Disorders of acid-base equilibrium

Pathobiochemistry and diagnostics of acid-base and mineral metabolism

Physiologic pH

- **Plasma and most extracellular fluids**

pH = 7.40 ± 0.02

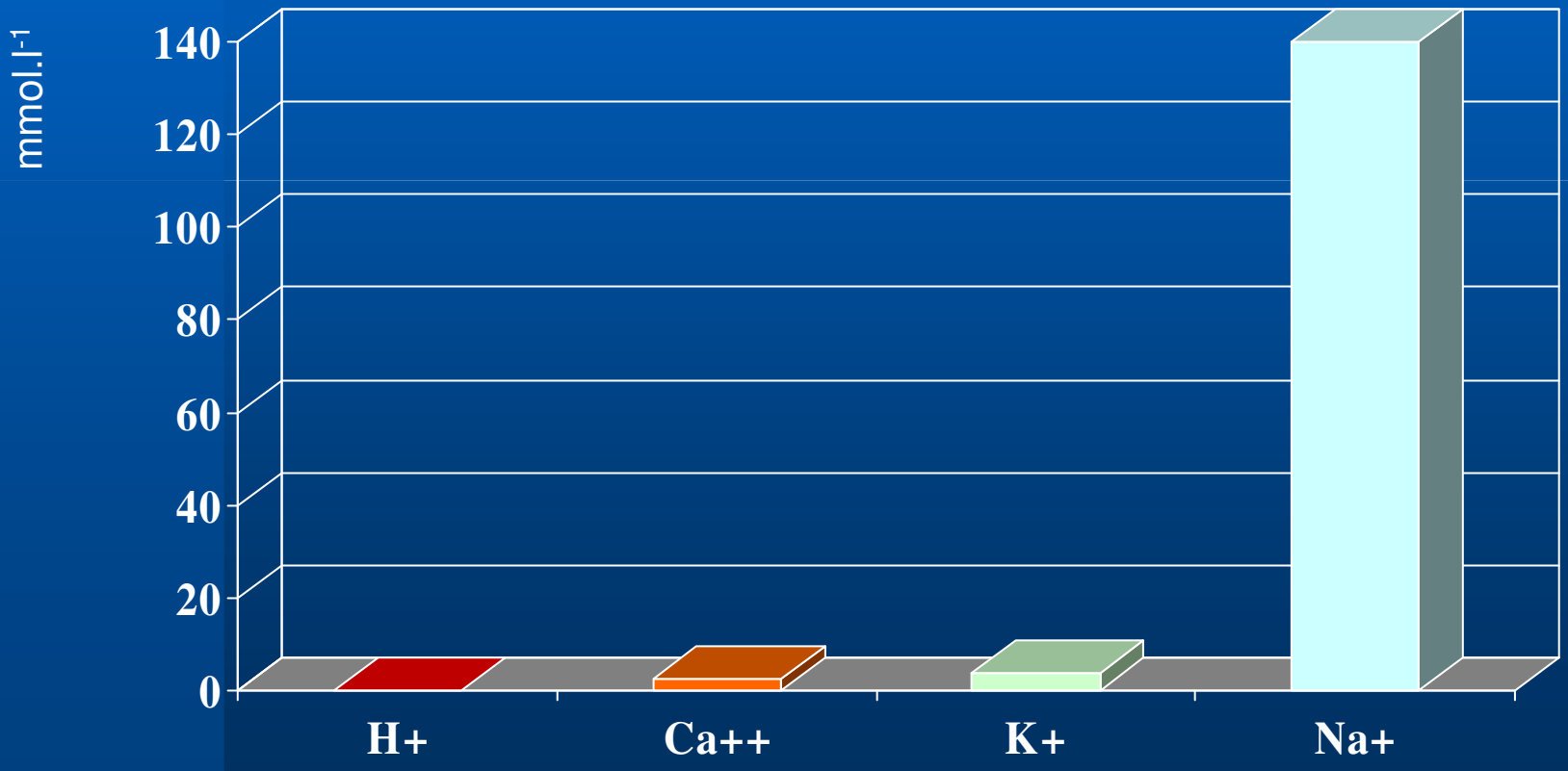
Significance of constant pH

pH influences

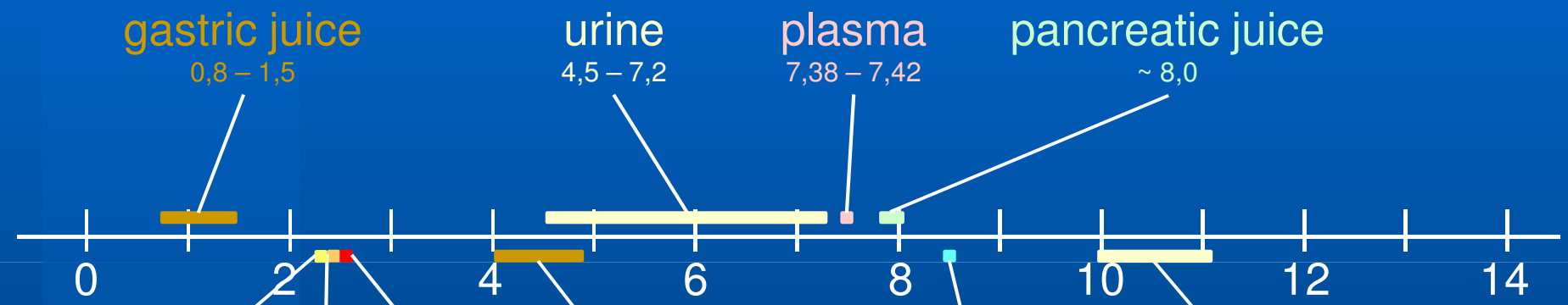
- **properties of proteins**
  - **enzyme activity**
  - **structure of cell components**
- **permeability of membranes**
  - **distribution of electrolytes**

pH < 7.0 or > 7.7 is lethal

H^+ and other cathions



pH



lemon juice
2,3

vinegar
2,4

Coca-Cola
2,6

beer
4,0 – 4,9

marine water
8,5

soap
10 – 11

http://www.edunet.ch

Proton sources

- **Anaerobic glycolysis**

  $1Glc \rightarrow 2lactate^{-} + 2H^{+}$

- **Lipolysis**

  $TAG \rightarrow 3FA^{-} + glycerol + 3H^{+}$

- **Formation of ketone bodies**

  $FA^{-} \rightarrow \rightarrow acetoacetate^{-} + hydroxybutyrate^{-} + nH^{+}$

Proton sources

- **Oxidation of S-containing AA**
- **Metabolism of org. phosphates**
- **Oxidation of other AA**
- **Ureasynthesis from NH_4^+**

$$CO_2 + 2NH_4^+ \rightarrow \text{urea} + H_2O + 2H^+$$

Consumption of protones

- **Oxidation of lactate**

$$lactate^- + 3O_2 + H^+ \rightarrow 3CO_2 + H_2O$$

Anaerobic glycolysis

$$1Glc \rightarrow 2lactate^- + 2H^+$$

May be separated in time or space

$$2lactate^- + 2H^+ + 6O_2 \rightarrow 6CO_2 + 2H_2O$$

Oxidation of lactate

Consumption of protones

- **Gluconeogenesis**

  $2\text{lactate}^- + 2\text{H}^+ \rightarrow \text{Glc}$

- **Oxidation of neutral AA**
- **Oxidation of dicarboxylic AA**
- **Oxidation of anions of org. acids**

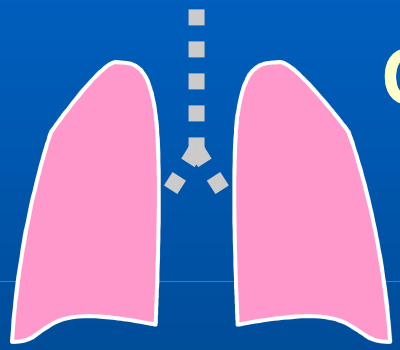
Proton sources

- **Food contains**
  - **salts of organic acids**
  - **compounds metabolised to sulphuric acid**
  - **compounds metabolised to phosphoric acid**

Maintaining pH

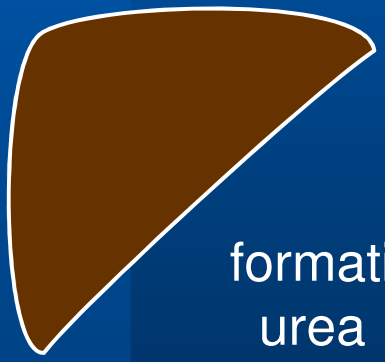
- **Fast but incomplete**
  - **BUFFERS**
- **Complete but slow**
  - **CONTROL of METABOLISM**
    respiration, transporting mechanisms…

Maintaining acidity of inner environment



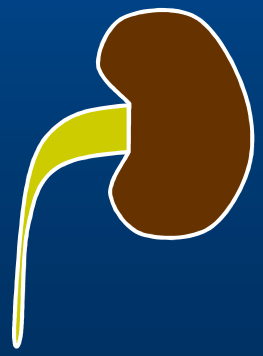
CO_2

NH_3



formation of
urea
glutamin

H^+
HCO_3^-



Respiration

- $CO_2 + H_2O \rightleftharpoons H_2CO_3$

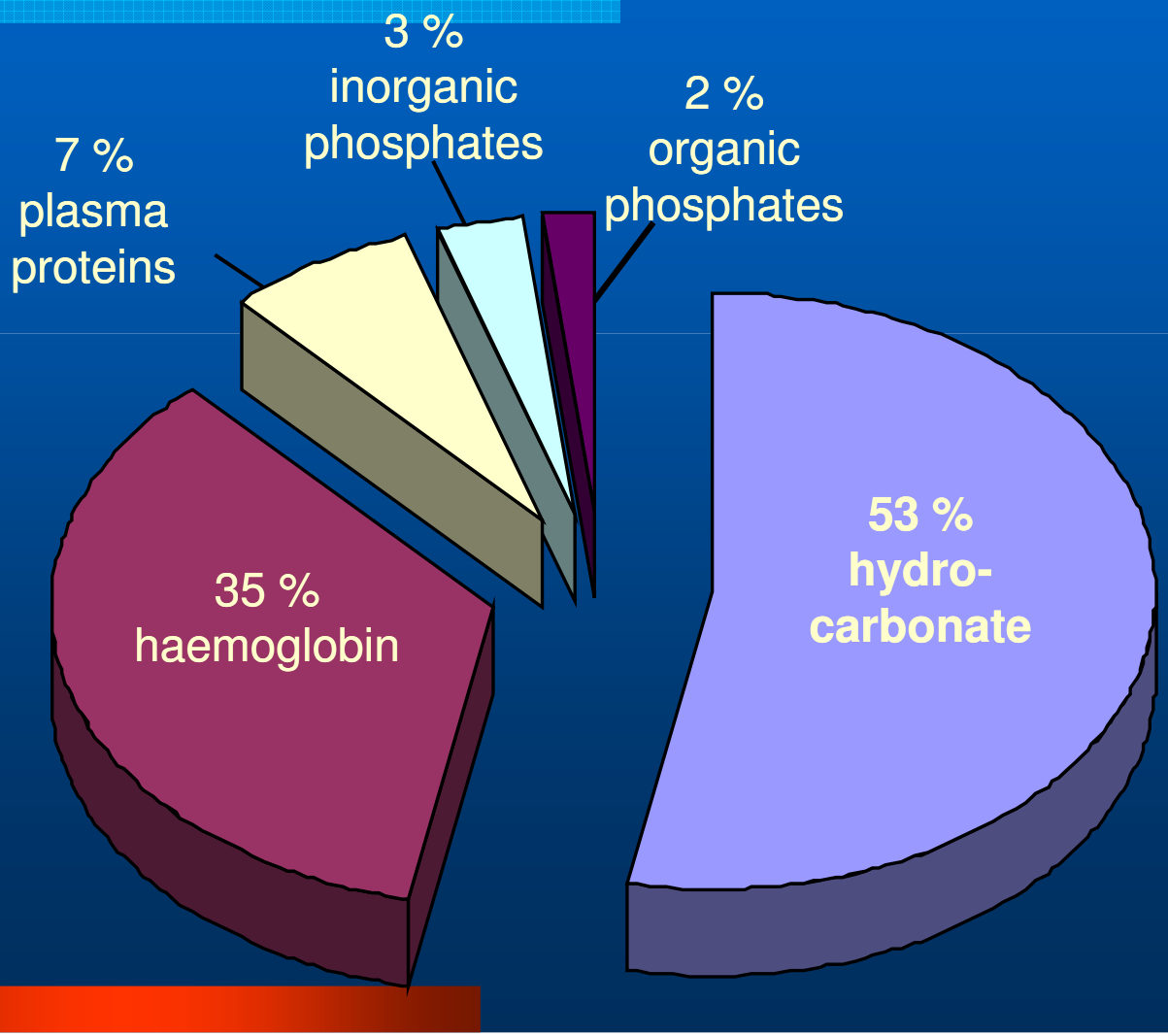
- ↑ ventilation → ↓ pCO_2 → alkalinisation
- ↓ ventilation → ↑ pCO_2 → acidification

Liver

$$CO_2 + 2NH_4^+ \rightarrow \text{urea} + 2H^+ + H_2O$$

$$NH_4^+ + Glu^- \rightarrow Gln + H_2O$$

Blood buffers



Bicarbonate buffer

Henderson-Hasselbalch equation

$$pH = pK_a + \log \frac{[HCO_3^-]}{[H_2CO_3]}$$

- pK_a = 6,1
- $[HCO_3^-]$ = 24 mmol.l^{-1}
- $[H_2CO_3]$ = 1,2 mmol.l^{-1}

$$\frac{[HCO_3^-]}{[H_2CO_3]} = 20$$

Henderson-Hasselbalch equation

$$pH = pK_a + \log \frac{[HCO_3^-]}{\alpha \cdot pCO_2}$$

- pK_a = 6,1
- $[HCO_3^-]$ = 24 mmol.l^{-1}
- α = 0,224 mmol.l^{-1} / kPa

pCO_2 = 5,3 kPa

Bicarbonate buffer

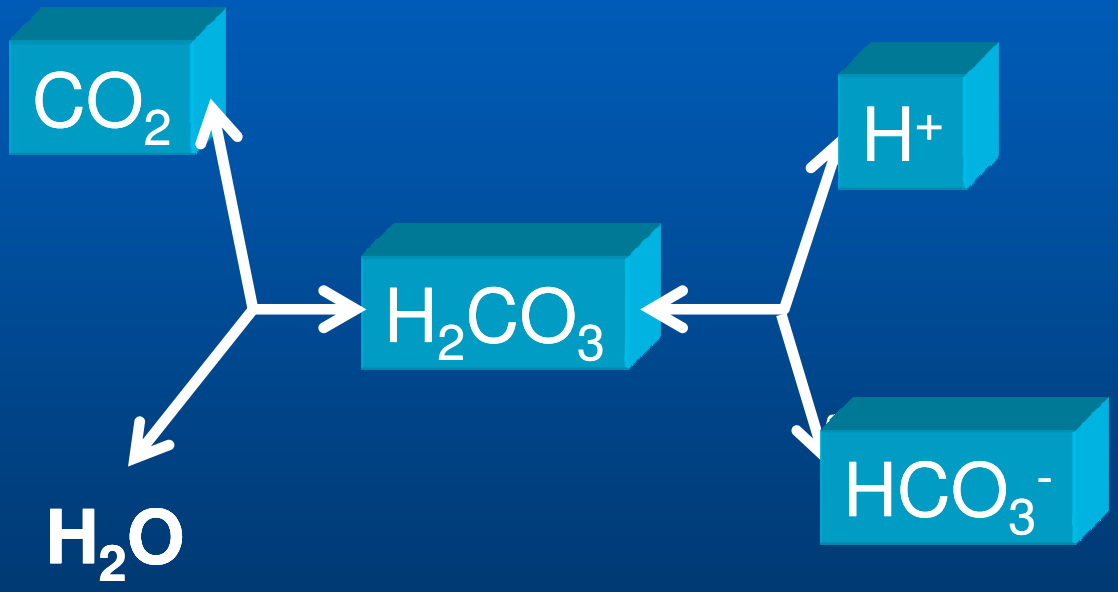
tissue

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

lungs

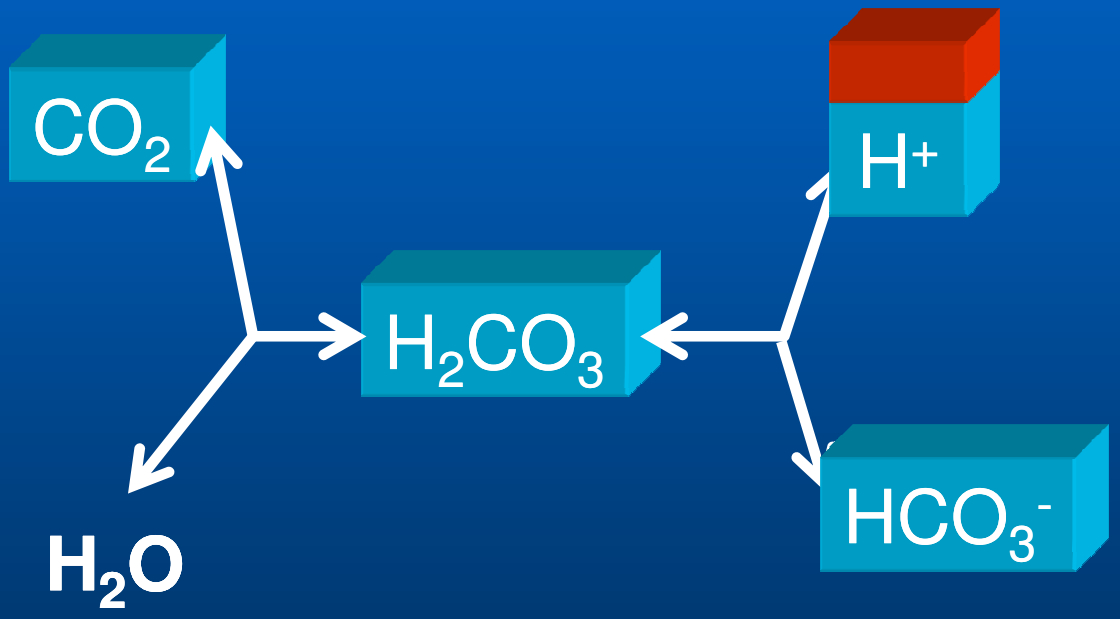
kidney

Bicarbonate buffer

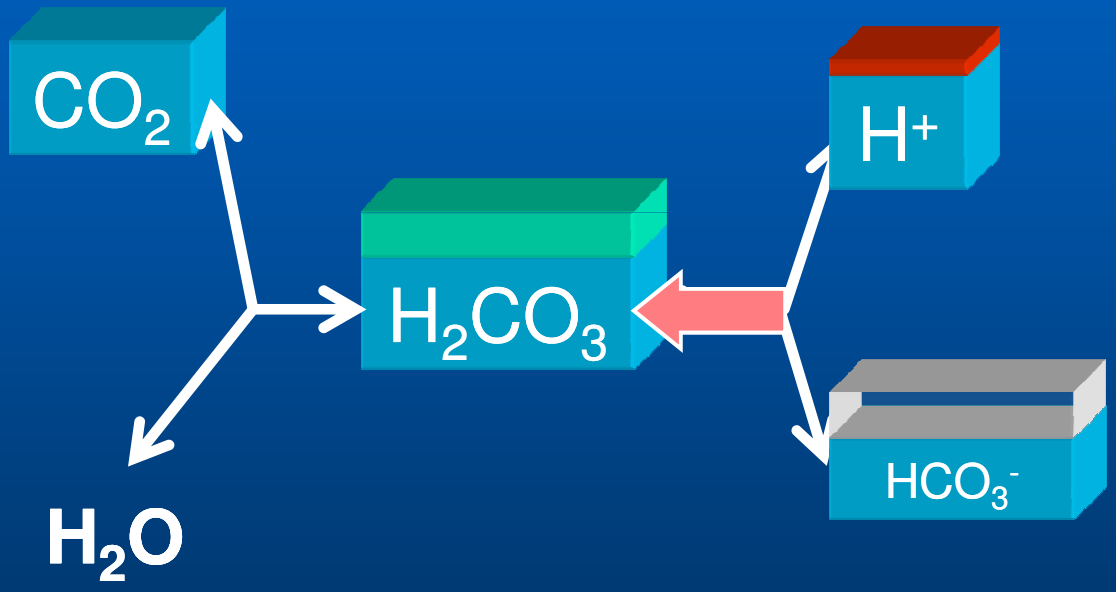


NB: box size does not correspond to concentration!

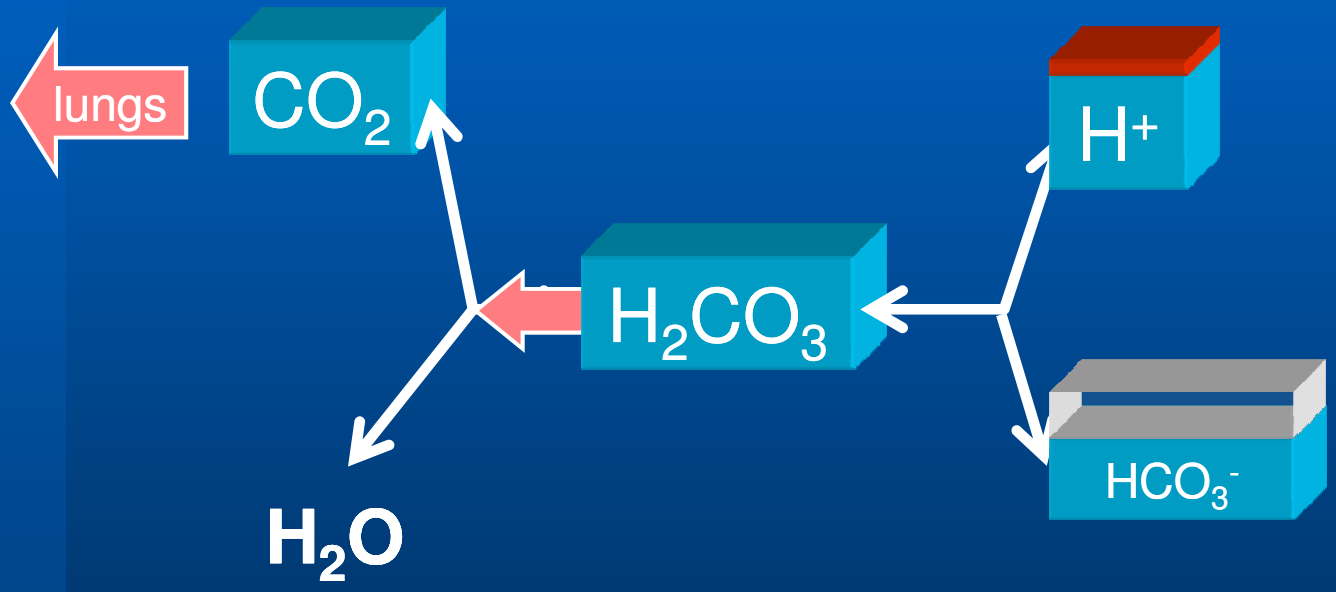
Bicarbonate buffer



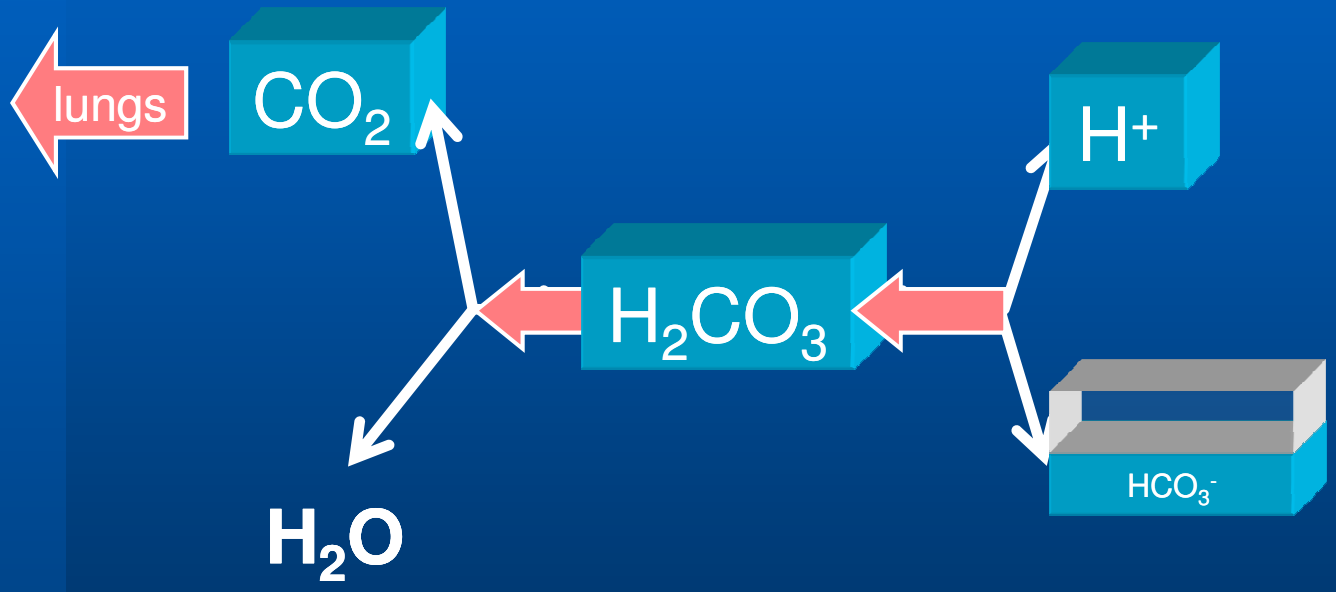
Bicarbonate buffer



Bicarbonate buffer



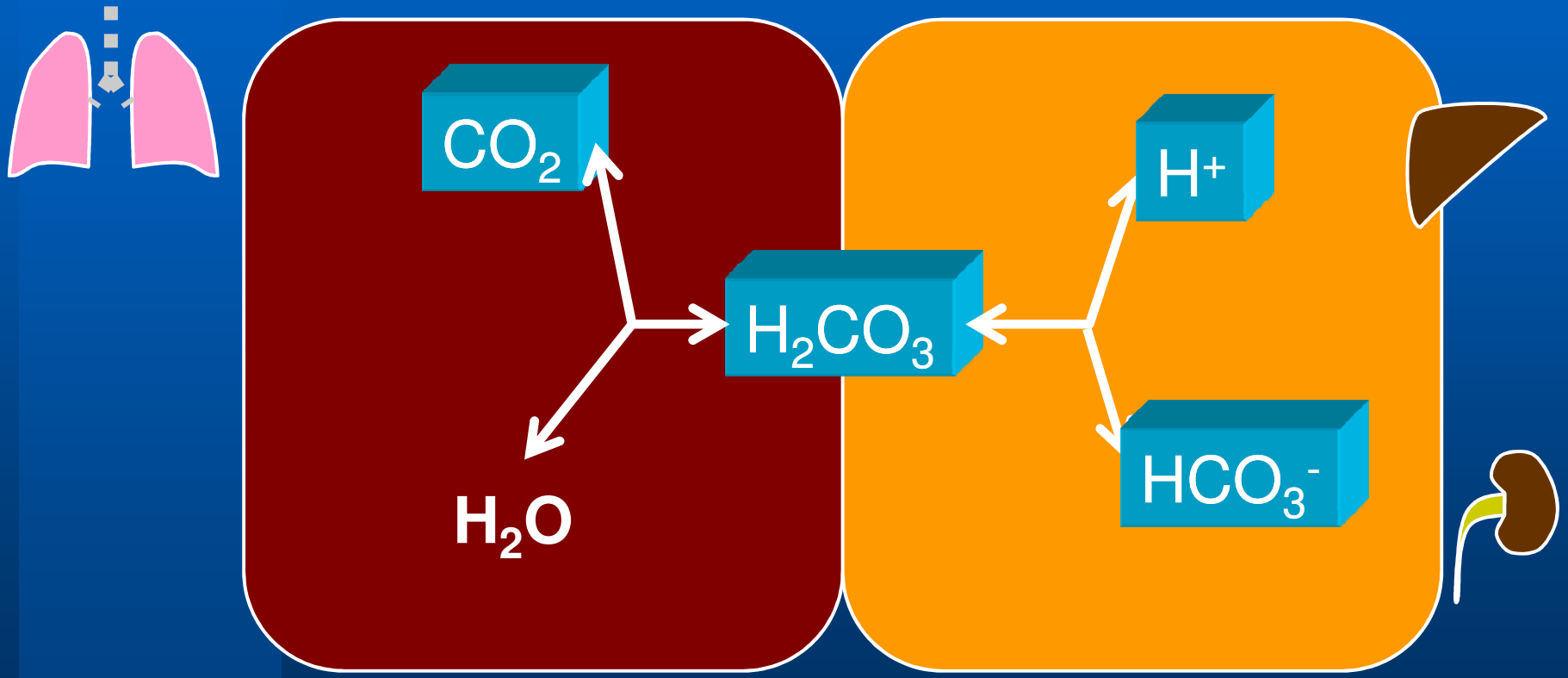
Bicarbonate buffer



pH change in vomiting

- **loss of ca. 0.5 L of gastric juice, pH 0.8**
  - **w/o buffer** **pH 7,4 → > 14**
  - **isolated system** **7,4 → 7,9**
  - **opened system** **7,4 → 7,415**

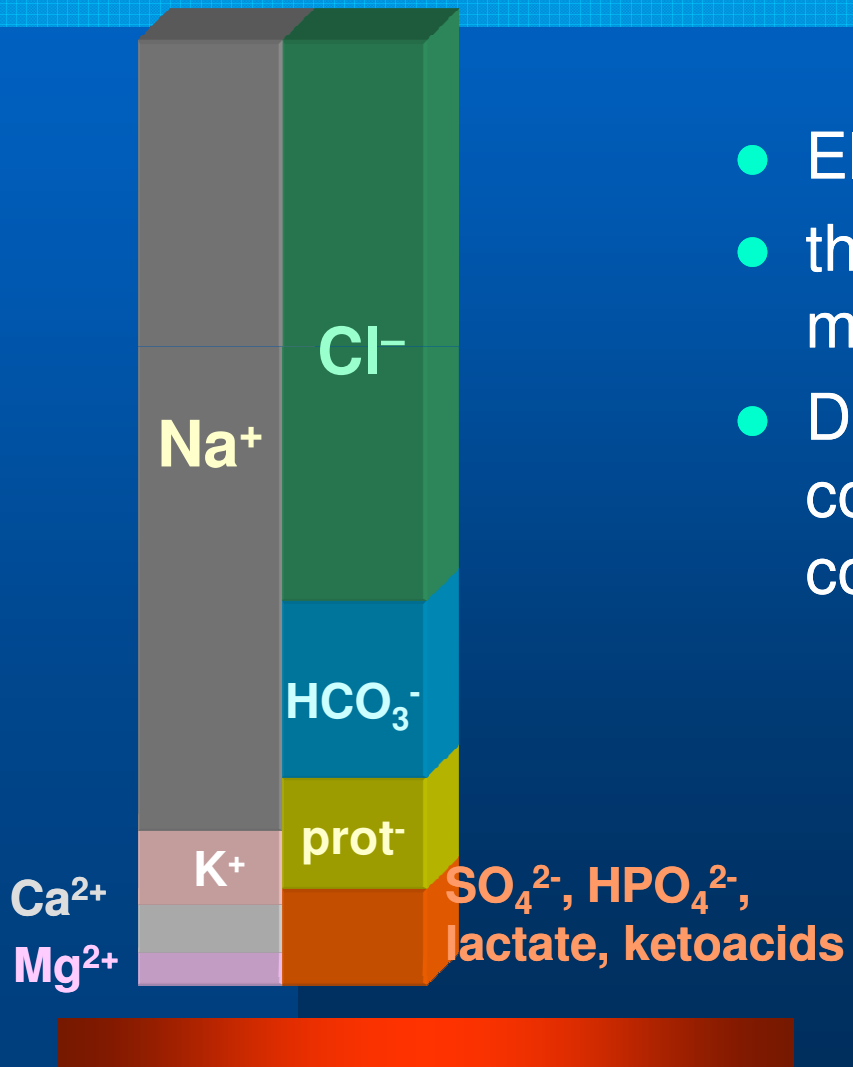
Bicarbonate buffer



Redistribution of ions among compartements

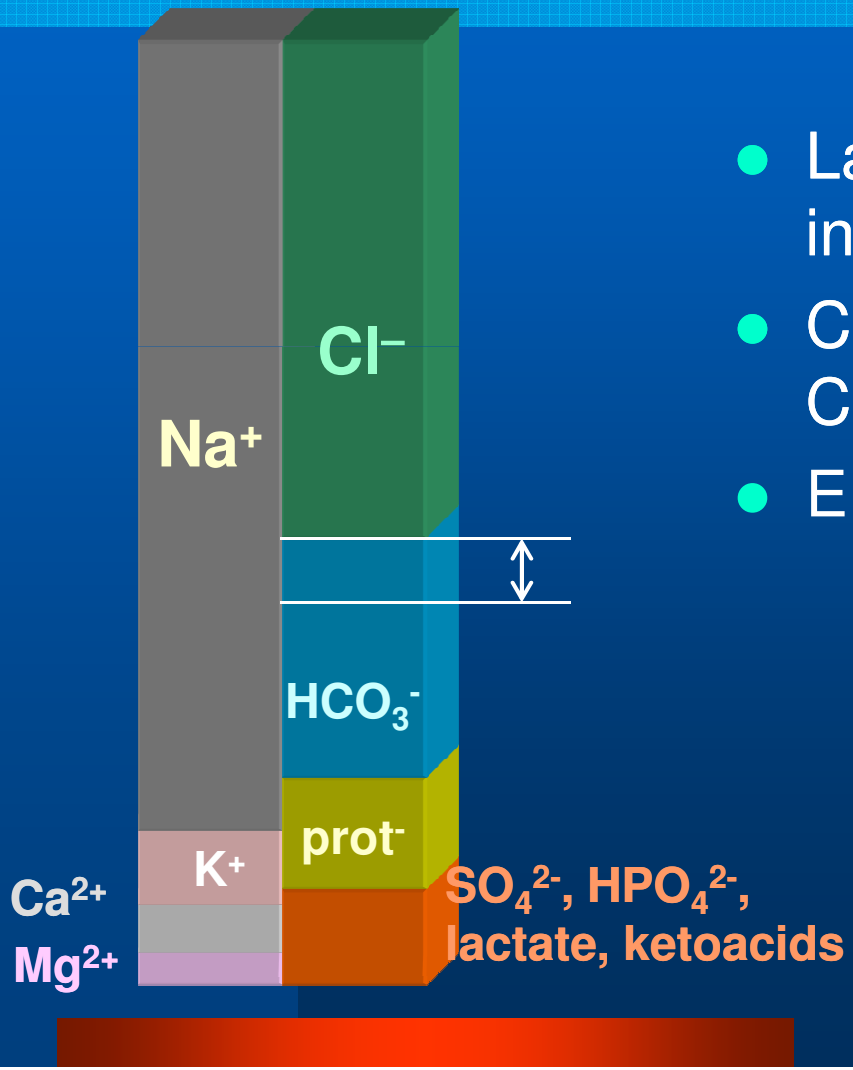
- **Transport of H^+, OH^- or HCO_3^- over membranes**
  - **Na^+-H^+ antiport**
  - **H^+ - K^+ exchange**
  - **H^+ - Ca^{2+} exchange**

ABE and ions



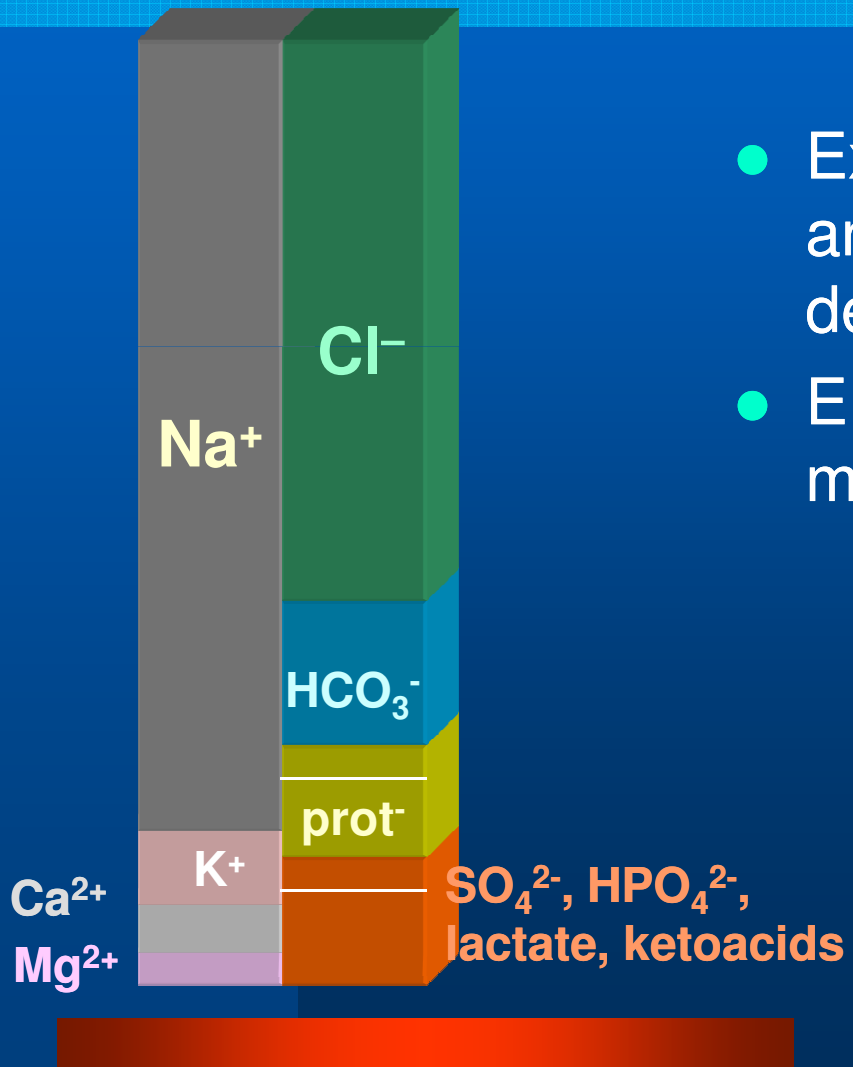
- Electroneutrality must be kept
- thus: ABE influences mineral metabolism
- Deviations in ion concentrations are most easily compensated by HCO_3^-

Hypochloremic alkalosis



- Lack of Cl^- is comensated by increased HCO_3^-
- Changed ratio bicarbonate / CO_2 causes alkalosis
- E.g. in vomiting

Ketoacidosis



- Excess of β-hydroxybutyric and acetacetic acid leads to decreased bicarbonate
- E.g. decompensed diabetes mellitus, starvation…

ABE disorders

- **Acidemia, alkalemia**
  - pH of blood deviation
- **Acidosis, alkalosis**
  - excess/lack of acids/bases

Alkalemia

- ↓ Ca^{2+} → ↑ neuromuscular excitability
- ↓ K^{+} → heart arrhythmias
- Shift of haemoglobin dissociation curve → tissue hypoxia

ABE disorders

- **Compensation**
  - Metabolic disorder is compensated by respiration and v.v.
- **Correction**
  - Metabolic disorder is corrected metabolically

- respiration: 12 - 24 hours
- kidney: about 5 days

Metabolic acidosis (MAC)

- **Lactate acidosis**
  - hypoxia, poor lactate degradation
- **Ketoacidosis**
  - diabetes, starvation, alcoholism…
- **Renal acidosis**
  - accumulation of sulphates, phosphates…
- **Intoxication**

MAC in loss of HCO_3^-

- **Diarrhoea and other loss from GIT**
- **Renal tubular acidosis**
  - disorder of HCO_3^- reabsorption in tubuli
- **Dilution acidosis**
  - large amount of infusions lacking buffering system
    (pCO_2 constant, HCO_3^- quickly diluted)

Treatment of MAC

- **$NaHCO_3$**
- **salts of organic acids**
  - metabolised to CO_2 in Krebs cycle

Ringer solution with lactate

Metabolic alkalosis (MAL)

- **Excessive loss of chlorides**
  - vomiting, diuretics
- **Dehydratation (concentration alkalosis)**
- **Hypoproteinemia**
- **Hyperaldosteronism**
  - retention of Na^+ at the expense of K^+ & H^+

MAL treatment

- **Arginin chloride**
- **NaCl**
  - Cl^- refill
  - Na_2HPO_4 excreted istead of NaH_2PO_4
  - HCO_3^- dilution
- **KCl**
  - additionaly: hypokalaemia corrected

Liver failure

- **Alkalosis**
  - hypoproteinaemia
  - hyperaldosteronism
  - ↓ of ureasynthesis from ammonia

Renal failure

- **Acidosis**
  - phosphate and sulphate retention
  - poor urine acidification

Combined ABE disorders

- **MAC + MAL**
  - vomiting + starvation
  - vomiting + diarrhoea
  - renal failure + uraemic vomiting
  - hepatorenal failure
- **MAC + RAL**
  - salicylate intoxication

Combined ABE disorders

- **2× MAC**
  - decompensated diabetes mellitus ketoacidosis + hypovolaemia → lactate MAC
- **RAC + MAC**
  - cardiopulmonary failure