Acid-Base Balance I.

Seminar No. 9

- Chapter 21, I. part -

Homeostasis = maintenance of constant parameters of internal environment (= ECF)

- volumes of all body fluids (isovolemia)
- concentrations of cations/anions in body fluids (isoionia)
- osmolality of body fluids (isotonia)
- body temperature (isothermia)
- pH of body fluids (isohydria)

Q.

Which (general biological) factors influence the volume and distribution of body fluids?

A.

age

- newborn baby ~ 78 % TBW, adults ~ 60 % TBW

sex

- males 55-70 %, females 45-60 % (more fat in the body)

Cations and anions in plasma (average concentrations)

Cation	**Molarity (mmol/l)**	
	Cation	**Pos. charge***
Na^+	142	142
K^+	4	4
Ca^{2+}	2.5	5
Mg^{2+}	1.5	3

Total positive charge: 154

Anion	**Molarity (mmol/l)**	
	Anion	**Neg. charge***
Cl^-	103	103
HCO_3^-	25	25
$Prot^-$	2	18
HPO_4^{2-}	1	2
SO_4^{2-}	0.5	1
Org. A	4	5

Total negative charge: 154

* Molarity of charge = miliequivalents per liter (mEq/l)

Compare: Isotonic solution of NaCl

Physiological sol. 0.9 % = 9 g/l = 154 mmol/l

Na$^+$	**Cl$^-$**
154 mmol/l	154 mmol/l

Commentary - Cations and anions in plasma

- every body fluid is **electroneutral system**
- in univalent ionic species ⇒

  molarity of charge = molarity of ion (Na^+, K^+, Cl^-, HCO_3^-, lactate$^-$)
- in polyvalent ionic species ⇒

  molarity of charge = charge × molarity of ion

  Mg^{2+} ⇒ $[\text{pos. charge}] = 2 \times [Mg^{2+}] = 2 \times 1 = 2$

  SO_4^{2-} ⇒ $[\text{neg. charge}] = 2 \times [SO_4^{2-}] = 2 \times 0.5 = 1$
- proteins (mainly albumin) are at pH 7.40 polyanions
- org. acid anions (OA) – mainly lactate (AA, oxalate, citrate, ascorbate ...)
- charge molarity of proteins + OA is estimated by empirical formulas

Q.

Compare the ion composition of the plasma and ICF.

A.

Feature	**Plasma**	**ICF**
Main cation	Na^+	K^+
Main anion	Cl^-	HPO_4^{2-}
Protein content	★	★ ★ ★
Main buffer base	HCO_3^-	HPO_4^{2-}

Q.

What are the main dietary sources

of Na^+, K^+, Ca^{2+}, Mg^{2+}, Cl^- ?

A.

Ion	Main dietary source
Na^+	common (table) salt, salty products
K^+	potatoes, vegetables, dried fruits, soya flour
Ca^{2+}	milk products, (cottage) cheese, mineral waters
Mg^{2+}	green vegetable (chlorophyll)
Cl^-	common (table) salt, salty products

Q.

Calculate the approximate osmolality of blood plasma if:

$[Na^+]$ = 146 mmol/l

[urea] = 4 mmol/l

[glucose] = 5.6 mmol/l

A.

approximate osmolality is calculated according to empirical relationship:

$$2\,[\mathrm{Na}^+] + [\mathrm{urea}] + [\mathrm{glucose}] =$$

$$2 \times 146 + 4 + 5.6 = \mathbf{301.6\ mmol/kg\ H_2O}$$

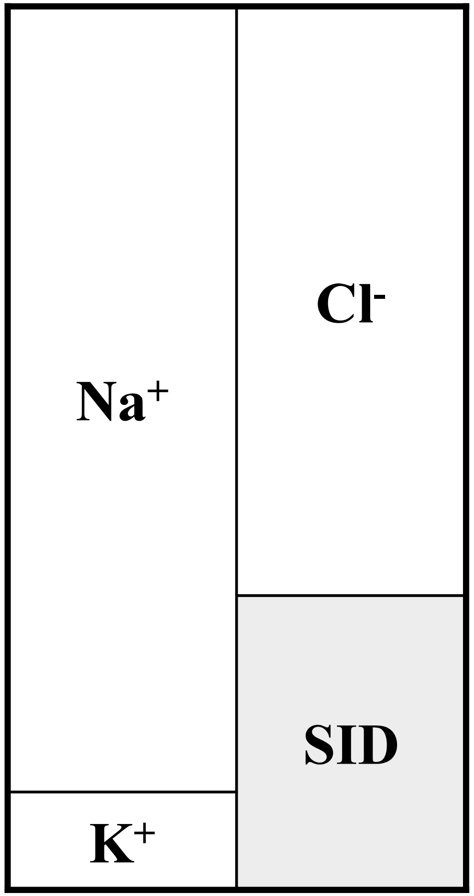
Data derived (calculated) from ionogram

SID, AG

SID (strong ion difference)

- strong ions **do not hydrolyze** in aqueous solution
- Na^+, K^+, Cl^-
- SID = $[Na^+]$ + $[K^+]$ **-** $[Cl^-]$ = 142 + 4 – 103 = 43 mmol/l
- physiological range of SID = 39 – 45 mmol/l

SID = buffer bases of plasma

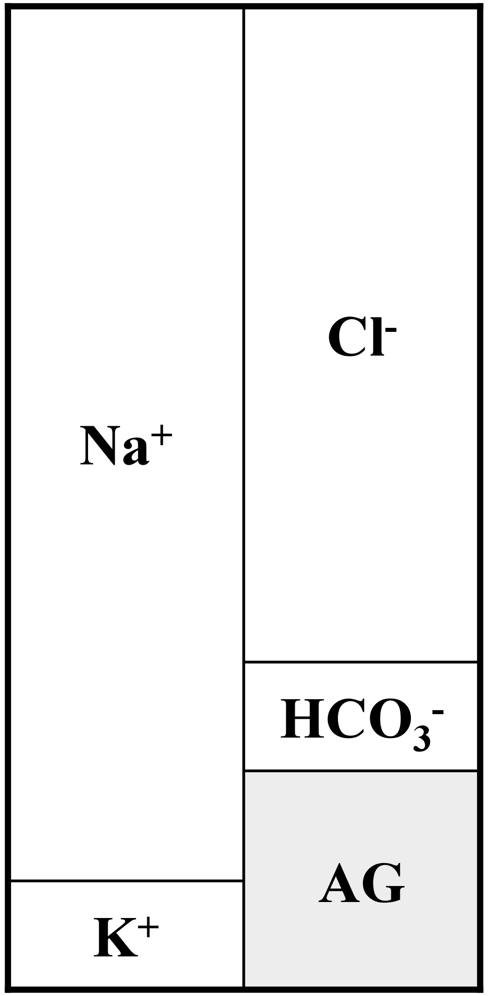


$$SID = HCO_3^- + HPO_4^{2-} + Prot^-$$

AG (anion gap)

- the extent of unmeasured or unusual anions
- AG = $[Na^+] + [K^+] - [Cl^-] - [HCO_3^-]$
- AG = 142 + 4 - 103 - 25 = 18 mmol/l
- physiological range of AG = 12 – 18 mmol/l

AG



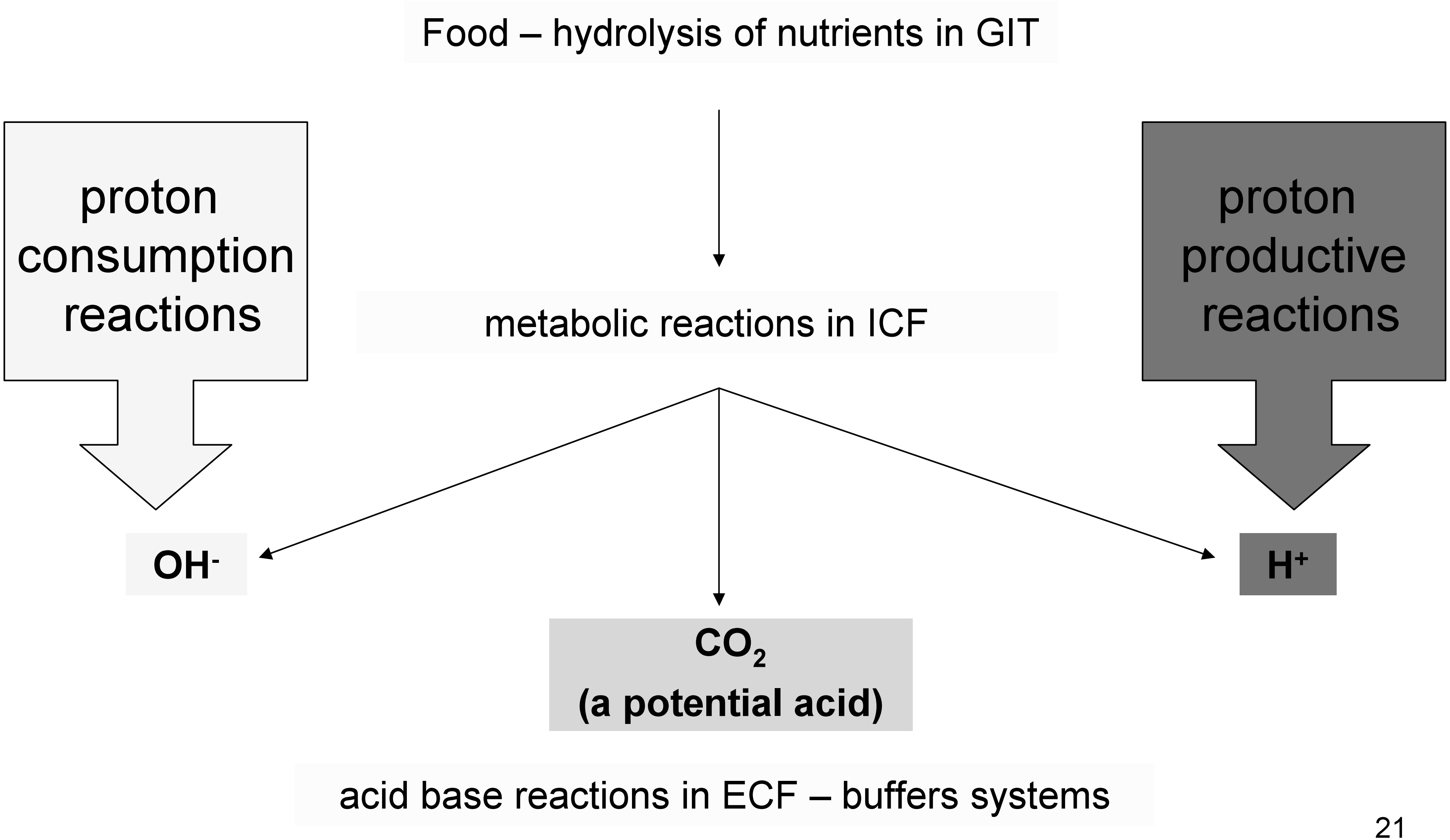
$$AG = HPO_4^{2-} + Prot^- + SO_4^{2-} + OA$$

Elevated AG may be caused by various conditions

- kidney insufficiency (↑ HPO_4^{2-} + ↑ SO_4^{2-})
- diabetes, starvation (↑ acetoacetate + ↑ β-hydroxybutyrate)
- poisoning by methanol (↑ formate $HCOO^-$)
- lactoacidosis (↑ lactate)
- severe dehydratation (↑ proteinates)

Metabolic processes produce or consume various acids

Metabolism of nutrients from acid-base point of view



Food – hydrolysis of nutrients in GIT

metabolic reactions in ICF

proton consumption reactions

proton productive reactions

OH^-

CO_2

(a potential acid)

H^+

acid base reactions in ECF – buffers systems

Proton consumption reactions

Gluconeogenesis from lactate:

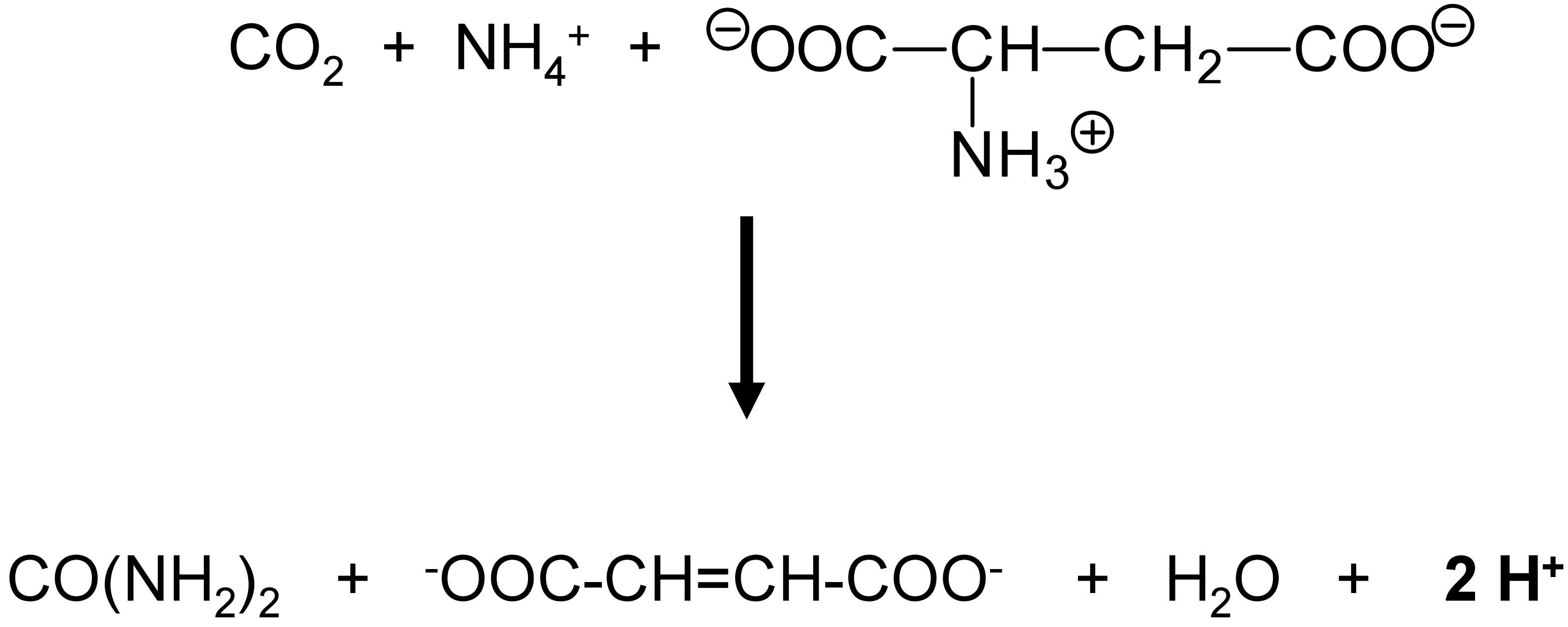
2 lactate$^-$ + $\mathbf{2\ H^+}$ → 1 glucose

anion + proton → neutral molecule

- protons are consumed in the synthesis of non-electrolyte from anion
- proton consumption is equivalent to OH^- production

Proton productive reactions

- **anaerobic glycolysis:** glucose → 2 lactate$^-$ + **2 H$^+$**
- **synthesis of urea:**



$$CO_2 + NH_4^+ + {}^{\ominus}OOC\text{—}\underset{\displaystyle NH_3^{\oplus}}{\underset{|}{C}}H\text{—}CH_2\text{—}COO^{\ominus}$$

$$\downarrow$$

$$CO(NH_2)_2 + {}^-OOC\text{-}CH{=}CH\text{-}COO^- + H_2O + \mathbf{2\ H^+}$$

Q.

Which compound is **the main acid product**

of metabolism in human body?

A.

carbon dioxide CO_2

compare daily production of acid equivalents:

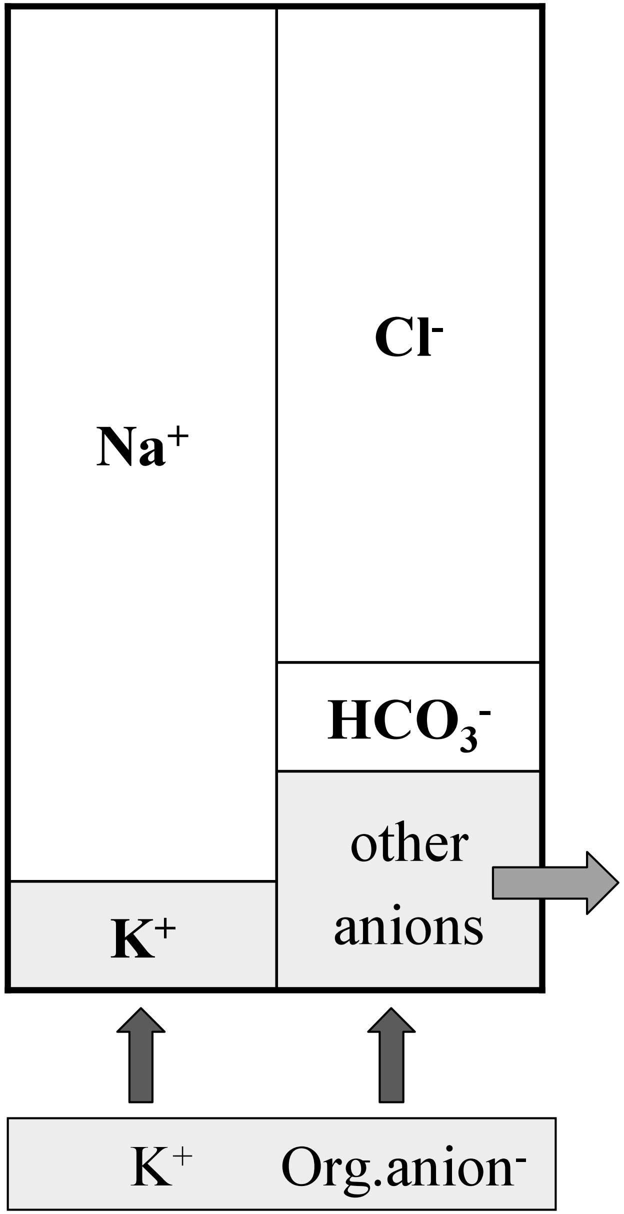
CO_2 - up to **25 000** mmol/day

H^+ as NH_4^+ and $H_2PO_4^-$ - up to **80** mmol/day

Q.

What kind of food leads to an increased production of OH^-?

A.



- **strictly vegetarian diet**
- contains a lot of potassium citrate/malate
- potassium salts get into blood plasma
- organic anions enter cells and are metabolized (CAC)
- K^+ cations remain in plasma
- to keep electroneutrality of plasma ⇒ HCO_3^- concentration increases
- **result: mild physiological alkalosis**

Q.

How is CO_2 formed in tissues?

Endogenous production of CO_2

- CO_2 is produced in **decarboxylation** reactions
- oxidative decarboxylation of pyruvate → acetyl-CoA
- two decarboxylations in CAC (isocitrate, 2-oxoglutarate)

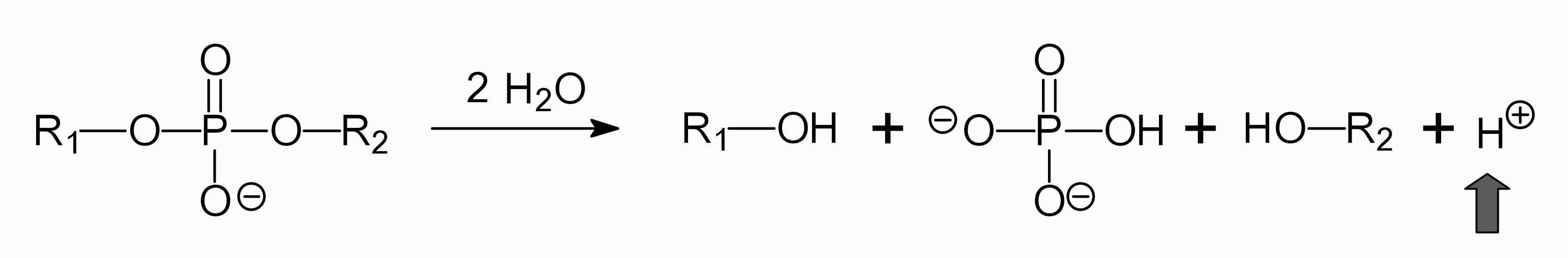
main sources of CO_2

- decarboxylation of aminoacids → biogenous amines
- non-enzymatic decarboxylation of acetoacetate → aceton
- catabolism of pyrimidine bases

  (cytosine, uracil $\rightarrow CO_2 + NH_3 + \beta$-alanine)
- catabolism of glycine $\rightarrow CO_2 + NH_3 +$ methylen-THF

Acid products of metabolism - Overview

- aerobic metabolism of nutrients → **CO_2**
- anaerobic glycolysis → **lactic acid**
- KB production (starvation) → **acetoacetic/β-hydroxybutyric acid**
- catabolism of cystein (-SH) → SO_4^{2-} + **2 H^+**
- catabolism of purine bases → **uric acid**
- catabolism of phospholipids → HPO_4^{2-} + **H^+**



Buffer systems in blood

Buffer system	Relevance	Buffer base	Buffer acid	pK_A
Hydrogencarbonate	50 %	HCO_3^-	H_2CO_3, CO_2	6.1
Proteins[a]	45 %	Protein-His	Protein-His-H^+	6.0-8.0[b]
Hydrogenphosphate	5 %	HPO_4^{2-}	$H_2PO_4^-$	6.8

[a] In plasma mainly albumin, in erythrocytes hemoglobin

[b] The pK_A value depends on the type of protein

Buffer bases in (arterial) plasma

Buffer base	**mmol/l**
HCO_3^-	24
Proteins	17
HPO_4^{2-}	1
----------	**-------------**
Total	**42**

Q.

Write a general form of Henderson-Hasselbach equation.

A.

$$\mathrm{pH} = \mathrm{p}K_{\mathrm{A}} + \log \frac{[\text{buffer base}]}{[\text{buffer acid}]}$$

Q.

What does the buffering capacity depends on?

A.

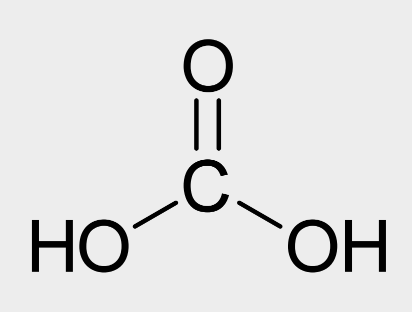
- buffering capacity depends on:

- concentration of both components
- the ratio of both components

- the best capacity if: [buffer base] = [buffer acid]

Hydrogencarbonate (bicarbonate) buffer

Carbonic acid *in vitro*



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

800 : 1 : 0.03

- weak diprotic acid (pK_{A1} = 6.37; pK_{A2} = 10.33)
- does exist only in aq. solution, easily decomposes to CO_2 and water
- CO_2 predominates 800 × in sol. ⇒ therefore CO_2 is included into K_A

$$K_{\mathrm{A\,eff}} = \frac{[\mathrm{H}^+][\mathrm{HCO_3}^-]}{[\underset{\Uparrow}{\mathrm{CO_2}} + \mathrm{H_2CO_3}]}$$

$K_{\mathrm{A\,eff}}$ = effective/overall dissociation constant

Carbonic acid *in vivo*

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

1 : traces : 20

- formation catalyzed by carbonic anhydrase
- under physiological conditions: $pK_{A1} = 6.10$
- CO_2 is continually eliminated from body by lungs
- the overall concentration of carbonic acid:

$$\mathbf{[CO_2 + H_2CO_3] \; = \; pCO_2 \times \boldsymbol{s} \; = \; 0.23 \; pCO_2 \; (kPa)}$$

Compare: CO_2 in water and blood !

Liquid	**pH**	**$[CO_2] : [HCO_3^-]$**
Carbonated water[a]	3.50 – 5.00	800 : 0.03
Blood[b]	7.36 – 7.44	1 : 20

[a] **Closed system** (PET bottle), 25 °C, $pK_{A1} = 6.37$
pH ~ pCO_2 ~ the pressure of CO_2 applied in saturation process

[b] **Open system**, 37 °C, $pK_{A1} = 6.10$
CO_2 continually eliminated, pCO_2 in lung alveoli ~ 5.3 kPa,
acid component of bicarbonate buffer

Q.

Give the Henderson-Hasselbalch equation for

the hydrogencarbonate buffer

A.

mmol/l

$$pH = 6.1 + \log \frac{[HCO_3^-]}{0.23 \times pCO_2}$$

kPa

Q.

Express the changes in the bicarbonate buffer after adding H^+.

A.

protons are eliminated in the reaction with buffer base

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

Q.

Express the changes in the bicarbonate buffer after adding OH^-.

A.

hydroxide ions are eliminated in the reaction with buffer acid

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

Q. Calculate changes in buffer system after adding 2 mmol H^+ into one liter

	Initial status	Closed system	Open system
$[HCO_3^-]$	24 mmol/l		
$[CO_2+H_2CO_3]$	1.2 mmol/l		
pH	7.40		

	Initial status	**Closed system**	**Open system**
$[HCO_3^-]$	24 mmol/l	**22**	
$[CO_2+H_2CO_3]$	1.2 mmol/l	**3.2**	
pH	7.40	**6.94**	

2 H^+ react with buffer base ⇒ $24 – 2 = \mathbf{22\ HCO_3^-} + 2\ CO_2$

newly formed CO_2 remain in the system ⇒ $1.2 + 2 = \mathbf{3.2\ CO_2}$

	Initial status	**Closed system**	**Open system**
$[HCO_3^-]$	24 mmol/l	22	**22**
$[CO_2+H_2CO_3]$	1.2 mmol/l	3.2	**1.2**
pH	7.40	6.94	**7.36**

2 H^+ react with buffer base $\Rightarrow$ 24 - 2 = **22** $\mathbf{HCO_3^-}$ + 2 CO_2

newly formed CO_2 is eliminated by lungs $\Rightarrow$ 3.2 - 2 = **1.2** $\mathbf{CO_2}$

Q.

Calculate the ratio of $[HCO_3^-]/[CO_2+H_2CO_3]$ at physiological pH.

A.

$7.40 = 6.1 + \log x$

$\log x = 1.3$

$x = 10^{1.3} = 20 = 20 : 1 = [HCO_3^-] : [CO_2 + H_2CO_3]$

Q.

Is the bicarbonate buffer more resistant to acids or bases?

A.

- see previous problem
- $[HCO_3^-] : [CO_2 + H_2CO_3] = 20 : 1$
- the concentration of buffer base is **20 × higher**

  than the concentration of buffer acid
- conclusion: bicarbonate buffer is 20 × more resistant to acids

Hydrogenphosphate buffer

- buffer base: HPO_4^{2-}
- buffer acid: $H_2PO_4^-$

- occurs mainly in ICF, bones, urine

Q.

What is the ratio of plasma phosphates at physiological pH?

A.

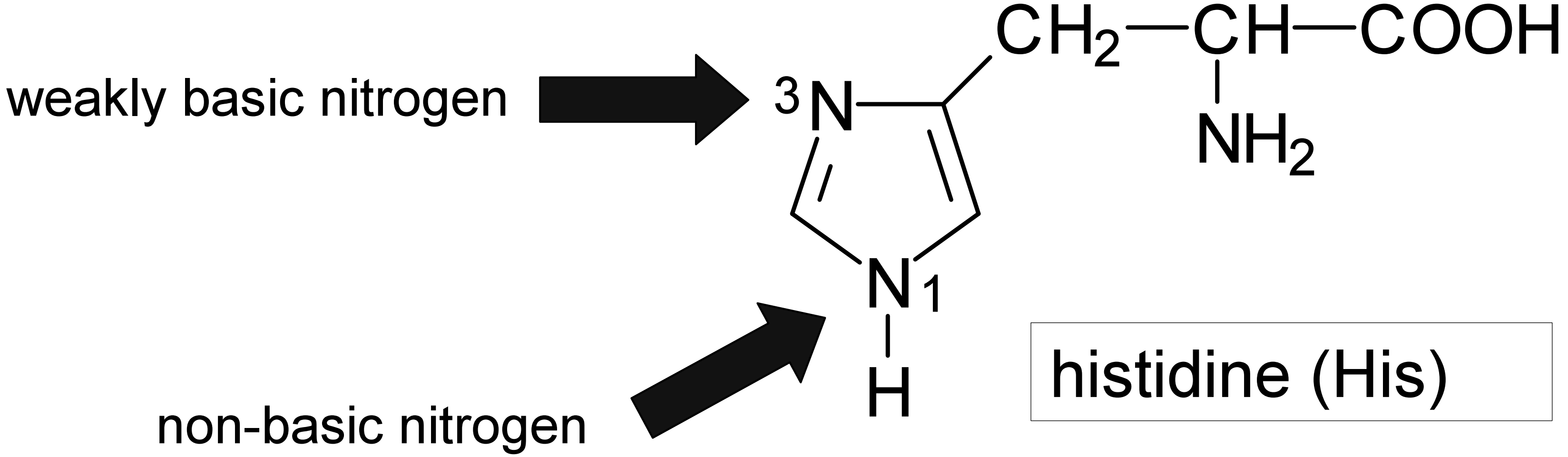
$7.40 = 6.80 + \log x$

$\log x = 0.6$

$x = 10^{0.6} = 4 \Rightarrow [HPO_4^{2-}] : [H_2PO_4^{-}] = 4 : 1$

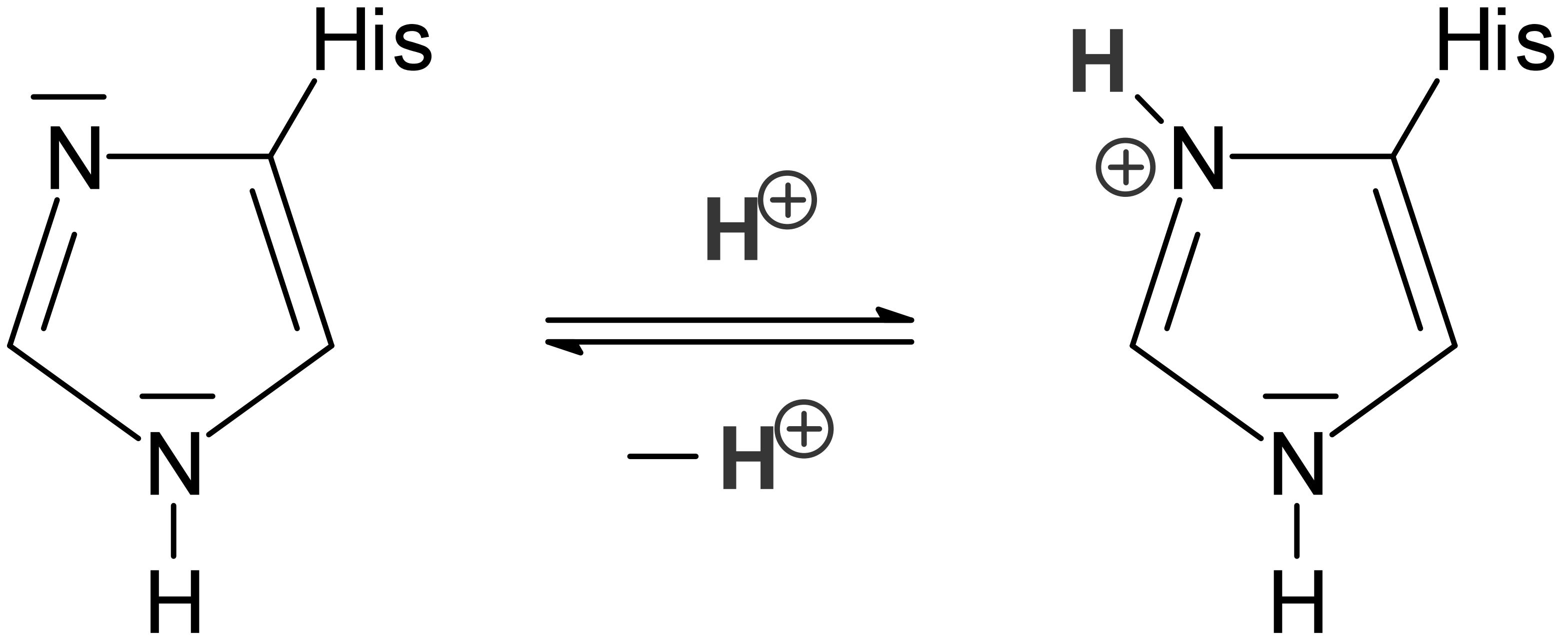
Hemoglobin buffer

- hemoglobin (Hb) contains a lot of histidine



histidine (His)

Buffering function of Hb is performed by side chain of histidine



imidazol

pK_B (His) = 8

imidazolium

pK_A (His) = 14 - 8 = 6

pK_A (His in proteins) = 6 - 8

The next seminar
May 15

- Chapter 21, II. part -