TUMS

Water and buffers

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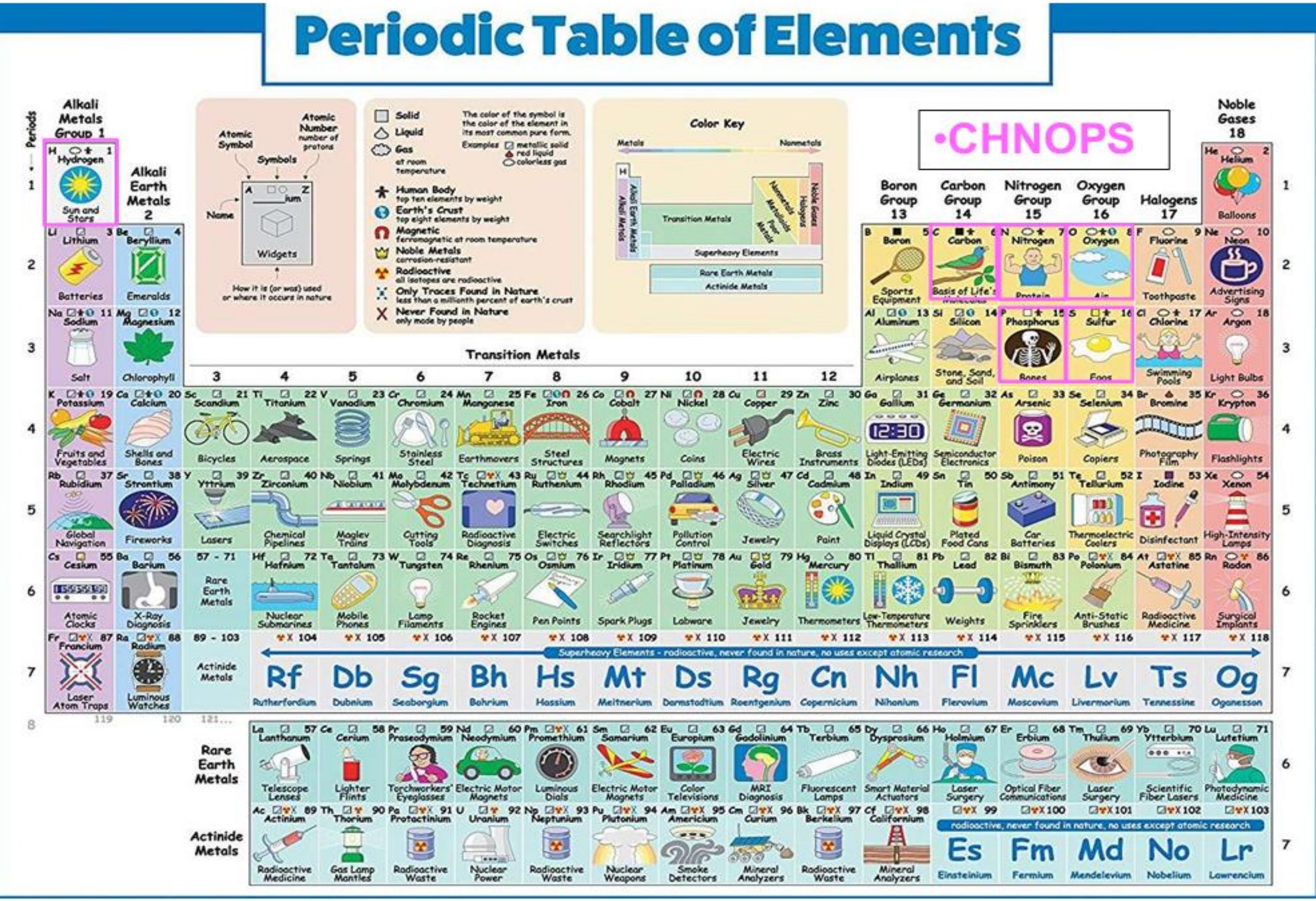
School of Medicine
Tehran University of Medical Sciences



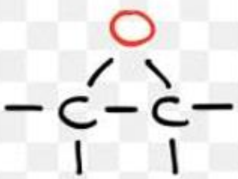
Periodic Table of Elements
Alkali Metals Group 1
Alkali Earth Metals 2
Transition Metals
Boron Group 13
Carbon Group 14
Nitrogen Group 15
Oxygen Group 16
Halogens 17
Noble Gases 18
Color Key
Metals
Nonmetals
Solid
Liquid
Gas
at room temperature
Human Body
Earth's Crust
Magnetic
Noble Metals
Radioactive
Only Traces Found in Nature
Never Found in Nature
Superheavy Elements - radioactive, never found in nature, no uses except atomic research
Rare Earth Metals
Actinide Metals

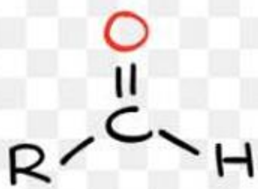
•CHNOPS

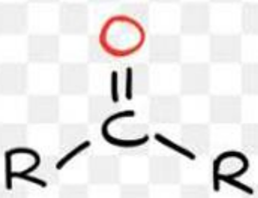
Important functional groups in biochemistry


alcohol


ether

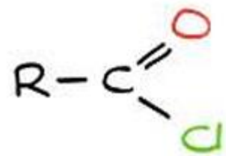

epoxide

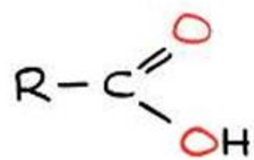

aldehyde

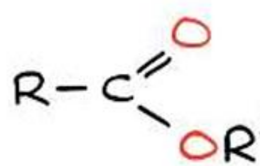

ketone

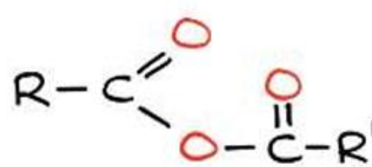

amine


nitrile

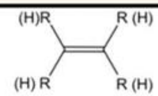
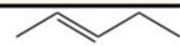
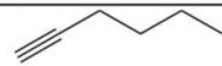
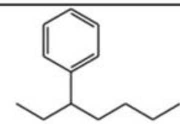
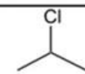
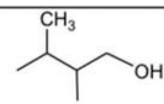
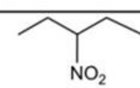

acid halide


carboxylic acid


ester

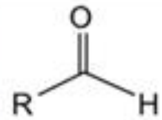
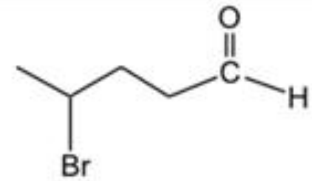
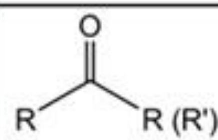
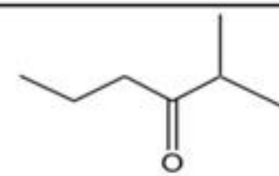
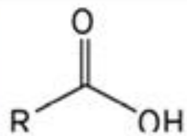
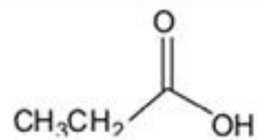
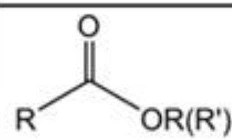
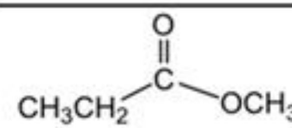
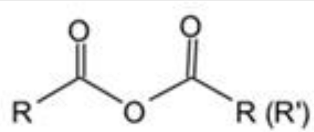
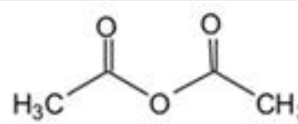
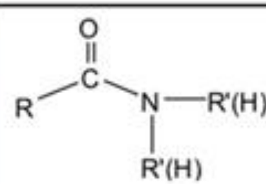
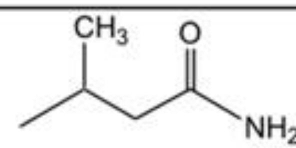

anhydride

Important functional groups in biochemistry

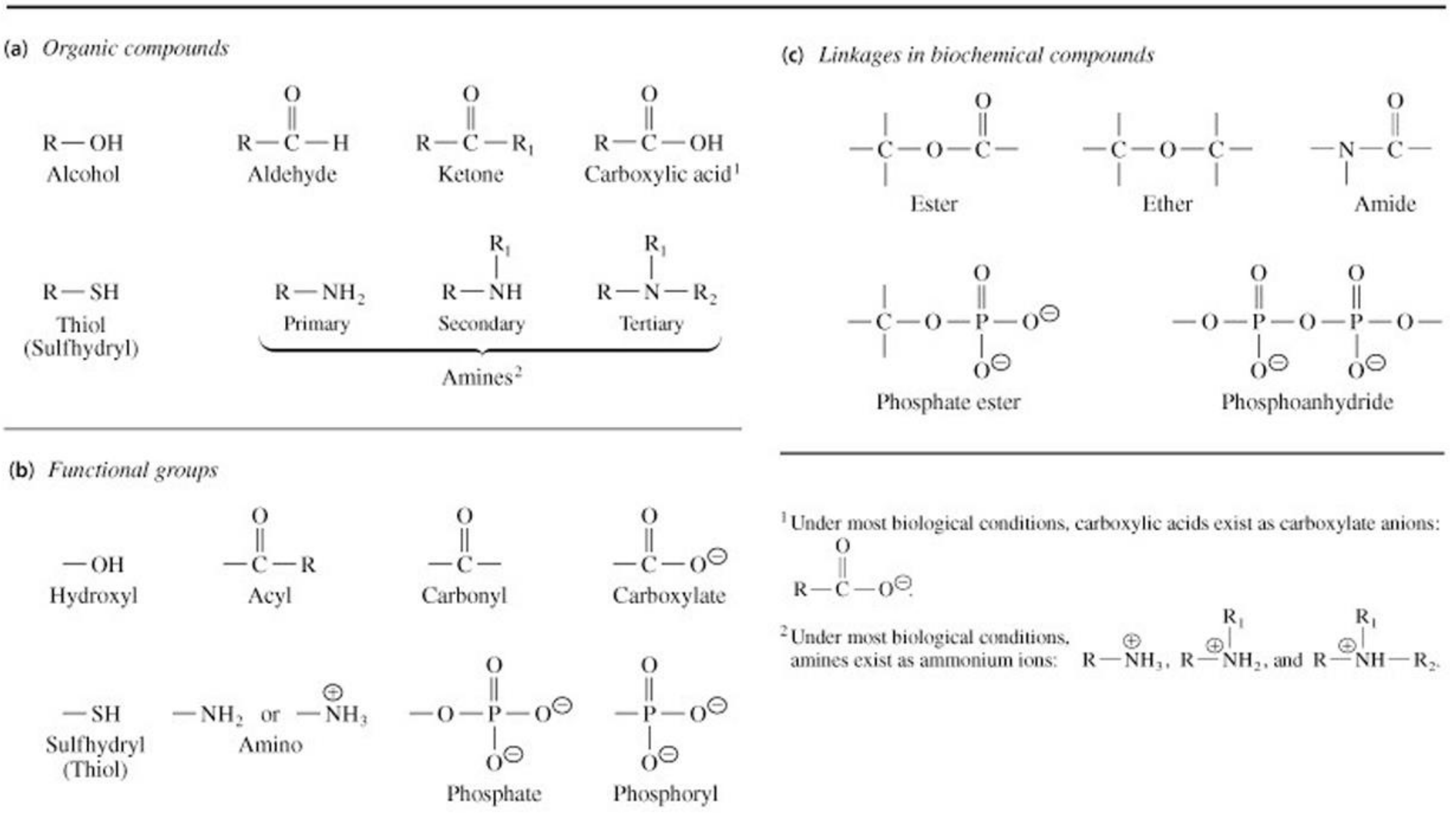
Class of Compounds	General Structure*	Specific Example	Notes
Alkene			
Alkyne	(H)R—≡—R (H)		
Aromatic ring			
Alkyl halide (Haloalkane)	R-X X: F, Cl, Br or I		$R\text{-}CH_2\text{-}X$: 1° halide $R_2\text{-}CH\text{-}X$: 2° halide $R_3\text{-}C\text{-}X$: 3° halide
Alcohol	R-OH		$R\text{-}CH_2\text{-}OH$: 1° alcohol $R_2\text{-}CH\text{-}OH$: 2° alcohol $R_3\text{-}C\text{-}OH$: 3° alcohol
Ether	R-O-R'	$CH_3—O—CH_2CH_3$ ethyl methyl ether (common name)	**Common name:** ** Alkyl alkyl ether (alphabetic order)
Nitrile	$R—C\equiv N$	$H_3C—C\equiv N$	
Nitro	$R—NO_2$		
Amine	RNH_2 R_2NH R_3N	$CH_3CH_2NH_2$: ethyl amine (common name) $(CH_3CH_2)_3N$: triethyl amine (common name)	**Common name:** ** Alkyl alkyl alkyl amine (alphabetic order)

** R: hydrocarbon group, alkyl or phenyl; for structure with multiple R, they can be same or different groups.*

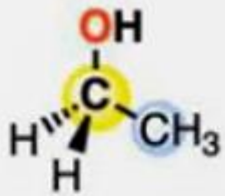
*** These common names are accepted by IUPAC.*

Class of Compounds	General Structure	Specific Example	Notes
Aldehyde	 or: R-CHO		C=O double bond is usually called as a **"carbonyl"** group. The function groups on this page all contain carbonyl group.
Ketone			
Carboxylic acid	 *or:* R-COOH		Reaction with base gives salt of carboxylic acid, $RCOO^{-}M^{+}$
Ester			Carboxylic acid derivative.
Anhydride			Carboxylic acid derivative.
Amide			Carboxylic acid derivative

Important functional groups in biochemistry

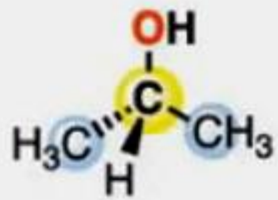


Alcohols are classified as primary (1°), secondary (2°), or tertiary (3°) according to the number of carbons **directly attached** to the carbon bonded to the OH.



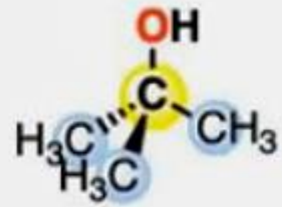
Primary (1°) alcohol

- C–OH carbon attached to **one** carbon



Secondary (2°) alcohol

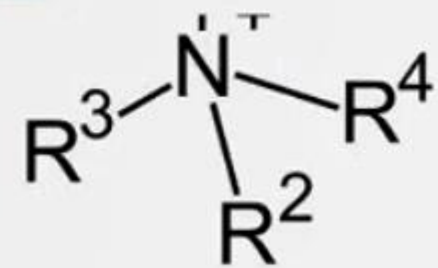
- C–OH carbon attached to **two** carbons



Tertiary (3°) alcohol

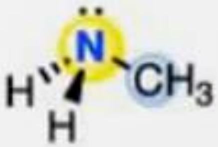
- C–OH carbon attached to **three** carbons

The quaternary ammonium cations are permanently charged, independent of the pH of their solution.



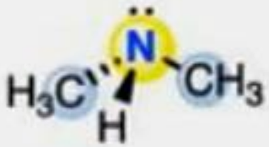
Quaternary ammonium cation. The R groups may be the same or different alkyl or aryl groups. Also, the R groups may be connected.

To name **amines**, we count the number of carbons directly attached to **nitrogen**



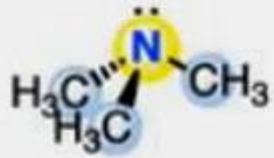
Primary (1°) amine

- N attached to **one** carbon



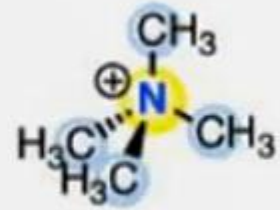
Secondary (2°) amine

- N attached to **two** carbons



Tertiary (3°) amine

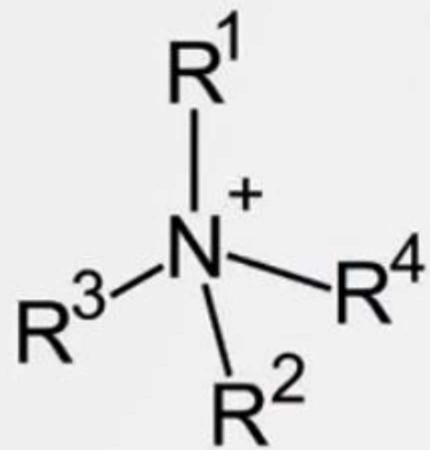
- N attached to **three** carbons



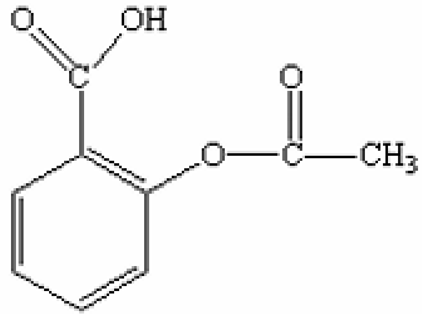
Quaternary (4°) ammonium salt

- N attached to **four** carbons

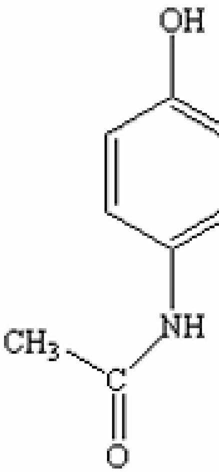
The quaternary ammonium cations are permanently charged, independent of the pH of their solution. The R groups may be the same or different.



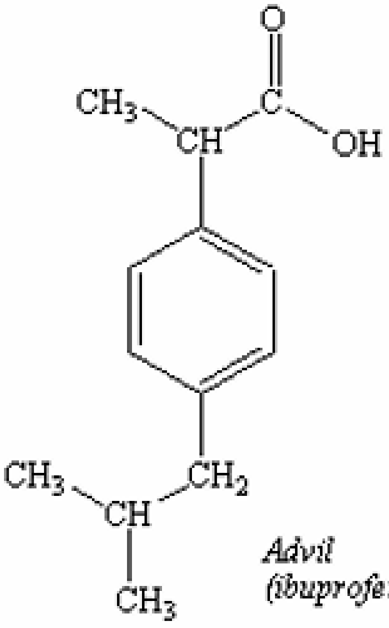
Structure of common painkillers



Aspirin
(acetylsalicylic acid)

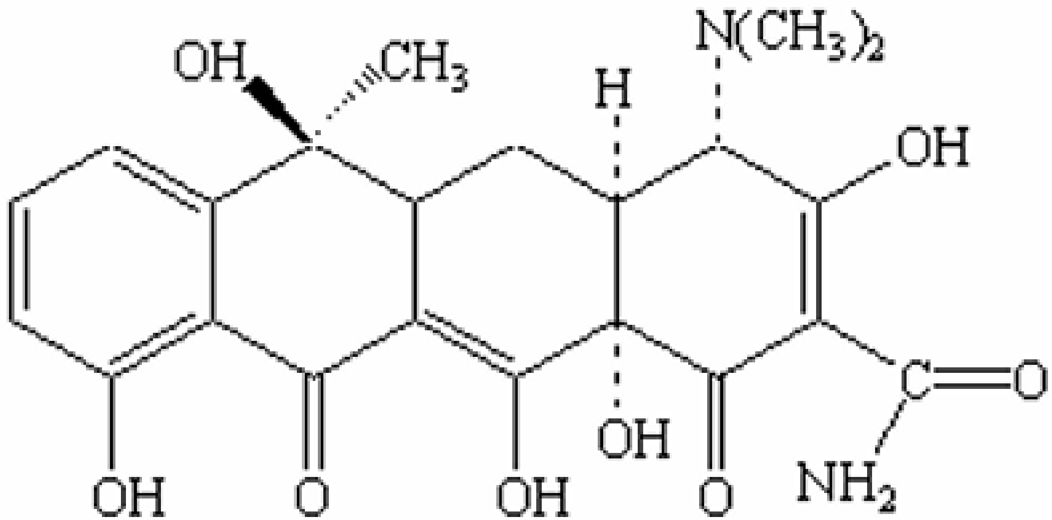


Tylenol
(acetaminophen)

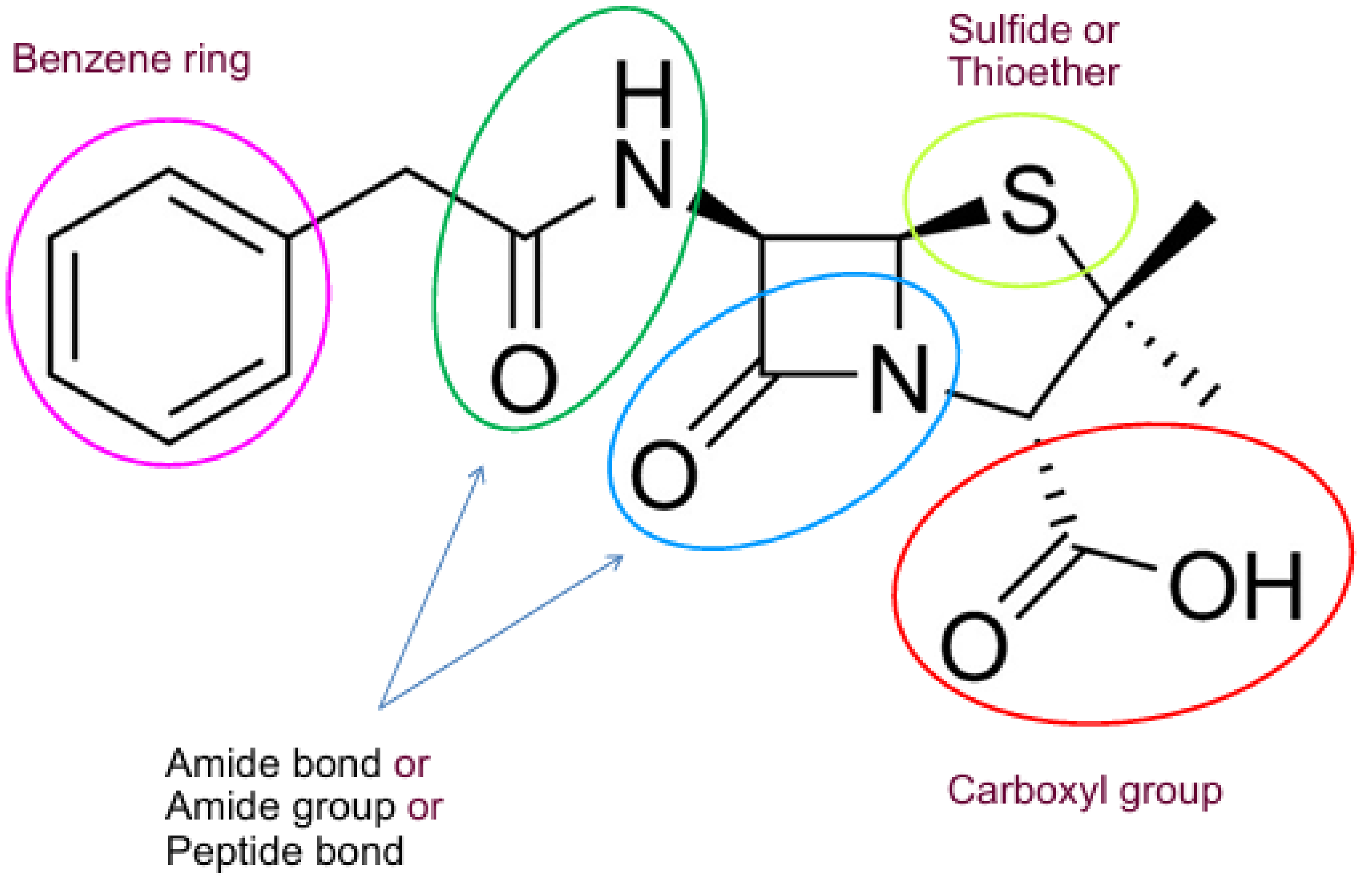


Advil
(ibuprofen)

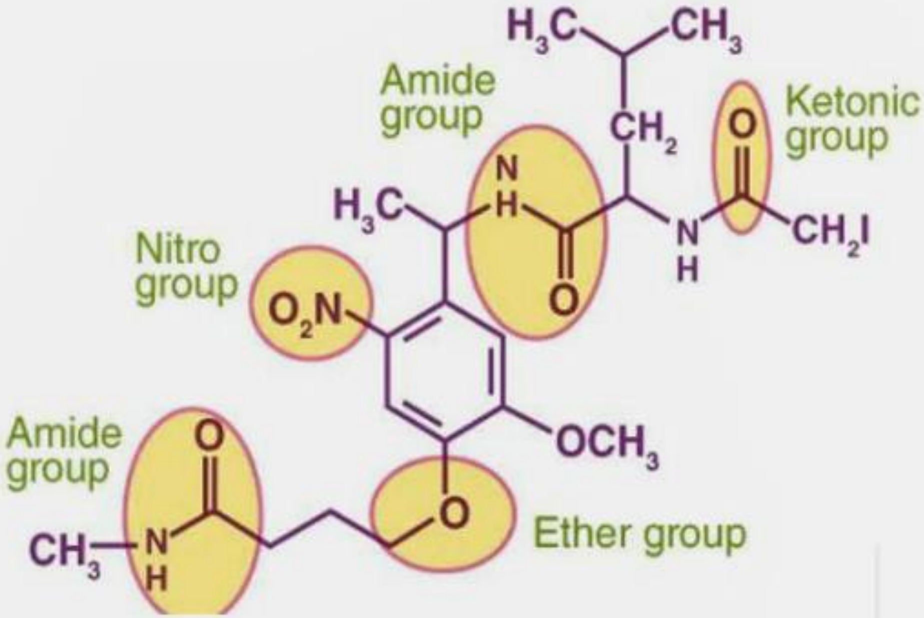
Structure of an antibiotic



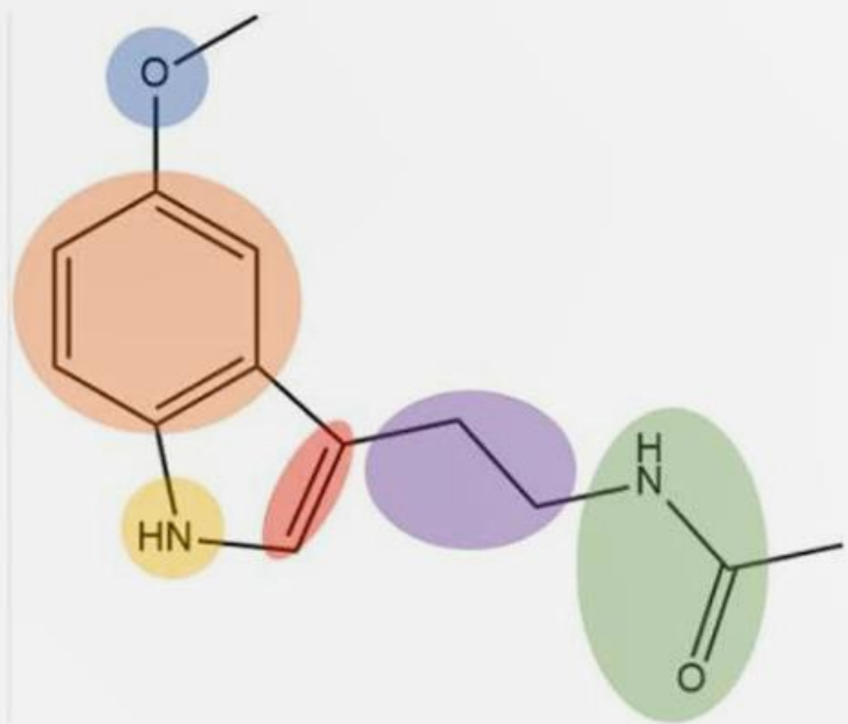
Tetracycline



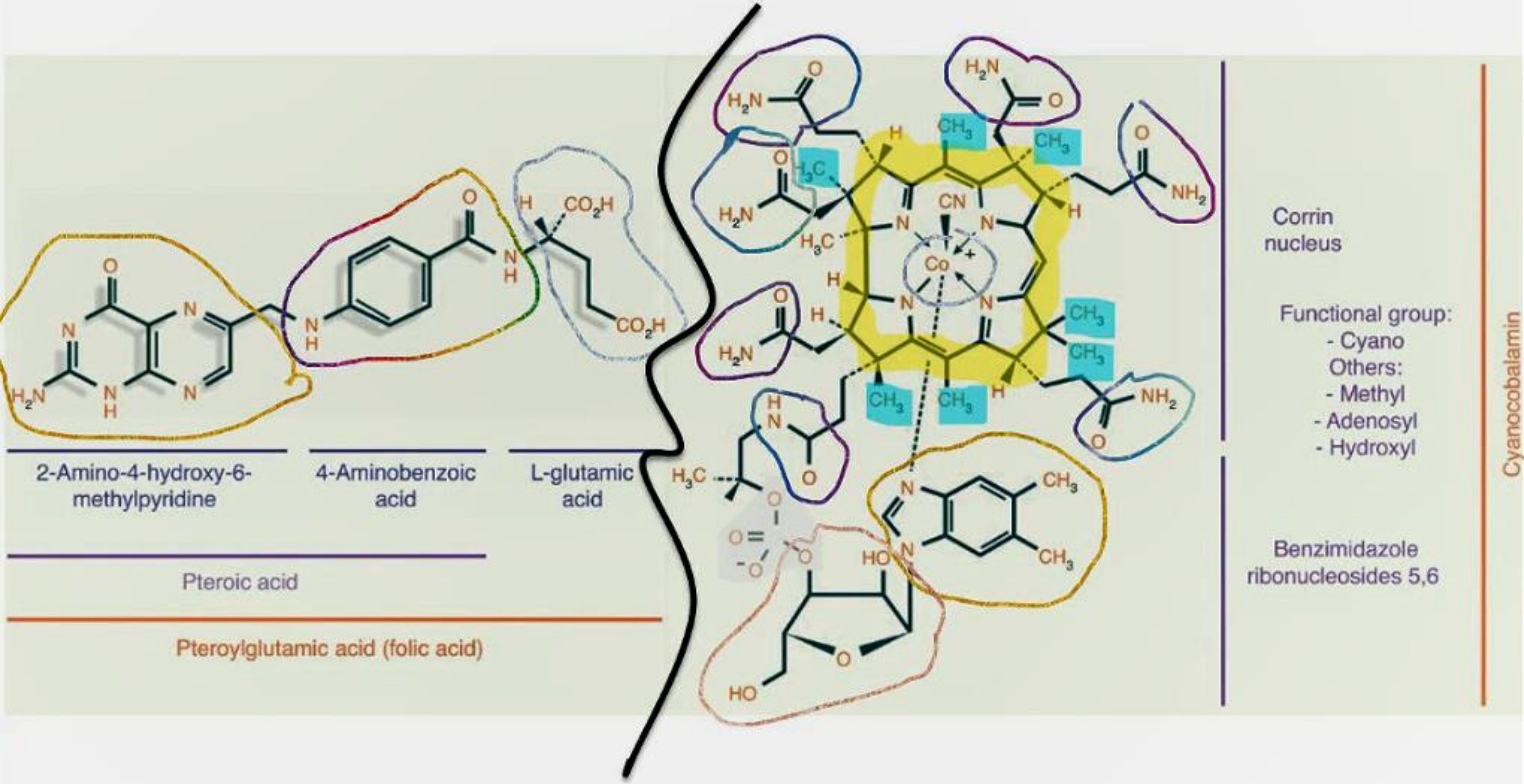
Penicillin G

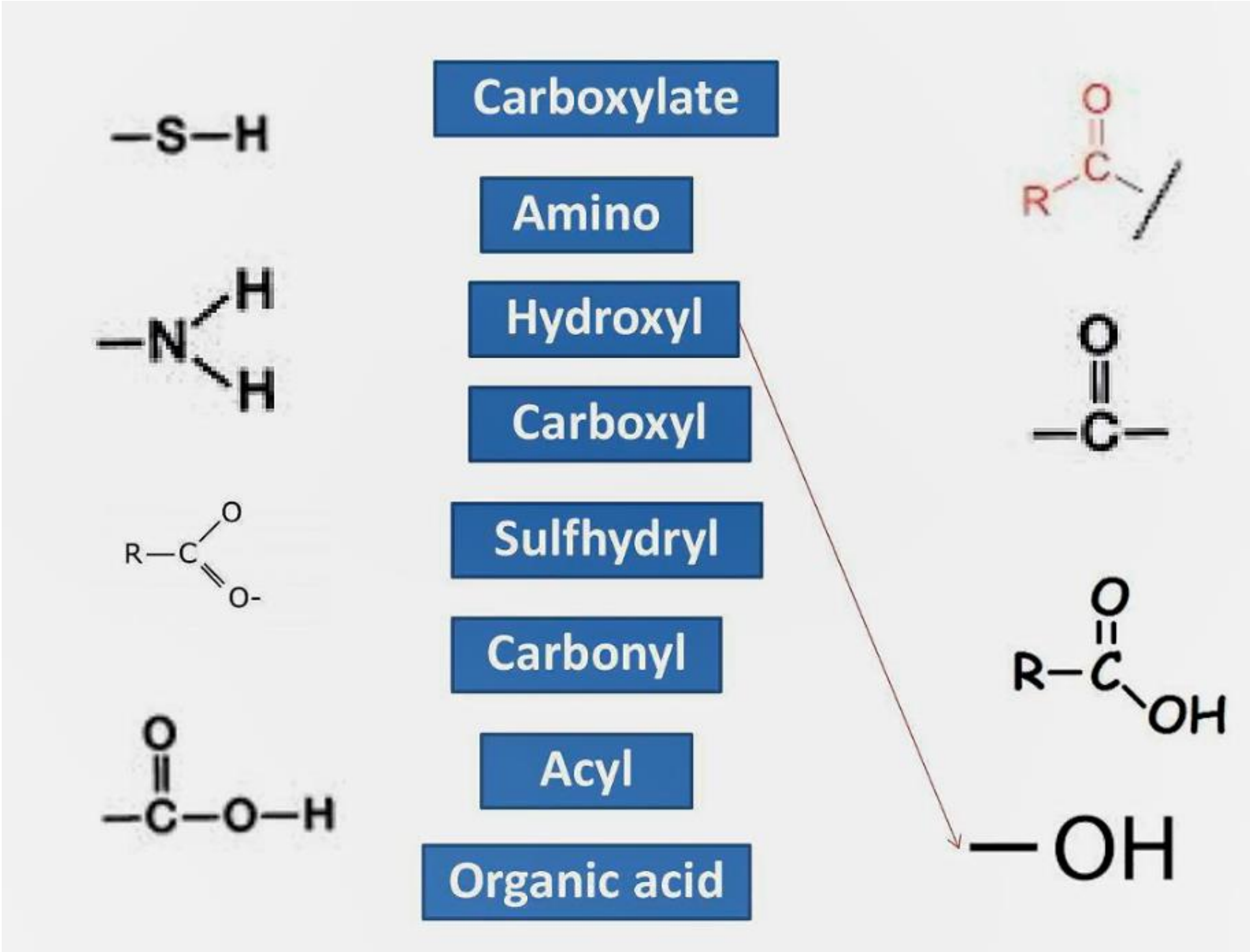


Amide group
Ketonic group
Nitro group
Amide group
Ether group



Vitamins Folic acid (B9) and B12

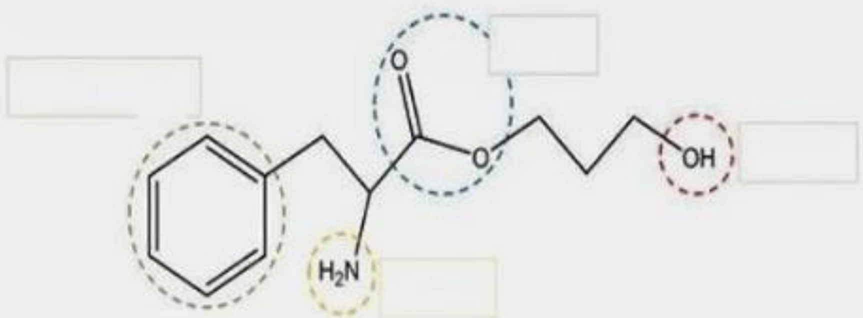



Carboxylate
Amino
Hydroxyl
Carboxyl
Sulfhydryl
Carbonyl
Acyl
Organic acid

Quiz

Which functional group typically has a pKa range of 5-6?

a. Alcohol with 5-6 carbons
b. Amine with 6-7 carbons
c. Ether with 4-5 carbons
d. Carboxylic acid group



در ساختار شیمیایی زیر کدام گروهها به ترتیب از **<u>راست به چپ</u>** وجود دارند؟

الف- الکل-استر-آمین-حلقه آروماتیک
ب-هیدروکسی-آنیدرید-آمین-حلقه بنزن
ج- الکل- اتر-آمین-حلقه بنزنی
د- حلقه آروماتیک- آمید- اسید کربوکسیلیک- هیدروکسی

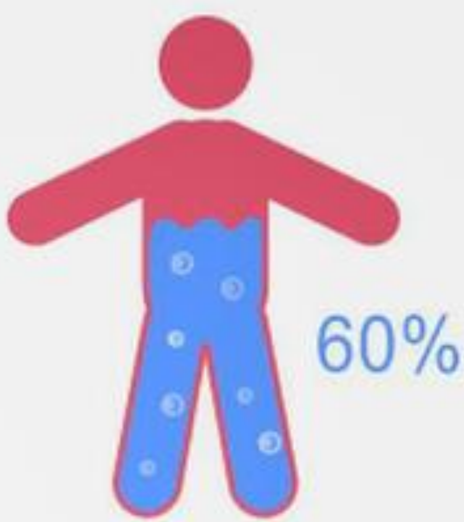
Types of chemical bonds

- Interactions that occur between atoms are called chemical bonds.

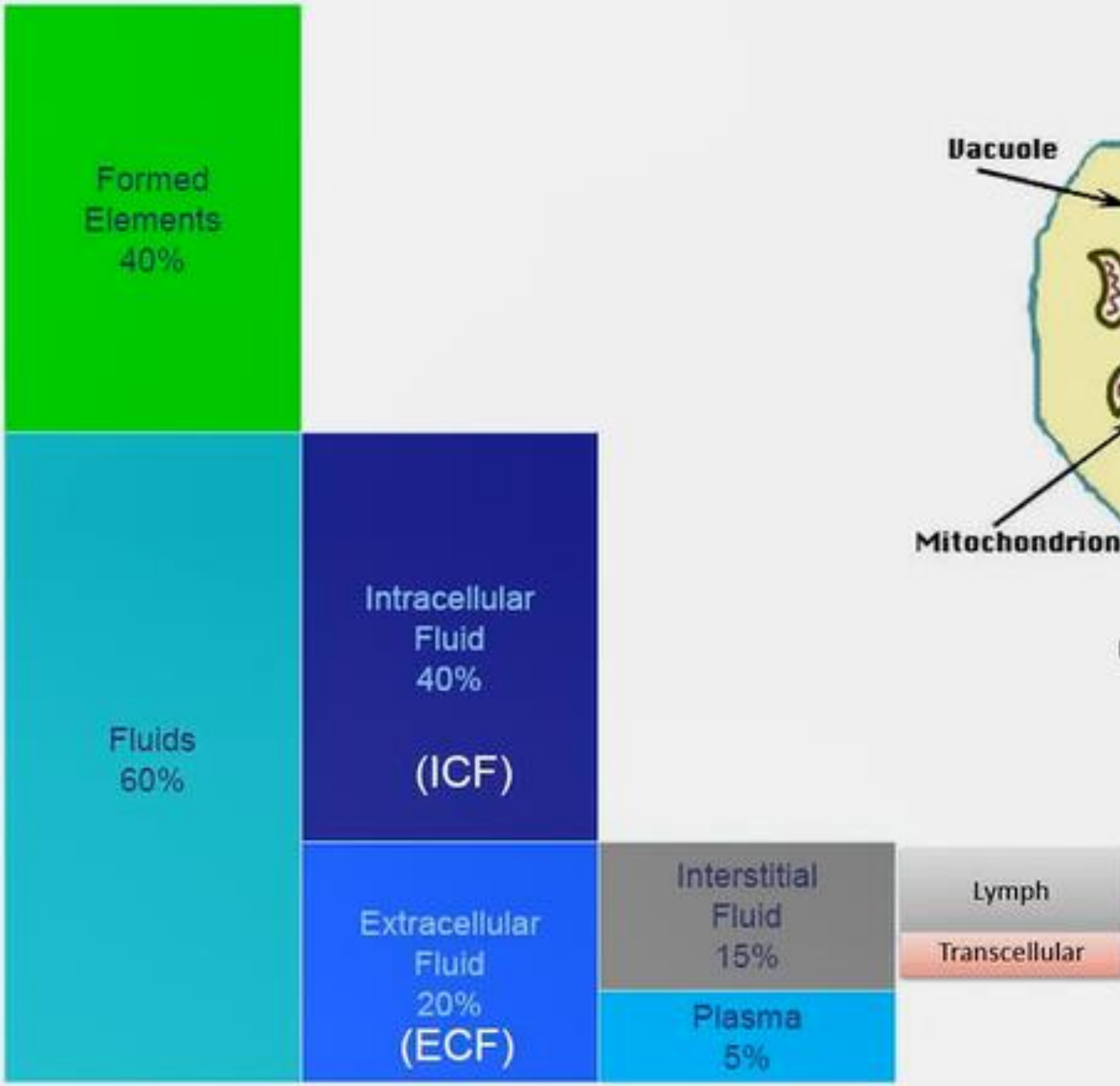
1. **Strong chemical bonds:**
   - covalent bond (between nonmetals)
2. **Weak chemical bonds:**
   - Ionic bond (between metals and nonmetals)
   - van der Waals forces (dipole-dipole attraction)
   - Hydrogen bonding (h-bond)
   - Hydrophobic interactions

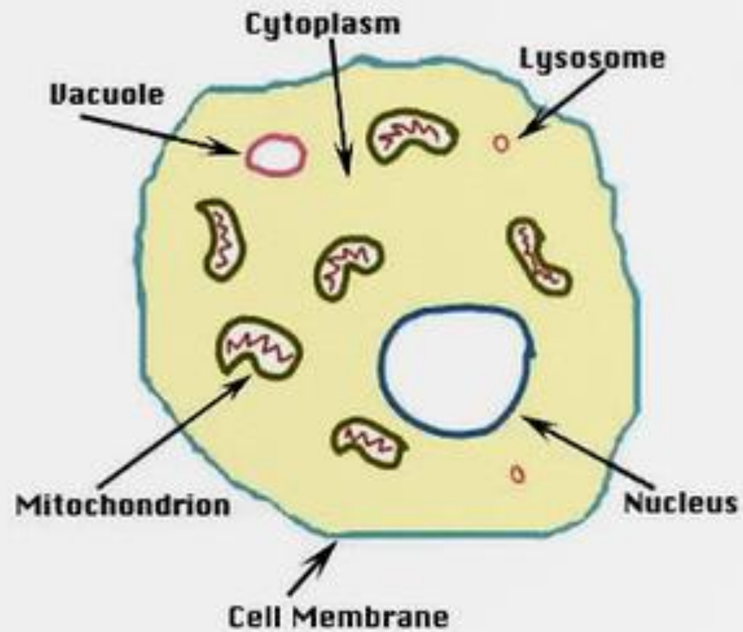
Water in different tissues

- Muscle consists of 75% water
- Brain consists of 80%-90% water
- Bone consists of 22% water
- Blood consists of 83% water



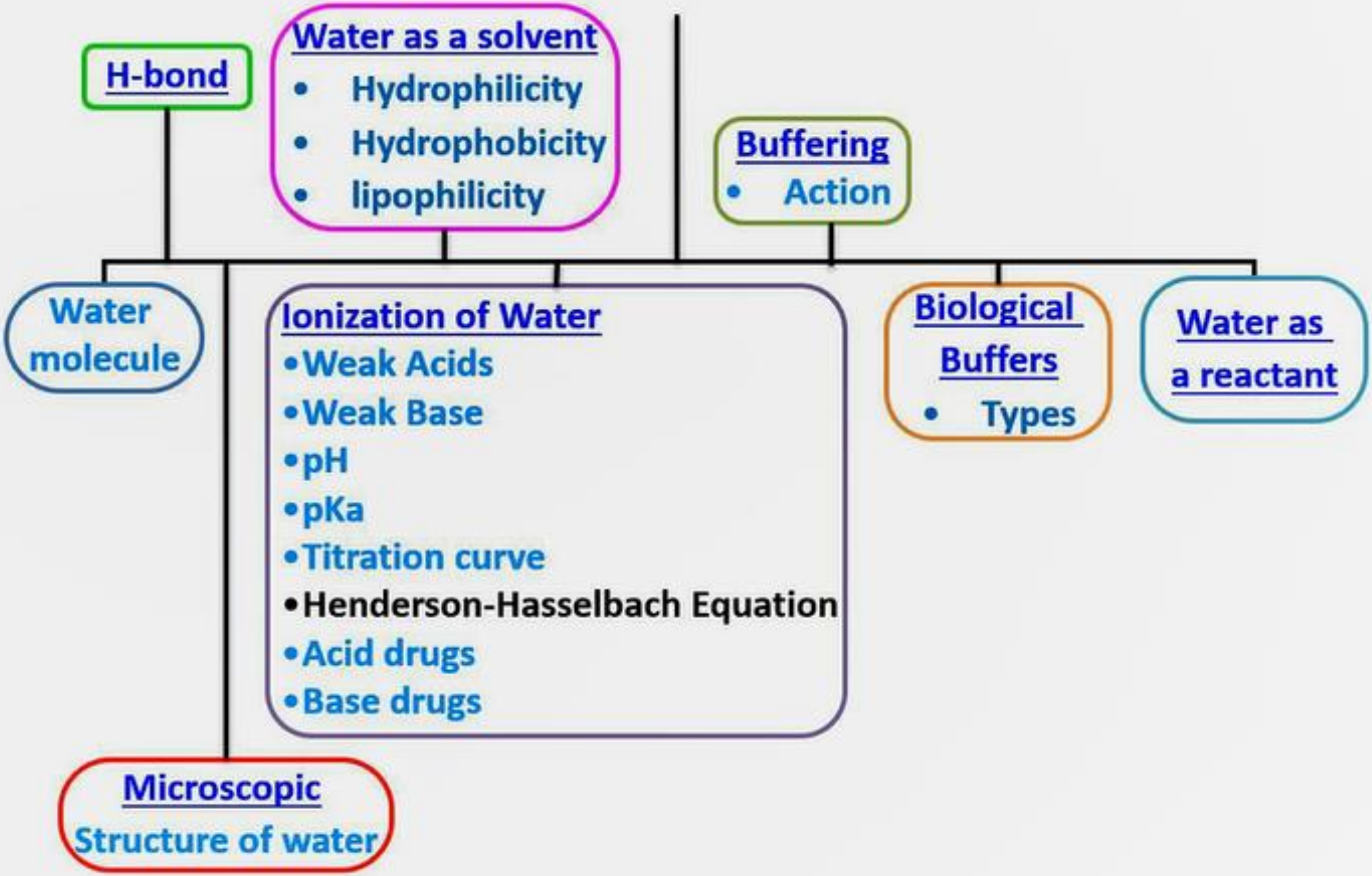
Fluid spaces in the human body





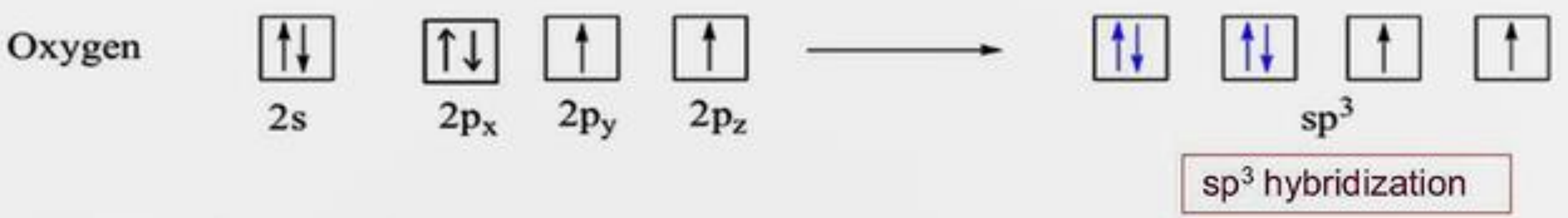
The content summary

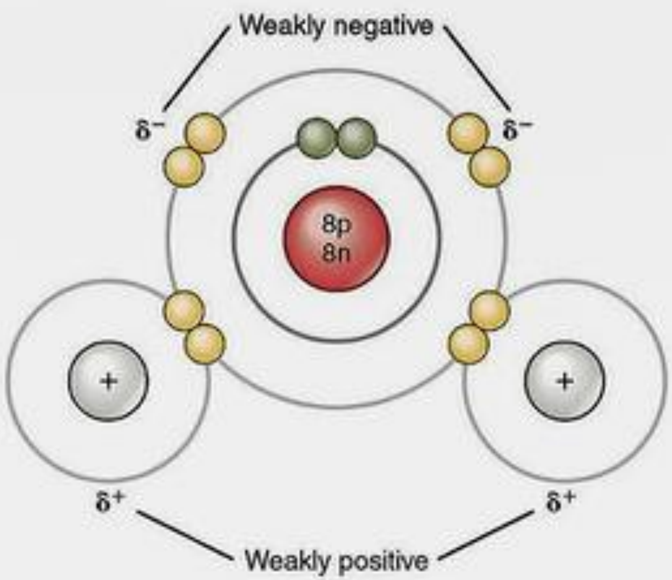
Water



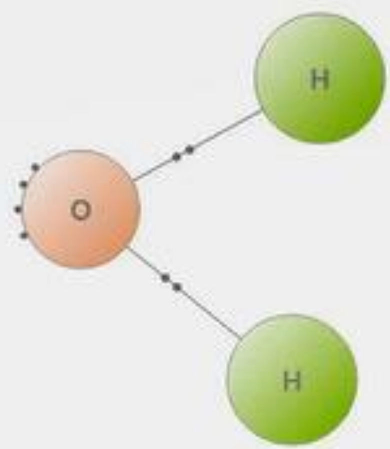
Hybrid orbitals - sp3 hybridization and tetrahedral bonding

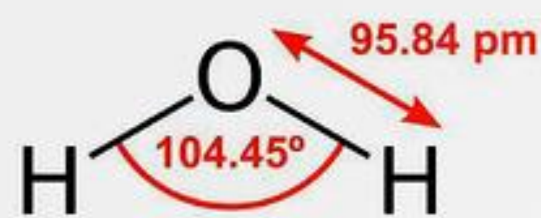
- Water has a simple structure.
- Oxygen has 6 electrons in the outer shell: $1s^2$, $2s^2$, $2p^4$.



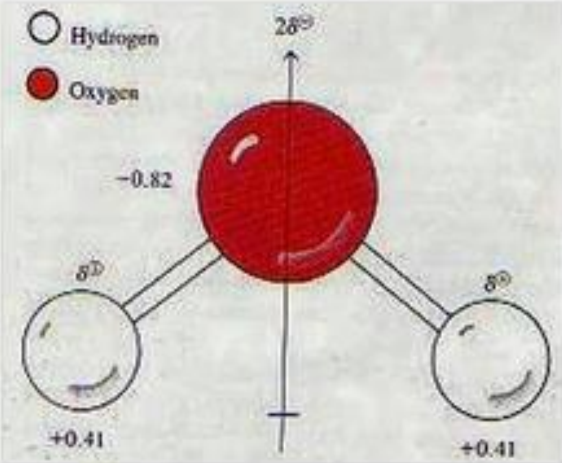


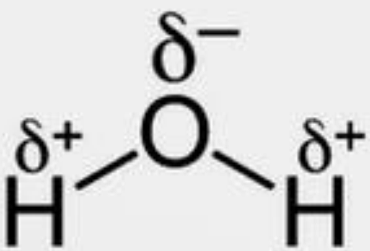
Planetary model of a water molecule

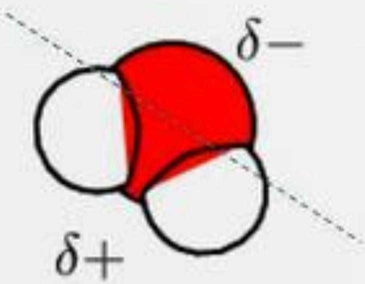




“Water molecule” is polar



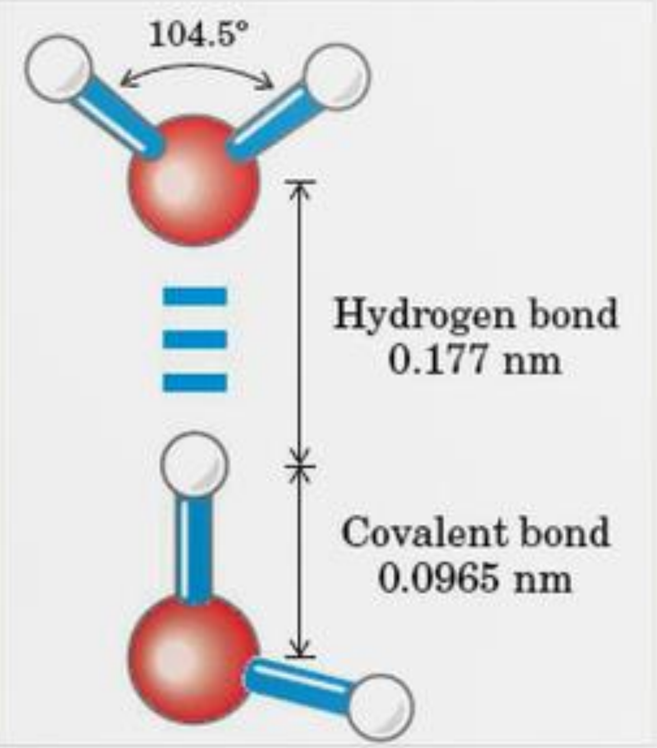


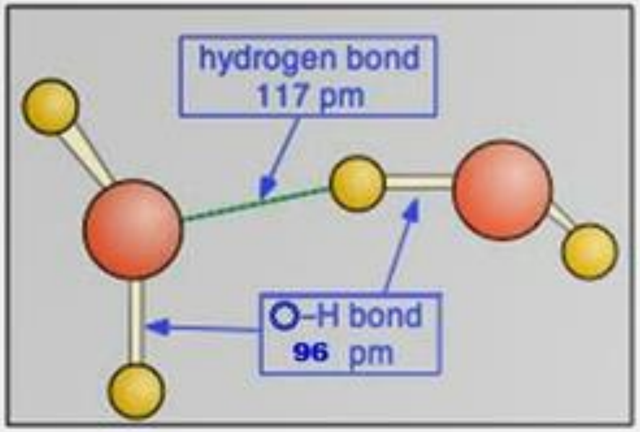


- The net charge of water molecule is zero. But O—H bond is polar because O is more electronegative than H. Sharing of electrons between H and O is unequal.
- The charge on O = -0.82 and on H = +0.41. This charge separation produces permanent dipoles.

Water molecules form H bond

- H bond is **10% covalent** and **90% electrostatic**.
- The **strength of H-bond** is 4 kcal/mol, less than 5% as strong as a typical covalent bond.
- The strength of O—H bond is 110 kcal/mol. H-bond is a weak interaction.
- Notice that the hydrogen bond (shown by the dashed line) is somewhat **longer** (117 pm) than the covalent O—H bond (99 pm). This means that it is considerably **weaker**.
- H-bond can form when a H atom that is bonded to O or N lies within **0.27-0.30 nm** of another O or N atom that has unshared e^-.





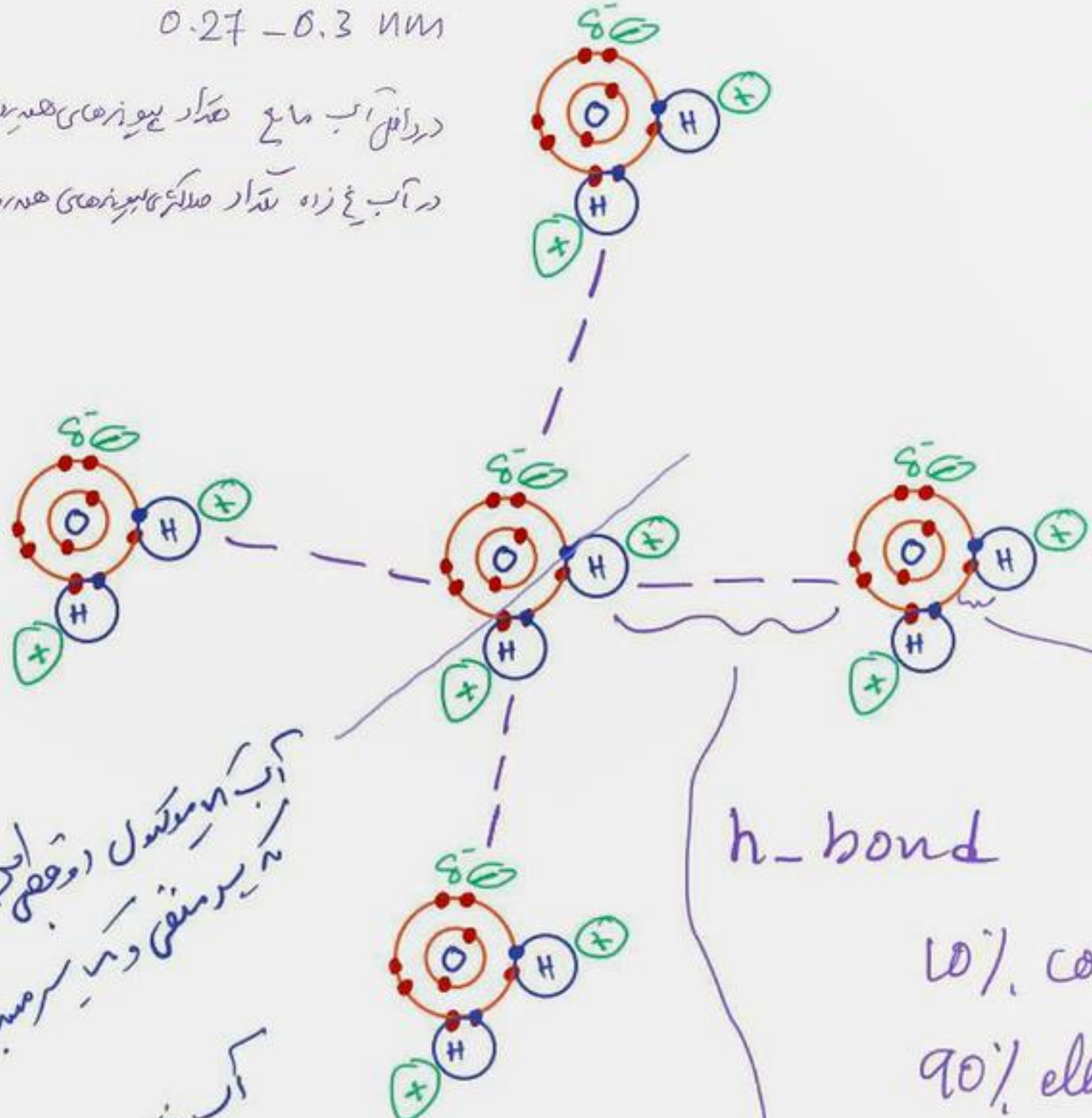
0.27 – 0.3 nm

در واقع آب مایع تعداد پیوندهای هیدروژنی به ازای هر مولکول آب ۳٫۴ است.

در آب یخ زده تعداد حداکثر پیوندهای هیدروژنی ایجاد م یعنی ۴ تا

$\delta =$ سمبل (کمی)

δ^- کمی منفی



کوتاه‌تر

آب یک مولکول دوقطبی است

۲ سر منفی و ۲ سر مثبت دارد

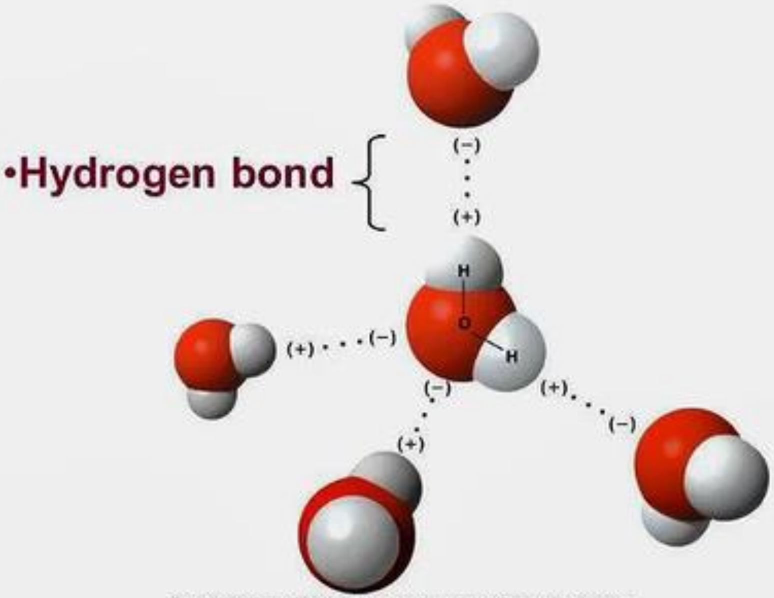
آب خاصیت لزجی هم دارد

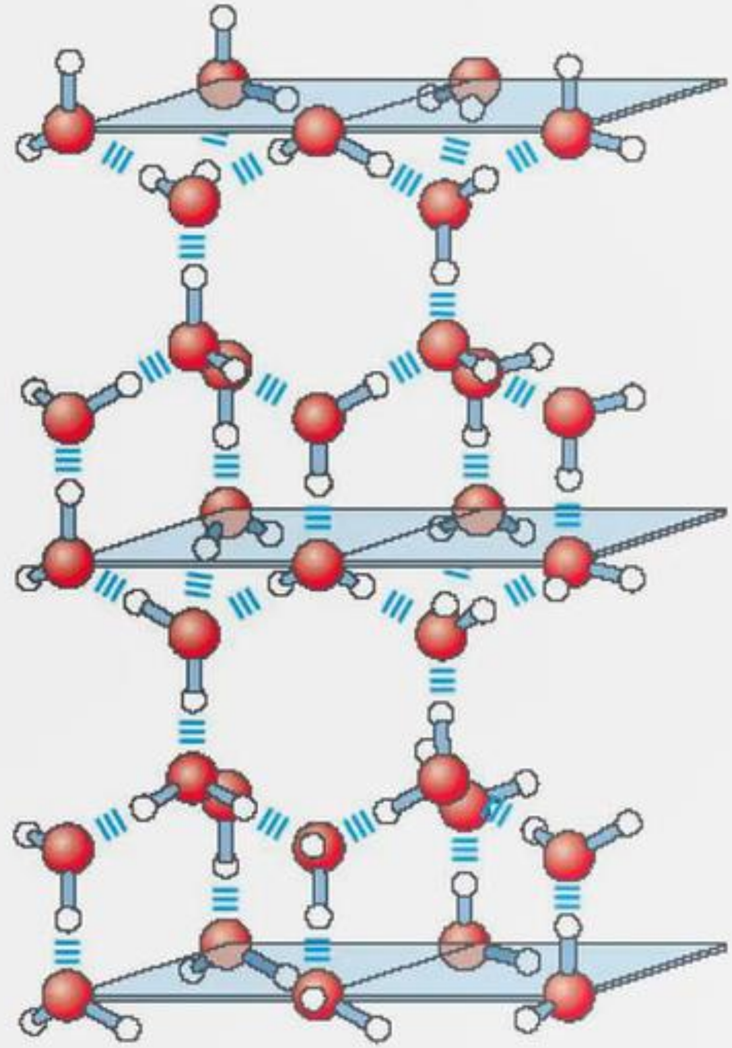
h_bond

10% covalent

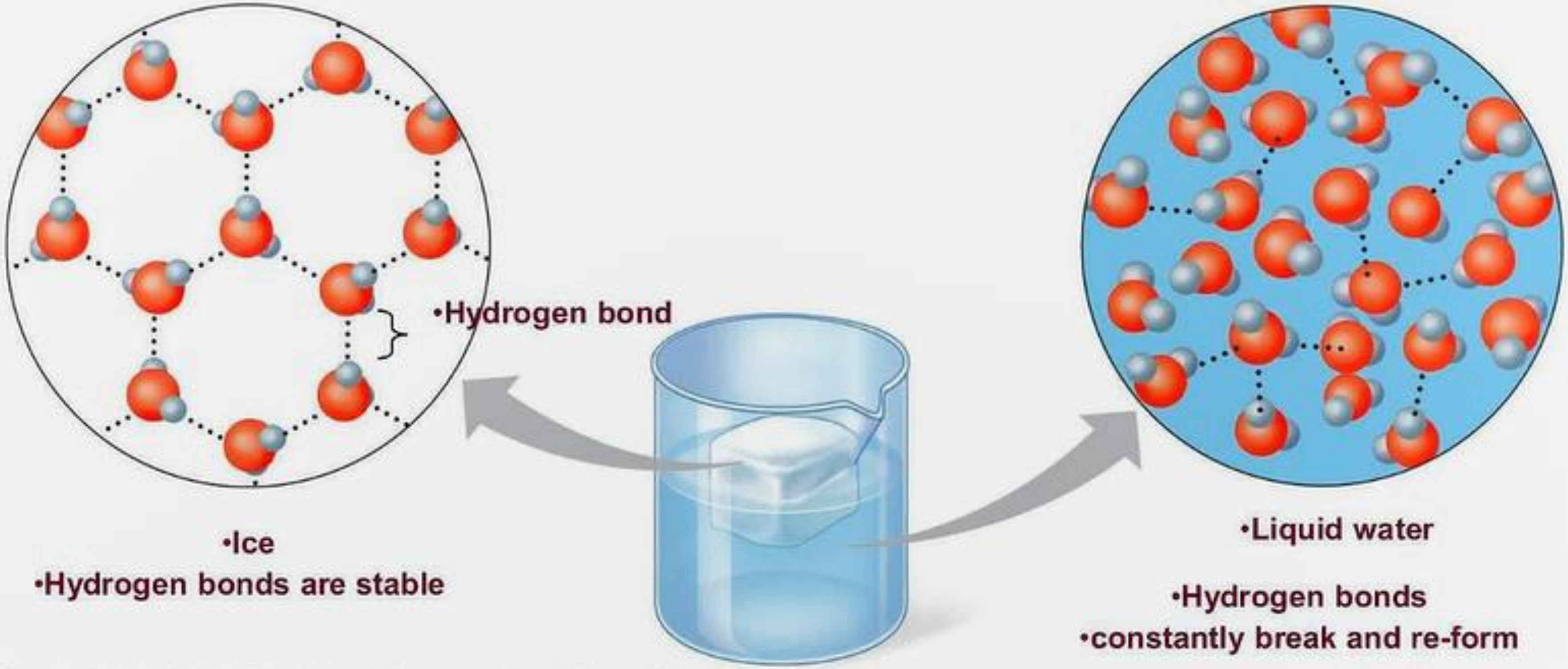
90% electrostatic

longer





•In ice crystal, each H2O is hydrogen bonded to 4 other H2O molecules.

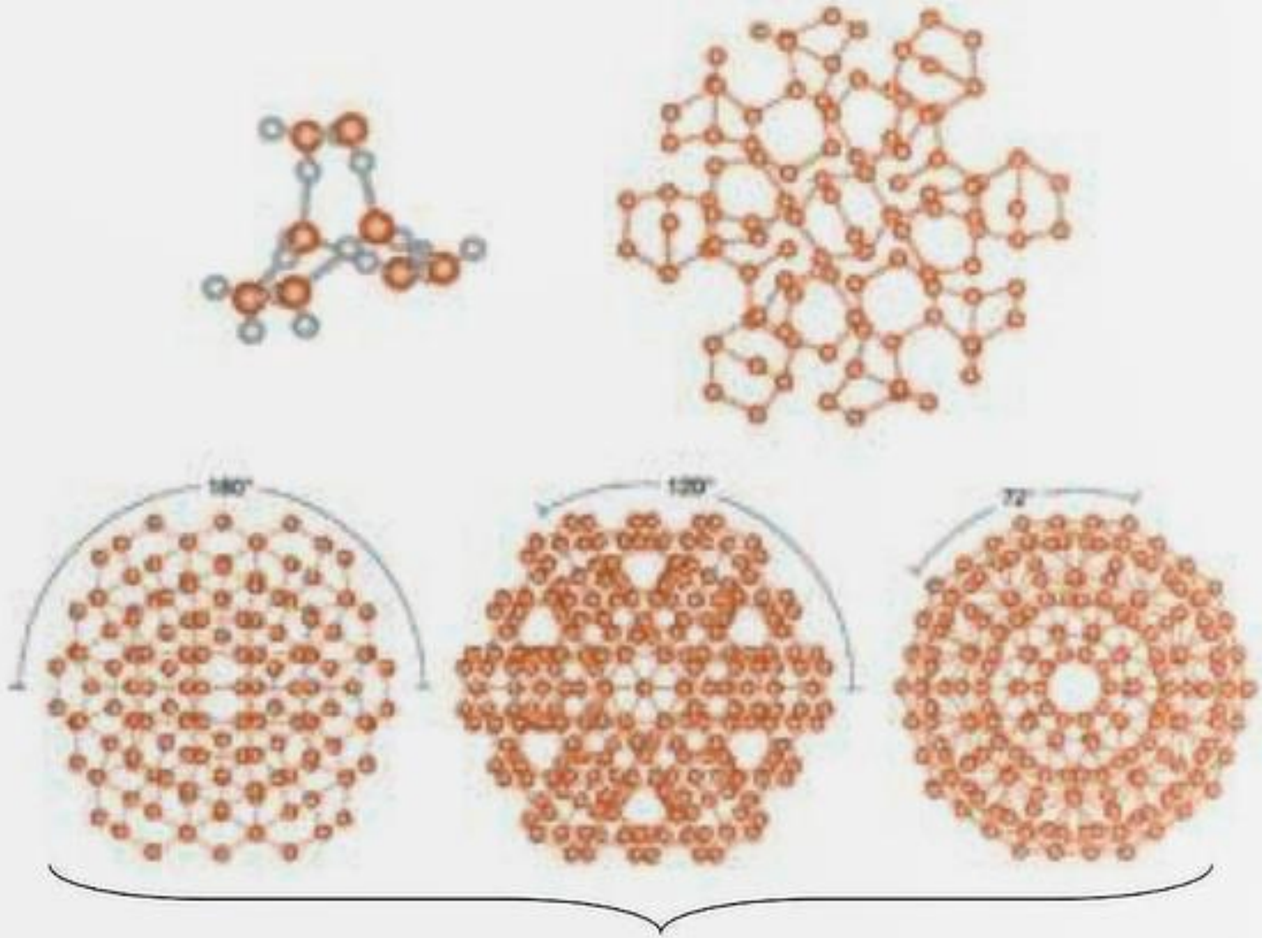


At any given time, most of the molecules in water are engaged in hydrogen bonding, but the lifetime of each hydrogen bond is just 1-20 picoseconds (1ps = 10^{-12}s).

In liquid water, molecules are disorganized and in continuous motion, so that each molecule forms H-bonds with an average of only 3.4 other molecules.

Structured Water Is Changing Models

$(H_2O)_8$
$(H_2O)_{14}$
$(H_2O)_{17}$
$(H_2O)_{21}$
$(H_2O)_{196}$
$(H_2O)_{280}$
$(H_2O)_{more}$



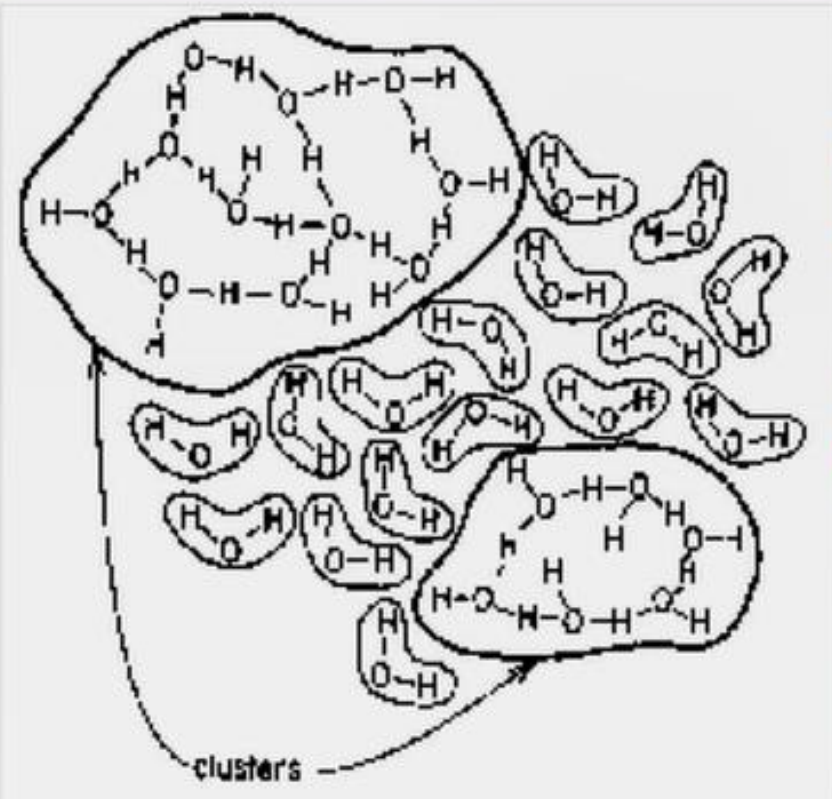
$(H_2O)_{280}$

Bennett Daviss

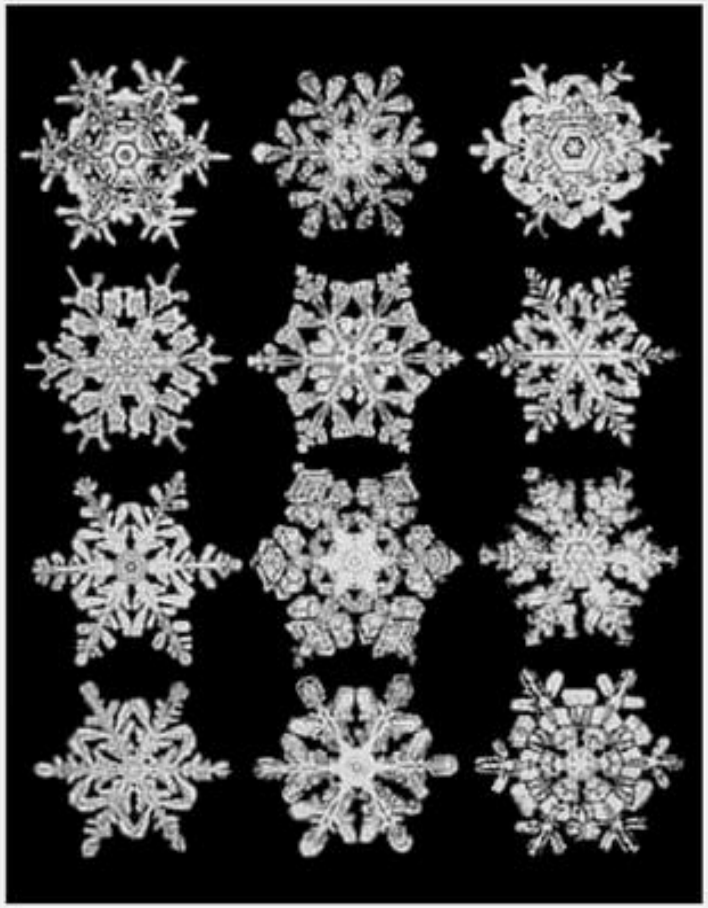
The Scientist 2004, **18**(21)**:**14.

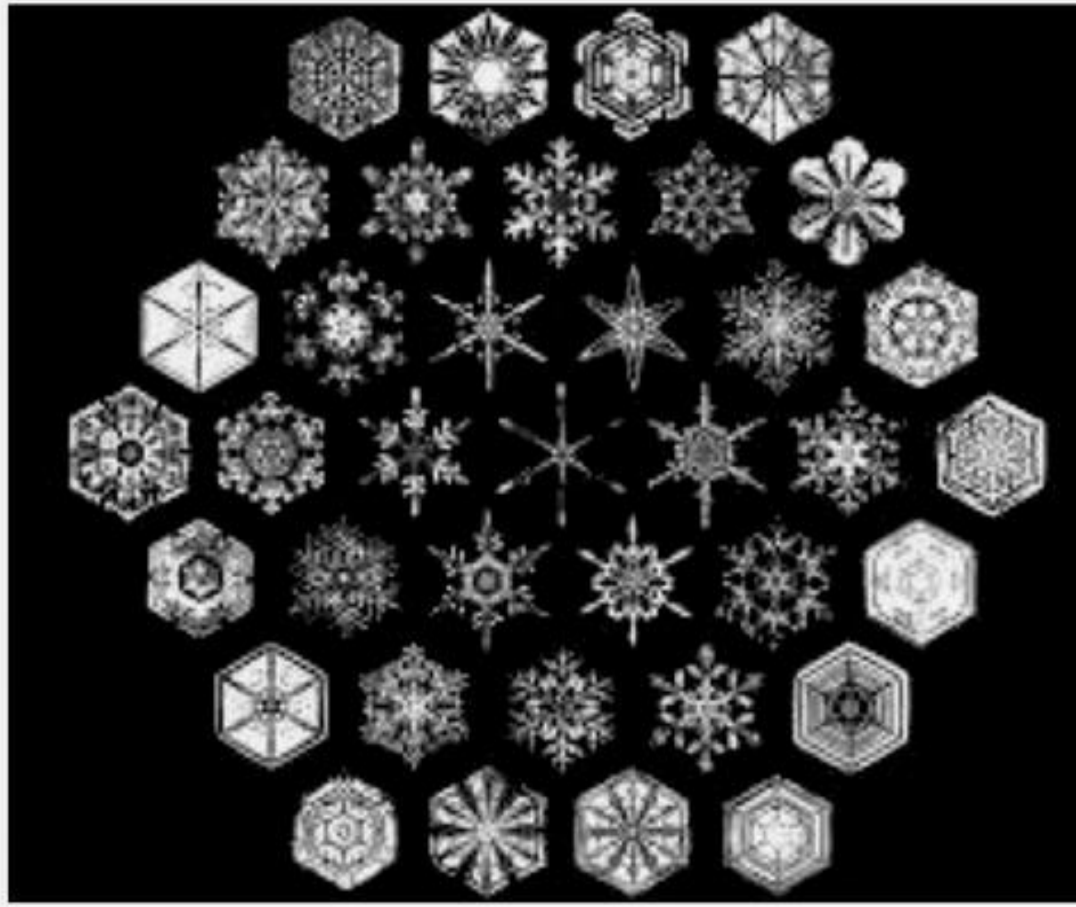
Microscopic structure of water

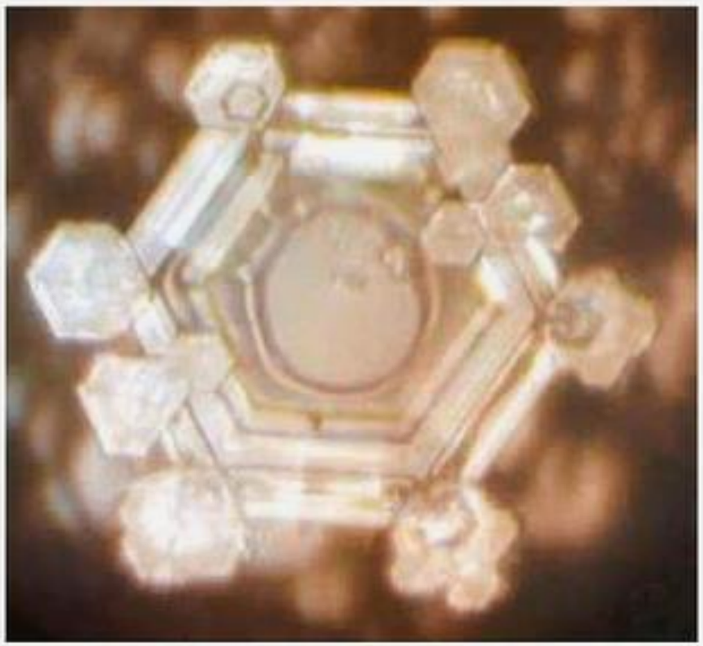
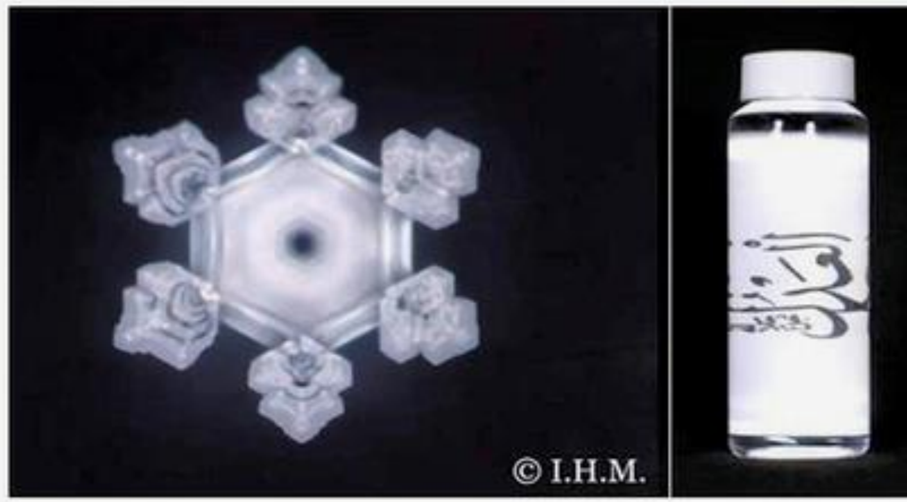
- Short-lived groups of water molecules interlinked by hydrogen bonds in liquid water are called **flickering clusters**.



Frozen water crystals (snowflakes)





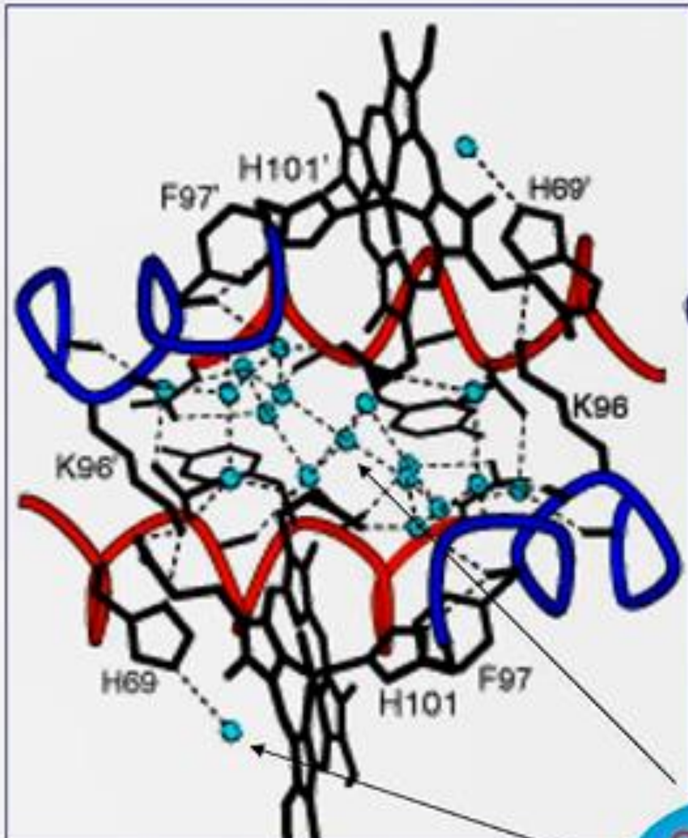




“Goldberg Variations”
Bach music

Frozen water crystals

Molecules are capable of imposing certain structures on the water.

A **solute** is a component of a solution which is present in a small amount relative to the solvent. A **solute** can be a solid, liquid, or gas.

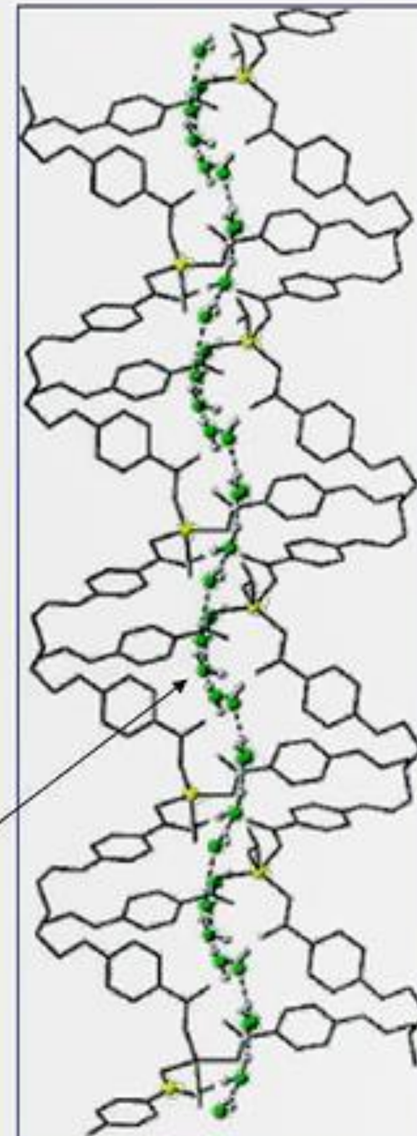


therapeutic powers of homeopathic remedies

Memory of water

Organized water molecules

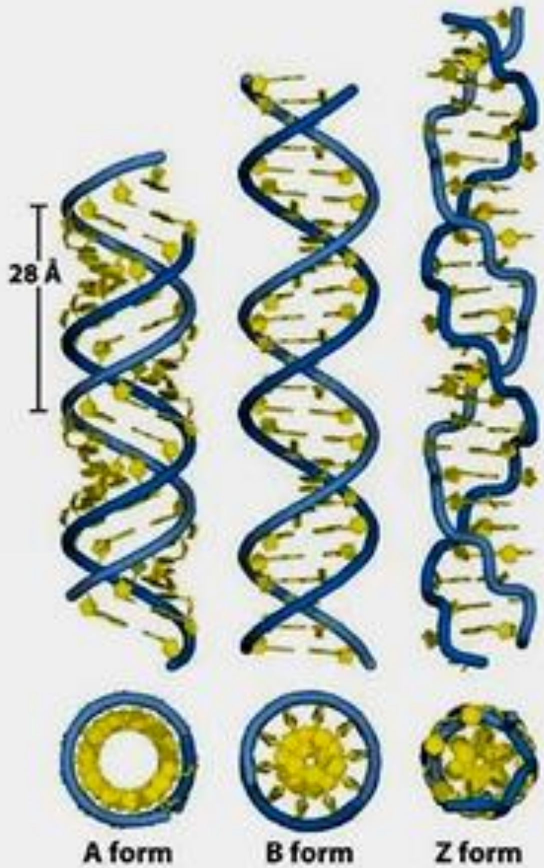
William Royer Jr.
U. of Mass. Medical school

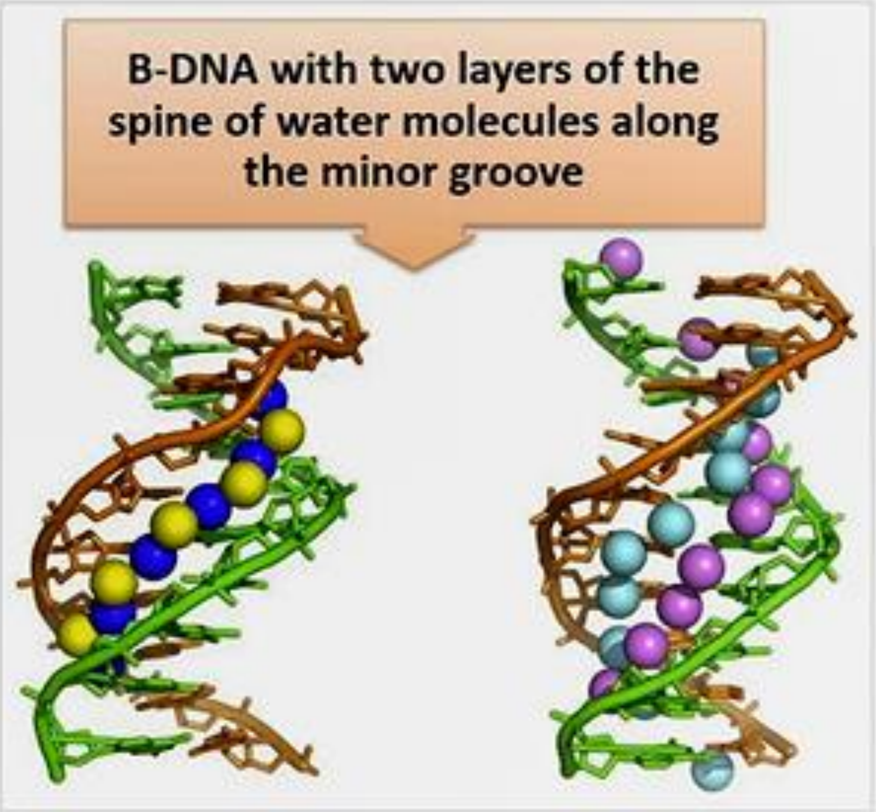


India, 2003

“**bound water**” molecules what do they do?

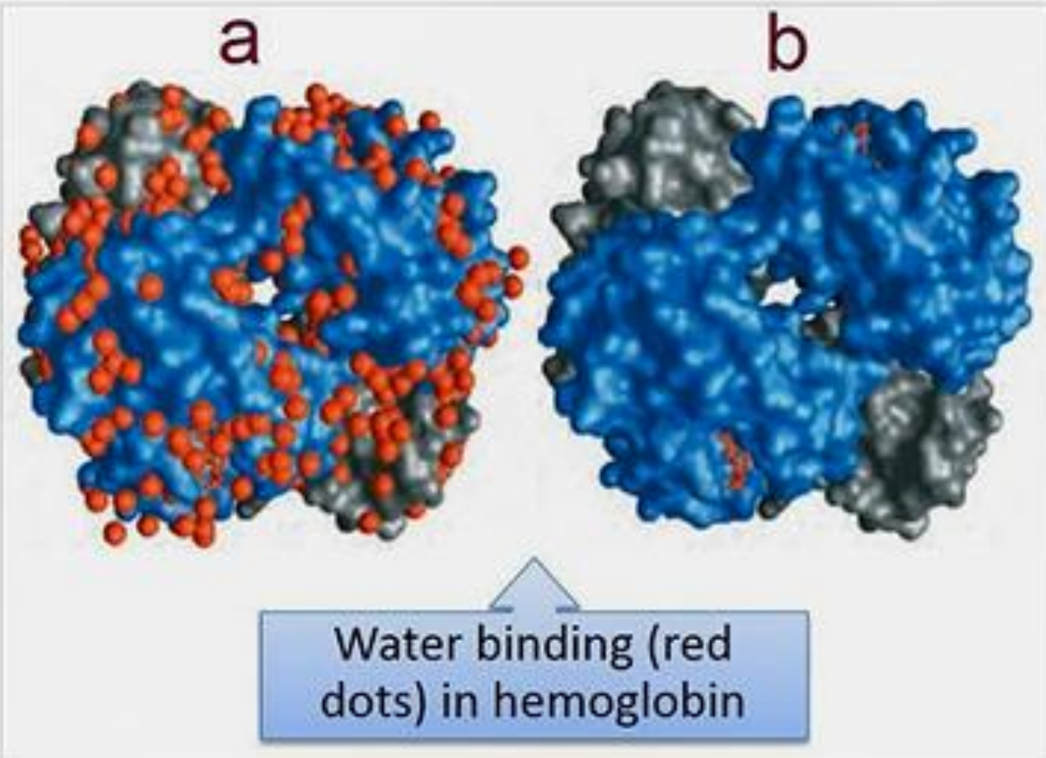
“Stabilization”



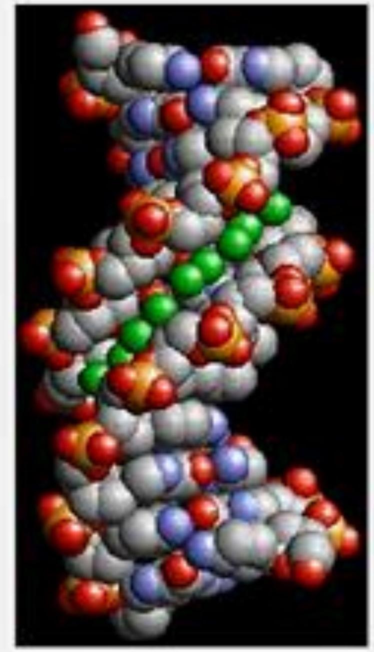


“**bound water**” molecules what do they do?

“Stabilization”

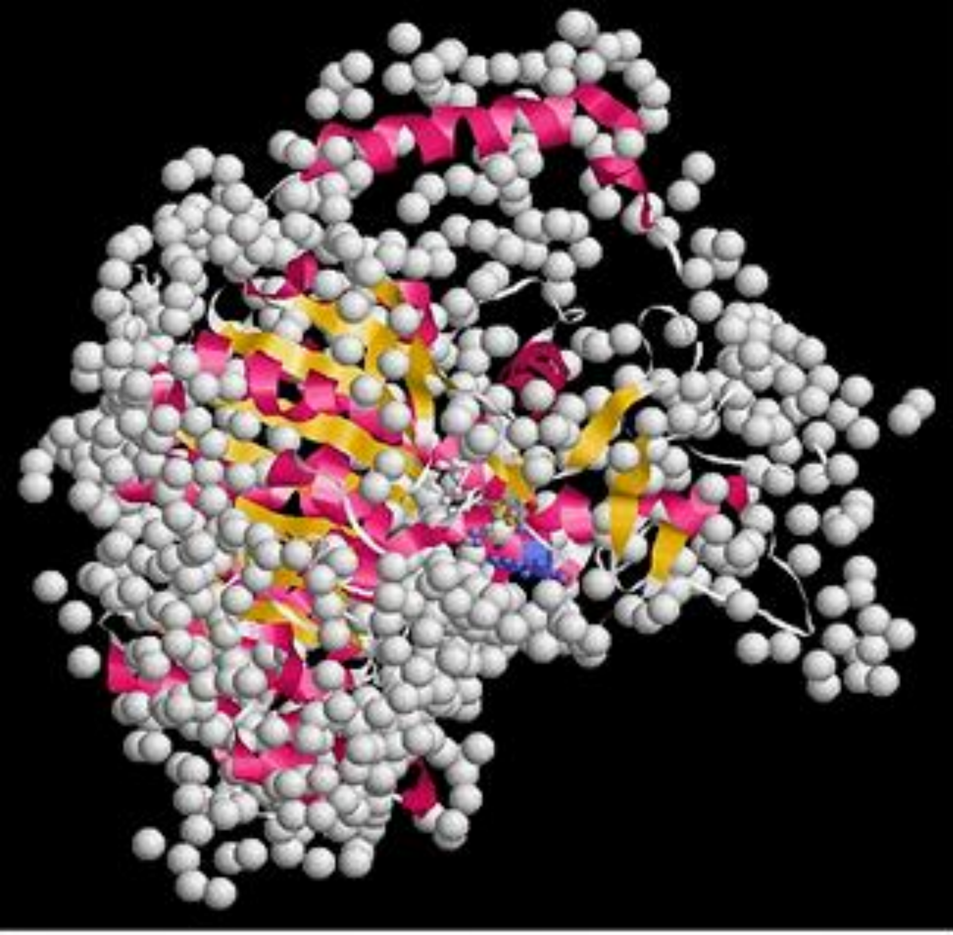


Bound water refers to the amount of water that are bound to macromolecules or organelles.



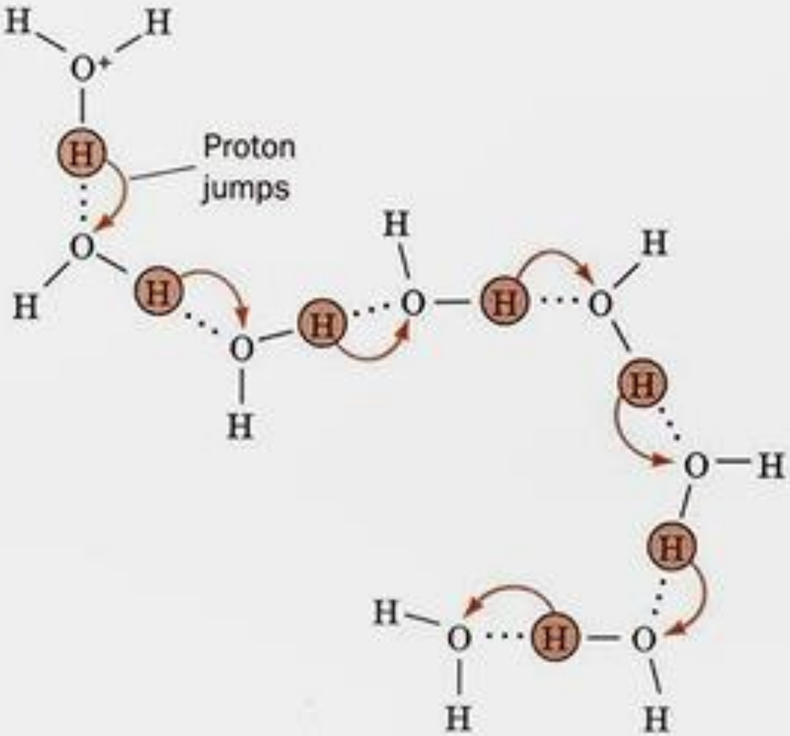
B-DNA with a spine of water molecules

مولکولهای آب در اطراف آنزیم آلکالن فسفاتاز (ALP)

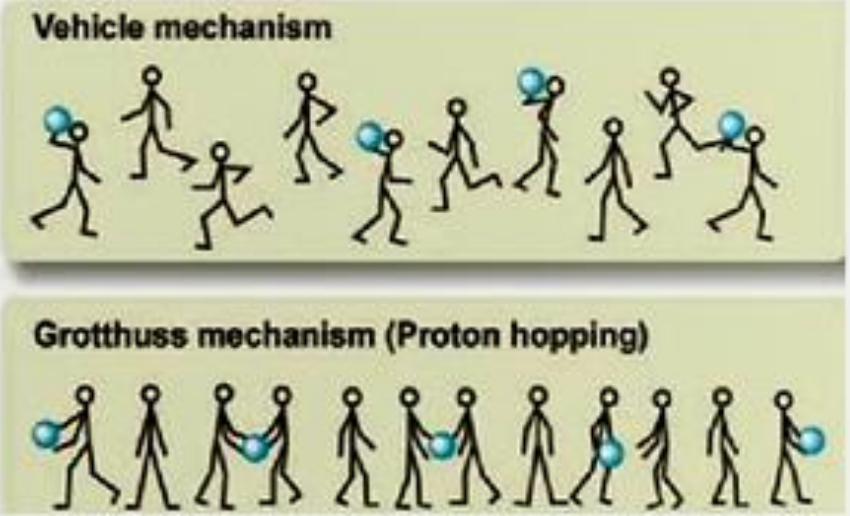


"Proton hopping"

- Hydronium ion migration; hops by switching partners at 10^{12} per second.



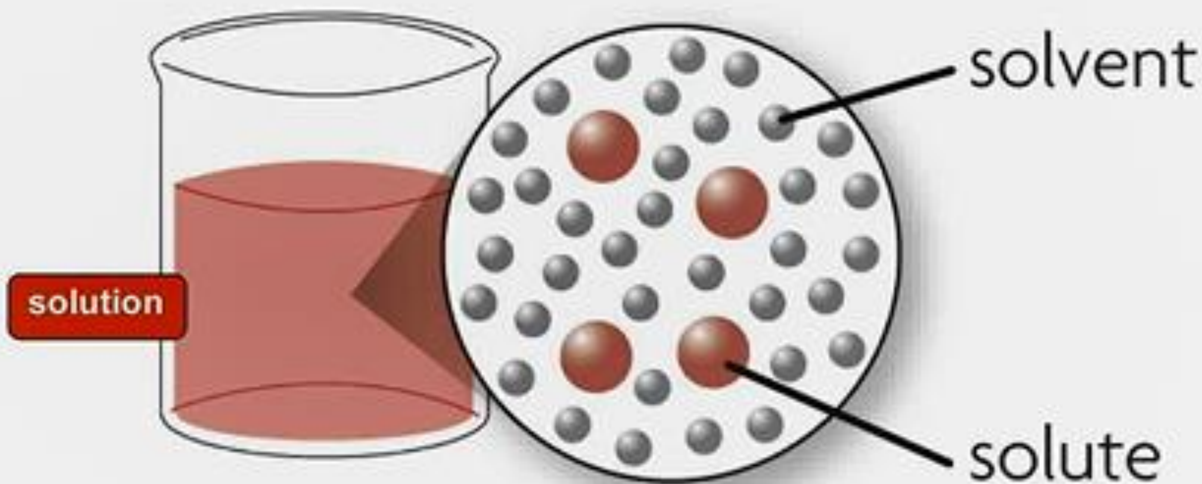
Proton hopping (hope) between a series of H-bonded water molecules cause rapid net movement of H+ and OH- ions over a long distance and hydroxide mobility is large compared to other ions.



- Myelinated axon nerve impulses travel 100 times more rapidly than impulses in non-myelinated axons.
- Proton Hopping: A Proposed Mechanism for Myelinated Axon Nerve Impulses.
  - CHEMISTRY & BIODIVERSITY – Vol. 10 (2013)
  - Lemont B. Kier

Solvent and Solute

- **Solutions:**
  - **Solvents** dissolve other substances.
  - **Solutes** dissolve in a solvent.



- Solvent rules: “Like dissolves like.”
  - Polar solvents dissolve polar solutes
  - *Hydrophilic*: “water-loving”
    1. Capable of forming H-bonds with H2O molecules
    2. Capable of being ionized in water

مکانیسم حل شدن مواد در آب

۲- حل کردن مواد متفاوت (حلال)

چون مولکول آب قطبی است لذا مواد قطبی را در خود حل می کند.

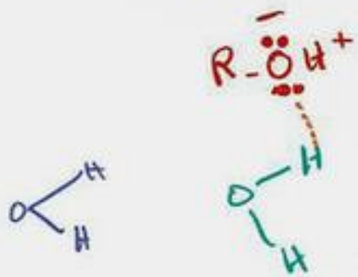
مواد قطبی به واسطه چه نوع ارتباطاتی با آب در آب حل می شوند؟

الکل، کتون، آلدئید به واسطه پیوندهای هیدروژنی در آب حل می شوند

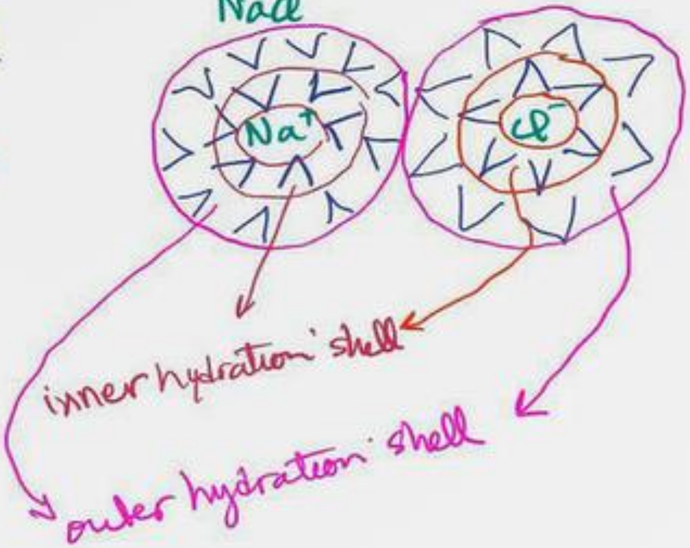
اندرکنش یا تعاملات یونی

موادی که به راحتی در آب حل می شوند، هیدروفیل محسوب می شوند.

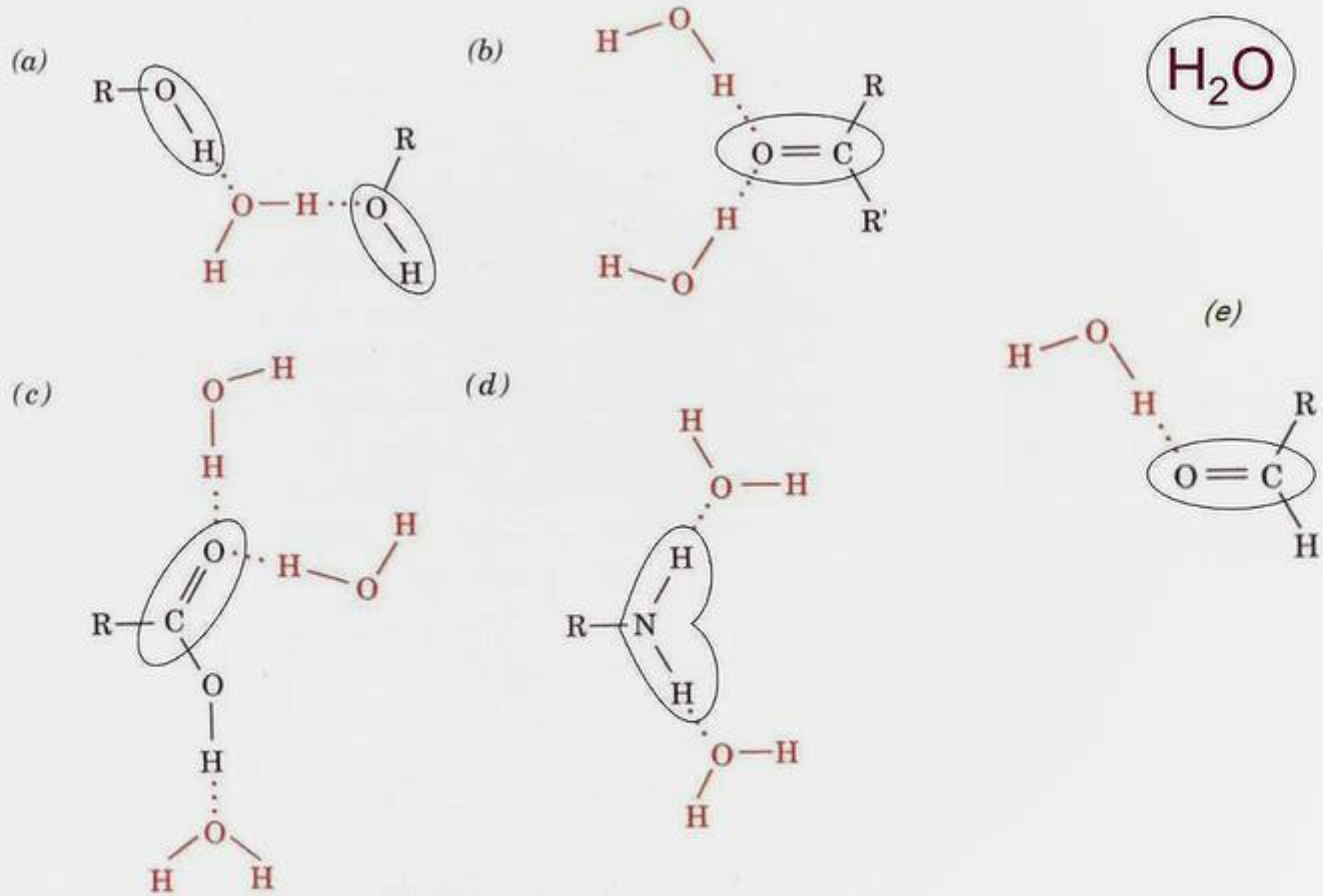
یا لیپوفوب



Na^+Cl^-

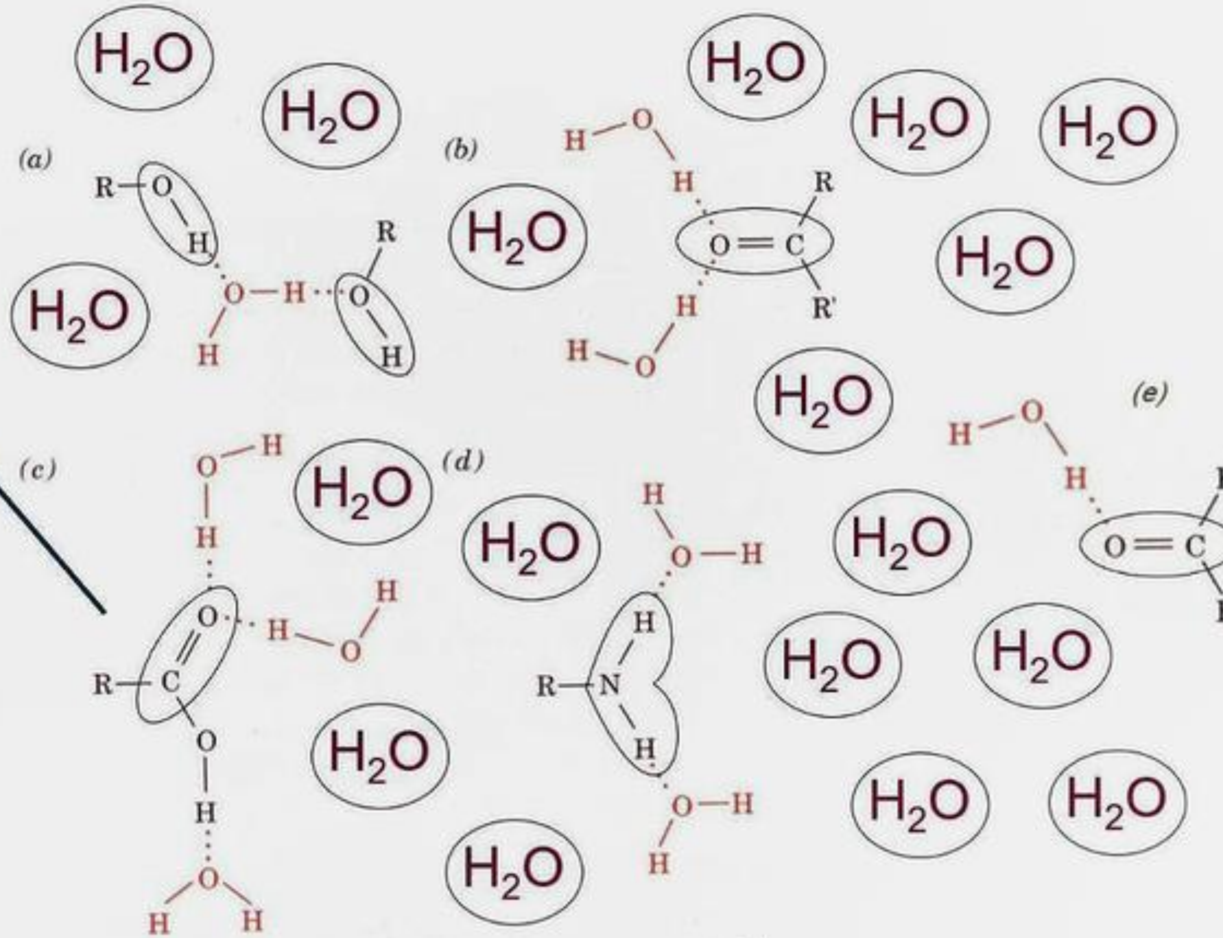


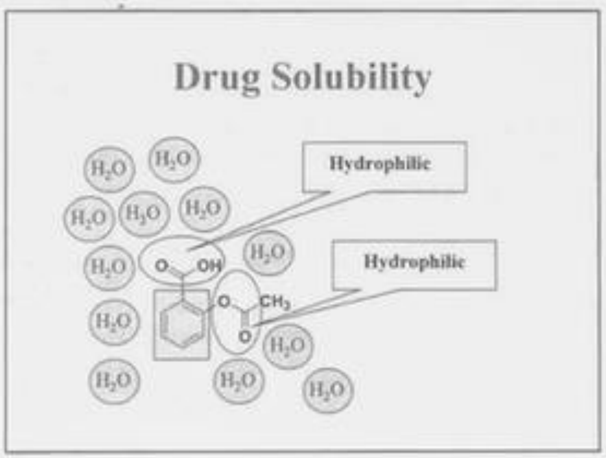
Water molecules form H-bonds with polar solutes and with functional groups



Solubility

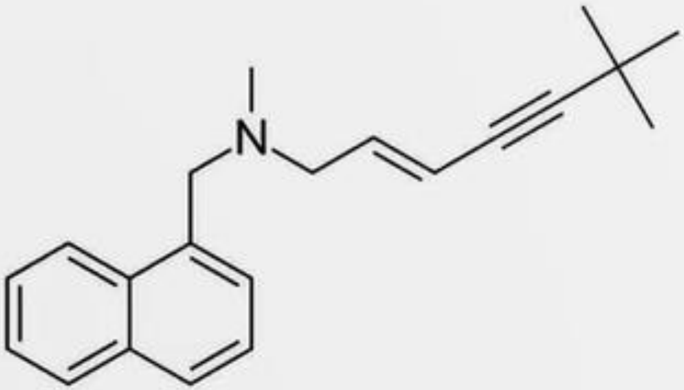
Hydrophilic





Water solubilization of functional groups

Functional group	Monofunctional compound	Polyfunctional compound
Alcohol	5-6 carbons	3-4 carbons
Phenol	6-7	3-4
Ether	4-5	2
Aldehyde	4-5	2
Ketone	5-6	2
Amine	6-7	3
Carboxylic acid	5-6	3
Ester	6	3
Amide	6	2-3

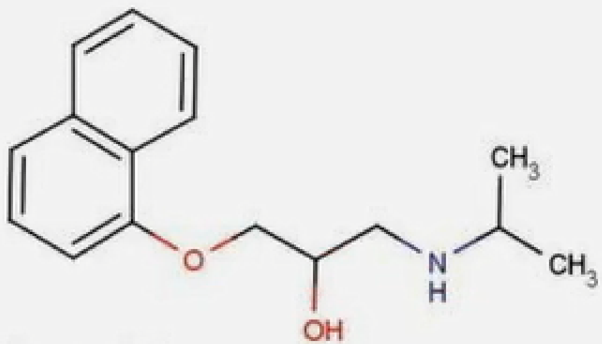


21 C atoms

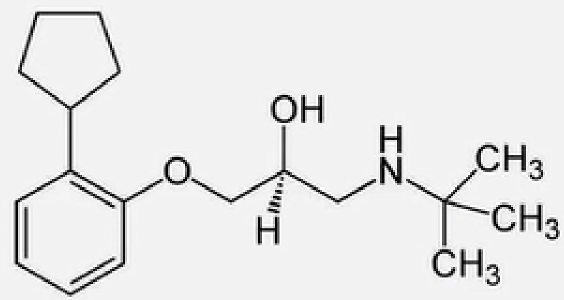
Tertiary amine Solubility = 6-7 C atoms

Neutral form = insoluble

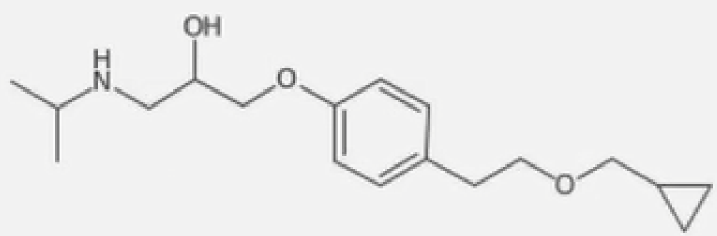
More practice problems



Propranolol

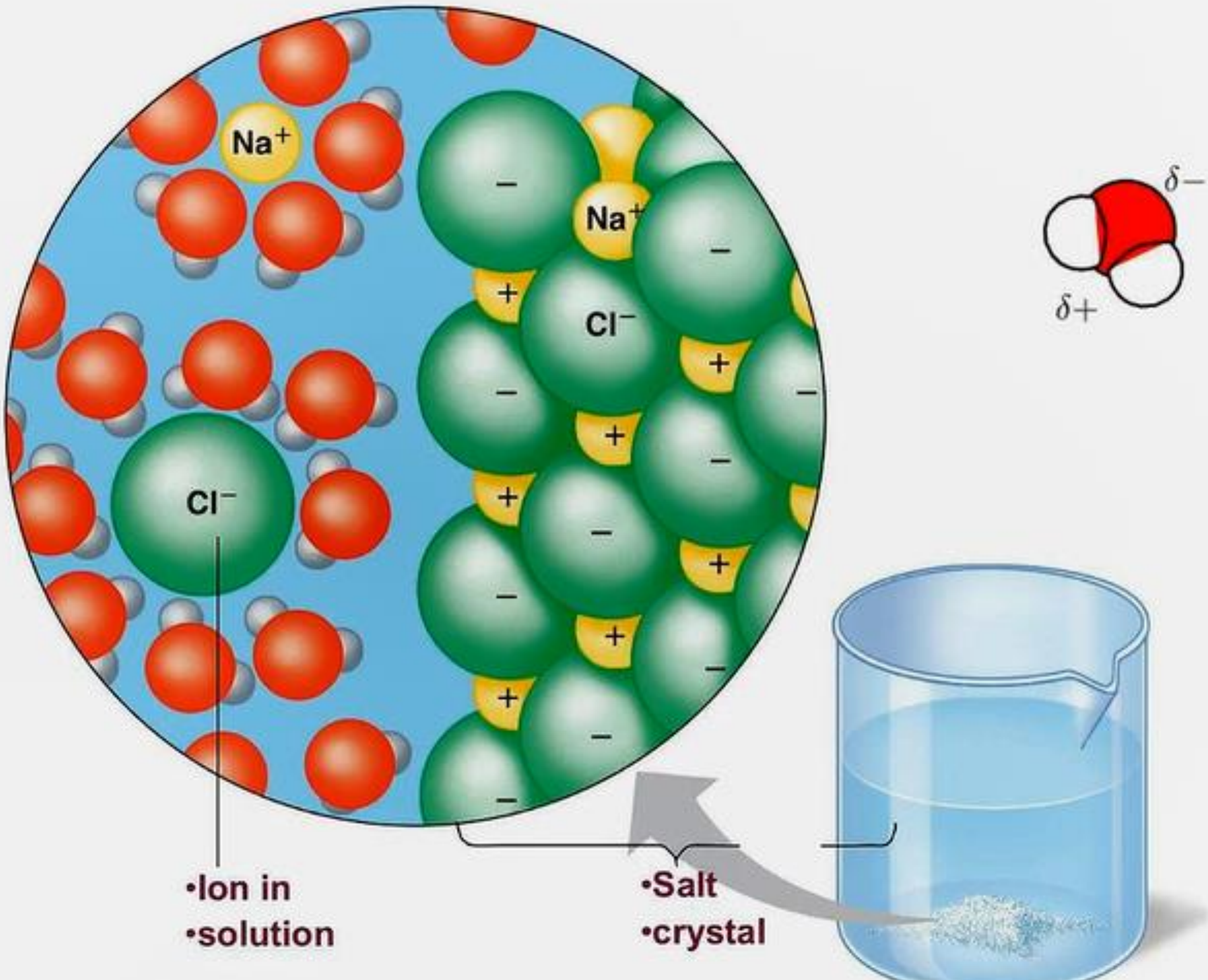


Penbutolol

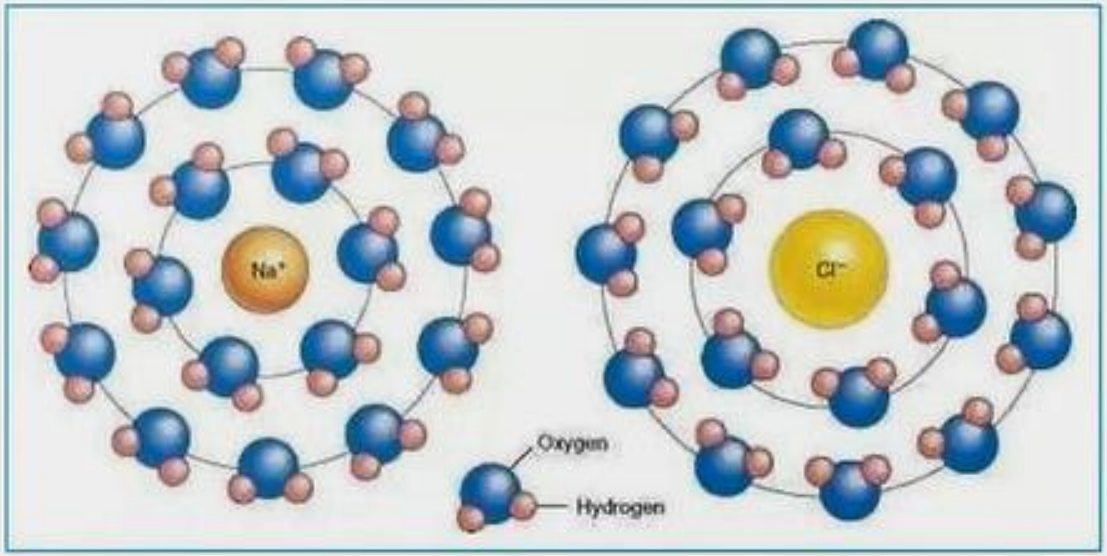


Betaxolol

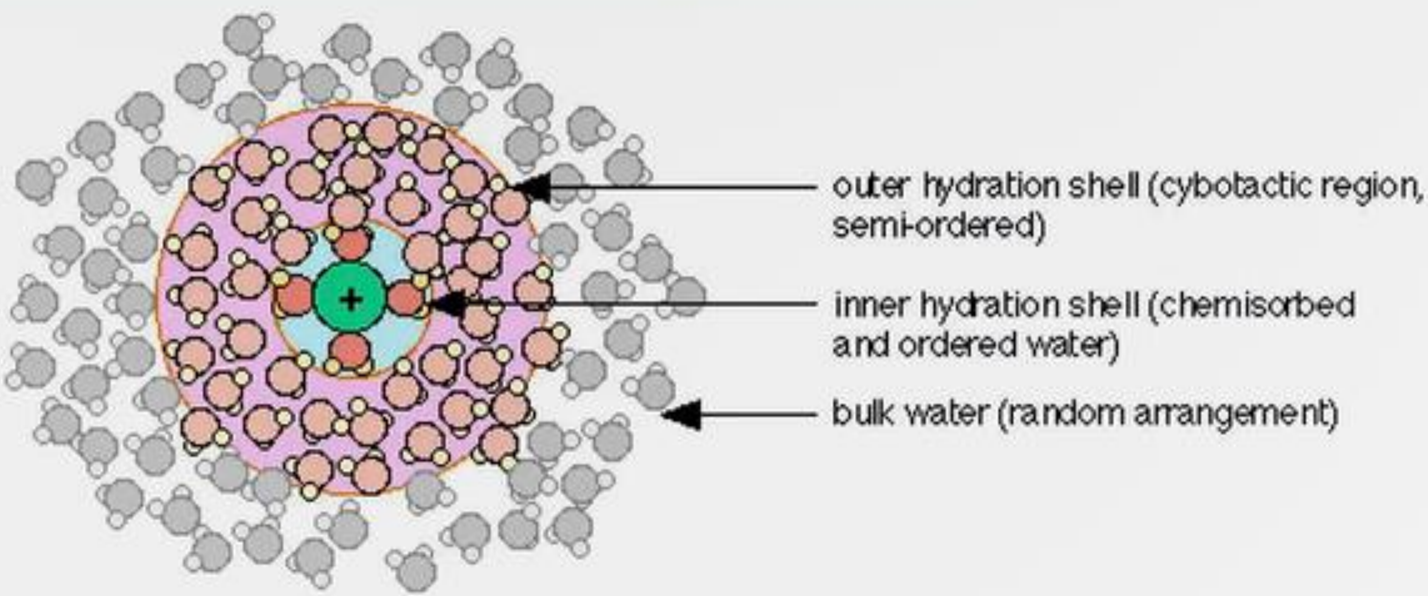
Electrostatic interaction with charged solutes



Ions change structure of liquid water

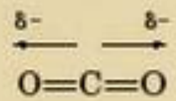
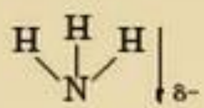
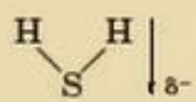


- Ionic substances are soluble because the net attraction of the + and – ions for water is greater than the attraction of oppositely charged ions for each other.
- Formation of **the Hydration shell**.



Nonpolar gases are poorly soluble in water: How are they carried in blood?

A **solute** is a component of a solution which is present in a small amount relative to the solvent. A **solute** can be a solid, liquid, or gas.

Gas	*Structure**	*Polarity*	*Solubility in water (g/L)*†
Nitrogen	$N\equiv N$	Nonpolar	0.018 (40 °C)
Oxygen	$O=O$	Nonpolar	0.035 (50 °C)
Carbon dioxide		Nonpolar	0.97 (45 °C)
Ammonia		Polar	900 (10 °C)
Hydrogen sulfide		Polar	1,860 (40 °C)

*The arrows represent electric dipoles; there is a partial negative charge (δ^-) at the head of the arrow, a partial positive charge (δ^+; not shown here) at the tail.

†Note that polar molecules dissolve far better even at low temperatures than do nonpolar molecules at relatively high temperatures.

Microscopic structures of water

ساختارهای میکروسکوپی خیلی کمک به درک هم دادن لذا از انرژی
مولکول آب به صورت منظم مکان ... که با پیوندهای هیدروژنی به هم متصل هستند.
در آب خالص این ساختارها مدام ایجاد می‌شوند. در آب ناخالص (شلوغ) شکل شلوغ‌تر [illegible]
رهسته هم [illegible] می‌دهند و حتی ممکن است تعدادشان در [illegible] و
کردن [illegible] بشکنند.

وقتی ماده‌ای در داخل آب ول می‌کنی در
مولکولای آب تحت تاثیر آن
ماده ساختار میکروسکوپی خود را تغییر می‌دهند
و از سوی دیگر جاهایی که ساختار مولکولی آن
ماده هم تغییر می‌کند از طریق تعامل با گروه‌های
شیمیایی تشکیل‌دهنده آن مولکول.

چون مولکول آب قطبی است لذا مواد
قطبی را در خود حل می‌کند.

60% وزن بدن آب است.

پس مولکولای آب اولاً کارهای مهمی انجام می‌دهند

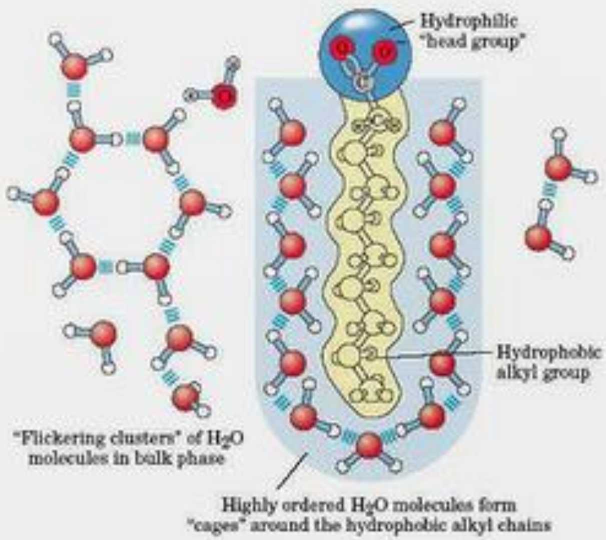
۱- پایدار کردن (افزودن به پایداری) بیومولکولها
۲- انتقال الکترون
۳- حل کردن مواد متفاوت (حلال)

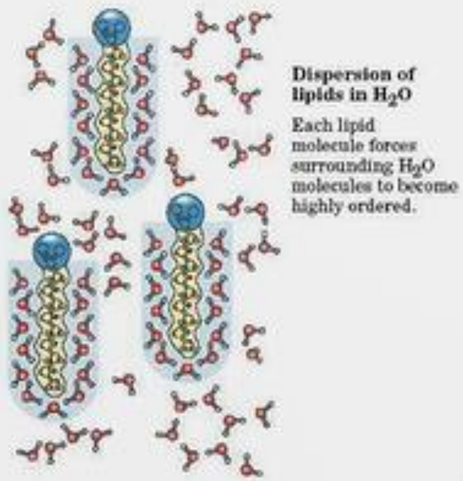
Nonpolar substances are fat soluble

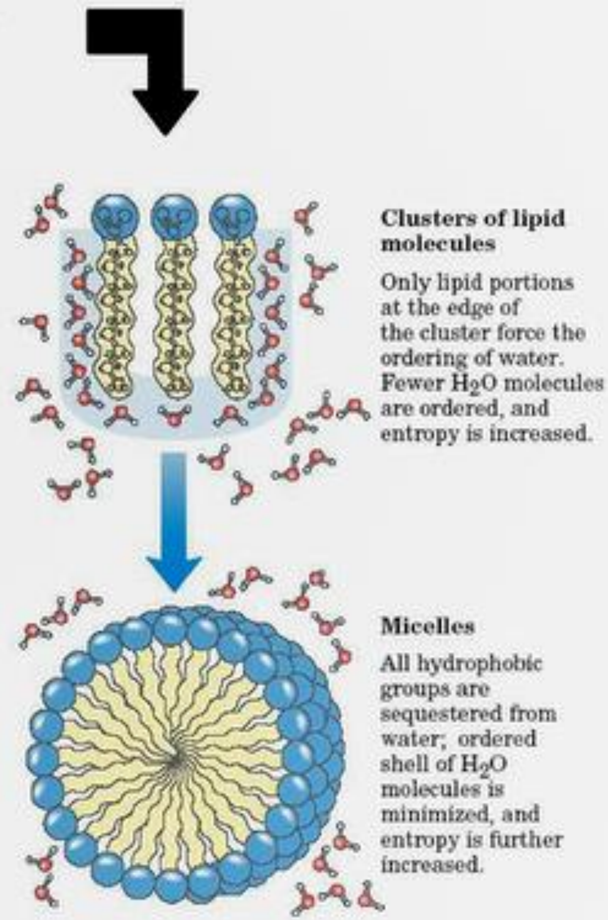
- Non-polar solvents dissolve non-polar solutes:
  - Polar and non-polar separate
  - *hydrophobic* – "water-fearing"
  - Lipophilic – "fat-loving"
  - Long chains of $–(CH2)_n$- are nonpolar; they are called "lipids" or "fats".

- Hydrocarbons and nonpolar molecules are insoluble because water-water interactions are stronger than water-hydrocarbon interactions.
- Oil droplets in water join together because water molecules force nonpolar molecules together and surround them.

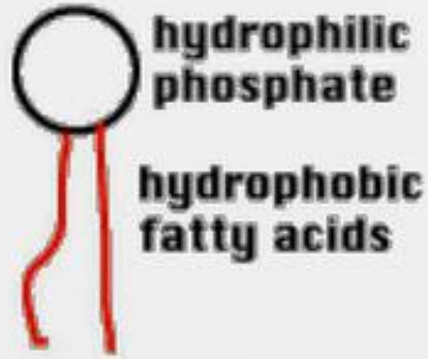
Hydrocarbons and lipids in water

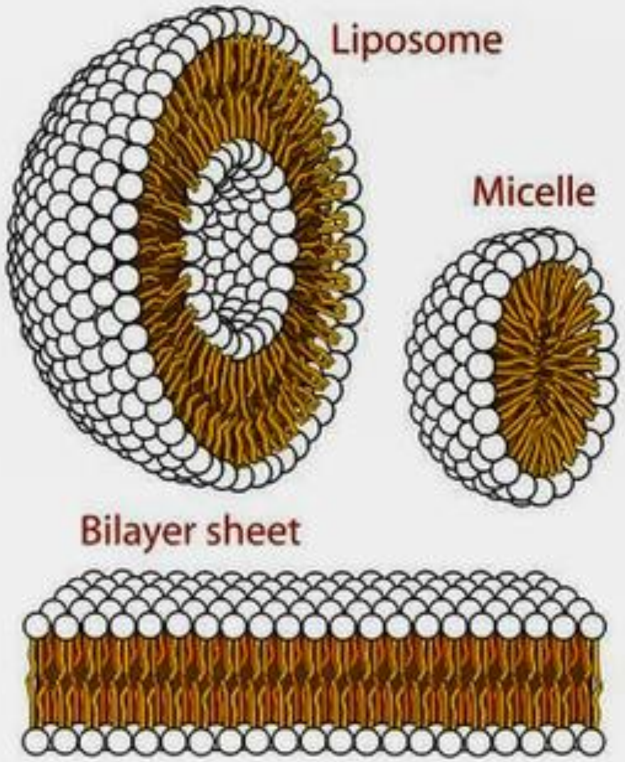


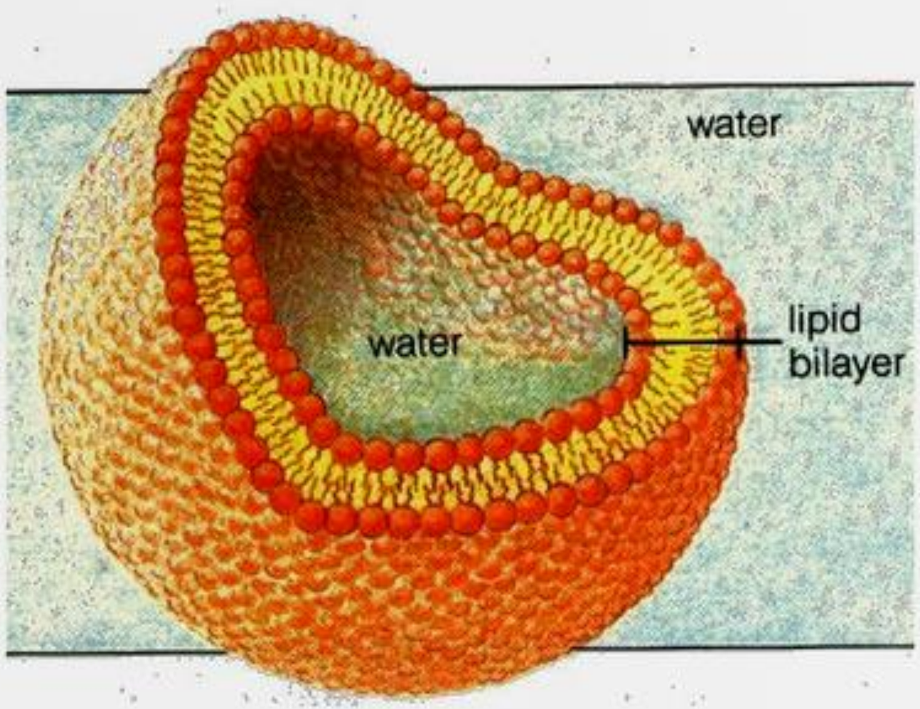




- Single-tail lipids are long-chain carboxylic acids.
- Substances that possess both hydrophilic and hydrophobic properties are called "amphipathic" or "amphiphilic".
- water molecules force nonpolar molecules together and surround them.
- This phenomenon is called hydrophobic effect or hydrophobic interaction.


hydrophilic
phosphate
hydrophobic
fatty acids


Liposome
Micelle
Bilayer sheet


water
water
lipid
bilayer

Water as a solvent

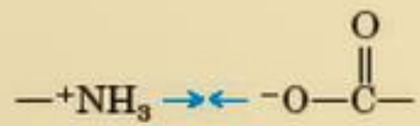
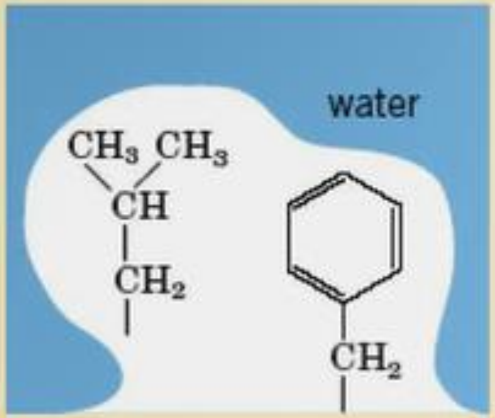
Water is a polar solvent:

- Compounds that dissolve easily in water are hydrophilic (Greek, “water-loving).

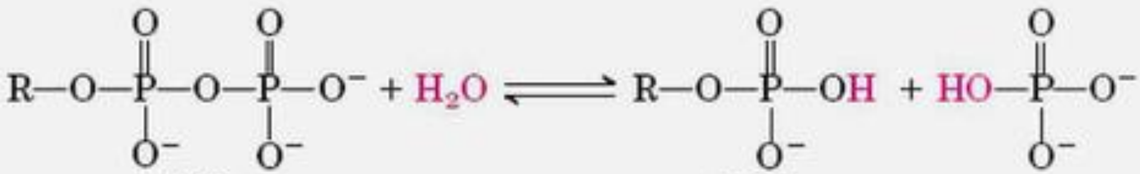
- Nonpolar molecules that are not dissolved in water can be dissolved in nonpolar solvents (chloroform, and benzene). These nonpolar molecules are called hydrophobic (water-fearing) or lipophilic (fat-loving).

- Compounds that contain regions that are polar (or charged) and regions that are nonpolar are called amphipathic or amphiphilic.

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

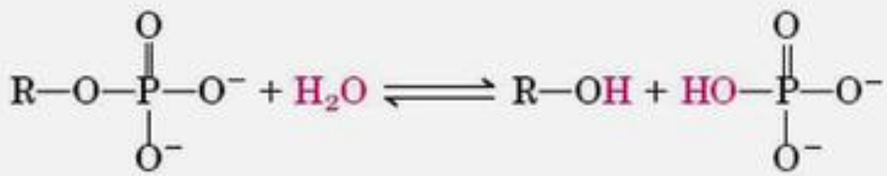
Water as a reactant



(ATP) (ADP)

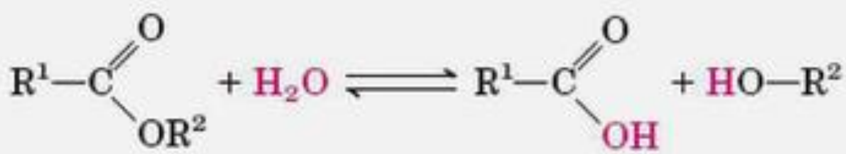
Phosphoanhydride

(a)



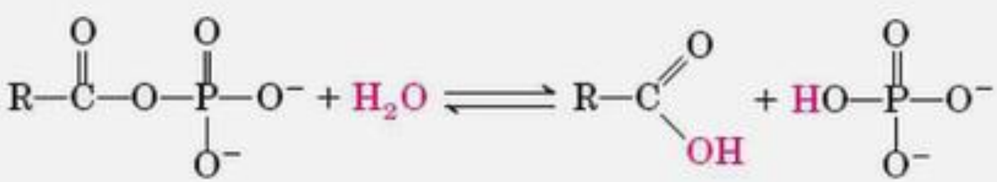
Phosphate ester

(b)



Carboxylate ester

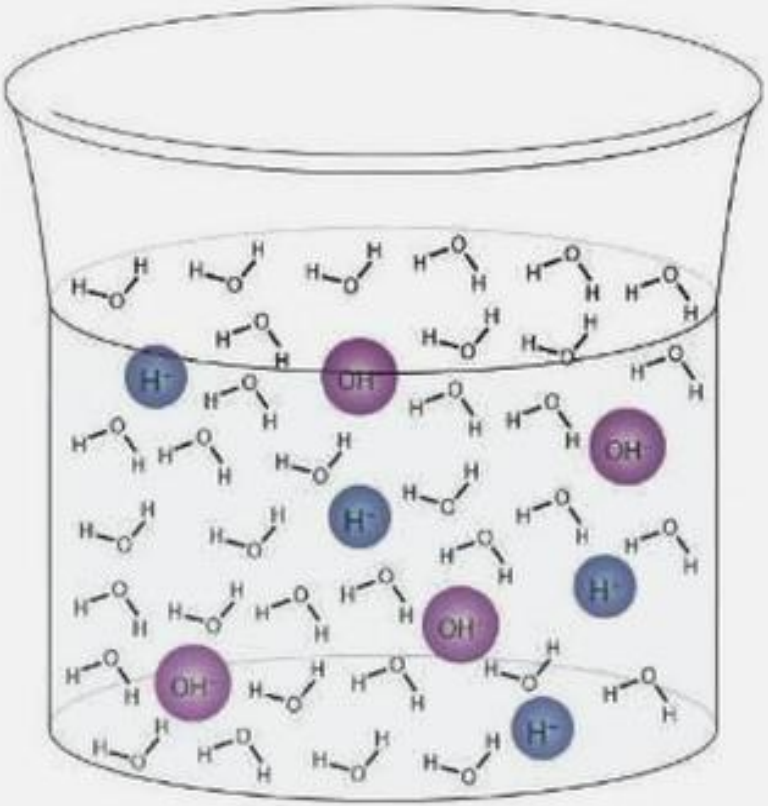
(c)



Acyl phosphate

(d)

Autoionization of water, giving hydroxide and hydronium ions.



- Autoionization.
- A small fraction of water molecules—approximately 6 in 100 million—ionize spontaneously into hydronium ions and hydroxide ions.

- This picture necessarily overrepresents the amount of autoionization that really occurs in pure water.

Ionization of water

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

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

$$[H2O] \times Keq = [H+] \times [OH-]$$

$$Kw = Keq \times [H2O] = (1.8 \times 10^{-15}) \times (55.5)$$

pOH = -log [OH^-] =7

pH = -log [H^+] = 7

pka = -log Ka = 14

Keq = 1.8×10^{-16}

[H2O]=55.5 M (this is the concentration of pure water in mol/L) [because (1000g/L)/(18.015 g/mol)].

(55.6)Keq = $[H^+][OH^-]$

(55.6)(1.8×10^{-16}) = $[H^+][OH^-] = K_w$

$K_w = 1.0 \times 10^{-14} = [H^+][OH^-] = [H^+]^2$

$[H^+] = 1.0 \times 10^{-7}$ M

$[OH^-]$ = = 1.0×10^{-7} M

$pK_H + pK_{OH} = pKa$

7 + 7 = 14

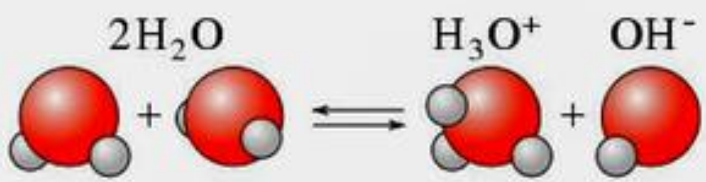
For pure water:
pH=7 and pOH=7
pH=pOH
pH + pOH = 14

An **acid** is a chemical species that can donate a proton (H+).
A **base** is a chemical species that can accept (gain) a proton.

Water is **amphoteric**, because it can act as either an acid or a base.

Autoionization of water, giving hydroxide and hydronium ions

$$\underbrace{H_2O}_{\text{acid}} + \underbrace{H_2O}_{\text{base}} \rightleftharpoons H_3O^+ + OH^-$$



$$K_w = [H_3O^+][OH^-] = 1.0 \times 10^{-14}$$

Summary of Relations for Acidic, Basic and Neutral Solutions

Classification	Relative Ion Concentrations	pH at 25 °C
acidic	$[H_3O^+] > [OH^-]$	pH < 7
neutral	$[H_3O^+] = [OH^-]$	pH = 7
basic	$[H_3O^+] < [OH^-]$	pH > 7

pH of a solution

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

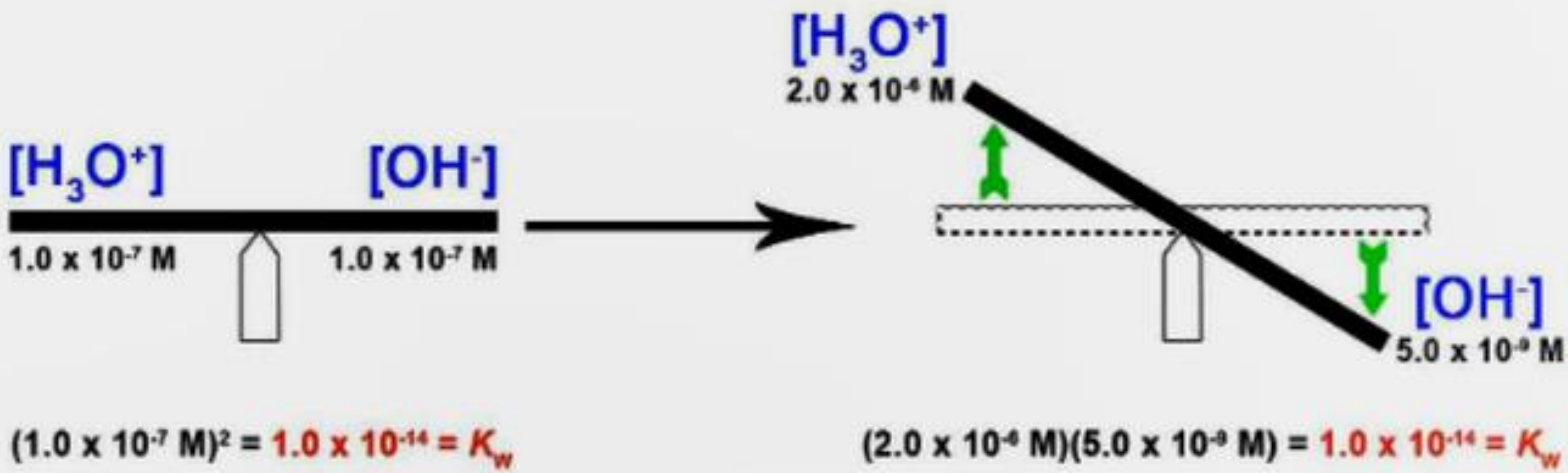
$[H^+] = [OH^-]$ **Neutral solution, pH=7**

$[H^+] > [OH^-]$ **Acidic solution, pH<7**

$[H^+] < [OH^-]$ **Basic (alkaline) solution; pH>7**

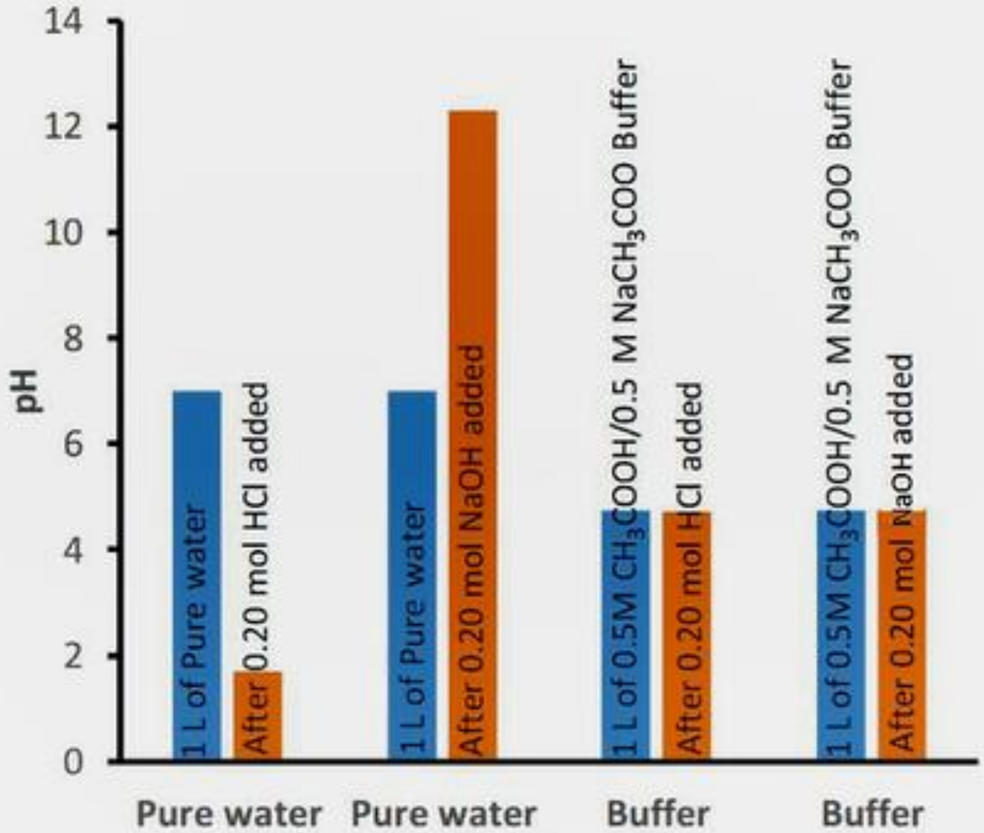
- Pure water is a neutral solution with a pH=7.

Adding acid into pure water



- The ion-product constant is $K_W = 1.0 \times 10^{-14}$ the whole time at 25°C. In pure water, $[H_3O^+] = [OH^-] = 1.0 \times 10^{-7}$.
- When we increase $[H_3O^+]$, like a seesaw, this is balanced and counteracted by a decrease in $[OH^-]$ – this keeps K_W constant.

Pure water vs. buffer solution after adding acid or base



- Effects of acid and base addition on pH change of pure water at pH 7.00 and on acetic acid/sodium acetate buffer at pH 4.74.

TYPES OF BUFFERS

Two types :

- ACIDIC BUFFERS –

Solution of a mixture of a weak acid and a salt of this weak acid with a strong base.

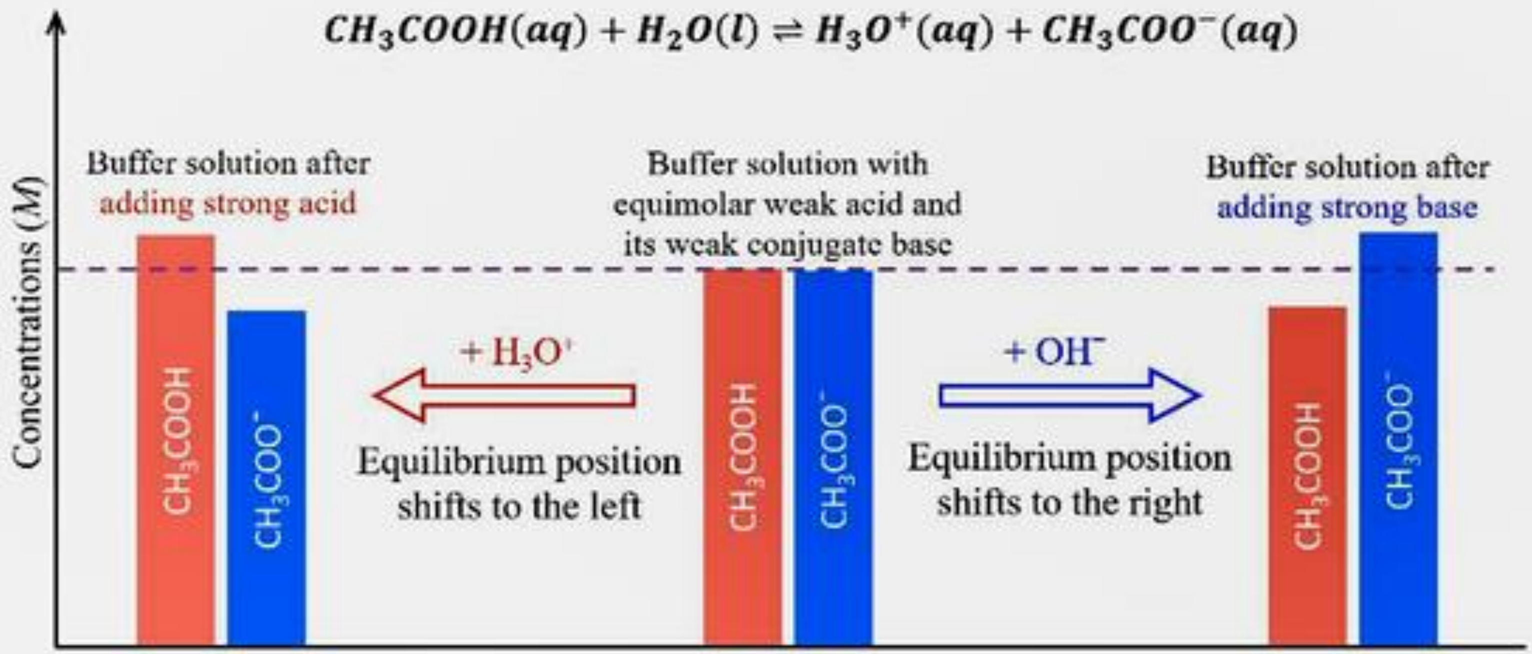
E.g. CH_3COOH + CH_3COONa
(weak acid) (Salt)

- BASIC BUFFERS –

Solution of a mixture of a weak base and a salt of this weak base with a strong acid.

e.g. NH_4OH + NH_4Cl
(Weak base) (Salt)

How does a buffer solution resist pH changes?



- *When a strong acid (producing H_3O^+) is added to a buffer solution, the weak base is converted to its weak conjugate acid. When a strong base (producing OH^-) is added to a buffer solution, the weak acid is converted to its weak conjugate base.*

Buffer solution mechanism

اسید ضعیف   باز مزدوج

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

The Major Body Buffer Systems		
Site	**Buffer System**	**Comment**
ISF interstitial space fluid	Bicarbonate	For metabolic acids
	Phosphate	Not important because concentration too low
	Protein	Not important because concentration too low
Blood	Bicarbonate	Important for metabolic acids
	Haemoglobin	Important for carbon dioxide
	Plasma protein	Minor buffer
	Phosphate	Concentration too low
ICF Intracellular fluid	Proteins	Important buffer
	Phosphates	Important buffer
Urine	Phosphate	Responsible for most of 'Titratable Acidity'
	Ammonia	Important - formation of NH_4^+
Bone	Ca carbonate	In prolonged metabolic acidosis

Dissociation of weak acids

- An **acid dissociation constant**, K_a, (also called **acidity constant**, or **acid-ionization constant**)
- It is a quantitative measure of the strength of an acid in solution.

$$\mathrm{p}K_\mathrm{a} = -\log K_\mathrm{a}$$

- Ka ∝ *acid strength (or acidity)*

- pKa $\propto \frac{1}{acid\ strength\ (or\ acidity)}$

K_a and pK_a values of some common of acids (25°C)

No.	Acid	K_a	pK_a
1	Hydroiodic acid (HI)	3.16×10^9	-9.5
2	Hydrobromic acid (HBr)	1.0×10^9	-9
3	Hydrochloric acid (HCl)	1.0×10^6	-6
4	Sulfuric acid (H_2SO_4)	1.0×10^3	-3
5	Hydronium ion (H_3O^+)	55	-1.74
6	Nitric acid (HNO_3)	28.2	-1.45
7	Trifluoroacetic acid (CF_3COOH)	5.62×10^{-1}	0.25
8	Oxalic acid (HOOC–COOH)	5.37×10^{-2}	1.27
9	Acetic acid (CH_3COOH)	1.75×10^{-5}	4.76

$[H^+] > [OH^-]$

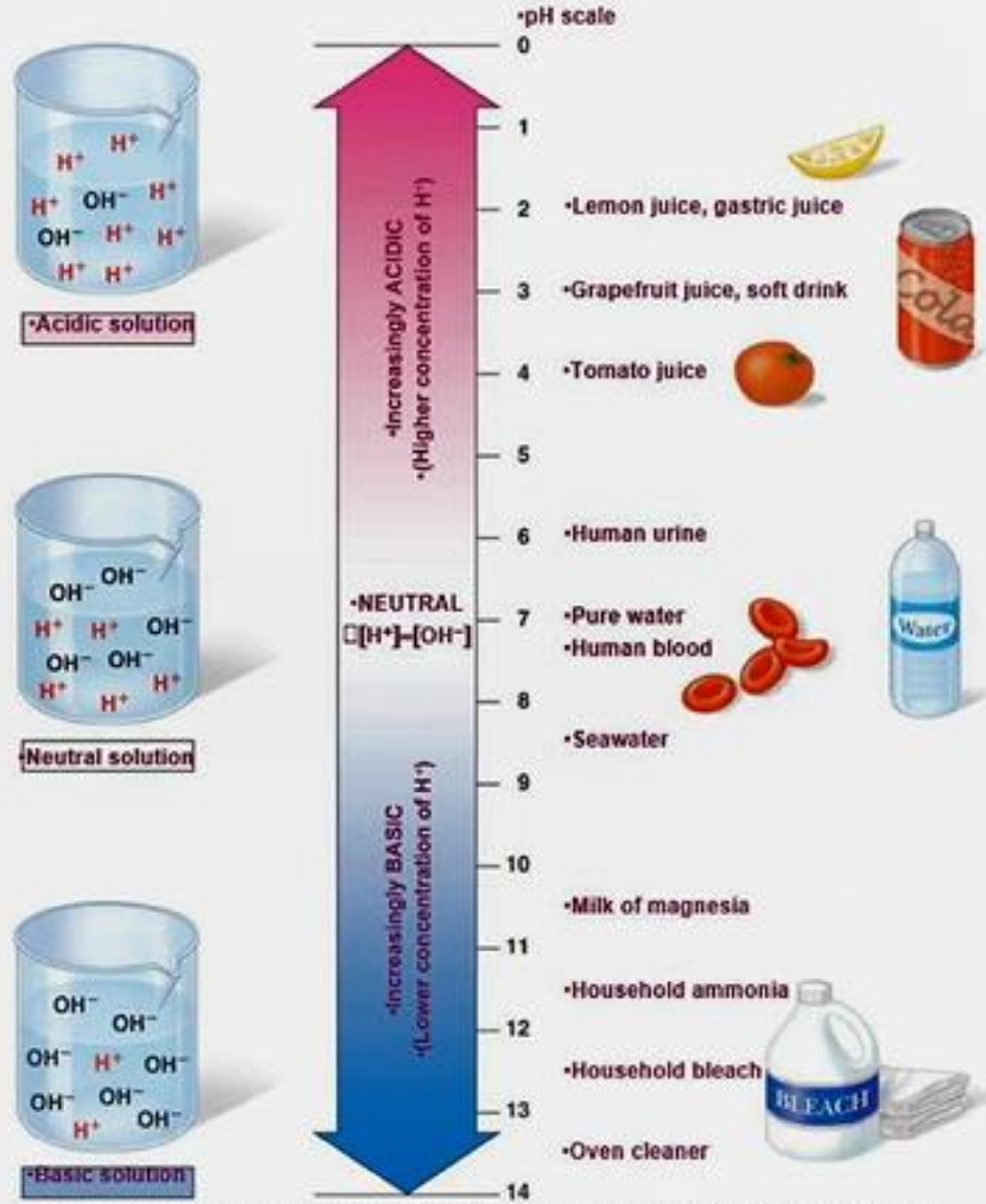
pH<7

$[H^+] = [OH^-]$

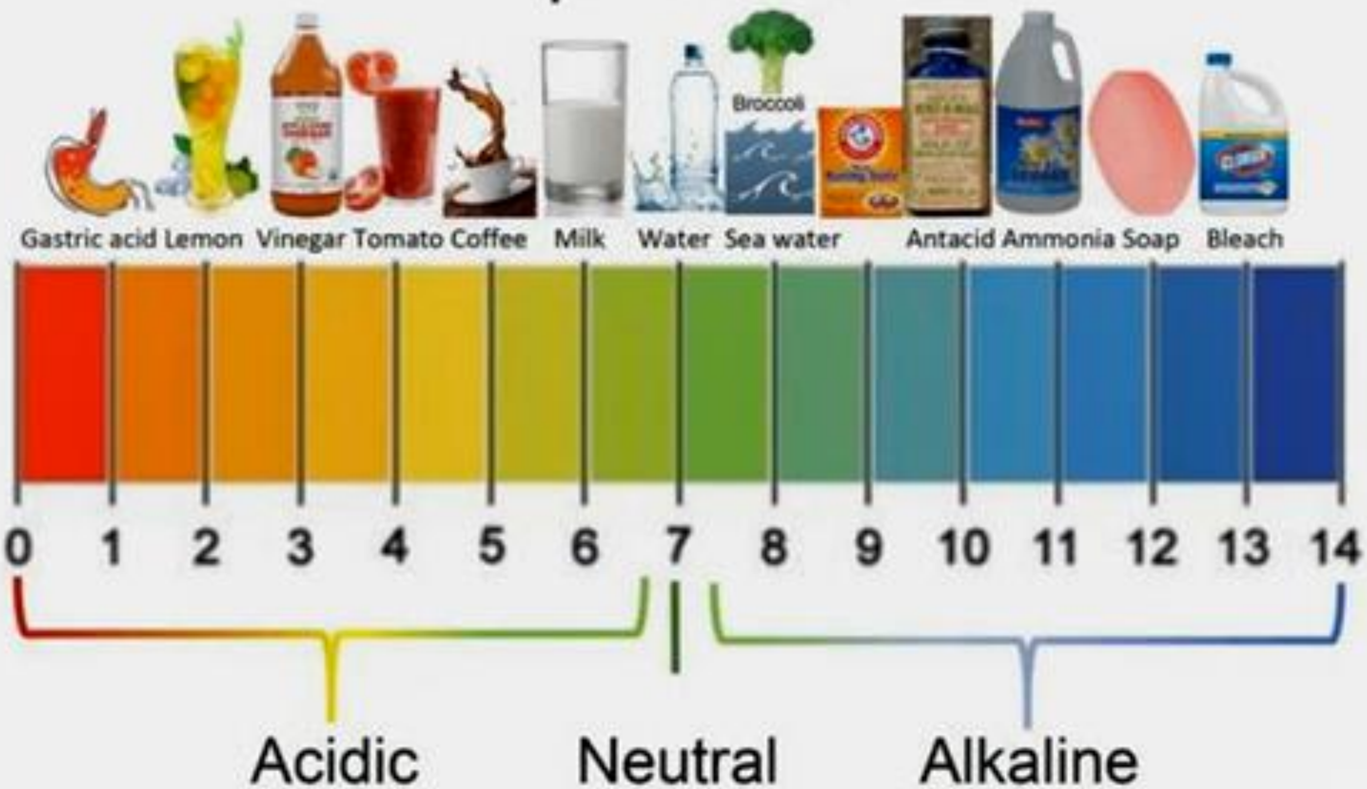
pH=7

$[H^+] < [OH^-]$

pH>7



pH Scale


Gastric acid
Lemon
Vinegar
Tomato
Coffee
Milk
Water
Broccoli
Sea water
Antacid
Ammonia
Soap
Bleach
0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
Acidic
Neutral
Alkaline

Buffers

- Function of buffers:
  1. Aqueous systems that resist changes in pH when small amounts of a strong acid or base are added.

- A buffered system:
  1. Consist of a weak acid and its conjugate base.
  2. The most effective buffering occurs at the region of minimum slope on a titration curve (i.e. around the pKa).

- Effectiveness of buffer solution:
  1. Are effective at pHs that are within +/-1 pH unit of the pKa.

Henderson-Hasselbalch Equation

$HA = [H^+] + [A^-]$

HA = weak acid
A^- = Conjugate base

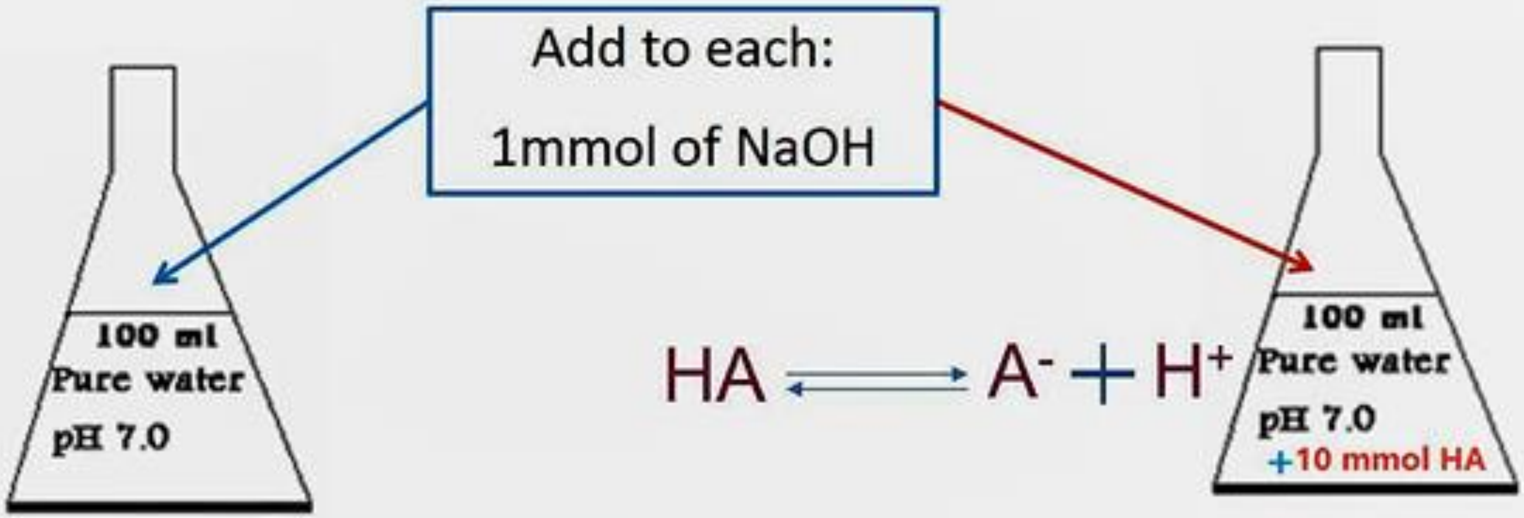
- 1) $K_a = \frac{[H^+][A^-]}{[HA]}$
- 2) $[H^+] = K_a \frac{[HA]}{[A^-]}$
- 3) $-\log[H^+] = -\log K_a - \log \frac{[HA]}{[A^-]}$
- 4) $-\log[H^+] = -\log K_a + \log \frac{[A^-]}{[HA]}$
- 5) $pH = pK_a + \log \frac{[A^-]}{[HA]}$

H-H equation describes the relationship between pH, pKa and buffer concentration

- When: $[HA] = [A^-]$

  ☞ pH = pKa

Comparison of buffered and unbuffered solutions



- $[OH^-]$ = 1.0 mmol/100ml

  = 0.01M

  pOH = - log $[OH^-]$ = 2.00

  pH = 12.0
- The change of pH is from 7.0 to 12.0 or 5 units.

1.0 mmol of OH^- reacts with 1.0 mmol of HA.

- ➢ mmol of HA decreases to 9.0.
- ➢ mmol of A^- increases to 11.0.

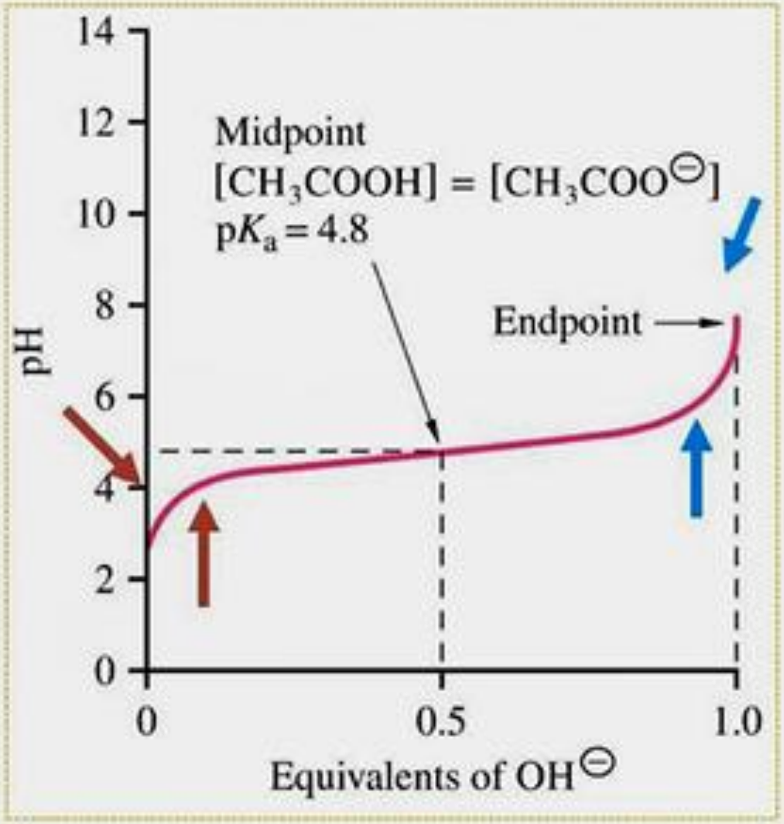
  pH = 7.0 + log 11/9

  pH = 7.09
- The change of pH is only from 7.00 to 7.09 or 0.09 units.

You can use H-H equation to draw titration curve

If 1% NaOH added:

- $pH = pK_a + \log_{10} \frac{[0.01]}{[0.99]}$
- $pH = 4.76 - 2.00$
- $pH = 2.76$



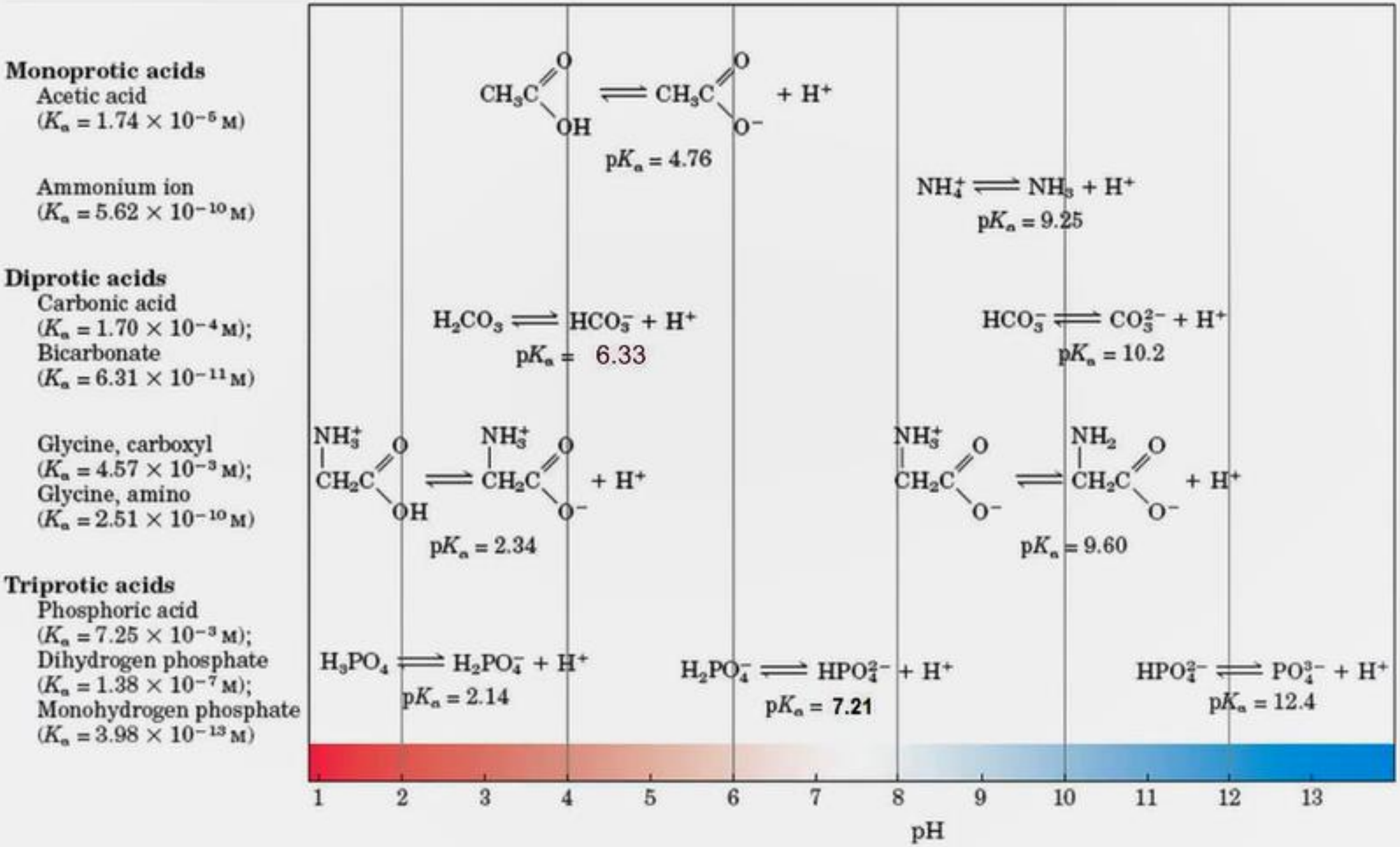
If 99% NaOH added:

- $pH = pK_a + \log_{10} \frac{[0.99]}{[0.01]}$
- $pH = 4.76 + 2.00$
- $pH = 6.76$

If 50% NaOH added:

- $pH = pK_a + \log_{10} \frac{[0.5]}{[0.5]}$
- $pH = 4.76 + 0$
- $pH = 4.76 = pK_a$

Types of acids



Titration curve

$$HA = [H^+] + [A^-]$$

$$K_a = \frac{[H^+][Ac^-]}{[HAc]}$$

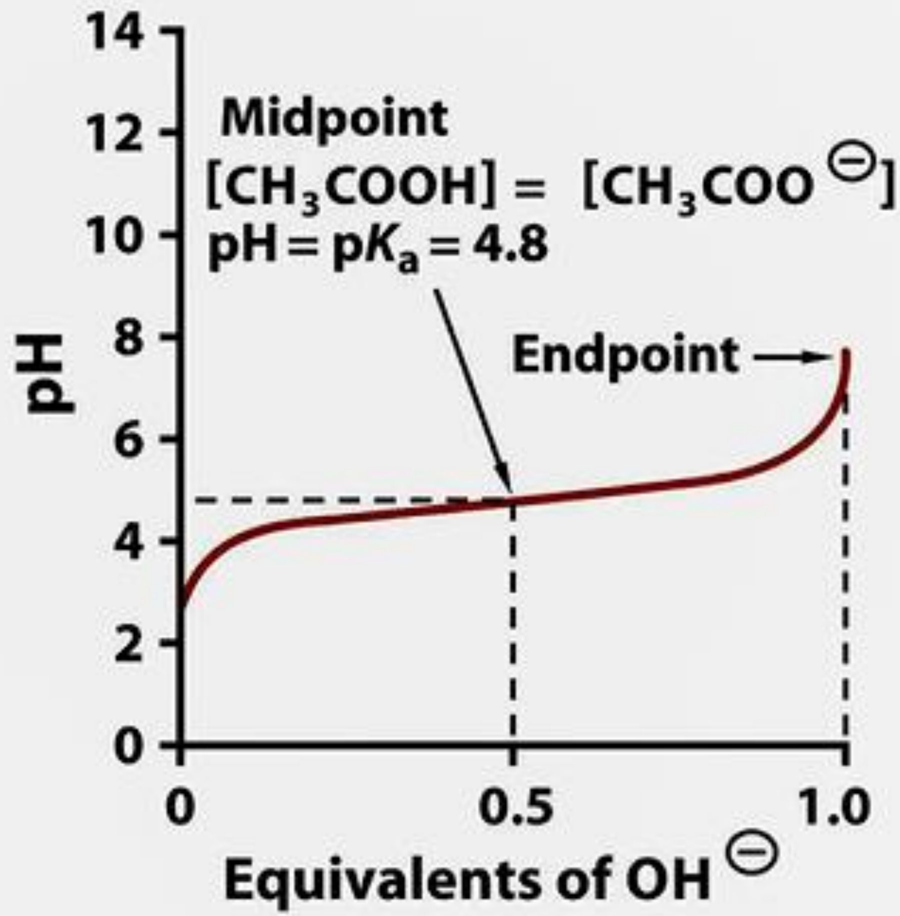
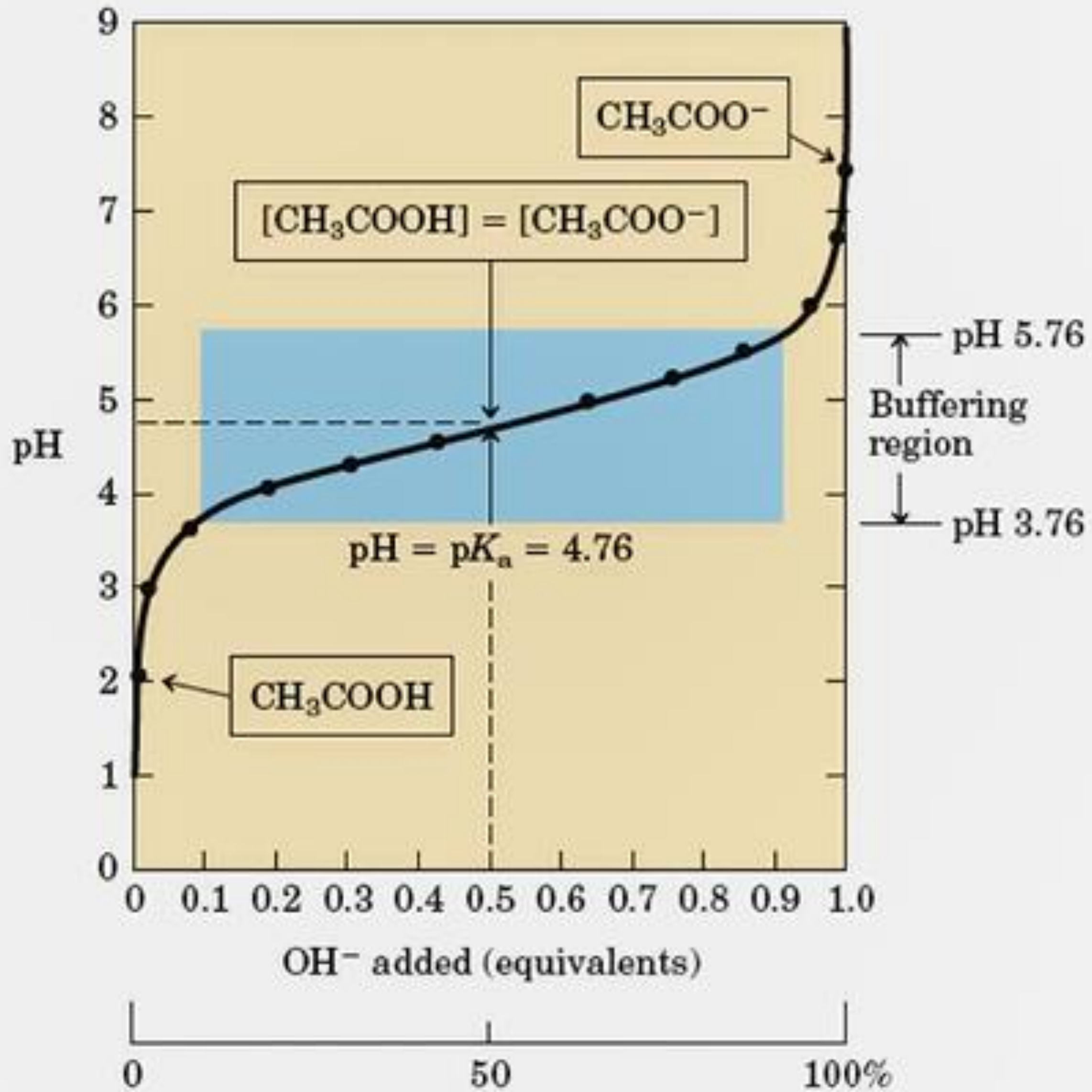
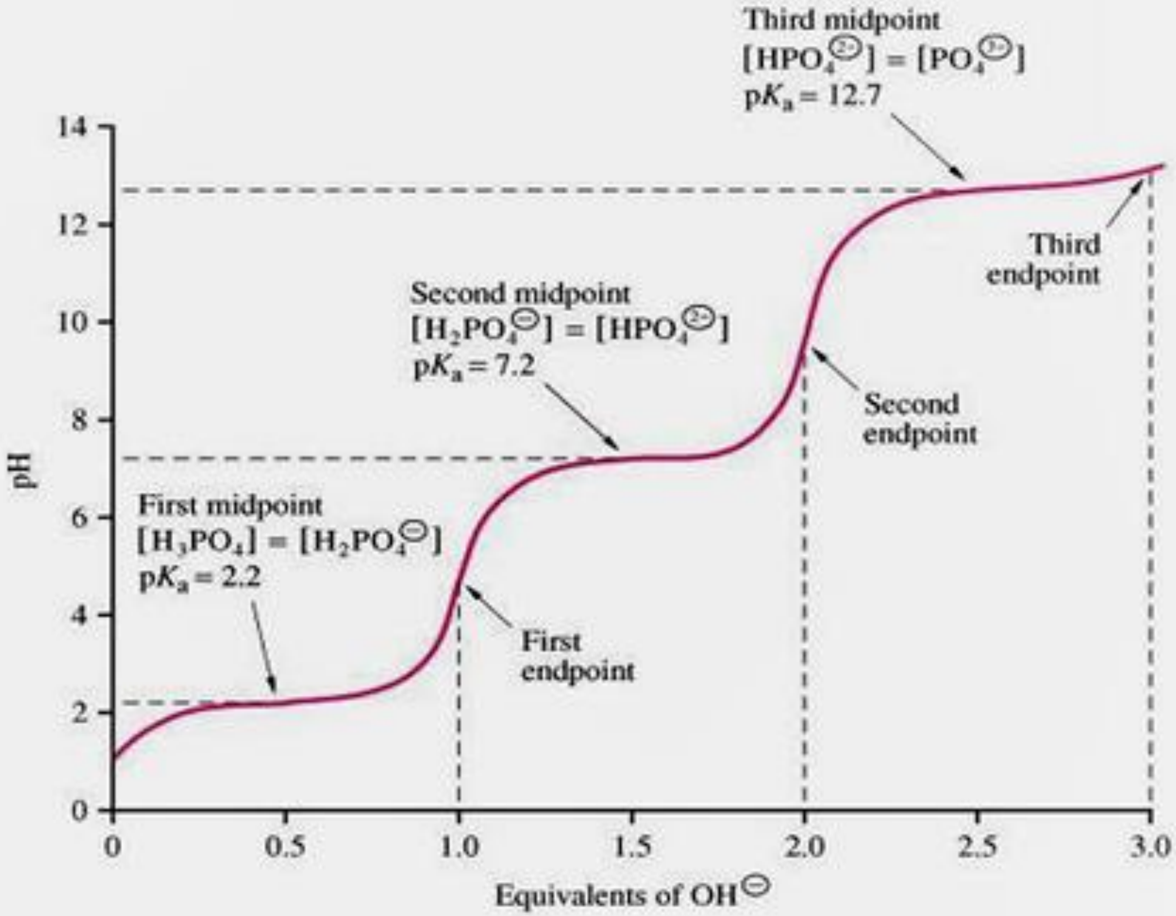


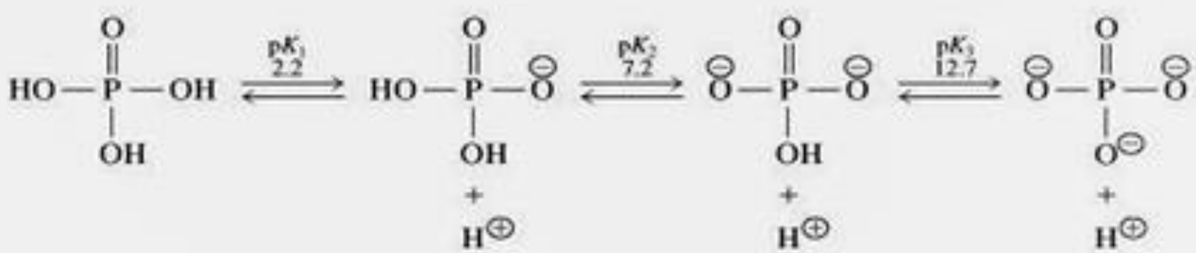
Figure 2-16 Principles of Biochemistry, 4/e

pKa values determined by titration



Phosphate has three ionizable H^+ and three pKas

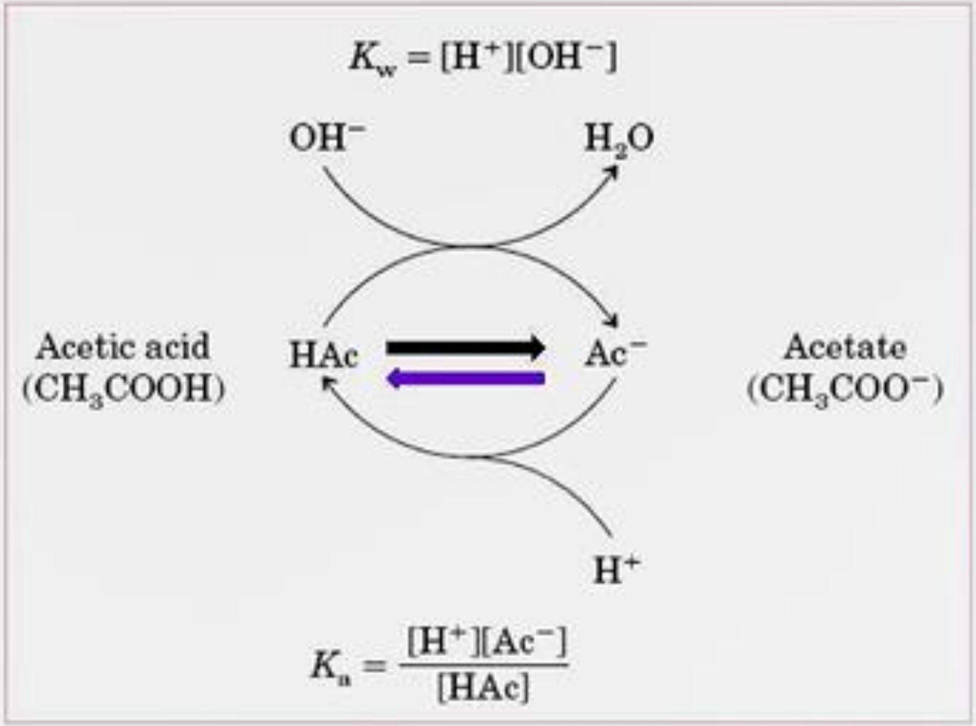




(2.19)

How does a buffer system work?

- Buffering results from two reversible reaction equilibria.
- It occurs in a solution of nearly equal concentrations of a proton donor and its conjugate proton acceptor.
- The decrease in concentration of one component of the system is balanced exactly by an increase in the other.



Titration can be used to calculate the concentration of a known acid

- Suppose you have 50 ml of HCl. But you do not know its concentration. You can put a drop of phenolphthalein (a pH indicator) and titrate with 0.5 M NaOH till the endpoint. At the endpoint (which is determined but a color change) you must record the total volume of NaOH that is used. You can then use the following equation to find the concentration of your acid. If 25 ml of NaOH solution was used for complete titration:

M=molarity

$$M=\frac{moles}{L}$$

$$M_{HCl} \cdot V_{HCL} = M_{NaOH} \cdot V_{NaOH}$$

$$M_{HCl} \times (50) = 0.5 \times 25$$

$$M_{HCl} = 0.25\ M$$

$$Moles = \frac{weight\ of\ substance\ (grams)}{Molecular\ weight\ of\ that\ substance\ (MW)}$$

weight of HCL in grams=0.25 x MW (which is 36.5)

What if the acid is diprotic or triprotic?

Suppose you have 50 ml of H2SO4. But you do not know its concentration. You can put a drop of phenolphthalein (a pH indicator) and titrate with 0.5 M NaOH till the endpoint. At the endpoint (which is determined by a color change) you must record the total volume of NaOH that is used. You can then use the following equation to find the concentration of your acid. If 25 ml of NaOH solution was used for complete titration:

- We know that sulfuric acid reacts with NaOH in the 1:2 ratio, so we can write:

$$2NaOH + H_2SO_4 \rightarrow Na_2SO_4 + 2\,H_2O$$

$$2M_{\,H2SO4} \cdot V_{\,H2SO4} = M_{\,NaOH} \cdot V_{\,NaOH}$$

$$2M_{\,H2SO4}\ x\ (50) = 0.5\ x\ 25$$

$$M_{\,H2SO4} = \frac{M_{\,NaOH} . V_{\,NaOH}}{2(V_{\,H2SO4})} = \frac{0.5\ x\ 25}{2\ (50)} = 0.125$$

So, the weight of H2SO4 in grams=0.125 x MW

What if the acid is diprotic or triprotic

Suppose you have 50 ml of $H2SO4$. But you do not know its concentration. You can put a drop of phenolphthalein (a pH indicator) and titrate with 0.5 N NaOH till the endpoint. At the endpoint (which is determined by a color change) you must record the total volume of NaOH that is used. You can then use the following equation to find the concentration of your acid. If 25 ml of NaOH solution was used for complete titration:

- Then you need to use normality instead of molarity.

$$N_{H2SO4} \cdot V_{H2SO4} = N_{NaOH} \cdot V_{NaOH}$$

$$N_{H2SO4} \times (50) = 0.5 \times 25$$

$$N_{HCl} = 0.25\ N$$

N=normality

$$N = \frac{Equivalents}{L}$$

$$Equivalents = \frac{weight\ of\ substance\ (grams)}{Molecular\ weight\ of\ that\ substance\ (MW)/n}$$

n = number of hydrogens an acid can release. n=2 for H2SO4

So, the weight of H2SO4 in grams=0.25 x MW/2 (or 98/2=49)

Molarity vs. Normality

$$\text{Normality} = \text{Molarity} \times n$$

- where n is the number of H^+ ions (for acids) or OH^- ions (for bases) per molecule. For example, sulfuric acid (H_2SO_4) has a basicity of 2, so its normality is twice its molarity.

Cell membrane is hydrophobic

بدن یک سیستم پیچیده است

اساساً یک محیط آبی (مائی)

در عین حال پر است از مقدار زیادی چربی

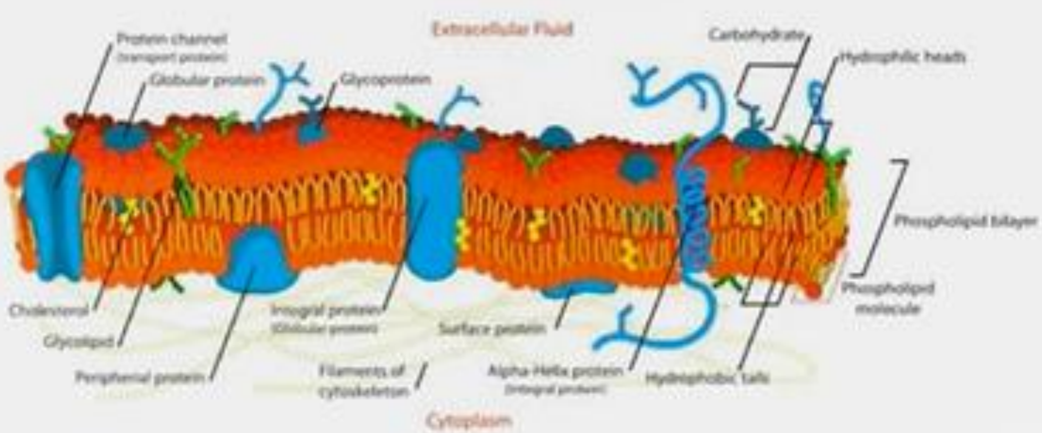
غشاءها، بافتها، سلولها، و غیره

داروها باید حل بشوند تا بتوانند به درون خون و بافتها وارد شوند.

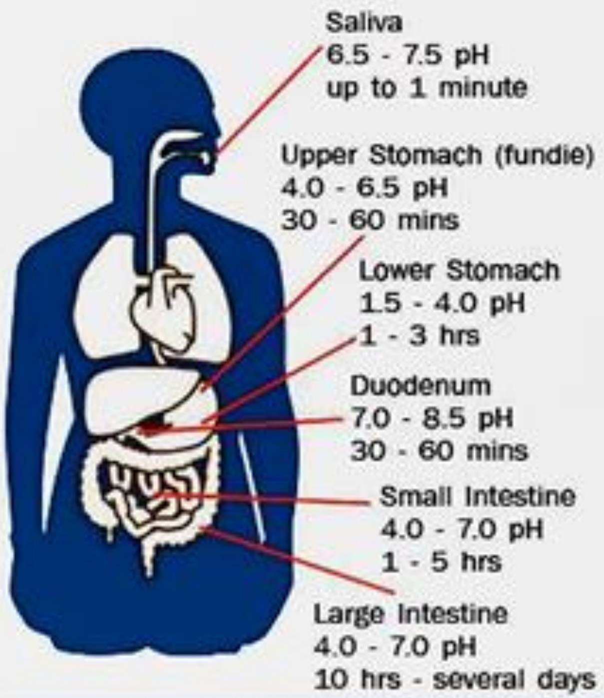
دو محیط در بدن وجود دارند))

محیط آبی (آب یک مولکول قطبی است و می تواند مولکول های قطبی را در خود حل کند)

محیط چربی: لیپیدها یا چربی ها مولکول های غیر قطبی هستند و می توانند مولکولهای غیر قطبی را در خود حل کنند.



pH environment in the GI tract



This diagram illustrates the average time food spends in each part of the digestive system along with the average pH.

- The **pH** is a way of measuring how acidic or alkaline the body is.
- The pH in the human digestive tract varies greatly (see Human Digestive Tract pH Range Chart on the left side).
- The pH of saliva is usually between 6.5 – 7.5.
- After we chew and swallow food it then enters the fundic or upper portion of the stomach which has a pH between 4.0 – 6.5.
- This is where "predigestion" occurs while the lower portion of the stomach is secreting hydrochloric acid (HCl) and pepsin until it reaches a pH between 1.5 – 4.0.
- After the food mixes with these juices, it then enters the duodenum (small intestine) where the pH changes to 7.0 – 8.5.
- This is where 90% of the absorption of nutrients is taken in by the body while the waste products are passed out through the colon (pH 4.0 – 7.0).

WEAKLY ACIDIC DRUGS		
Amoxicillin	Ibuprofen	Phenytoin
Acetazolamide	Levodopa	PTU
Aspirin	Methotrexate	Salicylic acid
Chlorothiazide	Warfarin	Sulfadiazine
Ciprofloxacin	Methyldopa	Sulfapyridine
Cephalexin	Penicillamine	Theophylline
Ethacrynic Acid	Pentobarbital	Tolbutamide
Furosemide	Phenobarbital	
WEAKLY BASIC DRUGS		
Alprenolol	Ephedrine	Morphine
Allopurinol	Epinephrine	Nicotine
Amphetamine	Imipramine	Norepinephrine
Atropine	Lidocaine	Pilocarpine
Chlorpheniramine	Methadone	Pseudoephedrine
Cocaine	Methamphetamine	
Diazepam	Methyldopa	
Diphenhydramine	Metoprolol	

Table 1: Drugs with corresponding pKa values

Drug	Nature	pK_a
Acetyl salicylic acid	Acid	3.49
Benzyl penicillin	Acid	2.76
Ethosunamide	Acid	9.3
Chlorpropamide	Acid	4.8
Sulfadrazine	Acid	6.48
Dephenghydantoin	Acid	8.3
Atropine	Base	9.65
Amphetamine	Base	9.8
Lignocaine	Base	7.9
Procaine	Base	8.8
Tetracycline	Base	3.3, 7.8, 9.7

Some common drugs that are weak acids

- Commonly used drugs that are weak acids include paracetamol, propofol, and thiopentone.
- Weak acids are better absorbed in the stomach due to the acidic environment, where they become less charged. Other examples of drugs that act as weak acids are barbiturates.
- Understanding whether a drug is a weak acid or base is important because it influences how the body absorbs and processes the drug, affecting its efficacy and how quickly it is eliminated.

- Levodopa (2.3)
- Amoxycillin (2.4)
- Aspirin (3.5)
- Cephalexin (3.6)
- Frusemide (3.9)
- Warfarin (5.0)
- Acetazolamide (7.2)
- Phenytoin (8.4)

Pka
of acid drug or base drug

pH of the environment lower than pKA

pH of the environment higher than pKA

Acid drug:
contains -COOH

-COOH

-COO^-

Base drug:
contains –NH2

-NH_3^+

-NH_2

نمونه سوال

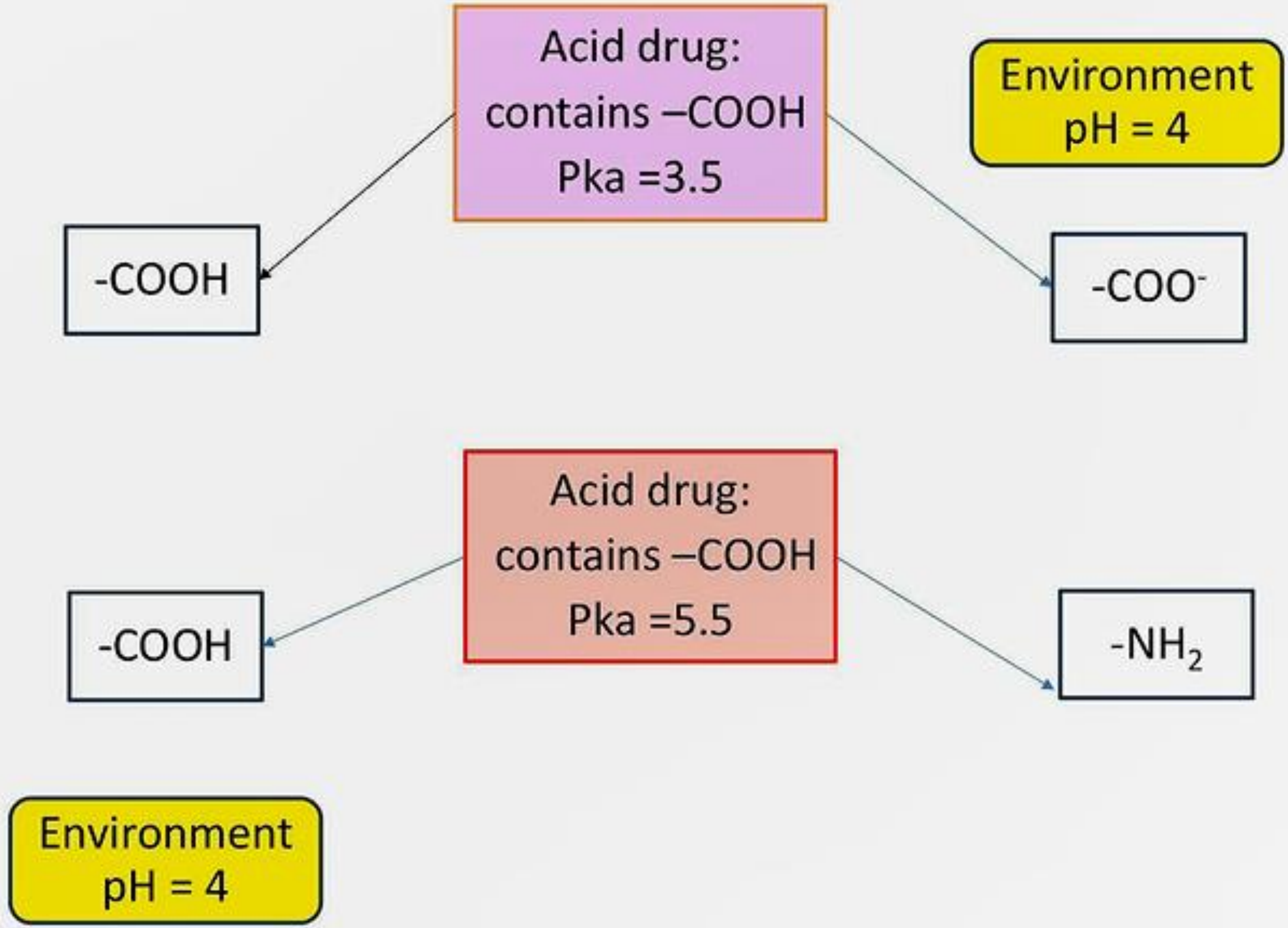
از میان دو داروی اسیدی ضعیف Drug A pKa = 3.5 و Drug B pKa = 5.5، کدامیک در محیط با pH = 4.0 بهتر جذب خواهد شد؟

الف- داروی A

ب- داروی B

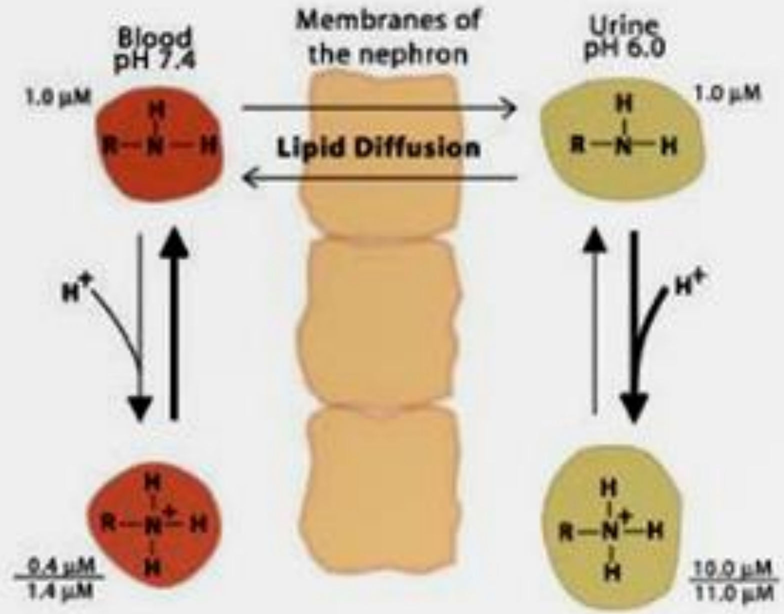
ج- هر دو به یک اندازه جذب می‌شوند

د- هر دو در روده بهتر جذب می‌شوند


Acid drug:
contains –COOH
Pka =3.5
Environment
pH = 4
-COOH
$-COO^-$
Acid drug:
contains –COOH
Pka =5.5
-COOH
$-NH_2$
Environment
pH = 4

Cell membrane and drugs

- Bilayer of amphipathic lipids with the hydrophobic chains pointing inwards and the hydrophilic heads pointing outwards.
- **like dissolves like**, thus charged (ionized) molecules will have a difficult time crossing this bilayer with uncharged (non-ionized) molecules crossing more easily.
- Urine pH
- tends to be acidic but pH ranges from 4.6 - 8.



Thank you