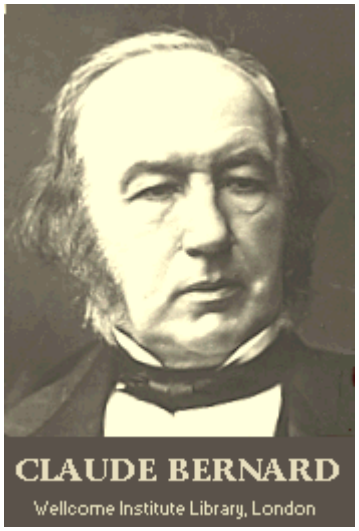
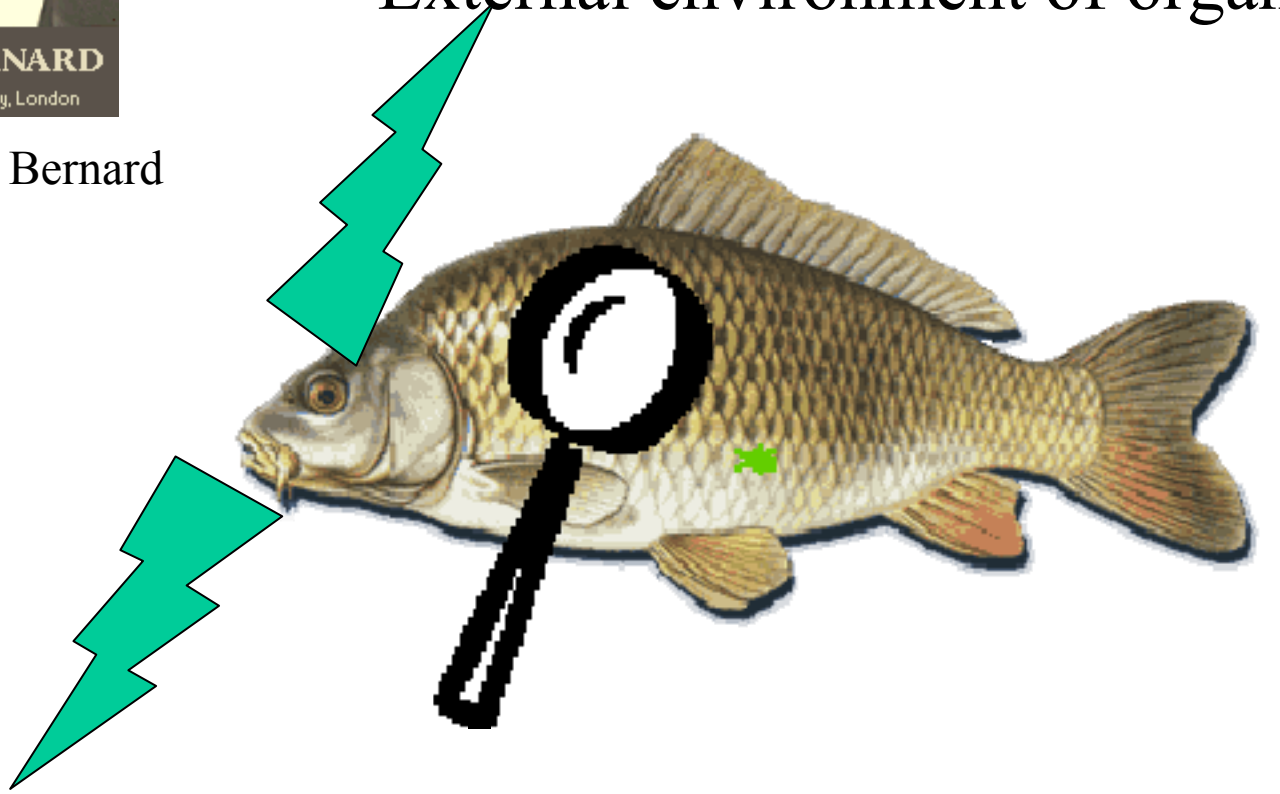
Homeostasis of internal enviroment

Disorders of the acid-base chemistry, influence of respiration, lungs and altered metabolism

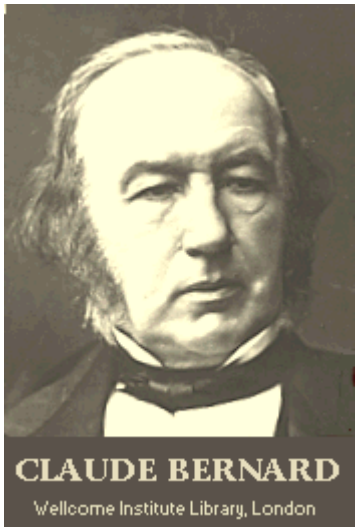


1865 Claude Bernard

External environment of organism



Internal environment of the cells



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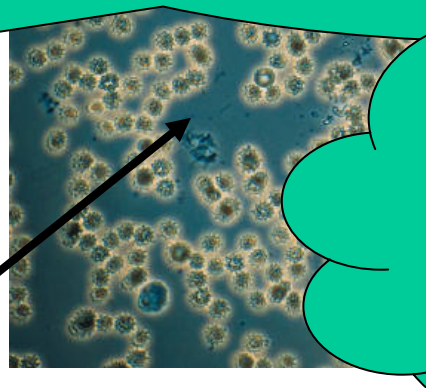
External environment of organism

i.e. temperature, volume, osmolarity, pH, ionic composition, O_2, CO_2 concentrations, concentration of glucose etc.

Their **properties** must enable optimal functioning of cellular structures



THEY ARE STAEDY AND INDEPENDENT ON FLOATING CONDITIONS OF EXTERNAL ENVIRONMENT AND ON VARIED LEVELS OF CELLULAR METABOLIC ACTIVITY

External environment of cells = **internal environment**

1932 Walter Cannon

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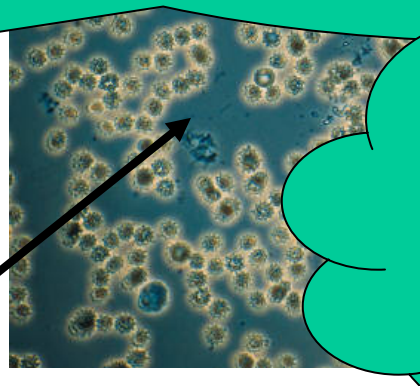

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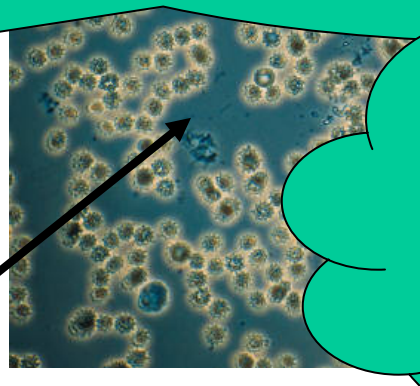

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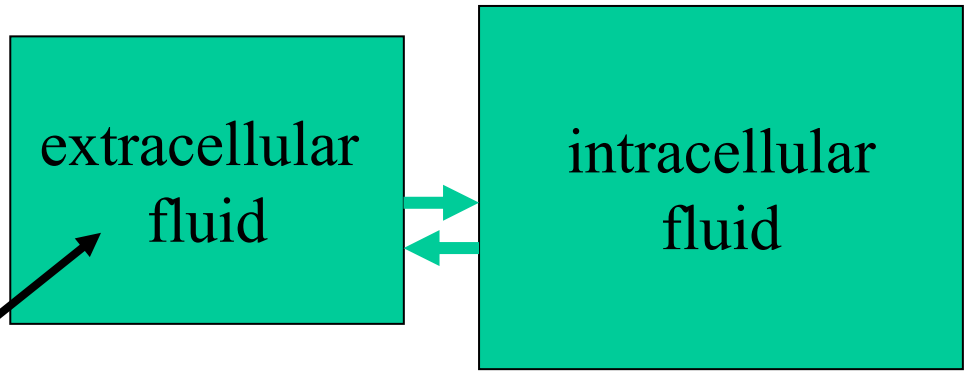

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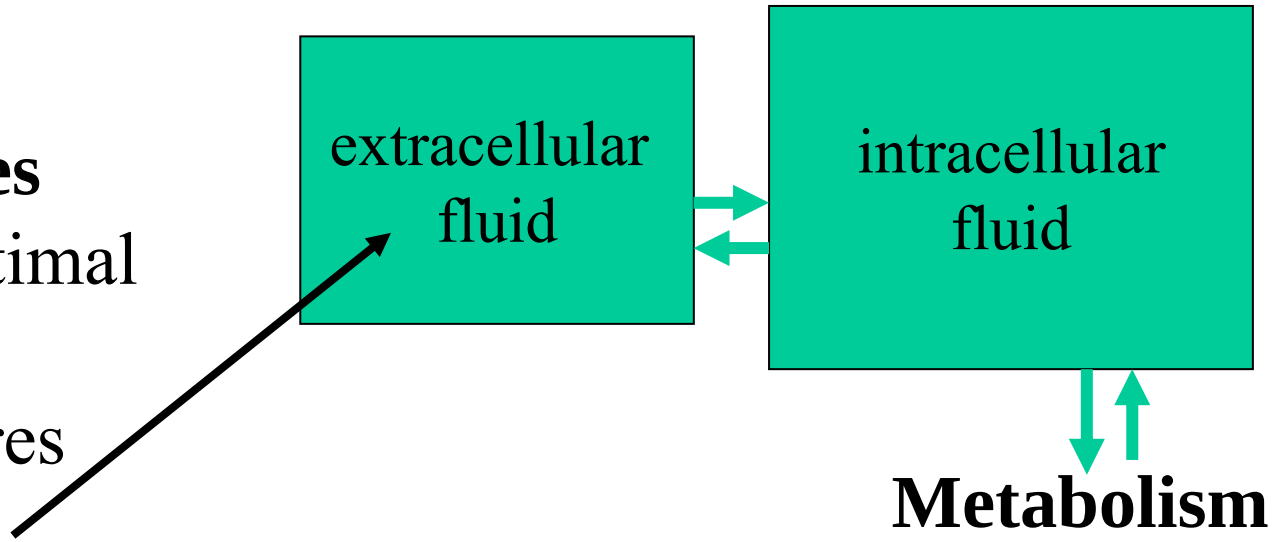

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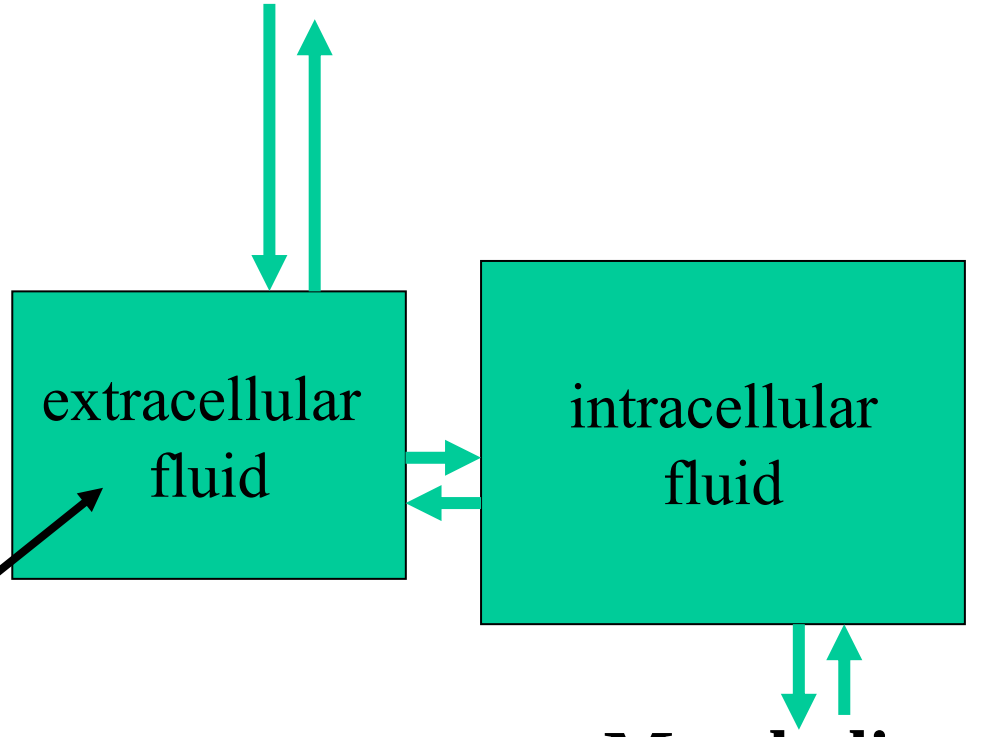

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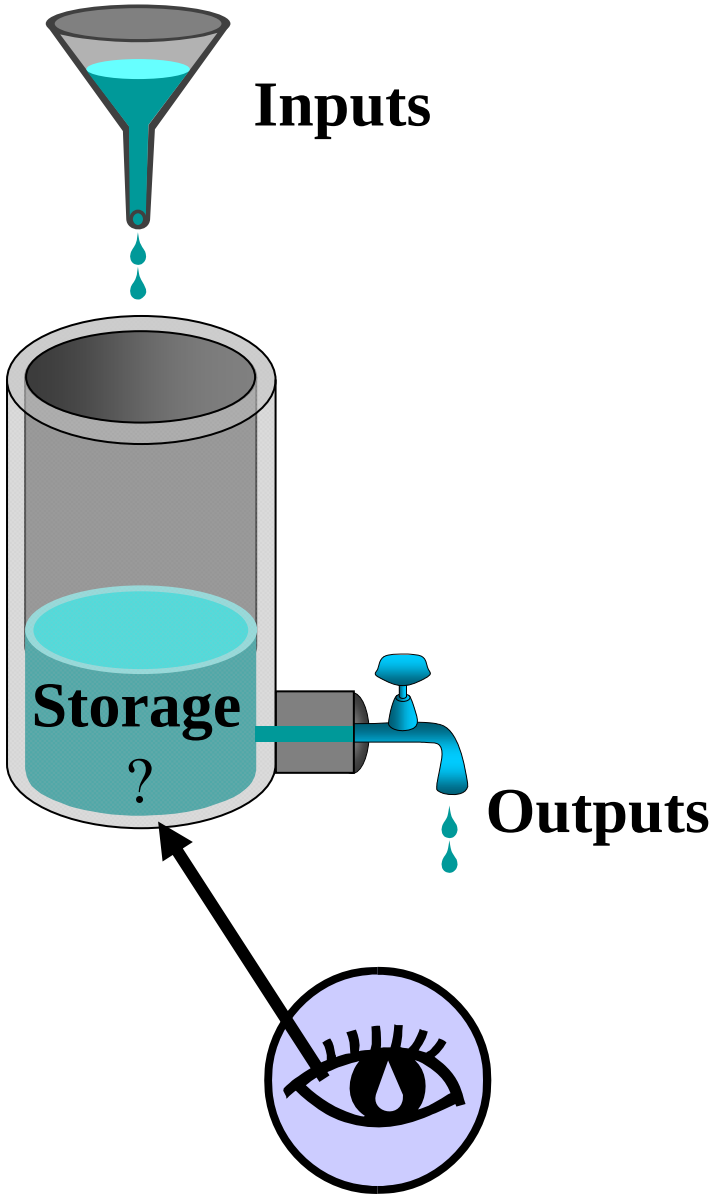
External environment of cells = **internal environment**

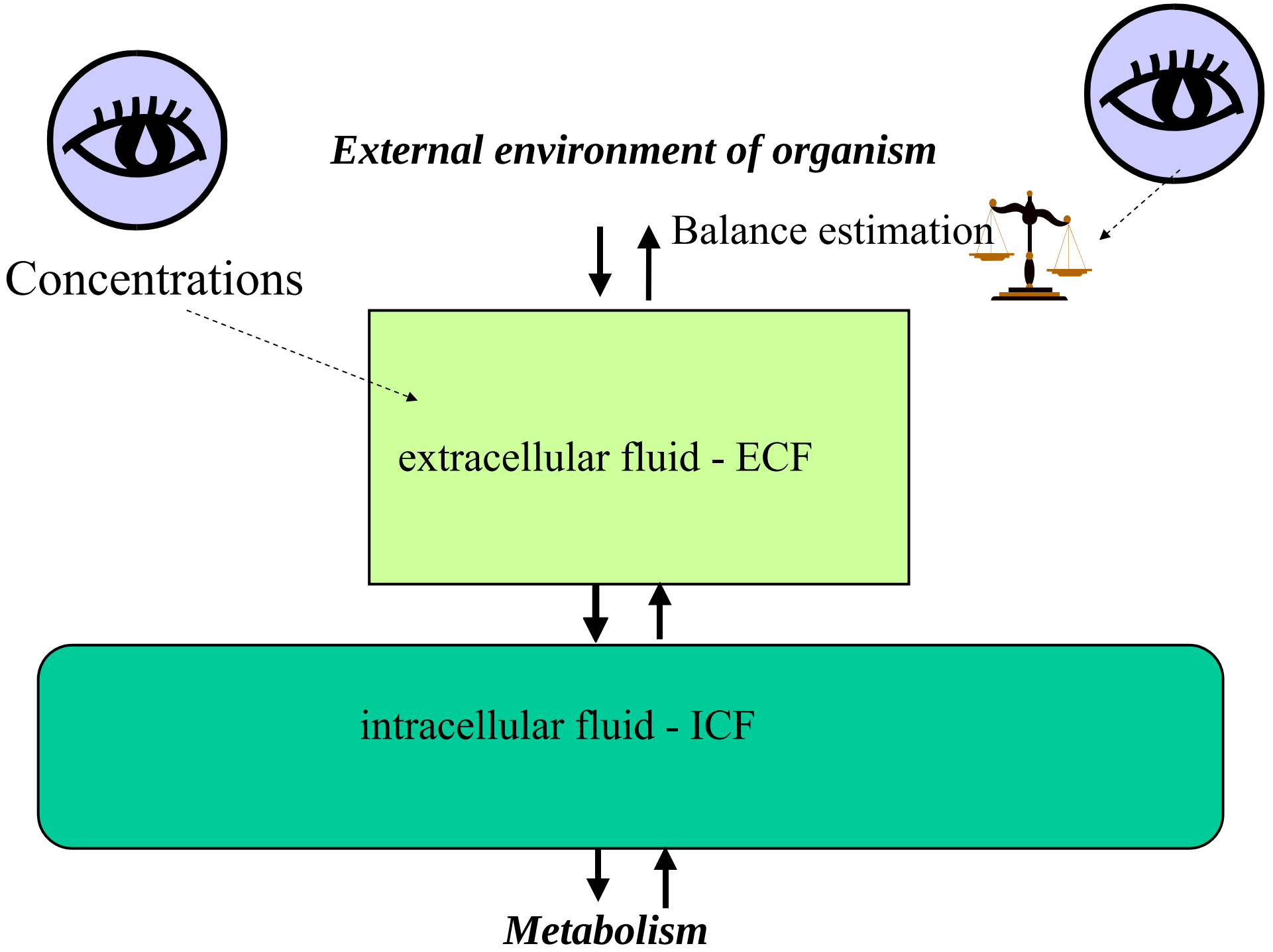
Balance between input and output flow

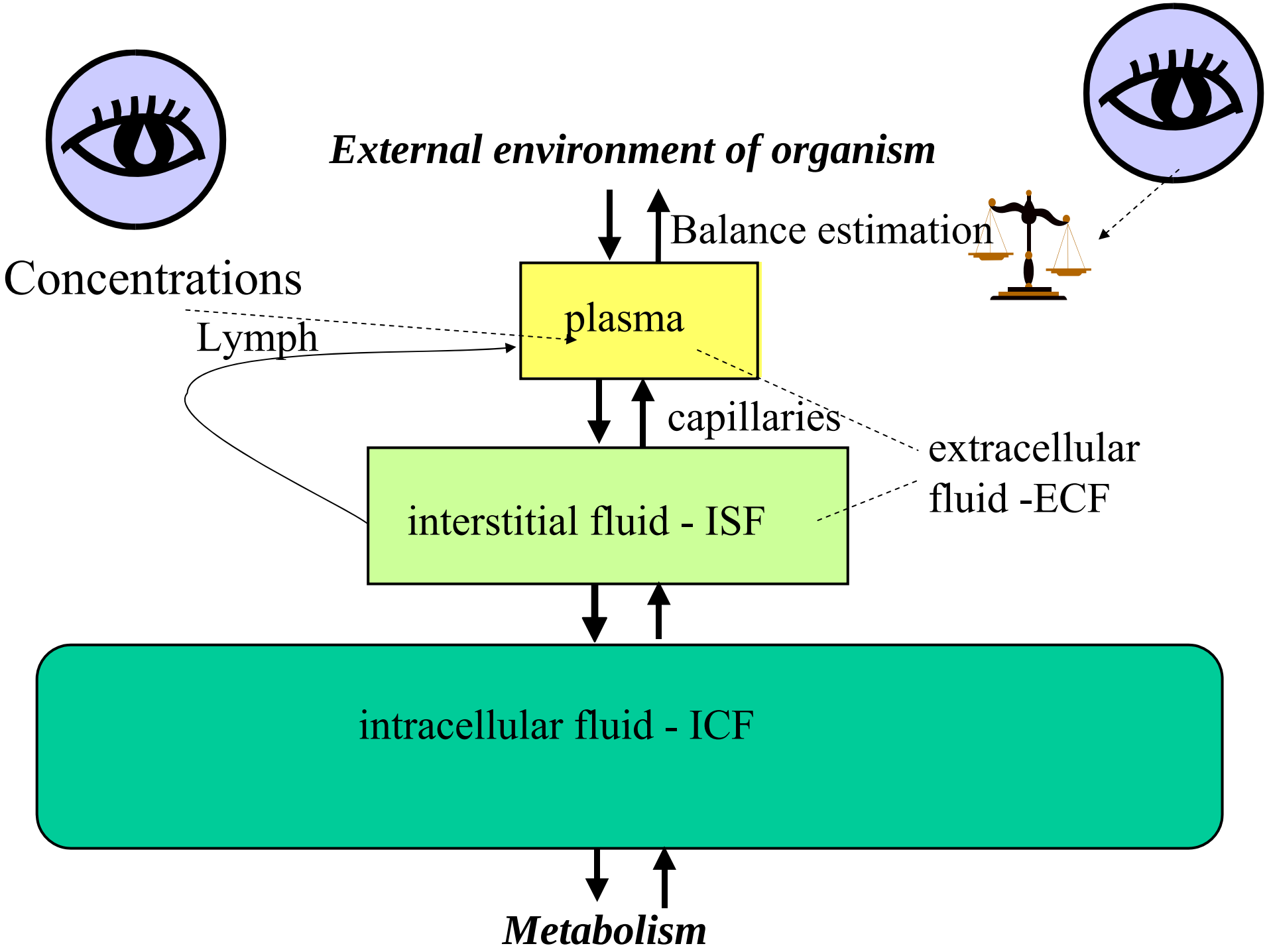
↑ **retention**

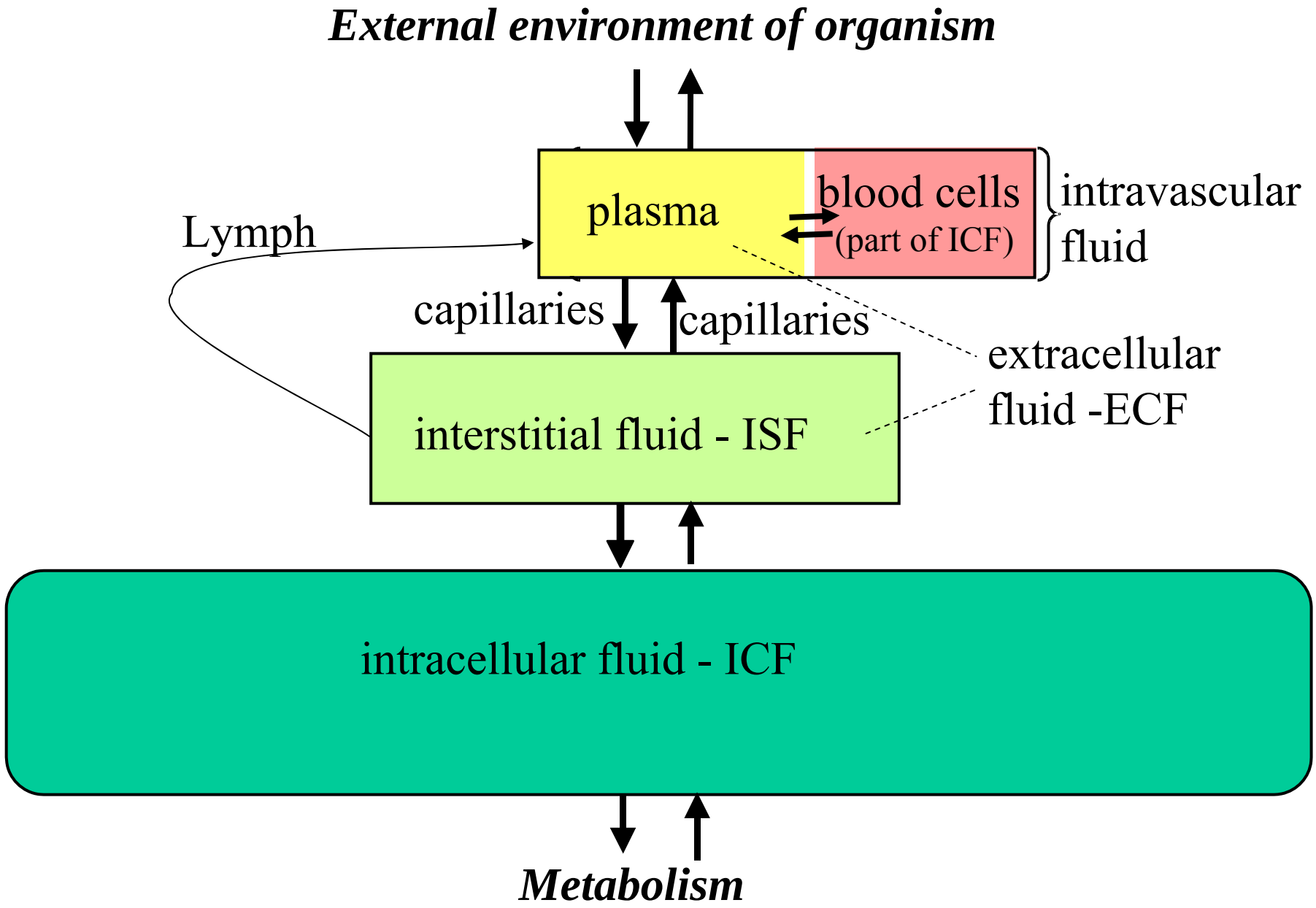
?

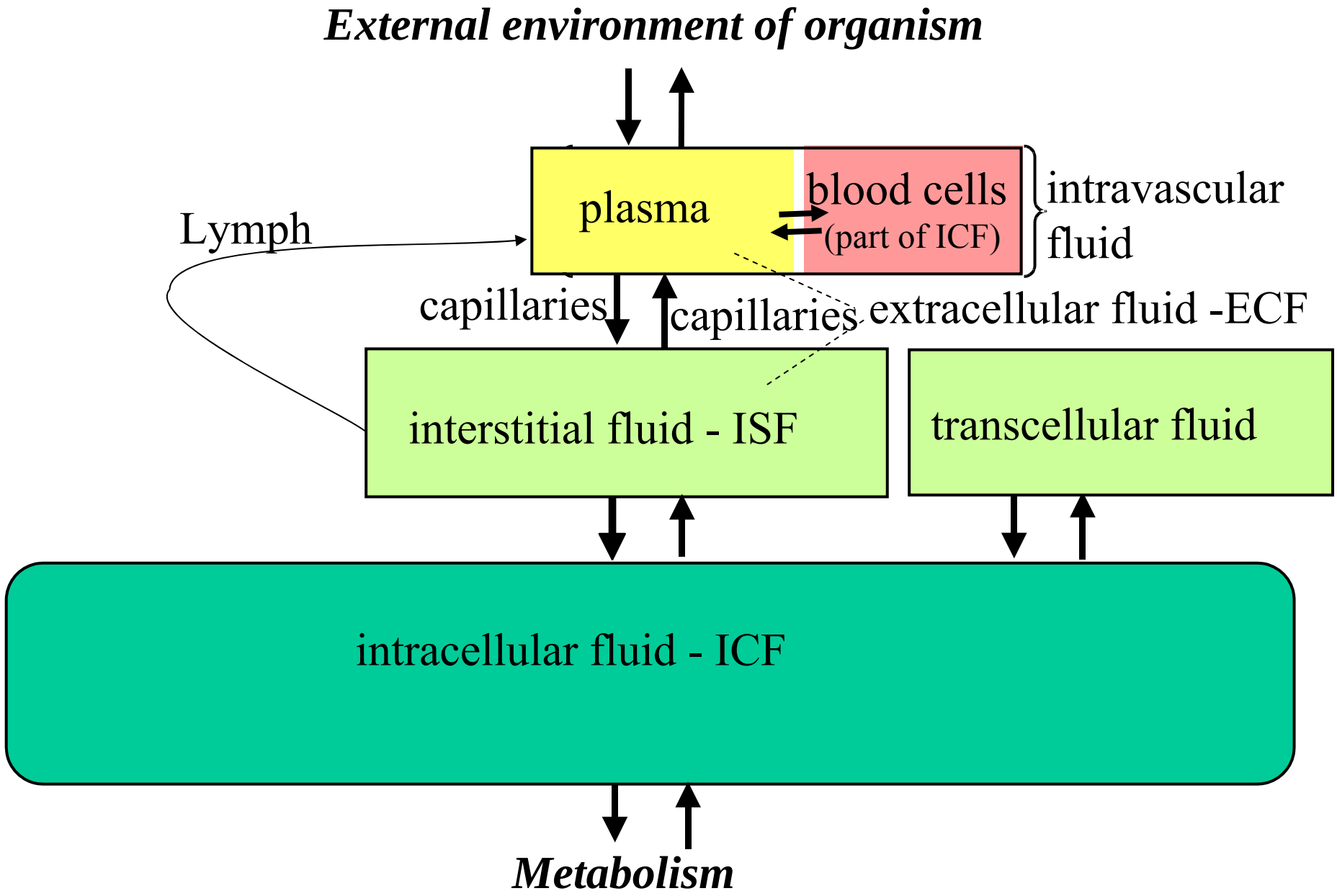
depletion ↓




External environment of organism
Concentrations
Balance estimation
extracellular fluid - ECF
intracellular fluid - ICF
Metabolism


External environment of organism
Balance estimation
Concentrations
Lymph
plasma
capillaries
extracellular
fluid -ECF
interstitial fluid - ISF
intracellular fluid - ICF
Metabolism


External environment of organism
plasma
blood cells
(part of ICF)
intravascular
fluid
Lymph
capillaries
capillaries
extracellular
fluid -ECF
interstitial fluid - ISF
intracellular fluid - ICF
Metabolism


External environment of organism
plasma
blood cells
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Lymph
capillaries
capillaries
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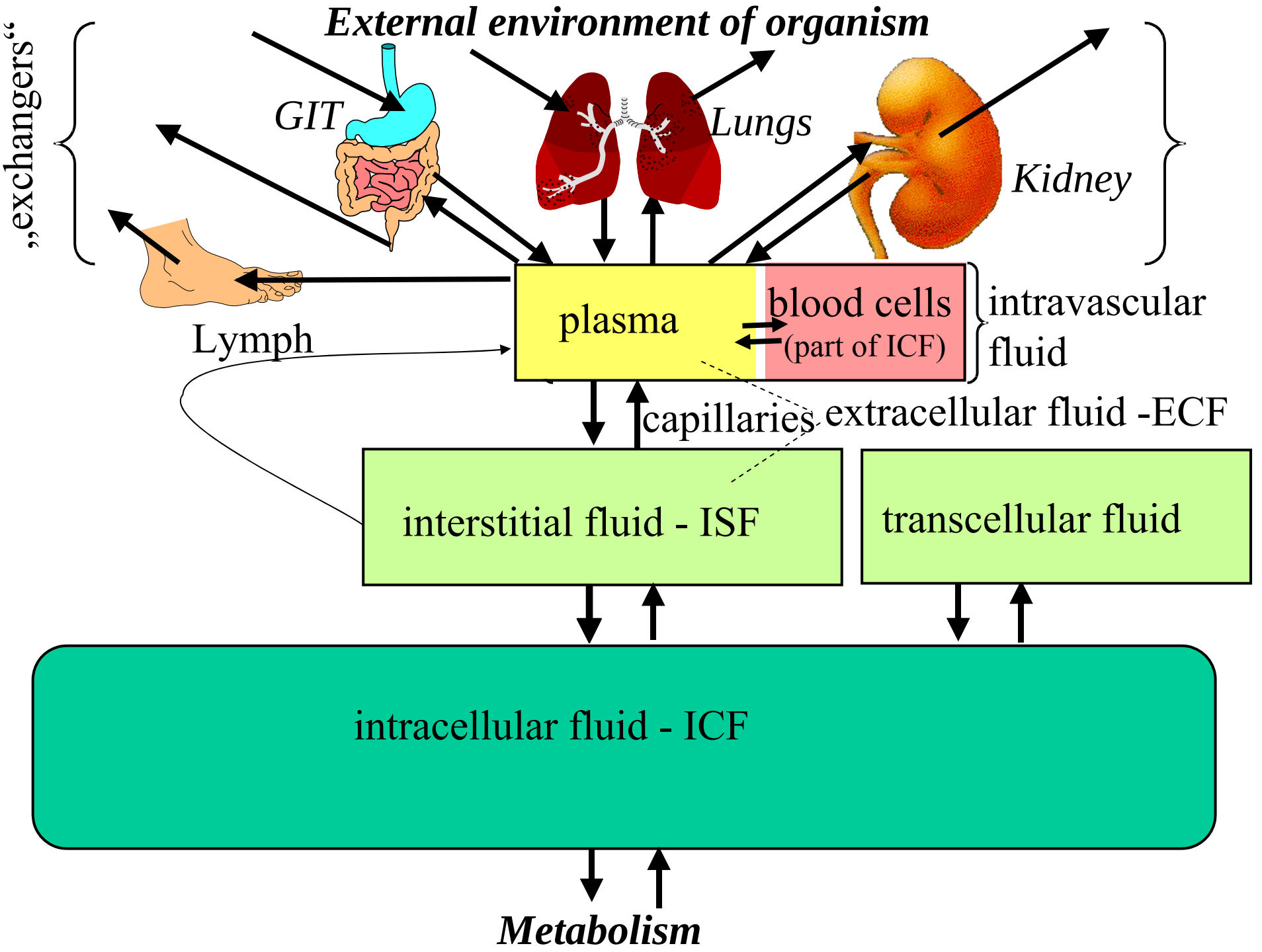
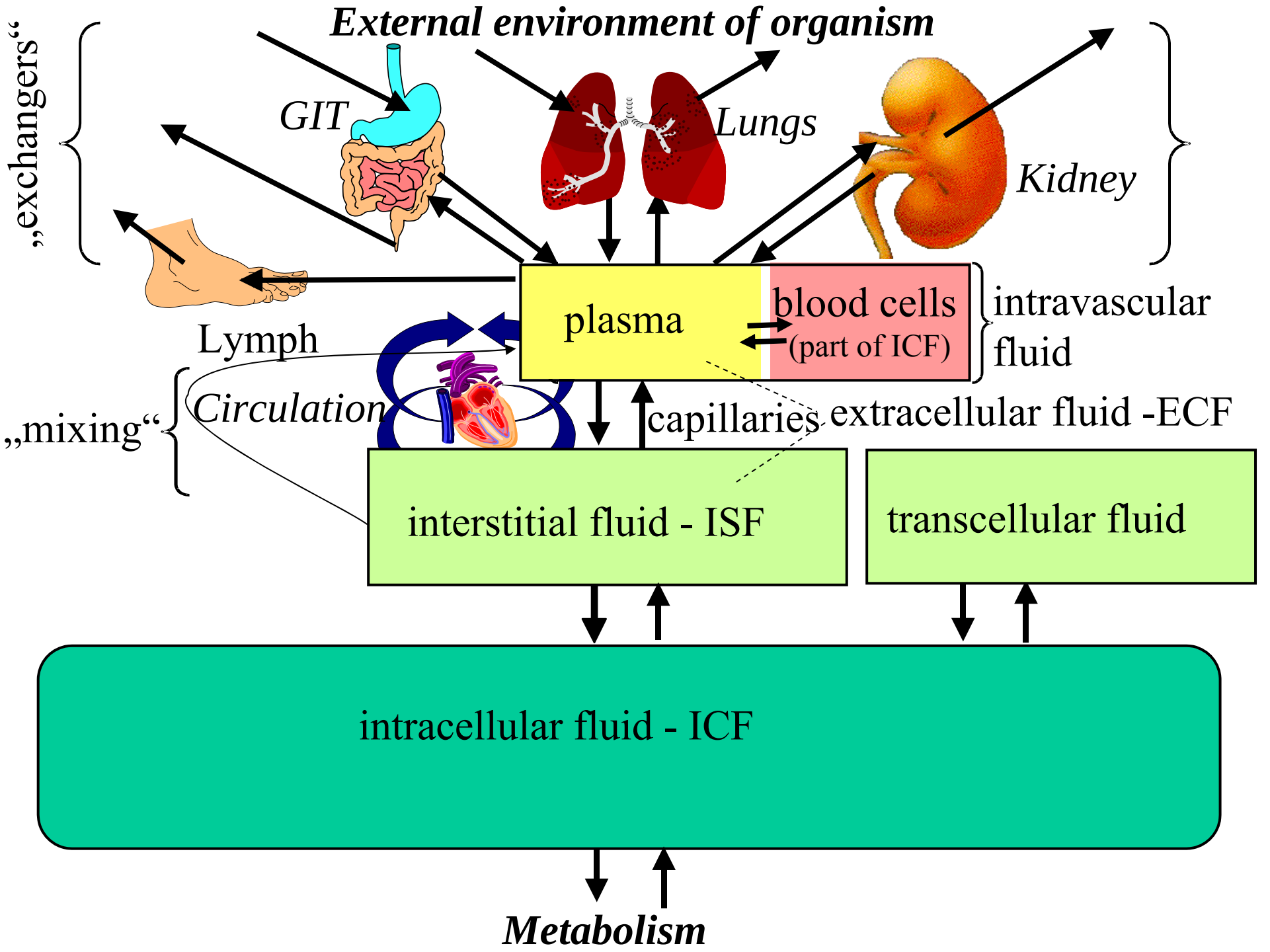
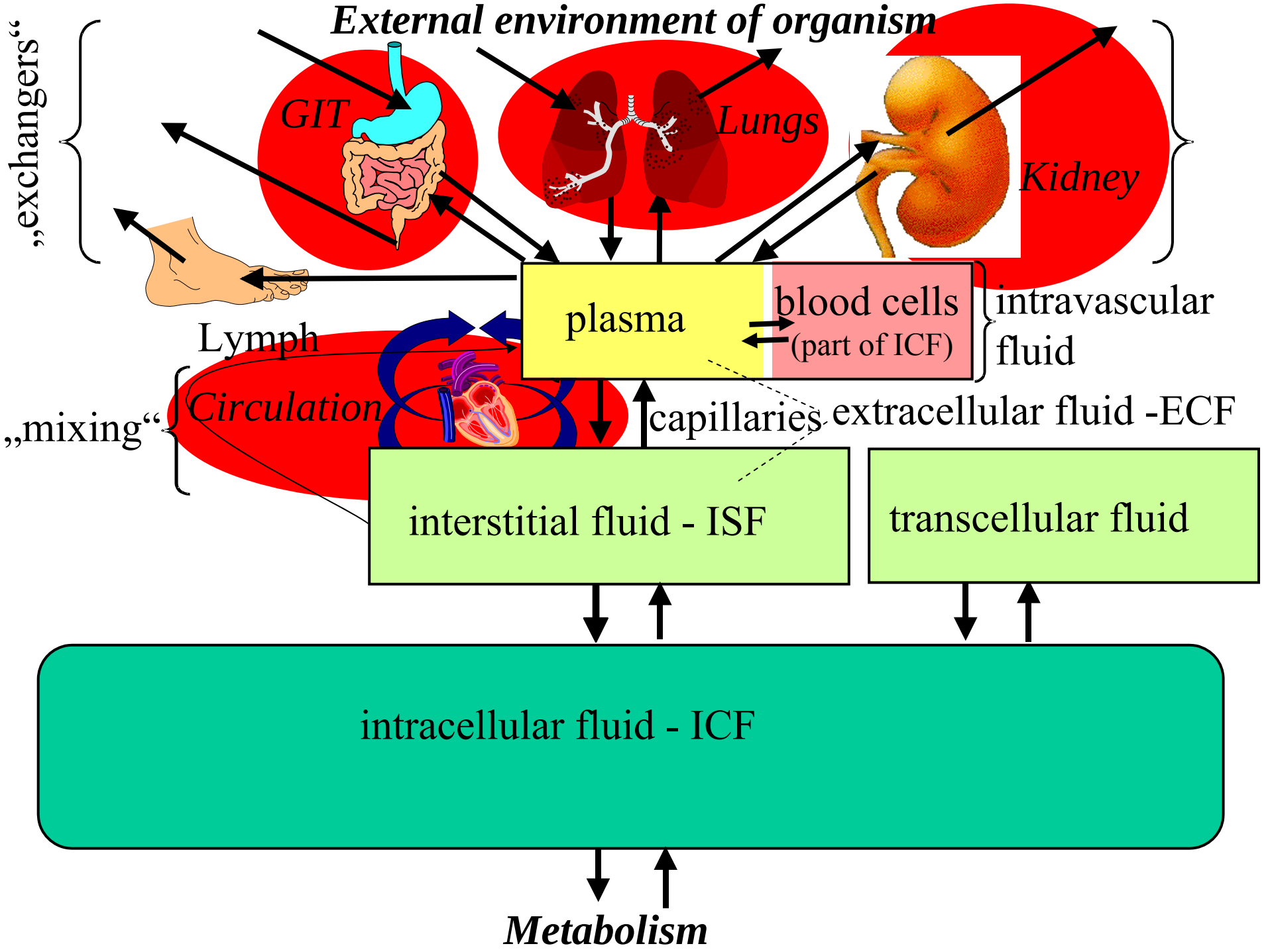
transcellular fluid
intracellular fluid - ICF
Metabolism


External environment of organism
„exchangers“
GIT
Lungs
Kidney
Lymph
plasma
blood cells
(part of ICF)
intravascular
fluid
capillaries
extracellular fluid -ECF
interstitial fluid - ISF
transcellular fluid
intracellular fluid - ICF
Metabolism


External environment of organism
„exchangers“
GIT
Lungs
Kidney
plasma
blood cells
(part of ICF)
intravascular
fluid
Lymph
„mixing“
Circulation
capillaries
extracellular fluid -ECF
interstitial fluid - ISF
transcellular fluid
intracellular fluid - ICF
Metabolism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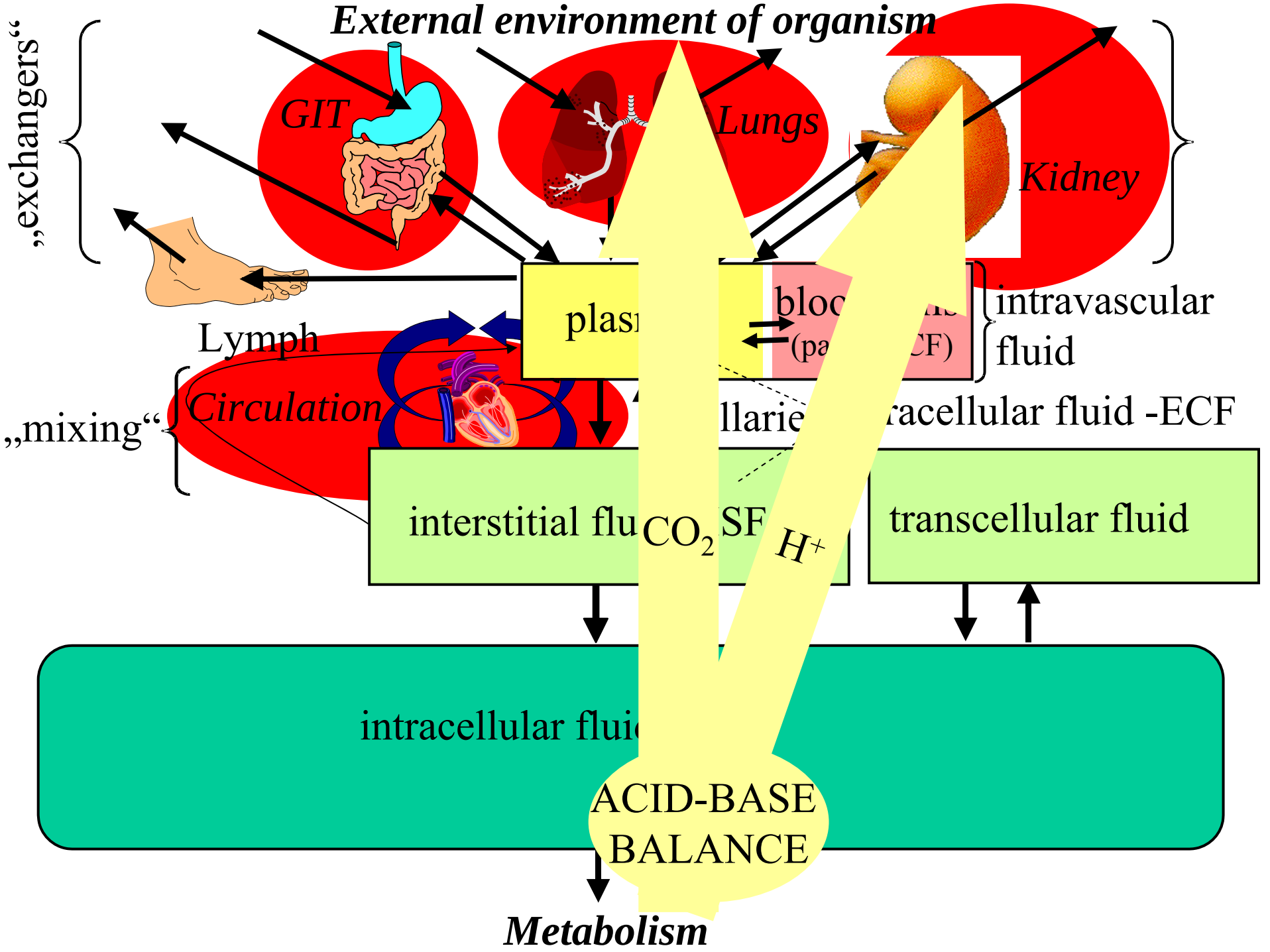
Metabolism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Circulation
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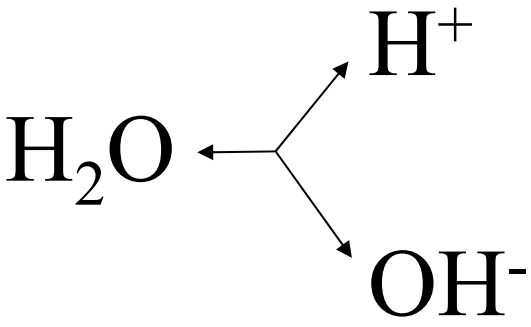
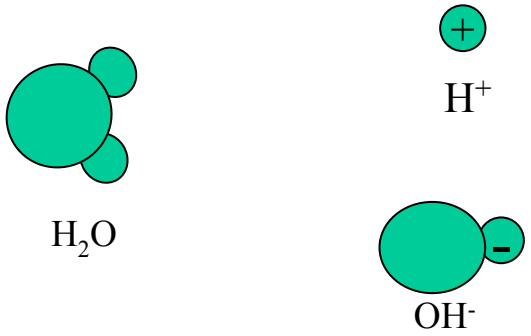
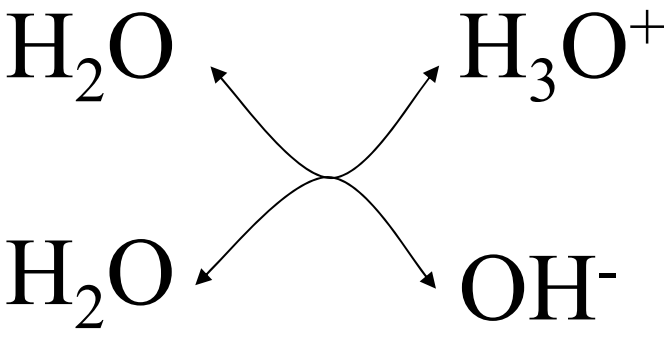
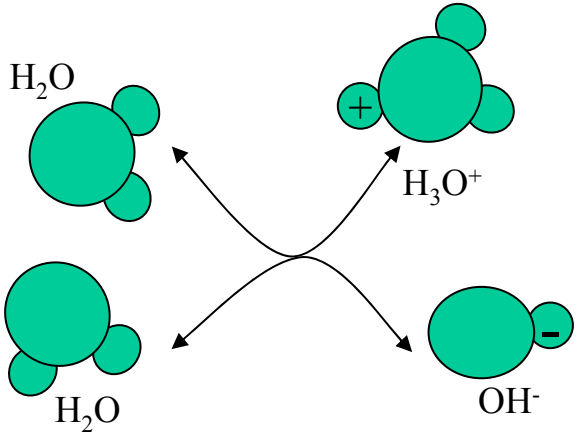
SF
transcellular fluid
CO_2
H^+
intracellular flui
ACID-BASE BALANCE
Metabolism


H_2O
H^+
OH^-


H^+
H_2O
OH^-


H_2O
H_2O
H_3O^+
OH^-


H_2O
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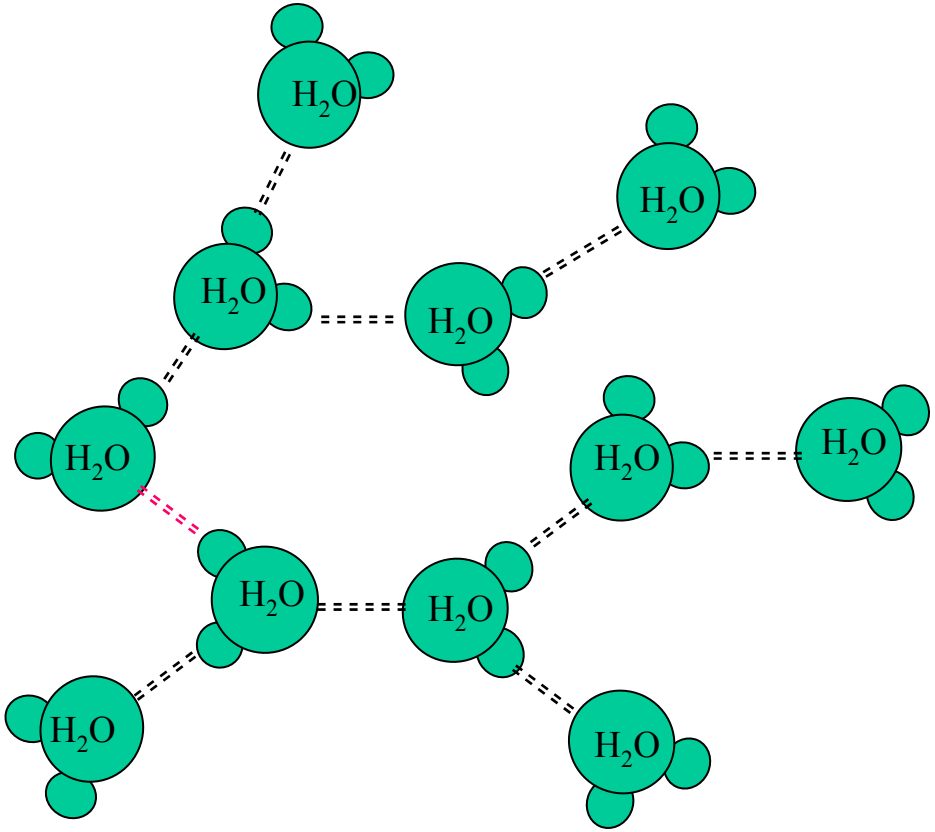
H2O
H2O
H2O
H2O
H2O
H2O
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H2O
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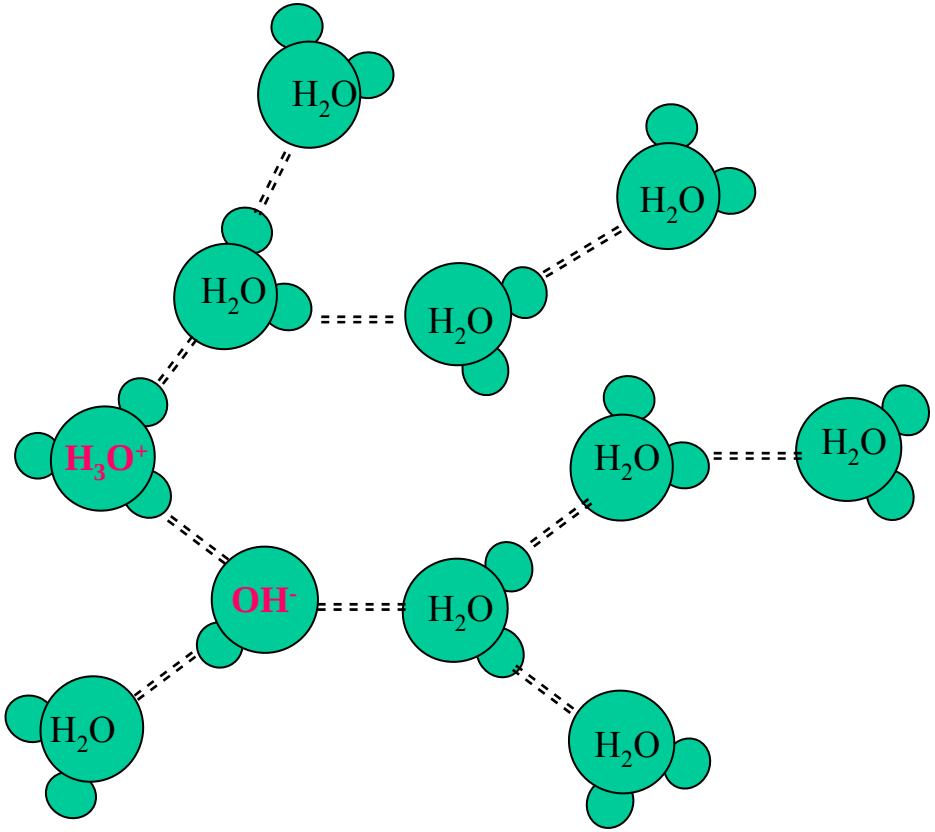
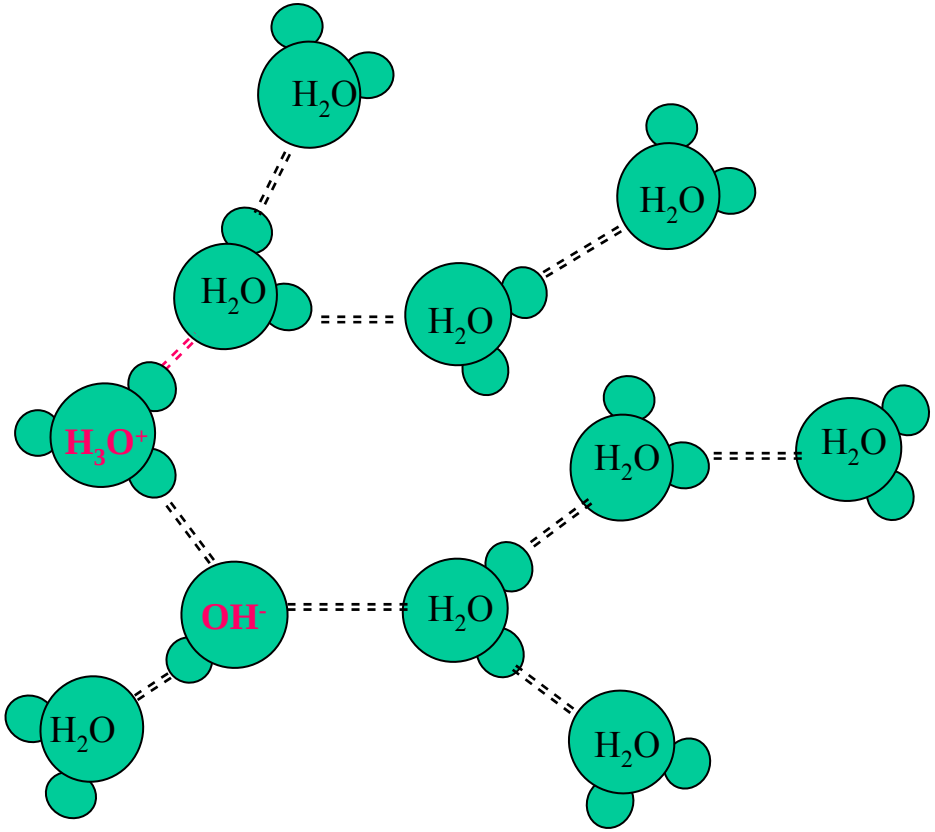
H2O


H2O
H2O
H2O
H2O
H3O+
H2O
H2O
OH-
H2O
H2O
H2O


H2O
H2O
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H3O+
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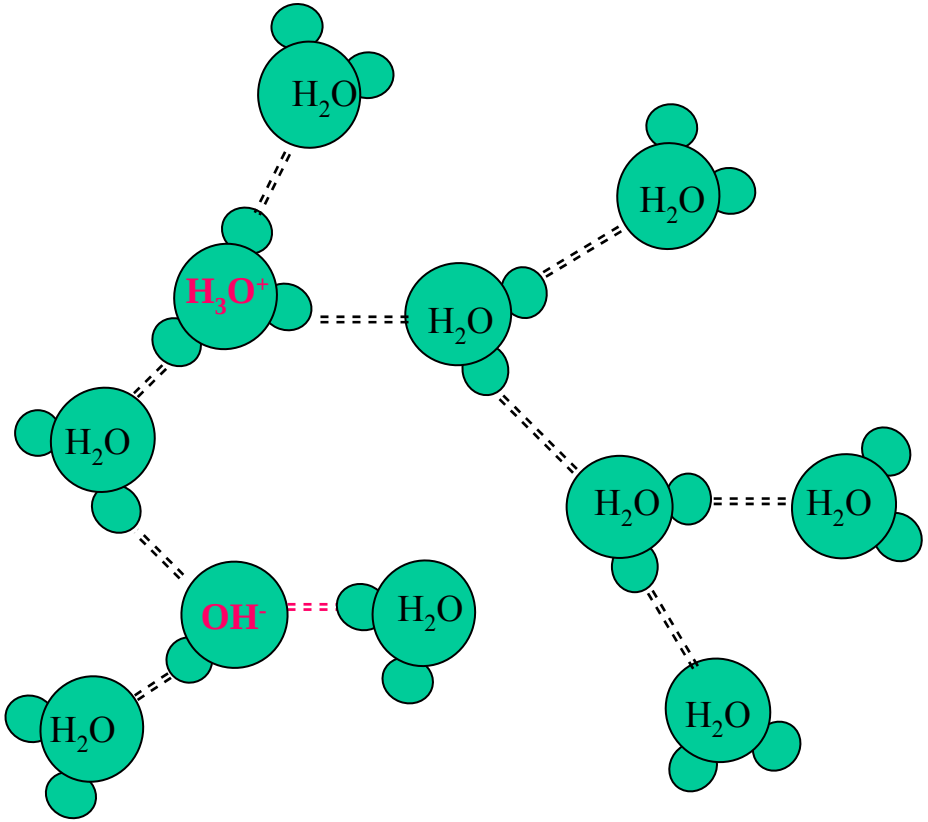
H2O
OH-
H2O
H2O
H2O


H2O
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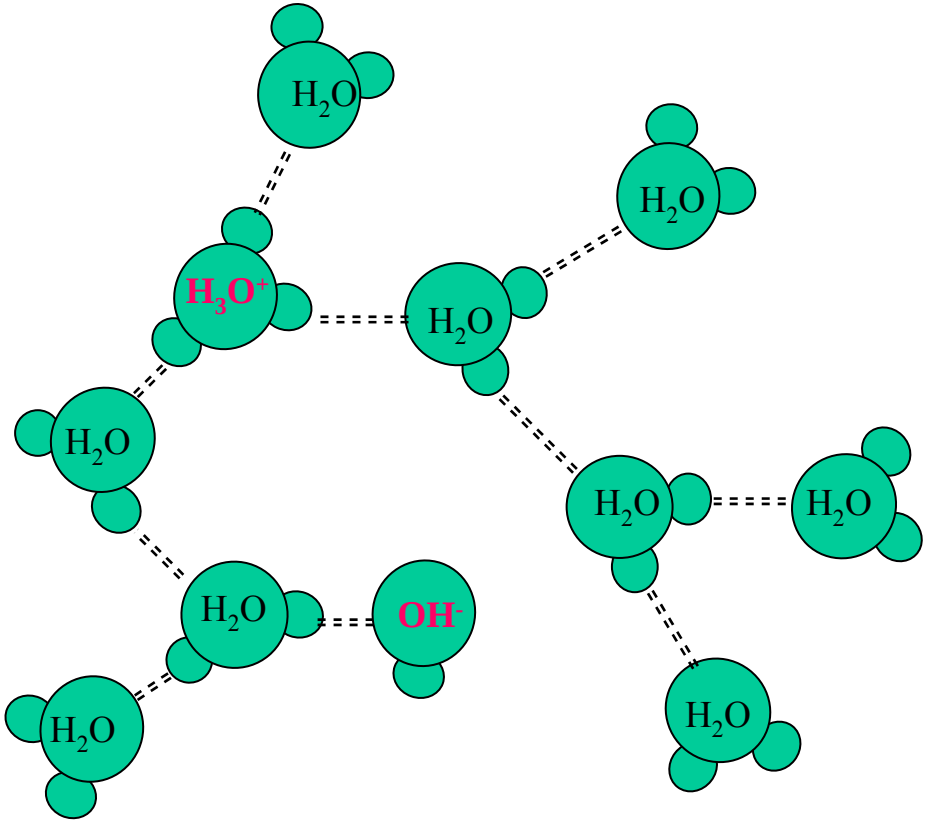
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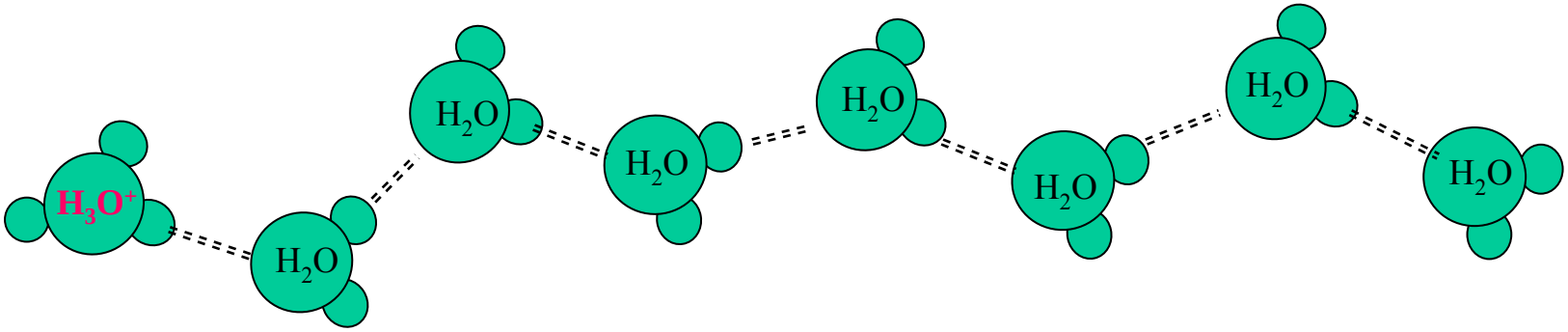
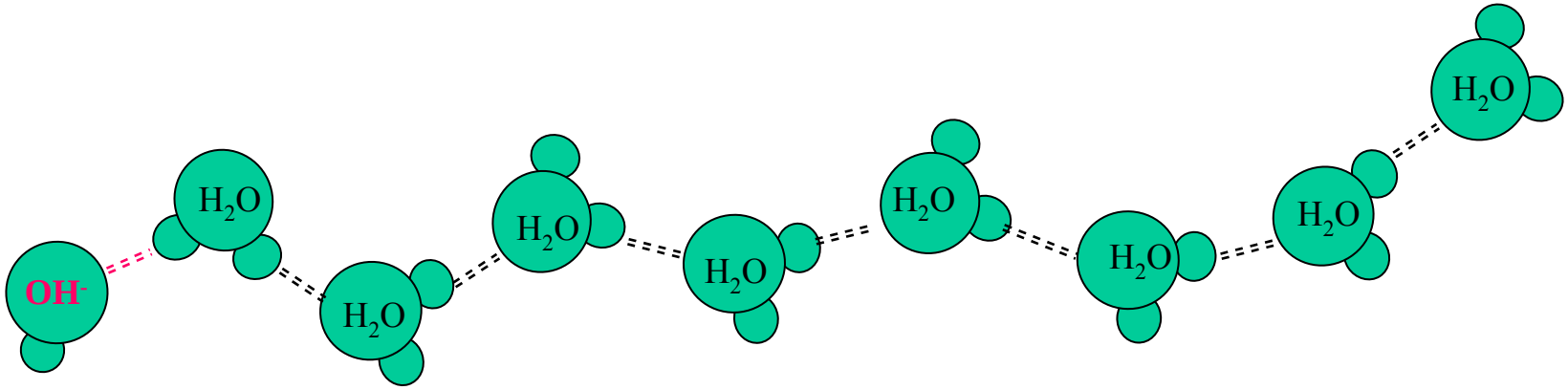
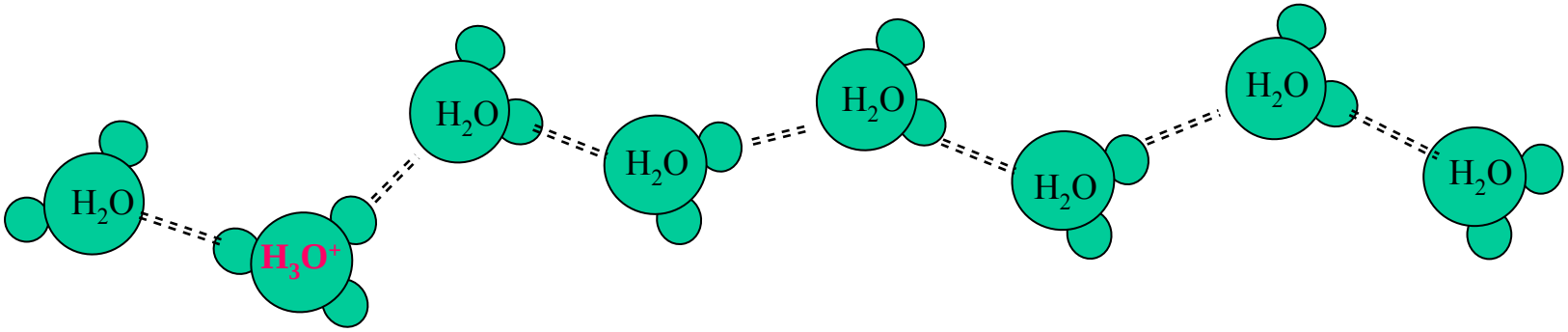


$$H_3O^+ + H_2O \longrightarrow H_2O + H_3O^+$$



$$OH^- + H_2O \longrightarrow H_2O + OH^-$$



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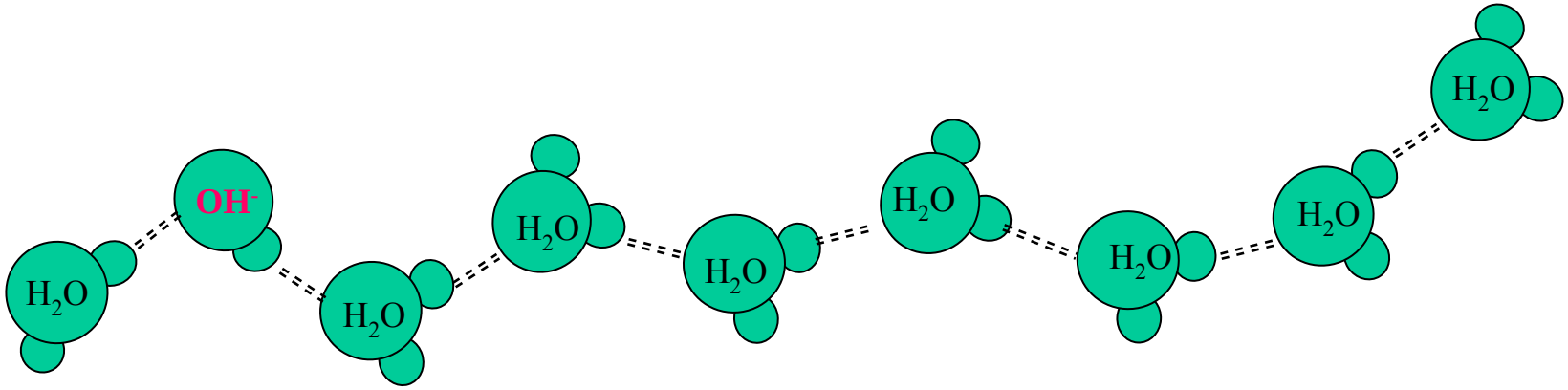

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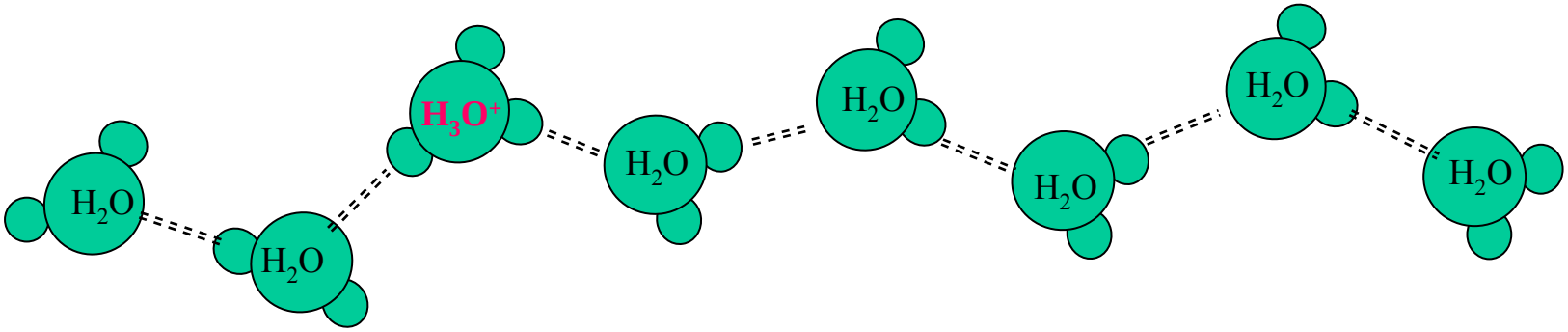

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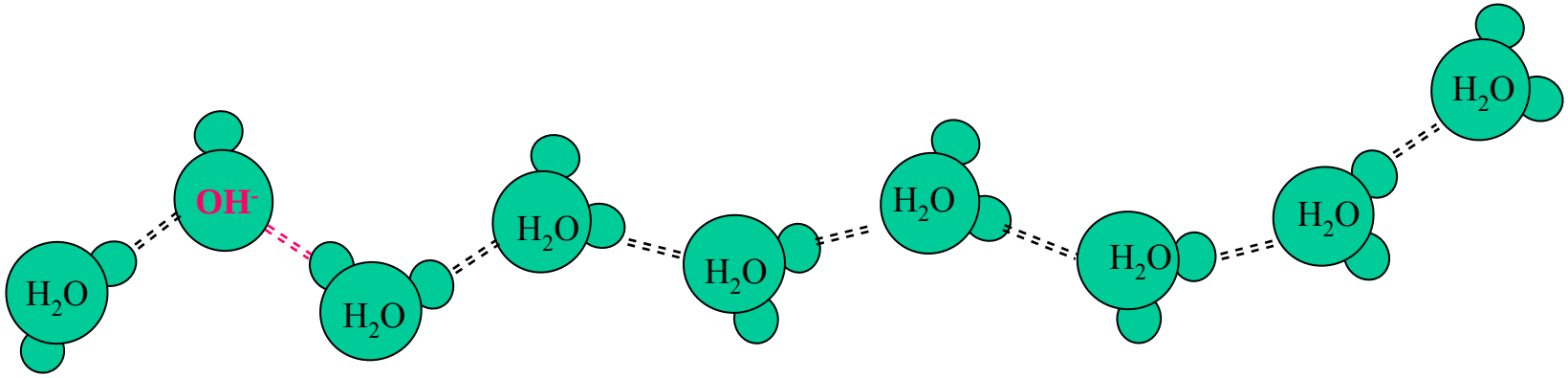

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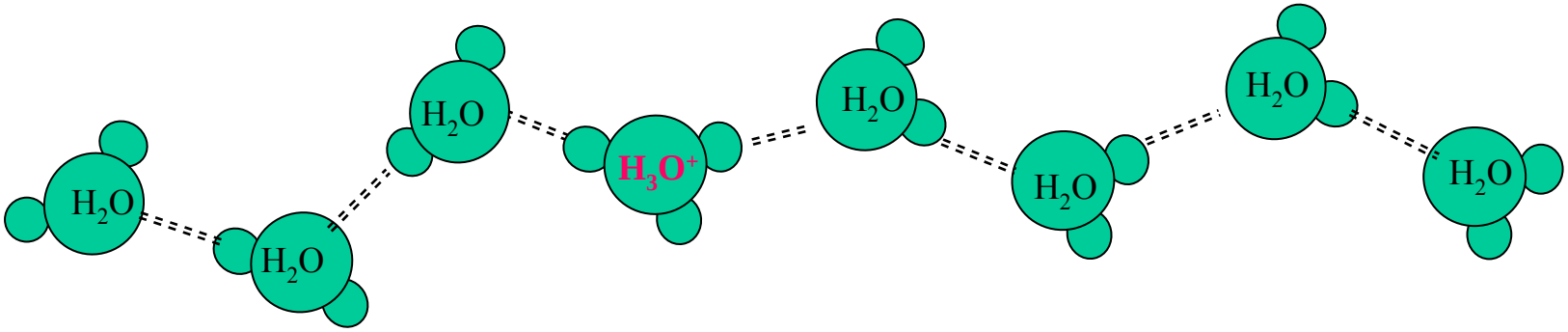

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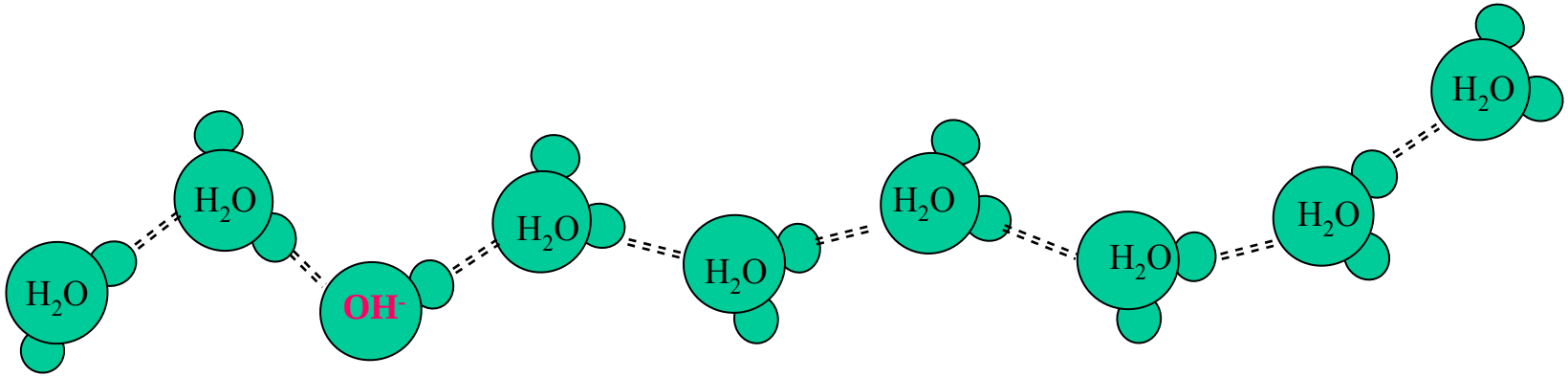

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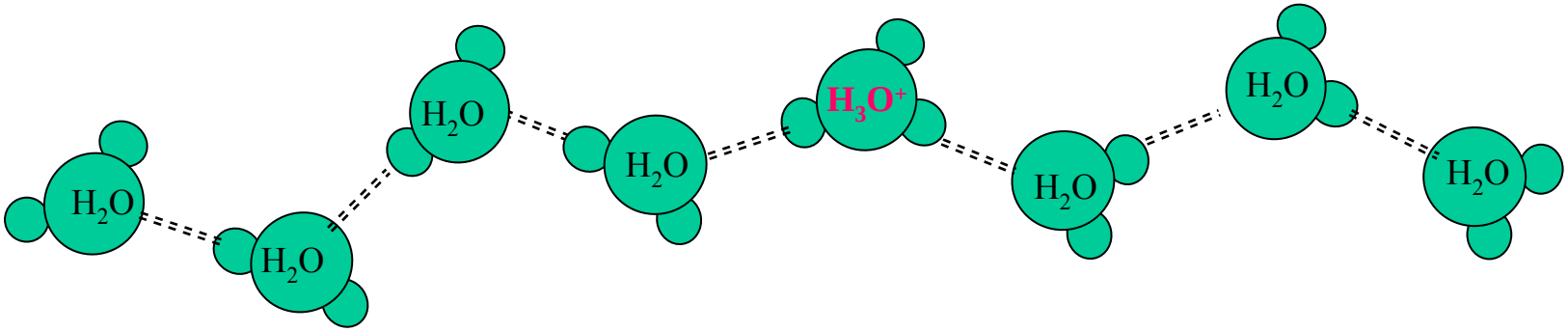

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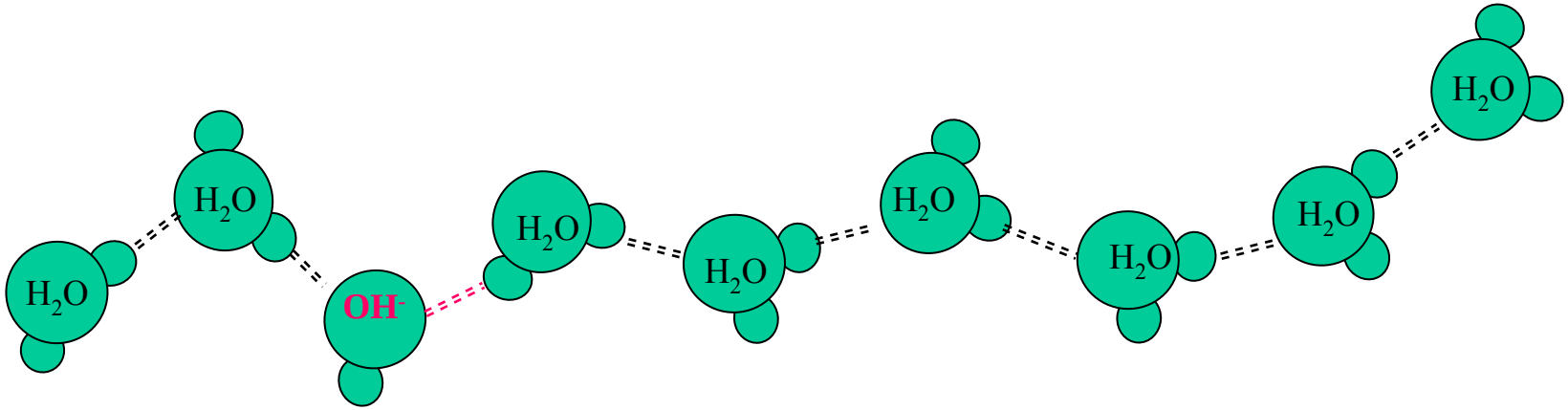

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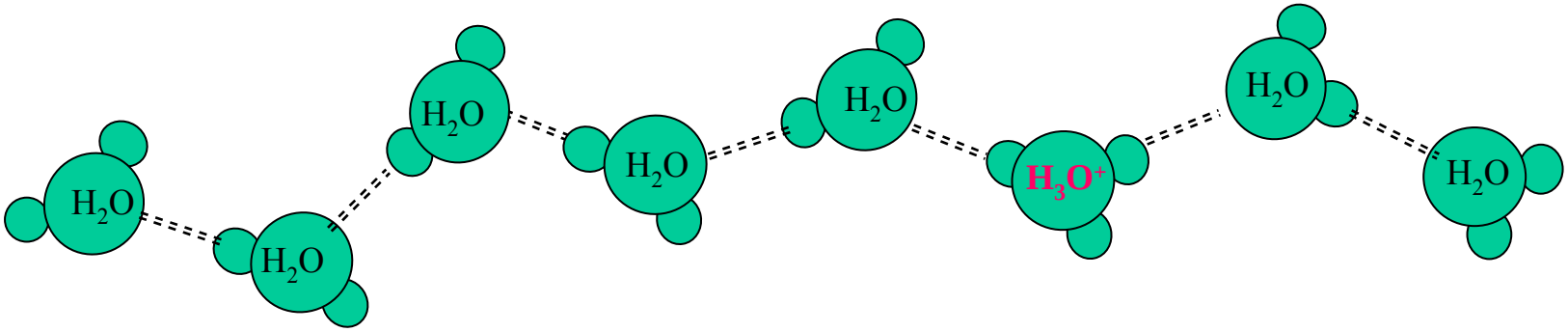

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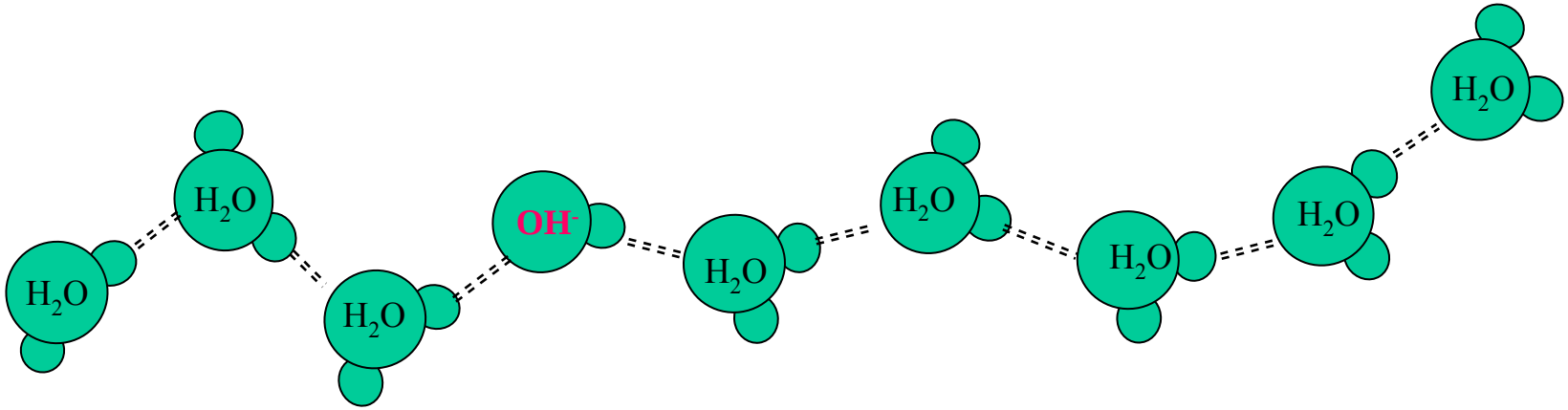

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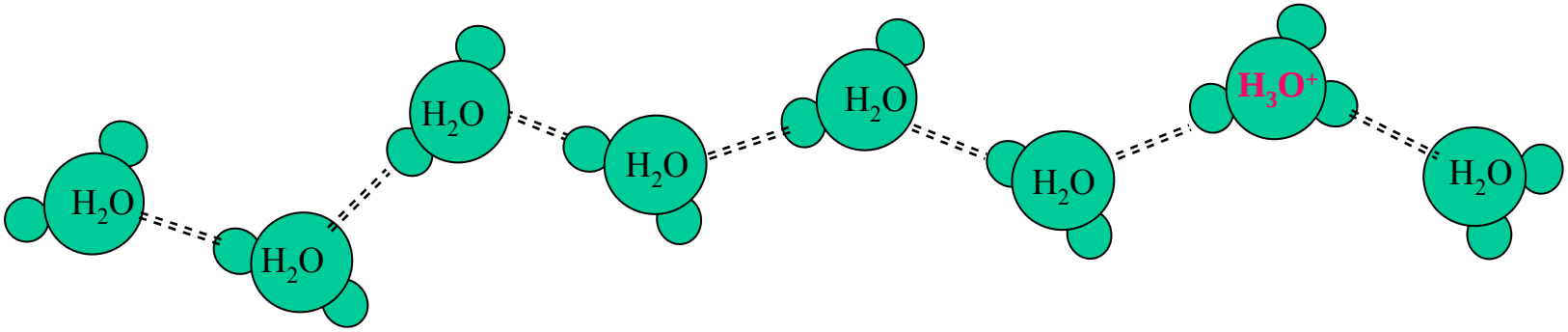

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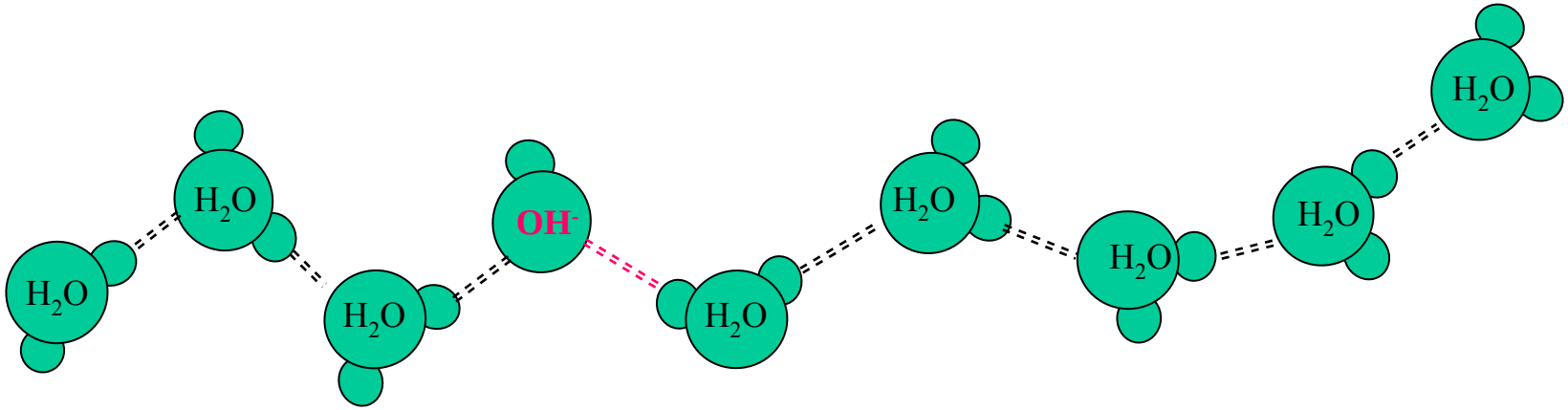

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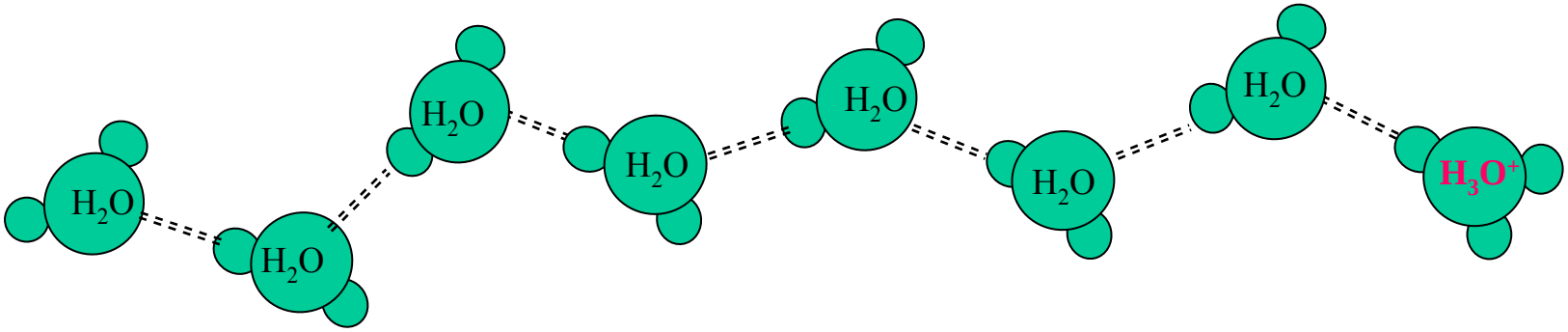

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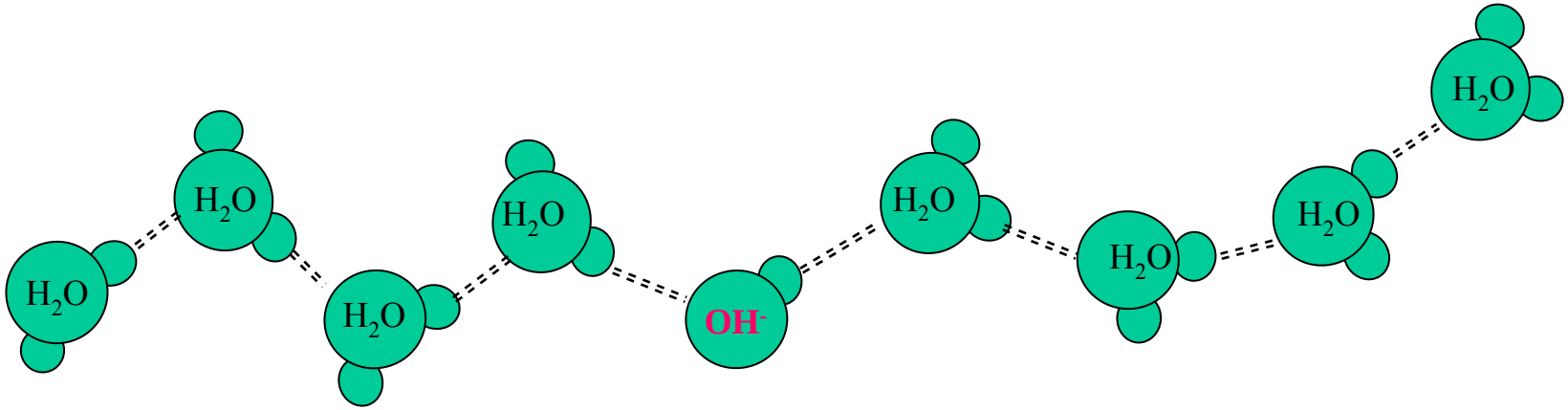

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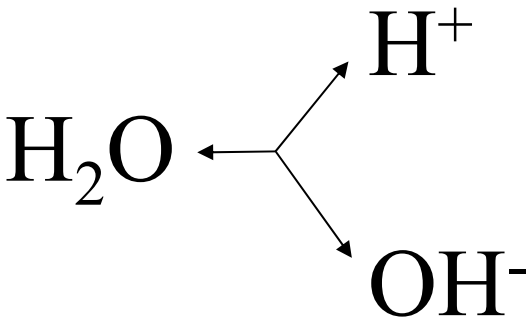
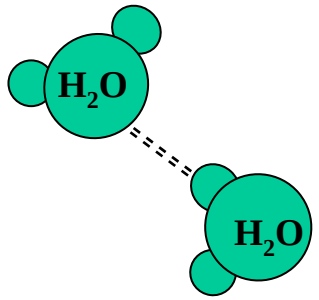
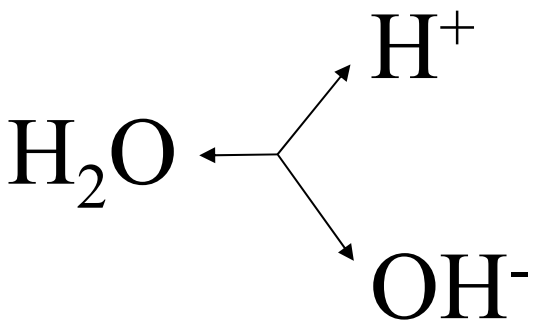
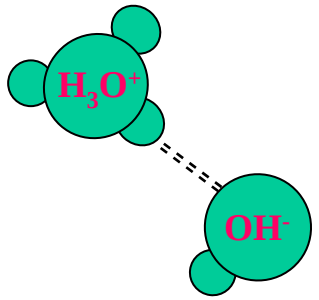

H+
H2O
OH-


H2O
H2O





$$H_2O \underset{v_2=k_2[H^+][OH^-]}{\overset{v_1=k_1[H_2O]}{\rightleftharpoons}} H^+ + OH^-$$

$v_1 = v_2$

$k_1[H_2O] = k_2[H^+][OH^-]$

$$K' = \frac{k_1}{k_2} = \frac{[H^+][OH^-]}{[H_2O]}$$

$K'\,[H_2O] = [H^+][OH^-]$

$[H_2O]$ = ***constant***

$K_w = [H^+][OH^-] = 2{,}4 \cdot 10^{-14}\ mol^2/l^2$ at 37°C

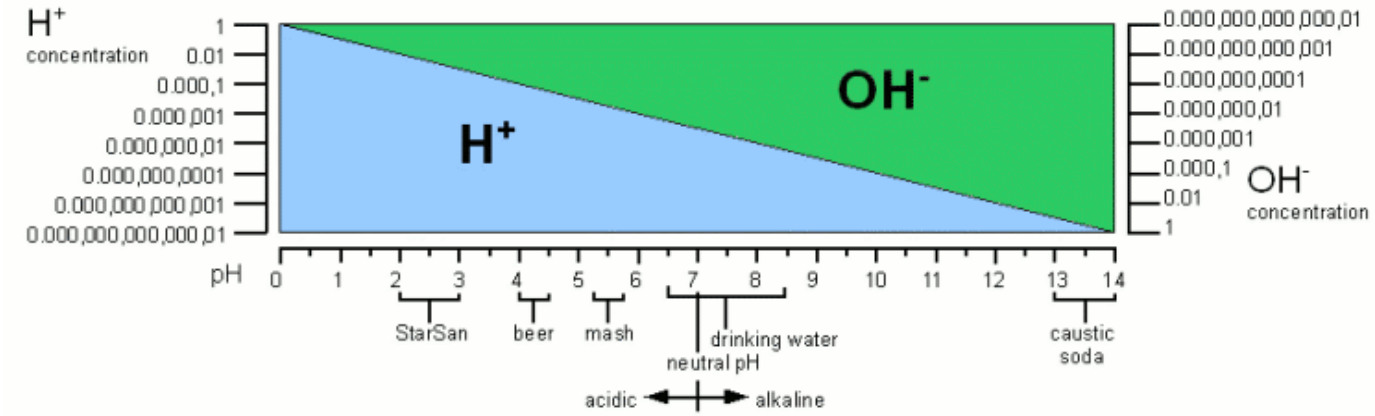
pH = 7.4

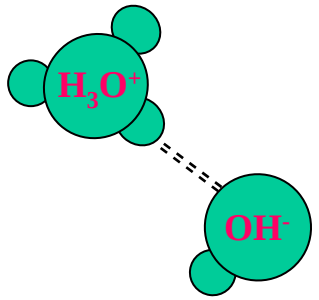
$[H^+] = 10^{-7{,}4}$ mol/l = 40 nmol/l

pH= -log $[H^+]$

$[H^+] = 1{,}55 \cdot 10^{-7}$ mol/l = 155 nmol/l

$[OH^-] = 1{,}55 \cdot 10^{-7}$ mol/l = 155 nmol/l





$$H_2O \underset{v_2=k_2[H^+][OH^-]}{\overset{v_1=k_1[H_2O]}{\rightleftharpoons}} H^+ + OH^-$$

$v_1 = v_2$

$k_1[H_2O] = k_2[H^+][OH^-]$

$$K' = \frac{k_1}{k_2} = \frac{[H^+][OH^-]}{[H_2O]}$$

$K'\,[H_2O] = [H^+][OH^-]$

$[H_2O]$ = ***constant***

$K_w = [H^+][OH^-] = 2{,}4 \cdot 10^{-14}\ mol^2/l^2$ at 37°C

pH = 7.4

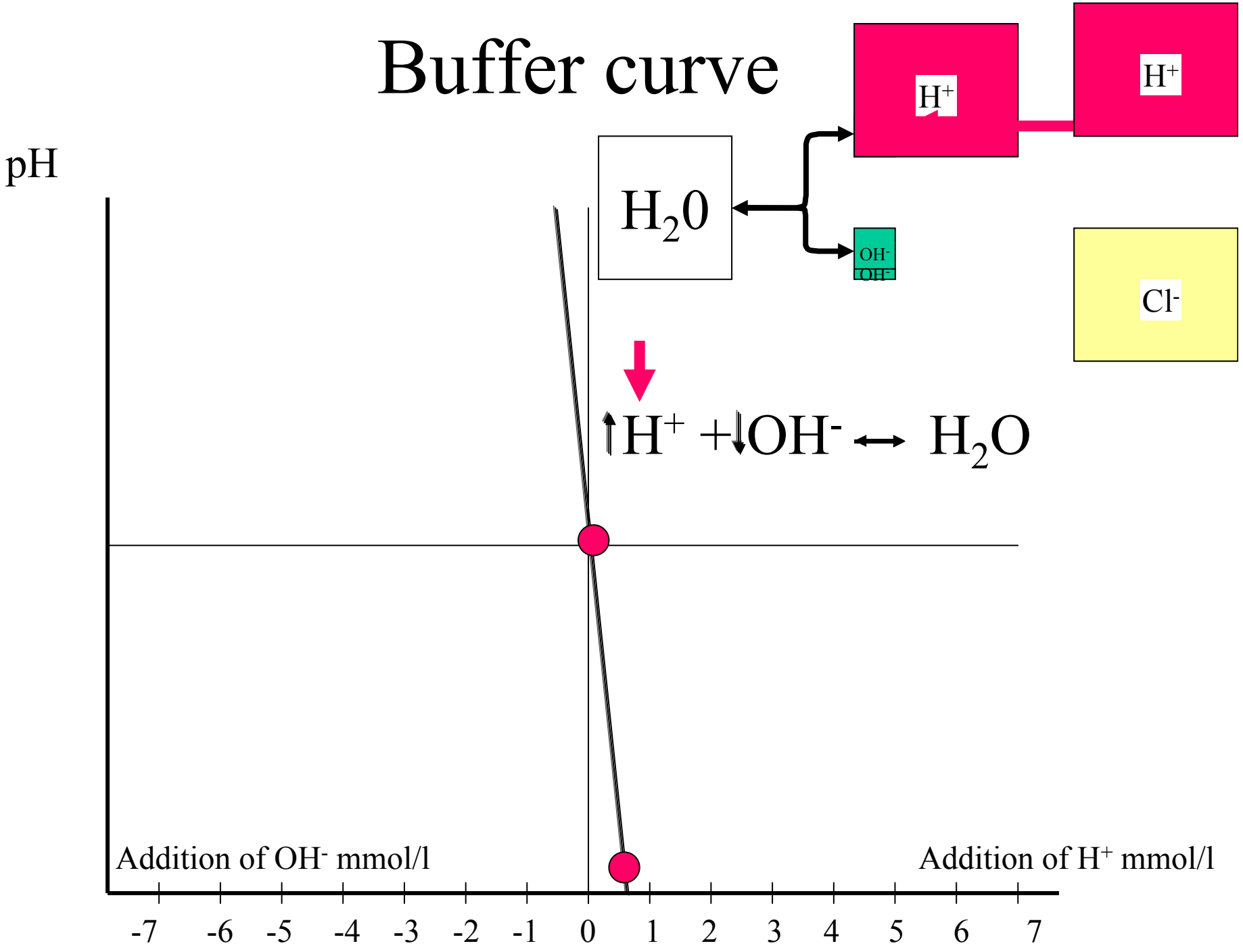
$[H^+] = 10^{-7{,}4}$ mol/l = 40 nmol/l

pH= -log $[H^+]$

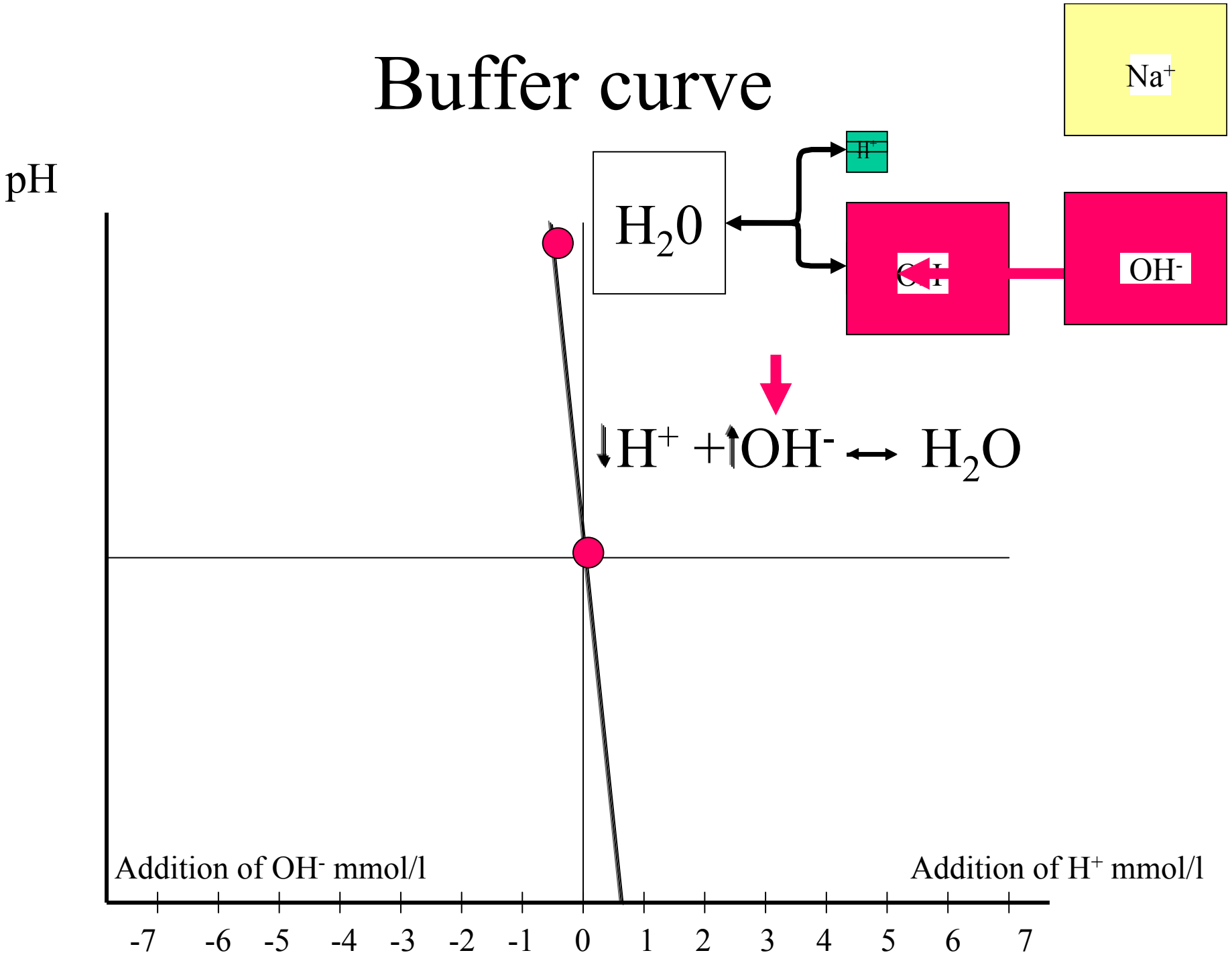
$[H^+] = 1{,}55 \cdot 10^{-7}$ mol/l = 155 nmol/l

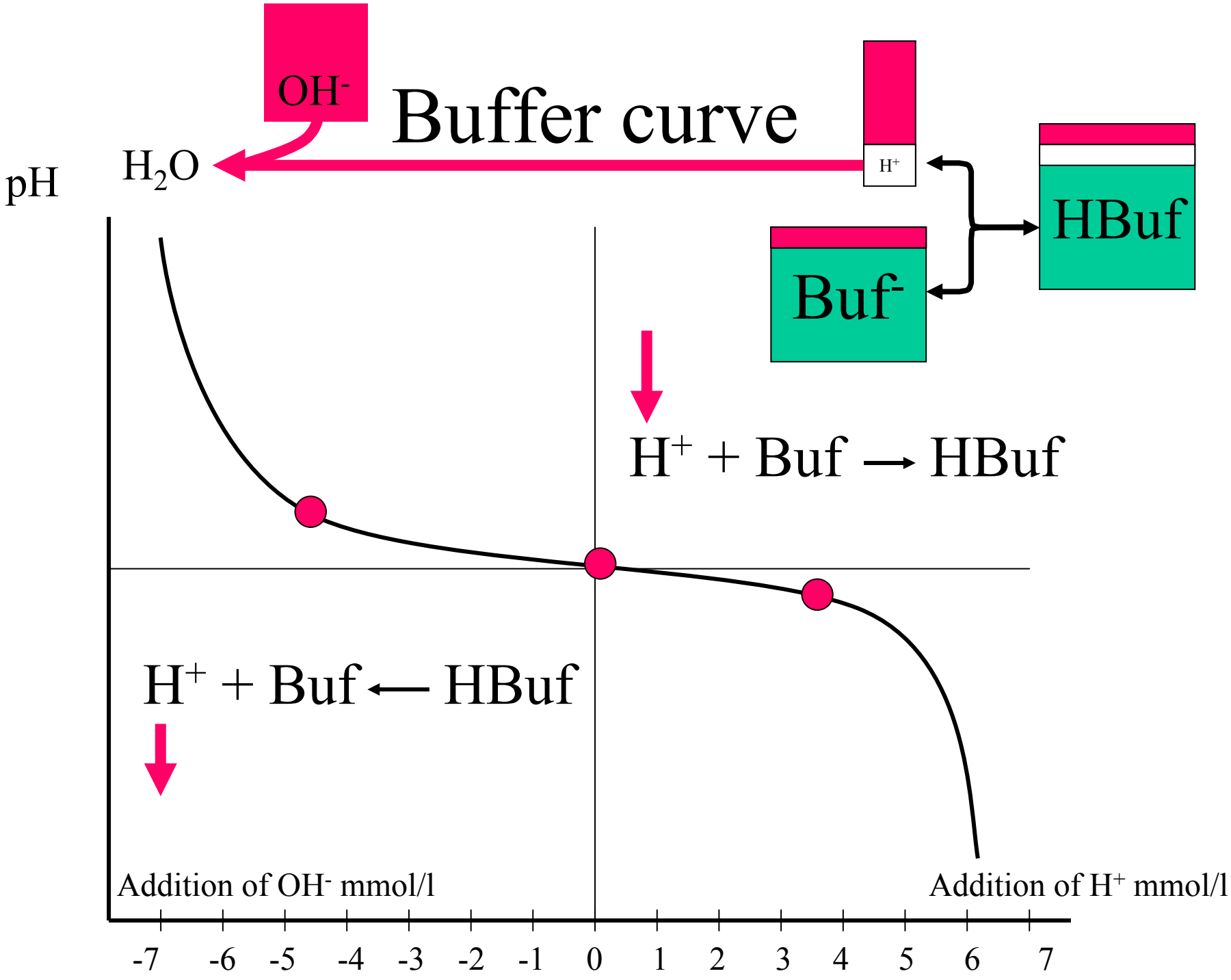
$[OH^-] = 1{,}55 \cdot 10^{-7}$ mol/l = 155 nmol/l

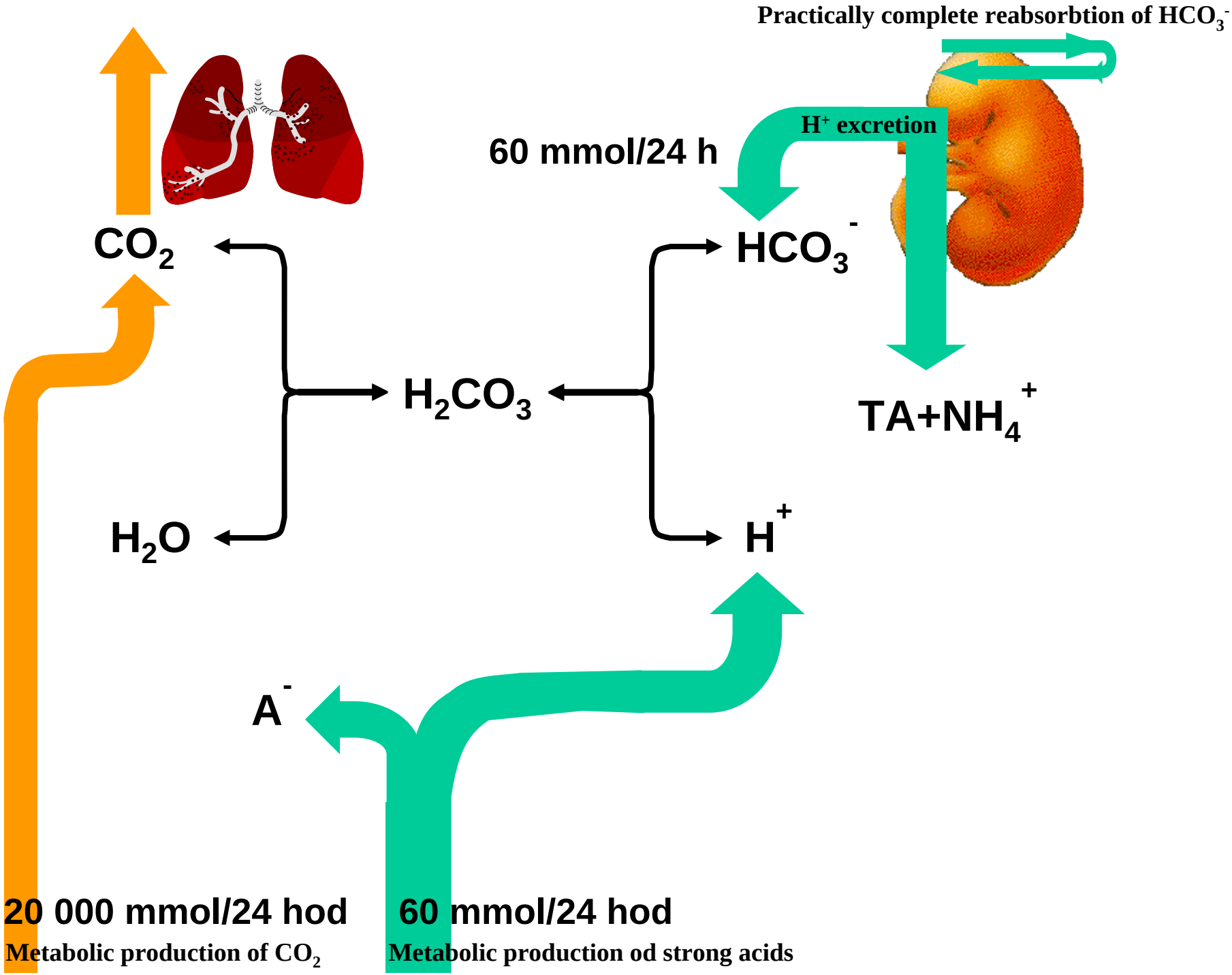
Buffer curve



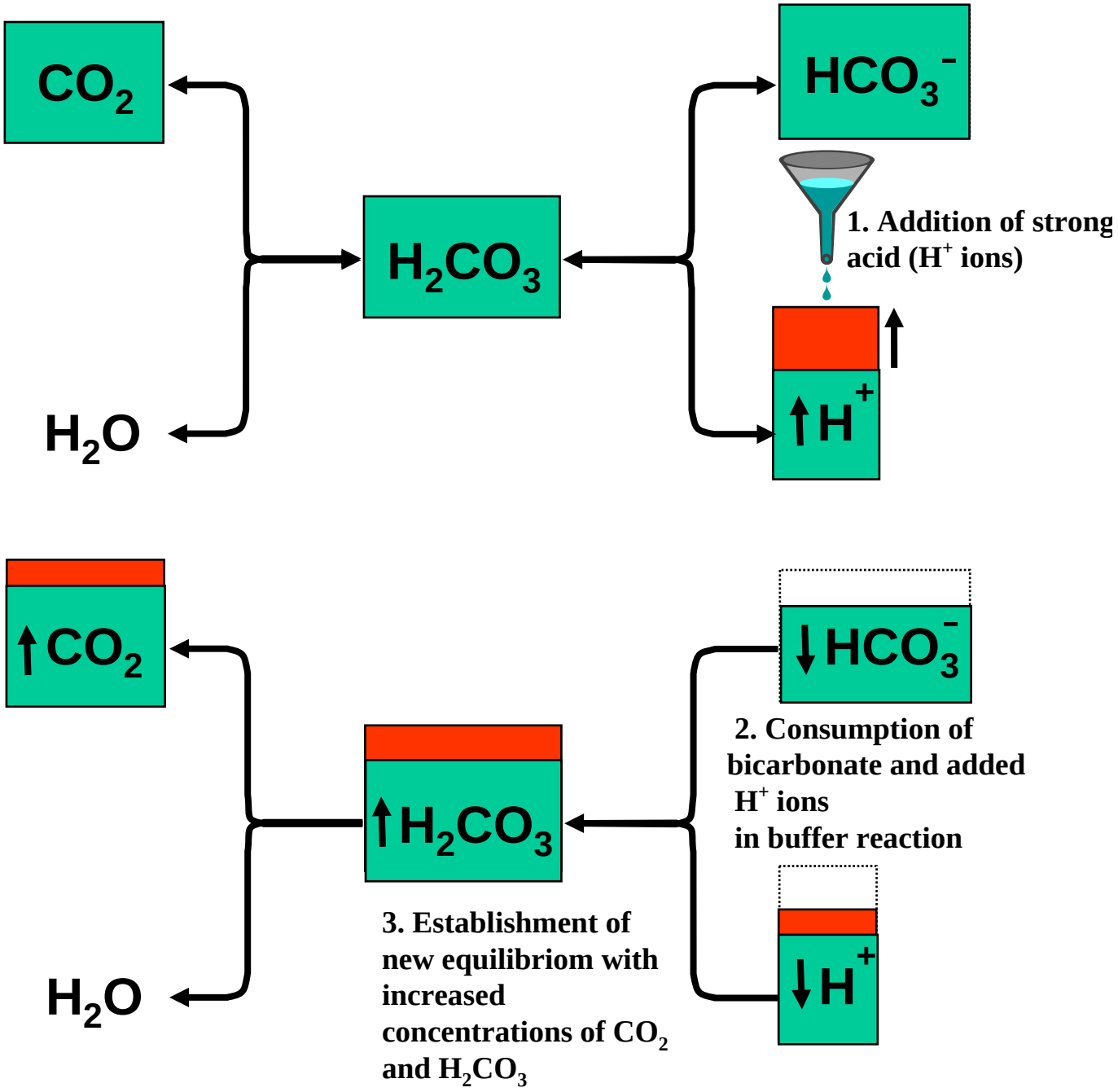
Buffer curve



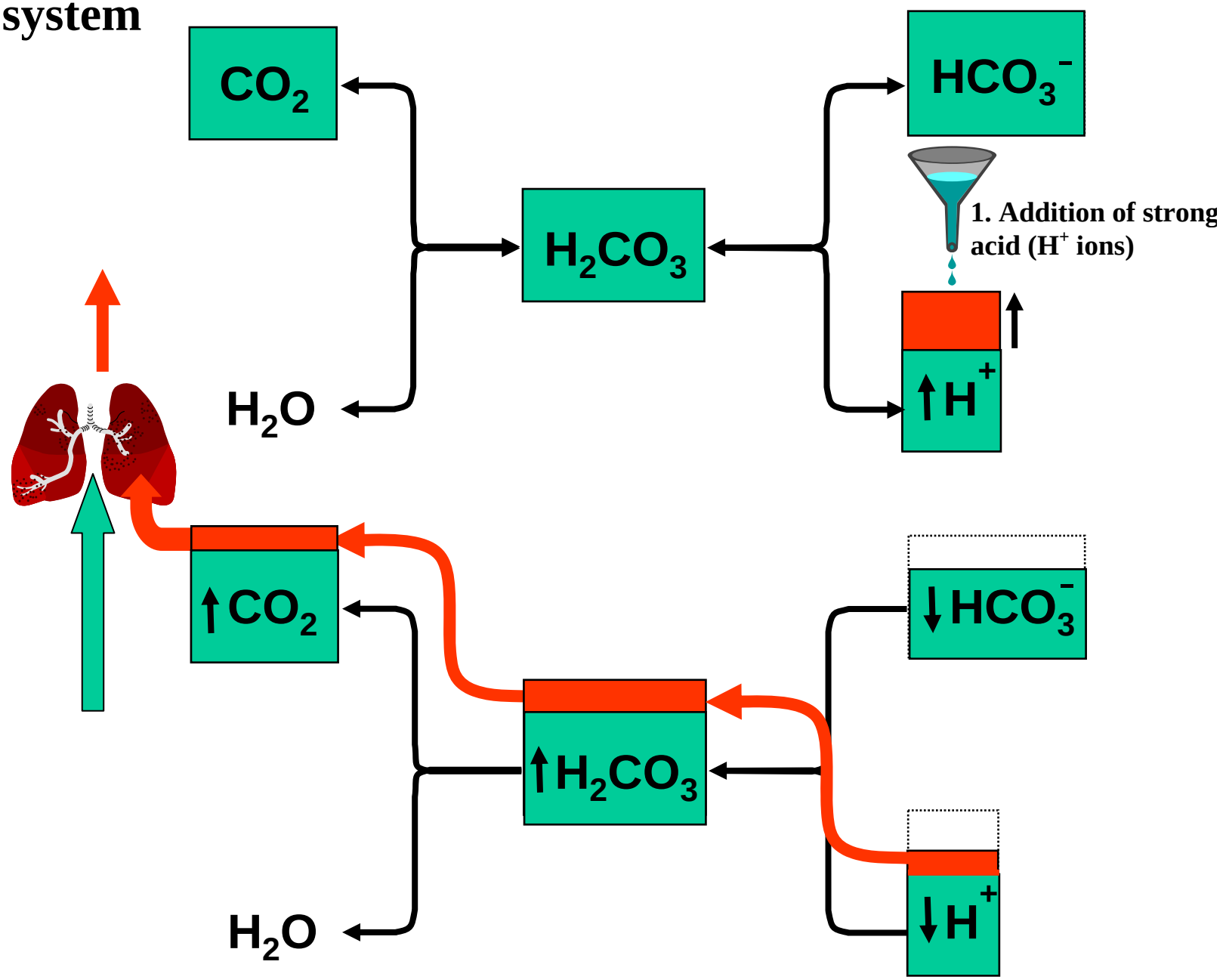

OH-
Buffer curve
pH
H2O
H+
HBuf
Buf-
H+ + Buf → HBuf
H+ + Buf ← HBuf
Addition of OH- mmol/l
Addition of H+ mmol/l
-7
-6
-5
-4
-3
-2
-1
0
1
2
3
4
5
6
7

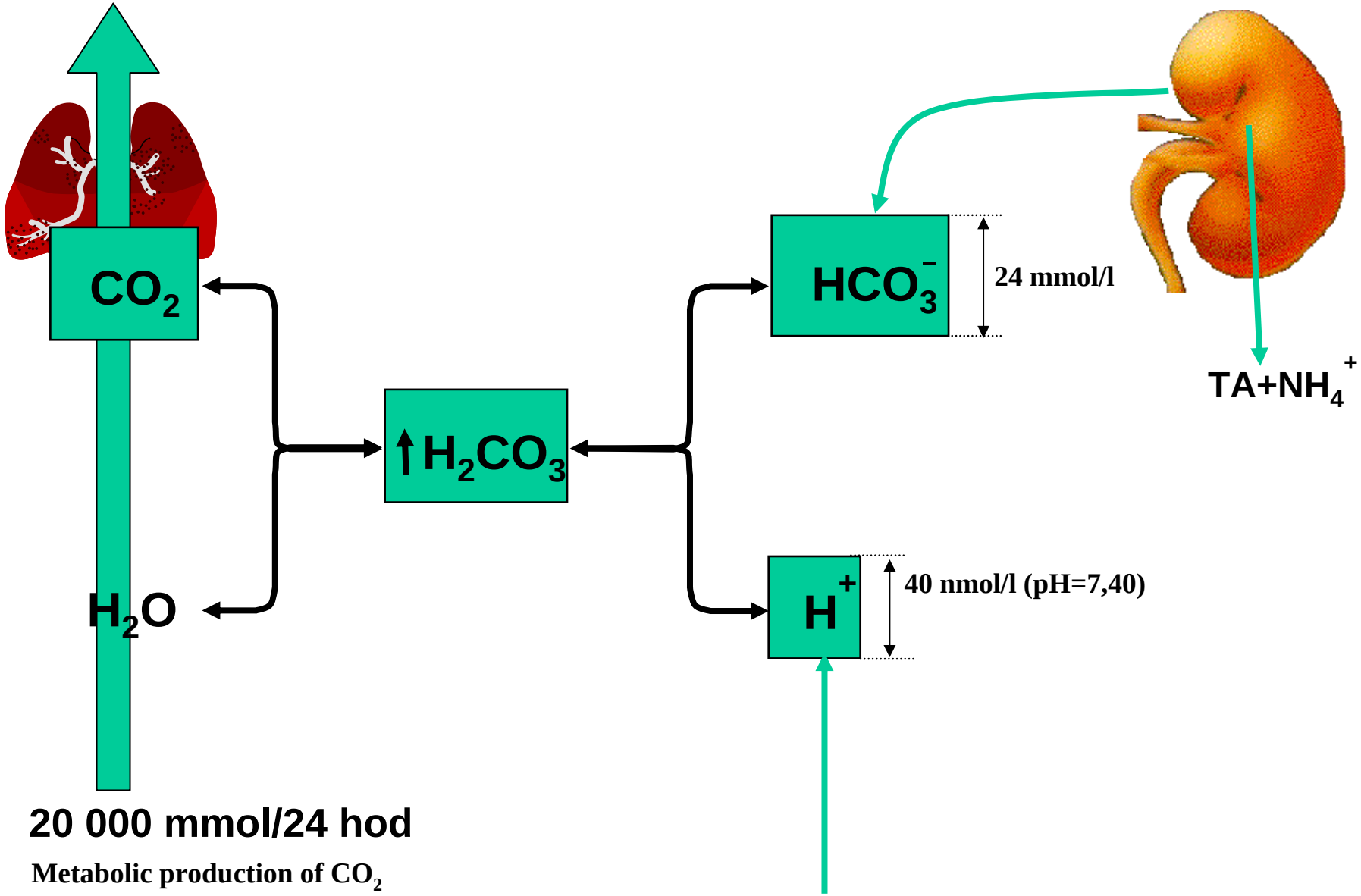

Practically complete reabsorbtion of HCO_3^-
H^+ excretion
60 mmol/24 h
CO_2
HCO_3^-
H_2CO_3
$TA+NH_4^+$
H_2O
H^+
A^-
20 000 mmol/24 hod
Metabolic production of CO_2
60 mmol/24 hod
Metabolic production od strong acids

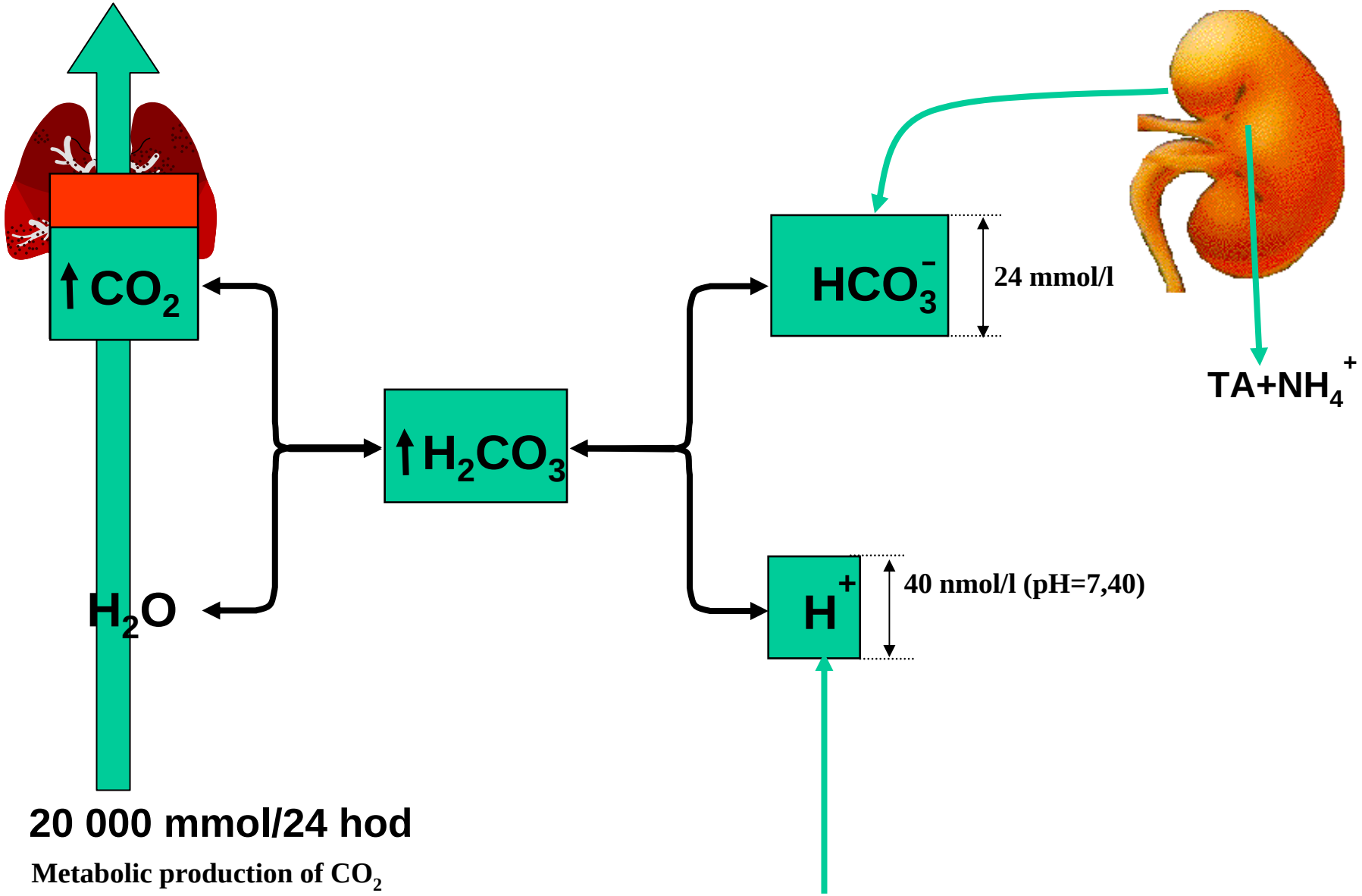
A: Closed system

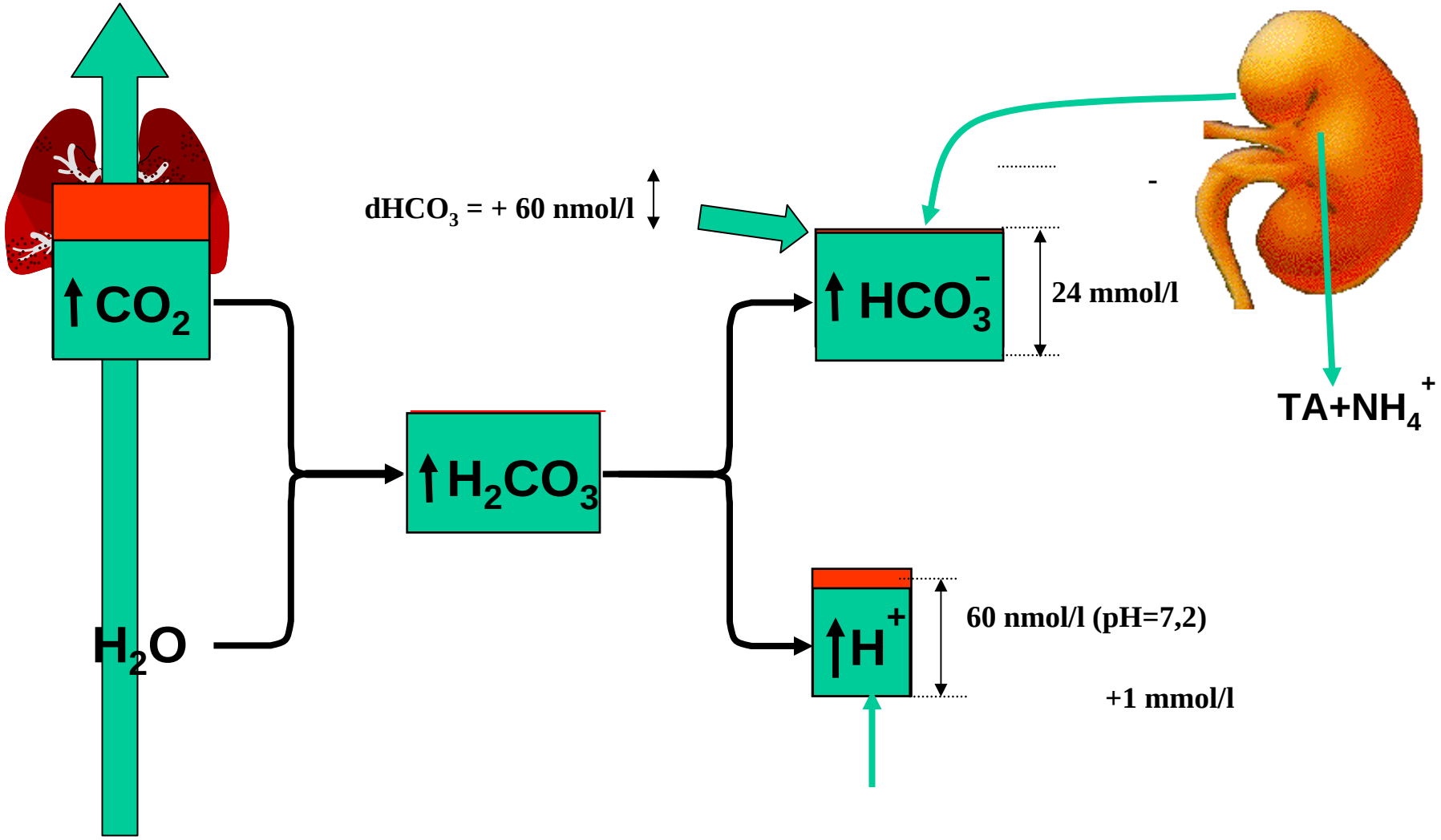


A: Open system



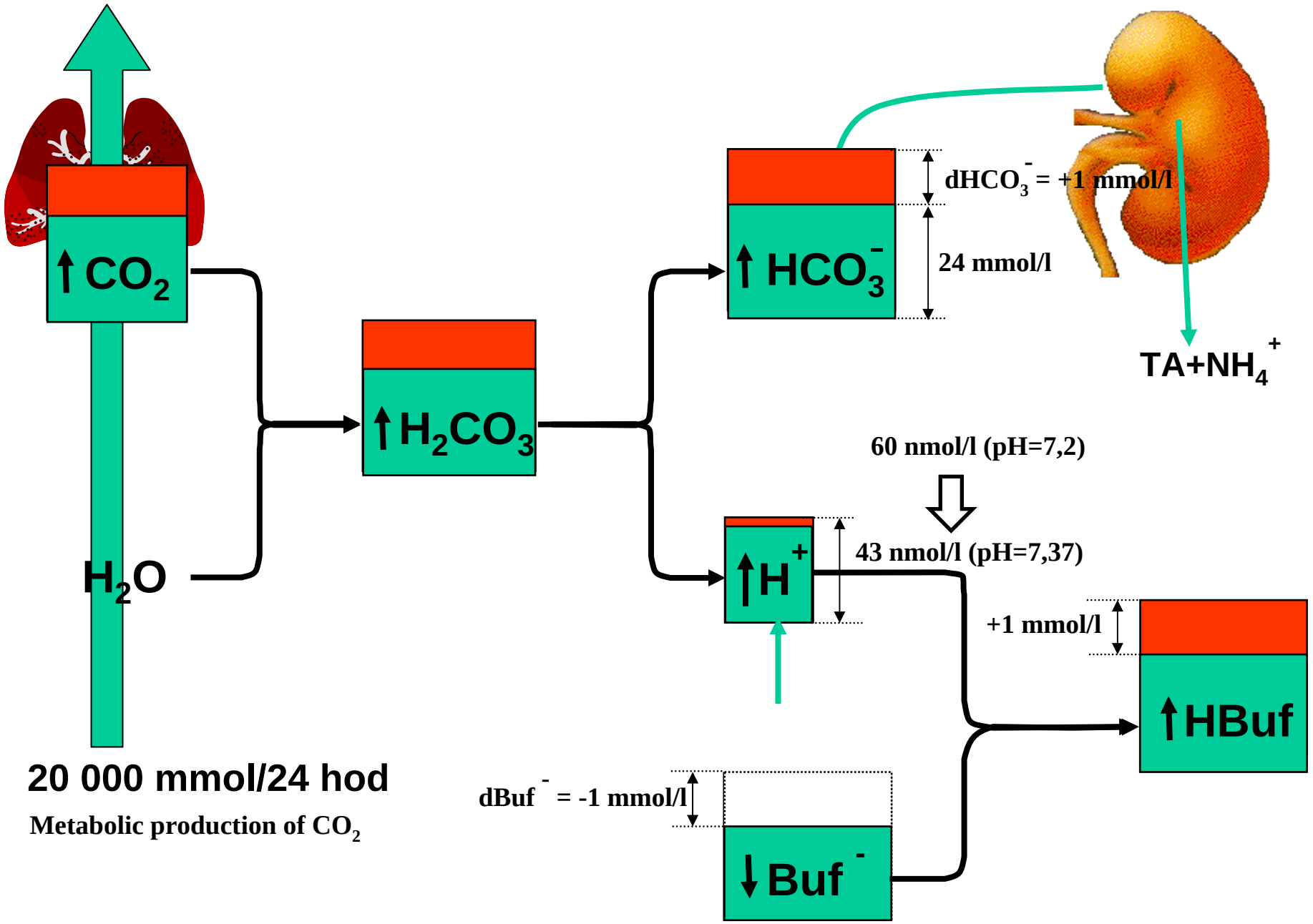

CO_2
H_2O
H_2CO_3
HCO_3^-
24 mmol/l
$TA+NH_4^+$
H^+
40 nmol/l (pH=7,40)
20 000 mmol/24 hod
Metabolic production of CO_2
60 mmol/24 hod
Metabolic production od strong acids


↑CO2
H2O
↑H2CO3
HCO3−
24 mmol/l
TA+NH4+
H+
40 nmol/l (pH=7,40)
20 000 mmol/24 hod
Metabolic production of CO2
60 mmol/24 hod
Metabolic production od strong acids

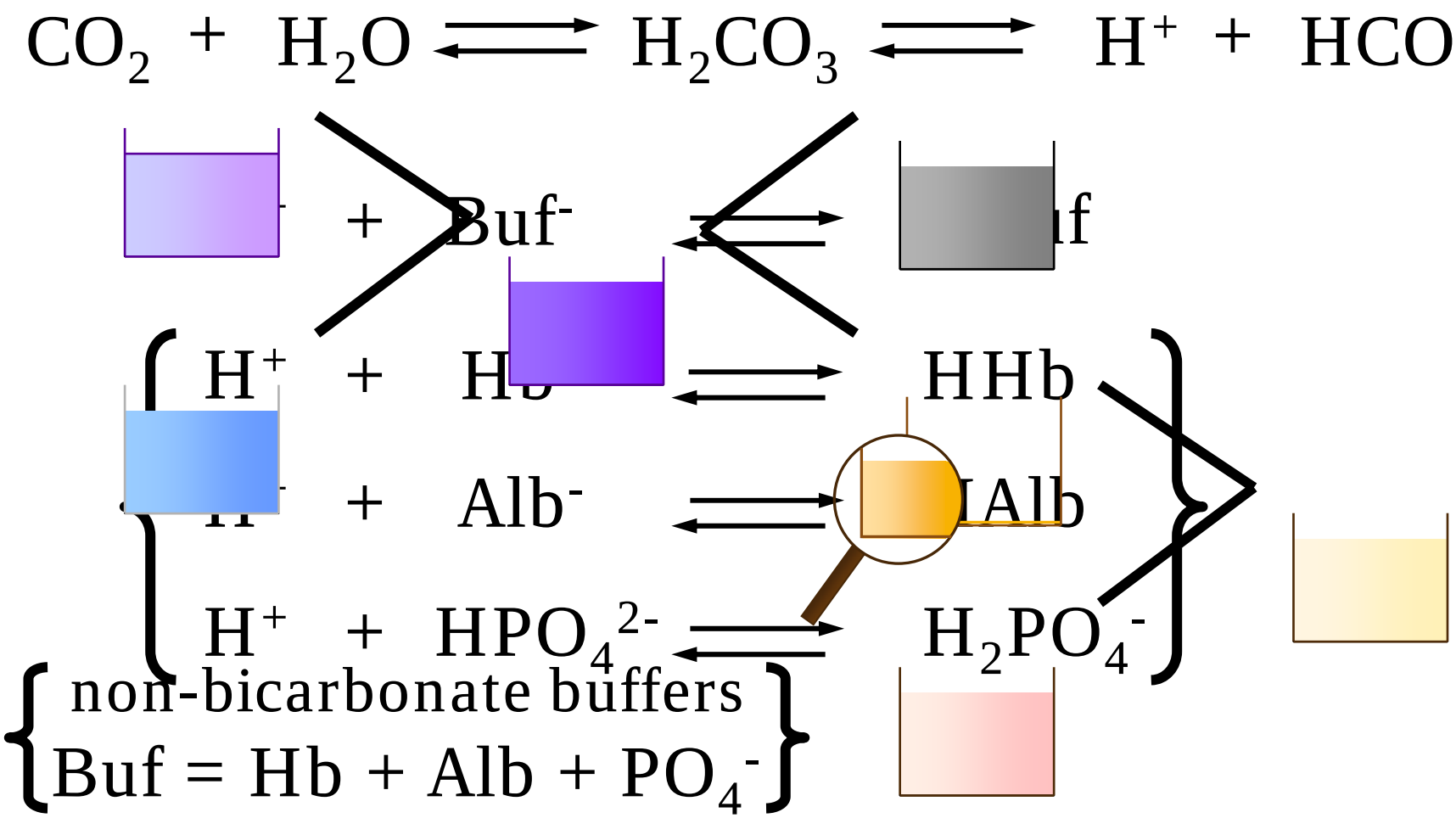


20 000 mmol/24 hod

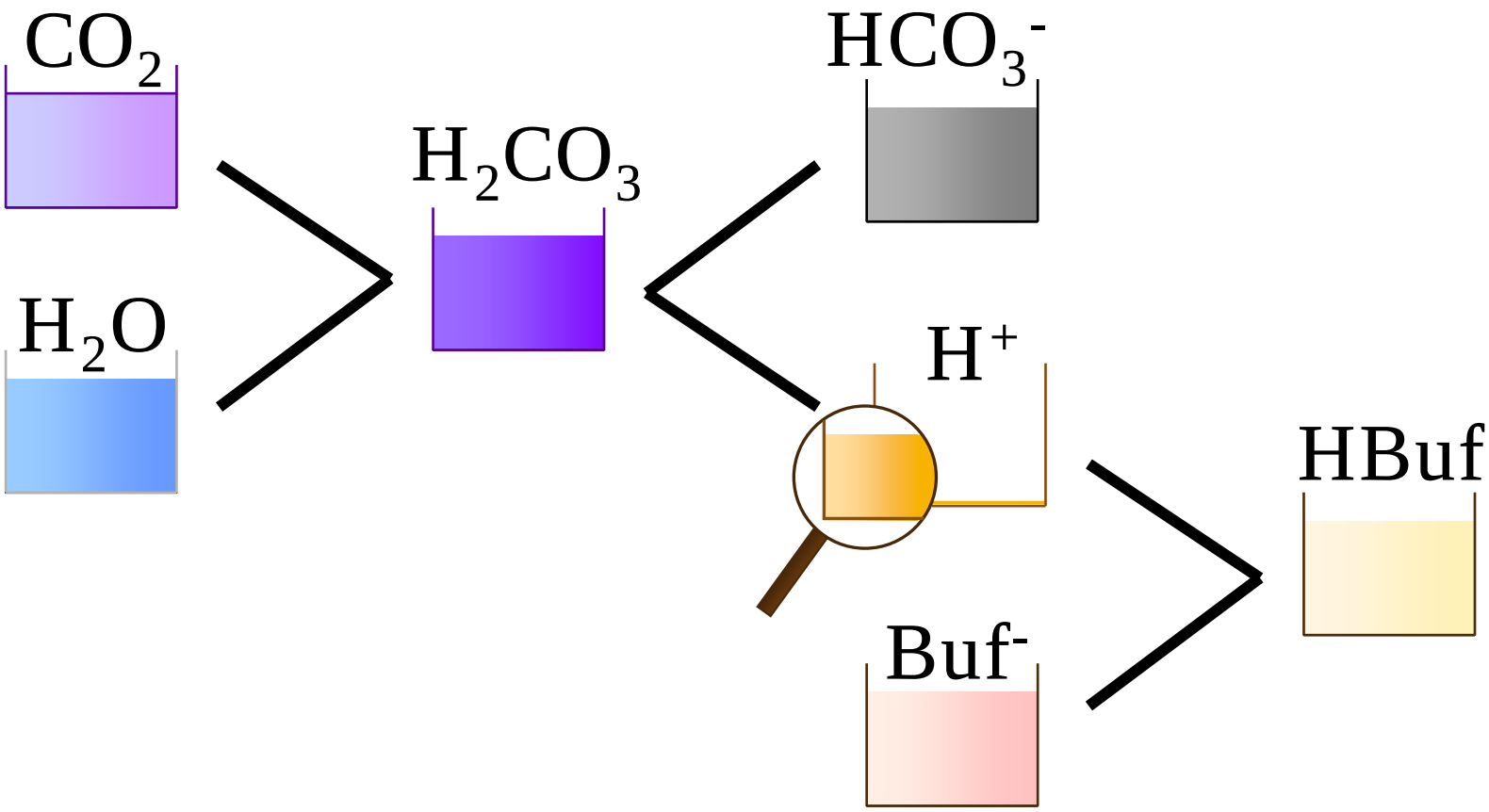
Metabolic production of CO_2


↑CO2
H2O
20 000 mmol/24 hod
Metabolic production of CO2
↑H2CO3
↑HCO3-
dHCO3- = +1 mmol/l
24 mmol/l
TA+NH4+
60 nmol/l (pH=7,2)
43 nmol/l (pH=7,37)
↑H+
+1 mmol/l
↑HBuf
dBuf - = -1 mmol/l
↓Buf -

Buffering systems of the blood



Buffering reactions



Bicarbonate buffer

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

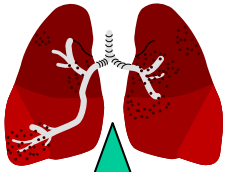
Hendersson- Hasselbalch equation:

$[H^+] = 24 . pCO2 / [HCO_3^-]$

or

$$pH = 6.1 + \log ([HCO_3^-] / [H_2CO_3])$$

$$= 6.1 + \log ([HCO_3^-] / 0.03\ pCO_2)$$



CO_2

H_2O

H_2CO_3

HCO_3^-

H^+

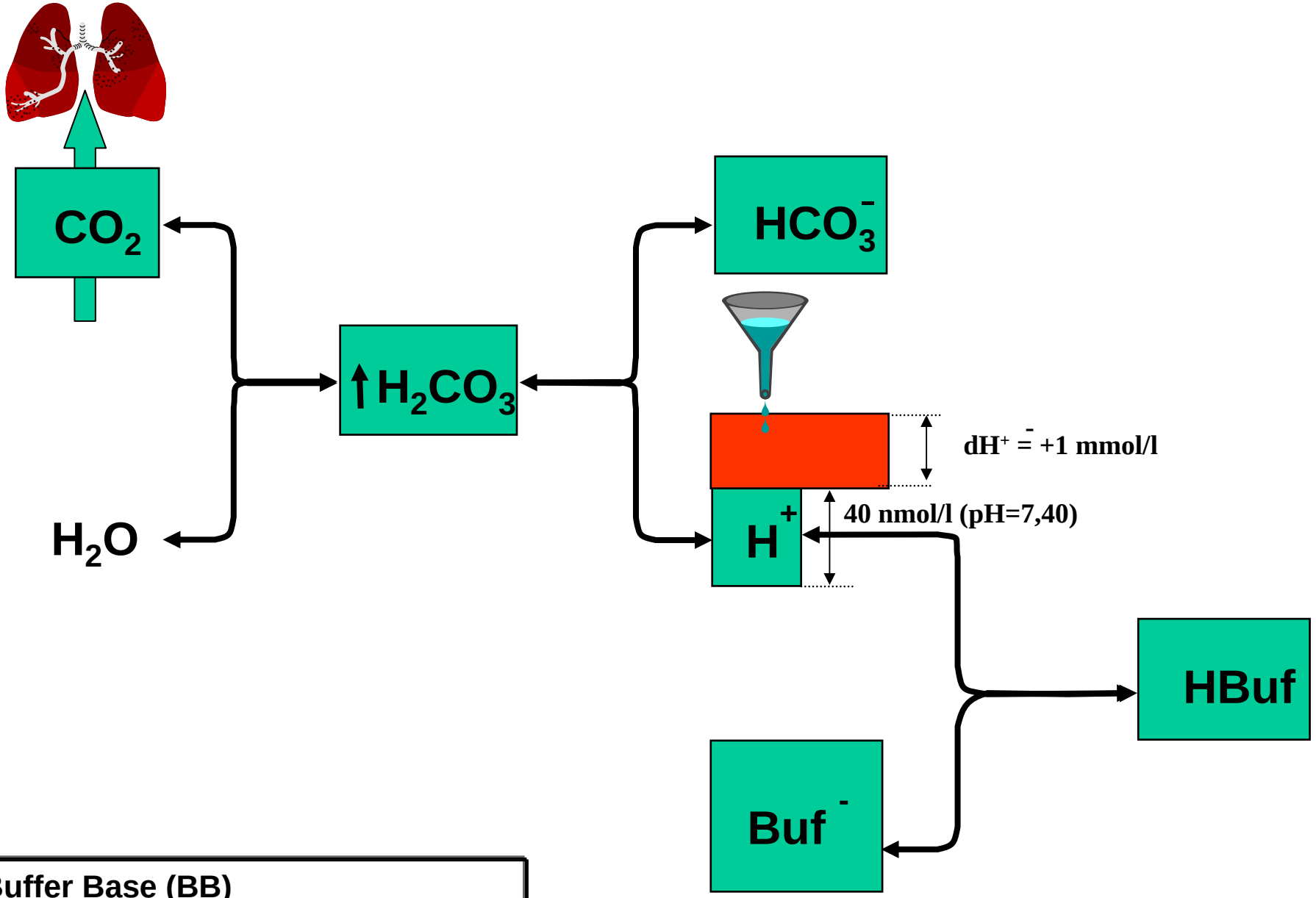
40 nmol/l (pH=7,40)

Buf^-

HBuf

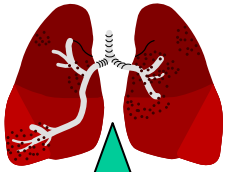
Buffer Base (BB)

$BB = [HCO_3^-] + [Buf^-]$



Buffer Base (BB)

$BB = [HCO_3^-] + [Buf^-]$



CO_2

H_2O

H_2CO_3

$dHCO_3^-$

HCO_3^-

$dH^+ = +1$ mmol/l

$dBuf^- + dHCO_3^- = -1$mmol/l

H^+

43 nmol/l (pH=7,37)

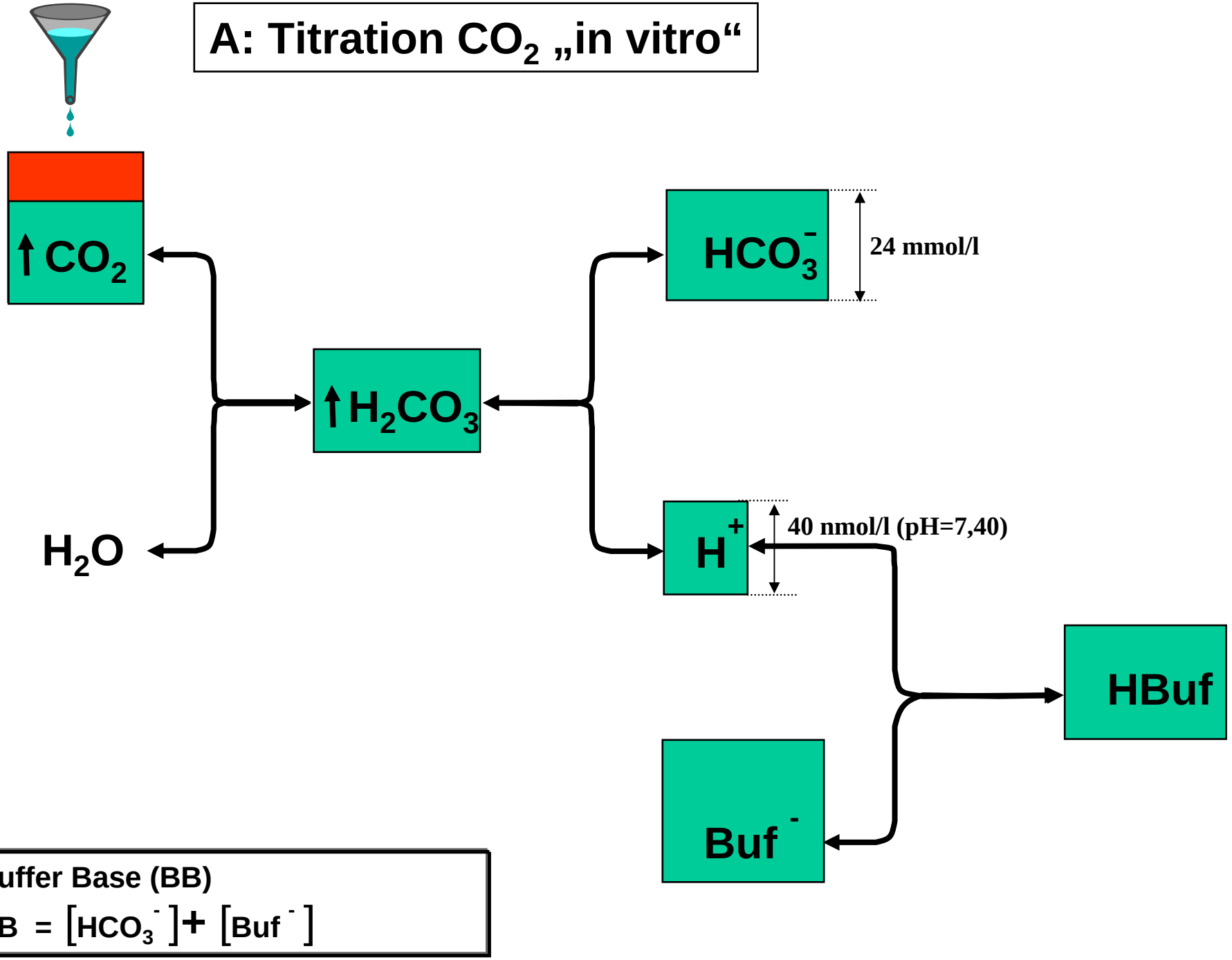
HBuf

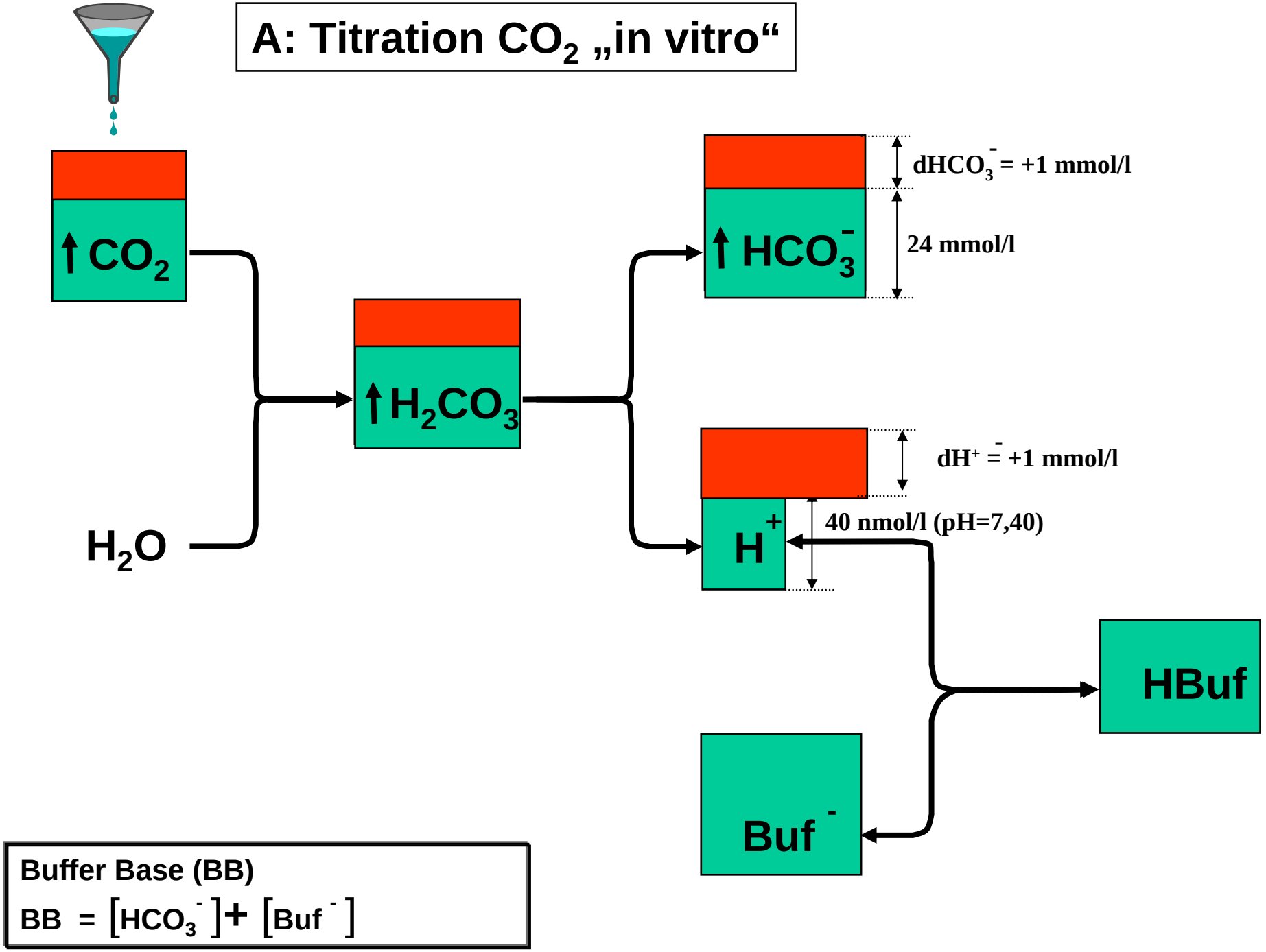
$dBuf^-$

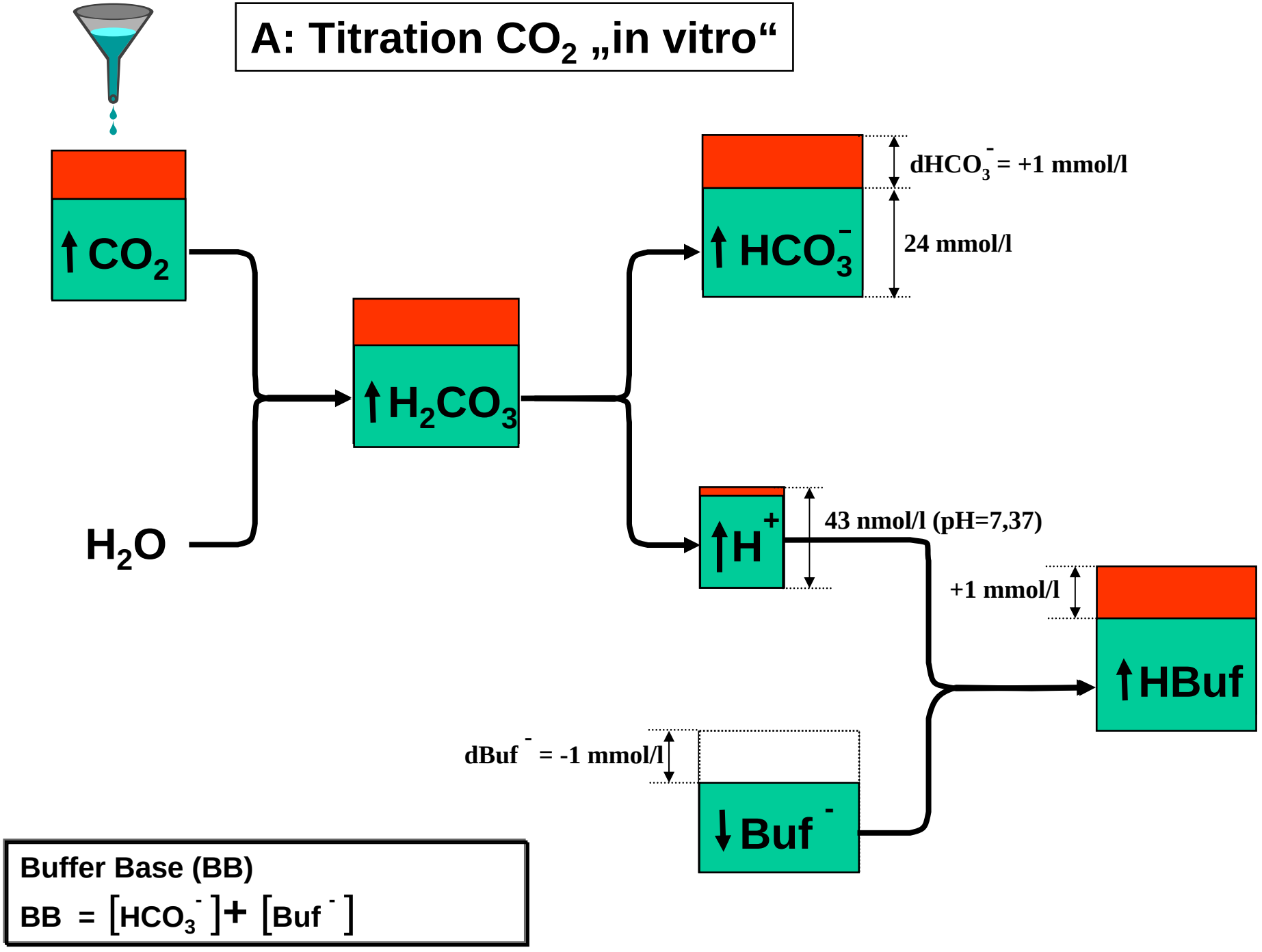
Buf^-

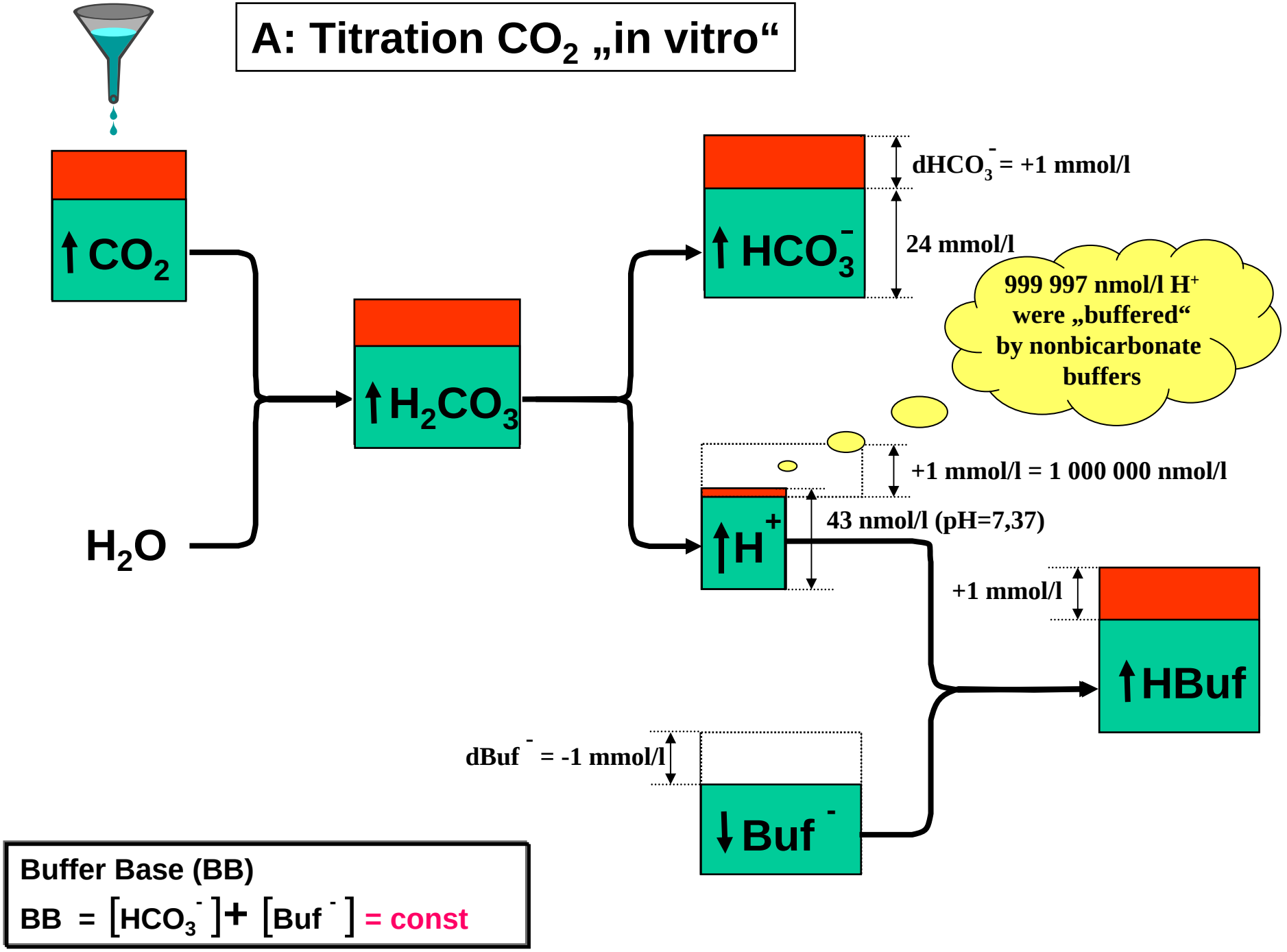
Buffer Base (BB)

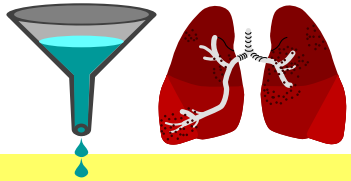
$BB = [HCO_3^-] + [Buf^-]$


A: Titration CO_2 „in vitro“
CO_2
H_2O
H_2CO_3
HCO_3^-
24 mmol/l
H^+
40 nmol/l (pH=7,40)
HBuf
Buf^-
Buffer Base (BB)
$BB = [HCO_3^-] + [Buf^-]$

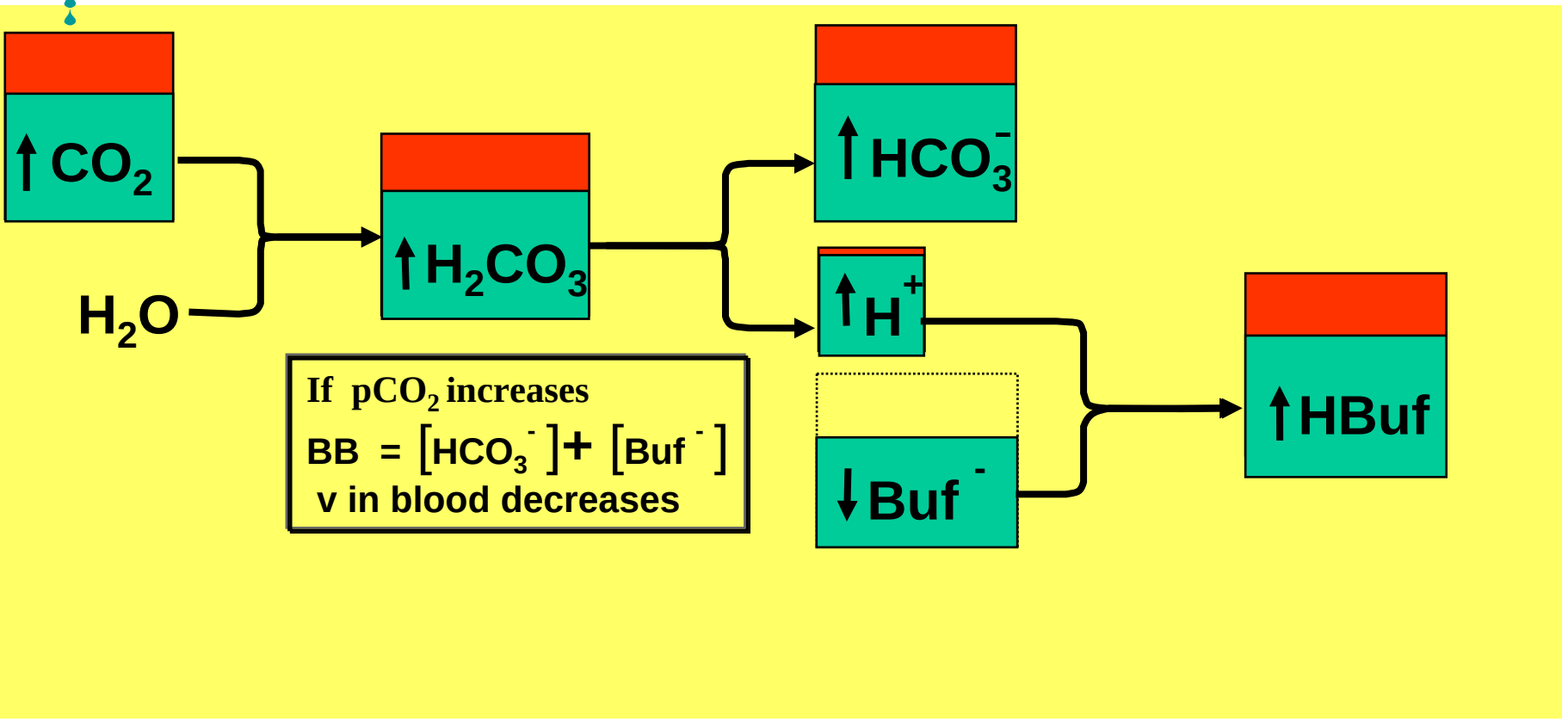

A: Titration CO_2 „in vitro“
CO_2
H_2O
H_2CO_3
HCO_3^-
$dHCO_3^-$ = +1 mmol/l
24 mmol/l
H^+
dH^+ = +1 mmol/l
40 nmol/l (pH=7,40)
HBuf
Buf^-
Buffer Base (BB)
$BB = [HCO_3^-] + [Buf^-]$


A: Titration CO_2 „in vitro“
CO_2
H_2O
H_2CO_3
HCO_3^-
$dHCO_3^-$ = +1 mmol/l
24 mmol/l
H^+
43 nmol/l (pH=7,37)
+1 mmol/l
HBuf
$dBuf^-$ = -1 mmol/l
Buf^-
Buffer Base (BB)
$BB = [HCO_3^-] + [Buf^-]$


A: Titration CO_2 „in vitro“
CO_2
H_2O
H_2CO_3
HCO_3^-
dHCO3- = +1 mmol/l
24 mmol/l
999 997 nmol/l H+ were „buffered“ by nonbicarbonate buffers
+1 mmol/l = 1 000 000 nmol/l
H^+
43 nmol/l (pH=7,37)
+1 mmol/l
HBuf
dBuf - = -1 mmol/l
Buf -
Buffer Base (BB)
BB = [HCO3-] + [Buf-] = const

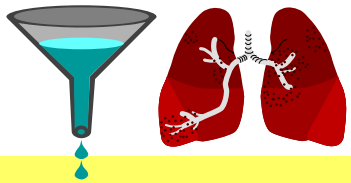


B: Titration CO_2 „in vivo“



Buffer Base (BB)

$BB = [HCO_3^-] + [Buf^-]$ =/= const



B: Titration CO_2 „in vivo“

↑ CO_2

H_2O

↑ H_2CO_3

↑ HCO_3^-

↑ H^+

↓ Buf^-

↑ HBuf

Diffusion by concentration gradient

If pCO_2 increases

BB = $[HCO_3^-] + [Buf^-]$

v in blood decreases

Blood

Interstitial fluid

↑ CO_2

H_2O

↑ H_2CO_3

↑ HCO_3^-

↑ H^+

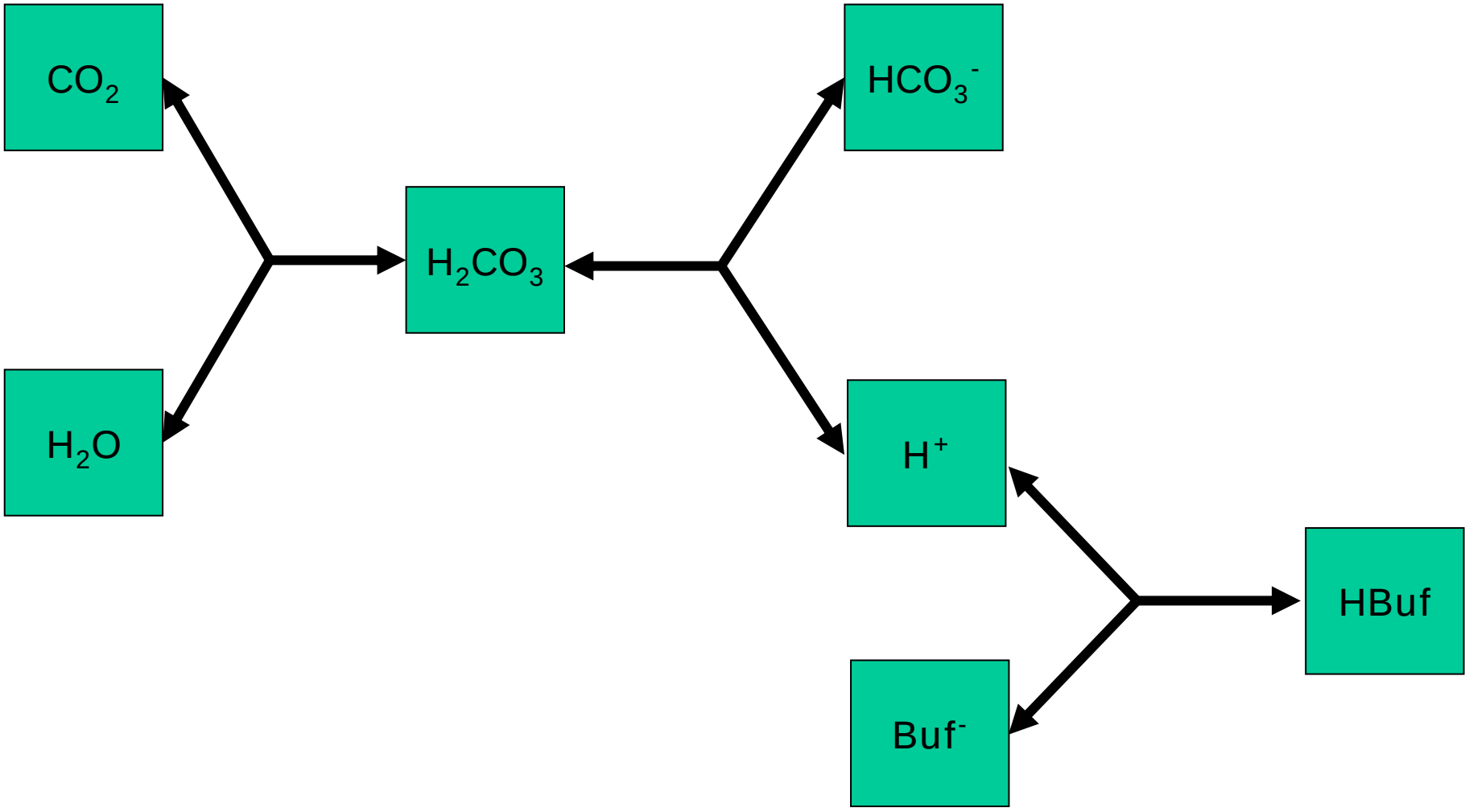
↓ Buf^-

↑ HBuf

There are small concentrations of non bicarbonate buffers in ISF

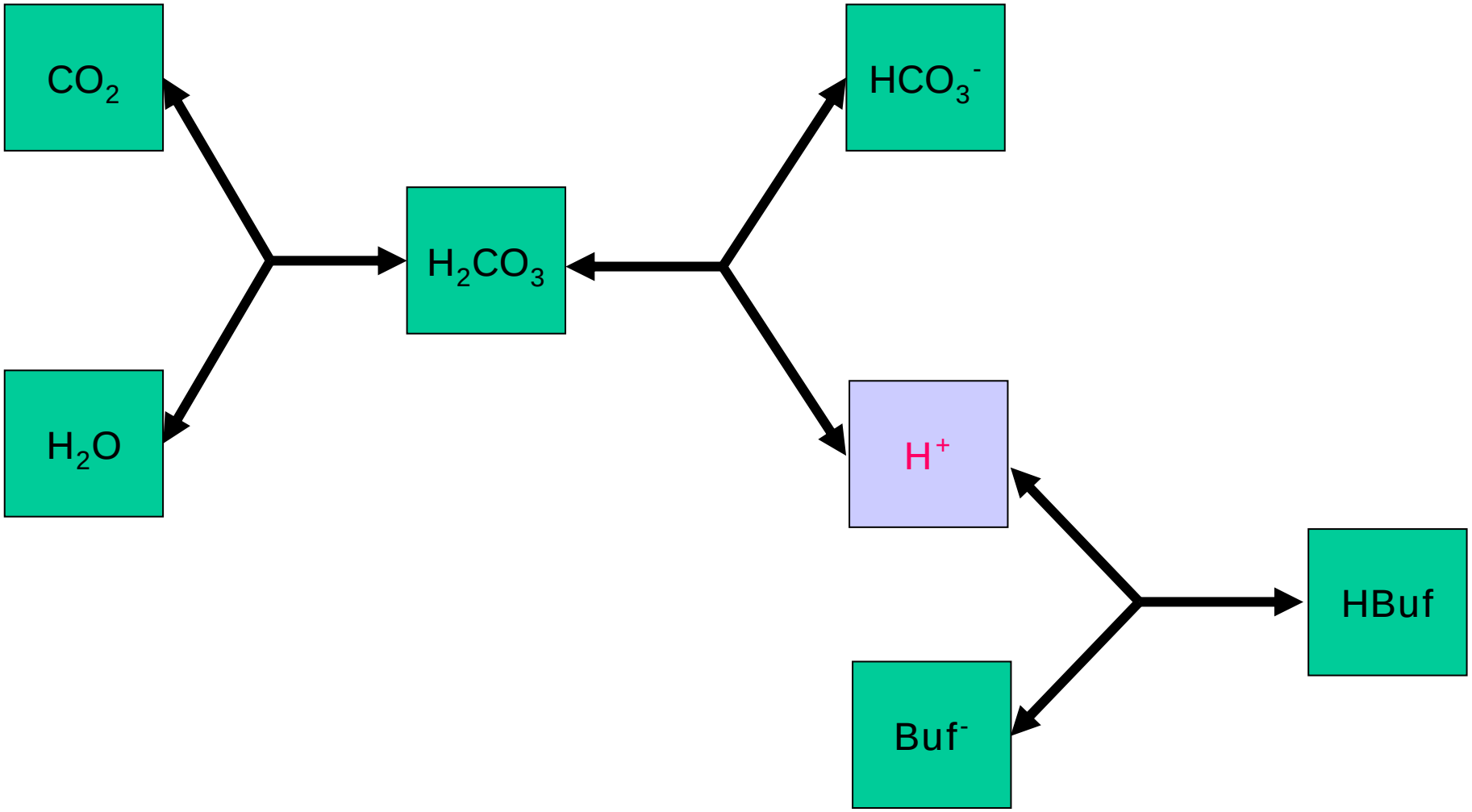
Measurement of Acid-Base parameters

pH, pCO2, [HCO_3^-]



Measurement of Acid-Base parameters

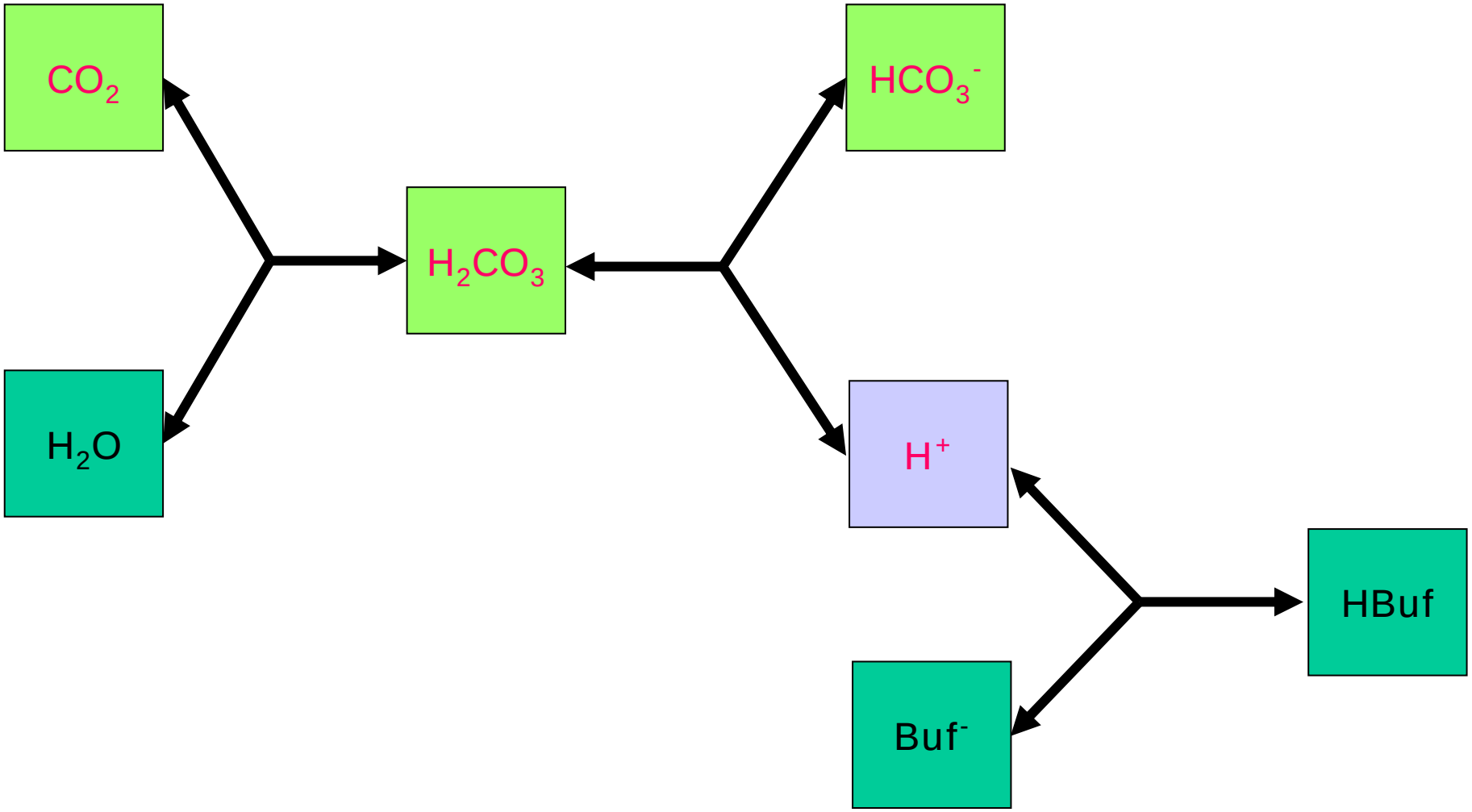
pH, pCO2, [HCO_3^-]



Measurement of Acid-Base parameters

pH, pCO2, [HCO_3^-]

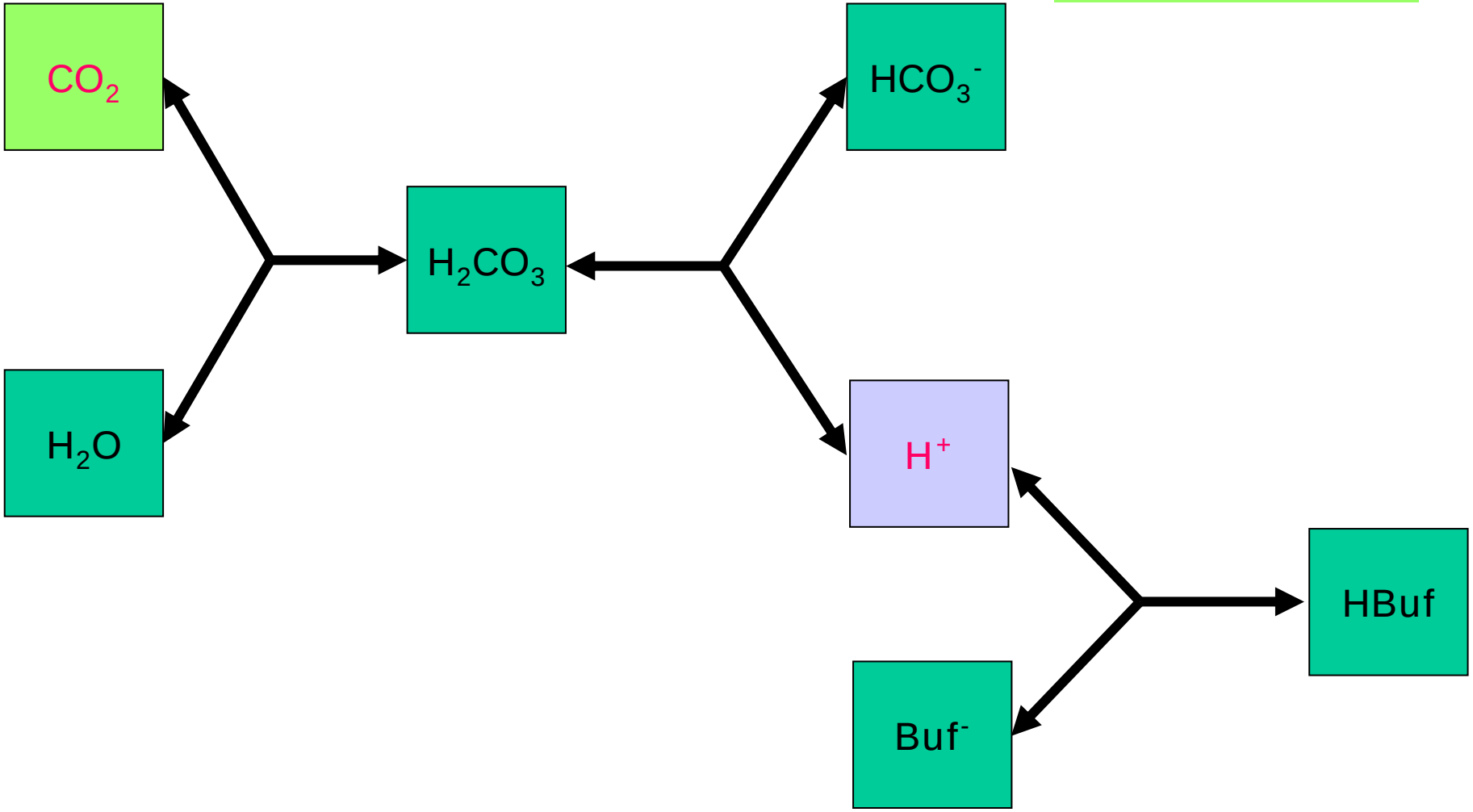
Alkaline reserve



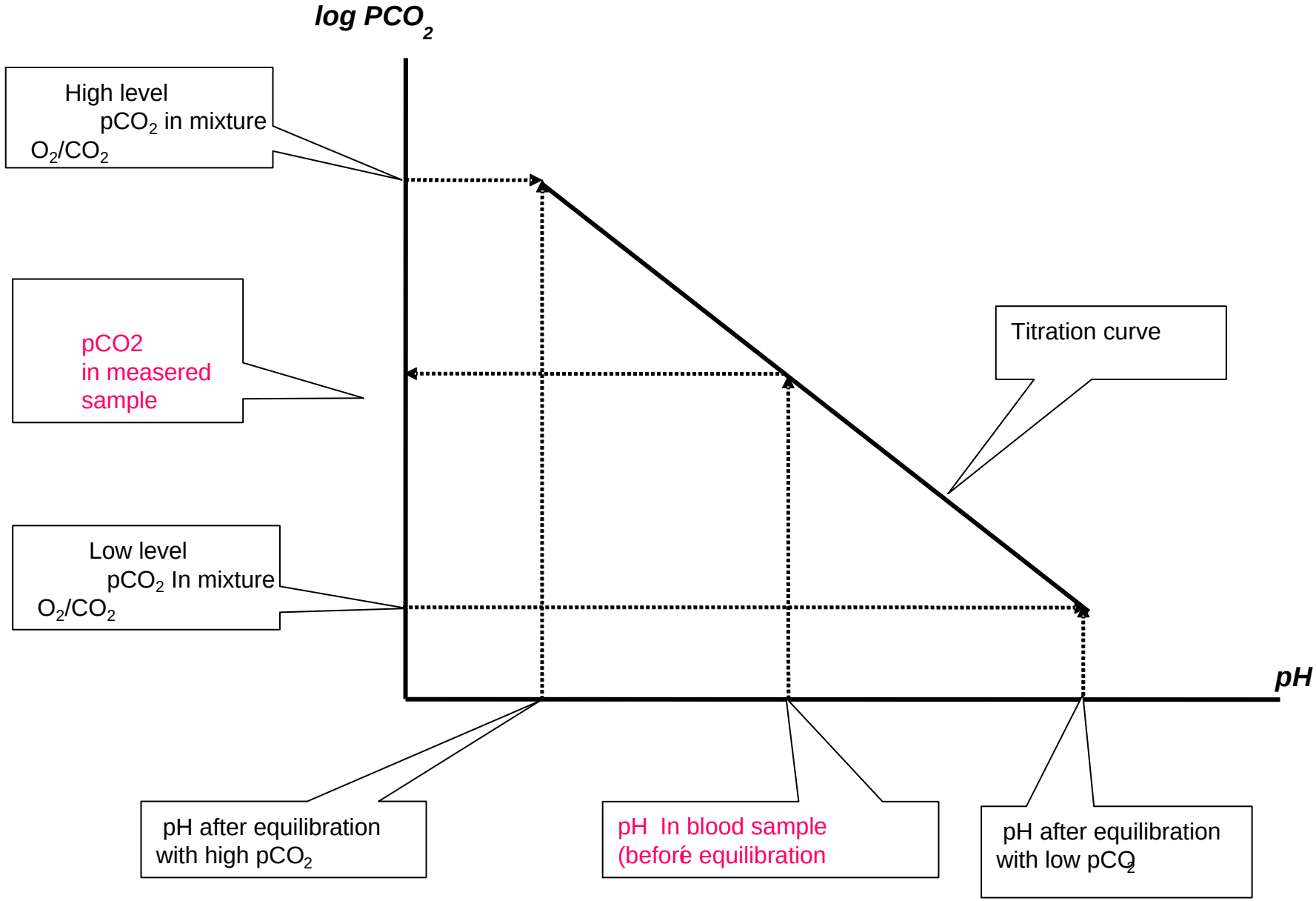
Measurement of Acid-Base parameters

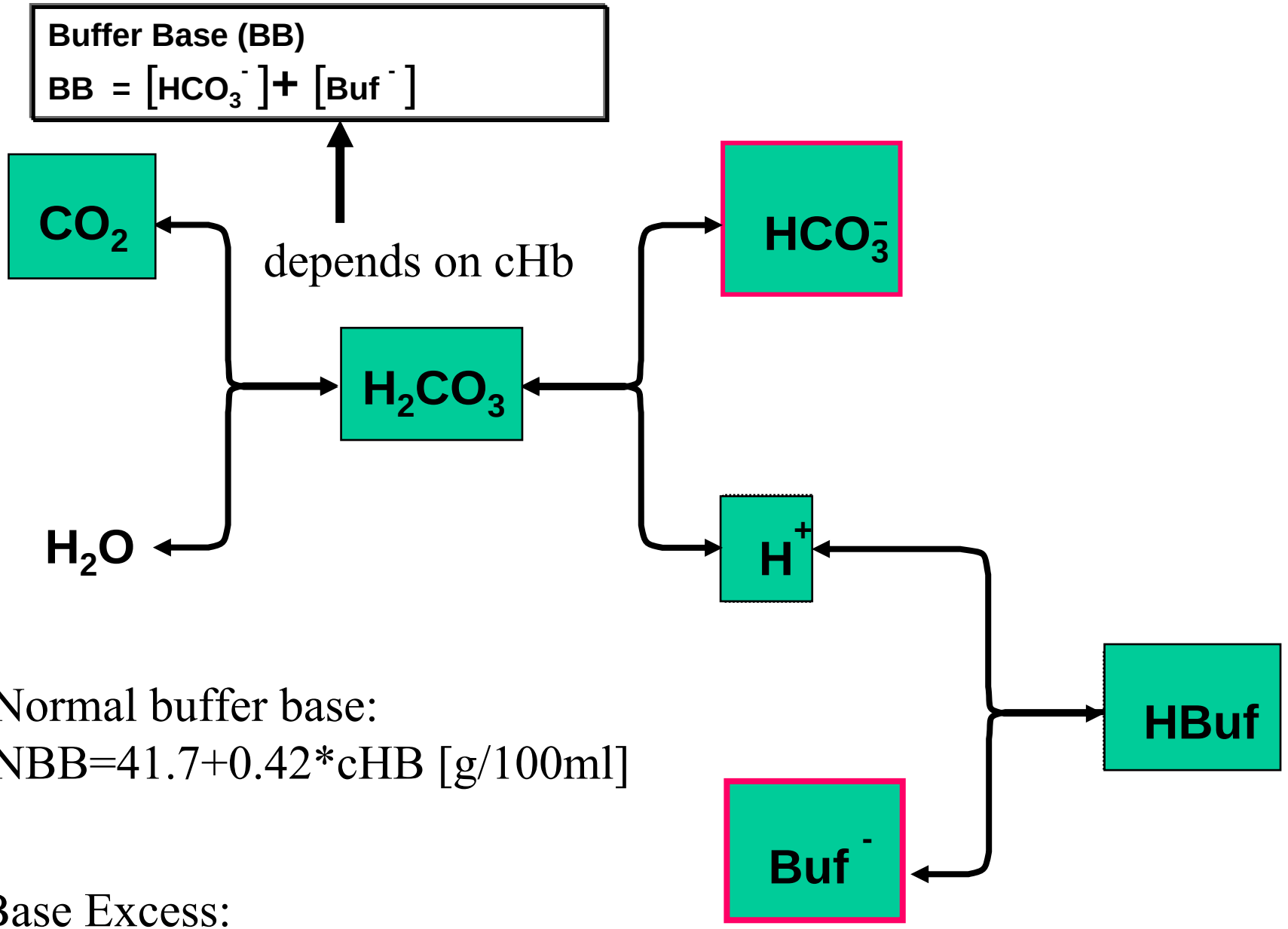
pH, pCO2, [HCO_3^-]

P. Astrup
1956



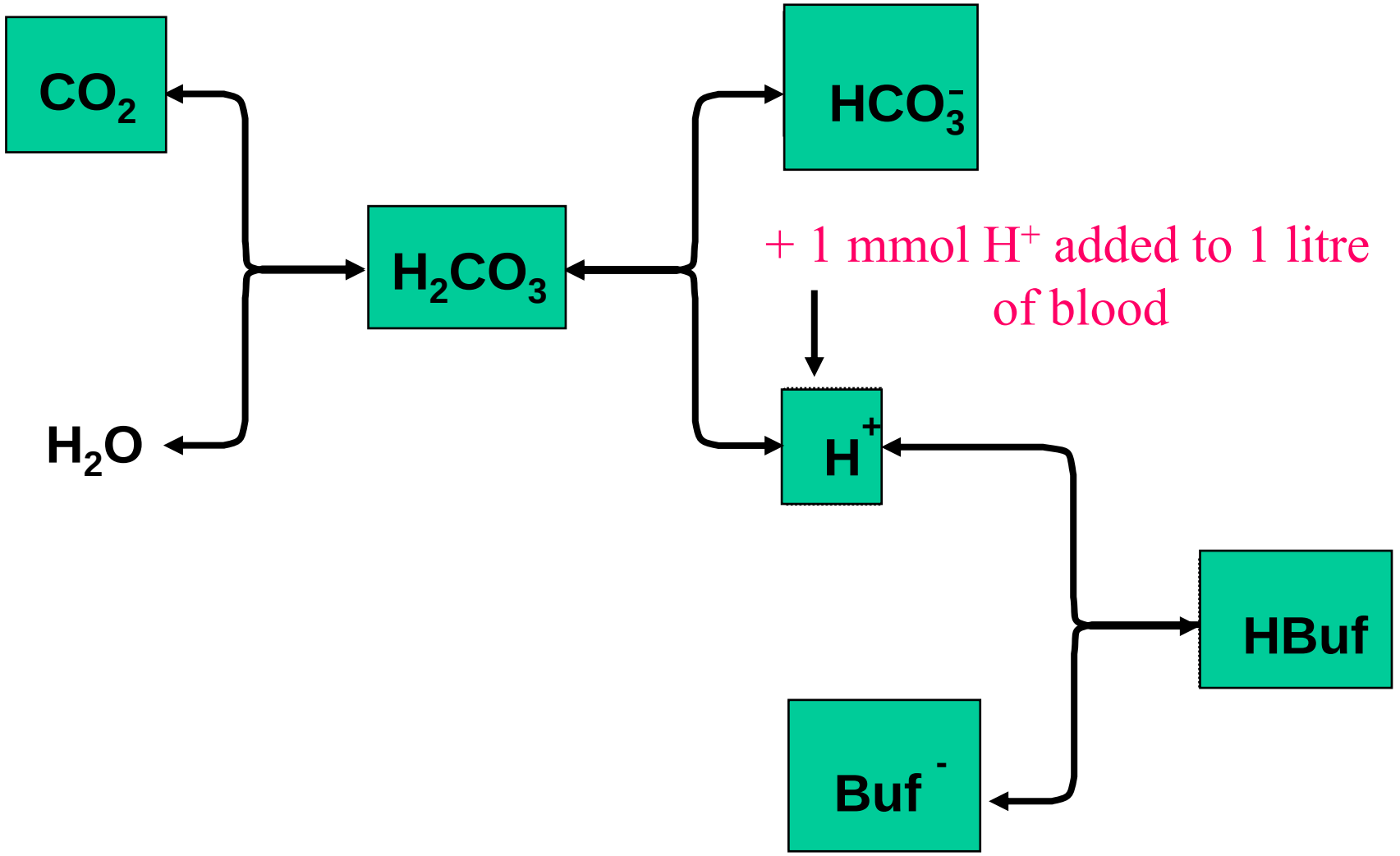
Equilibration method for pCO2 measurement by Astrup

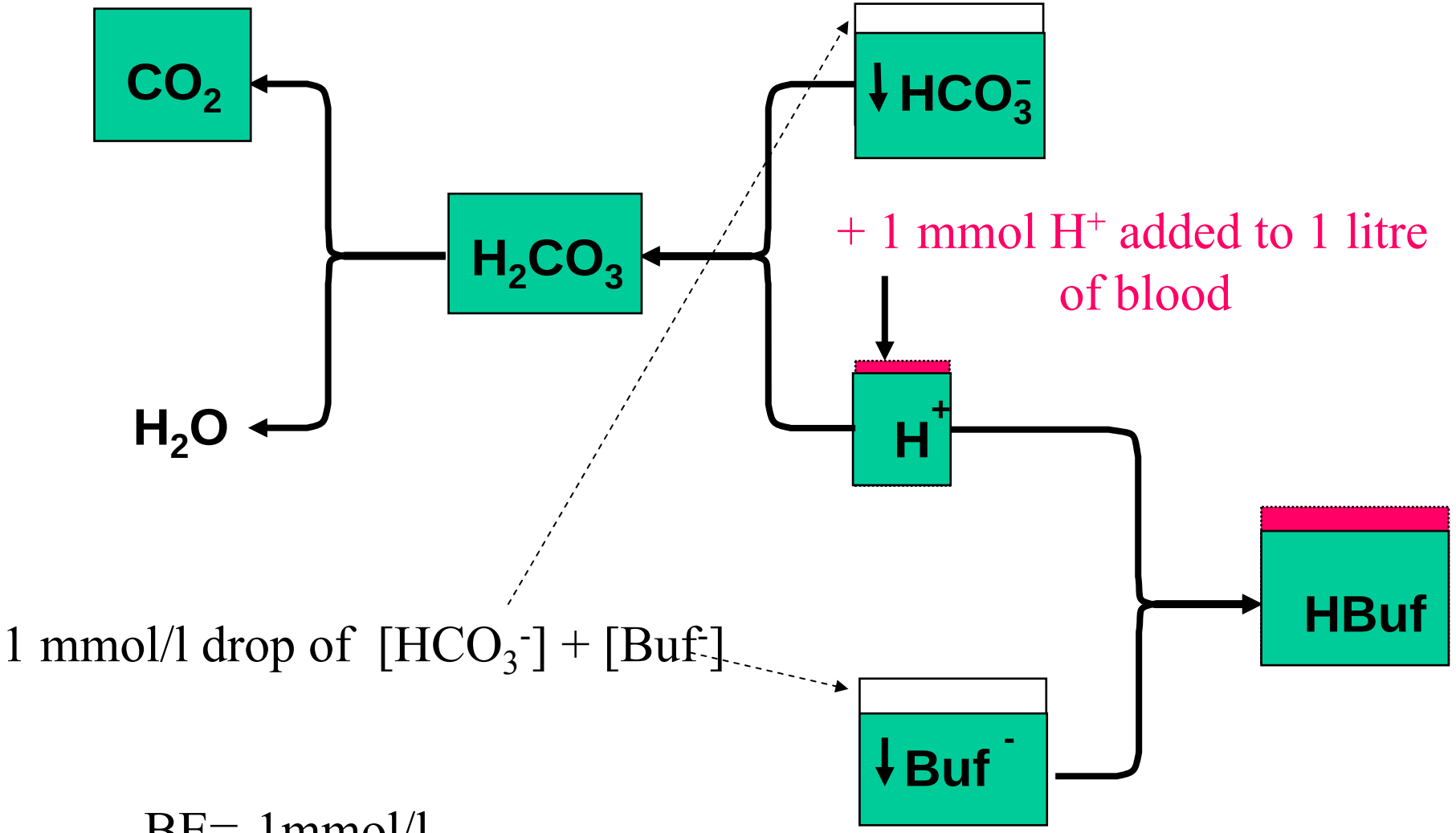


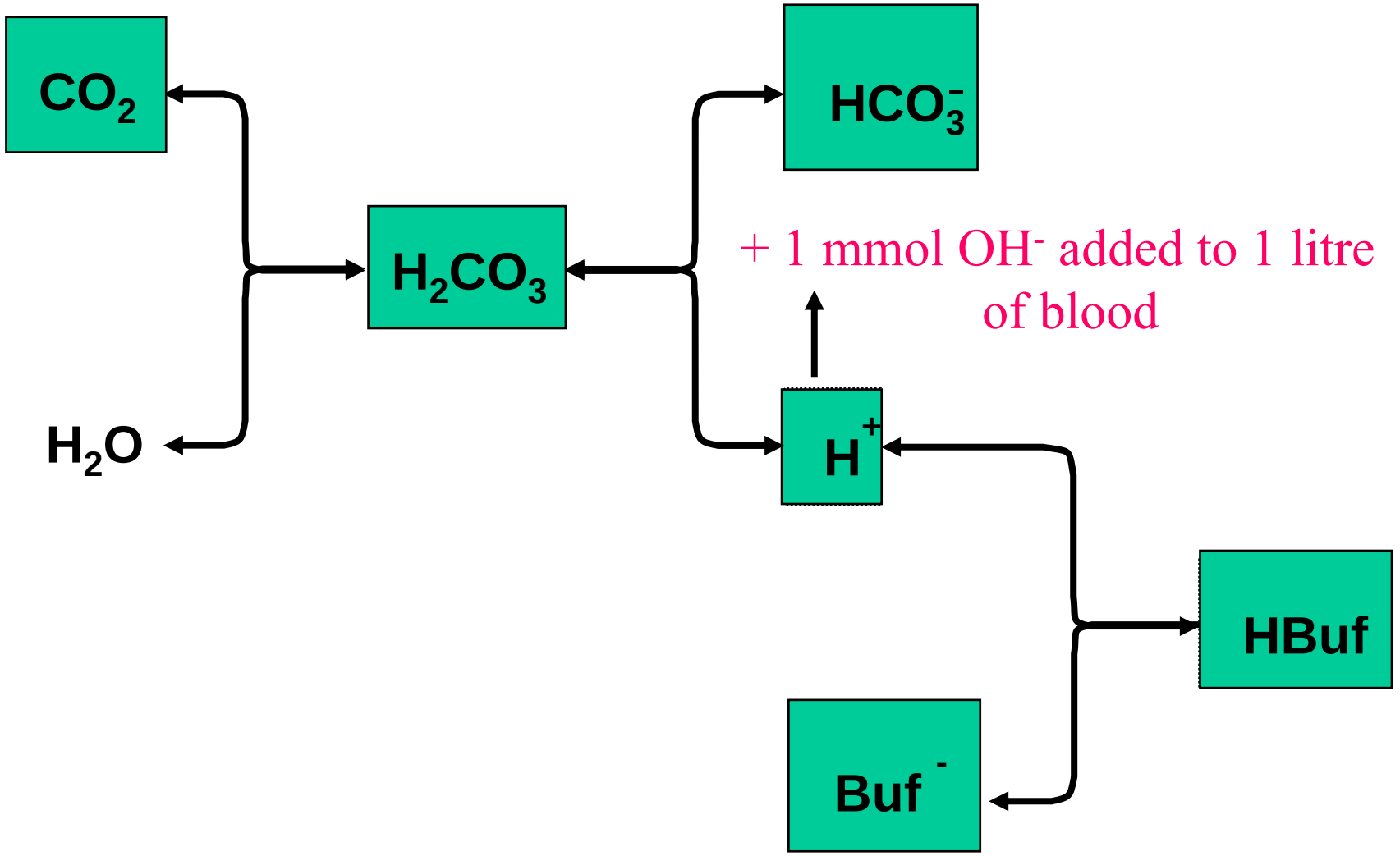


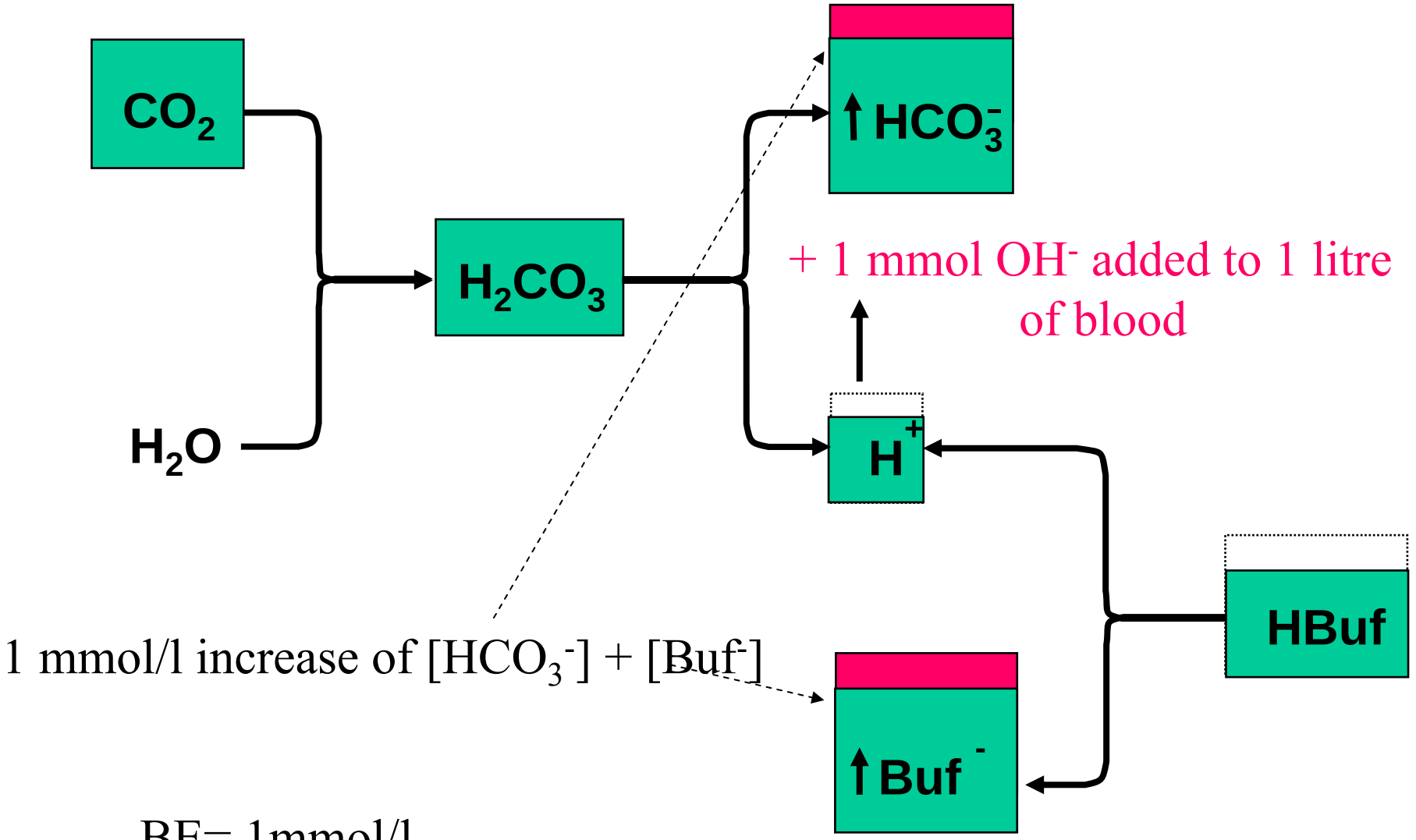
Normal buffer base:
NBB=41.7+0.42*cHB [g/100ml]

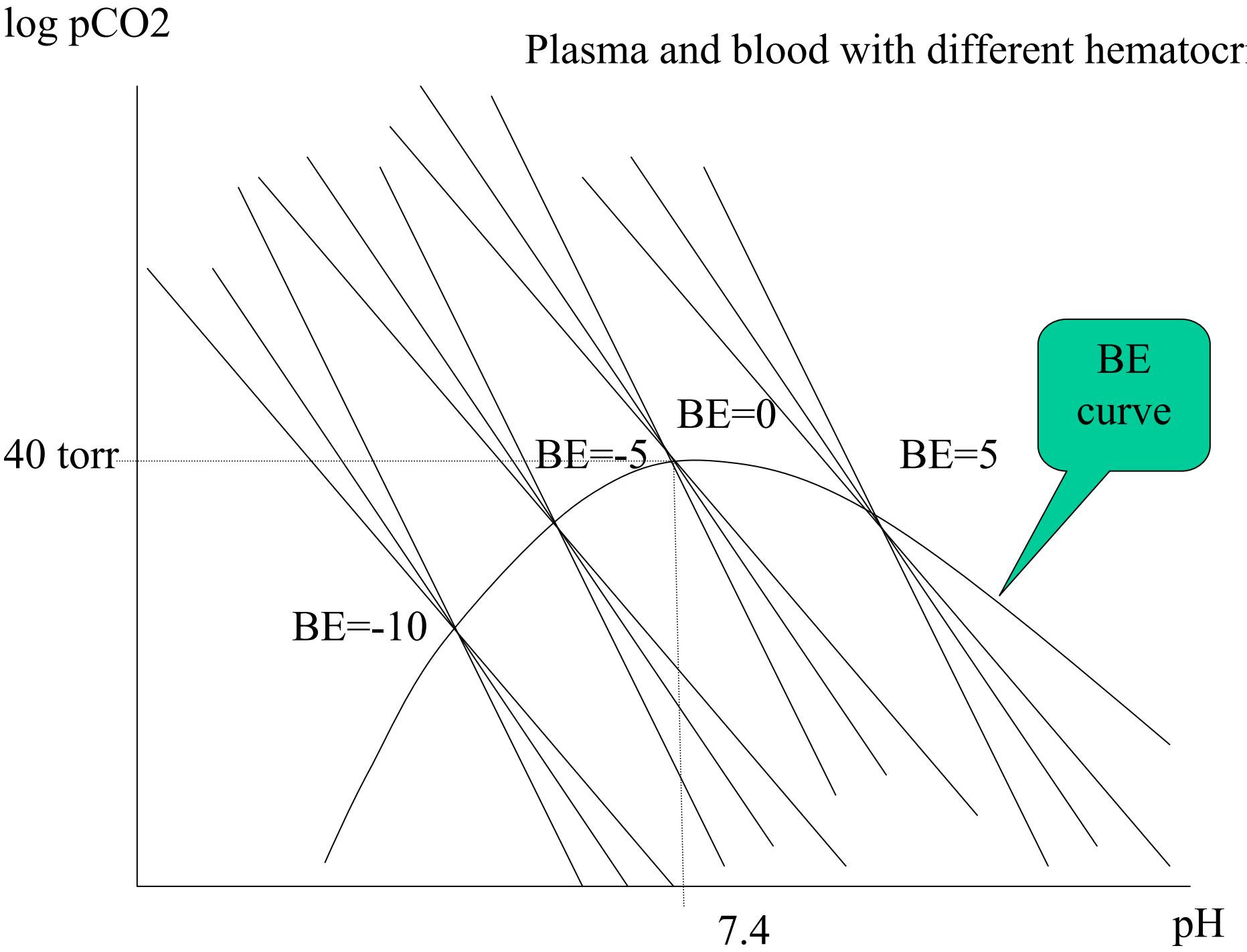
Base Excess:
BE=BB-NBB

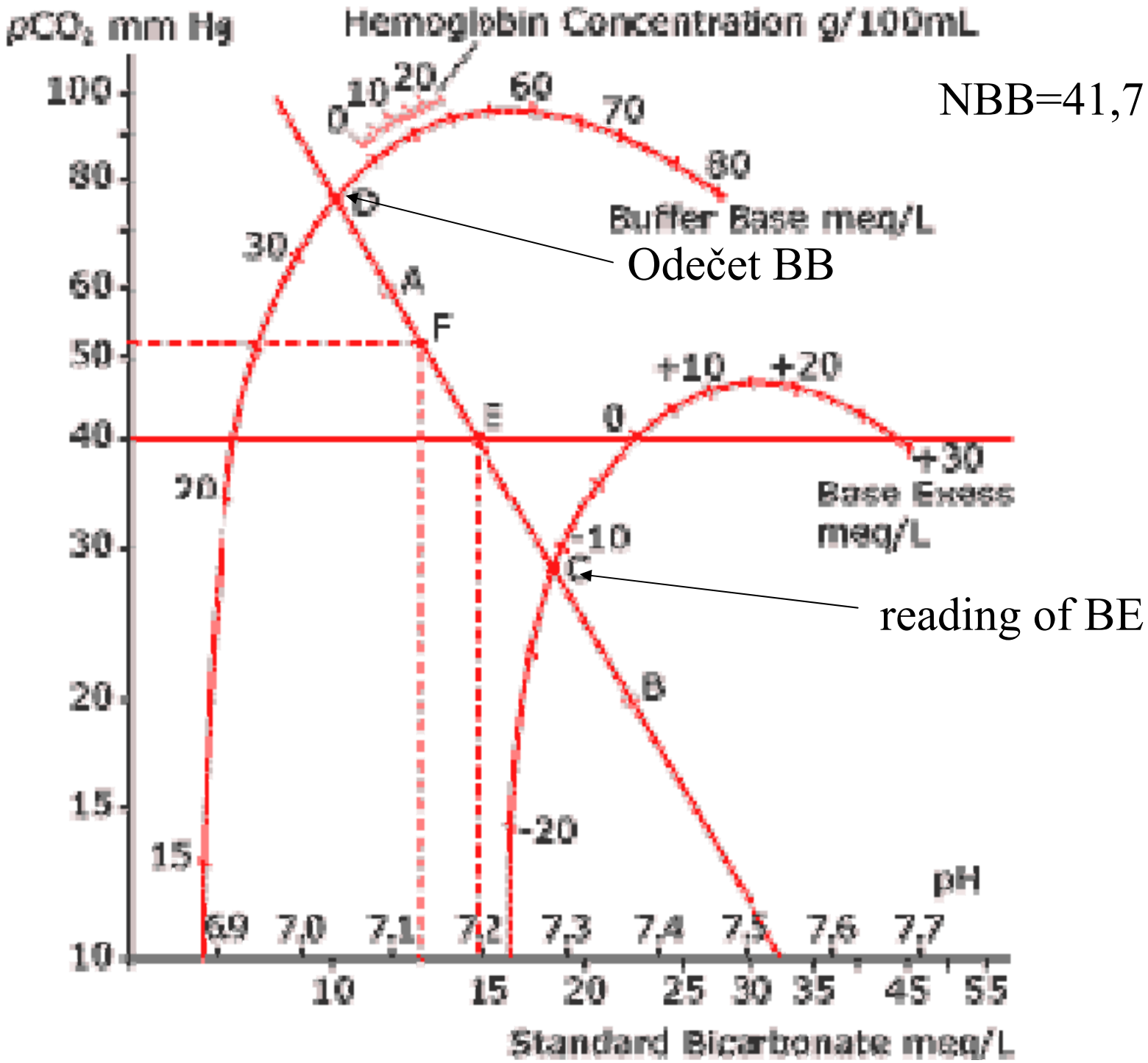

CO_2
H_2O
H_2CO_3
HCO_3^-
+ 1 mmol H^+ added to 1 litre of blood
H^+
HBuf
Buf^-


CO_2
H_2O
H_2CO_3
HCO_3^-
+ 1 mmol H^+ added to 1 litre of blood
H^+
HBuf
1 mmol/l drop of $[HCO_3^-]$ + $[Buf^-]$
Buf^-
BE=-1mmol/l

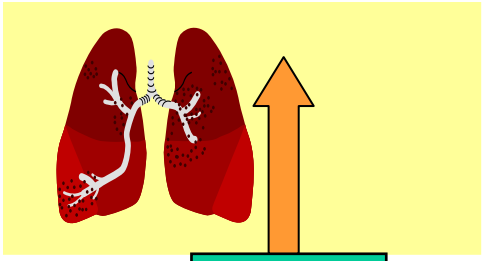

CO_2
H_2O
H_2CO_3
HCO_3^-
+ 1 mmol OH^- added to 1 litre of blood
H^+
HBuf
Buf^-

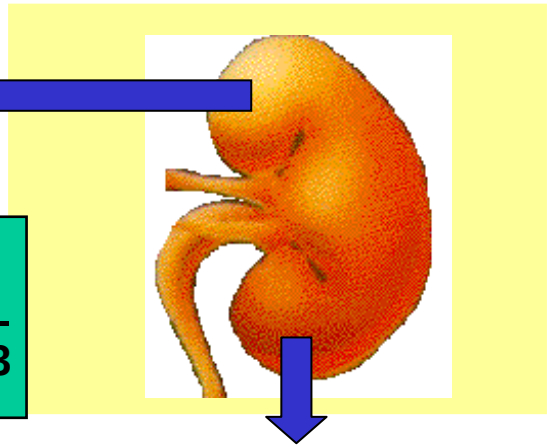

CO_2
H_2O
H_2CO_3
$\uparrow HCO_3^-$
+ 1 mmol OH^- added to 1 litre of blood
H^+
HBuf
1 mmol/l increase of $[HCO_3^-]$ + $[Buf^-]$
$\uparrow Buf^-$
BE= 1mmol/l


log pCO2
Plasma and blood with different hematocrit
40 torr
BE=0
BE=-5
BE=5
BE=-10
BE curve
7.4
pH


pCO2 mm Hg
Hemoglobin Concentration g/100mL
Buffer Base meq/L
Base Excess meq/L
Standard Bicarbonate meq/L
pH
Odečet BB
reading of BE
NBB=41,7 + 0,42 * cHB

Acid-base regulation





CO_2

CO_2 balance

H_2O

H_2CO_3

HCO_3^-

TA + NH_4^+

H^+

H^+ balance

HBuf

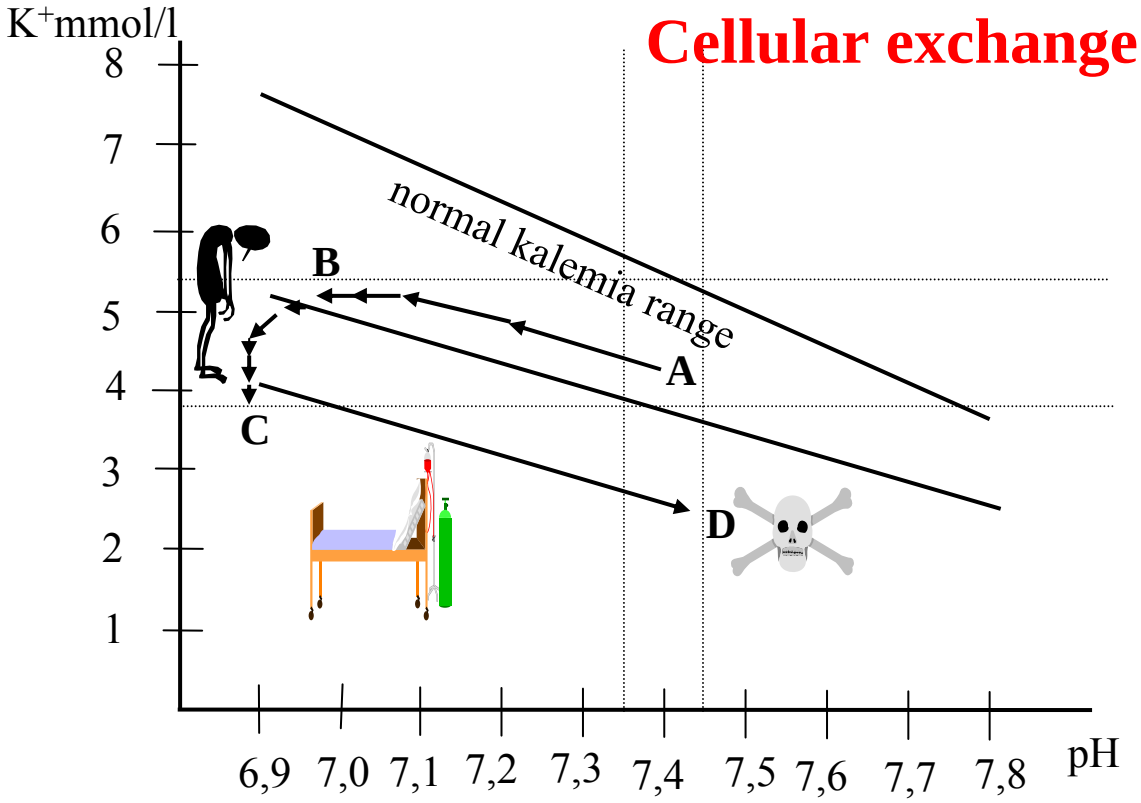
Buf^-

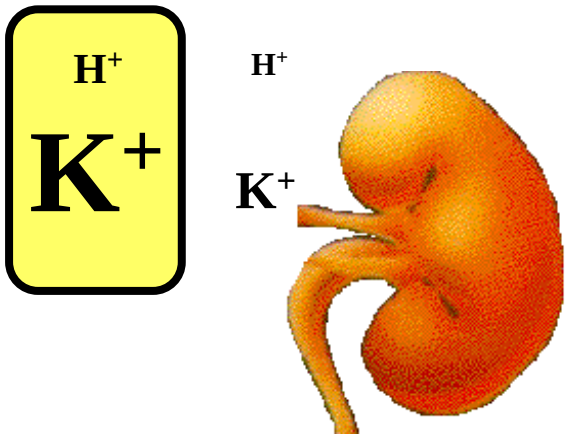
1. Buffer systems (msec)
2. Respiration control (12 hours)
3. Kidney control (3-5 days)

Exchange H^+/K^+ H^+/Na^+ between cells and ECF

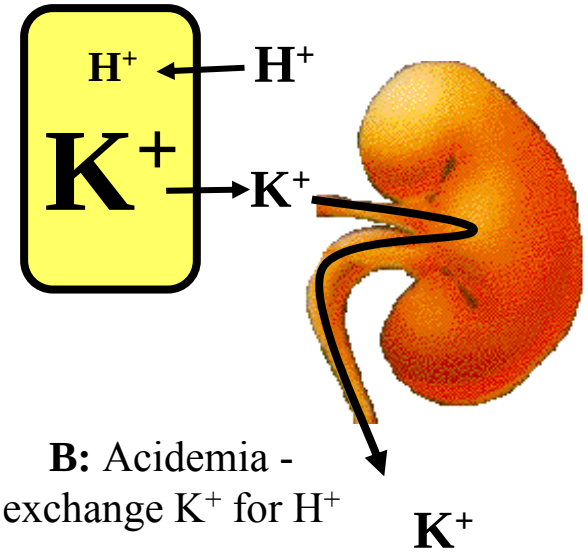
Role of liver in AB regulation

Cellular exchange K^+/H^+

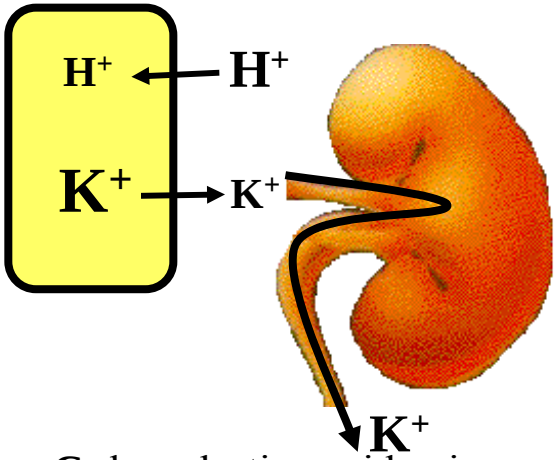




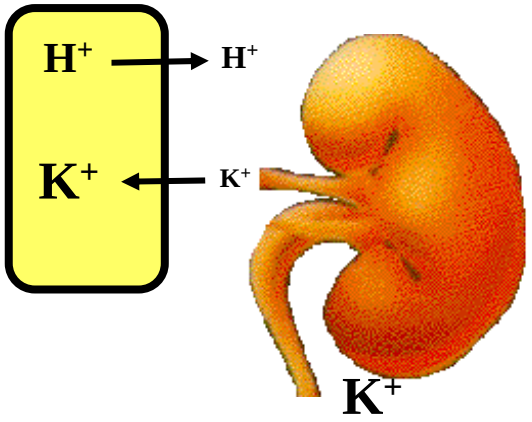
A: Norm



B: Acidemia - exchange K^+ for H^+



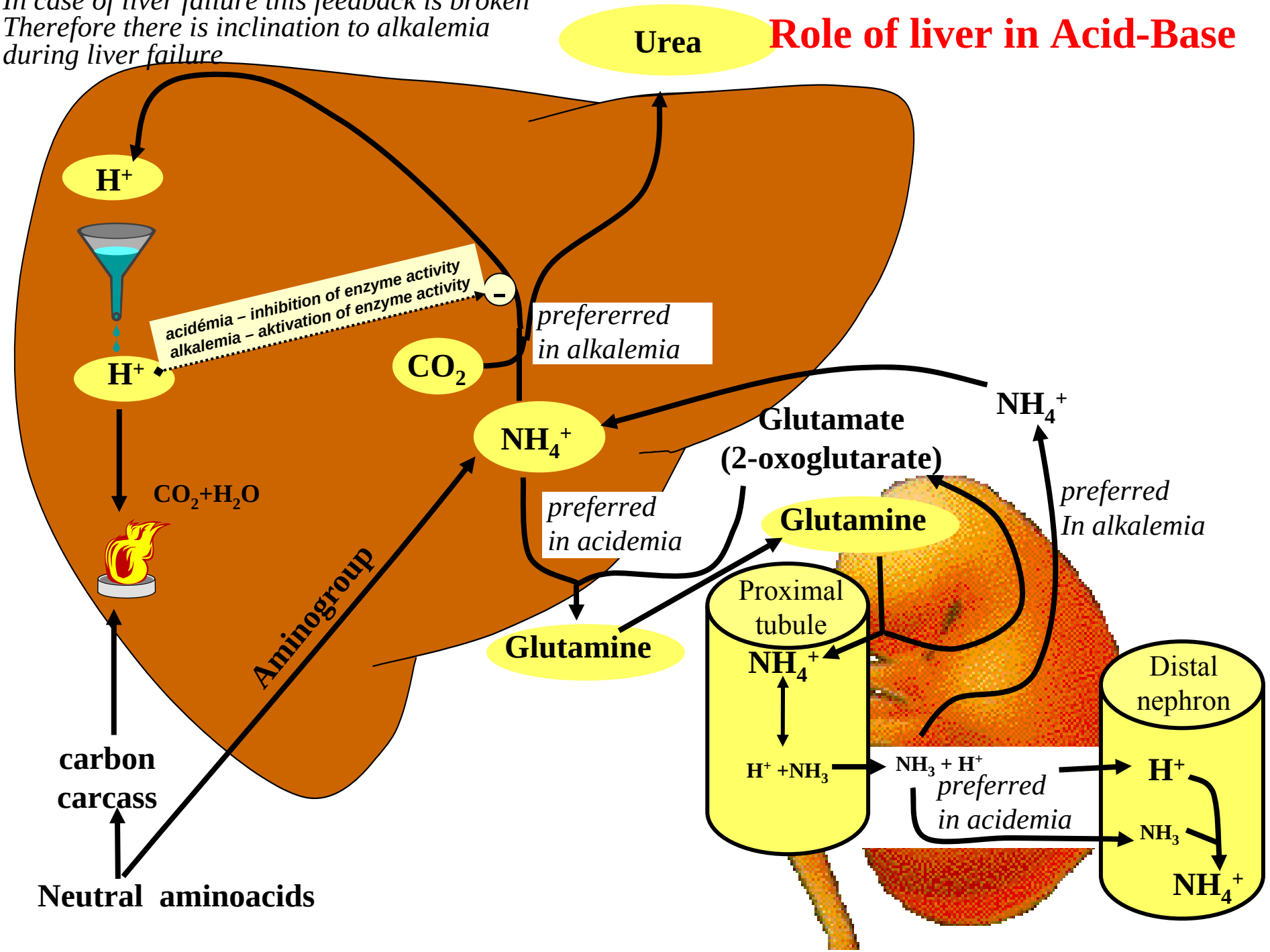
C: long-lasting acidemia - K^+ depletion



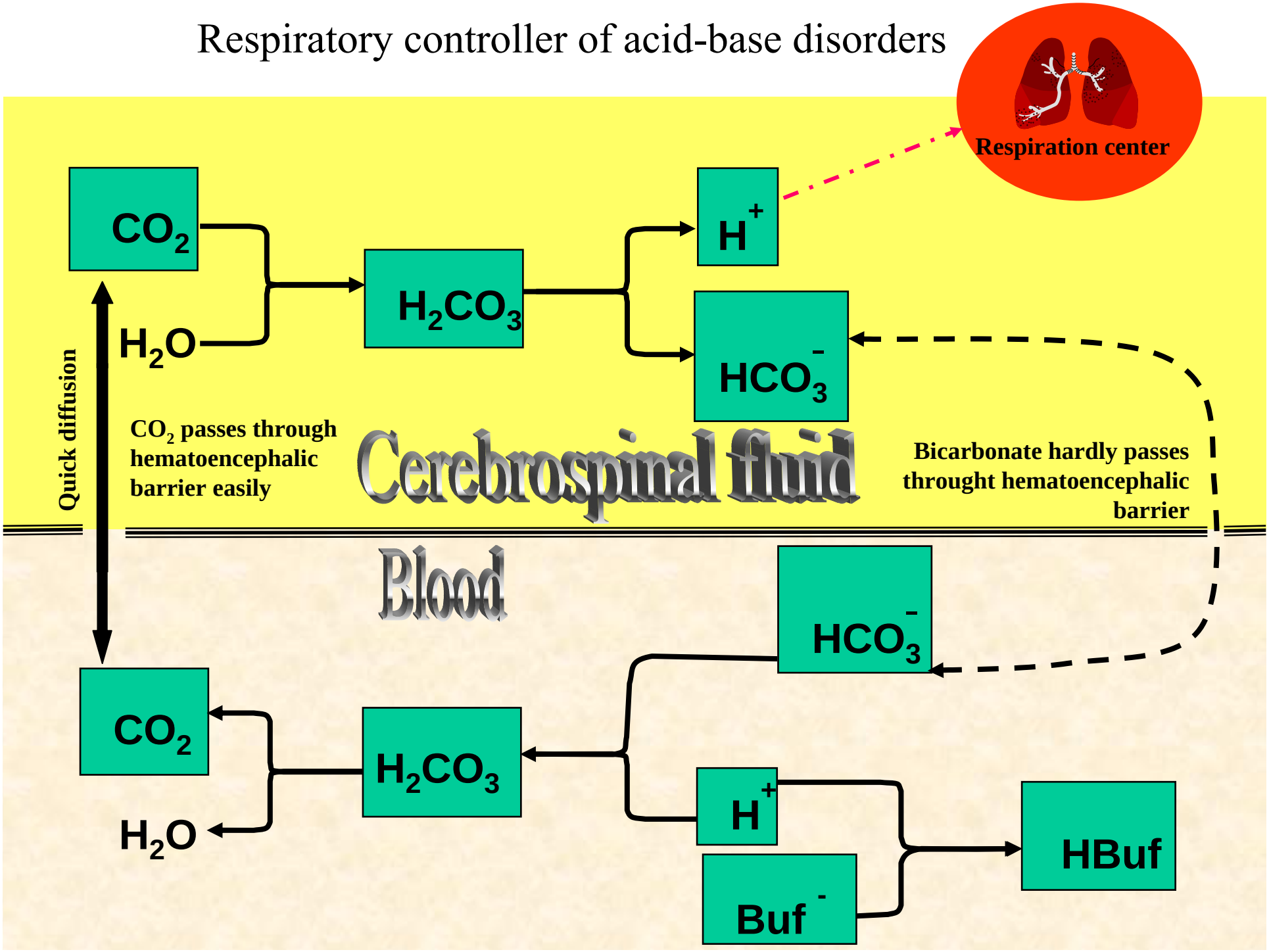
D: Quick alkalisation - exchange H^+ for K^+ - dangerous hypokalemia

In case of liver failure this feedback is broken
Therefore there is inclination to alkalemia during liver failure

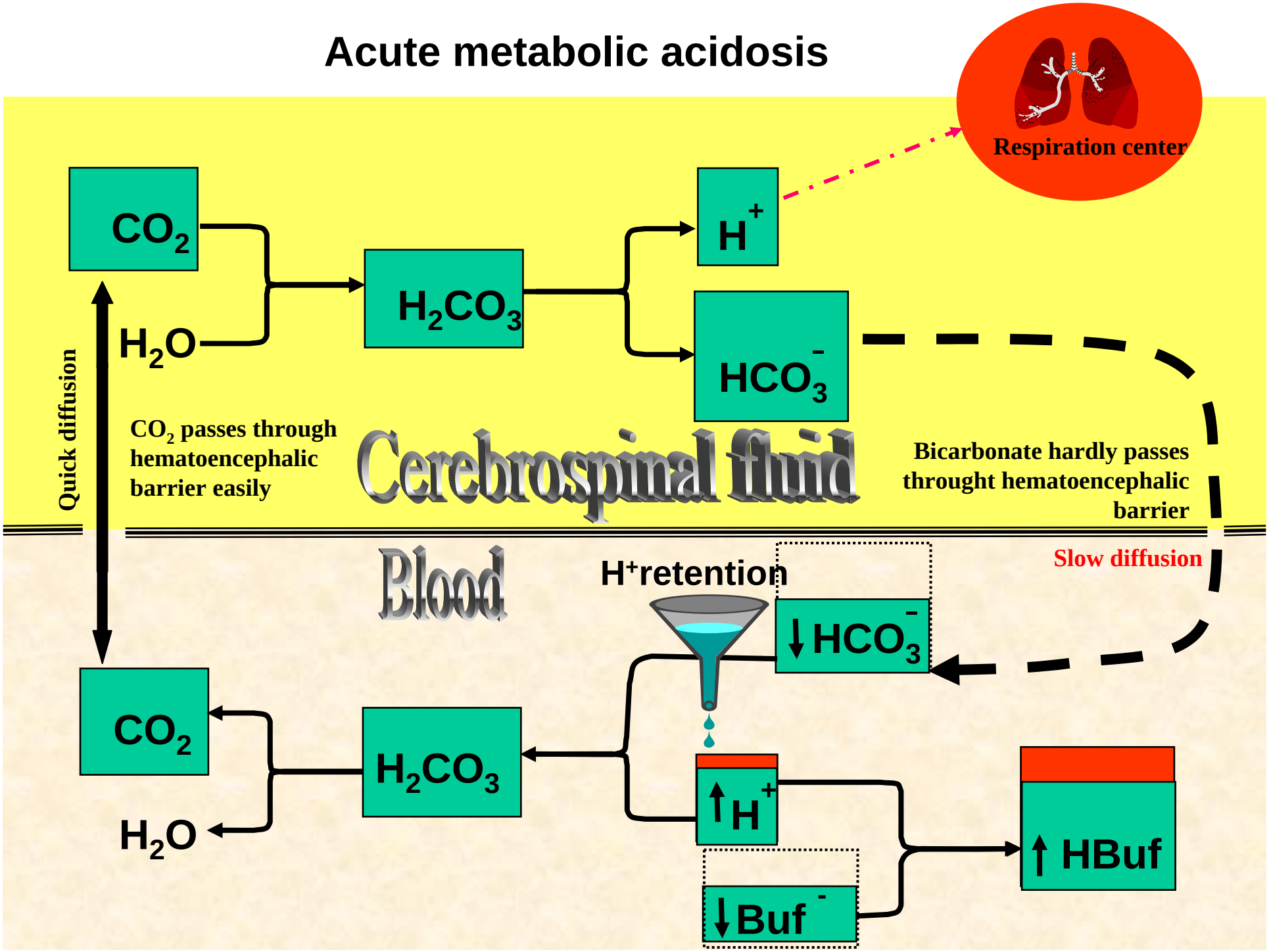
Role of liver in Acid-Base



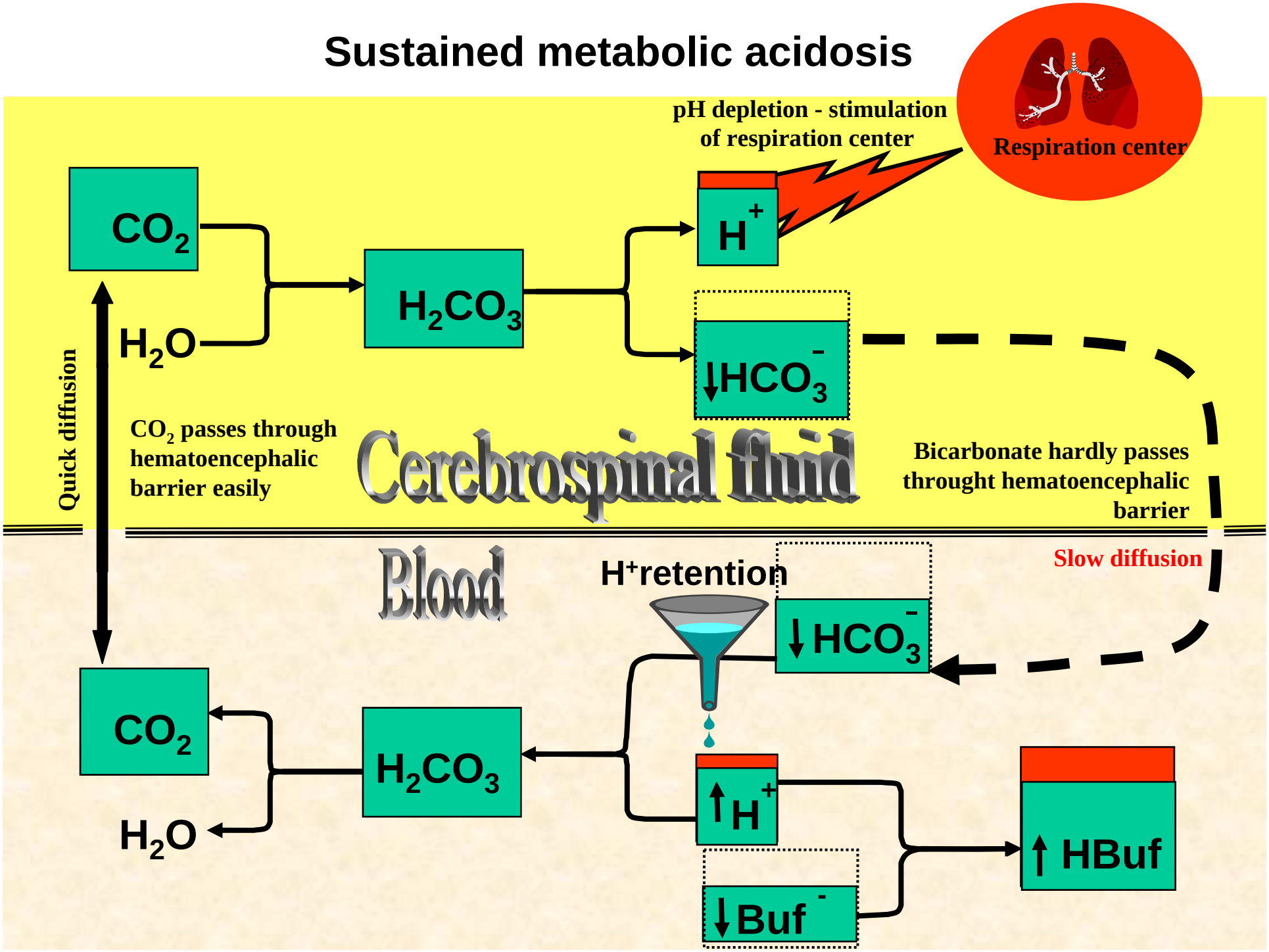
Respiratory controller of acid-base disorders

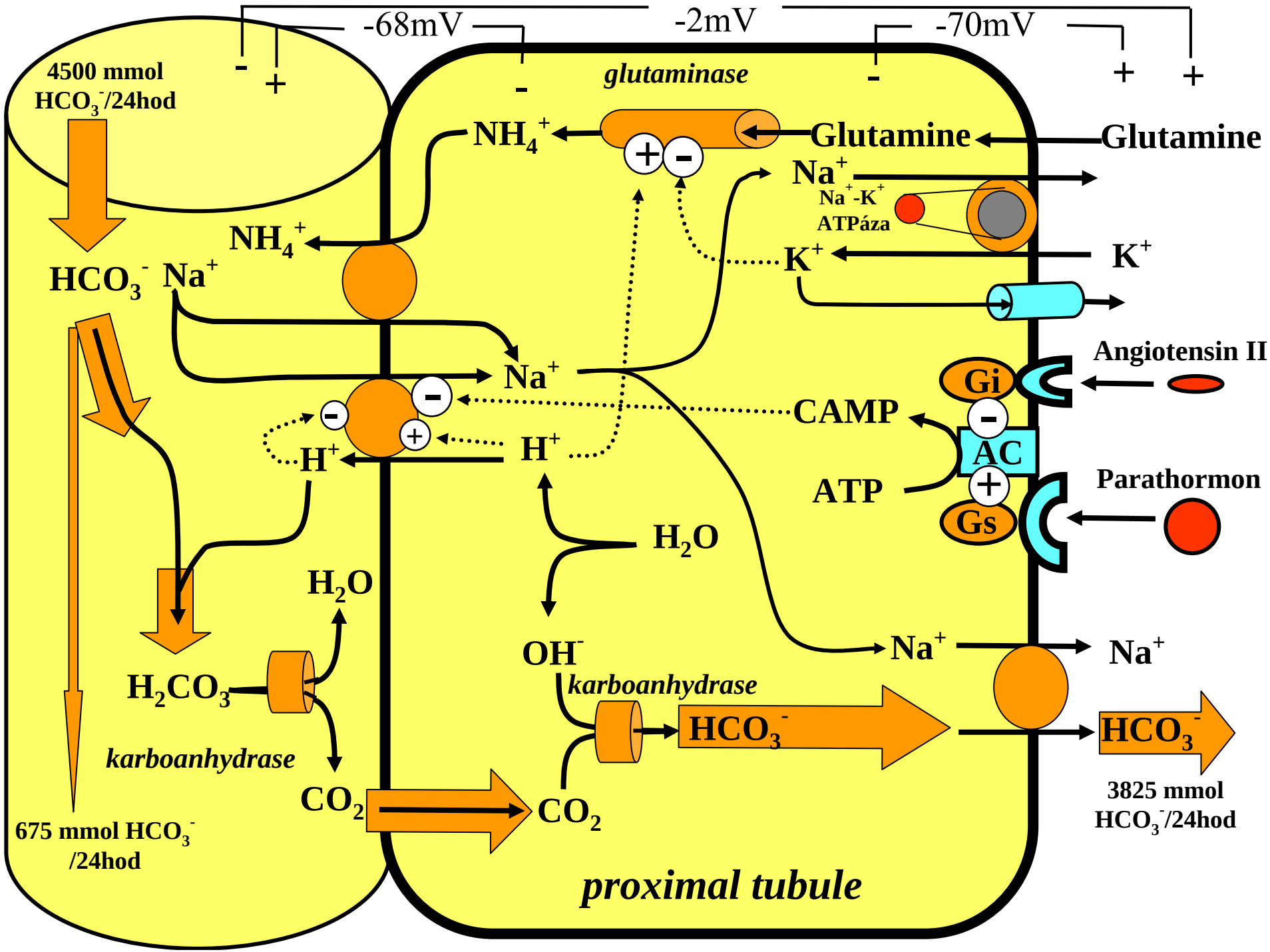


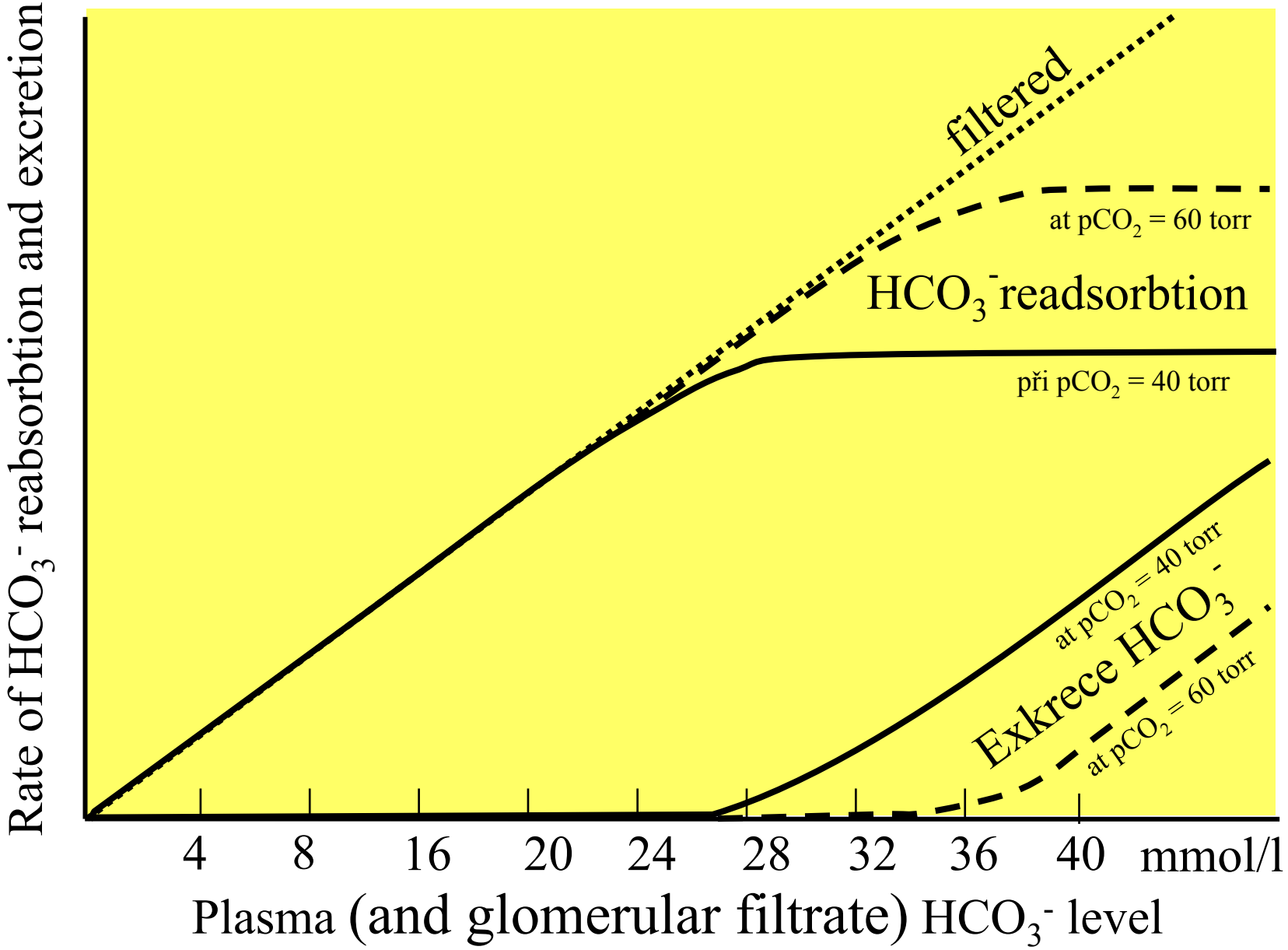
Acute metabolic acidosis

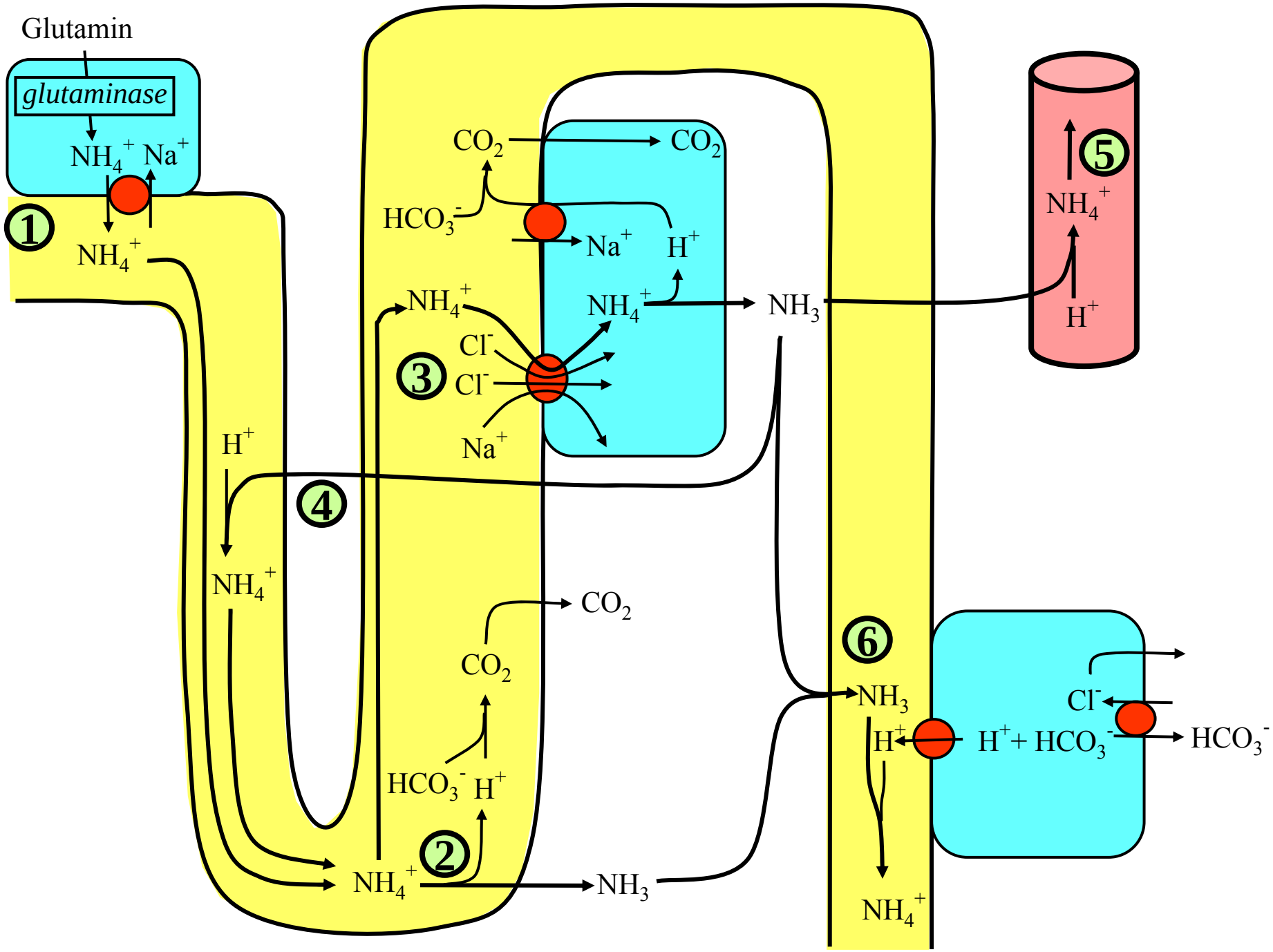


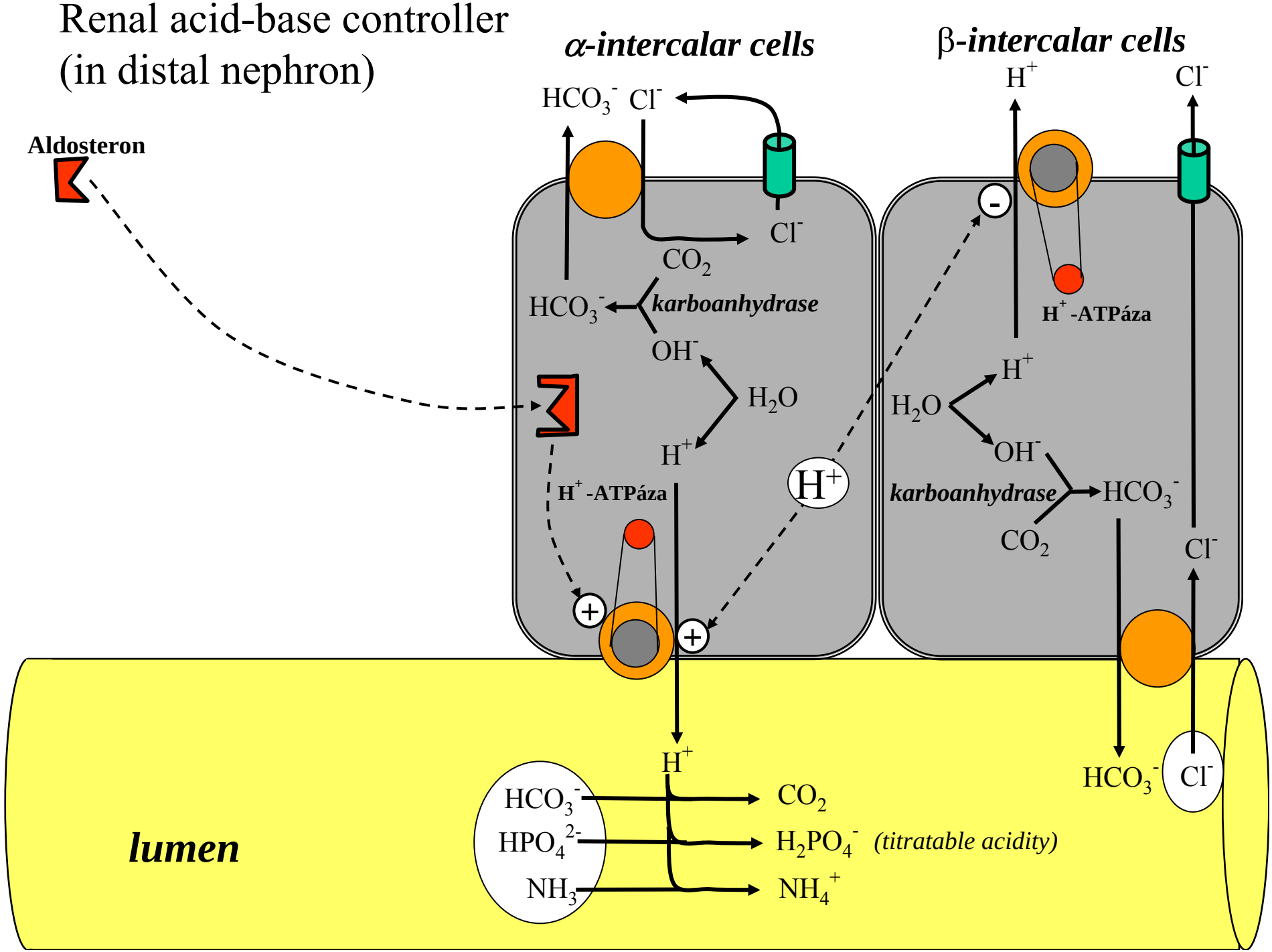
Sustained metabolic acidosis

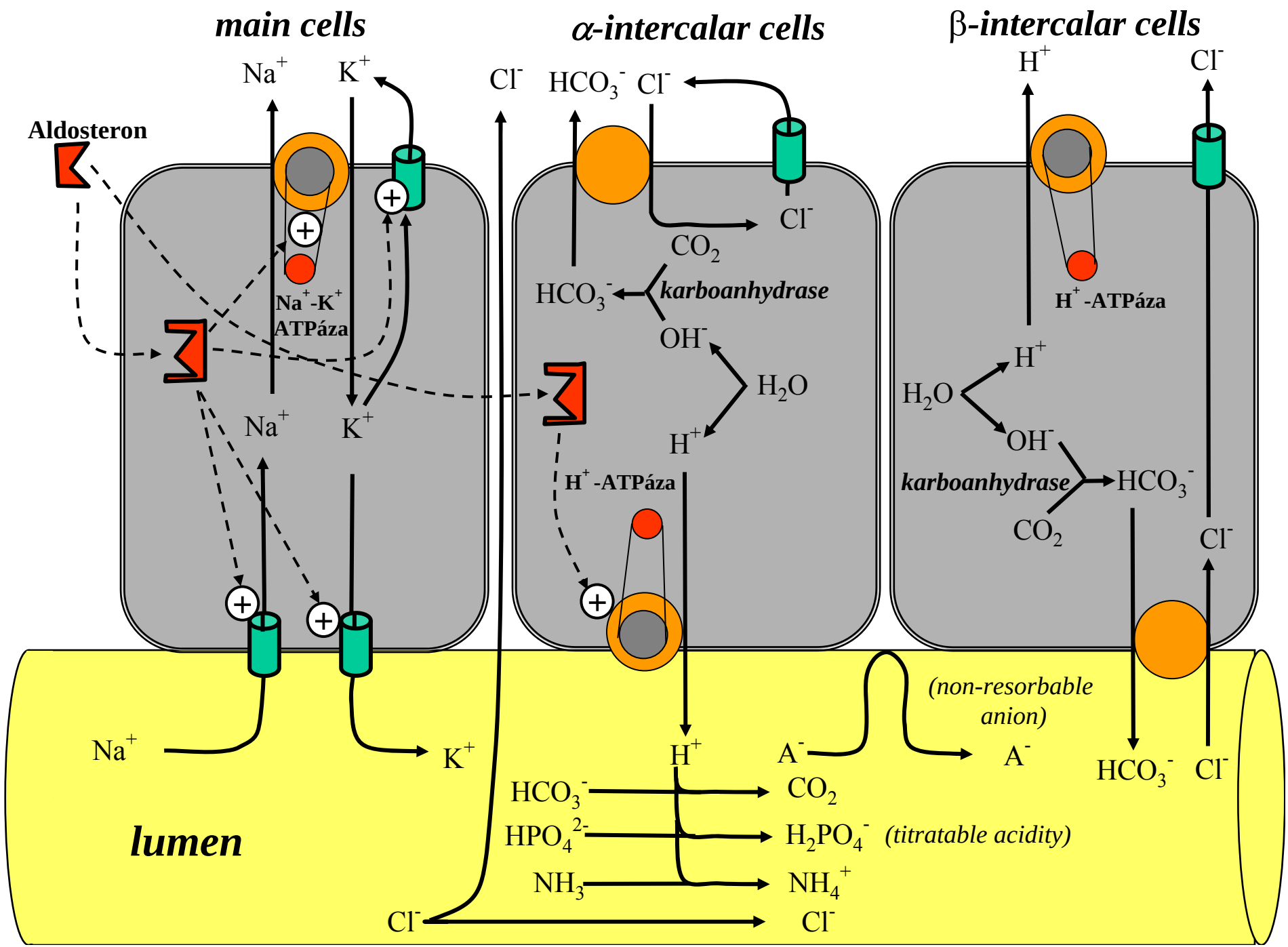



-68mV
-2mV
-70mV
4500 mmol HCO3-/24hod
glutaminase
NH4+
Glutamine
Glutamine
Na+
Na+-K+ ATPáza
K+
K+
HCO3- Na+
NH4+
Na+
Angiotensin II
Gi
CAMP
AC
ATP
Gs
Parathormon
H+
H+
H2O
H2O
OH-
Na+
Na+
karboanhydrase
H2CO3
HCO3-
HCO3-
karboanhydrase
CO2
CO2
675 mmol HCO3-/24hod
3825 mmol HCO3-/24hod
proximal tubule

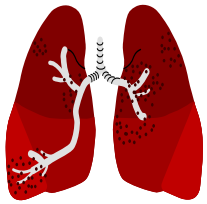

Rate of HCO_3^- reabsorbtion and excretion
filtered
at pCO_2 = 60 torr
HCO_3^- readsorbtion
při pCO_2 = 40 torr
at pCO_2 = 40 torr
Exkrece HCO_3^-
at pCO_2 = 60 torr
4
8
16
20
24
28
32
36
40
mmol/l
Plasma (and glomerular filtrate) HCO_3^- level

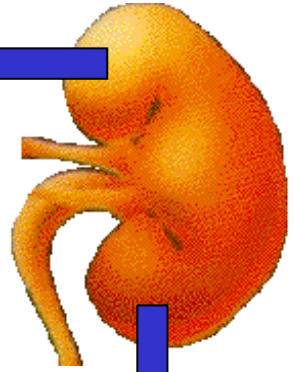

Glutamin
glutaminase
NH_4^+ Na^+
1
NH_4^+
CO_2
CO_2
HCO_3^-
Na^+
H^+
NH_4^+
NH_4^+
NH_3
3
Cl^-
Cl^-
Na^+
5
NH_4^+
H^+
H^+
4
NH_4^+
CO_2
CO_2
HCO_3^- H^+
2
NH_4^+
NH_3
6
NH_3
H^+
NH_4^+
Cl^-
$H^+ + HCO_3^-$
HCO_3^-


Renal acid-base controller
(in distal nephron)
α-intercalar cells
β-intercalar cells
Aldosteron
HCO3- Cl-
Cl-
CO2
HCO3-
karboanhydrase
OH-
H2O
H+
H+-ATPáza
H+
H+
H2O
OH-
karboanhydrase
HCO3-
CO2
H+-ATPáza
Cl-
Cl-
HCO3-
Cl-
lumen
H+
HCO3-
HPO4 2-
NH3
CO2
H2PO4-
(titratable acidity)
NH4+


main cells
α-intercalar cells
β-intercalar cells
Aldosteron
Na+
K+
Cl-
HCO3-
Na+-K+ ATPáza
CO2
karboanhydrase
OH-
H2O
H+
H+-ATPáza
(non-resorbable anion)
A-
HPO4 2-
H2PO4-
(titratable acidity)
NH3
NH4+
lumen

Acid-base disturbances:





CO_2

HCO_3^-

H_2CO_3

TA + NH_4^+

CO_2 balance

H_2O

H^+

H^+ balance

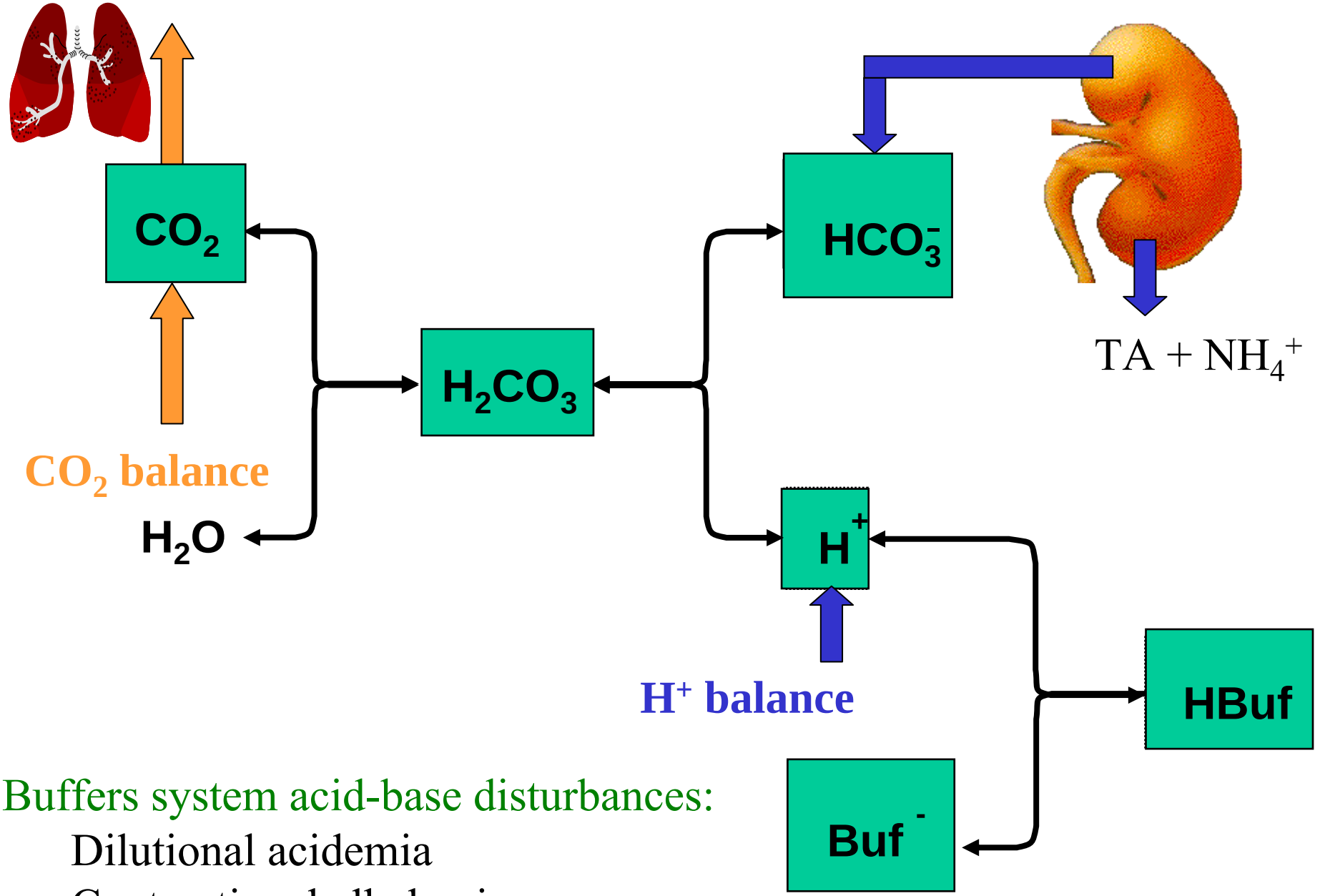
HBuf

Buf^-

Buffer system acid-base disturbances

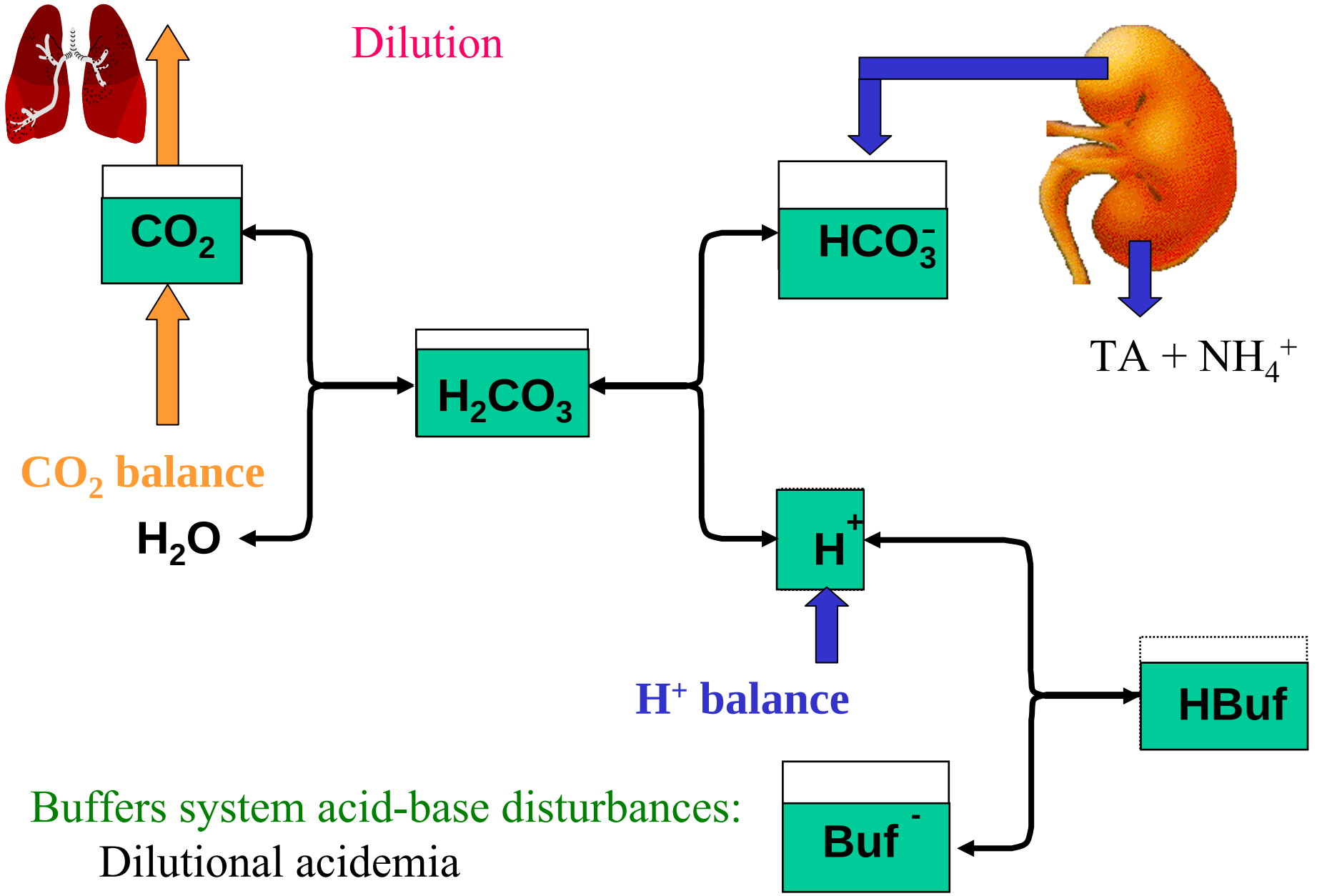
Balance acid-base disturbances:

- metabolic acidosis/alkalosis
- respiration acidosis/alkalosis



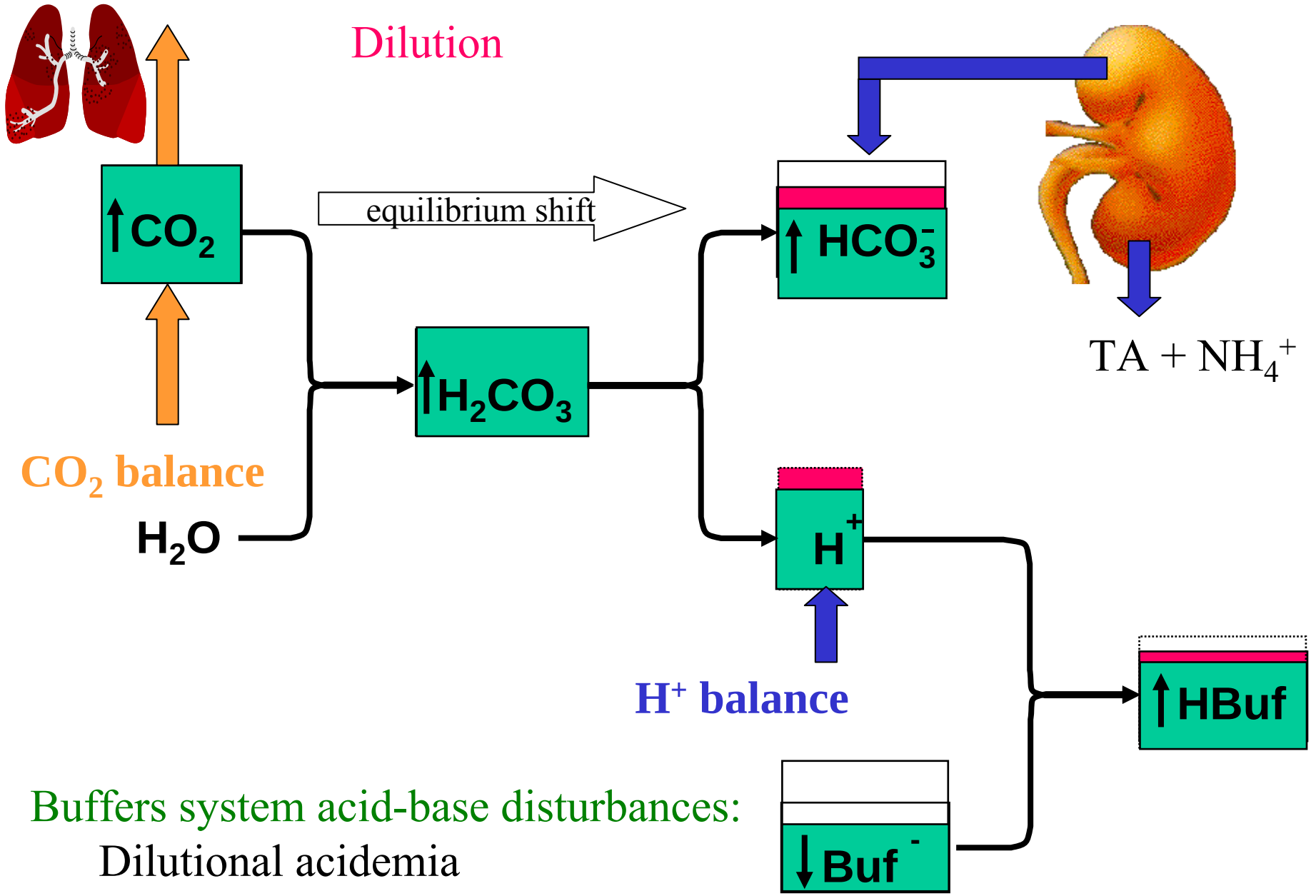
Buffers system acid-base disturbances:

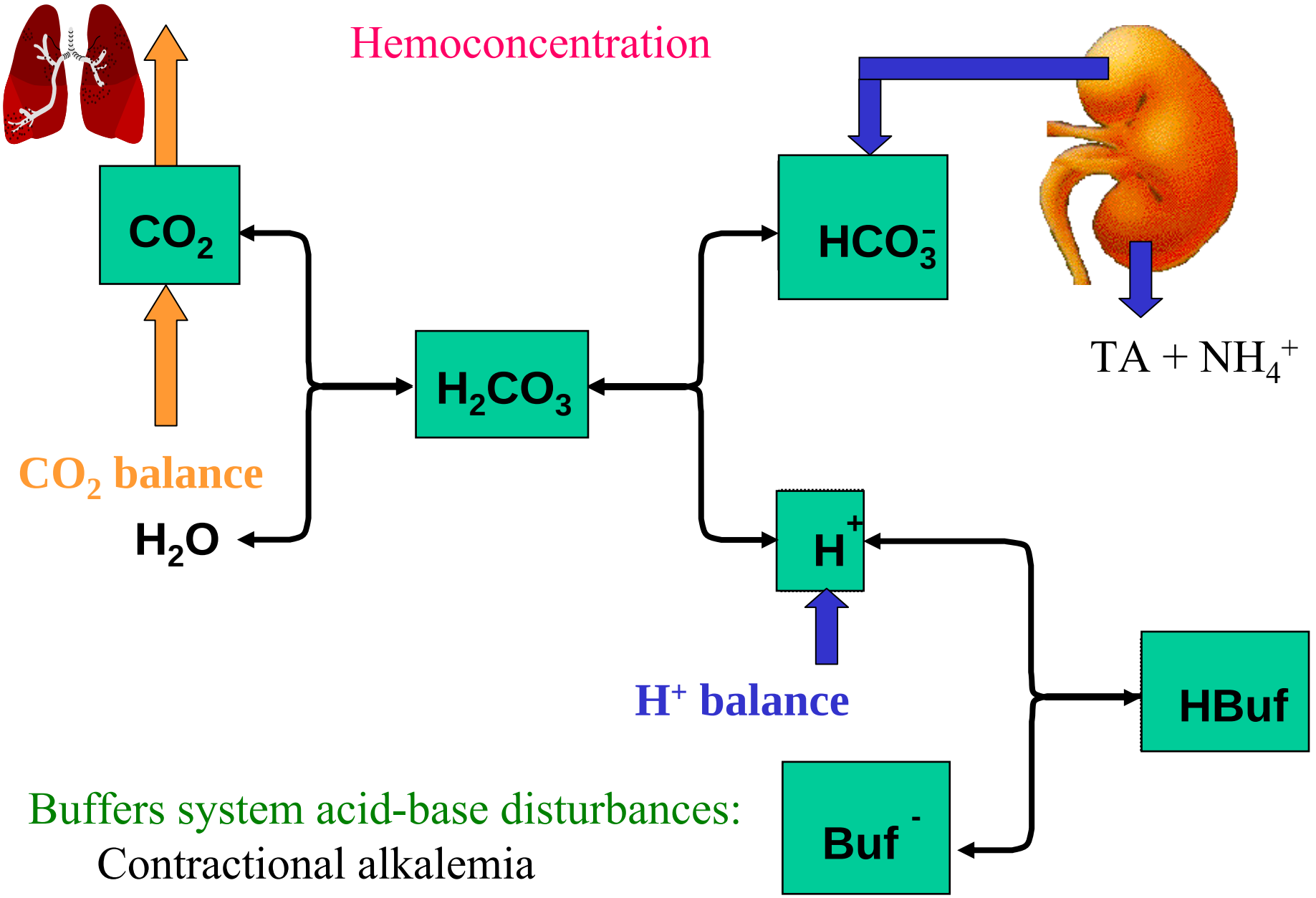
- Dilutional acidemia
- Contractional alkalemia
- Hypoproteinemic alkalemia



Buffers system acid-base disturbances:

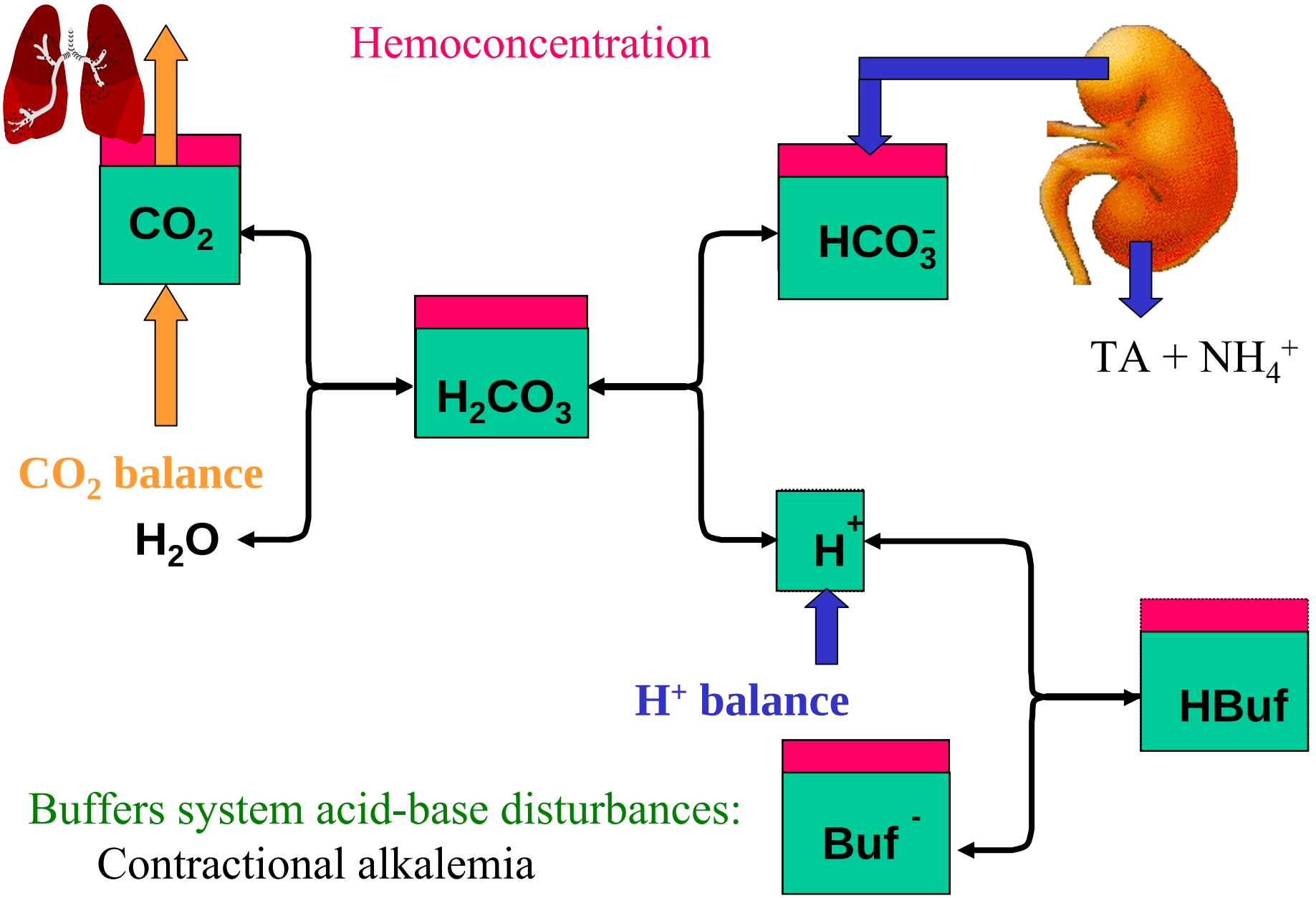
Dilutional acidemia

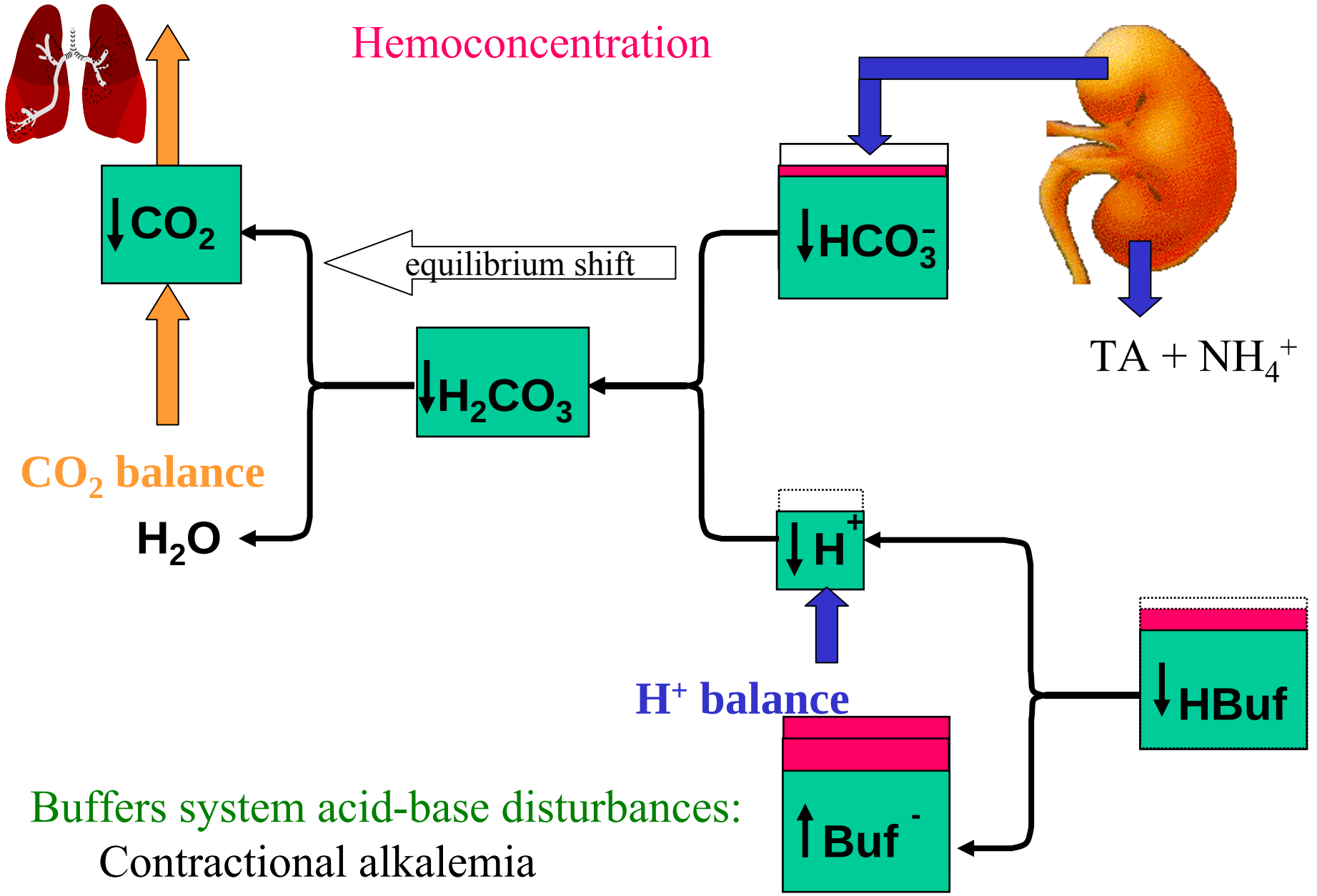

Dilution
↑CO2
equilibrium shift
↑HCO3-
TA + NH4+
↑H2CO3
CO2 balance
H2O
H+
H+ balance
↑HBuf
Buffers system acid-base disturbances:
Dilutional acidemia
↓Buf -

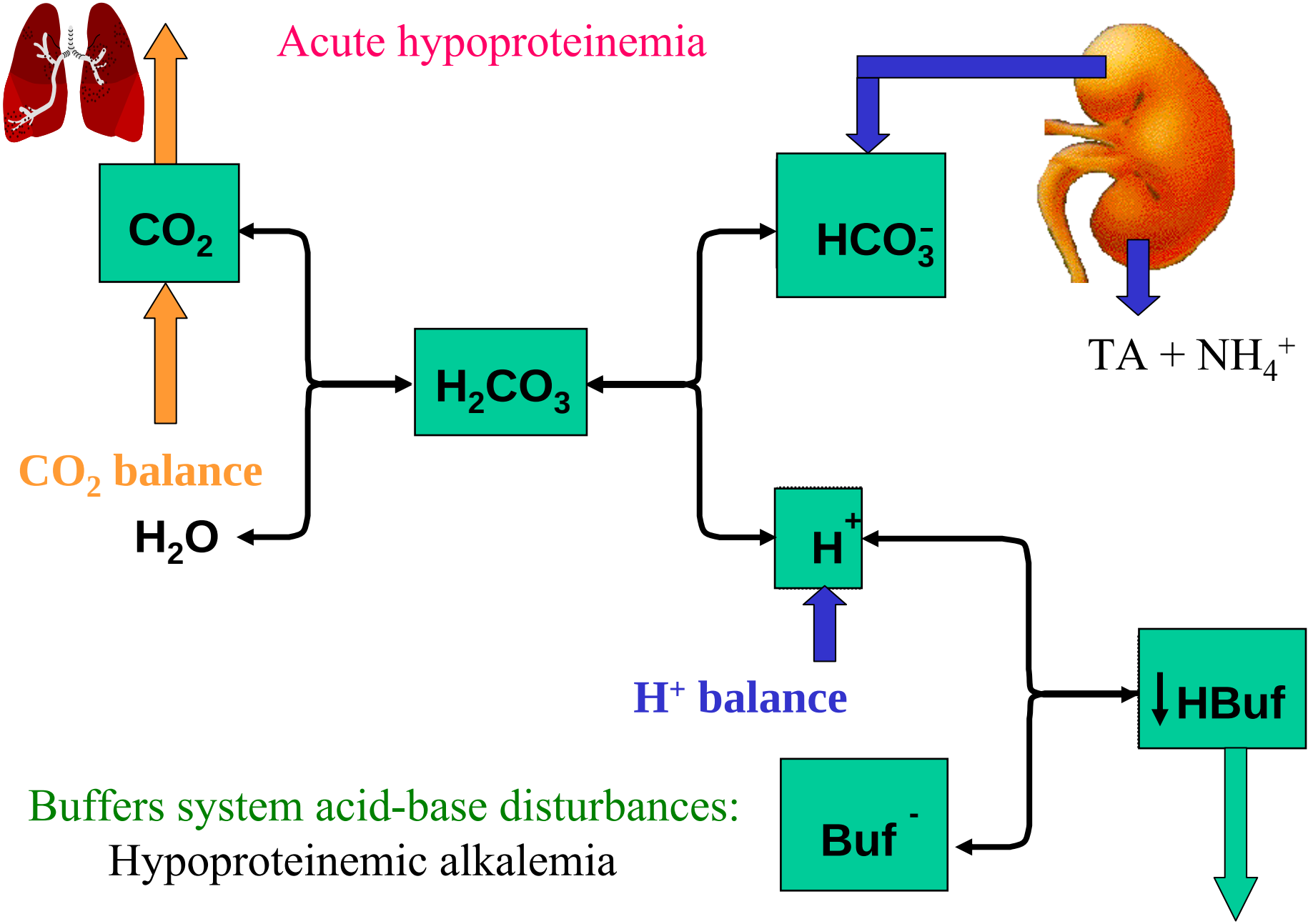


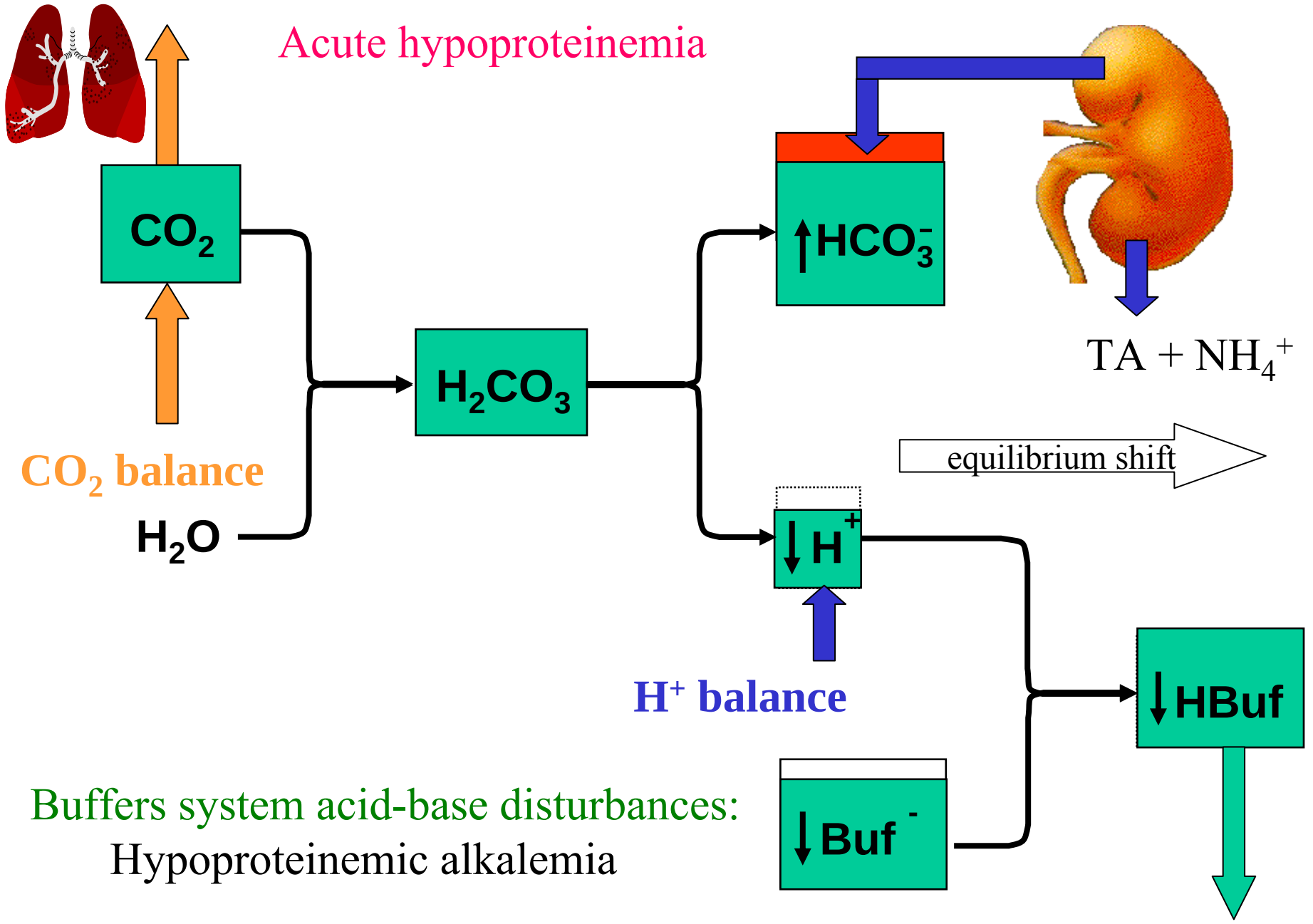
Buffers system acid-base disturbances:

Contractional alkalemia

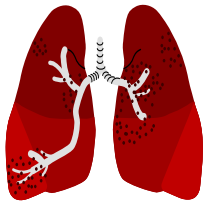

Hemoconcentration
CO_2
HCO_3^-
TA + NH_4^+
H_2CO_3
CO_2 balance
H_2O
H^+
H^+ balance
HBuf
Buf^-
Buffers system acid-base disturbances:
Contractional alkalemia

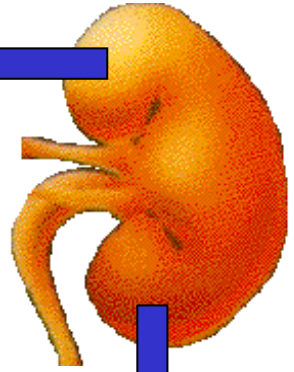

Hemoconcentration
↓CO2
equilibrium shift
↓HCO3-
TA + NH4+
↓H2CO3
CO2 balance
H2O
↓H+
H+ balance
↓HBuf
↑Buf -
Buffers system acid-base disturbances:
Contractional alkalemia


Acute hypoproteinemia
CO_2
H_2CO_3
HCO_3^-
TA + NH_4^+
CO_2 balance
H_2O
H^+
H^+ balance
HBuf
Buf^-
Buffers system acid-base disturbances:
Hypoproteinemic alkalemia


Acute hypoproteinemia
CO_2
H_2CO_3
HCO_3^-
TA + NH_4^+
CO_2 balance
H_2O
equilibrium shift
H^+
H^+ balance
HBuf
Buf^-
Buffers system acid-base disturbances:
Hypoproteinemic alkalemia

Acid-base disturbances:





CO_2

HCO_3^-

$TA + NH_4^+$

H_2CO_3

CO_2 balance

H_2O

H^+

H^+ balance

HBuf

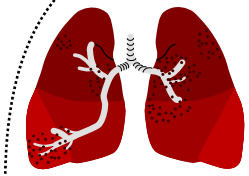
Buf^-

Buffer system acid-base disturbances

Balance acid-base disturbances:

- metabolic acidosis/alkalosis
- respiration acidosis/alkalosis

Acute metabolic acidosis



3. Respiration keep CO_2 level unchangeable – thereby increases buffer power of bicarbonate buffer

CO_2

H_2O

H_2CO_3

$\downarrow HCO_3^-$

2. Consumption of bicarbonate in buffer reaction

1. Primary disturbance: H^+ retention

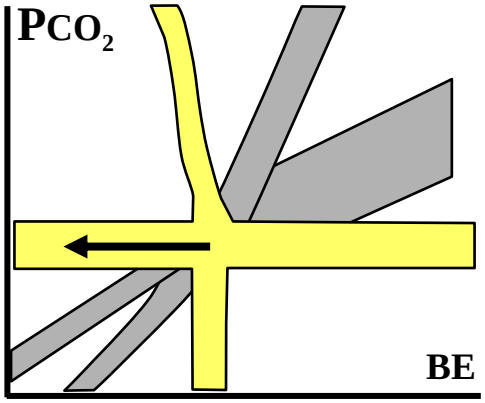
H^+

$\uparrow HBuf$

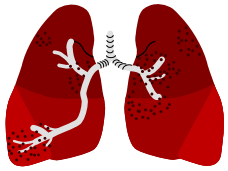
4. Pathophysiological concequence: H^+ level increases only a little bit due to buffer reaction

$\downarrow Buf^-$

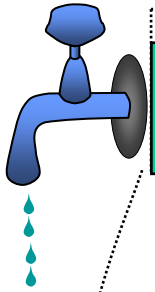
2. Consumtion of non-bicarbonate buffer bases in buffer reaction



Respiratory compensation of metabolic acidosis



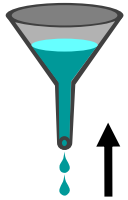
2. Respiratory response:
Decrease CO_2 level



↓ CO_2

↓ HCO_3^-

↓ H_2CO_3



H_2O

↓ H^+

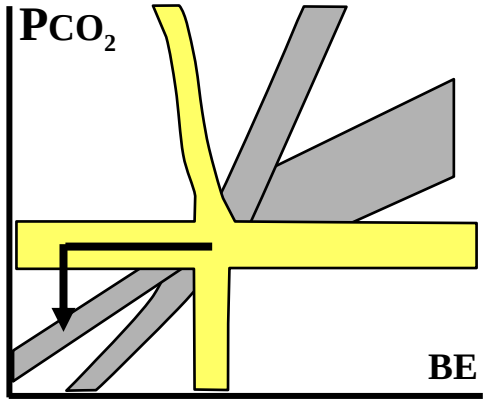
1. Primary failurea:
H^+ retention

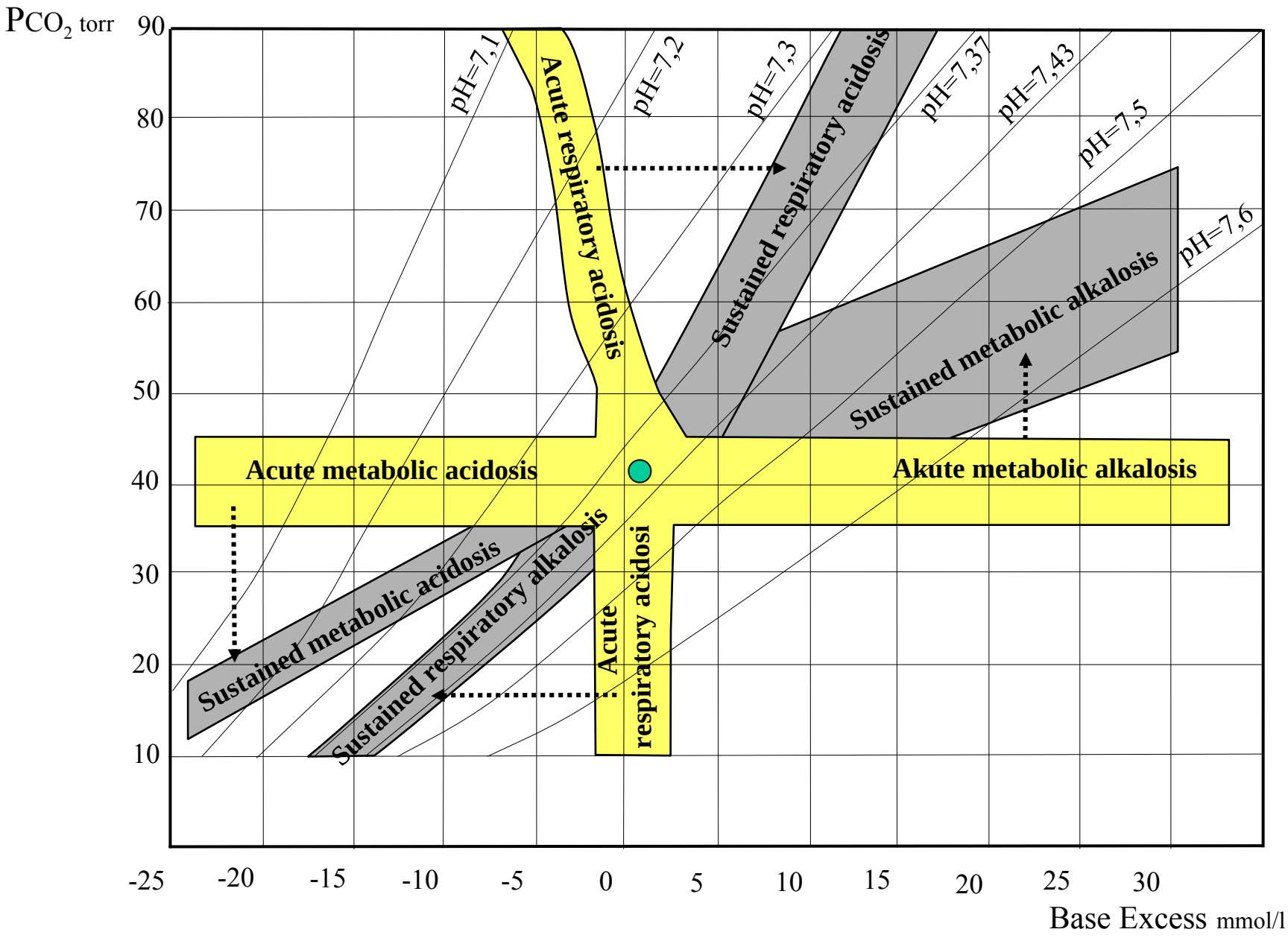
4. Pathophysiological concequence :
diminished H^+ level

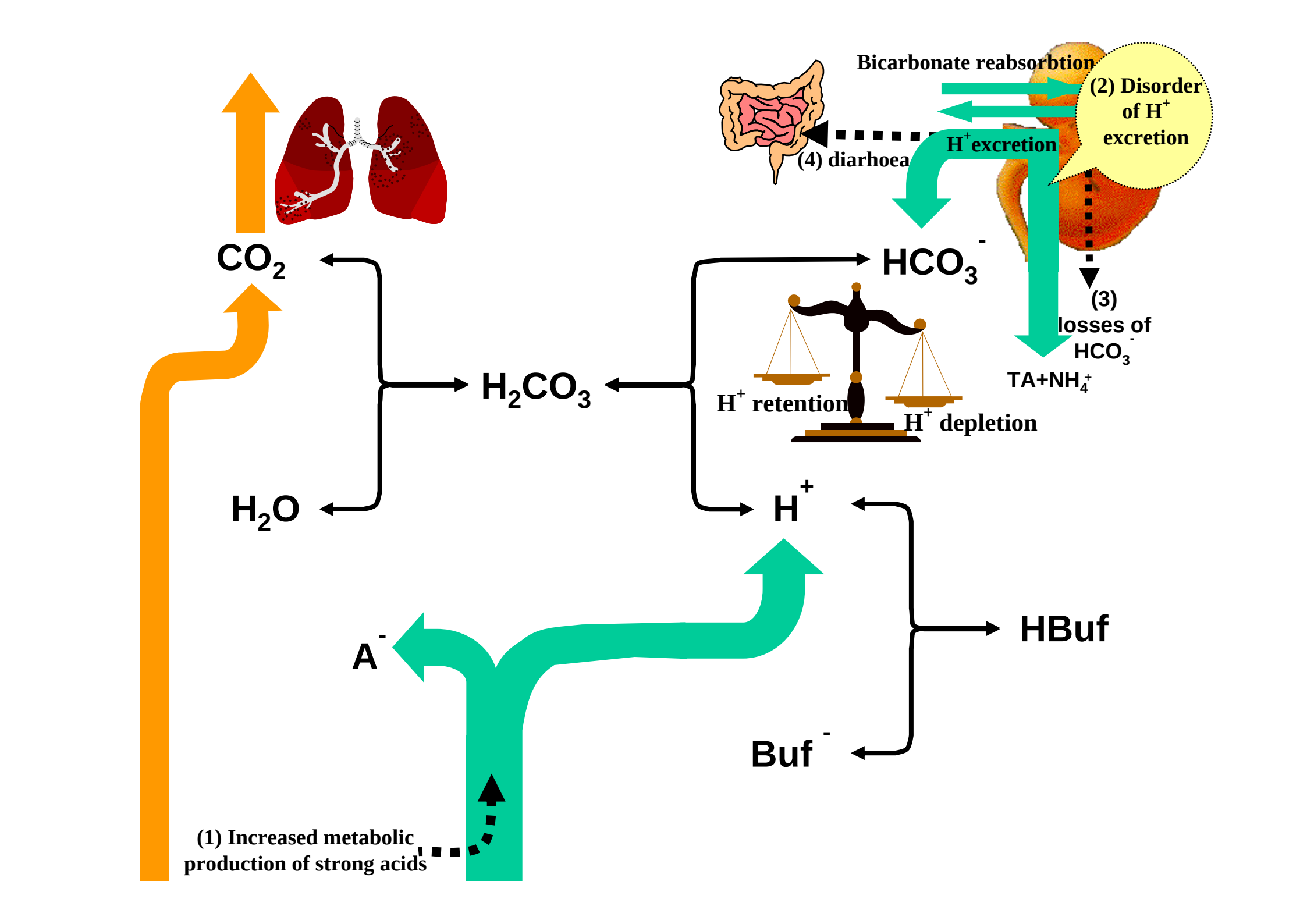
3. Shift of equilibrium to the left

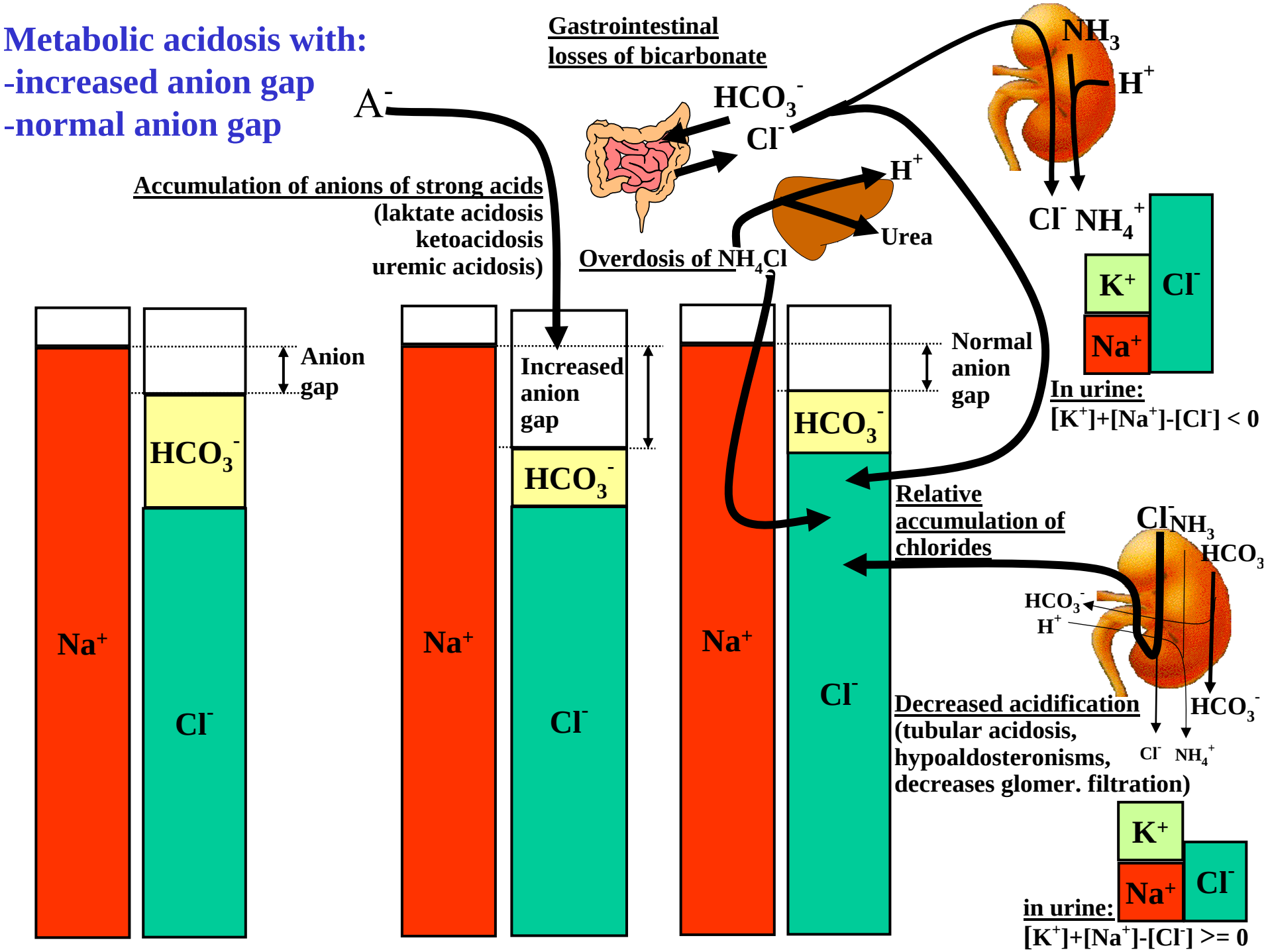
↓ HBuf

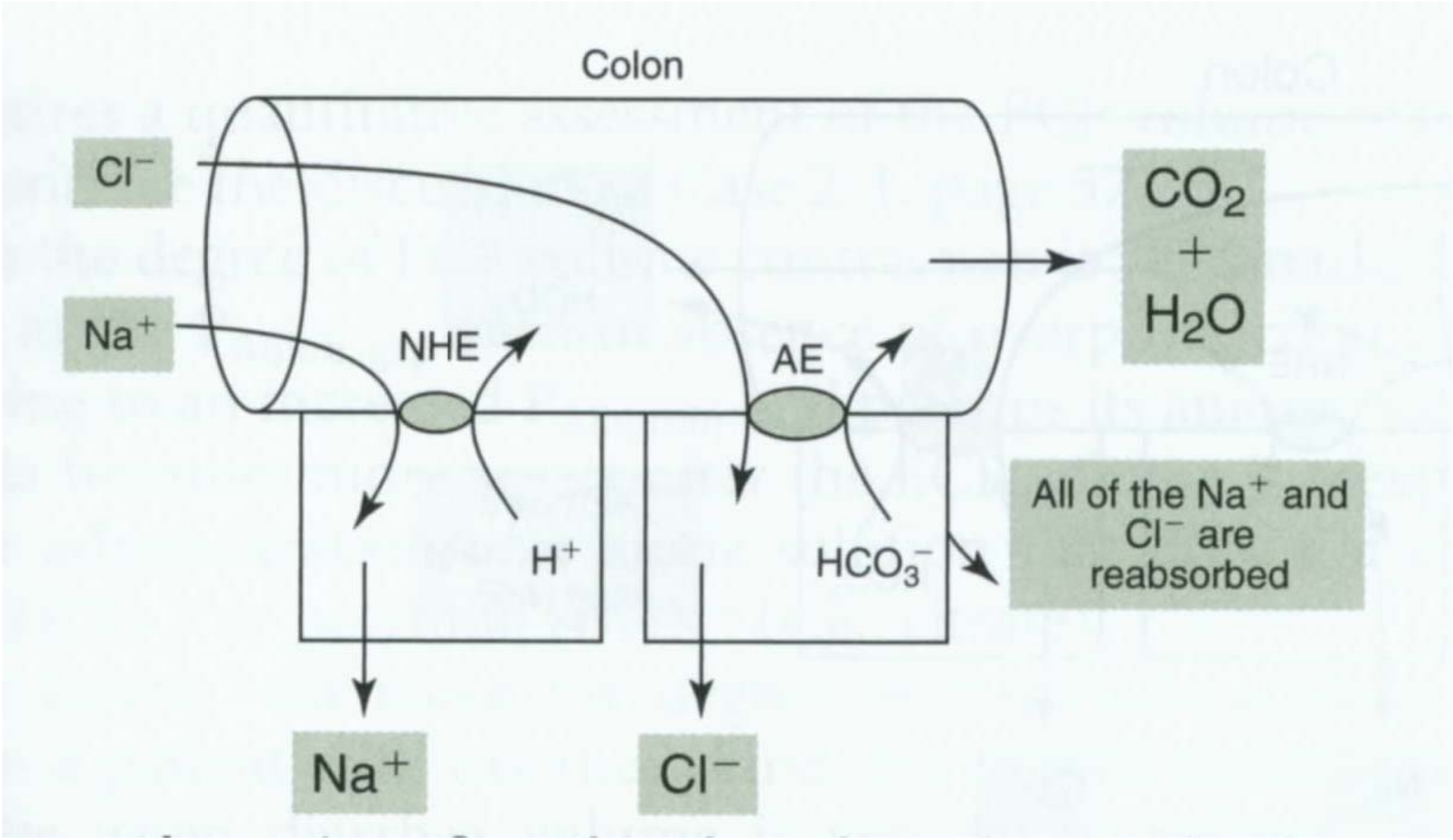
↑ Buf^-

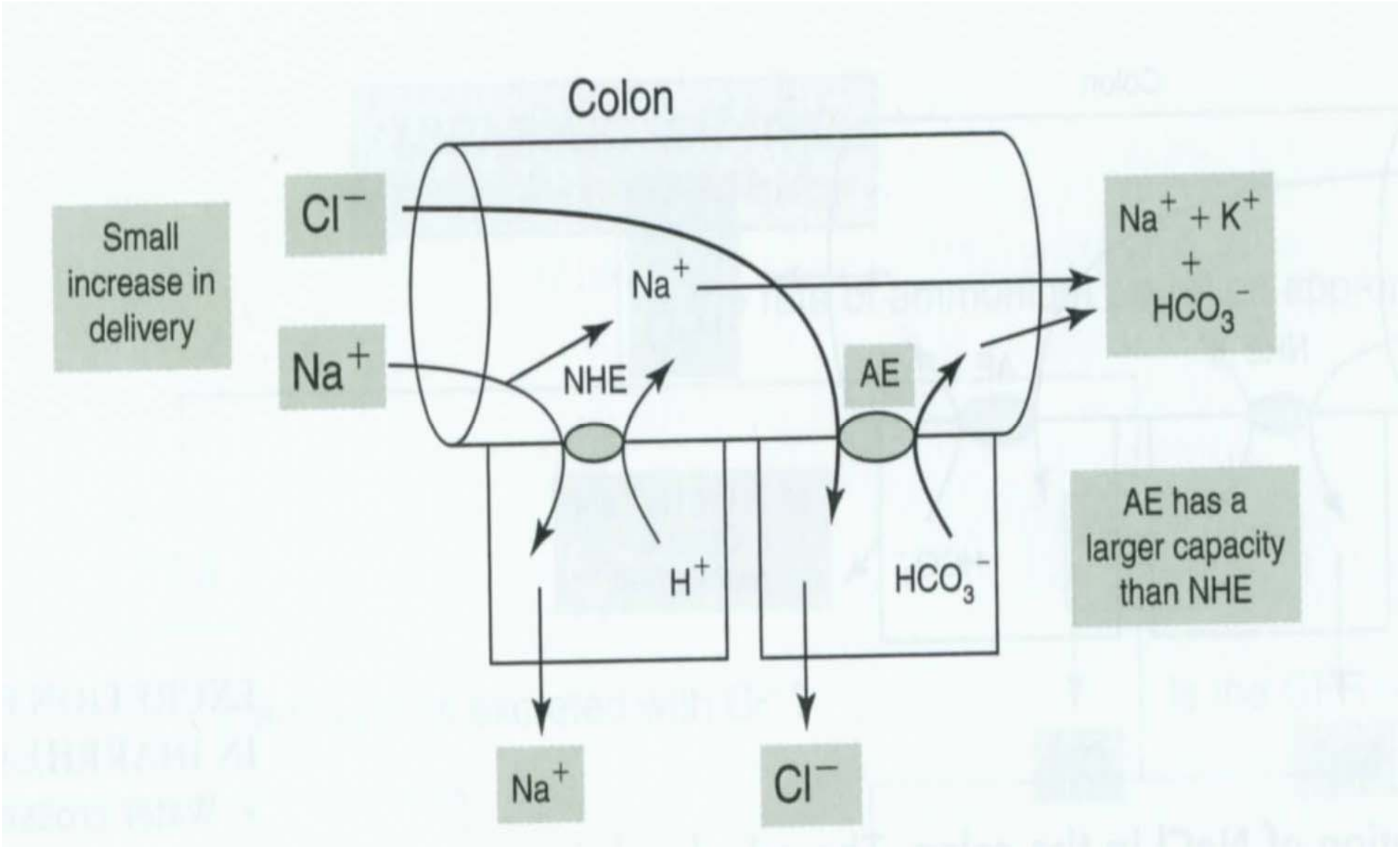



PCO2 torr
90
80
70
60
50
40
30
20
10
pH=7,1
pH=7,2
pH=7,3
pH=7,37
pH=7,43
pH=7,5
pH=7,6
Acute respiratory acidosis
Sustained respiratory acidosis
Sustained metabolic alkalosis
Acute metabolic acidosis
Akute metabolic alkalosis
Sustained metabolic acidosis
Sustained respiratory alkalosis
Acute respiratory acidosi
-25
-20
-15
-10
-5
0
5
10
15
20
25
30
Base Excess mmol/l

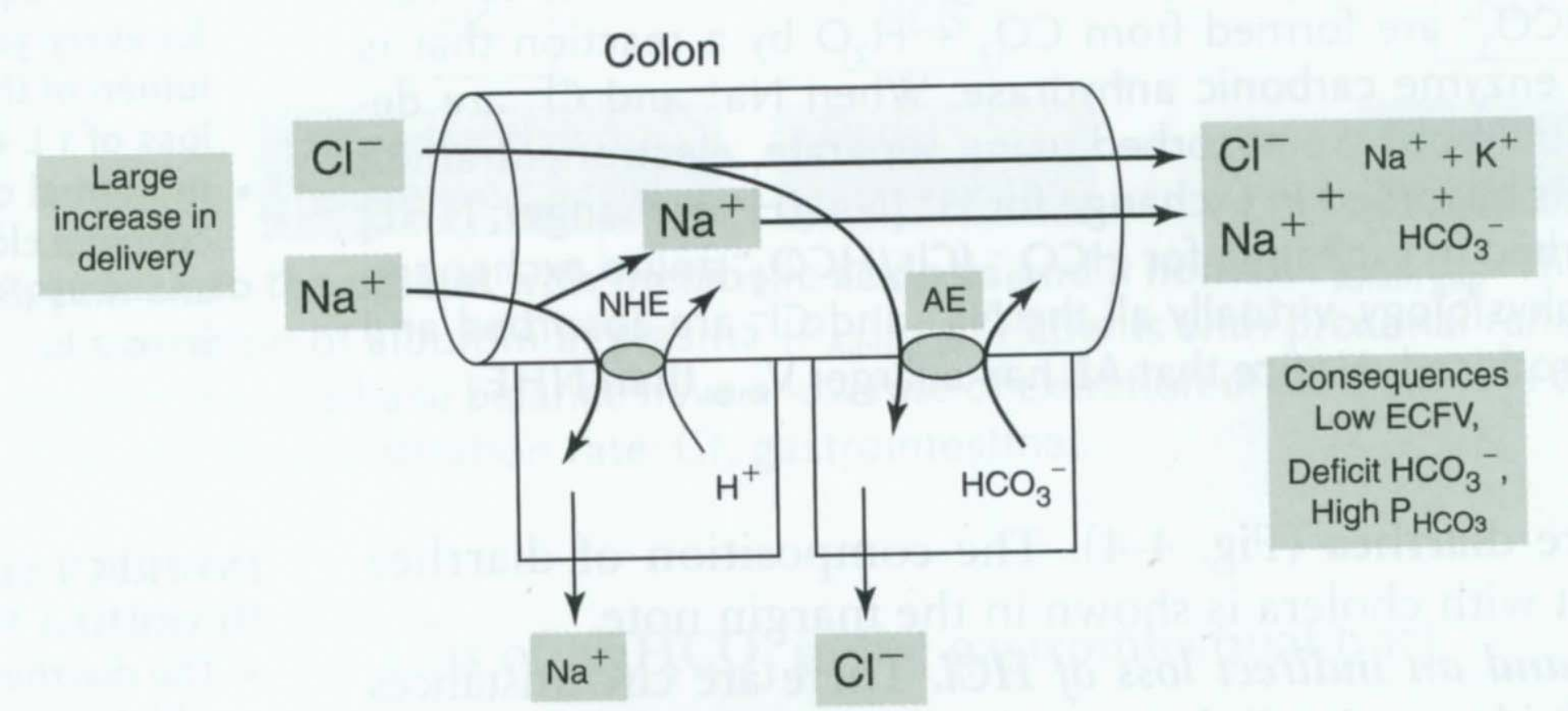

Bicarbonate reabsorbtion
(2) Disorder of H^+ excretion
H^+ excretion
(4) diarhoea
CO_2
HCO_3^-
(3) losses of HCO_3^-
$TA+NH_4^+$
H_2CO_3
H^+ retention
H^+ depletion
H_2O
H^+
HBuf
A^-
Buf^-
(1) Increased metabolic production of strong acids


Metabolic acidosis with:
-increased anion gap
-normal anion gap
Gastrointestinal losses of bicarbonate
A-
HCO3-
Cl-
NH3
H+
Accumulation of anions of strong acids (laktate acidosis ketoacidosis uremic acidosis)
Overdosis of NH4Cl
H+
Urea
Cl- NH4+
K+
Cl-
Na+
In urine:
[K+]+[Na+]-[Cl-] < 0
Anion gap
Increased anion gap
Normal anion gap
HCO3-
Na+
Cl-
Relative accumulation of chlorides
Cl-
NH3
HCO3
HCO3-
H+
HCO3-
Decreased acidification (tubular acidosis, hypoaldosteronisms, decreases glomer. filtration)
Cl- NH4+
K+
Na+
Cl-
in urine:
[K+]+[Na+]-[Cl-] >= 0

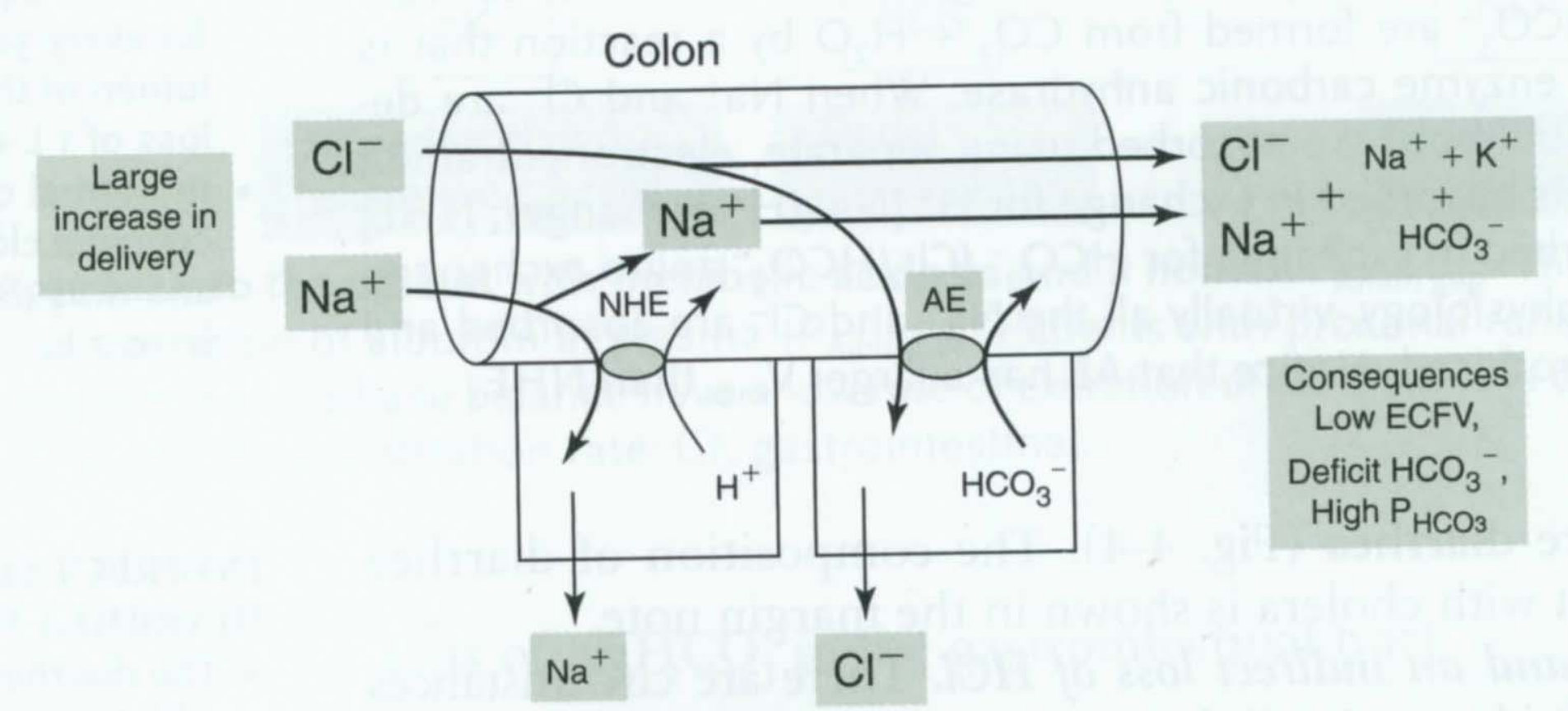

Colon
Cl^-
Na^+
NHE
AE
CO_2 + H_2O
H^+
HCO_3^-
All of the Na^+ and Cl^- are reabsorbed
Na^+
Cl^-



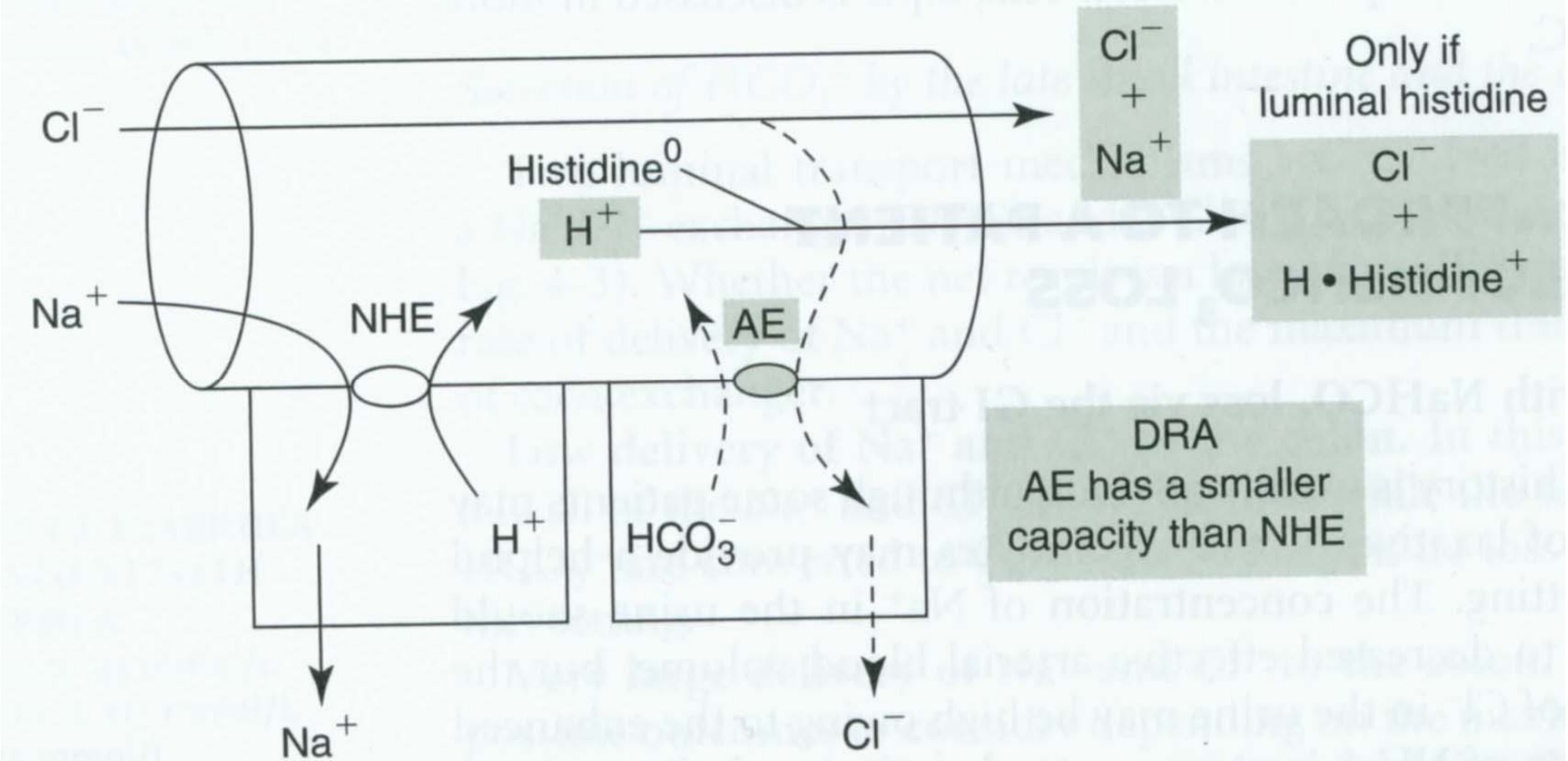
Alkalic diarrhoea



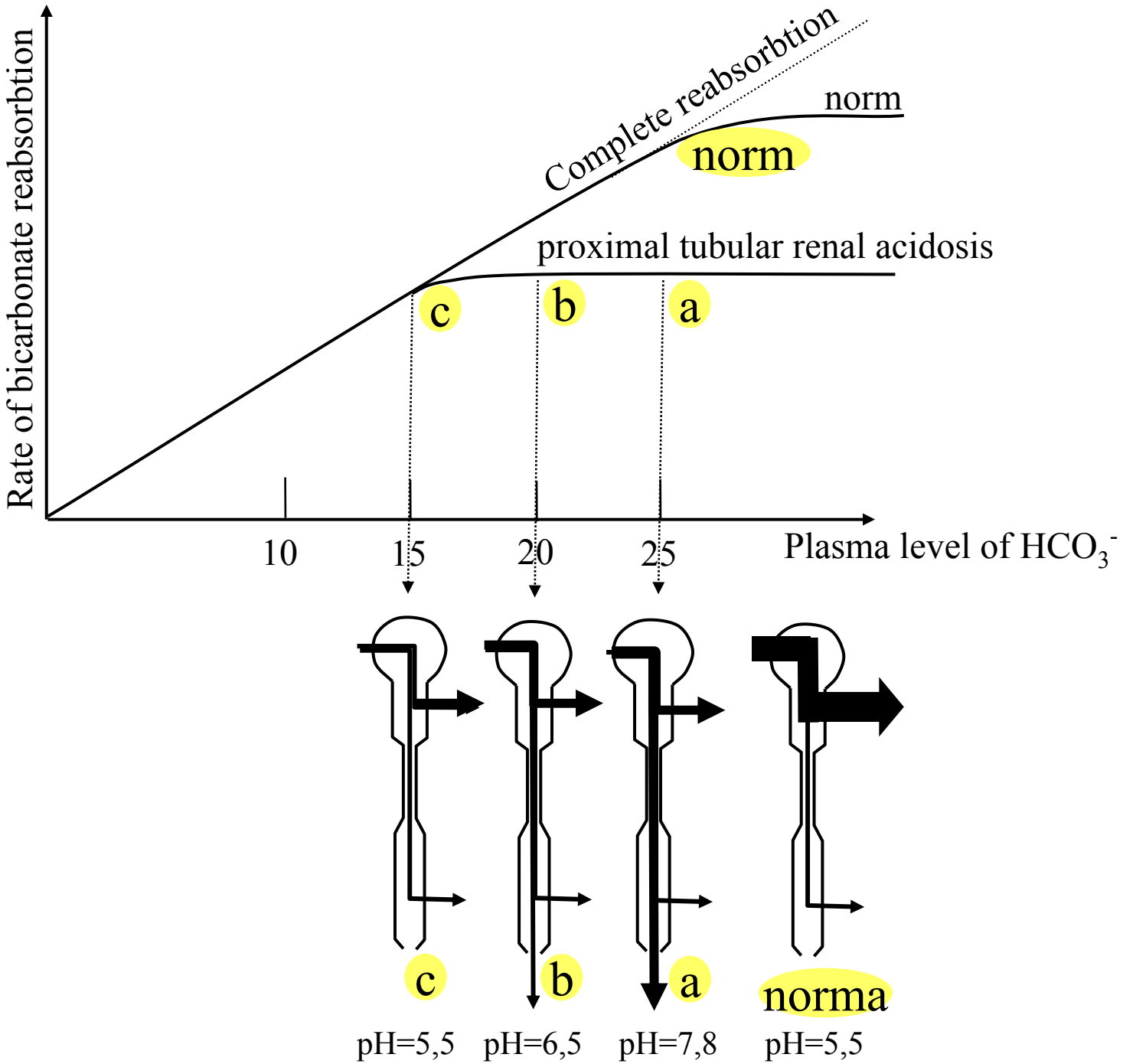
Severe alkalic diarrhoea

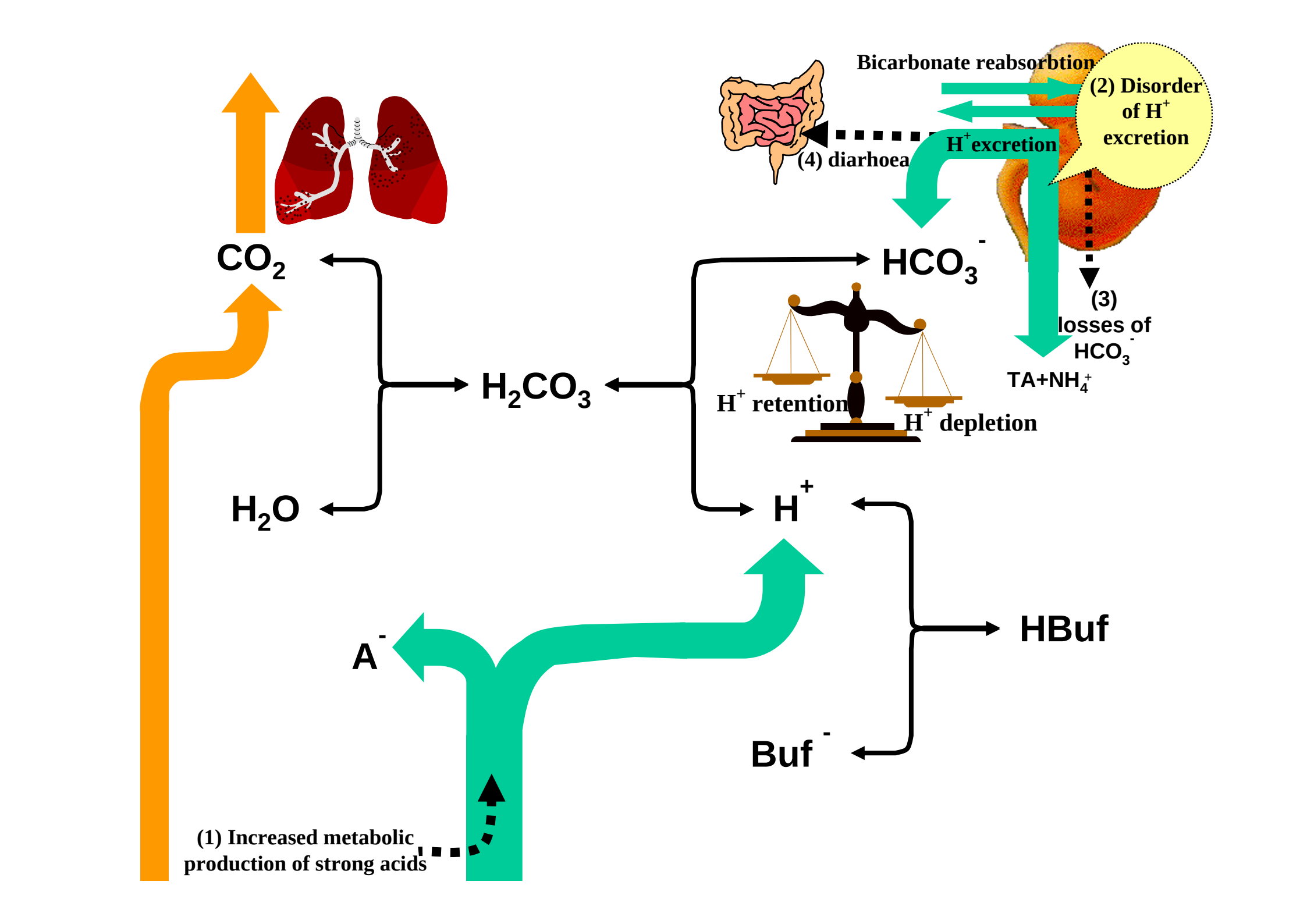


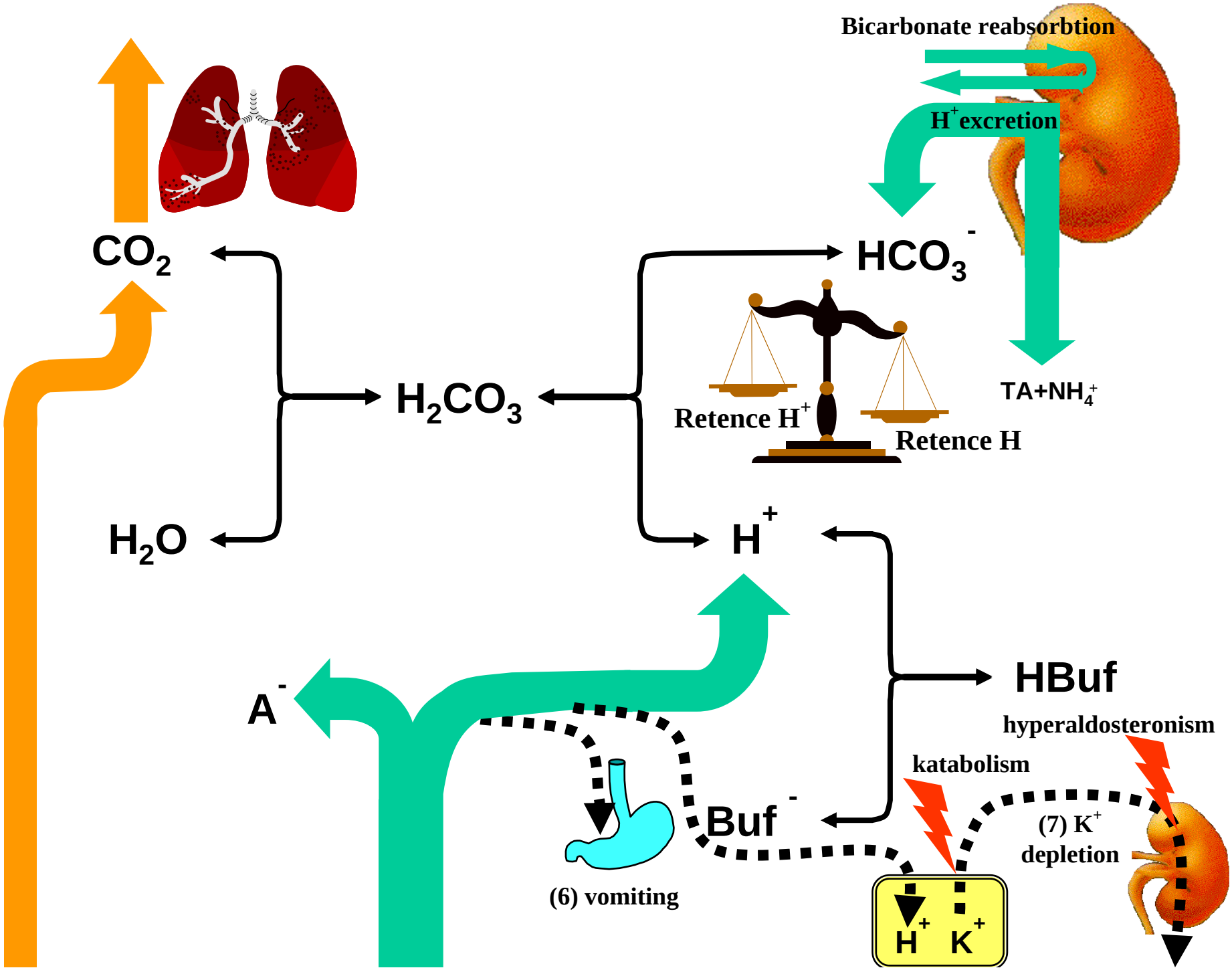
Severe alkalic diarrhoea



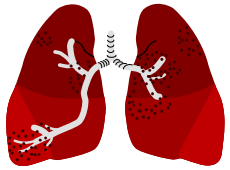
Acidic diarrhoea in DRA, down-regulated adenoma


Rate of bicarbonate reabsorbtion
Complete reabsorbtion
norm
norm
proximal tubular renal acidosis
c
b
a
10
15
20
25
Plasma level of HCO_3^-
c
b
a
norma
pH=5,5
pH=6,5
pH=7,8
pH=5,5


Bicarbonate reabsorbtion
(2) Disorder of H^+ excretion
H^+ excretion
(4) diarhoea
CO_2
HCO_3^-
(3) losses of HCO_3^-
$TA+NH_4^+$
H_2CO_3
H^+ retention
H^+ depletion
H_2O
H^+
HBuf
A^-
Buf^-
(1) Increased metabolic production of strong acids


Bicarbonate reabsorbtion
H+ excretion
CO2
HCO3-
H2CO3
H2O
Retence H+
Retence H
TA+NH4+
H+
HBuf
hyperaldosteronism
katabolism
A-
Buf-
(6) vomiting
(7) K+ depletion
H+ K+

Acute metabolic alkalosis



3. Respiration keep CO_2 level unchangeable – thereby increases buffer power of bicarbonate buffer

CO_2

H_2O

H_2CO_3

$\uparrow HCO_3^-$

2. Dissotiation of carbonic acid in buffer reaction

4. <u>Pathophysiological concequence:</u> H^+ level decreases only a little bit due to buffer reaction

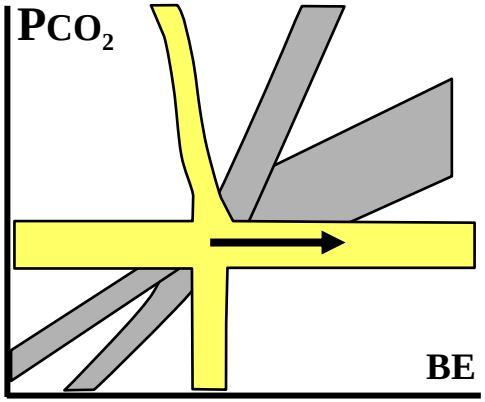
$\downarrow H^+$

1. <u>Primary disturbance:</u> H^+ loss

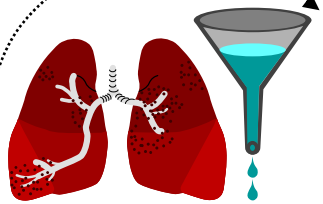
2. Dissotioation of non-bicarbonate acid in buffer reaction

$\downarrow HBuf$

$\uparrow Buf^-$



Respiratory compensation of metabolic alkalosis



2. **Regulatory response of respiration:**
Increase level of CO_2

3. Shift equilibrium in buffer system to the right

↑ CO_2

H_2O

↑ H_2CO_3

↑ HCO_3^-

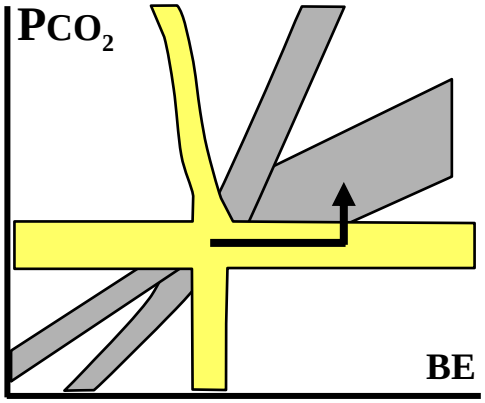
4. . **Pathophysiological concequence :**
increase diminished H^+ level

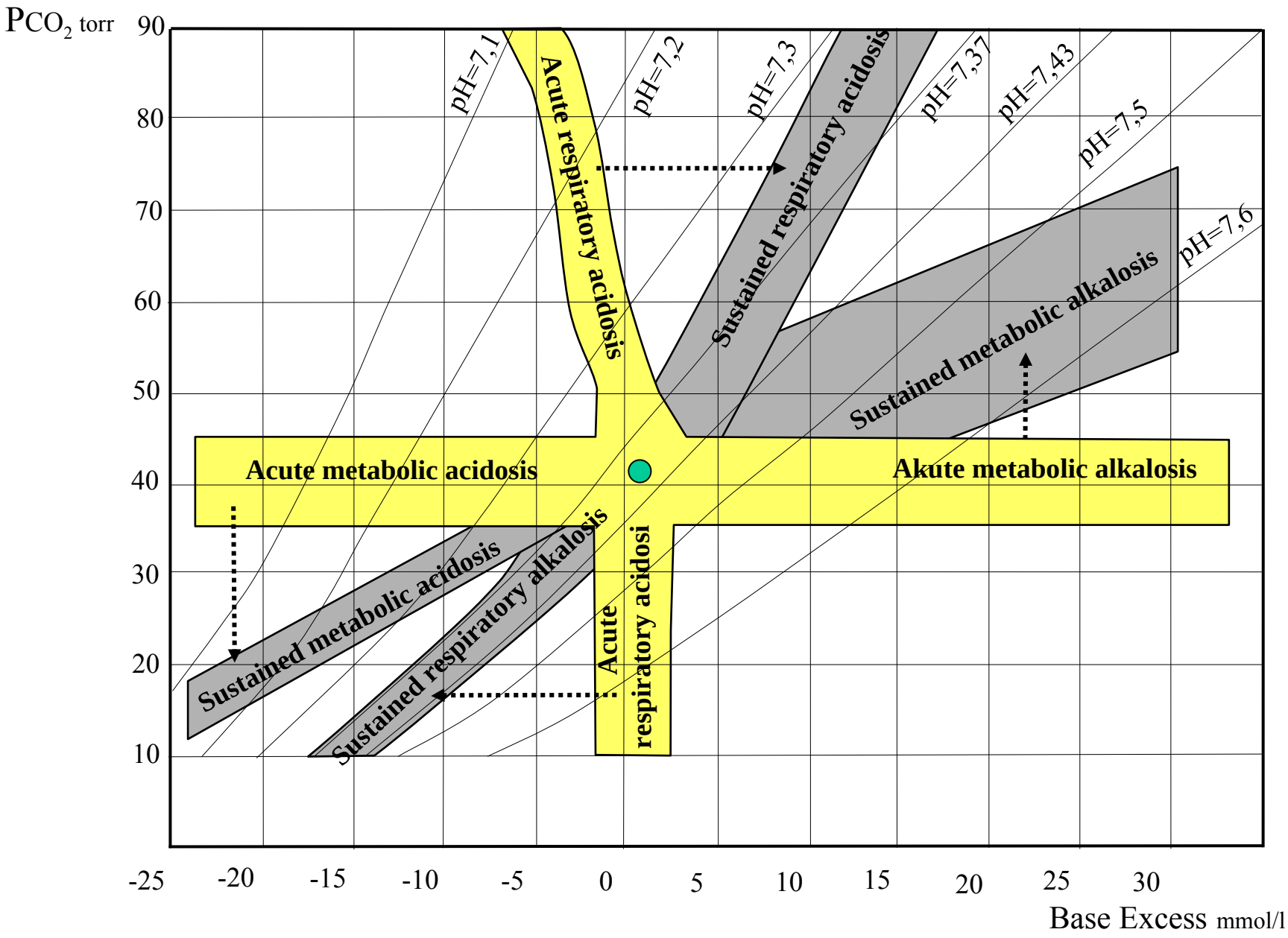
↑ H^+

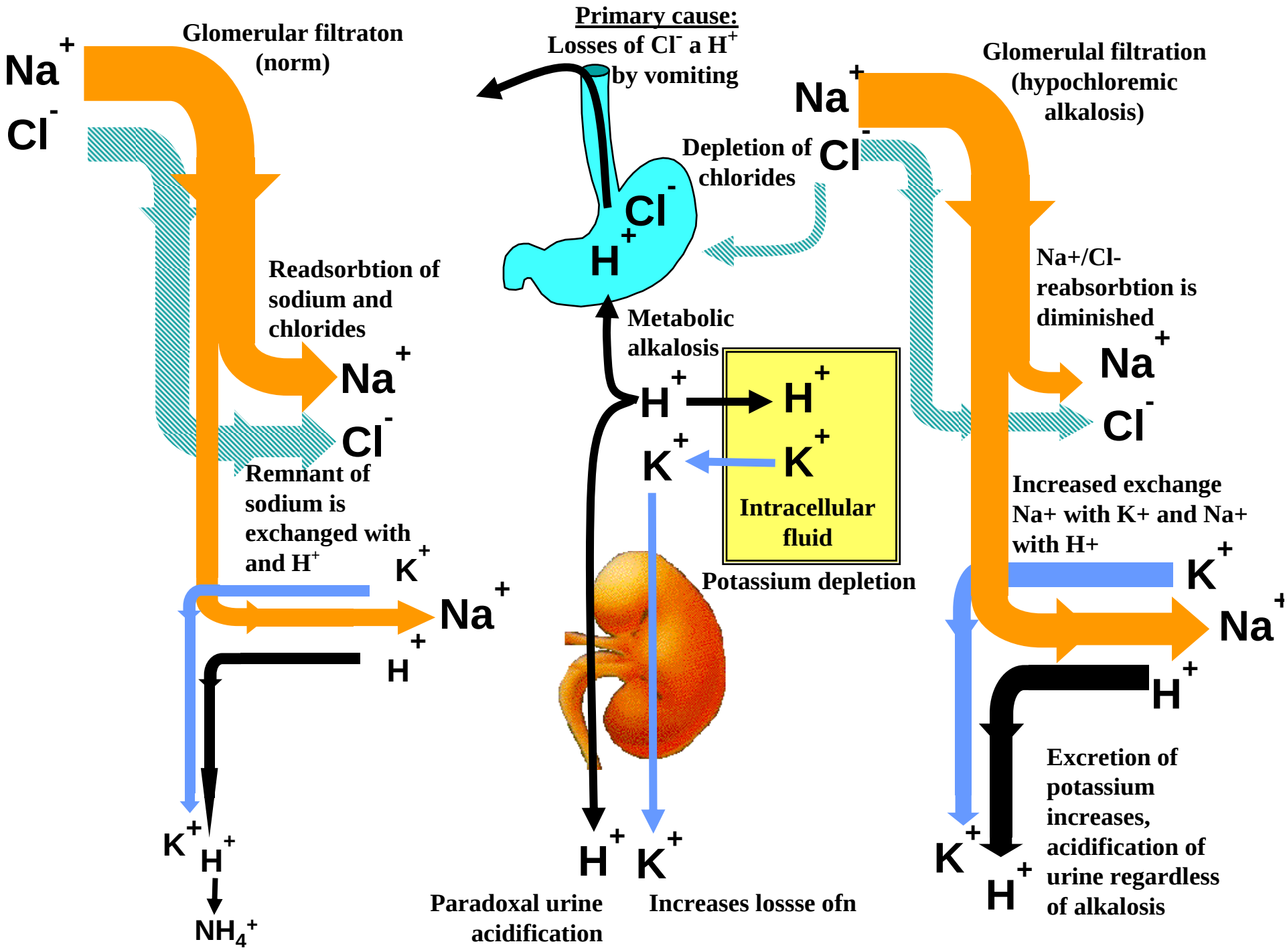
1. **Primary disturbance:**
H^+ loss

↓ Buf^-

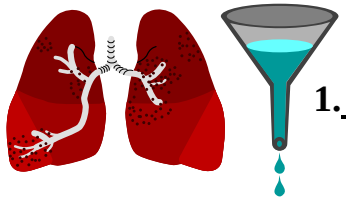
↑ HBuf




PCO2 torr
90
80
70
60
50
40
30
20
10
pH=7,1
pH=7,2
pH=7,3
pH=7,37
pH=7,43
pH=7,5
pH=7,6
Acute respiratory acidosis
Sustained respiratory acidosis
Sustained metabolic alkalosis
Acute metabolic acidosis
Akute metabolic alkalosis
Sustained metabolic acidosis
Sustained respiratory alkalosis
Acute respiratory acidosi
-25
-20
-15
-10
-5
0
5
10
15
20
25
30
Base Excess mmol/l


Glomerular filtraton (norm)
Na+
Cl-
Readsorbtion of sodium and chlorides
Na+
Cl-
Remnant of sodium is exchanged with and H+
K+
Na+
H+
K+
H+
NH4+
Primary cause:
Losses of Cl- a H+ by vomiting
Cl-
H+
Depletion of chlorides
Metabolic alkalosis
H+
K+
H+
K+
Intracellular fluid
Potassium depletion
H+
K+
Paradoxal urine acidification
Increases lossse ofn
Glomerulal filtration (hypochloremic alkalosis)
Na+
Cl-
Na+/Cl- reabsorbtion is diminished
Na+
Cl-
Increased exchange Na+ with K+ and Na+ with H+
K+
Na+
H+
K+
H+
Excretion of potassium increases, acidification of urine regardless of alkalosis

Acute respiratory acidosis



1. **Primary disturbance:**
CO_2 retention

2. Shift equilibrium to the left
- to carbonic acid dissociation

↑ CO_2

H_2O

↑ H_2CO_3

↑ HCO_3^-

3. Dissociation of carbonic acid,
creation of a huge amount of H^+ ions

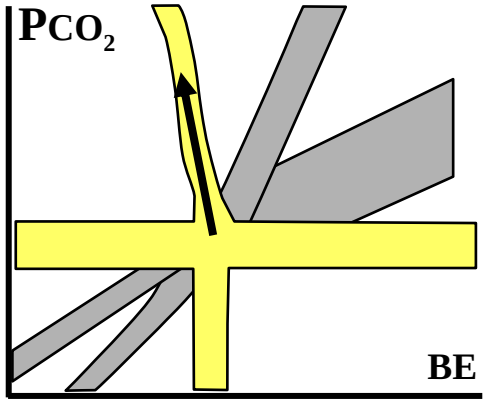
↑ H^+

4. **Pathophysiological concequence :**
H^+ level increases only a little bit due to buffer reaction

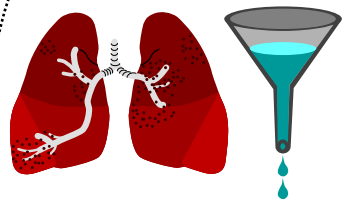
↑ HBuf

↓ Buf^-

3. H^+ ions are removed by the bounding with non-bicarbonate buffer bases

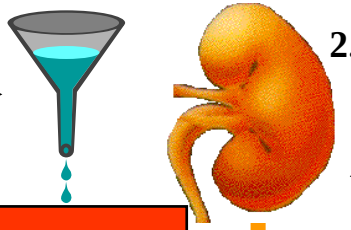


Renal compensation of respiratory acidosis



1. Primární disturbance:
CO_2 retention

(increased levels of CO_2 and H_2CO_3 are set to unchangeable values due to respiration)



2. Regulatory responce of kidney:
increasing excretion of titratable acids (TA) and ammonium ions accompanied by equimolar addition of bicarbonate ions into extracellular fluid

CO_2

H_2CO_3

$\uparrow HCO_3^-$

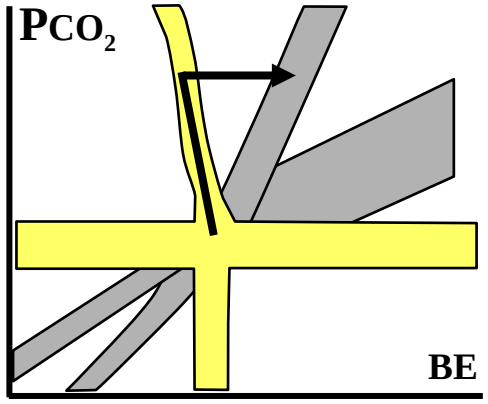
$TA+NH_4^+$

3. Addition of bicarbonates shifts equilibrium to the right, bicarbonates bind H^+ ions

H_2O

Increasing of H^+ level

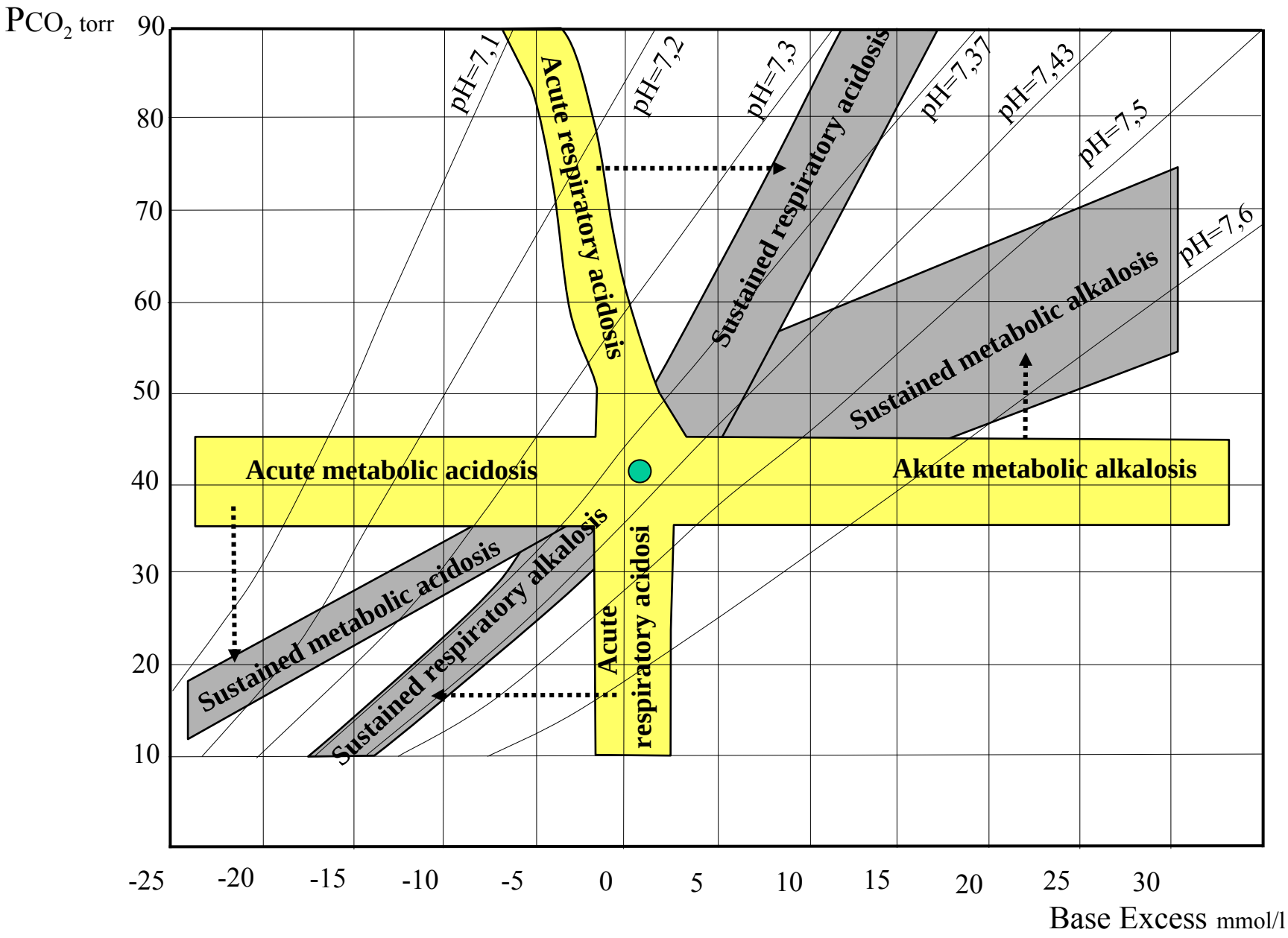
$\downarrow H^+$



4. Pathophysiological concequence :
decrease of H^+ level

$\downarrow$ HBuf

$\uparrow Buf^-$


PCO2 torr
90
80
70
60
50
40
30
20
10
pH=7,1
pH=7,2
pH=7,3
pH=7,37
pH=7,43
pH=7,5
pH=7,6
Acute respiratory acidosis
Sustained respiratory acidosis
Sustained metabolic alkalosis
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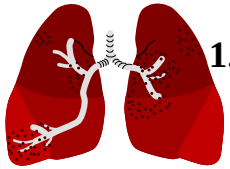
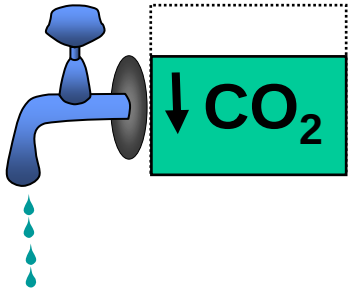
Sustained metabolic acidosis
Sustained respiratory alkalosis
Acute respiratory acidosi
-25
-20
-15
-10
-5
0
5
10
15
20
25
30
Base Excess mmol/l

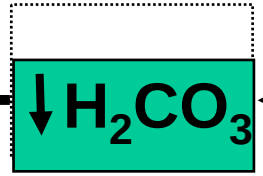
Acute respiratory alcalosis



1. Primary disturbance:
CO_2 depletion

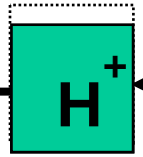
2. Shift equlibrium to the left, (to carbonic acid production)



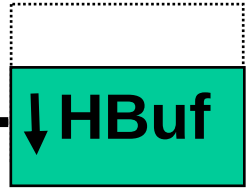


H_2O

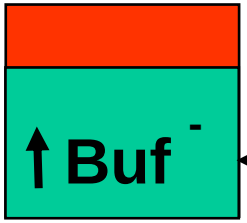
3. Due to carbonic acid production, A huge amount of H^+ ions are consumed

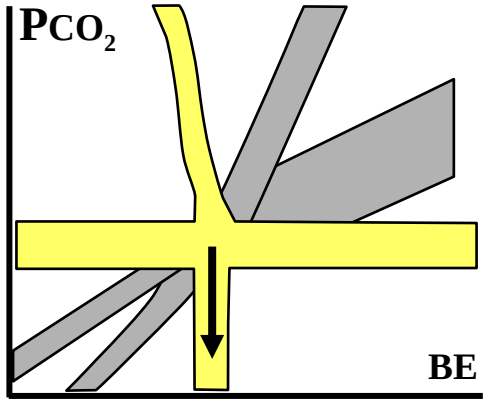


3. Consumed H^+ ions supplemented from non bicarbonate buffered acids

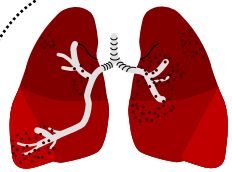


4. Pathophysiological concequence :
H^+ level due to buffering of non-bicarbonate acids decreases only a little bit.





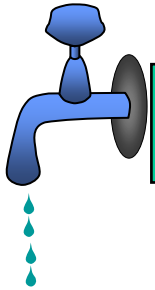
Renal compensation of respiratory alkalosis



1. Primary disturbance:
CO_2 depletion

2. Regulatory responce of kidney:
decreasing excretion of titratable acids (TA) and ammonium ions will be less then metabolic strong acids production.

(decreased levels of CO_2 and H_2CO_3 are set to unchangeable values due to respiration)



CO_2

$\downarrow HCO_3^-$

H_2CO_3

3. Metabolic H^+ ions production is greater then their renal excretion

H_2O

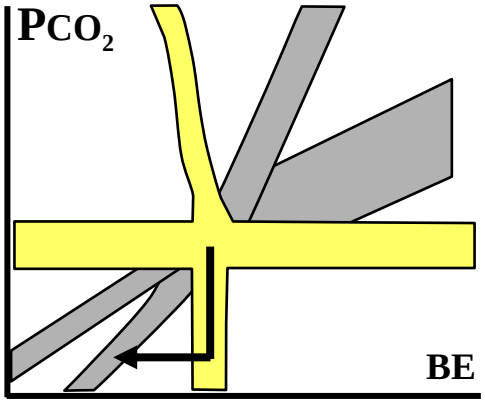
Decrease of H^+

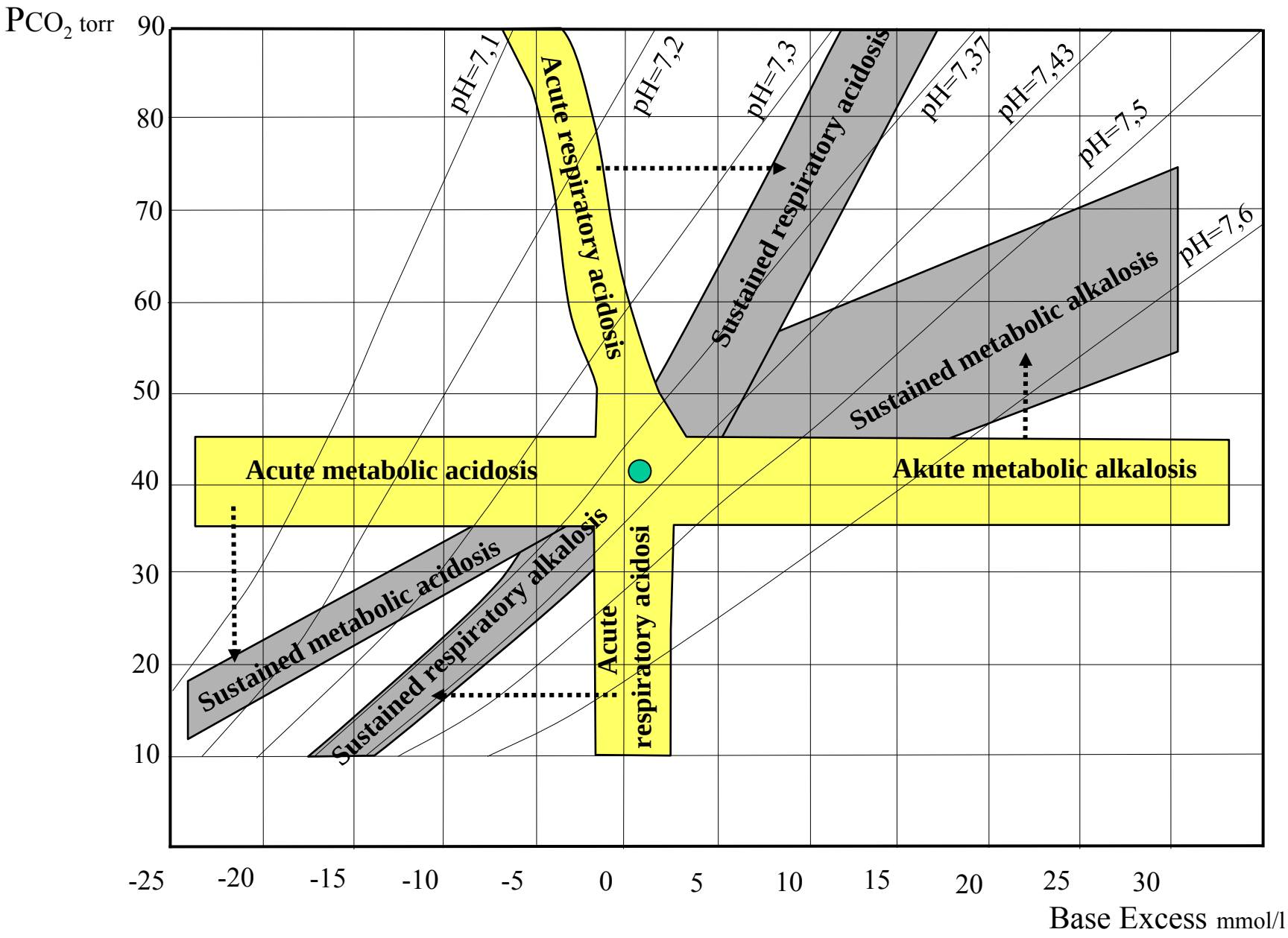
$\downarrow H^+$

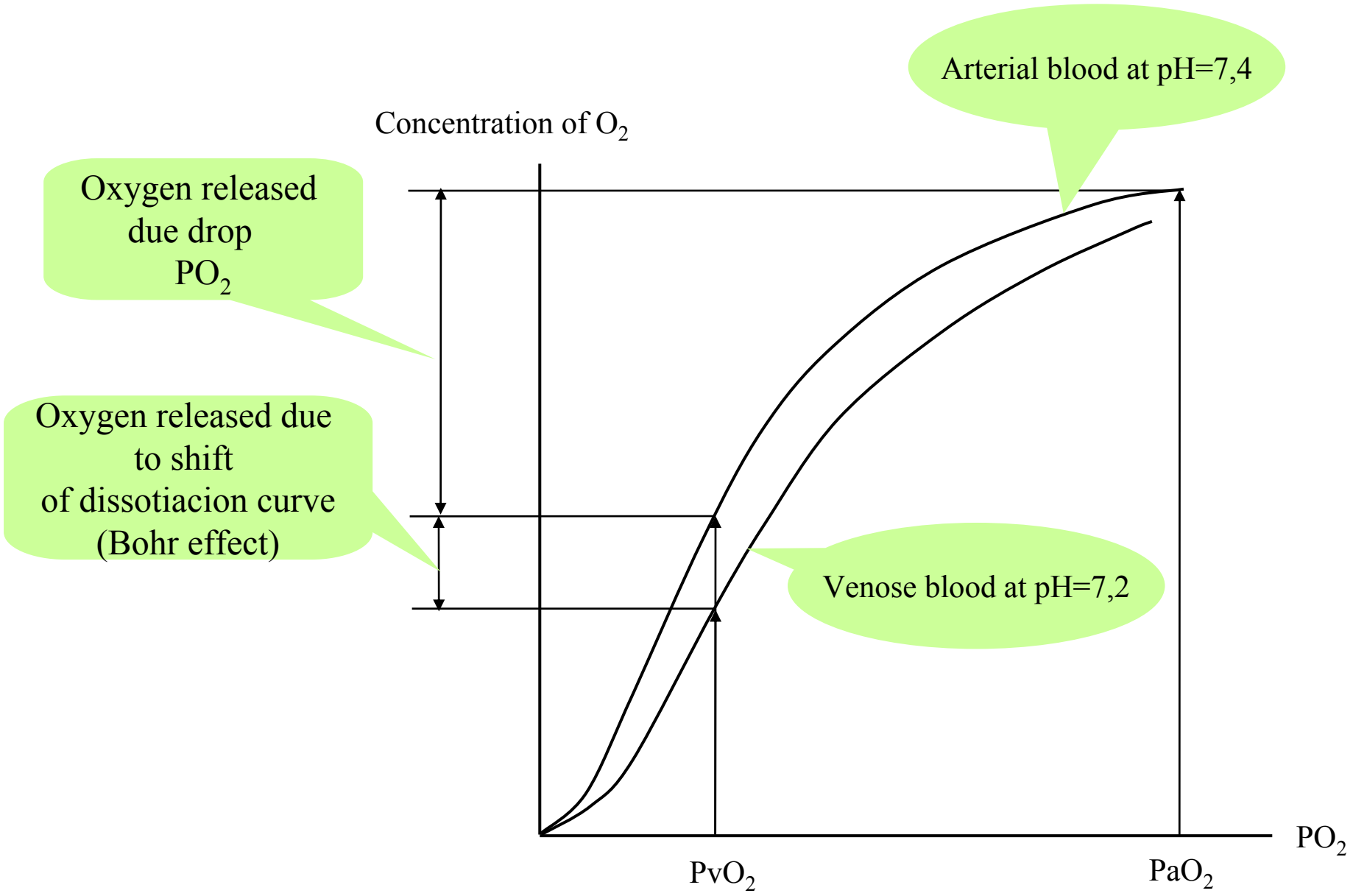
4. Pathophysiological consequence:
increase of H^+ level

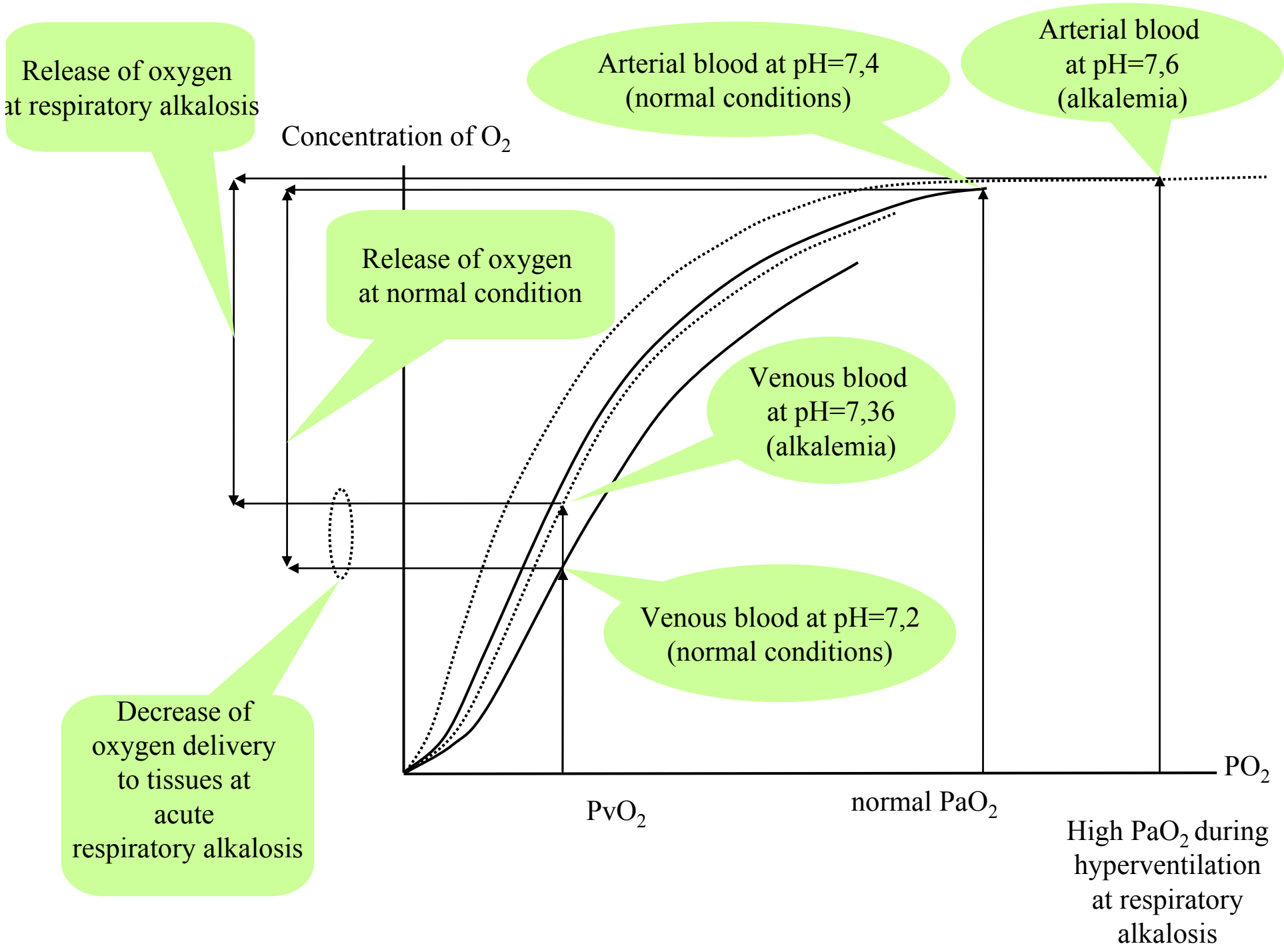
$\uparrow$HBuf

$\downarrow Buf^-$




PCO2 torr
90
80
70
60
50
40
30
20
10
pH=7,1
pH=7,2
pH=7,3
pH=7,37
pH=7,43
pH=7,5
pH=7,6
Acute respiratory acidosis
Sustained respiratory acidosis
Sustained metabolic alkalosis
Acute metabolic acidosis
Akute metabolic alkalosis
Sustained metabolic acidosis
Sustained respiratory alkalosis
Acute respiratory acidosi
-25
-20
-15
-10
-5
0
5
10
15
20
25
30
Base Excess mmol/l


Arterial blood at pH=7,4
Concentration of O_2
Oxygen released due drop PO_2
Oxygen released due to shift of dissotiacion curve (Bohr effect)
Venose blood at pH=7,2
PO_2
PvO_2
PaO_2


Release of oxygen
at respiratory alkalosis
Concentration of O_2
Arterial blood at pH=7,4
(normal conditions)
Arterial blood
at pH=7,6
(alkalemia)
Release of oxygen
at normal condition
Venous blood
at pH=7,36
(alkalemia)
Venous blood at pH=7,2
(normal conditions)
Decrease of
oxygen delivery
to tissues at
acute
respiratory alkalosis
PO_2
PvO_2
normal PaO_2
High PaO_2 during
hyperventilation
at respiratory
alkalosis

Mixed acid-base disturbances - examples