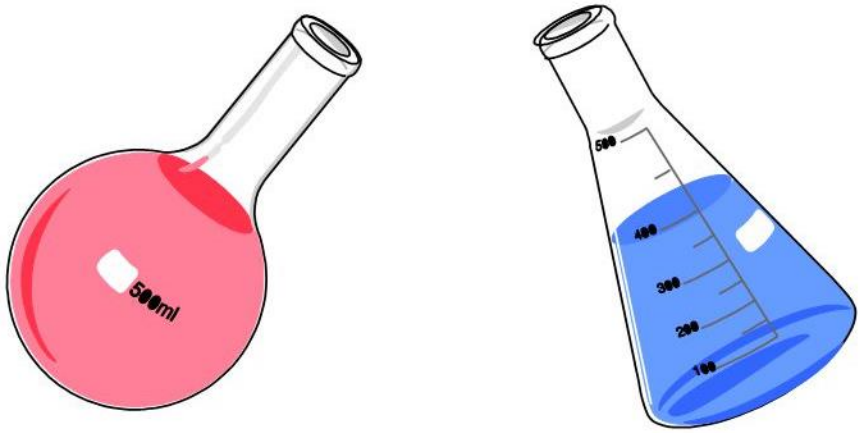

Acids, Bases and Water

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MD summer

Required material and further reading

Required:

Handout

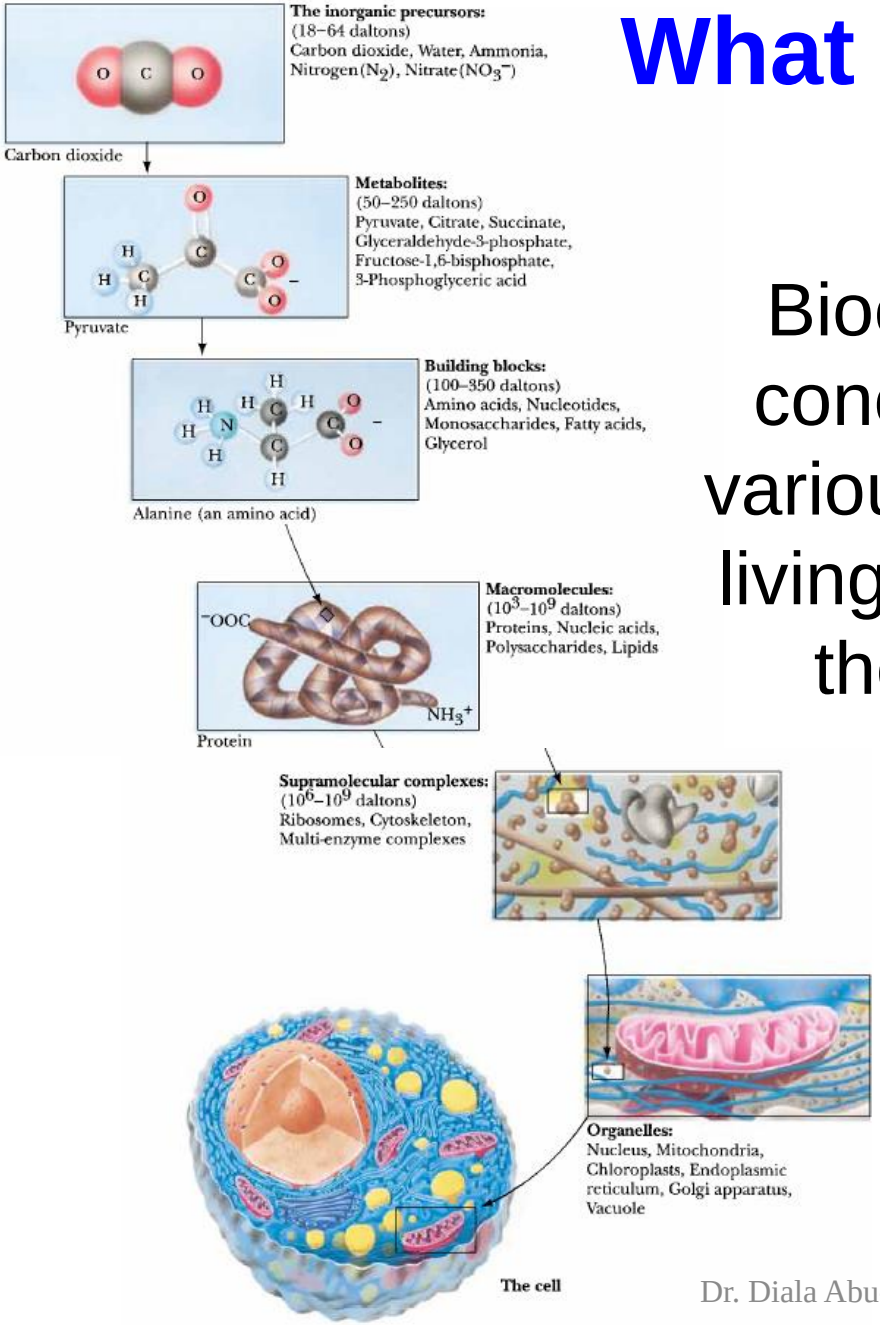
Text books:

Biochemistry. Campbell Chapter 2

Fundamentals of General, Organic, and Biological Chemistry. McMurry. Chapter 10

softcopy will be sent

What is Biochemistry?



Biochemistry is the science concerned with studying the various molecules that occur in living cells and organisms and their chemical reactions.

Garret *et al*

Why Biochemistry is important to Human Biology?

1. Biochemistry is an intrinsically beautiful and fascinating body of knowledge. “Lubert Stryer”
Because it unravels the details of the most fundamental processes in biological systems.

2. Biochemistry massively influences medicine and treatment development, ex. sickle-cell anemia, cystic fibrosis, hemophilia, etc.

3. By advances in biochemistry, researchers can tackle many questions in biology and medicine, ex. Biochemical changes in diseases, causes of diseases, lab tests..etc.

1. Molecular and biochemical basis of diseases become clear.

2. Manipulate the biochemical processes and simulating them in vivo and in vitro.

3. Molecules of life can be prepared on the bench

What makes biomolecules special?

Table 1.1

Functional Groups of Biochemical Importance

Class of Compound	General Structure	Characteristic Functional Group	Name of Functional Group	Example
Alkenes	$RCH{=}CH_2$ $RCH{=}CHR$ $R_2C{=}CHR$ $R_2C{=}CR_2$	C=C	Double bond	$CH_2{=}CH_2$
Alcohols	ROH	—OH	Hydroxyl group	CH_3CH_2OH
Ethers	ROR	—O—	Ether group	CH_3OCH_3
Amines	RNH_2 R_2NH R_3N	—N<	Amino group	CH_3NH_2
Thiols	RSH	—SH	Sulfhydryl group	CH_3SH
Aldehydes	R—C(=O)—H	—C(=O)—	Carbonyl group	CH_3CH=O
Ketones	R—C(=O)—R	—C(=O)—	Carbonyl group	$CH_3C(=O)CH_3$
Carboxylic acids	R—C(=O)—OH	—C(=O)—OH	Carboxyl group	$CH_3C(=O)OH$
Esters	R—C(=O)—OR	—C(=O)—OR	Ester group	$CH_3C(=O)OCH_3$
Amides	R—C(=O)—NR_2 R—C(=O)—NHR R—C(=O)—NH_2	—C(=O)—N<	Amide group	$CH_3C(=O)N(CH_3)_2$
Phosphoric acid esters	R—O—P(=O)(OH)—OH	—O—P(=O)(OH)—OH	Phosphoric ester group	CH_3—O—P(=O)(OH)—OH
Phosphoric acid anhydrides	R—O—P(=O)(OH)—O—P(=O)(OH)—OH	—P(=O)(OH)—O—P(=O)(OH)—	Phosphoric anhydride group	HO—P(=O)(OH)—O—P(=O)(OH)—OH

-The cellular apparatus of living organisms is made up of carbon compounds.

Arrhenius Definition of Acids and Bases and Their Reactions

Arrhenius Acids and Bases Acids are

- Acids in H_2O are H^+ donors
- Bases in H_2O are OH^- donors

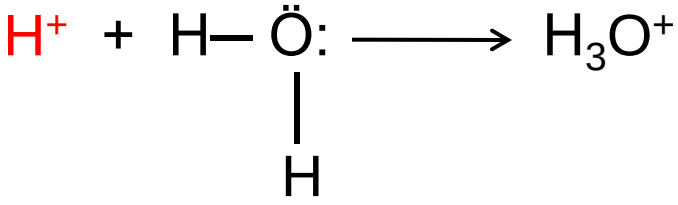
Arrhenius 1903

Nobel Prize

Neutralization of acids and bases produces salt and water.

$$NaOH \xrightarrow{H_2O} Na^+ + OH^-$$

$$HCL \xrightarrow{H_2O} Cl^- + H^+$$



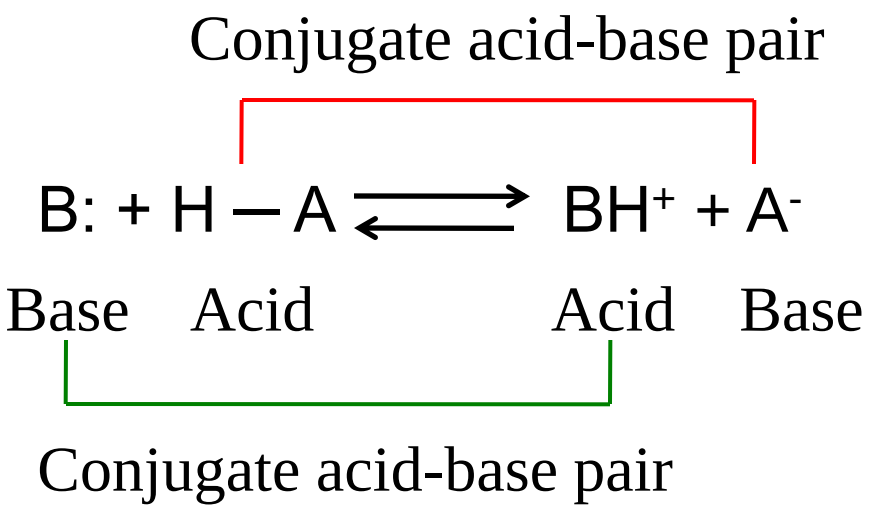
Drawbacks:

1. Reactions has to happen in aqueous solutions
2. H_3O^+ is released but not H^+

Bronsted-Lowry Definition of Acids and Bases and Their Reactions

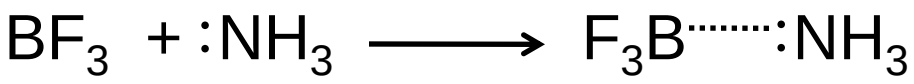
Bronsted-Lowry Acids and Bases (1923)

- Acids donate H^+
- Bases accept H^+ (non-bonding pairs)



Lewis Definition of Acids and Bases and Their Reactions

- Acids accept electrons
- Bases donate electrons (non-bonding pairs)



Acid **base**

Common Acids

- HCl- hydrochloric- stomach acid
- H_2SO_4- sulfuric acid - car batteries
- HNO_3 – nitric acid - explosives
- $HC_2H_3O_2$- acetic acid - vinegar
- H_2CO_3-carbonic acid – sodas
- H_3PO_4- phosphoric acid -flavorings

Common Bases

- NaOH- sodium hydroxide (LYE) soaps, drain cleaner
- $Mg(OH)_2$ - magnesium hydroxide-antacids
- $Al(OH)_3$-aluminum hydroxide-antacids, deodorants
- NH_4OH-ammonium hydroxide- “ammonia”

Water as both an acid and a base

Amphoterism - an ion or molecule can act as an acid or base depending upon the reaction conditions

Water in NH_3 serves as an acid

$$\underset{\text{acid}}{H_2O} + \underset{\text{base}}{NH_3} \rightleftharpoons \underset{\text{acid}}{NH_4^+} + \underset{\text{base}}{OH^-}$$

Water in acetic acid serves as a base

$$\underset{\text{base}}{H_2O} + \underset{\text{acid}}{CH_3CO_2H} \rightleftharpoons \underset{\text{acid}}{H_3O^+} + \underset{\text{base}}{CH_3CO_2^-}$$

Conjugate acid of H_2O

Conjugate base of acetic acid

Why water is important to our bodies?

1. ~60% of our body is water, 70-85% of the weight of a typical cell

2. A solvent of many substances our bodies need such as glucose, ions, etc.

3. Acts as a medium in which acids and bases release their chemical groups to maintain a constant cellular environment or homeostasis.

4. Essential buffer that maintain pH

5. Temperature regulation- high sppecific heat capacity.

6. A participant in many biochemical reactions.

Water distribution in body compartments

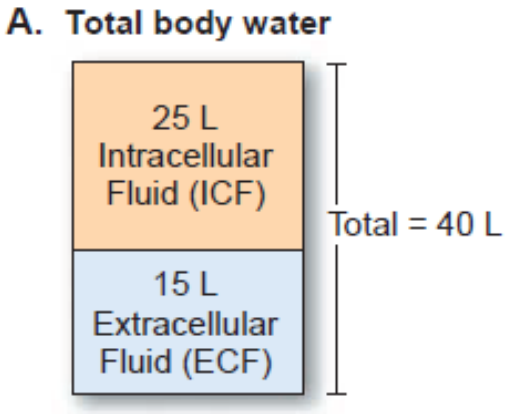


FIG. 4.2. Fluid compartments in the body based on an average 70-kg man.

Mark's 2012

Noncovalent Interactions

Electrostatic, or ionic interactions (salt bridges)

- Interactions between oppositely charged groups

Van der Waals forces

- Attractions between transient dipoles generated by the rapid movement of electrons of all neutral atoms. 1-5 kj/mole

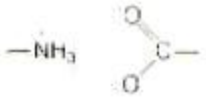
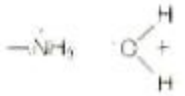
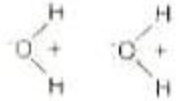
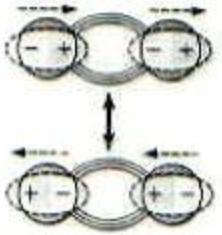
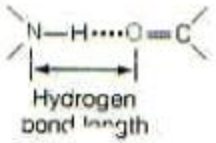
Hydrophobic interactions 5-30 kj/mole

- Self-association of nonpolar compounds in an aqueous environment.
- Minimize unfavorable interactions between nonpolar groups and water

Hydrogen bonds

- The two strands of the DNA helix. 10-30 kj/mole

Types of noncovalent interactions

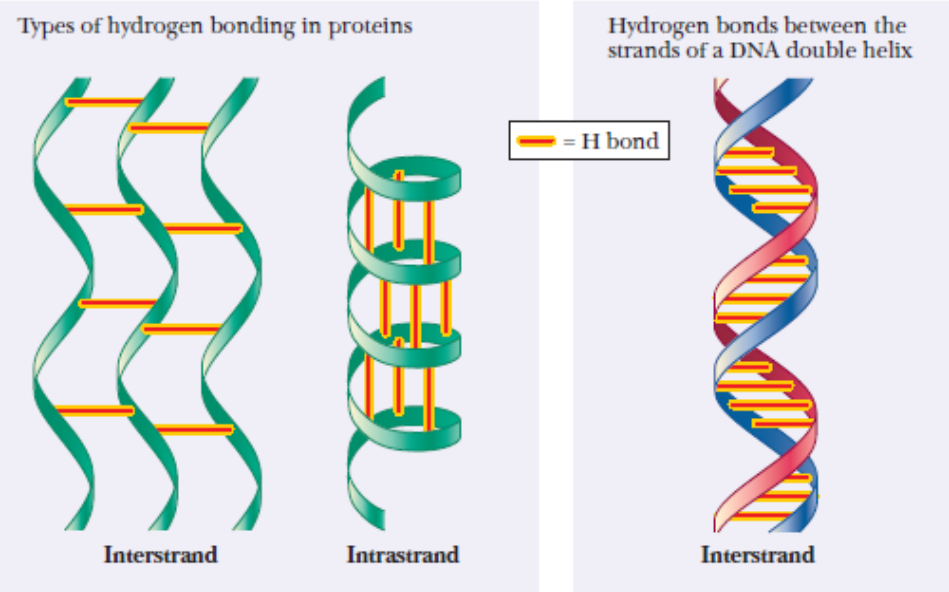
TYPE OF INTERACTION	MODEL	EXAMPLE	DEPENDENCE OF ENERGY ON DISTANCE	COMMENT
(a) Charge–charge			$1/r$	Longest-range force; nondirectional
(b) Charge–dipole			$1/r^2$	Depends on orientation of dipole
(c) Dipole–dipole			$1/r^3$	Depends on *mutual* orientation of dipoles
(d) Charge–induced dipole			$1/r^4$	Depends on polarizability of molecule in which dipole is induced
(e) Dipole–induced dipole			$1/r^5$	Depends on polarizability of molecule in which dipole is induced
(f) Dispersion			$1/r^6$	Involves mutual synchronization of fluctuating charges
(g) Hydrogen bond	DONOR—H···· ACCEPTOR		Length of bond fixed	Depends on donor–acceptor pair

Properties of Noncovalent Interactions

1. Reversible

2. Relatively weak.
1-30 kj/mole vs.
350 kj/mole in C–C bond

3. Molecules interact and bind specifically.



Covalent vs Noncovalent bonds

Table 2.3

Some Bond Energies

	Type of Bond	Energy ($kJ\ mol^{-1}$)	Energy ($kcal\ mol^{-1}$)
Covalent Bonds (Strong)	O—H	460	110
	H—H	416	100
	C—H	413	105
Noncovalent Bonds (Weaker)	Hydrogen bond	20	5
	Ion–dipole interaction	20	5
	Hydrophobic interaction	4–12	1–3
	Van der Waals interactions	4	1

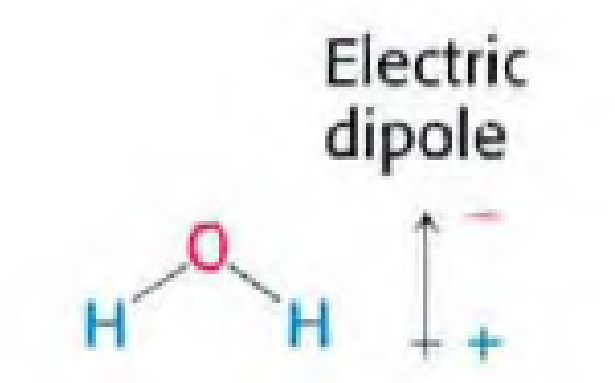
*Note that two units of energy are used throughout this text. The kilocalorie (kcal) is a commonly used unit in the biochemical literature. The kilojoule (kJ) is an SI unit and will come into wider use as time goes on. The kcal is the same as the "Calorie" reported on food labels.

-Noncovalent forces significantly contribute to the structure, stability, and functional competence of macromolecules in living cells.

- Can be either attractive or repulsive,

-Involve interactions both within the biomolecule and between it and the water of the surrounding environment.

Polarity



If straight?

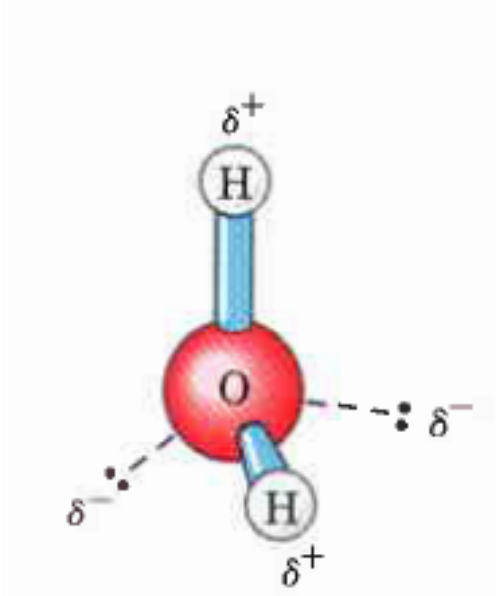
CO_2 has polar bonds but is nonpolar

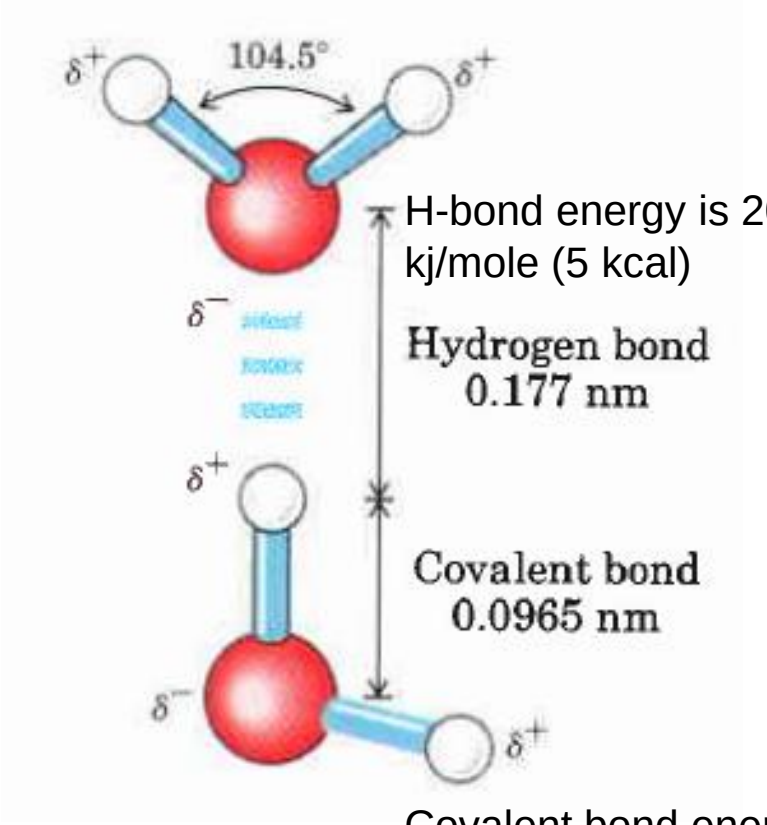
δ- δ+ δ-

O = C = O

Linear- no dipole moment

Water structure





H-bond energy is 20 kj/mole (5 kcal)

Covalent bond energy is 460 kj/mole (110 kcal)

Electronegativity of O atom is 3.5
Electronegativity of H atom is 2.1

Water is electrically neutral (net charge is zero)
Bent geometry → dipole

Water and Hydrogen Bonds (H-bonds)

-A hydrogen bond is a weak noncovalent interaction between the H of one molecule and the more electronegative atom of an acceptor molecule.

-A dipolar molecule with an uneven distribution of electrons between the hydrogen and oxygen atoms.

- Forms H-bonds with other polar molecules, thus acts as a solvent.

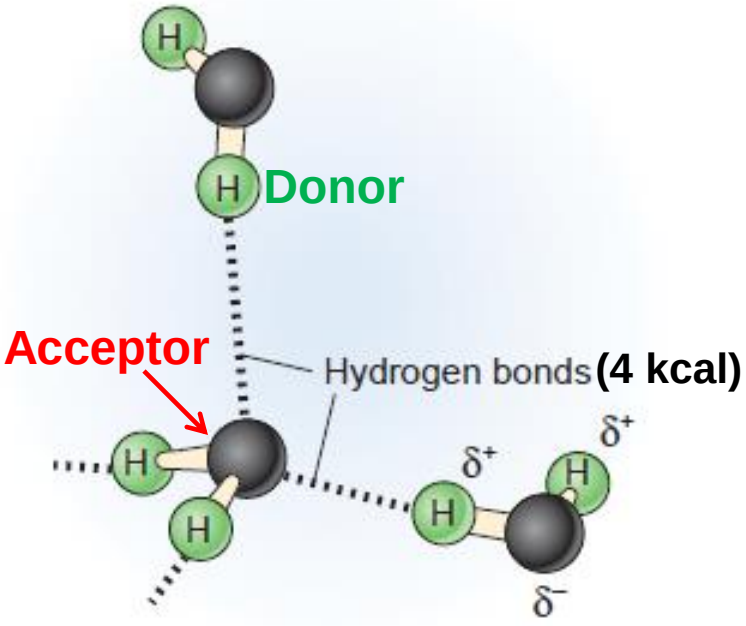
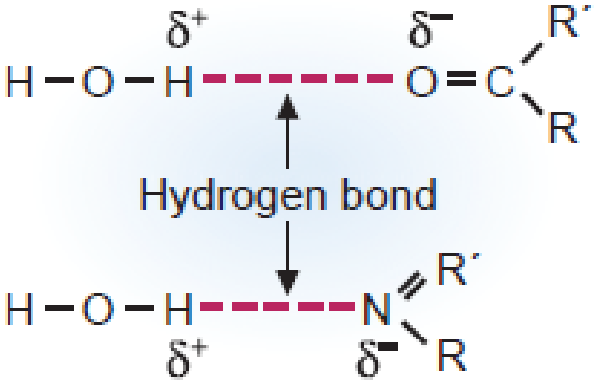


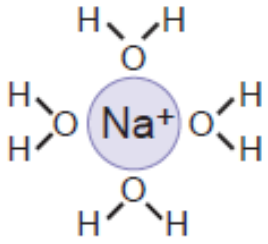
FIG. 4.3. Hydrogen bonds between water molecules. The oxygen atoms are shown in *black*.

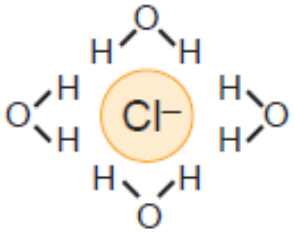
Mark's 2012

Water as a solvent



H-bonds between water and polar molecules. *R denotes additional atoms.*





Hydration shells surrounding anions and cations.

where water is

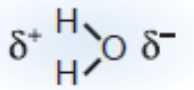
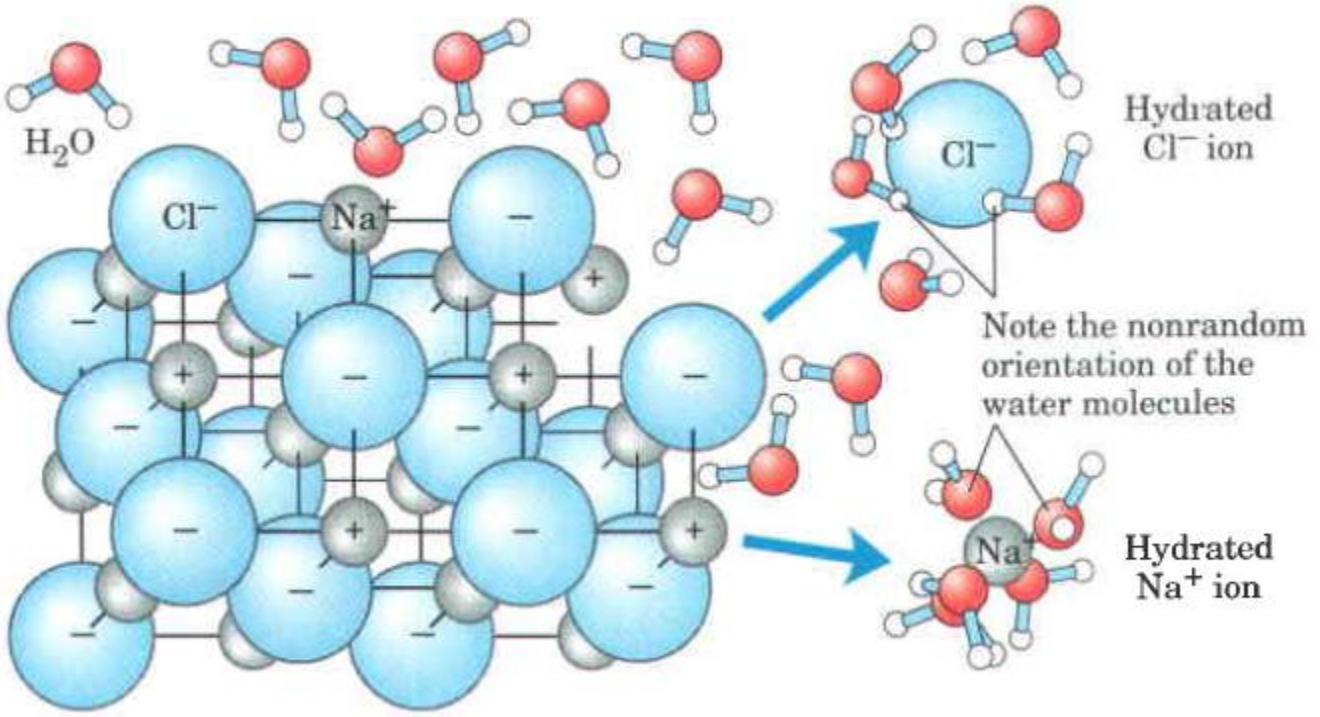


Table 4.1 Distribution of Ions in Body Fluids

	ECF[a] *(mmol/L)*	*ICF (mmol/L)*
Cations		
Na^+	145	12
K^+	4	150
Anions		
Cl^-	105	5
HCO_3^-	25	12
Inorganic phosphate	2	100

ECF, extracellular fluid; *ICF*, intracellular fluid.
[a]The content of inorganic ions is very similar in plasma and interstitial fluid, the two components of the ECF.

Water as a solvent



Lehninger 5th edition

Hydrogen Bonds (H-bonds) and Temperature

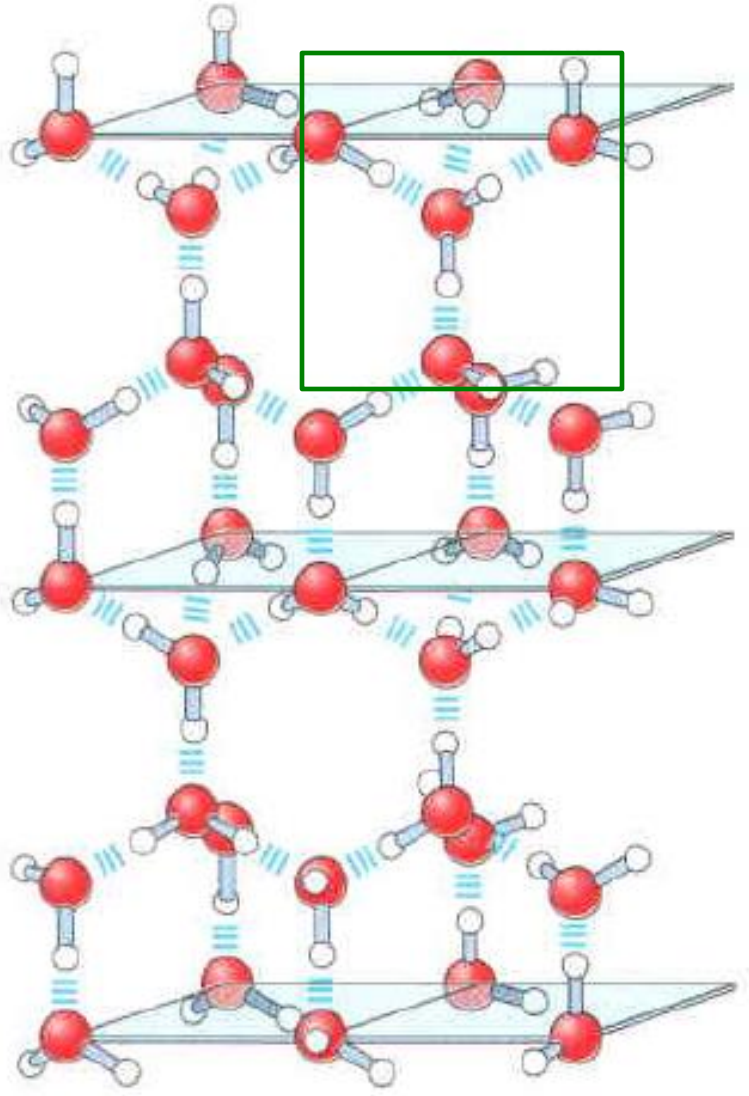
H-bond is stronger if

X–H ..... A

A is O, N or F
X is O, N or F

Average number of H-bond
in liquid water at 10°C is 3.4
in ice crystals is 4

Number of H-bonds decrease
with higher temperatures



Lehninger 5th edition

Physical properties of water

TABLE 2–1 Melting Point, Boiling Point, and Heat of Vaporization of Some Common Solvents

	Melting point (°C)	Boiling point (°C)	Heat of vaporization (J/g)*
Water	0	100	2,260
Methanol (CH_3OH)	−98	65	1,100
Ethanol (CH_3CH_2OH)	−117	78	854
Propanol ($CH_3CH_2CH_2OH$)	−127	97	687
Butanol ($CH_3(CH_2)_2CH_2OH$)	−90	117	590
Acetone (CH_3COCH_3)	−95	56	523
Hexane ($CH_3(CH_2)_4CH_3$)	−98	69	423
Benzene (C_6H_6)	6	80	394
Butane ($CH_3(CH_2)_2CH_3$)	−135	−0.5	381
Chloroform ($CHCl_3$)	−63	61	247

*The heat energy required to convert 1.0 g of a liquid at its boiling point and at atmospheric pressure into its gaseous state at the same temperature. It is a direct measure of the energy required to overcome attractive forces between molecules in the liquid phase.

H-bonding gives water its unusual properties

Higher melting and boiling points

Heat of vaporization

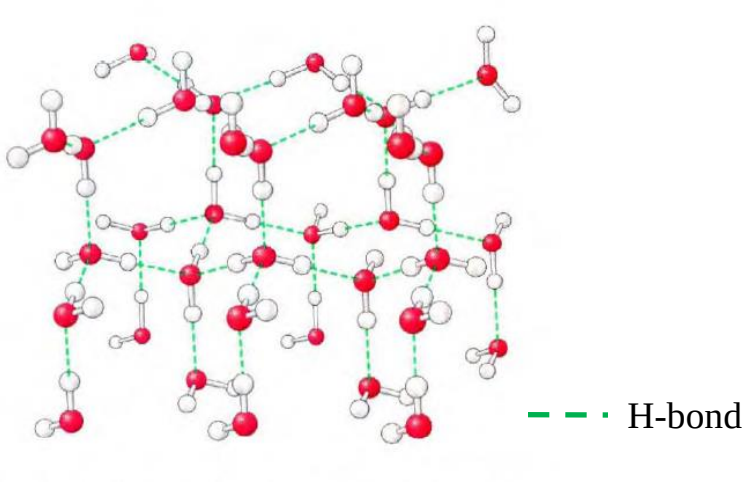
Higher freezing point

Surface tension

H-bond has:

A bond energy of 20 kj/mole

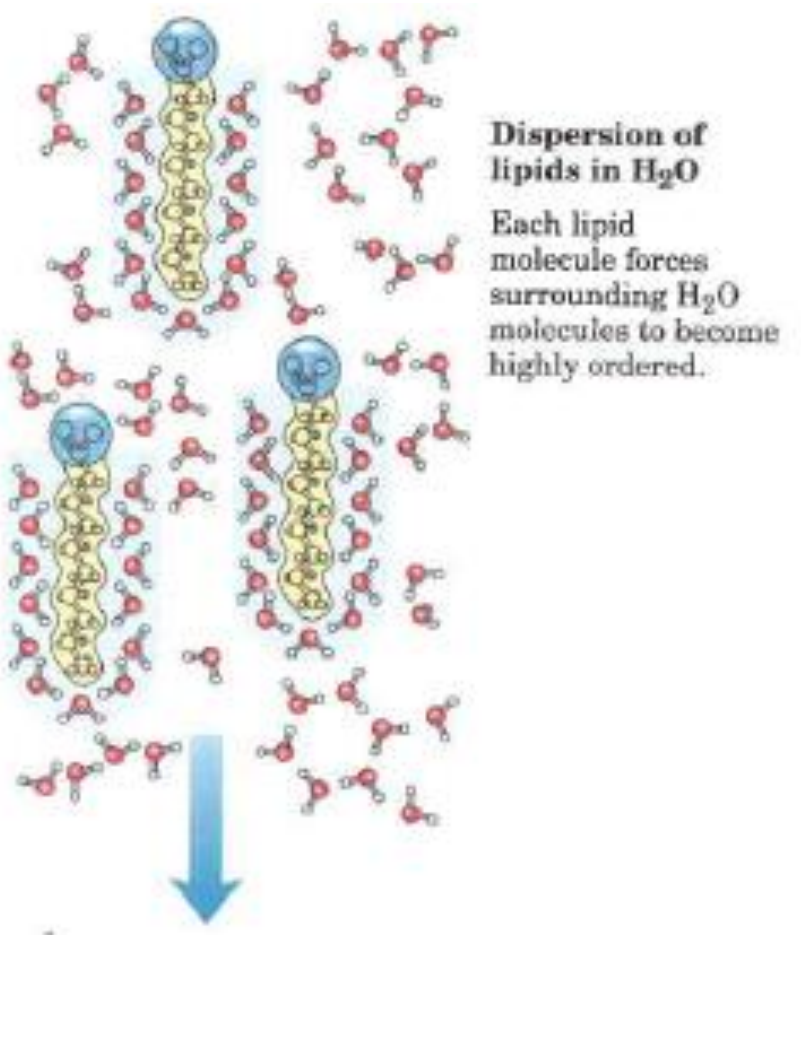
Life time 1x 10^{-9} second



Highly cohesive (ice)

Berg 2006

Hydrophobic interactions and micelle formation



in a cage like structure

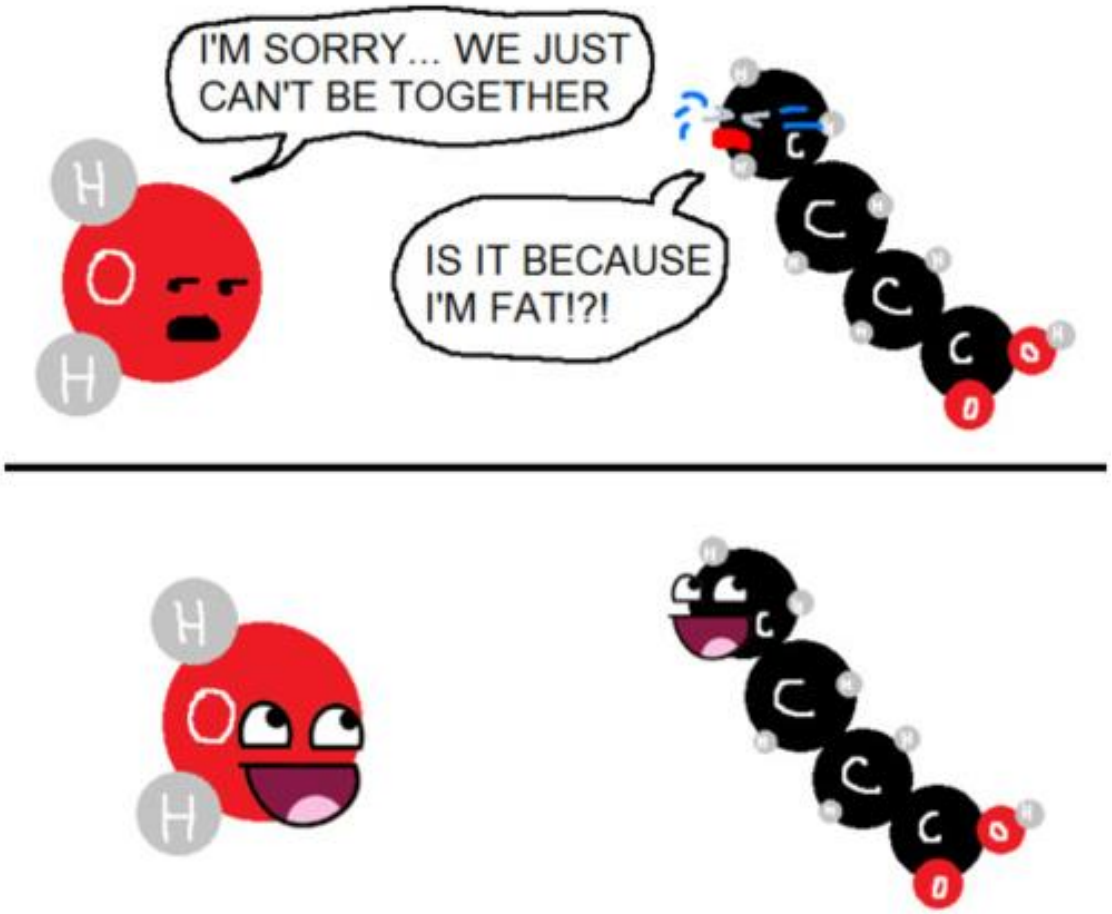
Water and Thermal Regulation

Water structure resists sudden and large temperature changes because:

High thermal conductivity thus, facilitates heat dissipation from high energy consumption areas into the body water pool.

High heat of fusion, so a large drop in temperature is needed to convert liquid water to ice.

High heat capacity and heat of vaporization; when liquid water (sweating) is converted to a gas and evaporates from the skin, we feel a cooling effect.


I'M SORRY... WE JUST CAN'T BE TOGETHER
IS IT BECAUSE I'M FAT!?!
H
O
H
C
O

Measuring concentrations

Molarity: the number of moles in a liter of solution

Unit: Mole/Liter = M

mM = 10^{-3} M, uM = 10^{-6} M

Symbol: [X]

$$\text{Concentration} = \frac{\text{Amount of solute}}{\text{Amount of solvent}}$$

Dissolve 2 moles of glucose in 5 liters of H_20. what is the concentration?

[Glucose] = 2/5 = 0.4 M

Acid and Base Strength

- Some acids can cause burns if come in contact with skin, other acids are safe. why?
- How easy can the acid produce proton

  – Strong acid: gives up H^+ easily (100% dissociated in water)

  $$HCl \longrightarrow H^+ + Cl^-$$

  – Weak acid: gives up H^+ with difficulty (less than 100% dissociated)

  $$CH_3COOH \rightleftharpoons H^+ + CH_3COO^-$$

Acid dissociation constant, K_a

– The general ionization of an acid is as follows:

$$HA + H_2O \rightleftharpoons H_3O^+ + A^-$$

So the acid dissociation constant is as follows:

$$K_a = \frac{[H_3O^+][A^-]}{[HA][H_2O]}$$

$[H_2O]$ = 55.5 M and is constant in all equations

$$K_a = \frac{[H_3O^+][A^-]}{[HA]}$$

Acid dissociation constant

– The general ionization of an acid is as follows:

$$HA \longleftrightarrow H^+ + A^-$$

So the acid dissociation constant is as follows:

$$K_a = \frac{[H^+][A^-]}{[HA]}$$

There are many orders of magnitude spanned by K_a values, so pK_a is used instead:

$$pK_a = \log 1/K_a = - \log_{10} K_a$$

The larger the value of the pK_a, the smaller the extent of dissociation.

The equilibrium constant, Ka

$$HA \leftrightarrow A^- + H^+$$

Acid **Conjugate base**

$$K_a = \frac{[H^+][A^-]}{[HA]}$$

Larger K_a means:
- More dissociation
- Smaller pK_a
- Stronger acid

Increase acid strength

Decrease acid strength

TABLE 8–2 Acidity Constants in Water at 25°C

Acid	Formula	Conjugate Base	K_a	pK_a
Hydriodic	HI	I^-	$\approx 10^{11}$	≈ -11
Hydrobromic	HBr	Br^-	$\approx 10^{9}$	≈ -9
Perchloric	$HClO_4$	ClO_4^-	$\approx 10^{7}$	≈ -7
Hydrochloric	HCl	Cl^-	$\approx 10^{7}$	≈ -7
Chloric	$HClO_3$	ClO_3^-	$\approx 10^{3}$	≈ -3
Sulfuric (1)	H_2SO_4	HSO_4^-	$\approx 10^{2}$	≈ -2
Nitric	HNO_3	NO_3^-	≈ 20	≈ -1.3
Hydronium ion	H_3O^+	H_2O	1	0.0
Urea acidium ion	$(NH_2)CONH_3^+$	$(NH_2)_2CO$ (urea)	6.6×10^{-1}	0.18
Iodic	HIO_3	IO_3^-	1.6×10^{-1}	0.80
Oxalic (1)	$H_2C_2O_4$	$HC_2O_4^-$	5.9×10^{-2}	1.23
Sulfurous (1)	H_2SO_3	HSO_3^-	1.5×10^{-2}	1.82
Sulfuric (2)	HSO_4^-	SO_4^{2-}	1.2×10^{-2}	1.92
Chlorous	$HClO_2$	ClO_2^-	1.1×10^{-2}	1.96
Phosphoric (1)	H_3PO_4	$H_2PO_4^-$	7.5×10^{-3}	2.12
Arsenic (1)	H_3AsO_4	$H_2AsO_4^-$	5.0×10^{-3}	2.30
Chloroacetic	$ClCH_2COOH$	$ClCH_2COO^-$	1.4×10^{-3}	2.85
Hydrofluoric	HF	F^-	6.6×10^{-4}	3.18
Nitrous	HNO_2	NO_2^-	4.6×10^{-4}	3.34
Formic	HCOOH	$HCOO^-$	1.8×10^{-4}	3.74

Acid dissociation constant

Acid Dissociation Constants and pK_a Values for Some Weak Electrolytes (at 25°C)

Acid	K_a (M)	pK_a
HCOOH (formic acid)	1.78×10^{-4}	3.75
CH_3COOH (acetic acid)	1.74×10^{-5}	4.76
CH_3CH_2COOH (propionic acid)	1.35×10^{-5}	4.87
$CH_3CHOHCOOH$ (lactic acid)	1.38×10^{-4}	3.86
$HOOCCH_2CH_2COOH$ (succinic acid) pK_1*	6.16×10^{-5}	4.21
$HOOCCH_2CH_2COO^-$ (succinic acid) pK_2	2.34×10^{-6}	5.63
H_3PO_4 (phosphoric acid) pK_1	7.08×10^{-3}	2.15
$H_2PO_4^-$ (phosphoric acid) pK_2	6.31×10^{-8}	7.20
HPO_4^{2-} (phosphoric acid) pK_3	3.98×10^{-13}	12.40
$C_3N_2H_5^+$ (imidazole)	1.02×10^{-7}	6.99
$C_6O_2N_3H_{11}^+$ (histidine–imidazole group) pK_R†	9.12×10^{-7}	6.04
H_2CO_3 (carbonic acid) pK_1	1.70×10^{-4}	3.77
HCO_3^- (bicarbonate) pK_2	5.75×10^{-11}	10.24
$(HOCH_2)_3CNH_3^+$ (*tris*-hydroxymethyl aminomethane)	8.32×10^{-9}	8.07
NH_4^+ (ammonium)	5.62×10^{-10}	9.25
$CH_3NH_3^+$ (methylammonium)	2.46×10^{-11}	10.62

*These pK values listed as pK_1, pK_2, or pK_3 are in actuality pK_a values for the respective dissociations. This simplification in notation is used throughout this book.
†pK_R refers to the imidazole ionization of histidine.

Data from *CRC Handbook of Biochemistry*, The Chemical Rubber Co., 1968.

Base dissociation constant

$$B + H_2O \rightleftharpoons BH^+ + OH^-$$

$$K_b = \frac{[BH+][OH^-]}{[B]}$$

Reverse the reaction:

$$BH^+ \rightleftharpoons B + H^+$$

$$K_a = \frac{[B][H^+]}{[BH^+]}$$

Weak Bases

TABLE 7.3 Values of K_b for Some Common Weak Bases

Name	Formula	Conjugate Acid	K_b
Ammonia	NH_3	NH_4^+	1.8×10^{-5}
Methylamine	CH_3NH_2	$CH_3NH_3^+$	4.38×10^{-4}
Ethylamine	$C_2H_5NH_2$	$C_2H_5NH_3^+$	5.6×10^{-4}
Aniline	$C_6H_5NH_2$	$C_6H_5NH_3^+$	3.8×10^{-10}
Pyridine	C_5H_5N	$C_5H_5NH^+$	1.7×10^{-9}

Strong Acids

- Dissociate readily
- Ka is very large
- Examples: Hydrochloric, Nitric; Sulfuric

Ex. $HCl \rightarrow H^+ + Cl^-$

$$Ka = \frac{[H^+]\,[Cl^-]}{[HCl]}$$

$$[H^+] = [acid]$$

Ex.1 M solution of HCl has a $[H^+]$ of 1 M

1 mM HCl solution has a $[H^+]$ of 1 mM

0.1 M H_2SO_4 solution has a $[H^+]$ of 0.2 M

Weak Acids

- Dissociate slightly
- Ka is smaller than strong acids
- Examples: Acetic, Boric, Nitrous, Phosphoric, Sulfurous

Ex. $CH_3COOH + H_2O \longleftrightarrow CH_3COO^- + H_3O^+$

$$Ka = \frac{[H+]\,[CH_3COO^-]}{[CH_3COOH]}$$

What is the H+ of a 0.1 M solution of acetic acid?
Ka= 1.74×10^{-5}

$1.74 \times 10^{-5} = x^2/0.1$

$x^2 = 1.74 \times 10^{-6}$, or $x = 1.32 \times 10^{-3}$ M

Equilibrium constant and the pH of water

H_2O dissociates to a slight extent to form hydrogen (H^+) and hydroxyl (OH^-) ions.

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

$$K_{eq} = \frac{[H^+][OH^-]}{[H_2O]}$$

$$K_{eq} = \frac{(10^{-7})(10^{-7})}{55.5} = 1.8 \times 10^{-16}$$

Because the concentration of H_2O in pure water is essentially constant, a new constant, K_w, the **ion product of water**, can be written as

$$K_w = 55.5\ K_{eq} = 10^{-14} = [H^+][OH^-]$$

[H+] of pure water is only 0.0000001 M

Dissociation of water

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

Example: A solution has an $[OH^-] = 10^{-9}$ M

$[H_3O^+] = 10^{-5}$ M

Problem solving

Example:

What is the $[H^+]$ of a 0.01 M NaOH solution?

$Kw = [H^+] \times [OH^-] = [H^+] \times 10^{-2} = 10^{-14}$

$[H^+] = 10^{-12}$ M

Example:

What is the $[OH^-]$ of a 0.01 M HCl solution?

$Kw = [H^+] \times [OH^-] = 10^{-2} \times [OH^-] = 10^{-14}$

$[OH^-] = 10^{-12}$ M

Example:

Find the K_a of a 0.04 M weak acid HA whose $[H^+]$ is 1×10^{-4}?

$$HA \rightleftharpoons H^+ + A^-$$

$K_a = [A^-][H^+] / [HA] = [H^+]^2 / [HA] = 10^{-4} \times 10^{-4} / 0.04 = 2.5 \times 10^{-7}$

Example 2:

What is the $[H^+]$ of a 0.05 M $Ba(OH)_2$?

$$Ba(OH)_2 \rightleftharpoons Ba + 2OH^-$$

$[OH^-] = 2 \times 0.05 = 0.10\ M = 1 \times 10^{-1}$

$[H^+] = 1 \times 10^{-13}$

Example 4:

The $[H^+]$ of a 0.03 M weak base solution is 1×10^{-10} M. Calculate pKb?

$$B + H_2O \rightleftharpoons BH^+ + OH^-$$

$[OH^-] = 10^{-4}$

$K_b = (10^{-4} \times 10^{-4}) / 0.03 = 3.33 \times 10^{-7}$ M

$pK_b = -\log K_b = 6.48$

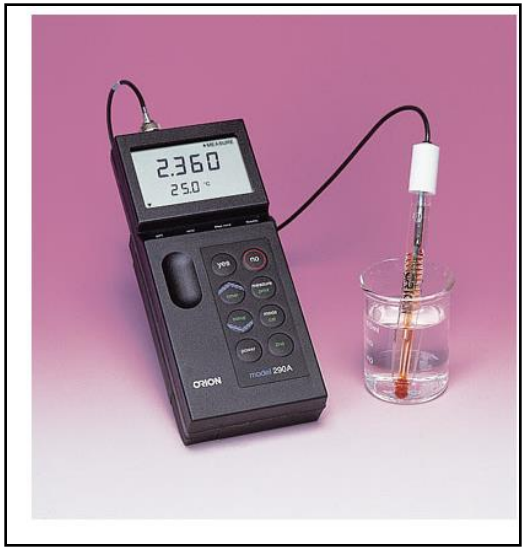
Measuring the acidity of solutions, pH

$$pH = -\log_{10} [H^+]$$

pH Scale

The hydrogen ion and hydroxyl ion concentrations are given in moles per liter at 25°C.

pH	[H⁺]		[OH⁻]	
0	(10^0)	1.0	0.00000000000001	(10^{-14})
1	(10^{-1})	0.1	0.0000000000001	(10^{-13})
2	(10^{-2})	0.01	0.000000000001	(10^{-12})
3	(10^{-3})	0.001	0.00000000001	(10^{-11})
4	(10^{-4})	0.0001	0.0000000001	(10^{-10})
5	(10^{-5})	0.00001	0.000000001	(10^{-9})
6	(10^{-6})	0.000001	0.00000001	(10^{-8})
7	**(10^{-7})**	**0.0000001**	**0.0000001**	**(10^{-7})**
8	(10^{-8})	0.00000001	0.000001	(10^{-6})
9	(10^{-9})	0.000000001	0.00001	(10^{-5})
10	(10^{-10})	0.0000000001	0.0001	(10^{-4})
11	(10^{-11})	0.00000000001	0.001	(10^{-3})
12	(10^{-12})	0.000000000001	0.01	(10^{-2})
13	(10^{-13})	0.0000000000001	0.1	(10^{-1})
14	(10^{-14})	0.00000000000001	1.0	(10^0)



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pH

The pH scale is a logarithmic scale.

One pH unit difference implies a 10-fold difference in [H+].

Example: lemon juice at pH 2.0 contains more than 100 times as much H+ as orange juice at pH 4.0

$pH = - \log [H_3O^+]$

$[H_3O^+] = 10^{-pH}$

Example 1: $[H_3O^+]$ in household bleach is 10^{-12} M

$pH = - \log [10^{-12}] = 12$

Example 2: Orange juice has a pH of 4

$[H_3O^+] = 10^{-4}$ M

The pH of Various Common Fluids

Fluid	pH
Household lye	13.6
Bleach	12.6
Household ammonia	11.4
Milk of magnesia	10.3
Baking soda	8.4
Seawater	8.0
Pancreatic fluid	7.8–8.0
Blood plasma	7.4
Intracellular fluids	
Liver	6.9
Muscle	6.1
Saliva	6.6
Urine	5–8
Boric acid	5.0
Beer	4.5
Orange juice	4.3
Grapefruit juice	3.2
Vinegar	2.9
Soft drinks	2.8
Lemon juice	2.3
Gastric juice	1.2–3.0
Battery acid	0.35

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pH problem solving

Example 1:

What is the pH of a solution whose hydrogen ion concentration is 3.2×10^{-4} mol/L?

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

$= -\log (3.2 \times 10^{-4})$

$= -\log (3.2) - \log (10^{-4})$

$= -0.5 + 4.0$

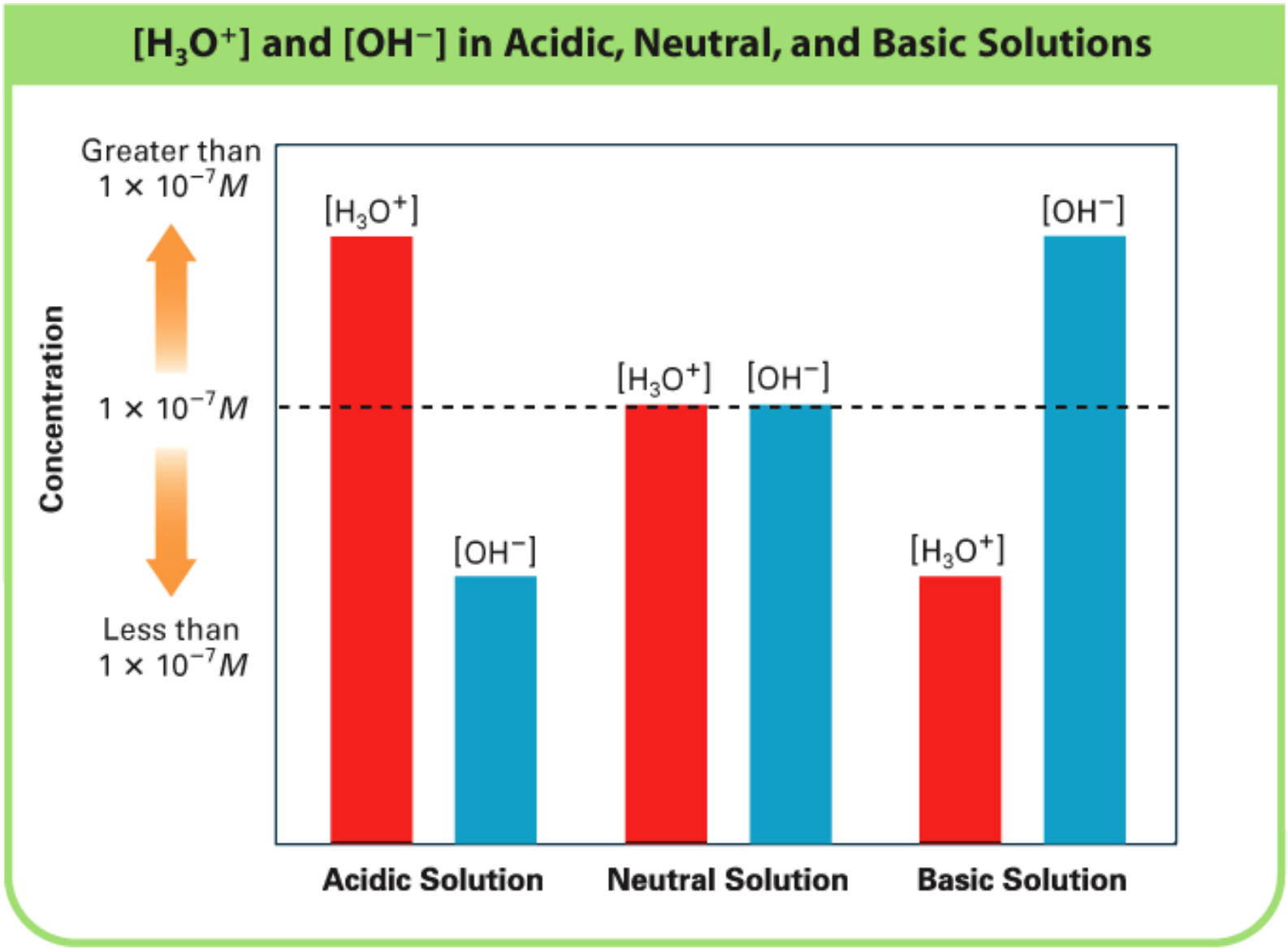
$= 3.5$

pH in solutions

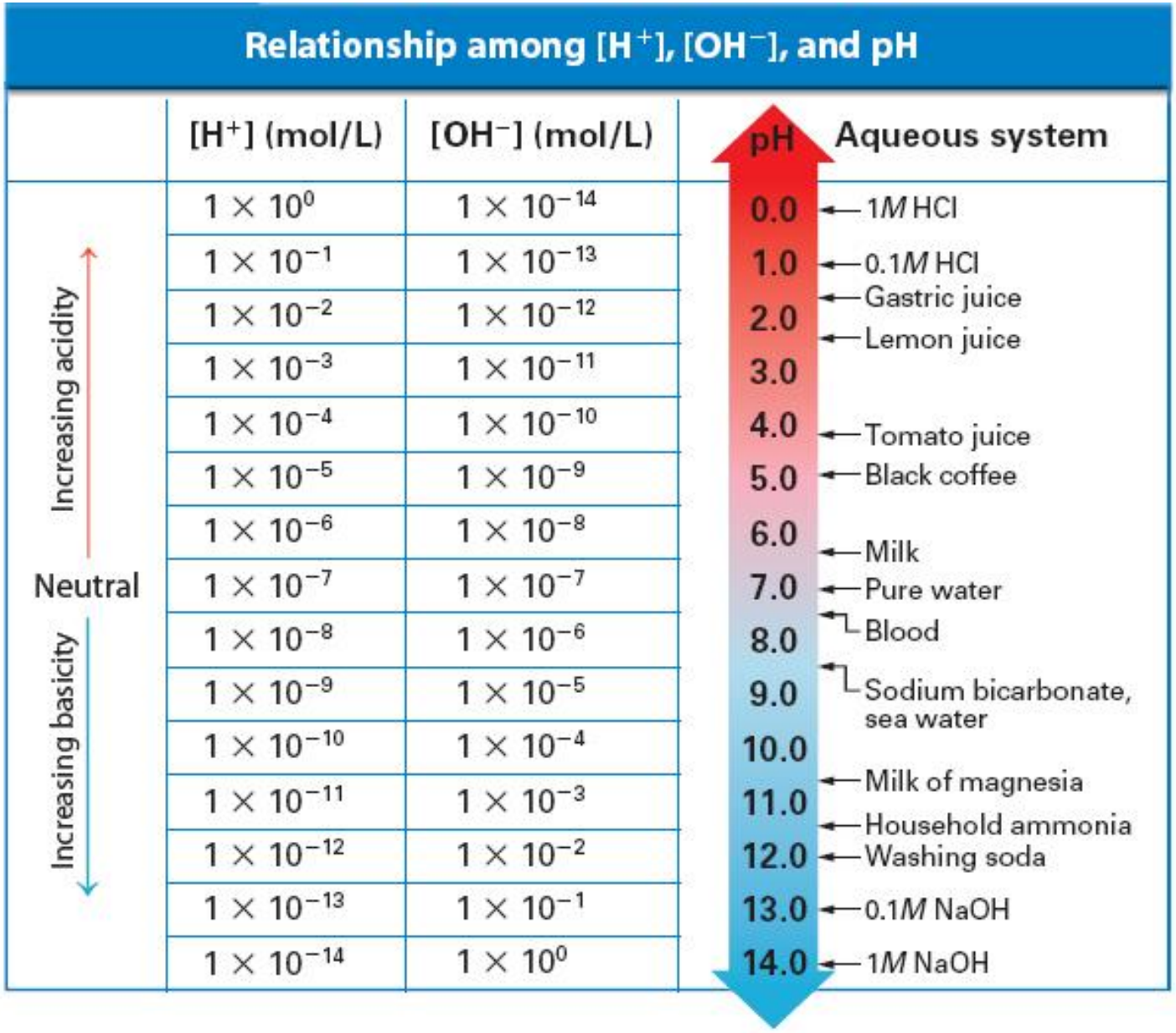
Acids

Neutral

Bases



pH scale for some common substances



Strong Acids and pH

$$HCl \rightarrow H^+ + Cl^-$$

$$Ka = \frac{[H^+]\,[Cl^-]}{[HCl]}$$

$$[H^+] = [acid]$$

Ex.1 M solution of HCl has a pH of 0

1 mM HCl solution has a pH of 3

0.1 M NaOH solution has a pH of 13

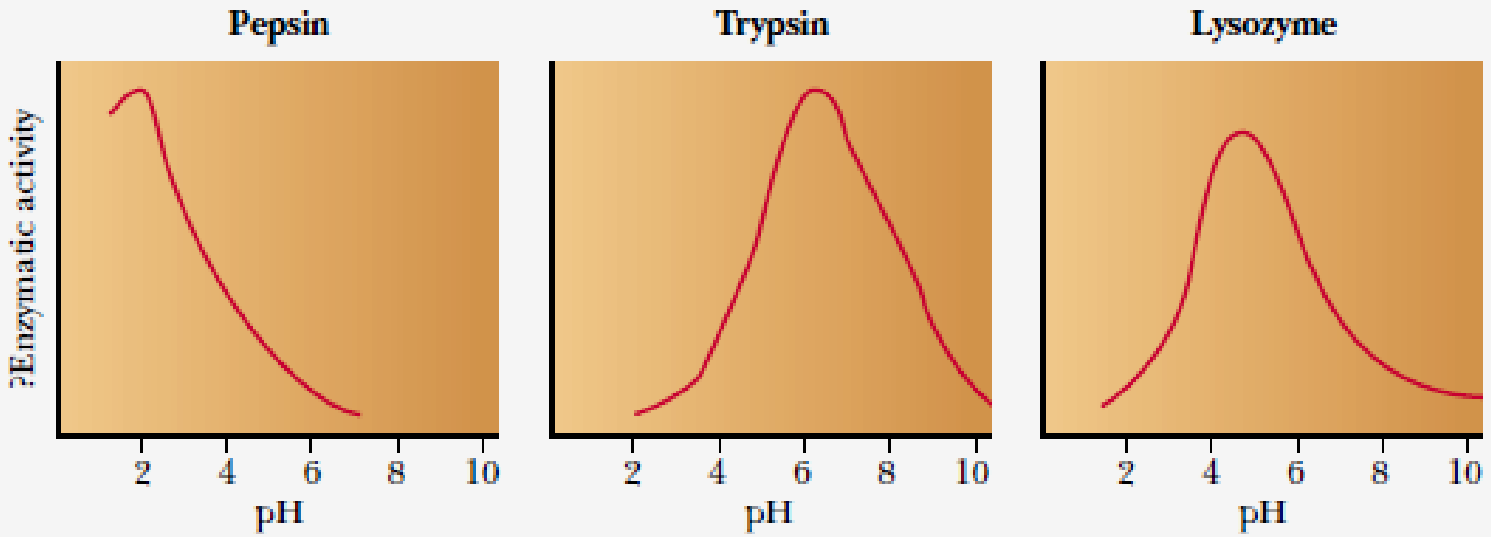
Dissociation of water

- $K_w = [H^+]\,[OH^-] = 10^{-14}$
- Valid for acidic, basic, neutral and pure H_2O
  - $pH = -\log [H^+]$
  - $pOH = -\log [OH^-]$
  - $pH + pOH = 14$

Example: A solution has an $[OH^-] = 10^{-9}$ M

$[H_3O^+] = 10^{-5}$ M $\rightarrow$ pH = 5

Enzyme activity and pH



■ **FIGURE 2.12 pH versus enzymatic activity.** Pepsin, trypsin, and lysozyme all have steep pH optimum curves. Pepsin has maximum activity under very acidic conditions, as would be expected for a digestive enzyme that is found in the stomach. Lysozyme has its maximum activity near pH 5, while trypsin is most active near pH 6.

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Example:

Find the K_a of a 0.04 M weak acid HA whose pH is 4.0?

$HA \rightleftharpoons H^+ + A^-$

$K_a = [A^-]\,[H^+] / [HA] = [H^+]^2 / [HA] = 10^{-4} \times 10^{-4} / 0.04 = 2.5 \times 10^{-7}$

Example 2:

What is the pH of a 0.05 M $Ba(OH)_2$?

$Ba(OH)_2 \rightleftharpoons Ba + 2OH^-$

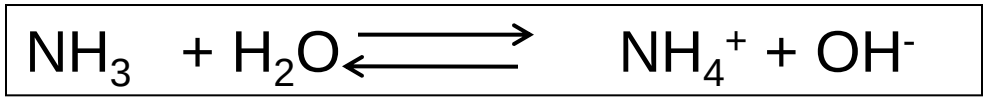
$[OH^-] = 2 \times 0.05 = 0.10\ M = 1 \times 10^{-1}$
$pOH = -\log 1 \times 10^{-1} = 1$

Remember $pOH = -\log [OH^-]$

$pH = 14 - 1 = 13$
$[H^+] = 1 \times 10^{-13}$

Example:

The K_b for ammonia is 1.8×10^{-5} M. What is the pH of 1×10^{-2} M of ammonia?



$K_b = [NH_4^+] [OH^-] / [NH_3]$

$1.8 \times 10^{-5} = [OH^-]^2 / 0.01$

$[OH^-] = 4.24 \times 10^{-4}$ M

$pOH = -\log 4.24 \times 10^{-4} = 3.37$

$pH = 14 - 3.37 = 10.63$

Henderson-Hasselbalch Equation

– The dissociation of a weak acid is as follows:

$$HA \longleftrightarrow H^+ + A^-$$

The acid dissociation constant is as follows:

$$K_a = \frac{[H^+][A^-]}{[HA]}$$

Rearranging this expression in terms of the parameter of interest [H+] gives the following:

$$[H^+] = \frac{K_a[HA]}{[A^-]}$$

Henderson-Hasselbalch Equation

Take the log of both sides:

$$\log[H^+] = \log K_a + \log \frac{[HA]}{[A^-]}$$

Change the signs , remember $pK_a = -\log K_a$:

$$pH = pK_a - \log \frac{[HA]}{[A^-]}$$

or

$$\mathbf{pH = pK_a + \log \frac{[A^-]}{[HA]}}$$

What happens when …..

pH = pKa

Substance protonation and deprotanation are in equillibruim.

pH < pKa

H^+ on, substance protonated

pH > pKa

H^+ off, substance deprotonated

$$pH = pK_a + \log \frac{[A^-]}{[HA]}$$

pH= pKa -1

Base/acid = 0.1

pH=pKa + 1

Base/acid = 10

Table 2.7

pH Values and Base/Acid Ratios for Buffers

If the pH equals	The ratio of base form/acid form equals
$pK_a - 3$	1/1000
$pK_a - 2$	1/100
$pK_a - 1$	1/10
pK_a	1/1
$pK_a + 1$	10/1
$pK_a + 2$	100/1
$pK_a + 3$	1000/1

Monoprotic- and PolyproticAcids

1. Monoprotic acids have only one ionizable proton.
2. Polyprotic acids have more than one ionizable proton.
3. The protons are removed in steps, not all at once.

$$CH_3COOH + NaOH \rightleftharpoons CH_3COO^-Na^+ + H_2O$$

$$H_3PO_4 \overset{pK_{a1} = 2.14}{\rightleftharpoons} H_2PO_4^- + H^+ \overset{pK_{a2} = 7.20}{\rightleftharpoons} HPO_4^{-2} + H^+ \overset{pK_{a3} = 12.4}{\rightleftharpoons} PO_4^{-3} + H^+$$

Polyprotic Acids

Sulfuric acid is a **strong acid** in its first dissociation step and a **weak acid** in its second step.

$H_2SO_4\ (aq) \rightarrow H^+\ (aq) + HSO_4^-\ (aq)$ $\qquad K_{a1} \approx 1.0 \times 10^{2}$

$HSO_4^-\ (aq) \rightleftharpoons H^+\ (aq) + SO_4^{2-}\ (aq)$ $\qquad K_{a2} \approx 1.2 \times 10^{-2}$

Polyprotic Acids

TABLE 7.4 Stepwise Dissociation Constants for Several Common Polyprotic Acids

Name	Formula	K_{a_1}	K_{a_2}	K_{a_3}
Phosphoric acid	H_3PO_4	7.5×10^{-3}	6.2×10^{-8}	4.8×10^{-13}
Arsenic acid	H_3AsO_4	5×10^{-3}	8×10^{-8}	6×10^{-10}
Carbonic acid*	H_2CO_3	4.3×10^{-7}	4.8×10^{-11}	
Sulfuric acid	H_2SO_4	Large	1.2×10^{-2}	
Sulfurous acid	H_2SO_3	1.5×10^{-2}	1.0×10^{-7}	
Hydrosulfuric acid†	H_2S	1.0×10^{-7}	$\approx 10^{-19}$	
Oxalic acid	$H_2C_2O_4$	6.5×10^{-2}	6.1×10^{-5}	
Ascorbic acid (vitamin C)	$H_2C_6H_6O_6$	7.9×10^{-5}	1.6×10^{-12}	

*This is really $CO_2(aq)$.

†The K_{a_2} value for H_2S is quite uncertain. Its small size makes it very difficult to measure.

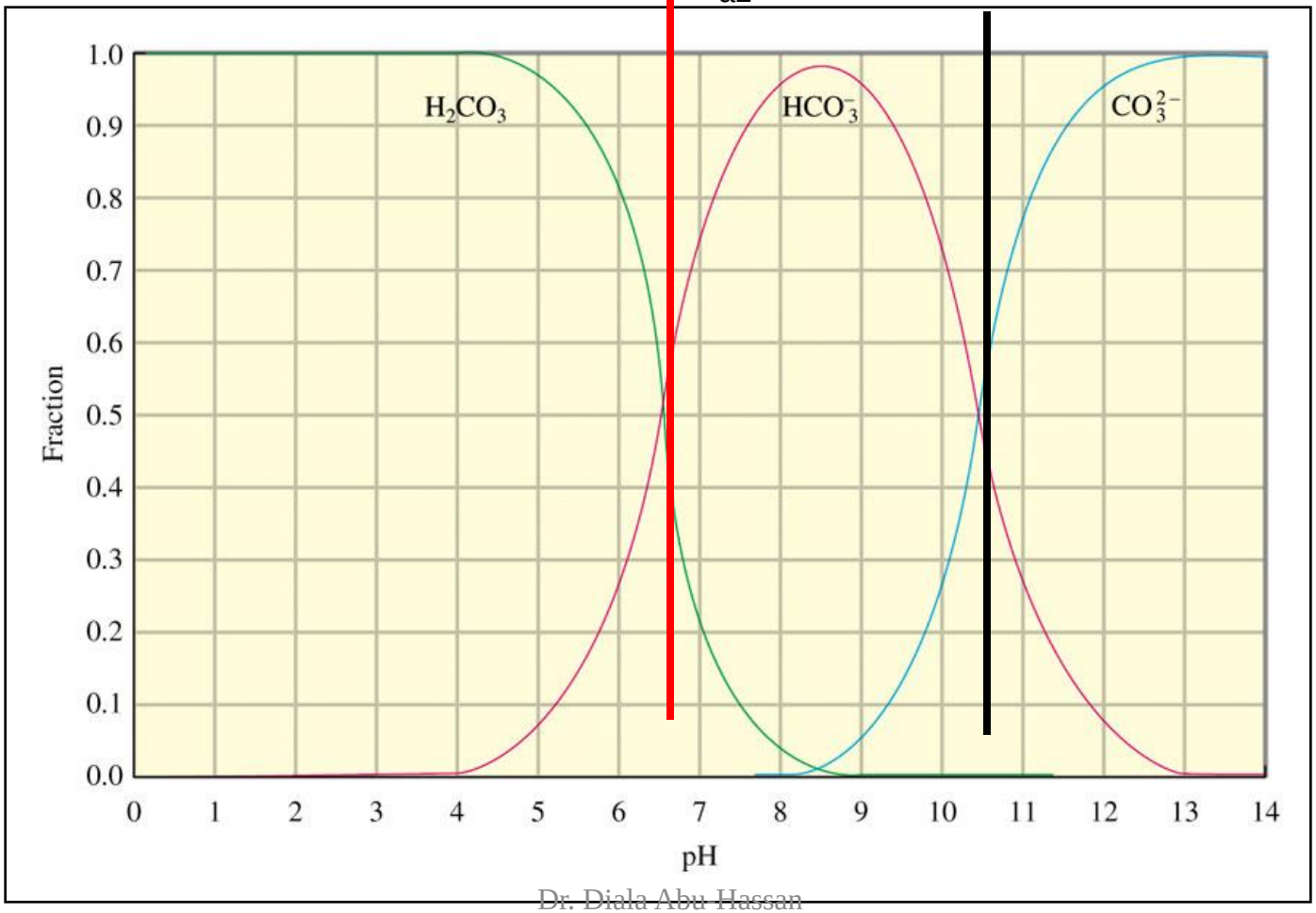
- **It is <u>always</u> easier to remove the first proton in a polyprotic acid than the second.**
- **$K_{a1} > K_{a2} > K_{a3}$**

A plot of the fractions of H_2CO_3, HCO^-_3 and CO_3^{2-}

At pH = 9.00 $H_2CO_3 \approx 0\%$, $HCO^-_3 = 95\%$ and $CO_3^{2-} = 5\%$

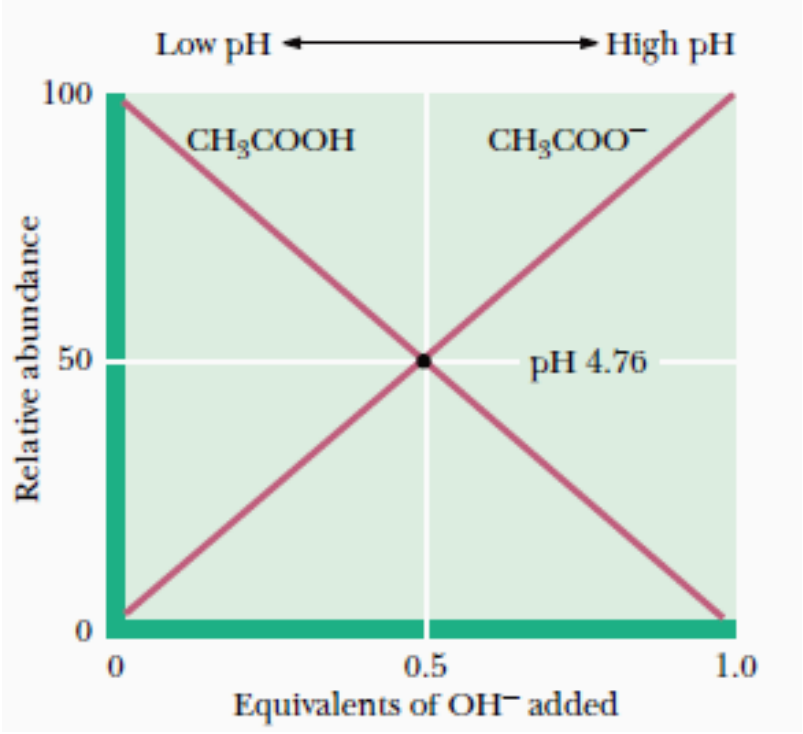
At pH = 10.00 $H_2CO_3 \approx 0\%$, $HCO^-_3 = 68\%$ and $CO_3^{2-} = 32\%$

K_{a1} = **4.3 x10^{-7}** K_{a2} = **4.8 x10^{-11}**



Titration

Titration is an experiment in which measured amounts of base are added to a measured amount of acid while following up changes in pH using a pH meter.

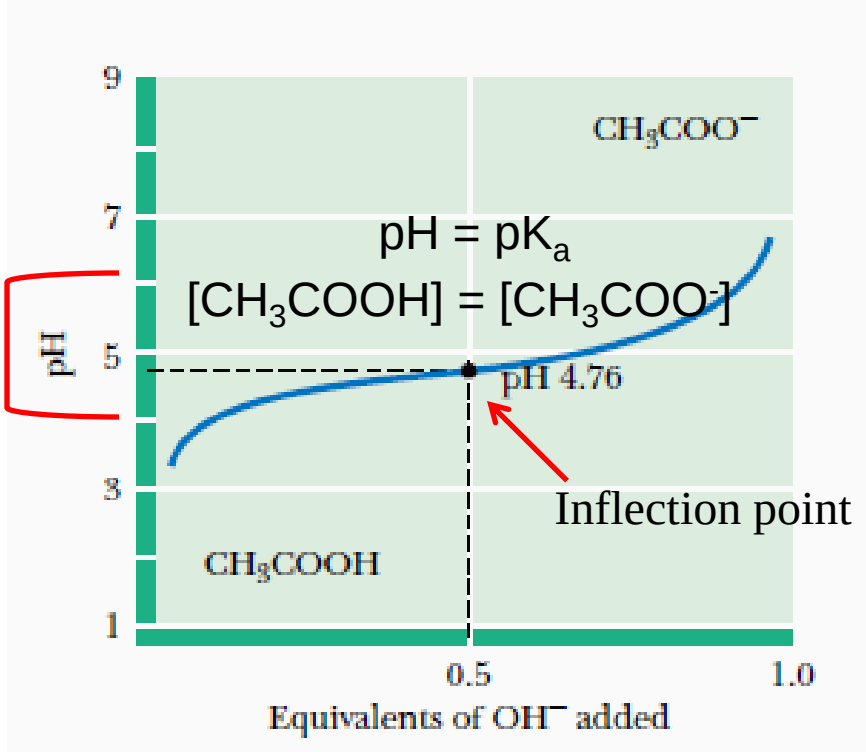


Titration curves

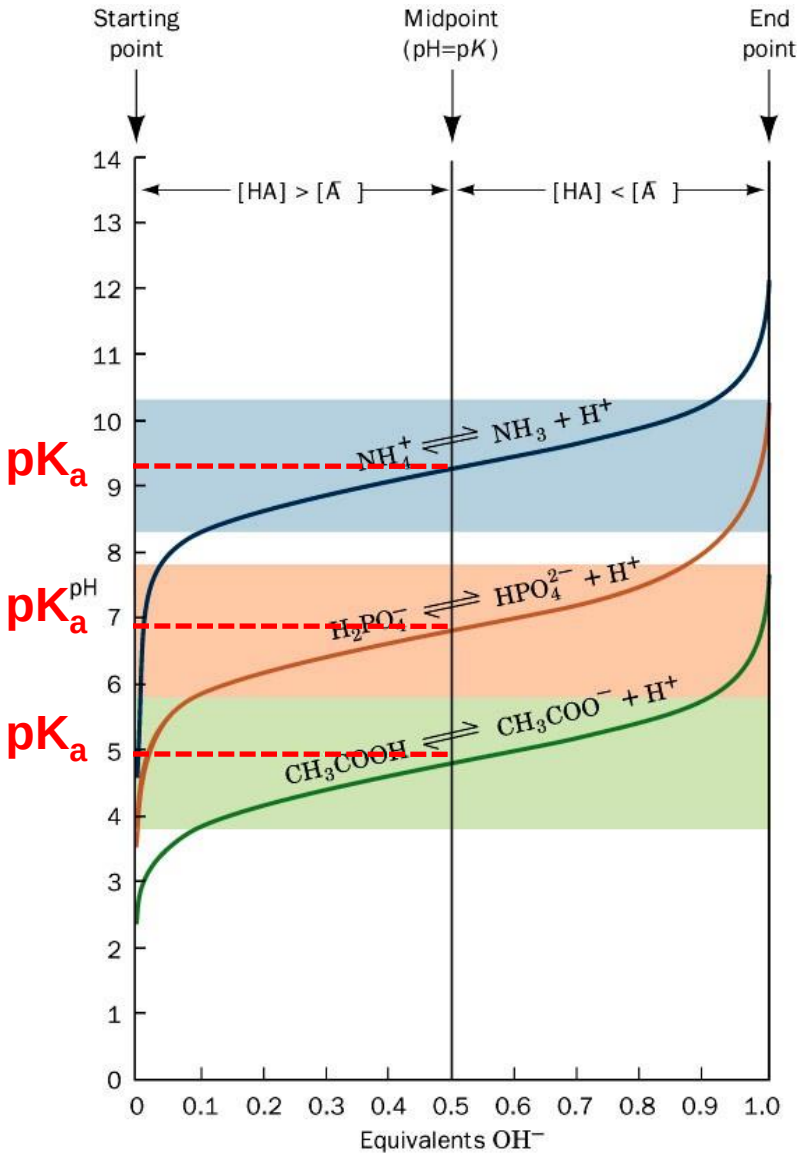
$$CH_3COOH + OH^- \rightleftharpoons CH_3COO^- + H_2O$$

In the region small pH changes upon addition of acid or base, the acid/base ratio varies within a narrow range (10:1 at one end and 1:10 at the other end).

The point in the titration at which the acid is exactly neutralized is called the **equivalence point.**



Titration curves



– Once OH^- is added to the reaction, it reacts completely with HA to form A^-

$$[A^-] = \frac{X}{V}$$

x = the equivalents of OH^- added

V represents the volume of the solution.

$$[HA] = \frac{\mathbf{HA_i\text{-}Base}}{V}$$

$$\mathbf{pH = pK_a + \log\left(\frac{[Base]}{[HA_i]\text{-}[Base]}\right)}$$

Example:

$$CH_3COOH + OH^- \rightleftharpoons CH_3COO^- + H_2O$$

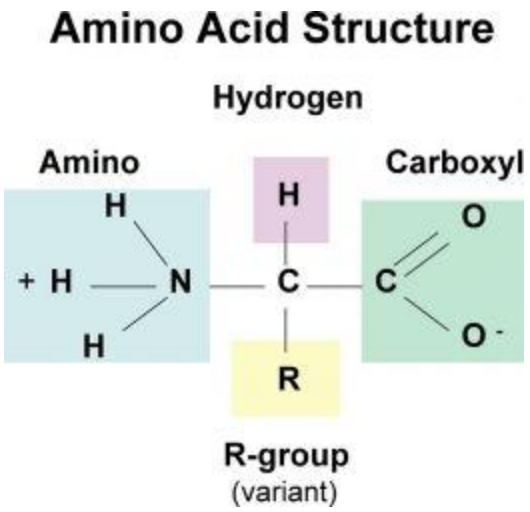
Calculate the relative amounts of acetic acid and acetate ion present and pH values when 1 mol of acetic acid is titrated with sodium hydroxide.

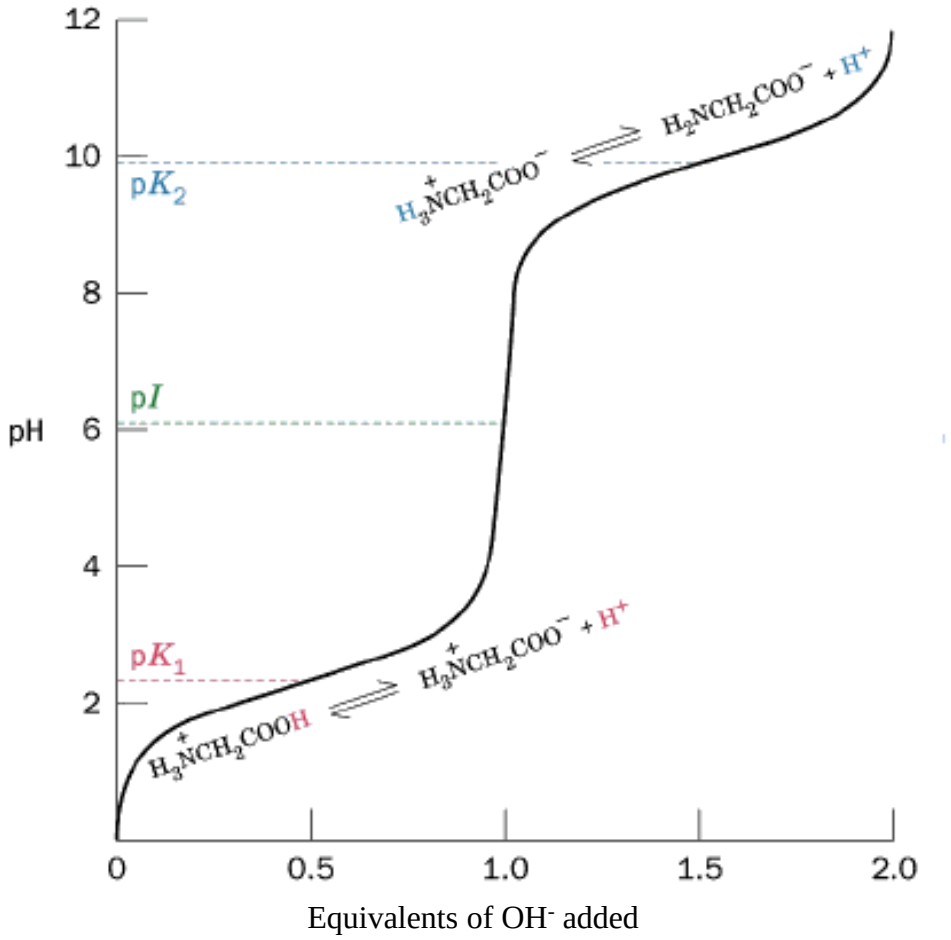
0.1 mol of NaOH is added

When 0.1 mol of NaOH is added, 0.1 mol of acetic acid reacts with it to form 0.1 mol of acetate ion, leaving 0.9 mol of acetic acid. The composition is 90% acetic acid and 10% acetate ion.

pH = pKa + log 0.1/0.9
pH = 4.76 + log 0.1/0.9
pH = 4.76 - 0.95
pH = 3.81

Titration curve of Glycine



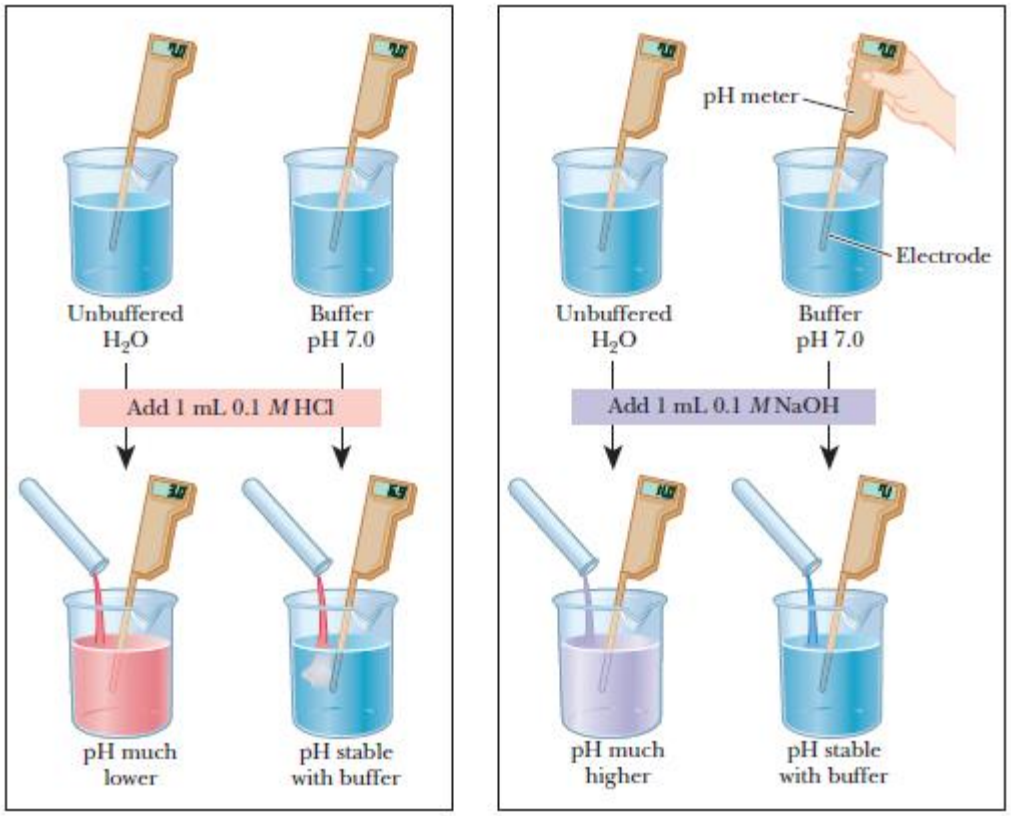


http://www.nd.edu/

Buffers

Significant changes in pH are harmful, ex. disruption of DNA double helix, disruption of protein structure, etc…

Buffers are solutions that resist abrupt and sudden changes in pH.



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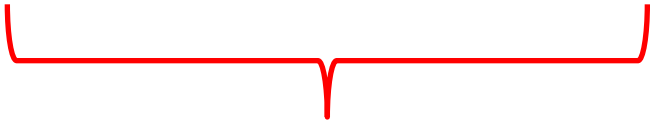
Preparation of buffers

$NaOH + CH_3COOH \rightarrow CH_3COONa + H_2O + CH_3COOH$

Limiting Reagent — Salt — excess weak acid



Buffer solution

Alkali Buffer:

PH > 7.0

Weak base + Salt of the base

$$NH_4Cl \rightarrow NH_4^+ + Cl^-$$

$$NH_3 + H_2O \leftrightarrow NH_4^+ + OH^-$$

Excess H^+ combines with OH^-

Excess OH^- combines with $NH_4^+ \rightarrow NH_3$

Buffer Action

Resists changes in PH when small amount of Acids or Alkali are
added.
Acidic Buffer = Weak acid + salt of the acid (Acid + strong Base)

$CH_3COONa \rightarrow CHCOO^- + Na^+$
$CH_3COOH \leftrightarrow CH_3COO^- + H^+$

If an acid is added, the extra H^+ combine with acetate → un-dissociated HA, so [H+] remains constant.
$CH_3COO^- + H^+ \leftrightarrow CHCOOH$

If an alkali is added, the OH^- ions are removed by reactions with
un-dissociated and to form water so [H+] remains constant
$CH_3COOH + OH- \rightarrow CH_3COO- + H_2O$

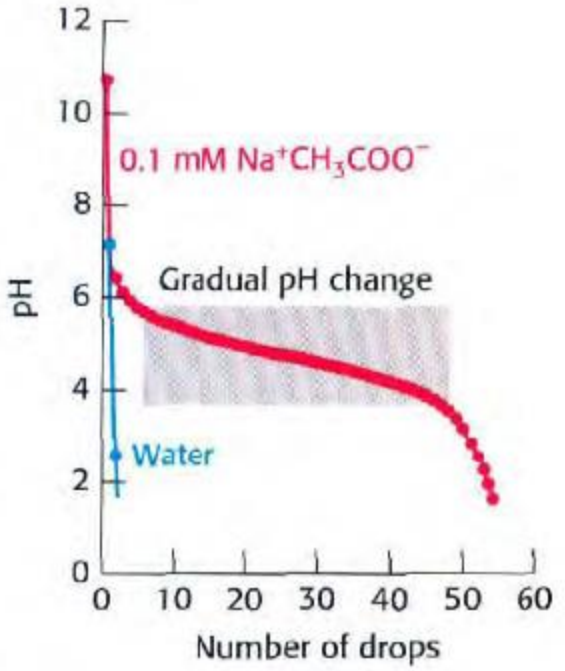
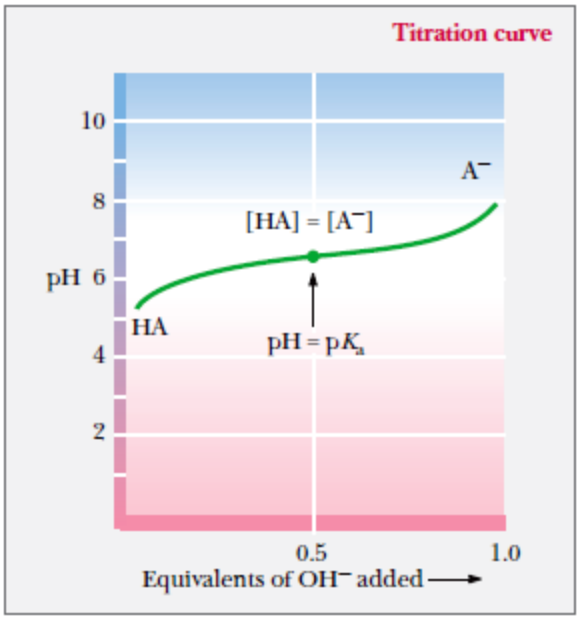


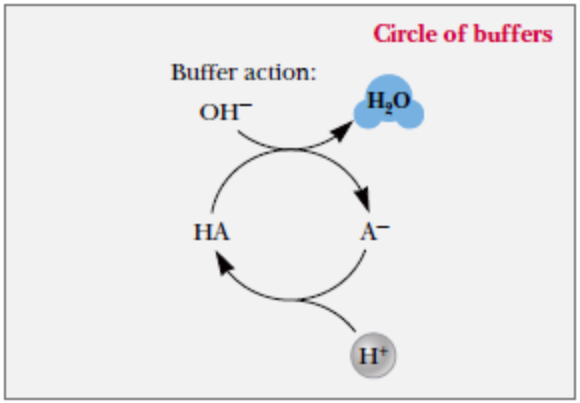
Figure 1.17 Buffer action. The addition of a strong acid, 1 M HCl, to pure water results in an immediate drop in pH to near 2. In contrast, the addition of the acid to a 0.1 M sodium acetate ($Na^+CH_3COO^-$) solution results in a much more gradual change in pH until the pH drops below 3.5.

Buffering action

Buffers work because the concentration of the weak acid and base is kept in the narrow window of the acid titration curve.

The buffer capacity is the amount of acid or base that can be added to a buffer solution before a significant change in pH occurs





■ **ACTIVE FIGURE 2.16 Two ways of looking at buffers.** In the titration curve, we see that the pH varies only slightly near the region in which [HA] = [A⁻]. In the circle of buffers, we see that adding OH⁻ to the buffer converts HA to A⁻. Adding H⁺ converts A⁻ to HA.

Factors affecting buffering capacity

Buffering Capacity depends on:

1. Buffer concentration
2. pKa of the buffer
3. The desired pH

How do we choose buffers?

Buffer selection criteria:

1. Suitable pKa for the buffer.

   pKa ±1 pH unit from the pH of the reaction

   pKa ±½ pH unit is even better

2. No interference with the reaction.

3. Suitable buffering capacity.

4. No precipitation of reactants or products due to presence of the buffer.

5. Non biological nature of the buffer.

Example:

Calculate the ratio of the concentration of acetate ion to the concentration of acetic acid in a titration process of sodium acetate. The pKa of acetic acid is 4.75.
At:

A. pH 4.75
B. pH 9
C. pH 3

$pH = pK_a + \log([\text{Acetate ion}] / [\text{Acetic acid}])$

$[\text{Acetate ion}] / [\text{Acetic acid}] = 10^{(pH-pKa)}$

A. $[\text{Acetate ion}] / [\text{Acetic acid}] = 1$

B. $[\text{Acetate ion}] / [\text{Acetic acid}] = 10^{4.25} = 17{,}782.79 = \sim 18{,}000$

C. $[\text{Acetate ion}] / [\text{Acetic acid}] = 10^{-1.75} = 0.0178 = \sim 0.02$

Buffer Calculations

Example 1:

A buffer consist of 0.2 mole $CH3COO^-$ in 500 ml of 0.1 M $CH3COOH$. (Ka = 1.8×10^{-5} M). What is the PH?

PH = pKa+ log Base/ Acid

PH = - log 1.8×10^{-5} + Log 0.4/0.1

OR

Ka = [H+] x 0.4 / 0.1=1.8×10^{-6}

[H+] = 4.5×10^{-6} M

PH = - log 4.5×10^{-6}

= 5.4

Buffer Calculations

Calculate the mass of sod. propionate to be dissolved in 1L of 1M propionic acid (M.W = 96.08 gr/mole) to give a buffer of PH=4.5 (pKa = 4.87)

pH = 4.5 $[H+]= 10^{-4.5}$

pKa = 4.87 $Ka= 10^{-4.87}$

Ka = [H+] [propionate]／ [propionic acid]

[propionate] = 1 x $10^{-4.87}$／ $10^{-4.5}$

= 0.427 M

Mass= 0.427x 96.08 = 41.0 gr

Buffer Calculations

Calculate pH of a buffer when 18 ml of 0.1 M HCL is added to 32 ml of 0.1 M NH3 (pKb = 4.75)

Calculate excess NH3 and salt forms:

HCL moles = $18/1000 \times 0.1 = 1.8 \times 10^{-3}$

NH3 moles = $32/1000 \times 0.1 = 3.2 \times 10^{-3}$

Ammonium salt = 1.8×10^{-3}

Excess Ammonia = $3.2 \times 10^{-3} - 1.8 \times 10^{-3} = 1.4 \times 10^{-3}$

Molar conc. of salt = $1.8 \times 10^{-3} / (50/1000)$

$= 3.6 \times 10^{-2}$

Molar conc. of NH3 = $1.4 \times 10^{-3} / (50/1000)$

$= 3.2 \times 10^{-2}$

$Kb = [NH_4^+] [OH^-] / NH_3$

$10^{-4.75} = (3.6 \times 10^{-2} \times [OH^-]) / 3.2 \times 10^{-2}$

$[OH^-] = 0.889 \times 10^{-4.75}$

$= 1.58 \times 10^{-5}$ M

$p\,OH = -\log 1.58 \times 10^{-5}$

$= 4.8$

$p\,H = 14 - 4.8$

$= 9.2$

OR

$p\,OH = p\,Kb + \log [Salt] / [weak\ Base]$

$p\,OH = 4.75 + \log [3.6 \times 10^{-2}] / [3.2 \times 10^{-2}]$

$= 4.75 + 0.05$

$= 4.8$

$PH = 14 - 4.8$

$= 9$

pH in the body

-Blood pH is between 7.36 and 7.44

-Intracellular pH is between 6.9 and 7.4

-The widest range of extracellular pH over which the metabolic functions can be maintained is 6.8 to 7.8

- When pH< 7.36, acidosis results. pH<7.25 life threatening

-Acidosis causes CNS depression and coma

-pH<7 death occurs.

Buffer systems in the body:

1. The bicarbonate–carbonic acid buffer system (main ECF)
2. The hemoglobin buffer system in RBCs
3. The phosphate buffer system in all types of cells
4. The protein buffer system of cells and plasma.

-Buffers act quickly but not permanently

-Respiratory and renal mechanisms essentially act for final elimination.

-Buffers do not remove acids or replenish alkali in the body

Types of acids produced in the body

Two types of metabolic acids produced:

1. Fixed Acids, non-gaseous

- Phosphoric and Sulphuric acids

Produced from Sulphur and Phosphorus of proteins and lipoprotein

- Organic Acids as pyravic, lactic, ketoacids (e.g acetoacetic,

B-hydroxy butyric acid and uric acid). Buffered and then H+ is excreted by the kidneys

2. Volatile Acids

The physiological importance = Carbonic acid

Amount produced daily equivalent to 36 liters of 1.0 M acids

Excreted as CO_2 by the lungs

20,000 mEq/day

Acidosis

-Metabolic acidosis:

Starvation, untreated diabetes,
high-protein diet, low-fat diet

-Respiratory acidosis

- When pH< 7.36, acidosis results. pH<7.25 life threatening

-Acidosis causes CNS depression and coma

-pH<7 death occurs.

Alkalosis

-pH> 7.44

-pH>7.55 is dangerous and >7.60 results in death.

-Metabolic alkalosis:

Excess clinical administration of salts and metabolic acids as Na lactate and $NaHCO_3$

Deamination of amino acids, citrate

Severe vomiting

-Respiratory alkalosis :

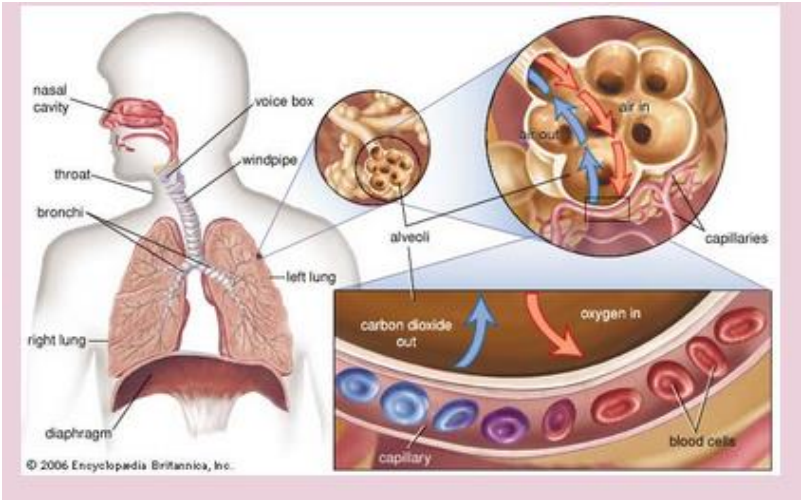
Hyperventilation (heavy breathing)

Hysteria, anxiety or altitude sickness

Buffer systems in the body:

1. The bicarbonate–carbonic acid buffer system (ECF)
2. The hemoglobin buffer system in RBCs
3. The phosphate buffer system in all types of cells
4. The protein buffer system of cells and plasma.

The bicarbonate–carbonic acid buffer system in blood



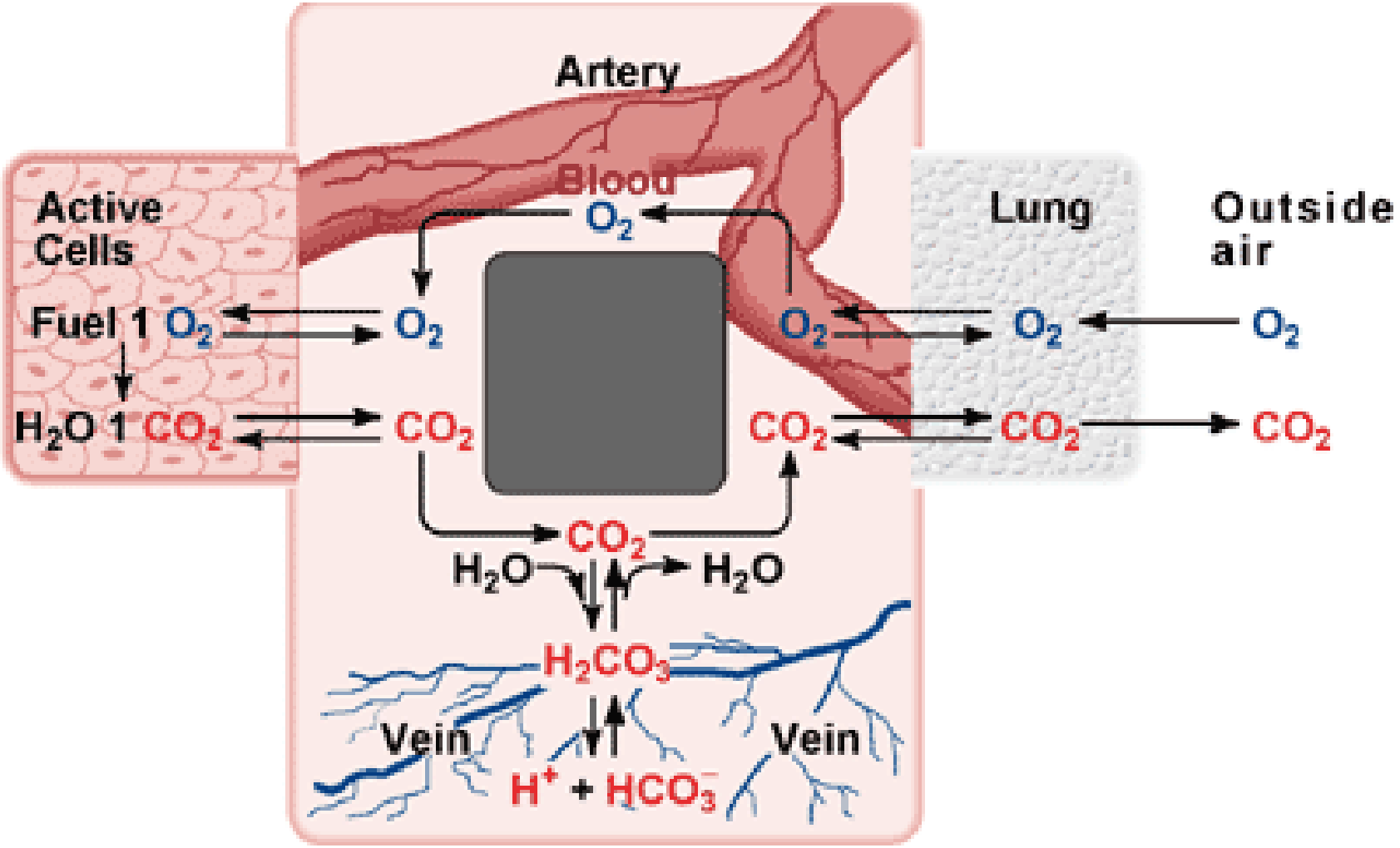
$CO_{2(g)} \rightleftharpoons CO_{2(aq)}$

$CO_{2(aq)} + H_2O_{(l)} \rightleftharpoons H_2CO_{3(aq)}$

$H_2CO_{3(aq)} \rightleftharpoons H^+_{(aq)} + HCO_3^-{}_{(aq)}$

Net: $CO_{2(g)} + H_2O_{(l)} \rightleftharpoons H^+_{(aq)} + HCO_3^-{}_{(aq)}$

Bicarbonate buffer system



The bicarbonate–carbonic acid buffer system in blood

$$CO_{2(g)} + H_2O_{(l)} \rightleftharpoons H^+_{(aq)} + HCO_3^-{}_{(aq)}$$

pKa of H_2CO_3 is 6.1, while the pH of human blood is 7.4

$7.4 = 6.1 + \log [HCO_3^-] / [CO_2]$
$1.3 = \log [HCO_3^-] / [CO_2]$
$[HCO_3^-] / [CO_2] = 20$

⟶ most of the dissolved CO_2 is present as HCO_3^-

Normal values:
pH = 7.4
pCO_2 = 40 mm Hg (~ 1.2 mM)
$[HCO_3^-]$ = 25 mM

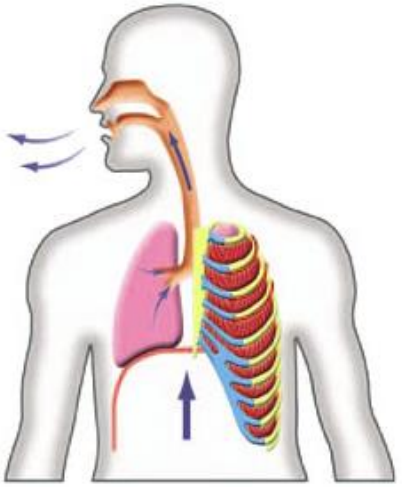
What happens when the pH of the blood drops?

- Low pH means more H^+

$$H^+_{(aq)} + HCO_3^-{}_{(aq)} \rightleftharpoons H_2CO_{3(aq)}$$

$$H_2CO_{3(aq)} \rightleftharpoons CO_{2(aq)} + H_2O_{(l)}$$

$$CO_{2(aq)} \rightleftharpoons CO_{2(g)}$$ exhaled by the lungs



-Aspirin

-High altitudes - rate of respiration increases.

-Athelete example

What happens when the pH of the blood increases?

- Higher pH means more OH^-

$NaOH + H_2CO_3 \longrightarrow NaHCO_3 + H_2O$

$CO_2 + H_2O \longrightarrow H_2CO_3$ to replace the consumed acid

$[CO_2]$ decrease and respiration decrease to reduce the rate of CO_2 consumption.

$[HCO_3^-] / [CO_2] = 25\ mM / 1.25\ m\ M = 20$

Buffer range = $6.1 \pm 1 = 5.1\text{-}7.1$

The Henderson-Hasselbalch equation for blood buffering

$$CO_2(aq) + H_2O(l) \rightleftharpoons H_2CO_3(aq) \rightleftharpoons HCO_3^-(aq) + H_3O^+(aq)$$

$$[H_3O^+] = K_a \frac{[CO_2]}{[HCO_3^-]}$$

An increase in $[CO_2]$ raises $[H_3O^+]$ and lowers pH.

A decrease in $[CO_2]$ lowers $[H_3O^+]$ and raises pH.

$$pH = pK_a + \log\left(\frac{[HCO_3^-]}{[CO_2]}\right)$$

The normal ratio of $[HCO_3^-/CO_2]$ in the blood is about 20 to 1 at pH 7.4. What is this ratio at pH 7.3 (acidosis) and at 7.5 (alkalosis)?

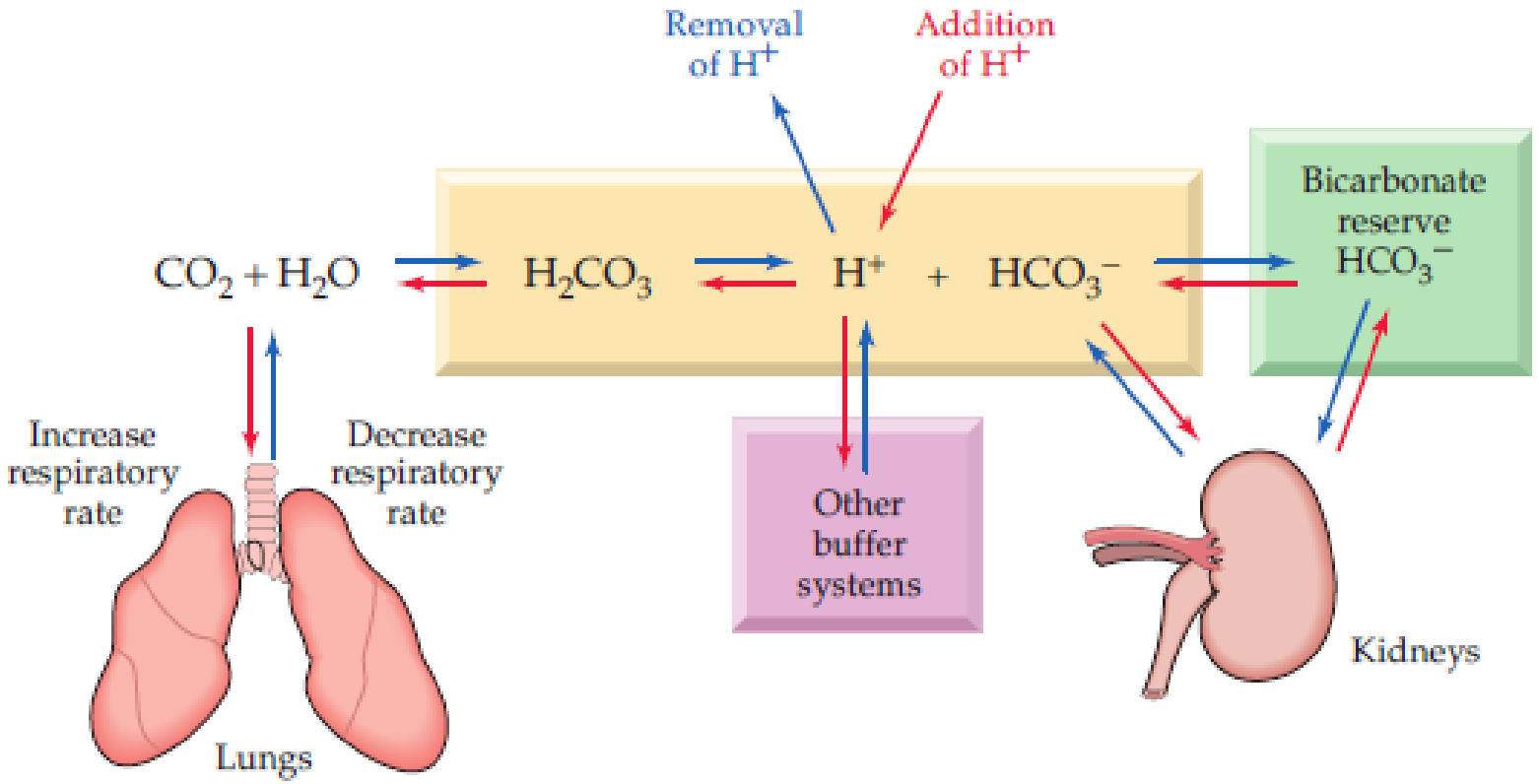
Regulatory Mechanism against changes in [H+] of blood

- Buffer Mechanism- first line of dense
- Respiratory Mechanism -second line of defense
- Renal Mechanism- third line of defense

The first two lines of defense keep the [H+] from changing too much until the more slowly responding third line of defense, the kidney's can eliminate the excess acid or base from body

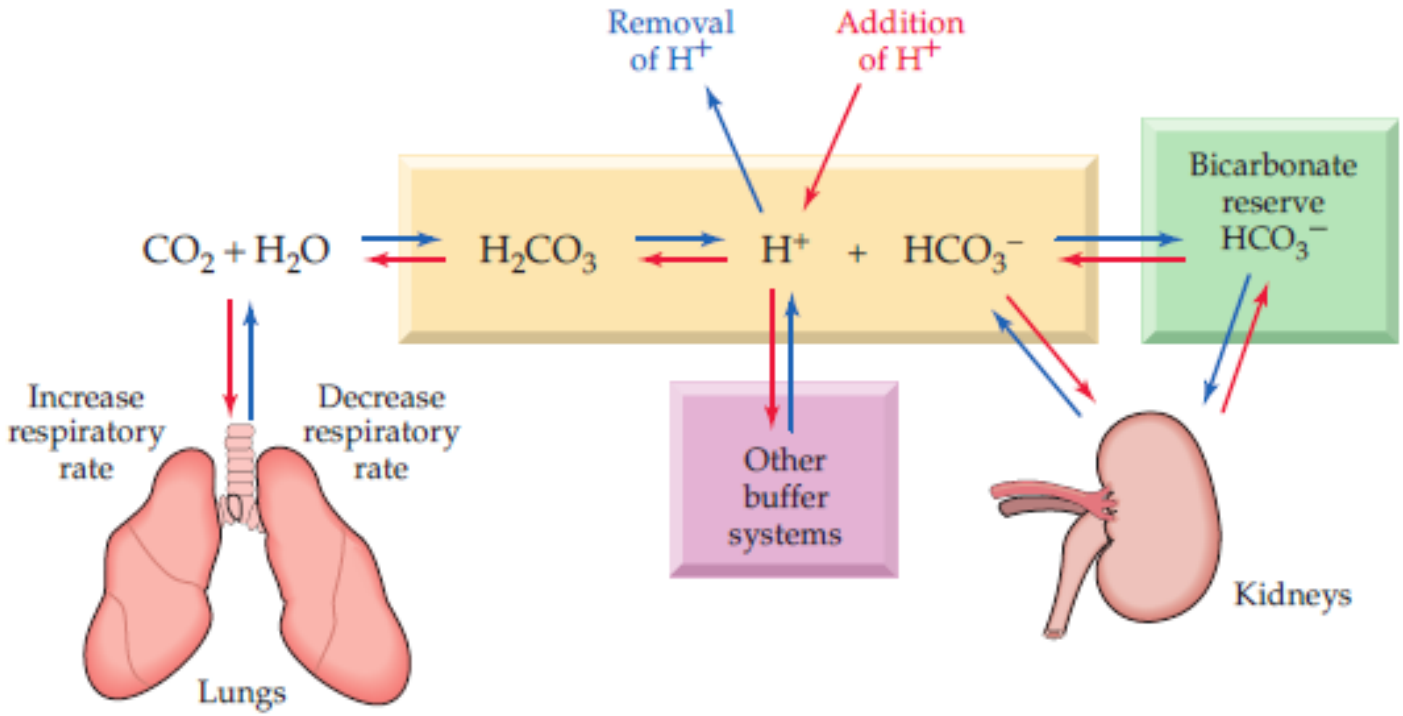
The equation

- **Relationships of the bicarbonate buffer system to the lungs and the kidneys.**



Roles of lungs and kidneys

- Maintaining blood is balanced by the kidneys and the lungs
- Kidneys control blood HCO_3^- concentration ($[HCO_3^-]$)
- Lungs control the blood CO_2 concentration (P_{CO2})

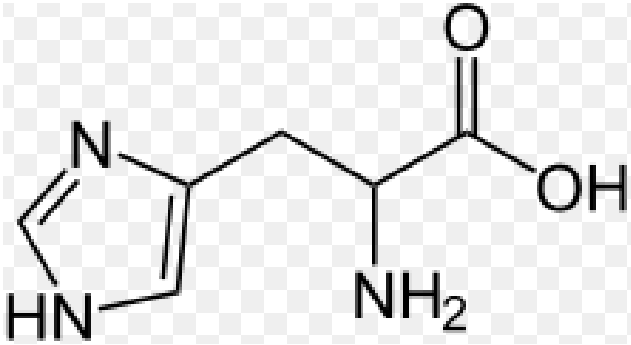


Protein Buffers

-Because of the presence of the dissociable acidic (-COOH) and basic (-NH2) groups, proteins act as buffers.

-Particularly the imidazole group of the side chain of histidine residue (pKa = 7.3)

Proteins, specifically Albumin, account for 95% of non-carbonate buffering action in plasma (has 16 His/mole)



Histidine

Phosphate Buffer systems

-Phosphate anions and proteins are important buffers that maintain a constant pH of ICF.

-Intracellular and tubular fluids of kidney

- $H_2PO_4^-$ dissociates to H^+ and HPO_4^{-2}

-pKa is 7.1-7.2

- In RBCs 2,3 BPG is 4.5 mM contributing to ~16% Non carbonate buffer function.

- Glu-6P, ATP act as buffers

$H^+ + Na_2HPO_4$

$OH^- + NaH_2PO_4$

Hemoglobin (Hb) Buffer

-Major intracellular buffer of the blood

-Hb has a high number of His (38 molecules/mole of Hb)

-Works cooperatively with the bicarbonate buffer system

-It buffers CO_2 and H_2CO_3

More details in the 3rd year

Buffer systems of the body

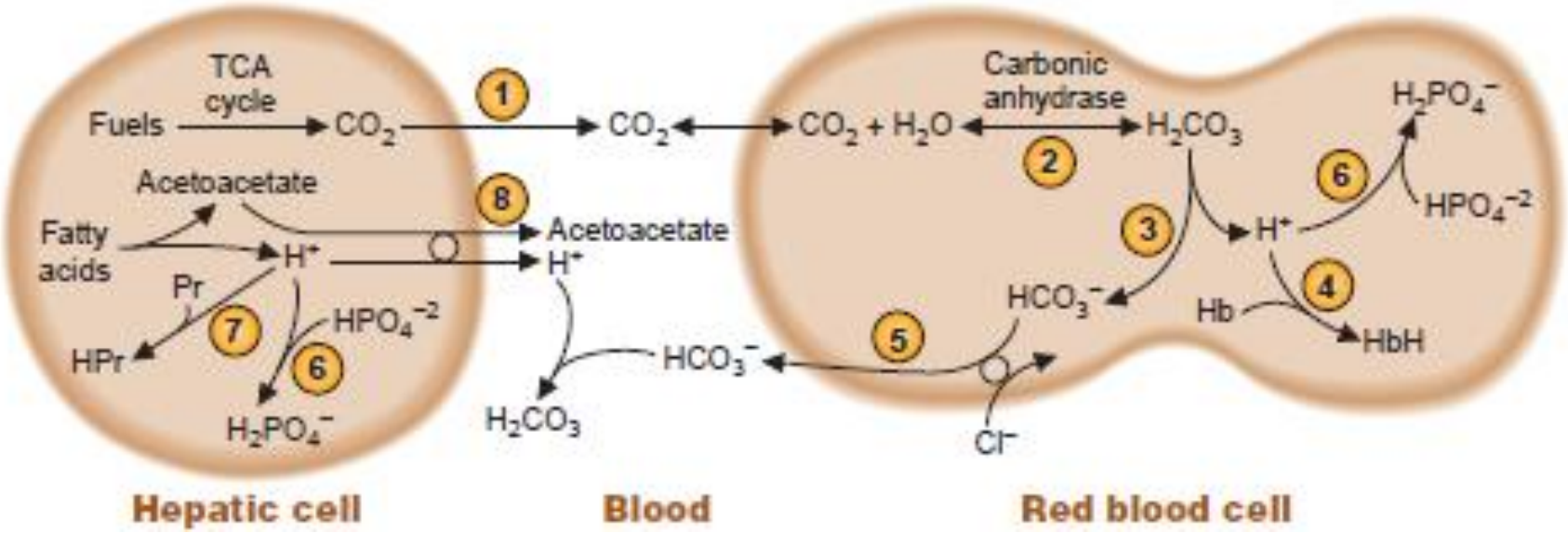


FIG. 4.9. Buffering systems of the body. CO_2 produced from cellular metabolism is converted to bicarbonate and H^+ in the red blood cells. Within the red blood cells, the H^+ is buffered by hemoglobin (Hb) and phosphate (HPO_4^{2-}) (*circles 4 and 6*). The bicarbonate is transported into the blood to buffer H^+ generated by the production of other metabolic acids, such as the ketone body acetoacetic acid (*circle 5*). Other proteins (Pr) also serve as intracellular buffers. See the text for more details.

Done or not yet?!