Medical chemistry

Autumn 2010

Recommended textbooks:

Táborská, Sláma: Medical Chemistry I (General and Inorganic Chemistry) Brno 2006

Dostál: Medical Chemistry II (Organic Chemistry) Brno 2006

Lecture files (ppt,pdf).

Solutions of electrolytes

Acid-base reactions

- acid-base theory (recapitulation)
- pH of acids and bases (recapitulation)
- hydrolysis of salts (recapitulation)
- buffers

Terms from the secondary school chemistry that is necessary to repeat to understand the lecture topics:

- electrolytes, their types and properties
- chemical equilibrium, equilibrium constant
- acids, bases, conjugate pairs
- autoprotolysis of water, pH
- strong and weak acids and bases
- calculation of pH of strong and weak acids

These terms are included in the textbook Medical chemistry I

Electrolytes and non-electrolytes

when a compound dissolves in water

Molecules are not changed

↓

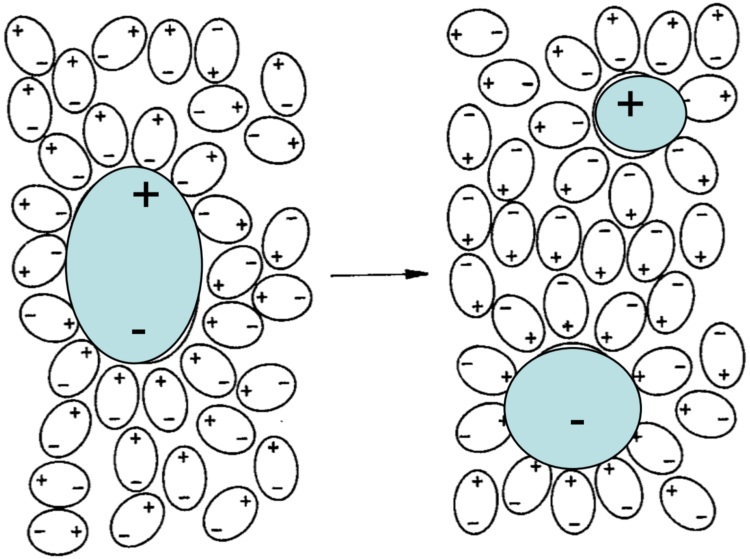
Nonelectrolyte

Dissociation to ions

↓

Electrolyte

Electrolytes



ions are surrounded by a certain number of water molecules (hydrated).

Compounds that dissolve in water with the formation of ions.
Electrolytes are ionic compounds or polar molecular compounds

Classification of electrolytes

Strong electrolytes

They are 100% ionized (fully dissociated)

Weak electrolytes

There is an equilibrium between ions and molecules

Characterization of electrolytes

Strong electrolytes: $AB(s) \xrightarrow{H_2O} A^+(aq) + B^-(aq)$

$NaCl(s) \rightarrow Na^+(aq) + Cl^-(aq)$

Dissociation is complete

Weak electrolytes: $AB(s) \xrightarrow{H_2O} AB(aq) \leftrightarrows A^+(aq) + B^-(aq)$

$HCN(g) \rightarrow HCN(aq) \leftrightarrows H^+(aq) + CN^-(aq)$

Dissociation is partial

Compare arrows in dissociation equations:

Strong electrolyte →

Weak electrolyte ⇆

Electrolytes

Strong

Strong acids

(HCl, HBr,HI, H_2SO_4, HNO_3, $HClO_4$, …………)

Strong hydroxydes

($NaOH$, KOH, $Ca(OH)_2$, $Mg(OH)_2$…

All salts

Na_2SO_4, $NaCl$, K_2CO_3, $FeCl_3$……….

Weak

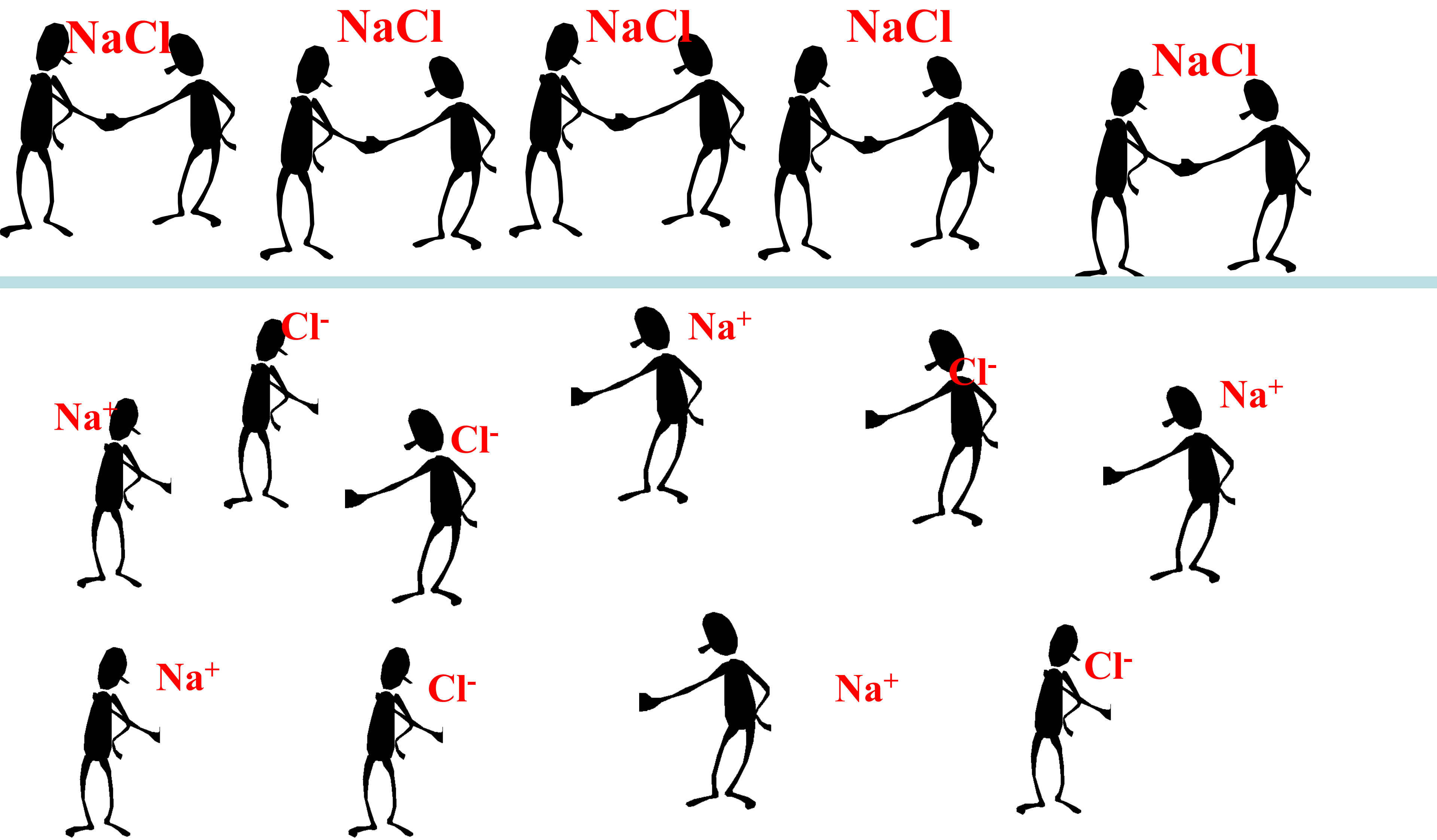
Weak acids

CH_3COOH, H_2CO_3, HNO_2…

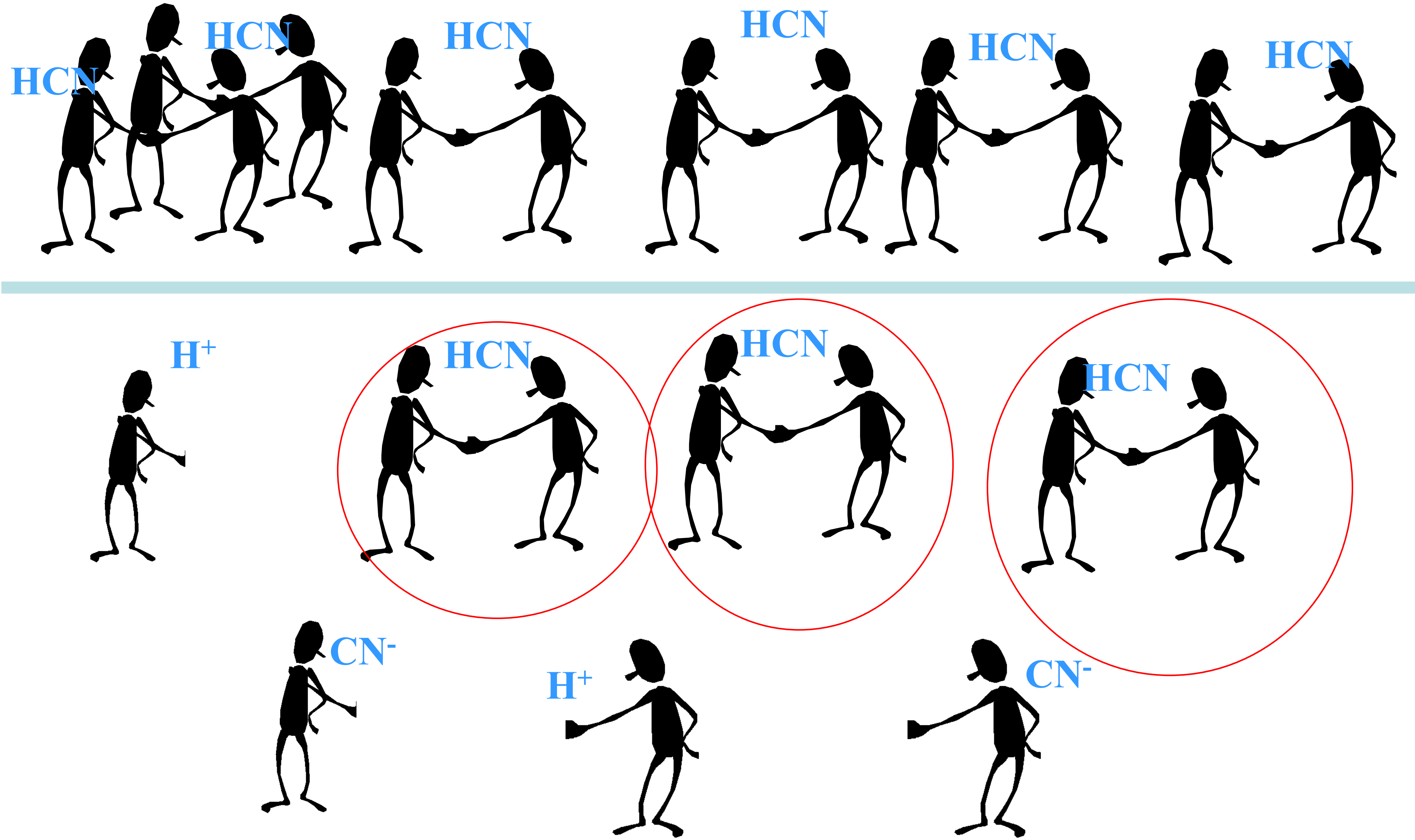
Weak bases

$Fe(OH)_3$, NH_3, $C_6H_5NH_2$…..

Strong electrolytes



Weak electrolytes



Examples

Nonelectrolyte	Strong electrolyte	Weak electrolyte
Ethanol	HCl	H_2CO_3
Urea	H_2SO_4	CH_3COOH
Glucose	NaOH	NH_3
Aceton	$Ca(OH)_2$	$Mg(OH)_2$
Sucrose	NaCl	HCN
Glycerol	Na_2SO_4	pyridine

Acids and bases according to Brønsted concept

Acid: molecule or ion that can lose a proton H^+

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

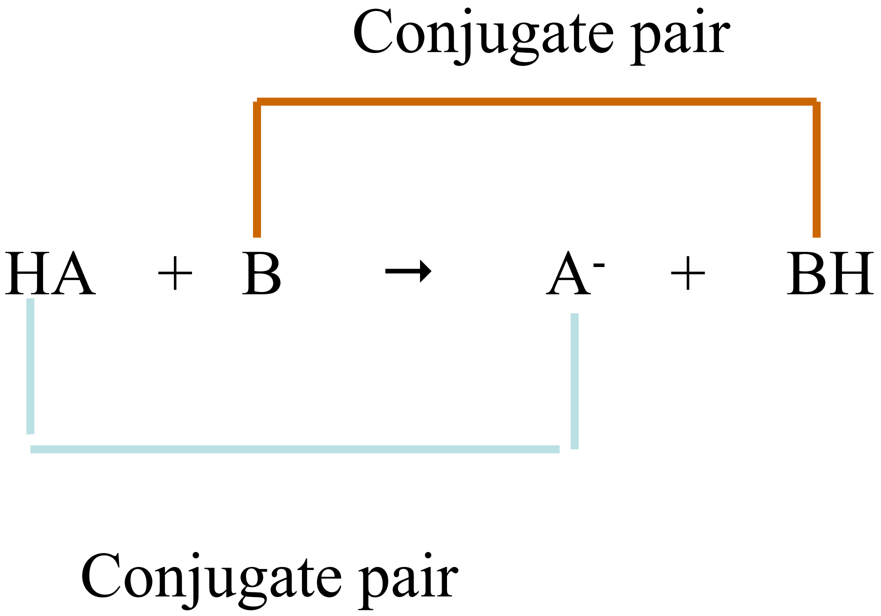
acid conjugate base

Base: molecule or ion that can bind a proton H+

$B + H^+ \rightarrow BH^+$

base conjugate acid

Conjugate pair acid/base



Conjugate pair

$$HA \quad + \quad B \quad \rightarrow \quad A^{-} \quad + \quad BH$$

Conjugate pair

Acids and bases in water

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

Water behaves as a base

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

Water behaves as an acid

pH

Acidity of a medium is assessed according to the concentration of hydrogen cations

$$pH = -\log\left[H^{+}\right]$$

similarly

$$pOH = -\log\left[OH^{-}\right]$$

$$\Downarrow$$

$$14 = pH + pOH$$

pH values of some body fluids

Body fluid	pH
Blood plasma	7,34 - 7,43
Urine	4,8 - 7,5
Gastric juice	≈ 2
Pancreatic juice	7,5 - 8,8
Intracelular fluid (liver cells)	6,4 - 6,5
Saliva	7 - 8

pH of strong acids and strong hydroxides solutions

Strong acid and strong hydroxides are **strong electrolytes** that are fully dissociated in aqueous solutions.

Dissociation of a strong acid: $HA + H_2O \rightarrow H_3O^+ + A^-$

The concentration **$[H^+]$** is equal to the total strong acid concentration **c_{HA}** :

$$[H^+] = c_{HA} \quad \text{and} \quad pH = -\log [H^+] = -\log c_{HA}$$

Dissociation of a strong hydroxide: $MeOH(aq) \rightarrow Me^+ + OH^-$

In solutions of monobasic **strong hydroxides**,

$$[OH^-] = c_{MeOH}, \quad pOH = -\log [OH^-] = -\log c_{MeOH},$$

$$\text{and} \quad pH = 14 - pOH$$

pH of weak acids and bases

What pH has vinegar ?

What pH has a solution of vitamin C?

Why can I drink solutions of carbonic and phosphoric acid, but not hydrochloric acid?

Disssociation of weak acids and bases

Weak monoprotic acid

Weak monobasic base

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

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

equilibrium constant of ionization

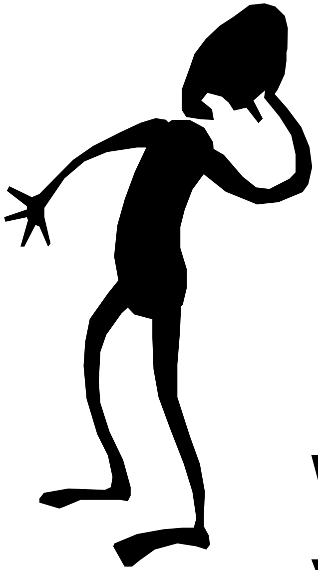
$$K_c = \frac{[H_3O^+].[A^-]}{[HA].[H_2O]}$$

$$K_c = \frac{[BH^+].[OH^-]}{[B].[H_2O]}$$

acid and base ionization constant

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

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



K_A – acid ionization constant

K_B – base ionization constant

$$pK = -\log K$$

What does express the pK_A (pK_B) values ?

The **lower** the value of pK_A, the **stronger is the weak acid**.

pK ~

1- 3……………moderately strong

4-8………………weak

>8………………very weak

pK_A values of weak acids

Kyselina	pK_{A1}	pK_{A2}	pK_{A3}
$(COOH)_2$	1,25	4,3	
HNO_2	2,29		
H_3PO_4	2,16	7,2	12,3
CH_3COOH	4,76		
H_2CO_3	6,35	10,3	
H_2S	7,07	12,2	
H_3BO_3	9,24	12,7	

pK_B values of weak bases

Báze	pK_B	pK_A
guanidin	1,50	12,5
methylamin	3,36	10,64
amoniak	4,75	9,25
imidazol	6,90	7,1
pyridin	8,82	5,18
anilin	9,38	4,62
kofein	13,40	0,6

Relation between K_A a K_B (pK_A a pK_B)

$$K_A \,.\, K_B = K_v = 1.\ 10^{-14}$$

$$\boxed{pK_A + pK_B = 14}$$

Calculation of pH of weak acids and bases

Weak monoprotic acid

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

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

$$pH = \tfrac{1}{2}\, pK_A - \tfrac{1}{2} \log c_A$$

Weak monobasic base

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

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

$$pOH = \tfrac{1}{2}\, pK_B - \tfrac{1}{2} \log c_B$$

$$pH = 14 - \tfrac{1}{2}\, pK_B + \tfrac{1}{2} \log c_B$$

Strong and weak acid with the same concentration– comparison of pH

HCl c=0,1 mol/l

$$pH = -\log c_{HA} = -\log 0{,}1 = \mathbf{1}$$

CH_3COOH c=0,1 mol/l $\quad pK_A = 4{,}7$

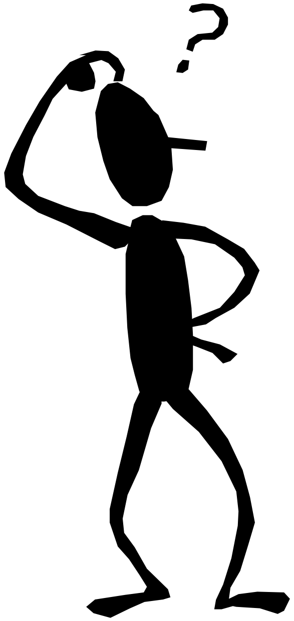
$$pH = \tfrac{1}{2}\, pK_A - \tfrac{1}{2} \log c_{HA}$$

$$pH = 2{,}35 + 0{,}5 = \mathbf{2{,}85}$$

Why soap has alkaline reaction?

Why solution of soda (Na_2CO_3) is alkaline?

Why solution of Na_3PO_4 is alkaline?



Hydrolysis of salts

Salts are formed in reaction between an acid and base – neutralization.

The final pH of a solution after the neutralization reaction is not always neutral.

This is because some salts undergo to hydrolysis

Differences in properties of ions

Cl^- CH_3COO^-

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

Cl^- is a spectator anion, it does not react with water

CH_3COO^- is an anion of weak acid, it tends to react with water and form acetic acid.

Such amount of CH_3COOH will be formed, to be in equilibrium with CH_3COOH given by ionization constant

Reactions of salts in water

examples

Example 1:

CH_3COONa – sodium acetate

(salt of weak acid CH_3COOH and strong hydroxide NaOH)

1. Dissociation

$$CH_3COONa \rightarrow CH_3COO^- + Na^+$$

2. Hydrolysis of the anion of weak acid

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

↓

pH is slightly alkaline

Example 2:

NH_4Cl – ammonium chloride

(salt of weak base NH_3 and strong acid HCl)

1. Dissociation

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

2. Hydrolysis of cation of weak base

$$NH_4^+ + H_2O \leftrightarrows H_3O^+ + NH_3$$

⬇

pH is slightly acidic

Example 3:

$CuCl_2$ – copper (II) chloride

(salt of Cu^{2+} cation derived from weak $Cu(OH)_2$ and strong HCl)

1. Dissociation

$$CuCl_2 \rightarrow Cu^{2+} + 2Cl^-$$

2. Hydration of a metal cation

$$Cu^{2+} + 6\ H_2O \rightarrow [Cu(H_2O)_6]^{2+}$$

3. Hydrolysis of hydrated cation

$$[Cu(H_2O)_6]^{2+} + H_2O \leftrightarrows [Cu(H_2O)_5OH]^+ + H_3O^+$$

↓

pH is slightly acidic

Example 4:

NH_4NO_2

(salt of weak base NH_3 and weak acid HNO_2)

1. Dissociation

$NH_4NO_2 \rightarrow NH_4^+ + NO_2^-$

2. hydrolysis of cation of a weak base and anion of a weak acid

$NH_4^+ + H_2O \leftrightarrows NH_3 + H_3O^+$ ➡ $pH \approx 7$

$NO_2^- + H_2O \leftrightarrows HNO_2 + OH^-$ ➡

Example 5:

$NaNO_3$

(salt of strong hydroxide NaOH and strong acid HNO_3)

1. Dissociation

$NaNO_2 \rightarrow Na^+ + NO_2^-$

2. No hydrolysis of cation nor anion

$Na^+ + H_2O \leftrightarrows \times$

$NO_3^- + H_2O \leftrightarrows \times$

pH = 7

Hydrolysis of salts - summary

Complete

Composition of salt - origin of ions		
cation	anion	pH
Strong base	Strong acid	
Weak base	Strong acid	
Strong base	Weak acid	
Weak base	Weak acid	

How to maintain the constant pH of our blood?

Buffer solutions

- A **buffer solution** is a solution able to absorb a certain quantity of acid or base without undergoing a strong variation in pH

- It serves to maintain a fairly constant pH value.

Simple buffer solutions are mixtures of

a weak acid and the conjugate base of that
(e.g. acetic acid and sodium acetate)

or

a weak base and its conjugate acid
(e.g. ammonia and ammonium chloride)

Function of a buffer

Example: solution of ($CH_3COOH + CH_3COONa$)

Particles present in the solution:

CH_3COO^-	CH_3COOH	Na^+	H^+
↓	↓	↓	↓
mainly from the salt	from the acid	from the salt	from the acid

The presence of CH_3COO^- from the salt supresses dissociation of CH_3COOH

The equilibrium in the solution: $CH_3COOH \leftrightarrows CH_3COO^- + H^+$

$$K_A = \frac{[H^+]\cdot[A^-]}{[HA]} = \frac{[H^+]\cdot[CH_3COO^-]}{[CH_3COOH]} = \frac{[H^+]\cdot c_{salt}}{c_{acid}}$$

$$H^{+} = K_{A}\frac{CH_{3}COOH}{CH_{3}COO^{-}} = K_{A}\frac{c_{acid}}{c_{salt}}$$

The concentration of H^{+} ions (and also pH) depends on the ratio **of the acidic and basic component concentrations and K$_{A}$.**

The logarithmic form of that relation is known as **Henderson-Hasselbalch equation:**

$$\boxed{pH = pK_A + \log \frac{c_{Salt}}{c_{Acid}}}$$

How does the buffer work ?

- **H^+ ions of the strong acid are added to the solution:**

- concentration of H+ increases that upsets the equilibrium.

the buffer base binds most of the added H^+ ions which results in increase of the acidic buffer component

New equilibrium will settle :

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

$$K_A = \frac{[H^+] \cdot [CH_3COO^-]}{[CH_3COOH]}$$

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

[H+] increases proportionally to the increase of c_{acid} / c_{base},
pH decreases proportionally to the decrease of the log c_{base} / c_{acid} .

- **OH^- ions of the strong hydroxide are added to the solution**

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

Increase in OH– concentration withdraws H+ from the buffer acid that transforms into its conjugate base.

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

$$K_A = \frac{[H^+]\cdot[CH_3COO^-]}{[CH_3COOH]} \longrightarrow H^+ = K_A \frac{CH_3COOH}{CH_3COO^-}$$

[H+] decreases proportionally to the decrease of c_{acid} / c_{base},
pH increases proportionally to the increase of the log c_{base} / c_{acid} .

pH of a buffer

For the weak acid and its salt

with a strong base

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

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

from which

$$[H^+] = K_A \cdot \frac{c_{Acid}}{c_{Salt}} = K_A \cdot \frac{c_{Acid}}{c_{base}}$$

Salt can be considered as conjugate base to the acid

$$pH = pK_A + \log \frac{c_{Base}}{c_{Acid}}$$

Henderson-Hasselbalch equation

For weak base and its salt with the strong acid

$$pOH = pK_B + \log \frac{c_{Salt}}{c_{Base}} = pK_B + \log \frac{c_{acid}}{c_{base}}$$

⇩

$$pH = 14 - pK_B - \log \frac{c_{Salt}}{c_{Base}} = 14 - pK_B - \log \frac{c_{acid}}{c_{base}}$$

Henderson-Hasselbalch equation in general form:

$$\boxed{pH = pK_A + \log \frac{c_{Base}}{c_{Acid}}}$$

where c_{base} is the concentration of basic component and c_{Acid} the concentration of acidic component of conjugate pairs that form the buffer.

pH of a buffer depends on

$$pH = pK_A + \log \frac{c_B}{c_A}$$

pK_A value

ratio of buffer components

if $c_B/c_A = 1$

$$\Downarrow$$

$$\boxed{pH = pK_A}$$

Capacity of a buffer – expresses the effectivity of a buffer

$$\boxed{\mathrm{pH} = \mathrm{p}K_{A} + \log \frac{c_{B}}{c_{A}}}$$

Capacity is highest if **$c_B/c_A = 1$**

In sufficient buffer solutions, the ratio $c_{\mathrm{base}}/c_{\mathrm{acid}}$ should take values from 1:10 to 10:1, i.e. in the range pK_{A} 1.

Capacity depends also on the total buffer concentration

Buffer systems in human body

The pH value of blood is 7.40 ± 0.04 .

Most biological happenings occur in the pH range 6 to 8.

Blood buffer bases:	**Buffer:**
Hydrogen carbonate	$HCO_3^- / (H_2CO_3 + CO_2)$
Plasma proteins	protein / protein-H^+
Haemoglobin of red blood cells	haemoglobin / haemoglobin-H^+
Hydrogen phosphate	$HPO_4^{2-} / H_2PO_4^-$

All those buffer systems cooperate – a surplus of H^+ is accepted by all buffer bases but distributed proportionally to their concentration in blood.

Each of those four buffer systems has its own pK_A .

Hydrogencarbonate buffer

$$CO_2 + H_2O \leftrightarrows H_2CO_3 \leftrightarrows H^+ + HCO_3^-$$

- CO_2 originates from metabolism
- CO_2 dissolves in water and its small part forms H_2CO_3
- The concentration of H_2CO_3 depends on concentration of CO_2
- Instead the concentration $[H_2CO_3]$ is used effective concntration $[H_2CO_3]_{eff}$

$[CO_2 + H_2CO_3] = [H_2CO_3]_{ef}$ effective concentration

It is proportional to the partial pressure of CO_2 in blood

K_A of carbonic acid is replaced by K_{Aef}

$$K_{Aef} = \frac{[H^+]\,.\,[HCO_3^-]}{[CO_2 + H_2CO_3]} = 4{,}3\,.\,10^{-}$$

(water, 25 °C)

$pK_{Aef} = 6{,}37$

In blood (t =37 ^{o}C, higher ionic stregth)

$pK_{Aeff} = 6{,}10$

Henderson-Hasselbalch equation for hydrogencarbonate buffer in blood

$$\mathrm{pH} = \mathrm{p}K_{(H_2CO_3)} + \log \frac{[HCO_3^-]}{[CO_2 + H_2CO_3]} = 6{,}1 + \log \frac{[HCO_3^-]}{[H_2CO_3]_{ef}}$$

$$\mathrm{pH} = 6{,}1 + \log \frac{[HCO_3^-]}{pCO_2 \cdot 0{,}23}$$

parcial pressure of CO_2 in kPa

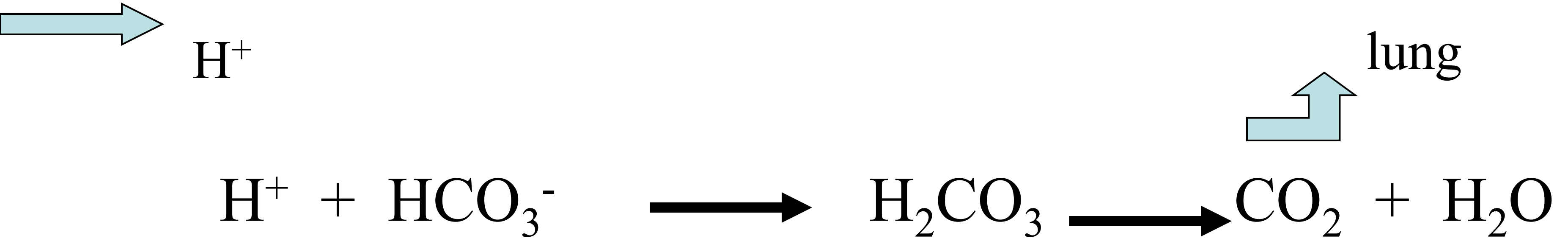
coeficient of solubility

For coefficient 0,23 and pressure in kPa is expressed in mmol/l !!!!!!

How does hydrogencarbonate buffer function?

Open system – the amount of CO_2 may be regulated by ventilation

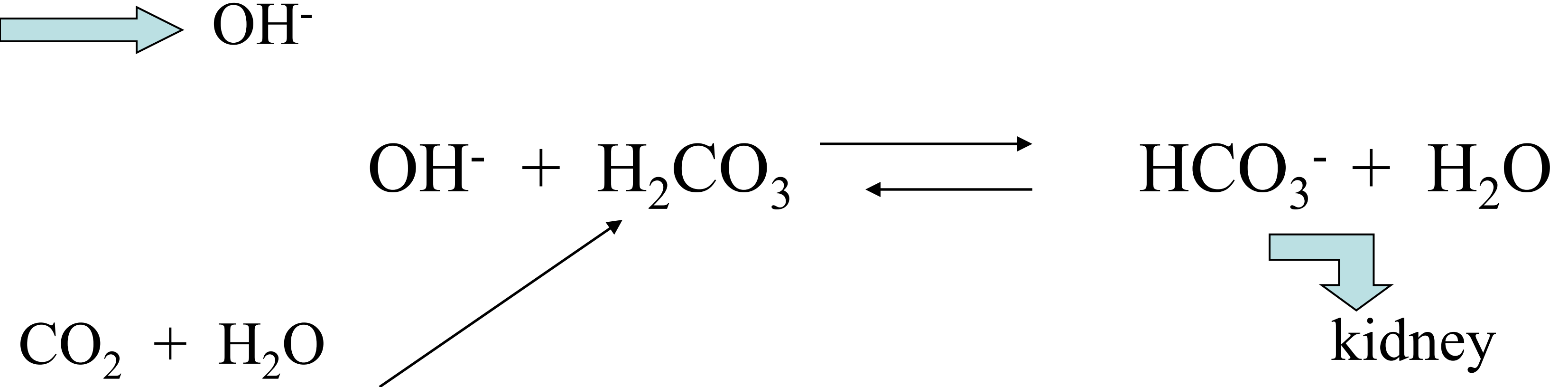
$$CO_2 + H_2O \rightleftharpoons H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$$



H^+

lung

$$H^+ + HCO_3^- \longrightarrow H_2CO_3 \longrightarrow CO_2 + H_2O$$



OH^-

$$OH^- + H_2CO_3 \rightleftharpoons HCO_3^- + H_2O$$

$CO_2 + H_2O$

kidney

Hydrogencarbonate buffer functions as open buffering system

Concentrations of both components can be regulated :

CO_2 by respiration

HCO_3^- by function of liver and kidney

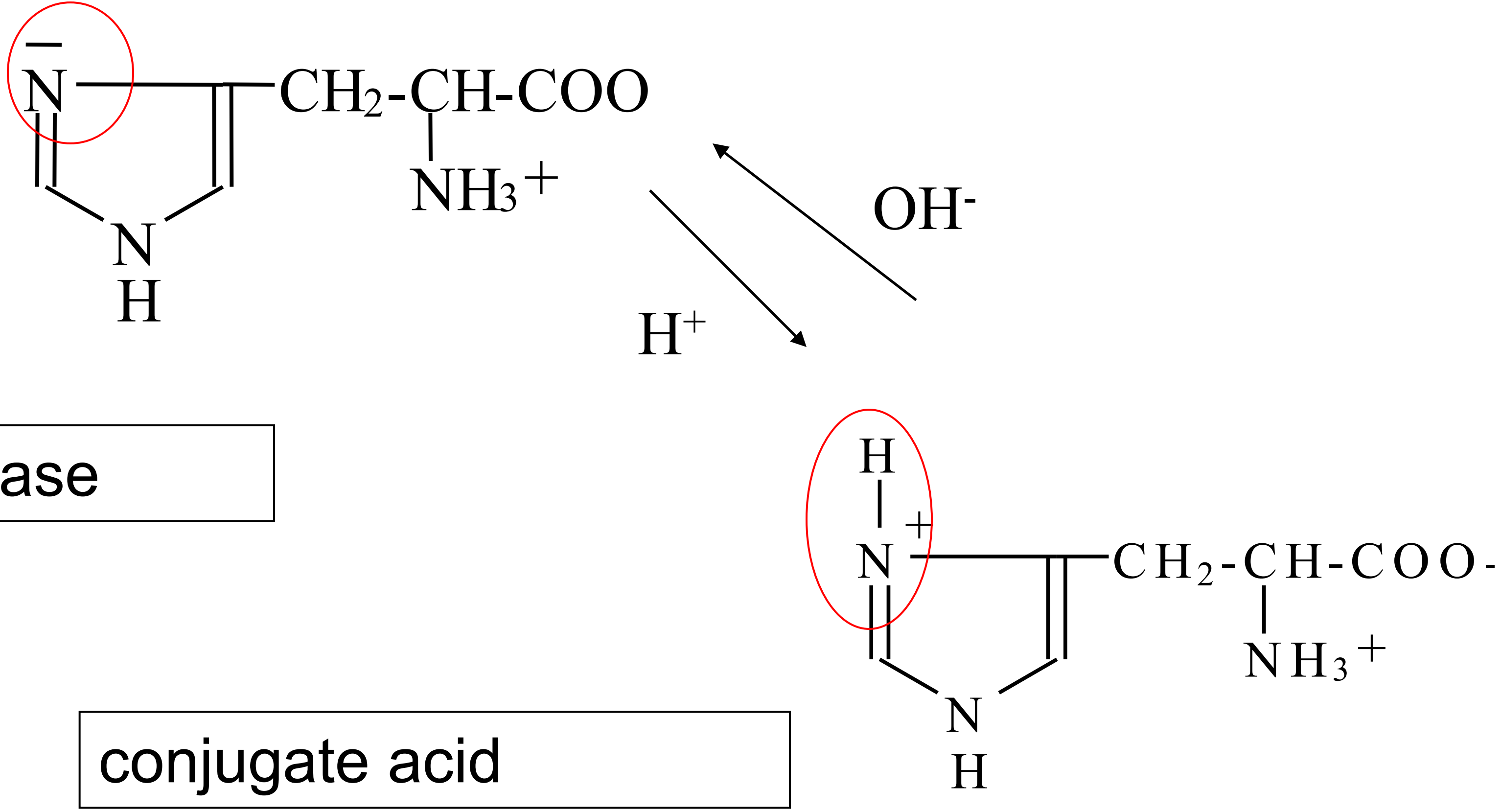
Plasma proteins and haemoglobin as buffers

In all proteins, only ionizable groups can take part in acid-base reaction
At physiological pH values, imidazol groups of histidine residues alone act as effective buffer bases.

Amino acid	**Ionizable group in the side chain**	**pK_A**
Glutamate	γ-carboxyl (-COOH)	4,3
Histidine	imidazolium	6,0
Cysteine	sulfanyl (-SH)	8,3
Tyrosine	phenolic hydroxyl	10,1
Lysine	ε-ammonium ($-NH_3^+$)	10,5
Arginine	guanidinium $–NH-C(NH_2)=NH_2^+$	12,5

The most important blood protein buffer is hemoglobin

Dissociation (protonization) of **histidine**



base

conjugate acid

Hydrogen/dihydrogenphosphate buffer

$H_2PO_4^-$ - acidic component

HPO_4^{2-} - bazic component

$pK_{A2} = 6{,}8$

$$\mathrm{pH} = 6{,}8 + \log \frac{HPO_4^{2-}}{H_2PO_4^{-}}$$

Buffer is of second-rate significance in the blood due to relatively low concentration.

However, within the cells, phosphates with proteins are the major buffer bases.