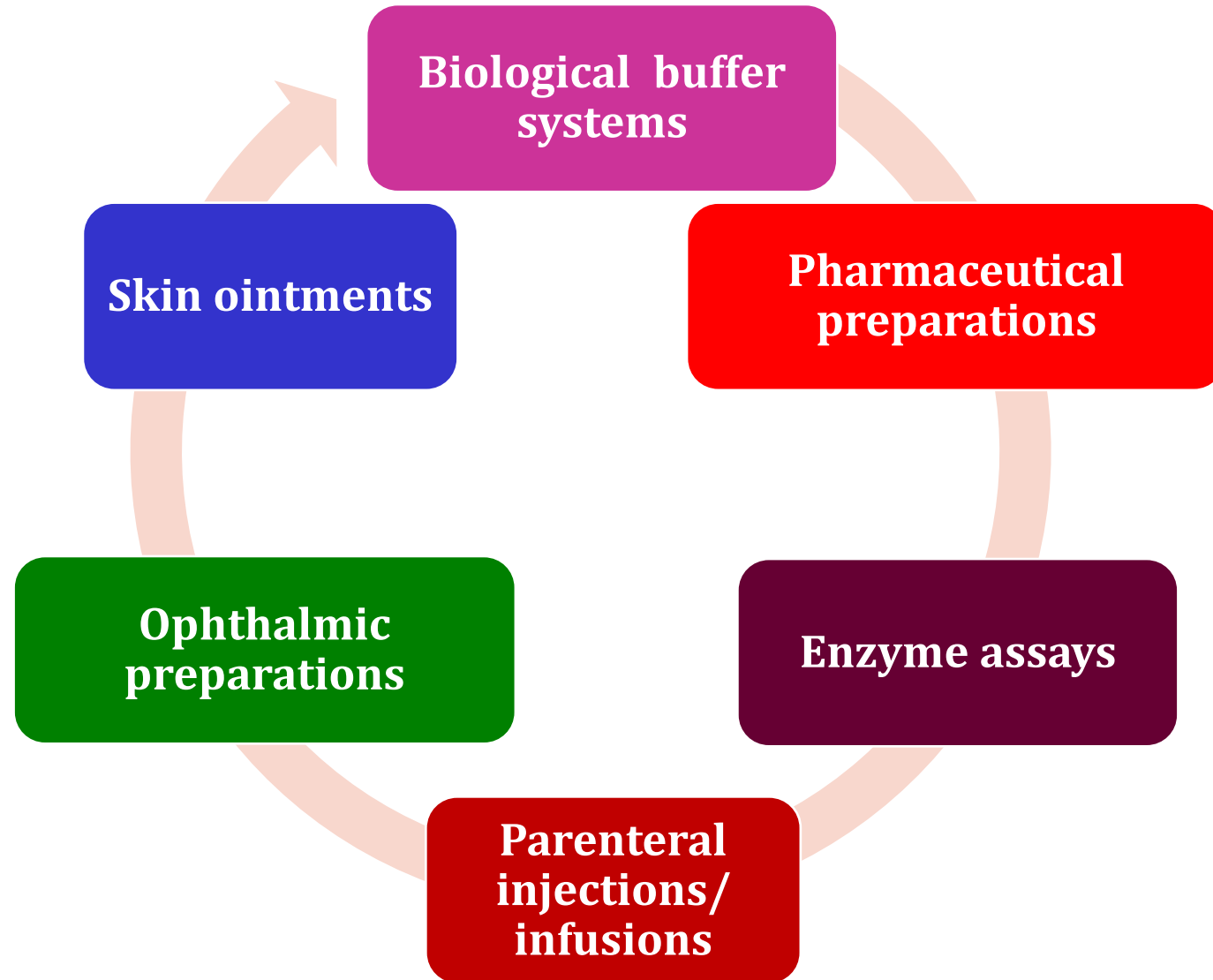


pH meter

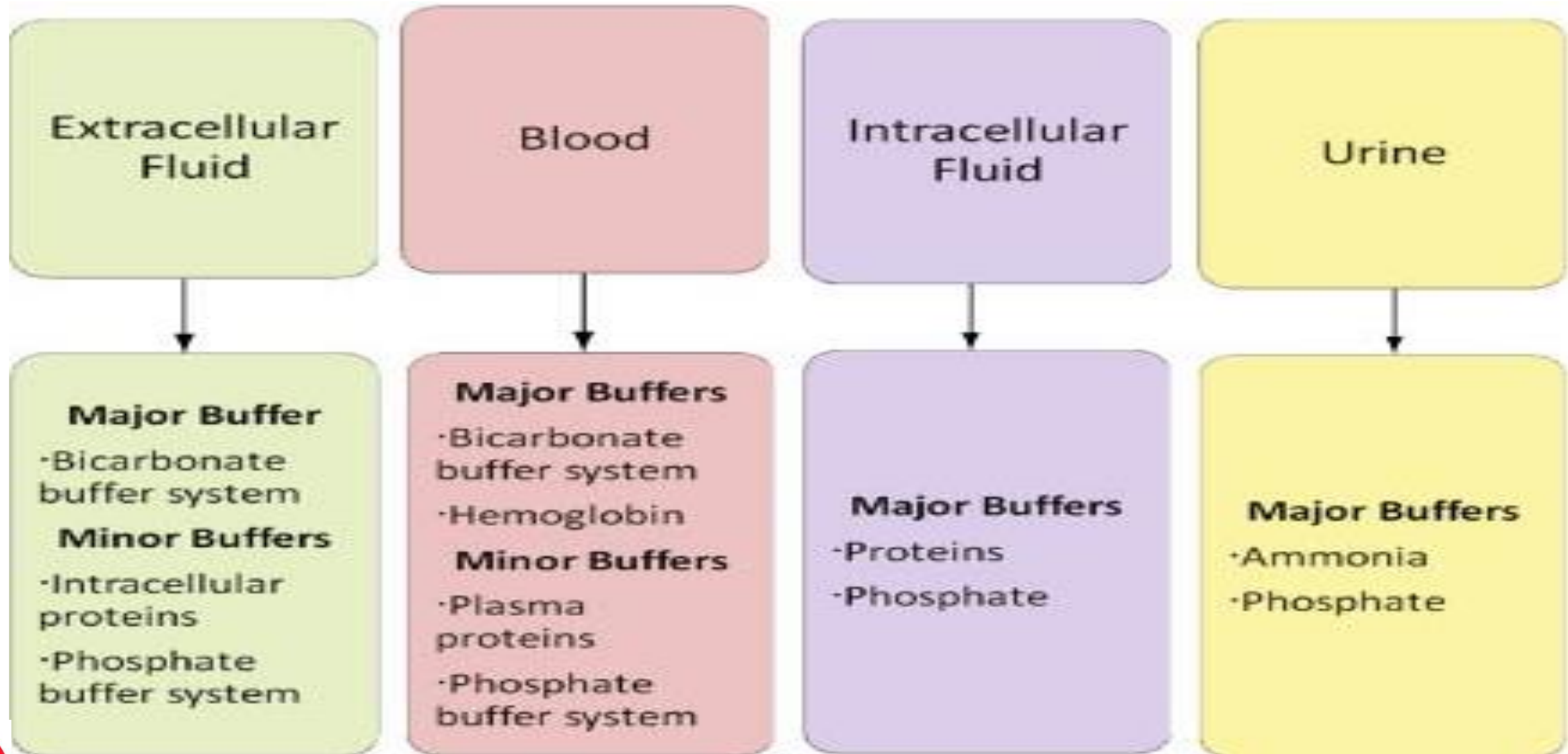
The pH Scale



SIGNIFICANCE OF BUFFER SYSTEMS



BIOLOGICAL BUFFER SYSTEMS IN HUMAN BODY



TYPES OF BLOOD BUFFERS

Primary buffer

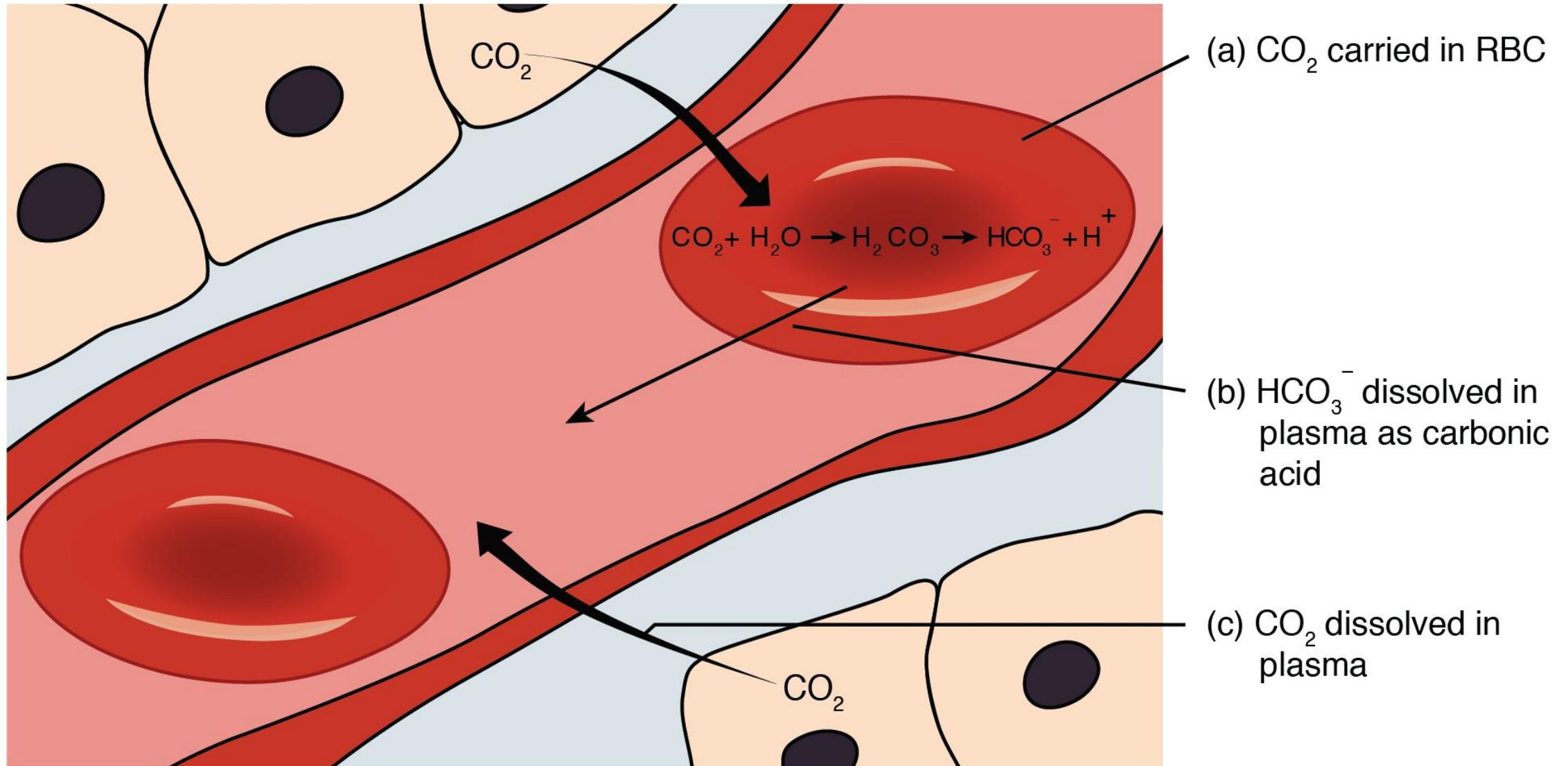
Present in plasma
E.g. Carbonic acid/
bicarbonate

Secondary buffer

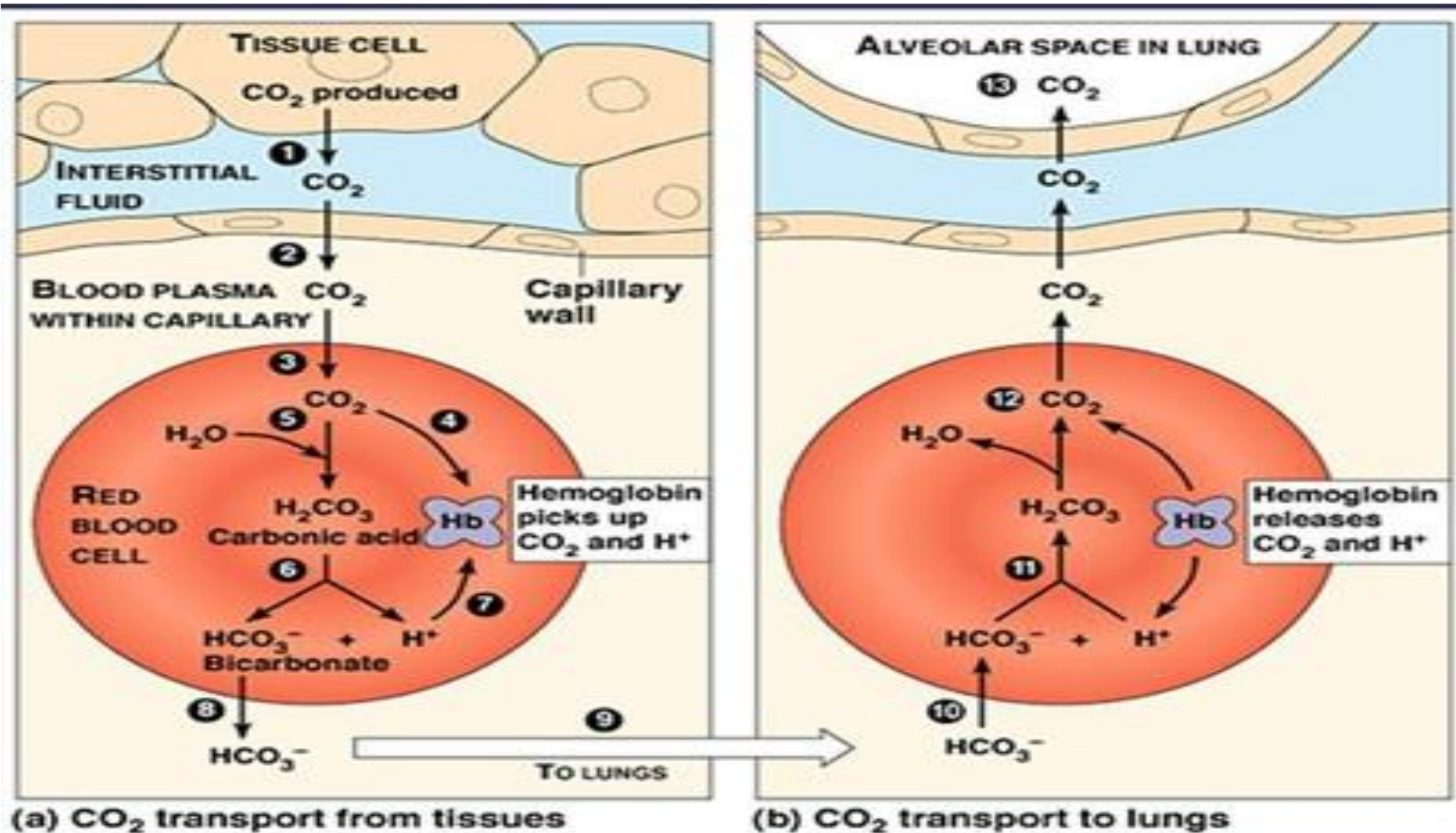
Present in erythrocytes
E.g. Hemoglobin/Oxy-
hemoglobin



BICARBONATE BUFFER SYSTEM



HEMOGLOBIN BUFFER SYSTEM



CONCEPT OF pK

- Dissociation behaviour of weak acids / bases influences pH and the structure and function of the entire molecule.
- E.g. *-COOH, -NH₂, phosphates present on proteins, nucleic acids, coenzymes*
- Relative strength of an acid is expressed as dissociation constant (K).



- **The numerical value of K** is a negative exponential number so it is usually expressed as

$$\text{pK} = -\log K$$



THE HENDERSON-HASSELBALCH EQUATION

- This equation provides us with the relationship of pH to pK.

$$\text{pH} = \text{pK} + \log [\text{salt}]/[\text{acid}]$$

- Derivation: $\text{HA} = \text{H}^+ + \text{A}^-$ [HA is a weak acid and dissociates to H^+ and A^-]

$$K = \frac{[\text{H}^+] \times [\text{A}^-]}{[\text{HA}]}$$

$$\text{Or } [\text{H}^+] = K[\text{HA}]/[\text{A}^-]$$



THE HENDERSON-HASSELBALCH EQUATION; CONTD..

- Taking negative logarithm on both sides,

$$-\log [\text{H}^+] = -\log K - \log [\text{HA}]/[\text{A}^-]$$

or

$$\text{pH} = \text{pK} - \log [\text{A}^-]/[\text{HA}]$$

or

$$\text{pH} = \text{pK} + \log [\text{A}^-]/[\text{HA}]$$

E.g. *Calculate the pH of a mixture of 0.1 M acetic acid and 0.2 M sodium acetate (pK of acetic acid is 4.76)*



SIGNIFICANCE OF HENDERSON-HASSELBALCH EQUATION IN ACTION OF BUFFER

- The pH of buffer system determined by the pK of the acid and the ratio of [A⁻] to [HA]
- Buffer has its greatest buffering capacity at its pK, that is, that pH at which the [A⁻] = [HA]

i.e. $\text{pH} = \text{pK} + \log 1$ which implies $\text{pH} = \text{pK}$



SIGNIFICANCE OF HENDERSON-HASSELBALCH EQUATION IN ACTION OF BUFFER; CONTD. .

- Capacity of buffer decreases as the ratio deviates from **1**
- In general buffers should be used at a $\text{pH} \pm 1$ from the pK
- If the ratio is beyond **50:1** or **1:50**, the system is considered to have lost its buffering capacity.



BOX 2-3 WORKING IN BIOCHEMISTRY

Solving Problems Using the Henderson-Hasselbalch Equation

1. Calculate the pK_a of lactic acid, given that when the concentration of lactic acid is 0.010 M and the concentration of lactate is 0.087 M, the pH is 4.80.

$$pH = pK_a + \log \frac{[\text{lactate}]}{[\text{lactic acid}]}$$


$$\begin{aligned} pK_a &= pH - \log \frac{[\text{lactate}]}{[\text{lactic acid}]} \\ &= 4.80 - \log \frac{0.087}{0.010} = 4.80 - \log 8.7 \\ &= 4.80 - 0.94 = 3.9 \quad (\text{answer}) \end{aligned}$$

2. Calculate the pH of a mixture of 0.10 M acetic acid and 0.20 M sodium acetate. The pK_a of acetic acid is 4.76.

$$\begin{aligned} pH &= pK_a + \log \frac{[\text{acetate}]}{[\text{acetic acid}]} \\ &= 4.76 + \log \frac{0.20}{0.10} = 4.76 + 0.30 \\ &= 5.1 \quad (\text{answer}) \end{aligned}$$

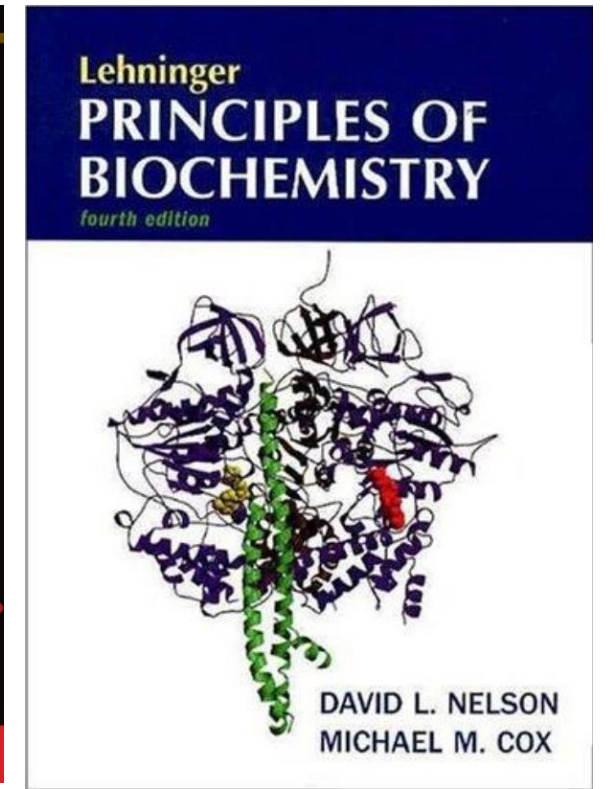
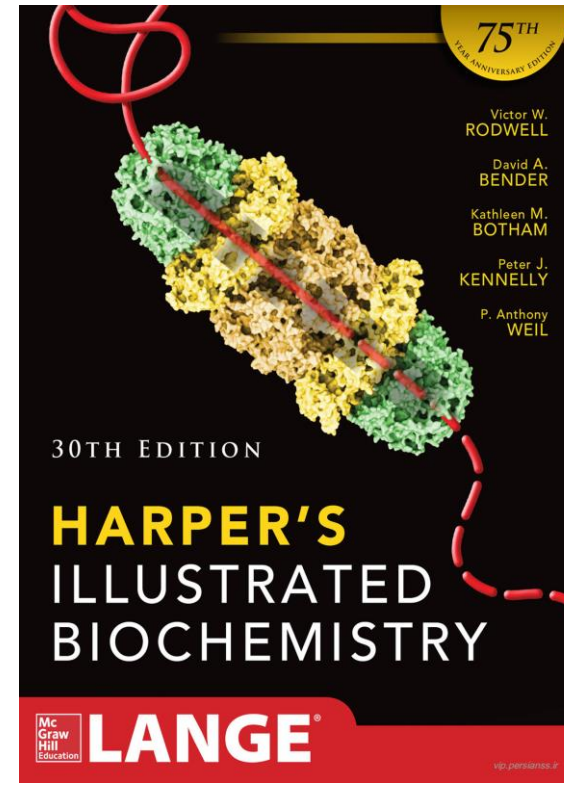
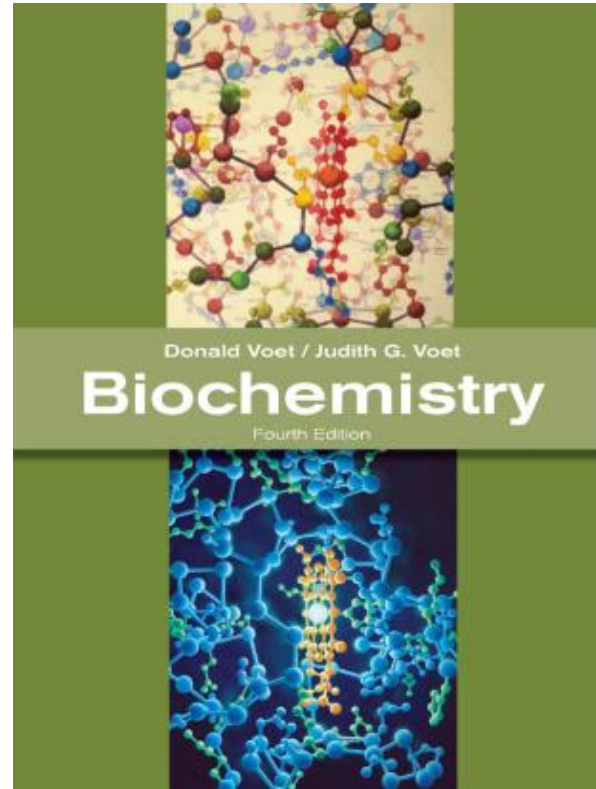
3. Calculate the ratio of the concentrations of acetate and acetic acid required in a buffer system of pH 5.30.

$$\begin{aligned} pH &= pK_a + \log \frac{[\text{acetate}]}{[\text{acetic acid}]} \\ \log \frac{[\text{acetate}]}{[\text{acetic acid}]} &= pH - pK_a \\ &= 5.30 - 4.76 = 0.54 \\ \frac{[\text{acetate}]}{[\text{acetic acid}]} &= \text{antilog } 0.54 = 3.5 \quad (\text{answer}) \end{aligned}$$

 To see the effect of pH on the degree of ionization of a weak acid, see the Living Graph for Equation 2-9.



Acknowledgement



For Query

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