Urinary system lecture 3

Process of urine Formation

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lecture 10

Factors affecting GFR

1- Glomerular Capillary Pressure:

The ↑ in *glomerular capillary pressure* → ↑ **GFR** and vice versa.

This pressure could be affected by the following:

***a*- Renal Blood Flow:** ↑**RBF** → ↑*glom. blood flow* → ↑*glom. cap. Pr.* → ↑**GFR** and *vice versa*.

***b*- Diameter of Afferent arteriole:**

- Dilatation → ↑ *glom. blood flow* → ↑ *glom. cap. Pr.* → ↑ **GFR**.
- Constriction has a reverse effect.

***c*- Diameter of Efferent arteriole:**

- Dilatation → ↓ *gl. cap. Pr* → ↓ **GFR**.
- Mild constriction → ↑ *glom. cap. Pr.* → slight ↑ in **GFR**.
- Moderate & sever constriction → ↓ **GFR** due to marked ↓ in *glom. blood flow*.

d- Sympathetic stimulation: → constriction of *afferent arteriole* → ↓*glo.cap.pr* → ↓ ***GFR***.

e- Arterial Blood Pressure (ABP) :

Change in **ABP** within physiological range (80 – 180 *mmHg*) has a little effect on renal blood flow or **GFR** due to ***autoregulation*** mechanism [mechanism by which **RBF** & **GFR** are maintained at a nearly constant rate inspite of changes in **ABP** within physiological range].

2- *Osmotic Pressure of Proteins in Bowman's Capsule:*

When ↑ → ↑ ***GFR*** and vice versa.

3- *Osmotic Pressure of Plasma Proteins:*

↓ ***Plasma Osmotic Pressure*** (as in ***Hypoproteinemia***) → ↑ **GFR** and vice versa.

4- *Hydrostatic pressure in Bowman's Capsule:*

↑ ***Intra-capsular Pressure*** as seen in obstructed ureter (e.g. due to stone) → ↓ **GFR**.

5- *Filtration Coefficient:*

It depends on:
- glomerular membrane surface area.
- glomerular membrane permeability.

The ↓ K_f (due to ↓ *permeability* or *surface area*) → ↓ **GFR**, and vice versa.

Effect of Changes in Starling Forces on Renal Plasma Flow, Glomerular Filtration Rate, and the Filtration Fraction

Effect	RPF	GFR	Filtration Fraction (GFR/RPF)
Constriction of afferent arteriole	↓	↓	N.C.
Constriction of efferent arteriole	↓	↑	↑
Increased plasma protein concentration	N.C.	↓	↓
Decreased plasma protein concentration	N.C.	↑	↑
Constriction of the ureter	N.C.	↓	↓

GFR, Glomerular filtration rate; *N.C.*, no change; *RPF*, renal plasma flow.

Starling forces

- **Starling forces** or Hydrostatic forces that control fluid transport between interstitium and peritubular capillaries they are the driving forces that act across the Peritubular capillaries and control fluid transport between interstitium and peritubular capillaries.

- **It is determined by 4 forces:**

1) Forces that favor absorption:

a) Colloid osmotic pressure in the peritubular capillaries

b) Hydrostatic pressure of the interstitial fluid

2) Forces that oppose absorption:

a) Colloid osmotic pressure of the interstitial fluid (normally = Zero).

b) Hydrostatic pressure in the peritubular capillaries

- Forces that help the filtration:

    1- Glomerular capillary hydrostatic pressure [60 mmHg].

    2- Osmotic pressure in Bowman's capsule [normally = zero].

- Forces that oppose the filtration:

    1- Osmotic pressure of Pl.Pr in the glomerular capillary [32 mmHg].

    2- Pressure in Bowman's capsule [18 mmHg].

Mechanism of urine formation:-

The urine is formed by 3 main processes:-

1_glomerular filtration: -

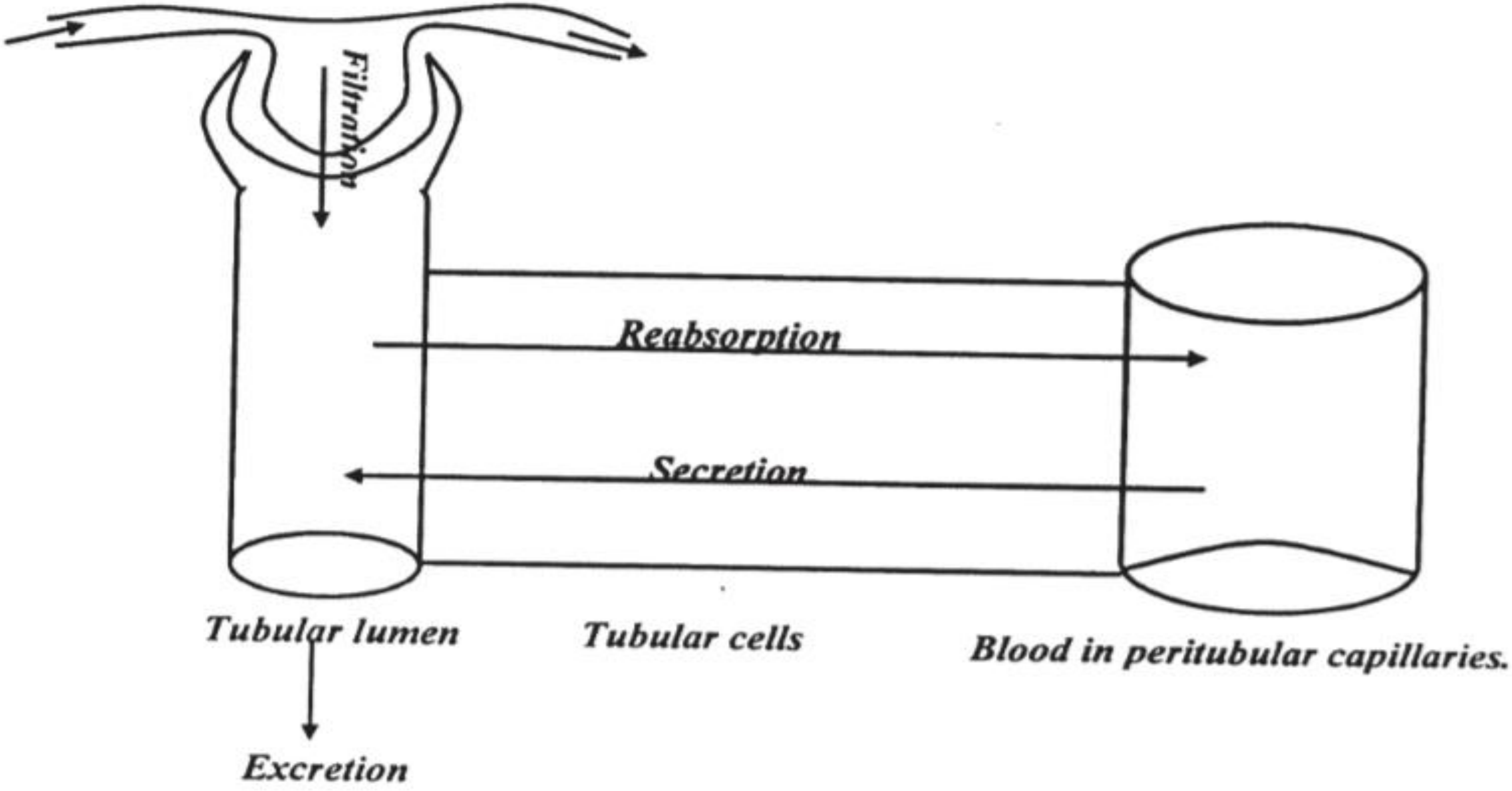
It is the filtration of fluid through the glomerular membrane into the Bowman's capsule. Usually 1/5 of the plasma flowing in the glomeruli filters.

2-Tubular reabsorption: -

It is the transport of substances from the tubular lumen to blood. The wanted substances, especially almost all of the water and many of the electrolytes are reabsorbed.

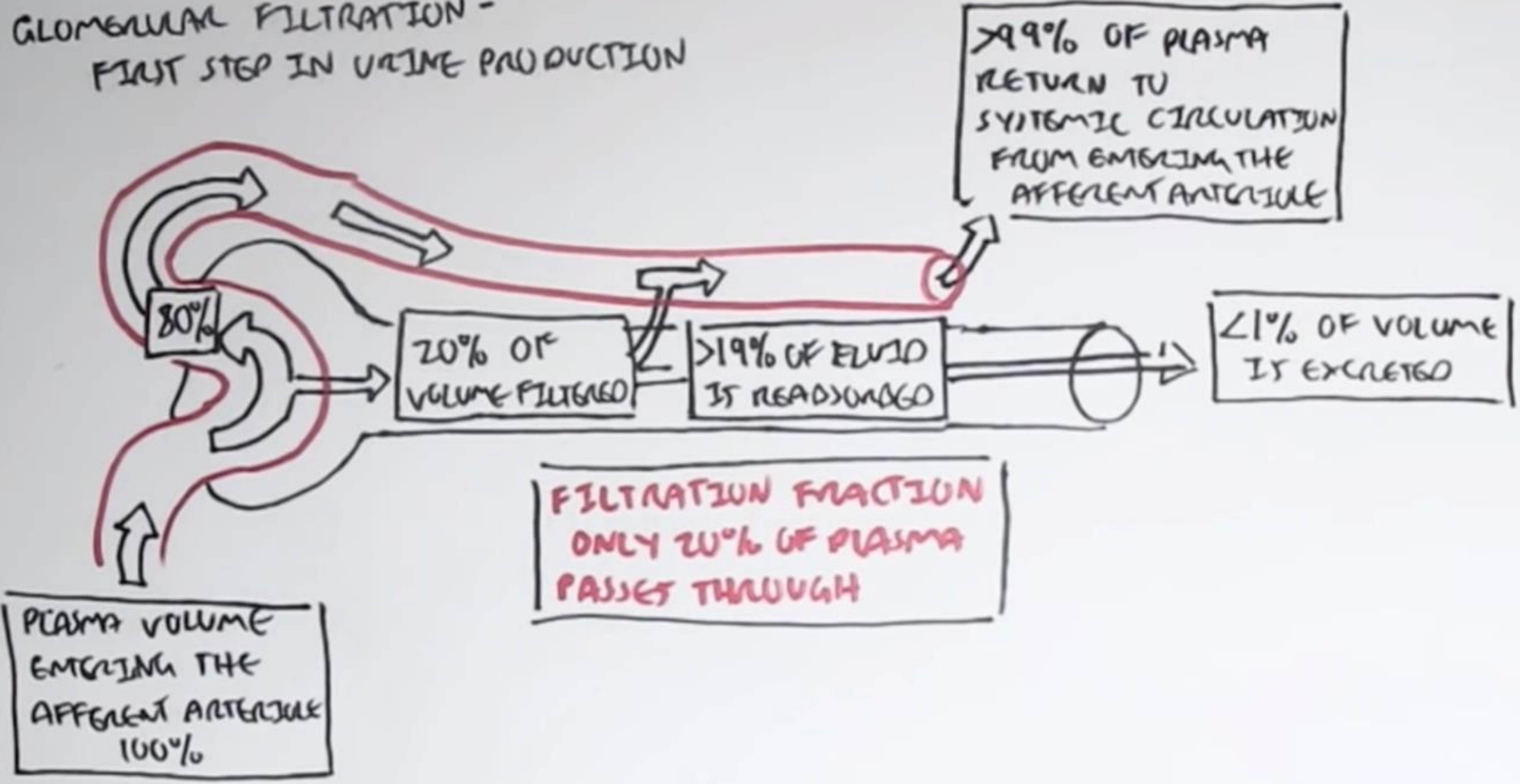
3_Tubular secretion: -

It is the transport of substances from the blood to the tubular lumen.



Note:- Excretion means substances that come out with the final urine

GLOMERULAR FILTRATION - FIRST STEP IN URINE PRODUCTION



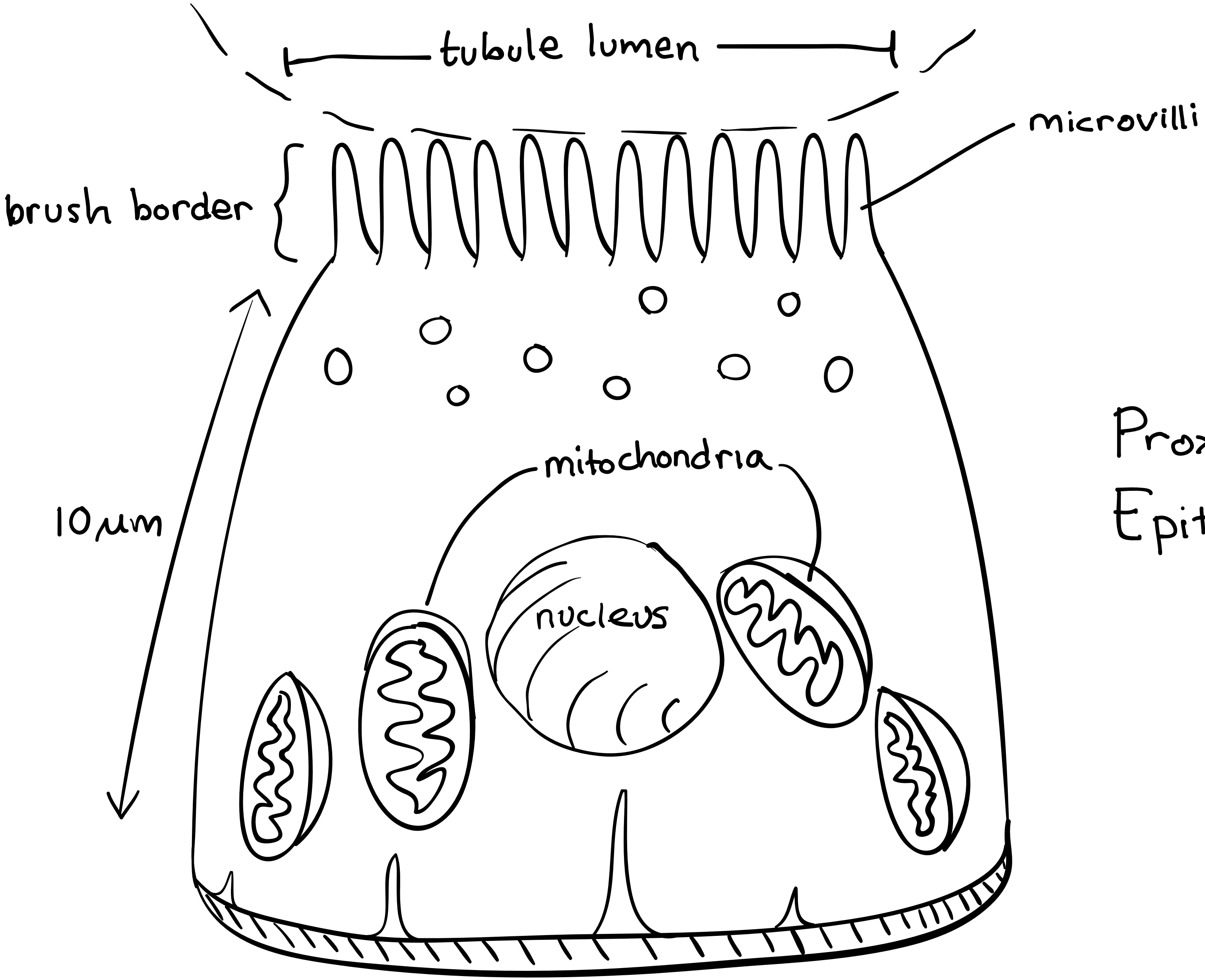
- The fluid that filters through the glomerulus and Bowman's capsule (glomerular filtrate) is very similar to blood plasma without the proteins, and at this point not at all like urine. If this filtrate flowed straight to your bladder and then out your body, you would lose more than 10-times the entire volume of your extracellular body fluids (plasma and interstitial fluid) every day. Fortunately, tubular reabsorption mechanisms in the nephrons of your kidneys return the water and solutes that you need back into your extracellular fluid and circulatory system. In addition to reabsorbing the substances that you need, your nephrons are able to secrete unwanted substances from your bloodstream into the filtrate. Together these processes complete the transformation of the glomerular filtrate into urine.

- Tubular reabsorption is the process that moves solutes and water out of the filtrate and back into your bloodstream. This process is known as reabsorption, because this is the second time they have been absorbed; the first time being when they were absorbed into the bloodstream from the digestive tract after a meal.

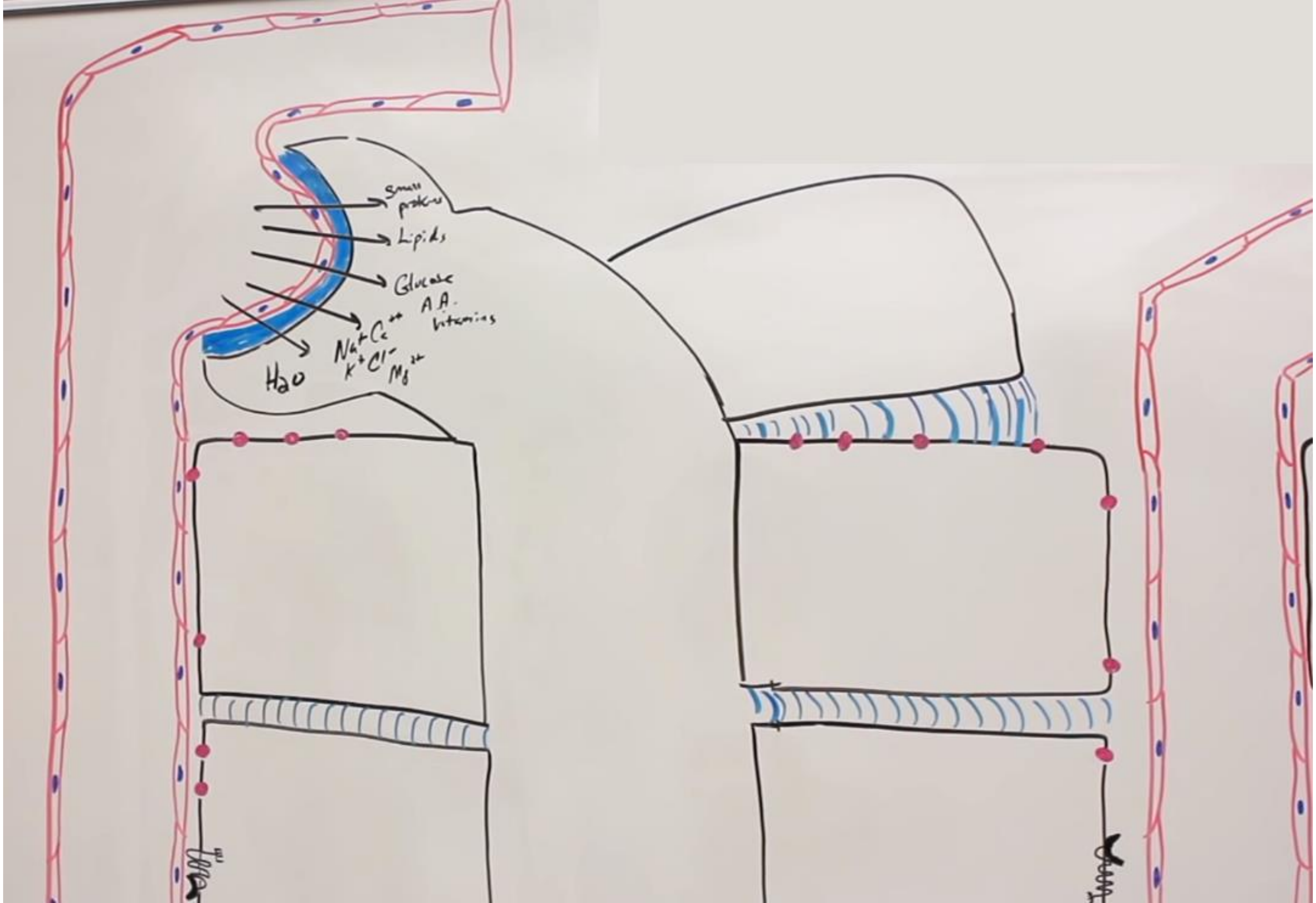
Reabsorption is a two-step process:

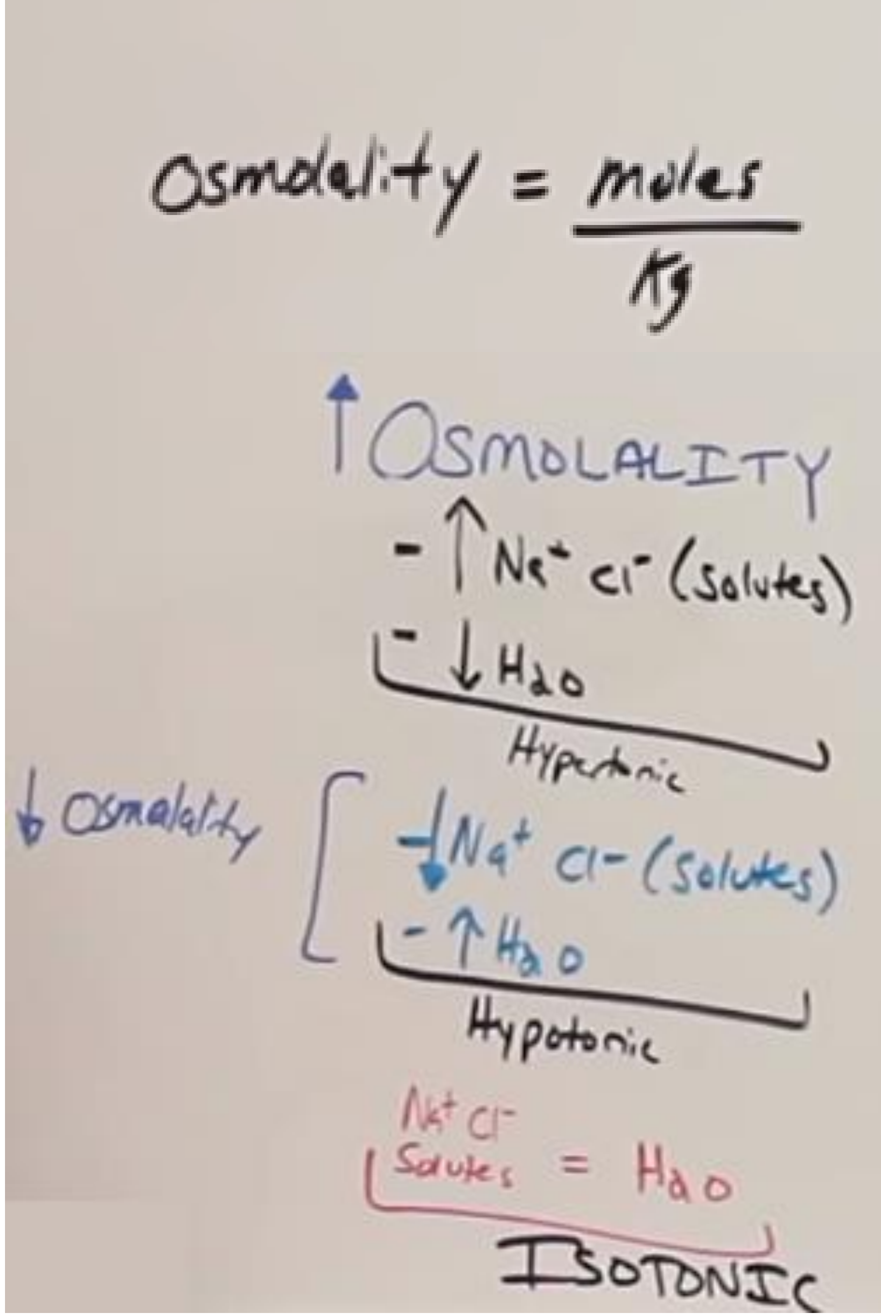
1) The first step is the passive or active movement of water and dissolved substances from the fluid inside the tubule through the tubule wall into the space outside.
2) The second step is for water and these substances to move through the capillary walls back into your bloodstream, again, either by passive or active transport.

- Nephrons are comprised of different segments that perform specific functions. The walls of the nephron are made of a single layer of cube-like cells, called cuboidal epithelial cells, and their ultrastructure changes depending on the function of the segment they are in. For example, the surface of the cells facing the lumen of the proximal convoluted tubule are covered in microvilli (tiny finger-like structures). This type of surface is called a brush border. The brush border and the extensive length of the proximal tubule dramatically increase the surface area available for reabsorption of substances into the blood enabling around 80% of the glomerular filtrate to be reabsorbed in this segment. Another notable feature of these cells is that they are densely packed with mitochondria (the cell’s energy generators). The mitochondria ensure a good supply of energy is available to fuel the active transport systems needed for efficient reabsorption.



Proximal Tubule Epithelial Cell

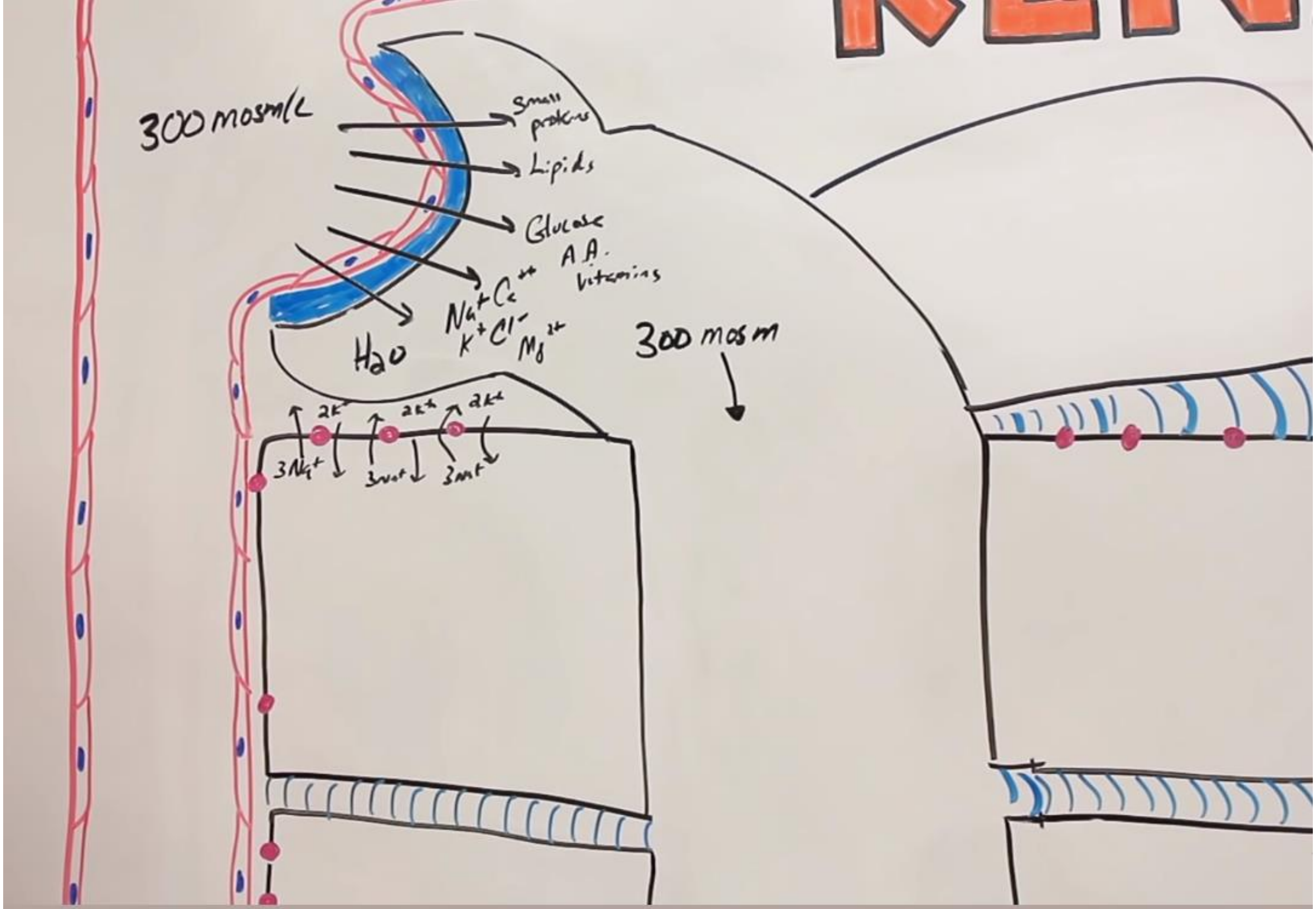

Small proteins
Lipids
Glucose
A.A.
Vitamins
Na+ Ca++
K+ Cl-
Mg++
H2O



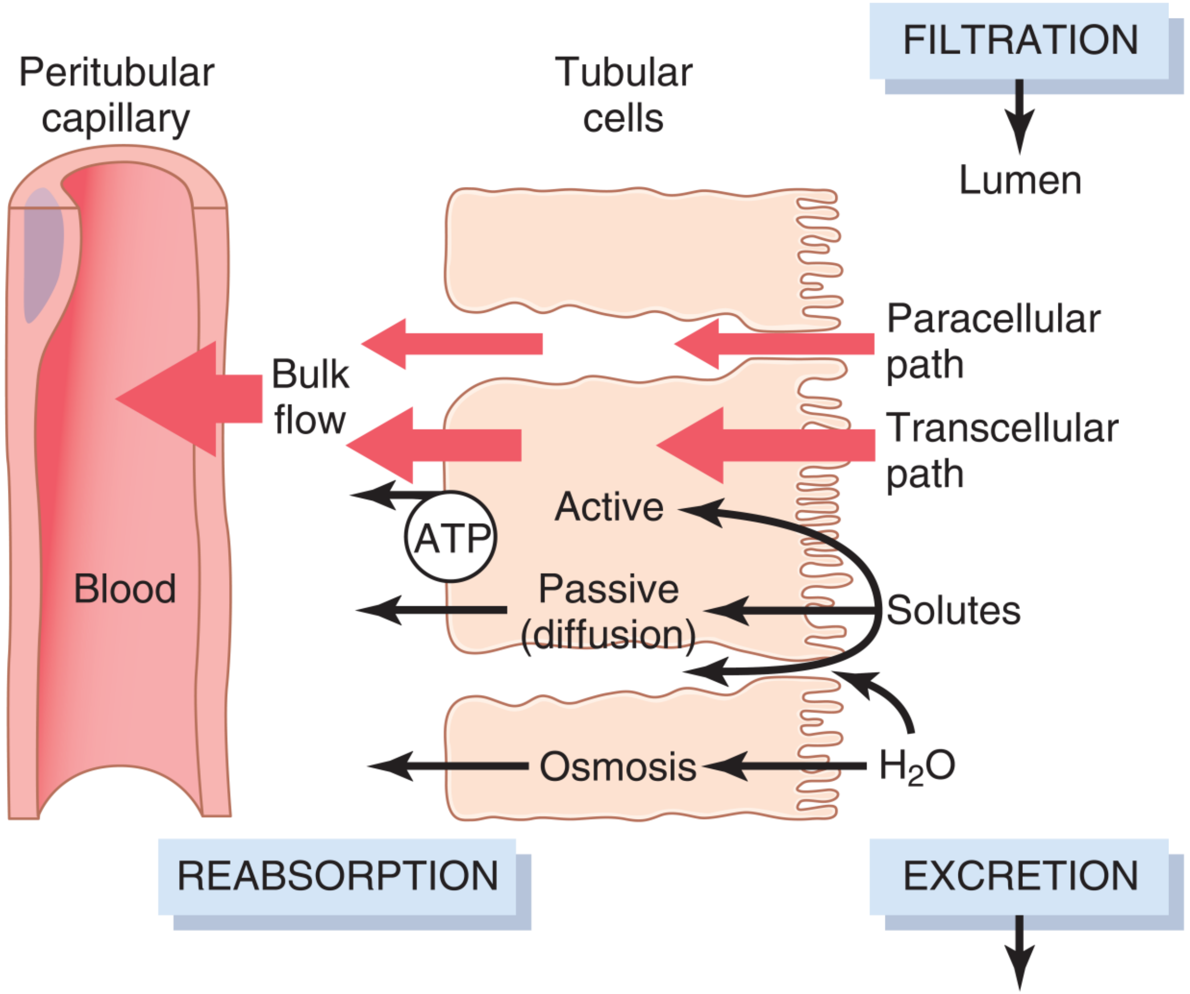
Osmolality is defined as the concentration of all solutes in a given weight of water and is expressed as units of either osmolality (milliosmoles of solute per kilogram of water, mOsm/kg H2O) or osmolarity (milliosmoles of solute per liter of water, mOsm/L H2O).

Osmolality & Osmolarity

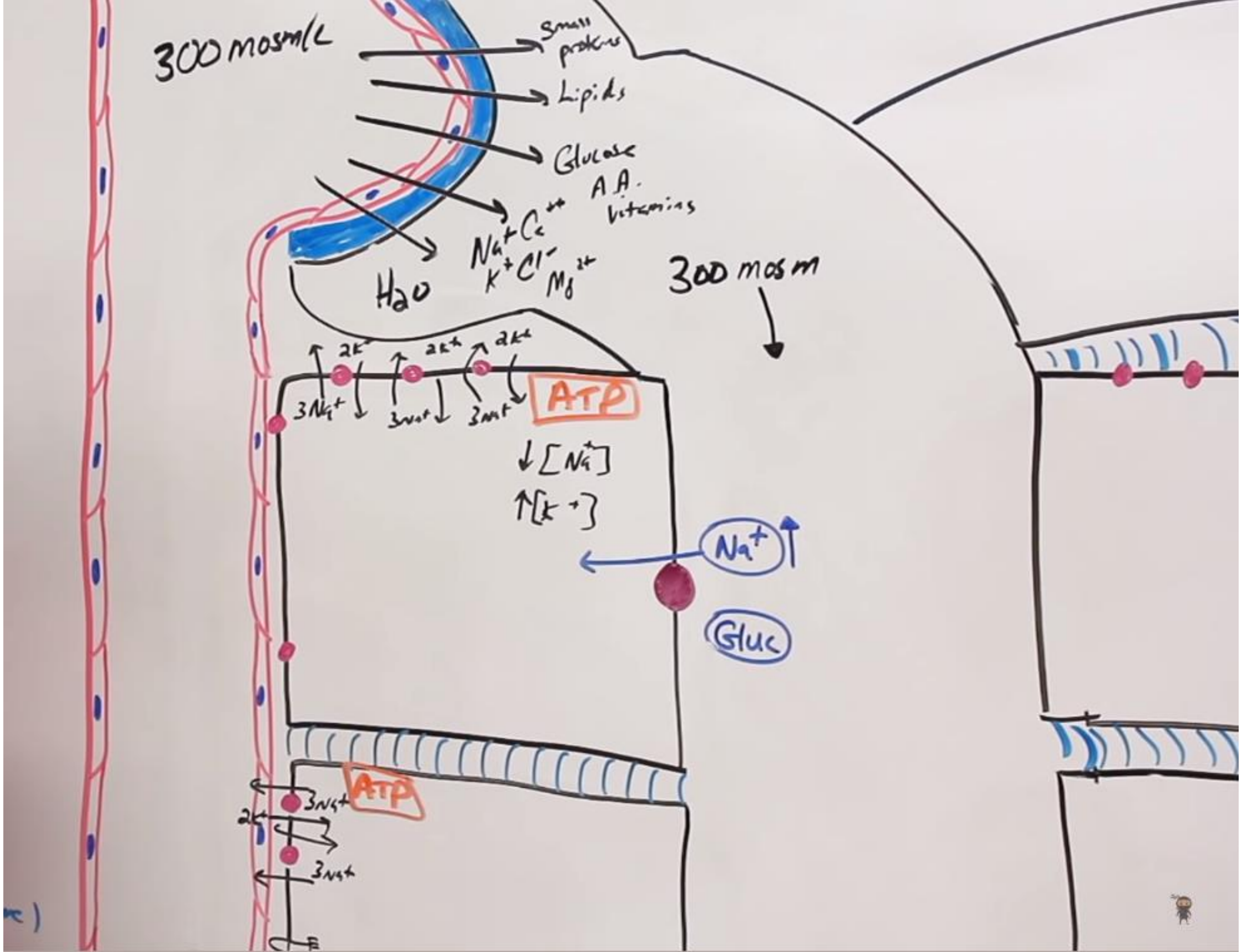
- Osmolality: Osmolality is a measure of the number of solute particles present in solution
- Is independent of the size or weight of the particles
- Expressed as : milliosmoles per kilogram of water (m Osmol/Kg)
- Osmolality of a solution is the number of osmoles of solute per kilogram of solvent (m Osmol/Kg)
- Osmolarity of a solution is the number of osmoles of solute per liter of solution (m Osmol/L)

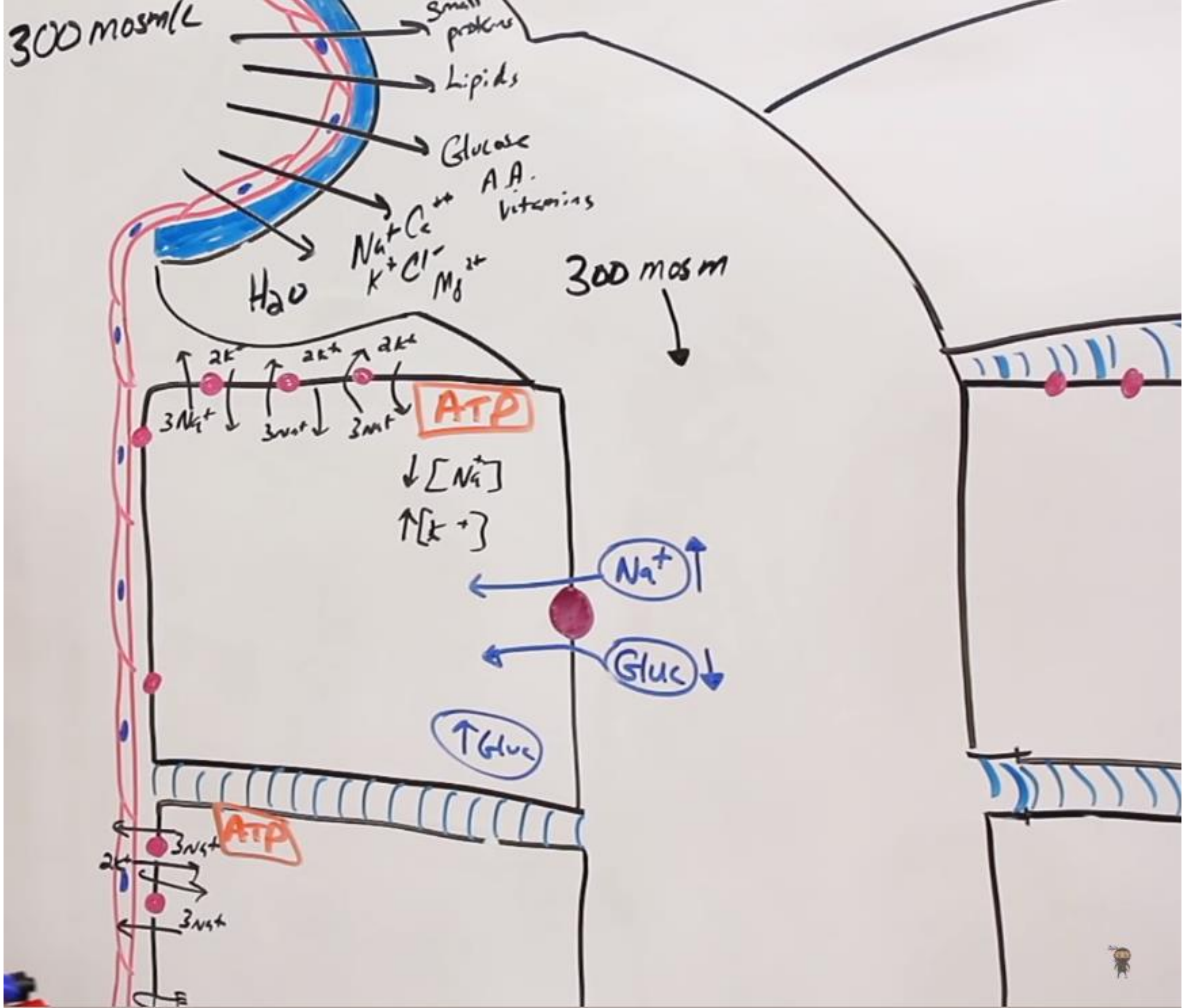


300 mosm/L
Small proteins
Lipids
Glucose
A.A.
Vitamins
Na+ Ca++
K+ Cl-
Mg2+
H2O
300 mosm
2K+
3Na+

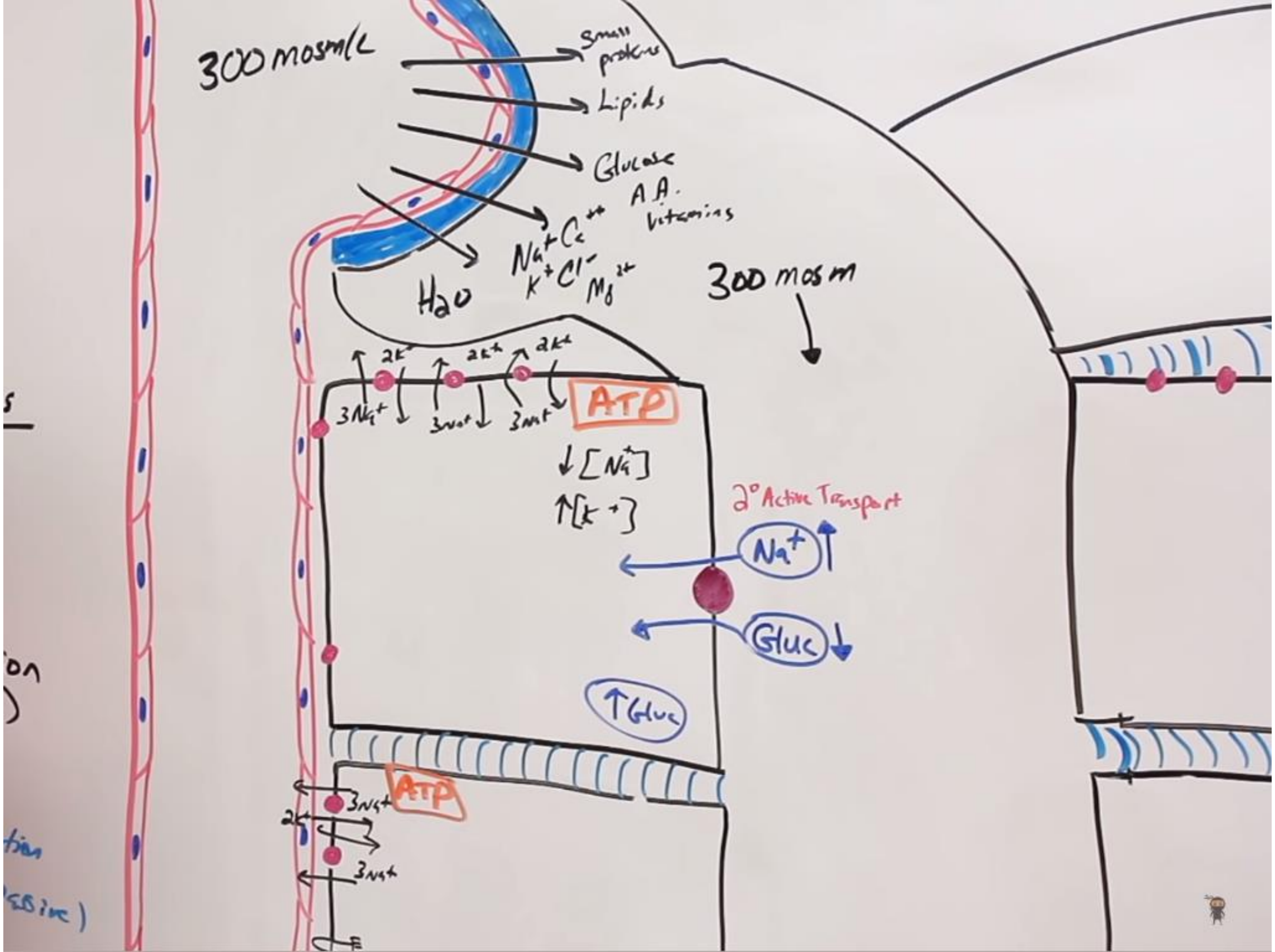


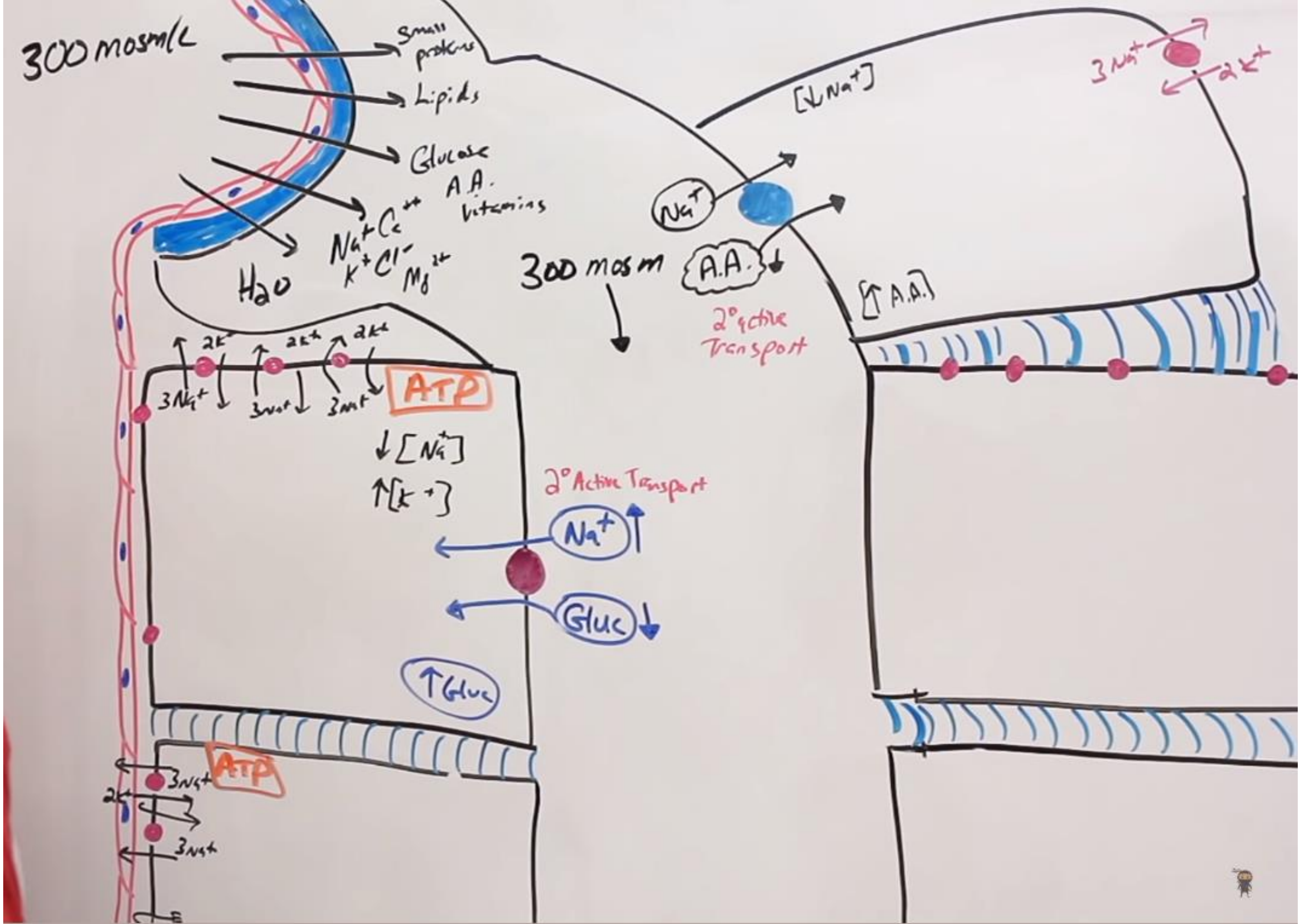
Reabsorption of filtered water and solutes from the tubular lumen across the tubular epithelial cells, through the renal interstitium, and back into the blood. Solutes are transported through the cells (*transcellular path)* by passive diffusion or active transport, or between the cells (*paracellular path*) by diffusion. Water is transported through the cells and between the tubular cells by osmosis. Transport of water and solutes from the interstitial fluid into the peritubular capillaries occurs by *bulk flow* .


300 mosm/L
Small proteins
Lipids
Glucose
A.A.
Vitamins
Na+ Ca2+
K+ Cl-
Mg2+
H2O
300 mosm
2K+
3Na+
ATP
↓[Na+]
↑[K+]
Na+
Gluc

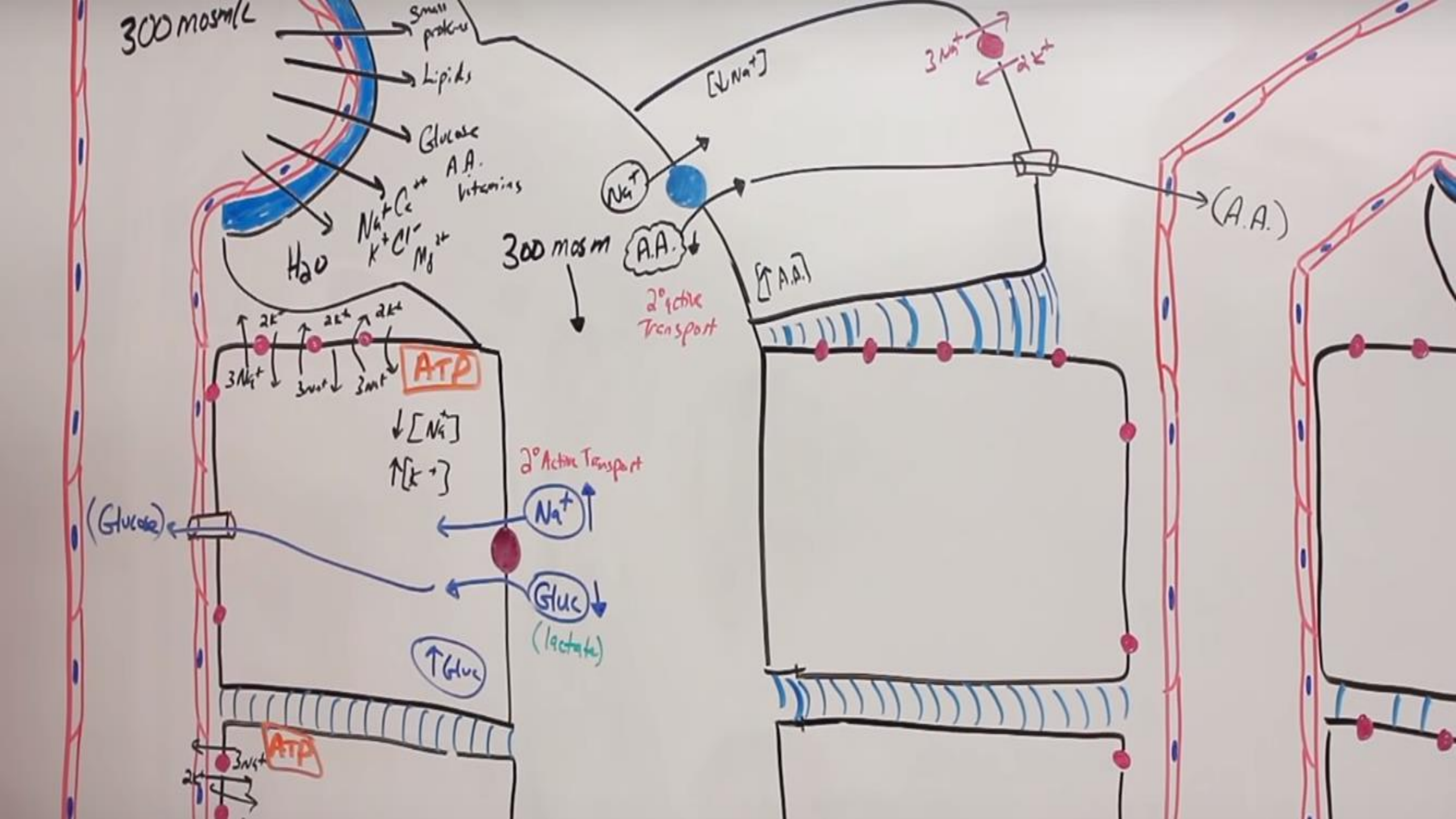


300 mosm/L
Small proteins
Lipids
Glucose
A.A.
Vitamins
Na+ Ca++
K+ Cl-
Mg2+
H2O
300 mosm
2K+
3Na+
ATP
↓[Na+]
↑[K+]
Na+
Gluc
↑Gluc

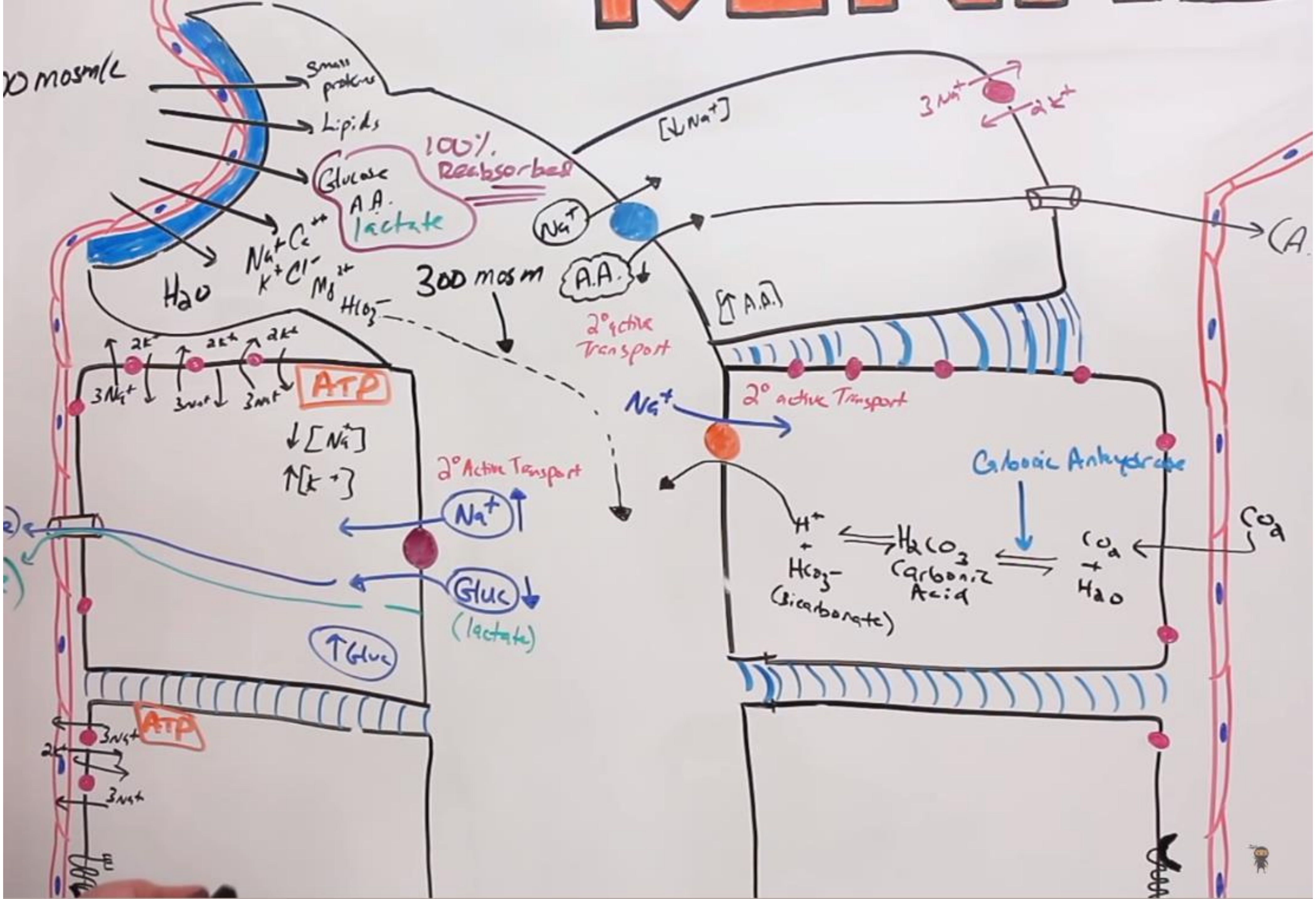

300 mosm/L
Small proteins
Lipids
Glucose
A.A.
Vitamins
Na+ Ca++
K+ Cl-
Mg2+
H2O
300 mosm
2K+
3Na+
ATP
↓[Na+]
↑[K+]
2° Active Transport
Na+
Gluc
↑Gluc



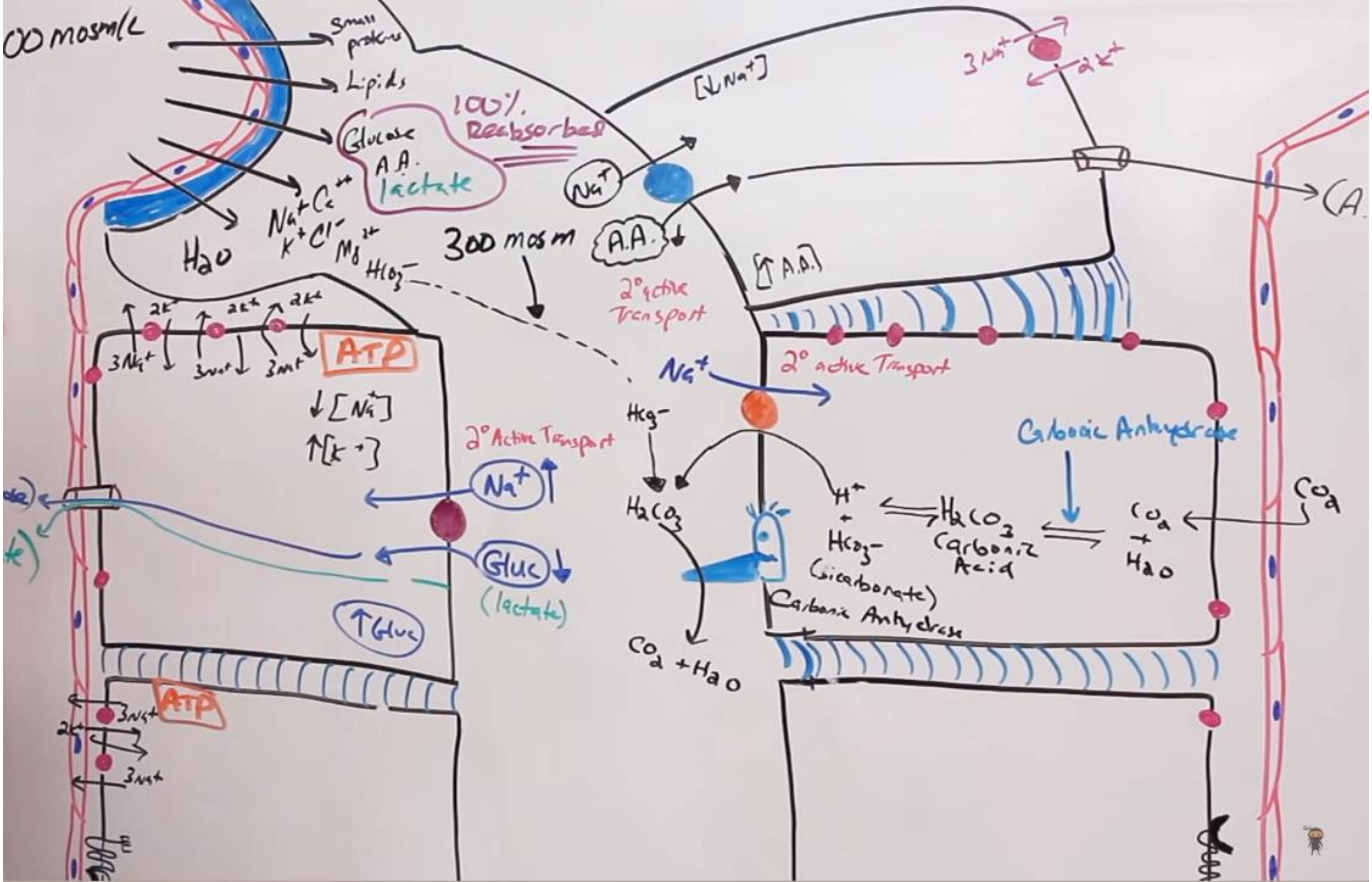
300 mosm/L
Small proteins
Lipids
Glucose
A.A.
Vitamins
Na^+ Ca^{++}
K^+ Cl^-
Mg^{2+}
H_2O
300 mosm
Na^+
A.A.
2° active Transport
[↓Na^+]
[↑A.A.]
$3Na^+$
$2K^+$
ATP
↓[Na^+]
↑[K^+]
2° Active Transport
Gluc
↑Gluc



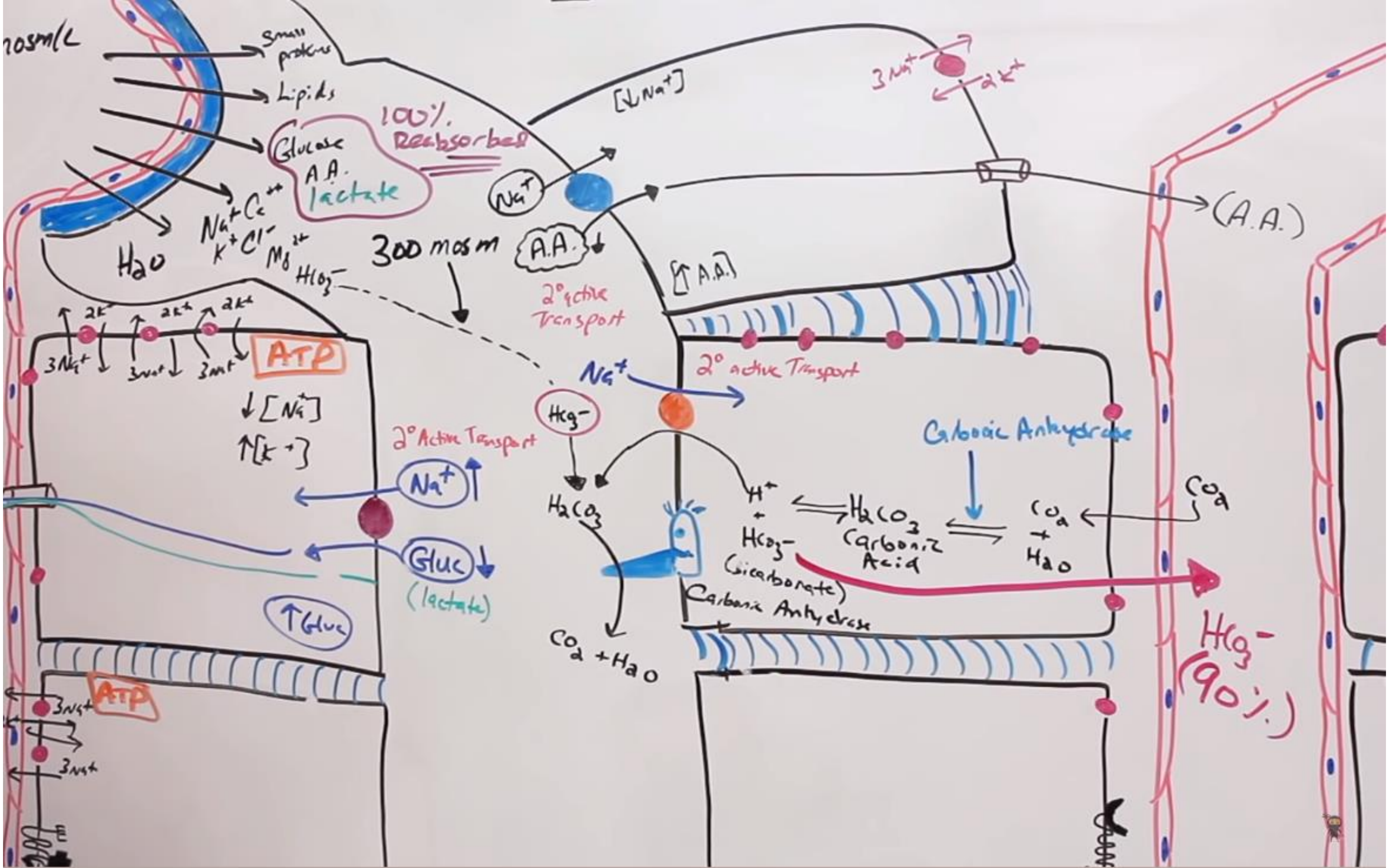
300 mosm/L
Small proteins
Lipids
Glucose
A.A.
Vitamins
Na^+ Ca^{++}
K^+ Cl^-
Mg^{2+}
H_2O
300 mosm
[↓Na+]
3Na+
2K+
Na+
A.A.
[↑A.A.]
2° Active Transport
(A.A.)
2K+
3Na+
ATP
↓[Na+]
↑[K+]
2° Active Transport
Na+
Gluc
(lactate)
(Glucose)
↑Gluc
ATP
3Na+
2K+



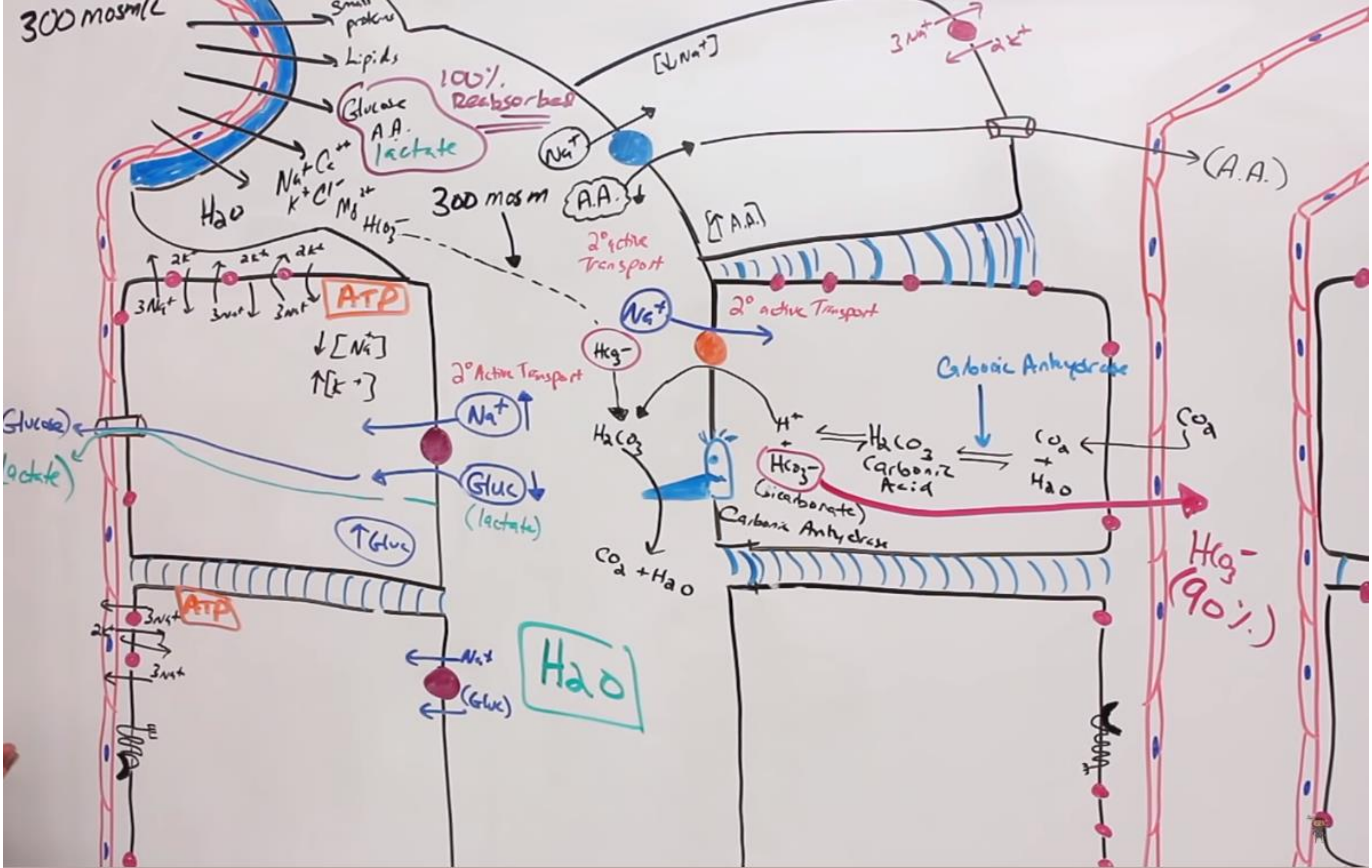
Small proteins
Lipids
Glucose
A.A.
lactate
100% Reabsorbed
Na^+ Ca^{++}
K^+ Cl^-
Mg^{2+}
HCO_3^-
H_2O
300 mosm
[↓Na^+]
$3Na^+$
$2K^+$
Na^+
A.A.
[↑A.A.]
2° active Transport
2° active Transport
ATP
↓[Na^+]
↑[K^+]
2° Active Transport
Na^+
Gluc
(lactate)
↑Gluc
Carbonic Anhydrase
H^+ + HCO_3^- (Bicarbonate)
H_2CO_3 Carbonic Acid
CO_2 + H_2O
CO_2

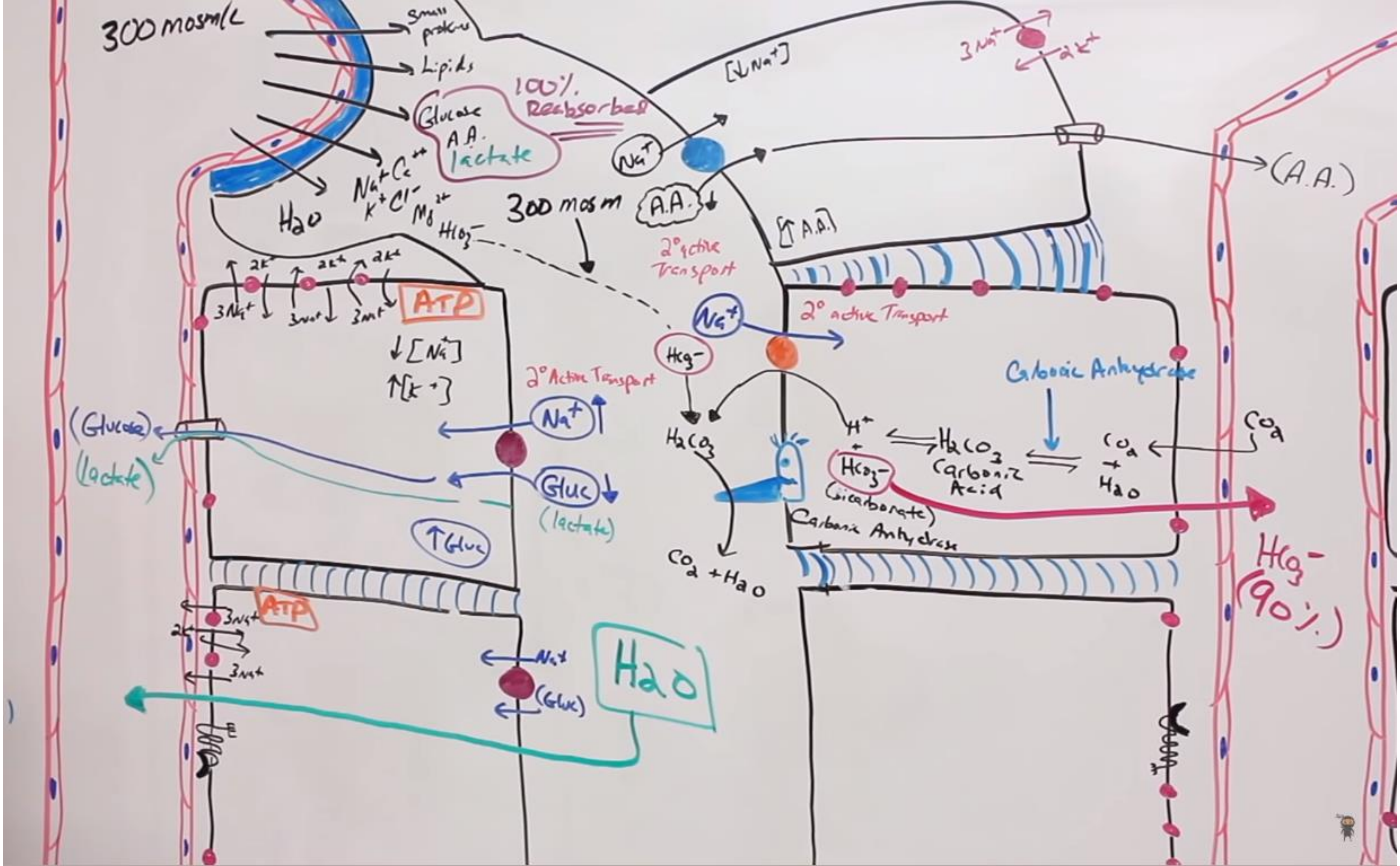


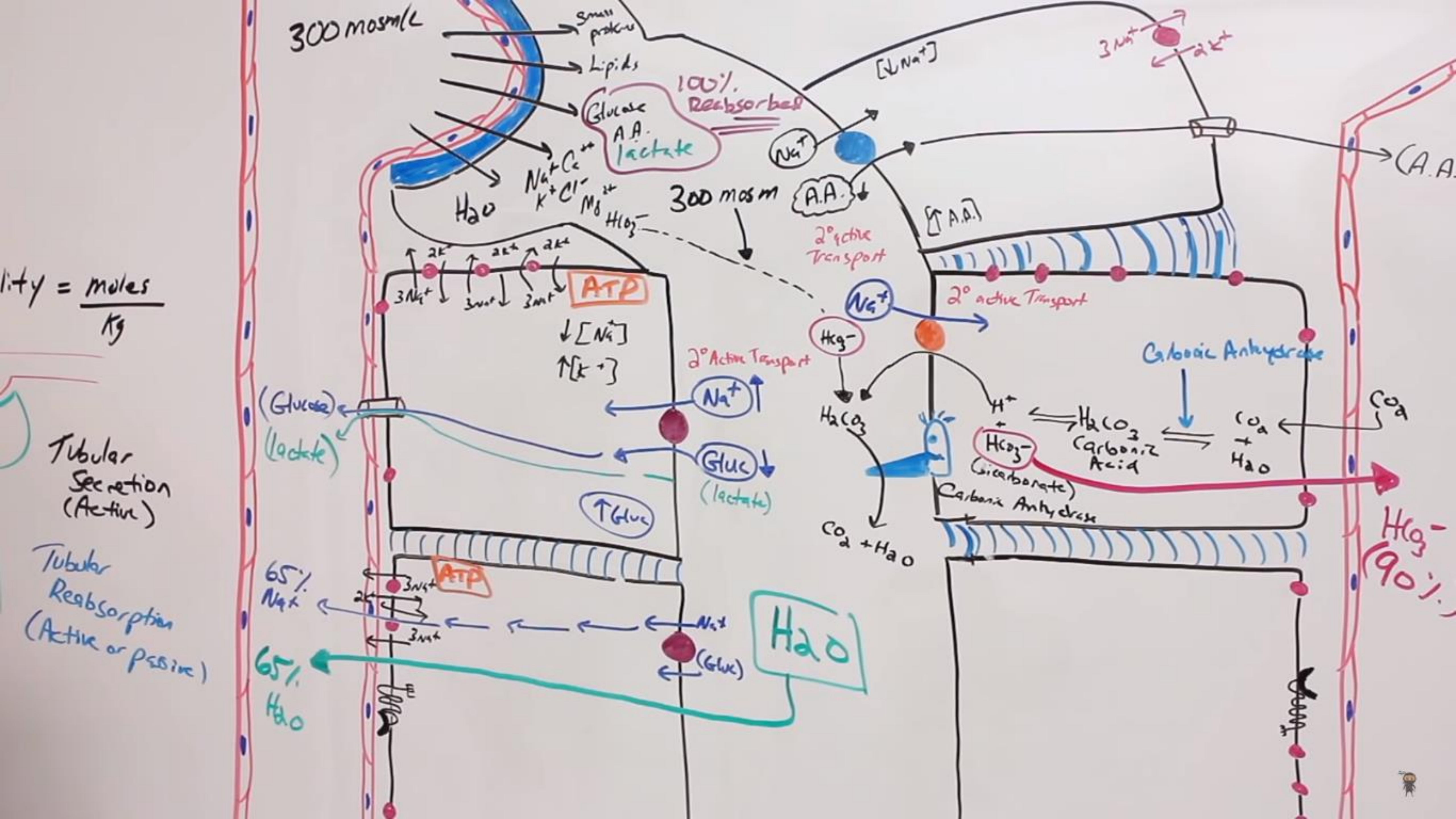
00 mosm/L
Small proteins
Lipids
Glucose
A.A.
lactate
100% Reabsorbed
Na+ Ca2+
K+ Cl-
Mg2+
HCO3-
H2O
300 mosm
[↓Na+]
3Na+
2K+
Na+
A.A.
[↑A.A.]
2° active Transport
2° active Transport
Na+
2K+
3Na+
ATP
↓[Na+]
↑[K+]
2° Active Transport
Na+
Gluc
(lactate)
↑Gluc
HCO3-
H2CO3
CO2 + H2O
H+ + HCO3- (bicarbonate)
H2CO3 Carbonic Acid
Carbonic Anhydrase
CO2 + H2O
CO2
Carbonic Anhydrase
ATP
3Na+
2K+
3Na+

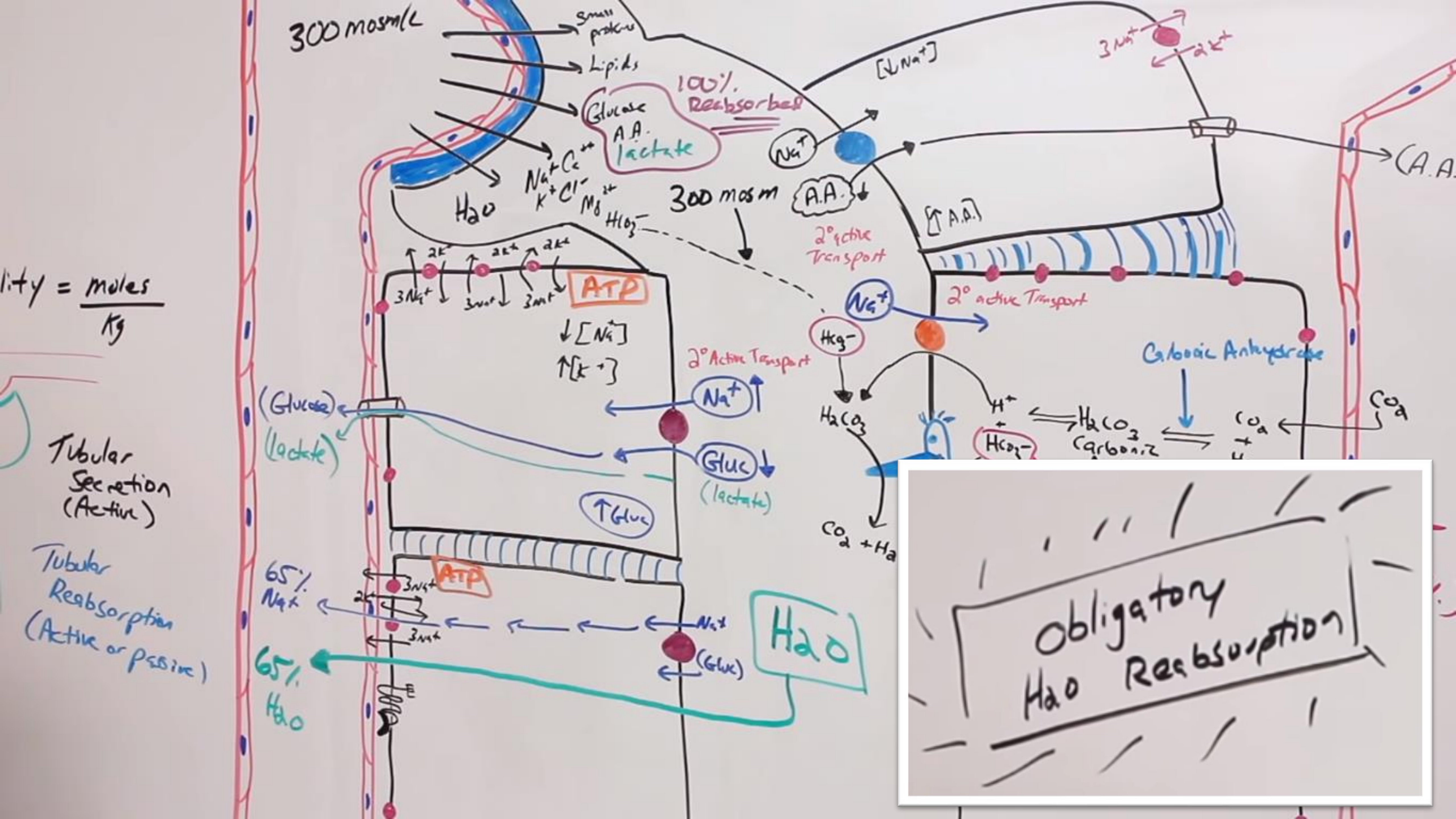


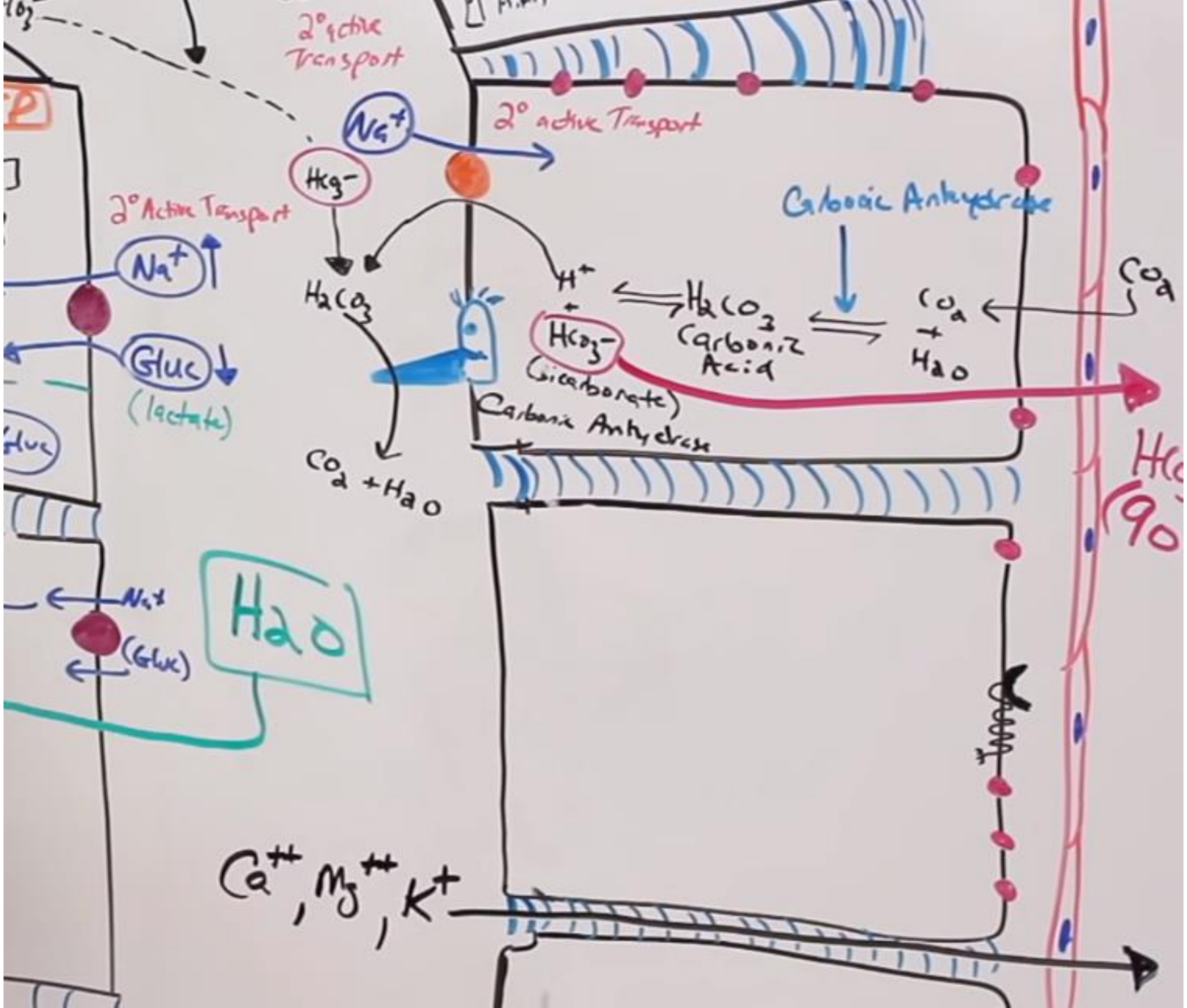
Small proteins
Lipids
Glucose
A.A.
lactate
100% Reabsorbed
Na^+ Ca^{++}
K^+ Cl^-
Mg^{2+}
HCO_3^-
H_2O
300 mosm
[↓Na+]
3Na+
2K+
Na+
A.A.
[↑A.A.]
2° active Transport
(A.A.)
ATP
↓[Na+]
↑[K+]
2° Active Transport
Na+
Gluc
(lactate)
↑Gluc
2° active Transport
Na+
HCO_3^-
H_2CO_3
$CO_2 + H_2O$
$H^+ + HCO_3^-$
Bicarbonate
H_2CO_3
Carbonic Acid
Carbonic Anhydrase
$CO_2 + H_2O$
CO_2
Carbonic Anhydrase
HCO_3^- (90%)


300 mosm/L
Small proteins
Lipids
Glucose
A.A.
lactate
100% Reabsorbed
Na+ Ca++
K+ Cl-
Mg2+
HCO3-
H2O
300 mosm
[↓Na+]
3 Na+
2 K+
Na+
A.A.
(A.A.)
[↑A.A.]
2° active Transport
ATP
↓[Na+]
↑[K+]
2° Active Transport
Na+
Gluc
(lactate)
(Glucose)
(lactate)
↑Gluc
HCO3-
H2CO3
CO2 + H2O
H+
H2CO3
Carbonic Acid
Carbonic Anhydrase
CO2
H2O
HCO3-
(Bicarbonate)
Carbonic Anhydrase
HCO3- (90%)
H2O
Na+
(Gluc)

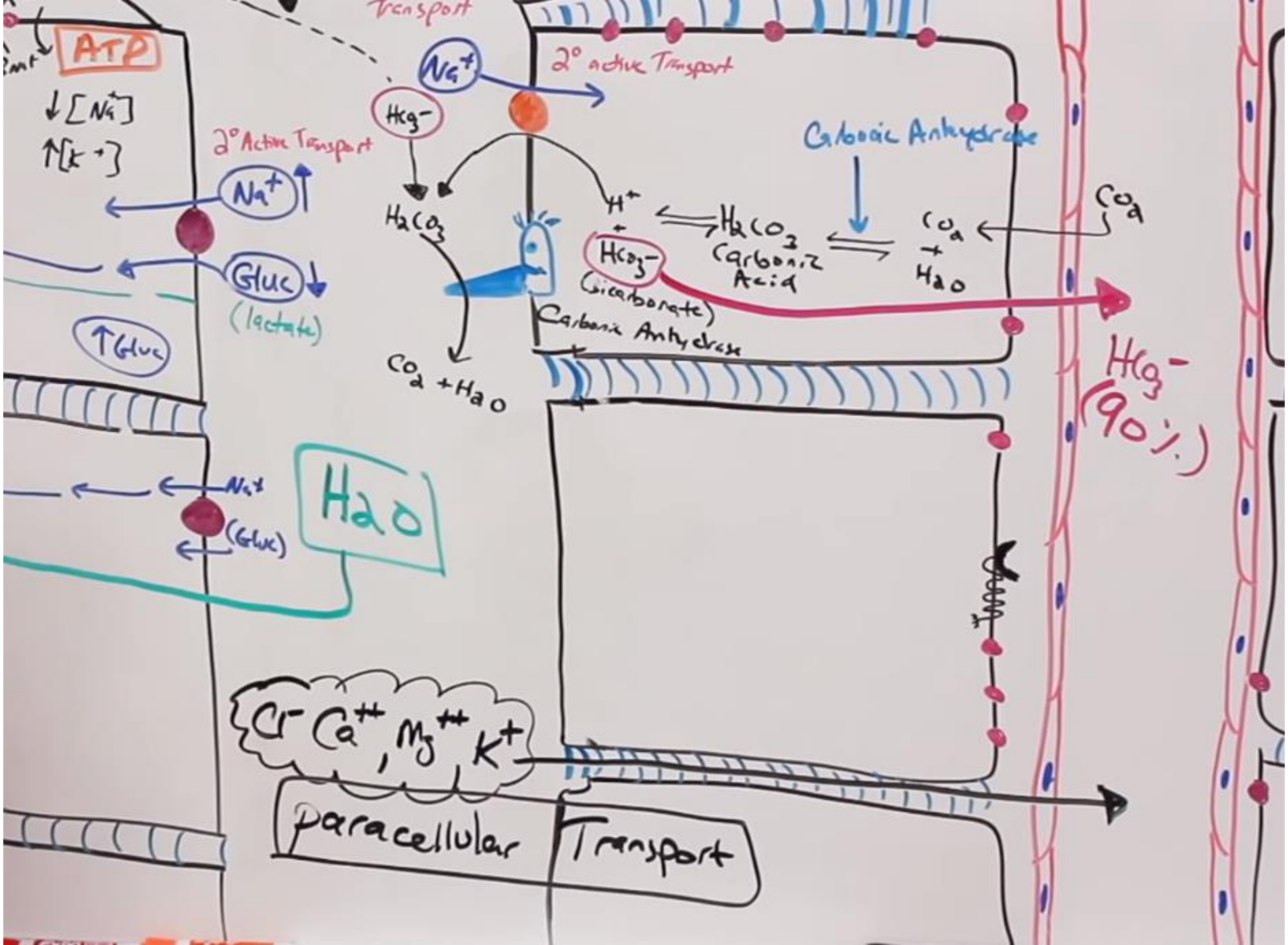

300 mosm/L
Lipids
Glucose
A.A.
lactate
100% Reabsorbed
H2O
300 mosm
Na+
A.A.
[↓Na+]
3Na+
2K+
(A.A.)
[↑A.A.]
2° active Transport
ATP
↓[Na+]
↑[K+]
2° Active Transport
(Glucose)
(lactate)
Gluc
(lactate)
↑Gluc
H2O
2° active Transport
H2CO3
CO2 + H2O
H+
H2CO3
Carbonic Acid
Carbonic Anhydrase
CO2
H2O
(Bicarbonate)
Carbonic Anhydrase
(90%)

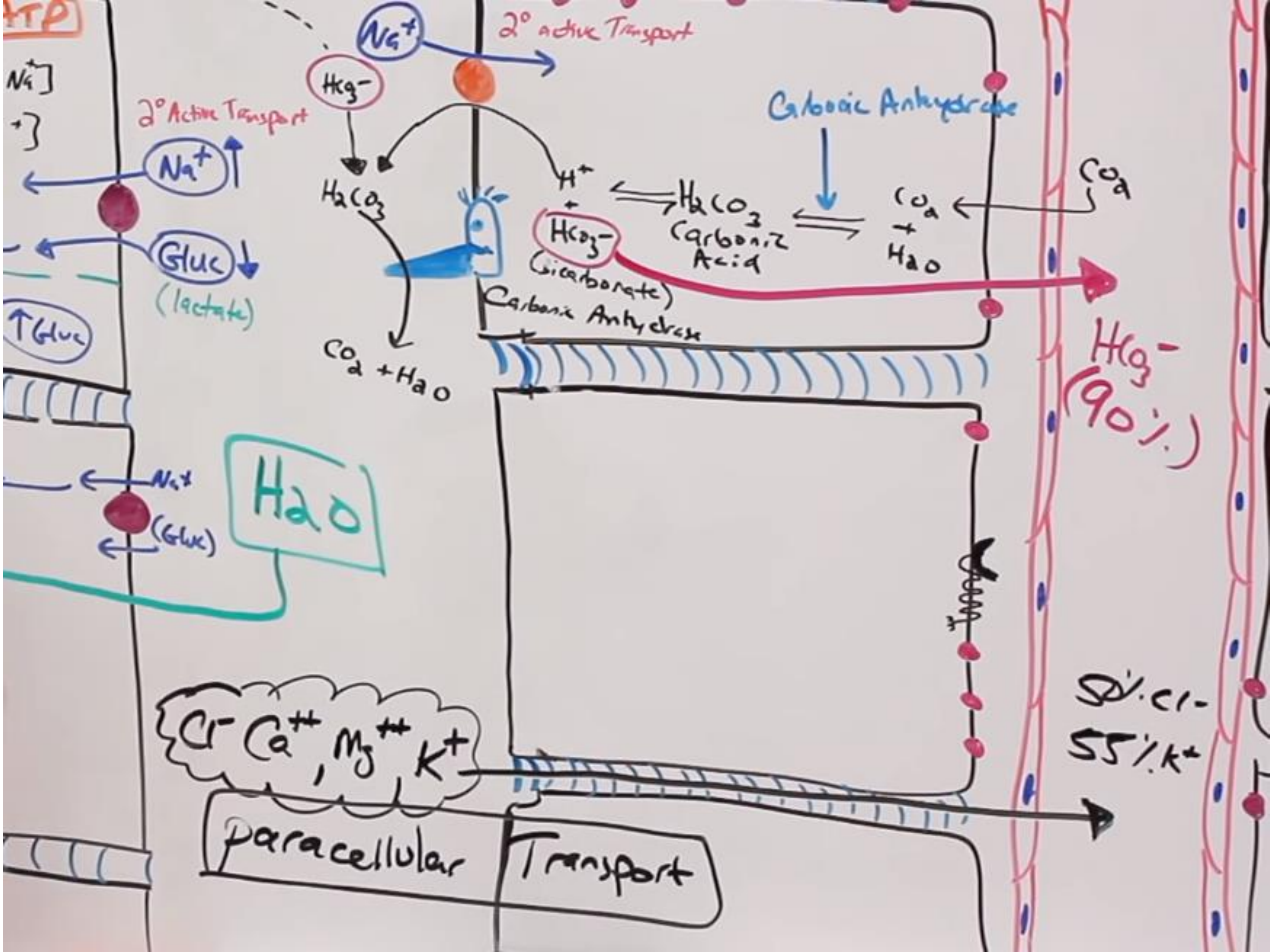

lity = moles / Kg
Tubular Secretion (Active)
Tubular Reabsorption (Active or passive)
300 mosm/L
Small proteins
Lipids
Glucose
A.A.
lactate
100% Reabsorbed
Na+ Ca++
K+ Cl-
Mg2+
HCO3-
H2O
300 mosm
[↓Na+]
[↑A.A.]
3Na+
2K+
Na+
A.A.
(A.A.)
2° active Transport
ATP
↓[Na+]
↑[K+]
2° Active Transport
(Glucose)
(lactate)
Gluc
↑Gluc
65% Na+
65% H2O
H2O
(Gluc)
HCO3-
H2CO3
CO2 + H2O
H+
Carbonic Anhydrase
Carbonic Acid
(bicarbonate)
HCO3- (90%)


300 mosm/L
Small proteins
Lipids
Glucose
A.A.
lactate
100% Reabsorbed
Na+ Ca2+
K+ Cl-
Mg2+
HCO3-
H2O
300 mosm
[↓Na+]
[↑A.A.]
3Na+
2K+
(A.A.
2° active Transport
2° active Transport
ATP
↓[Na+]
↑[K+]
2° Active Transport
Na+
Gluc
(lactate)
(Glucose)
(lactate)
↑Gluc
Carbonic Anhydrase
H2CO3
Carbonic
CO2
ility = moles / Kg
Tubular Secretion (Active)
Tubular Reabsorption (Active or passive)
65% Na+
65% H2O
H2O
(Gluc)
Obligatory H2O Reabsorption



2° active Transport
Na+
HCO3-
2° active Transport
2° Active Transport
Na+
Gluc
(lactate)
Carbonic Anhydrase
H2CO3
CO2 + H2O
H+
+
HCO3-
H2CO3
Carbonic Acid
CO2
+
H2O
CO2
(bicarbonate)
Carbonic Anhydrase
HCO3-
(90
Na+
(Gluc)
H2O
Ca++, Mg++, K+


Transport
ATP
↓[Na+]
↑[K+]
2° Active Transport
Na+
Gluc
(lactate)
↑Gluc
H2O
Na+
(Gluc)
HCO3-
Na+
2° active Transport
Carbonic Anhydrase
H2CO3
H+
HCO3-
Bicarbonate
H2CO3
Carbonic Acid
CO2 + H2O
CO2
Carbonic Anhydrase
CO2 + H2O
HCO3-
(90%)
Cl- Ca++, Mg++ K+
Paracellular Transport


2° active Transport
Na+
HCO3-
2° Active Transport
Na+
Gluc
(lactate)
↑Gluc
H2CO3
CO2 + H2O
H+
+
HCO3-
(bicarbonate)
Carbonic Anhydrase
H2CO3
Carbonic Acid
Carbonic Anhydrase
CO2
+
H2O
CO2
HCO3-
(90%)
H2O
Na+
(Gluc)
Cl- Ca++, Mg++, K+
Paracellular Transport
80% Cl-
55% K+

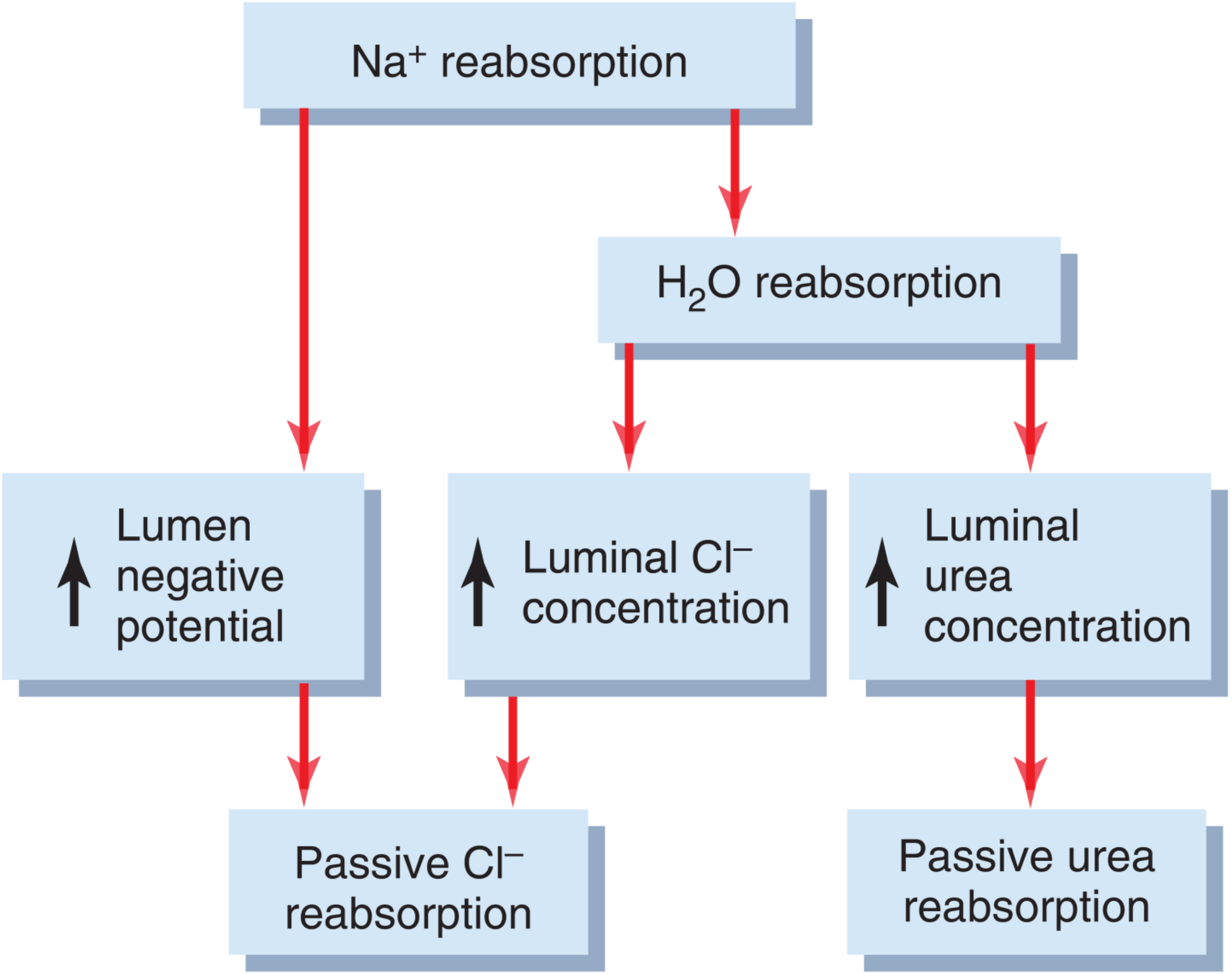
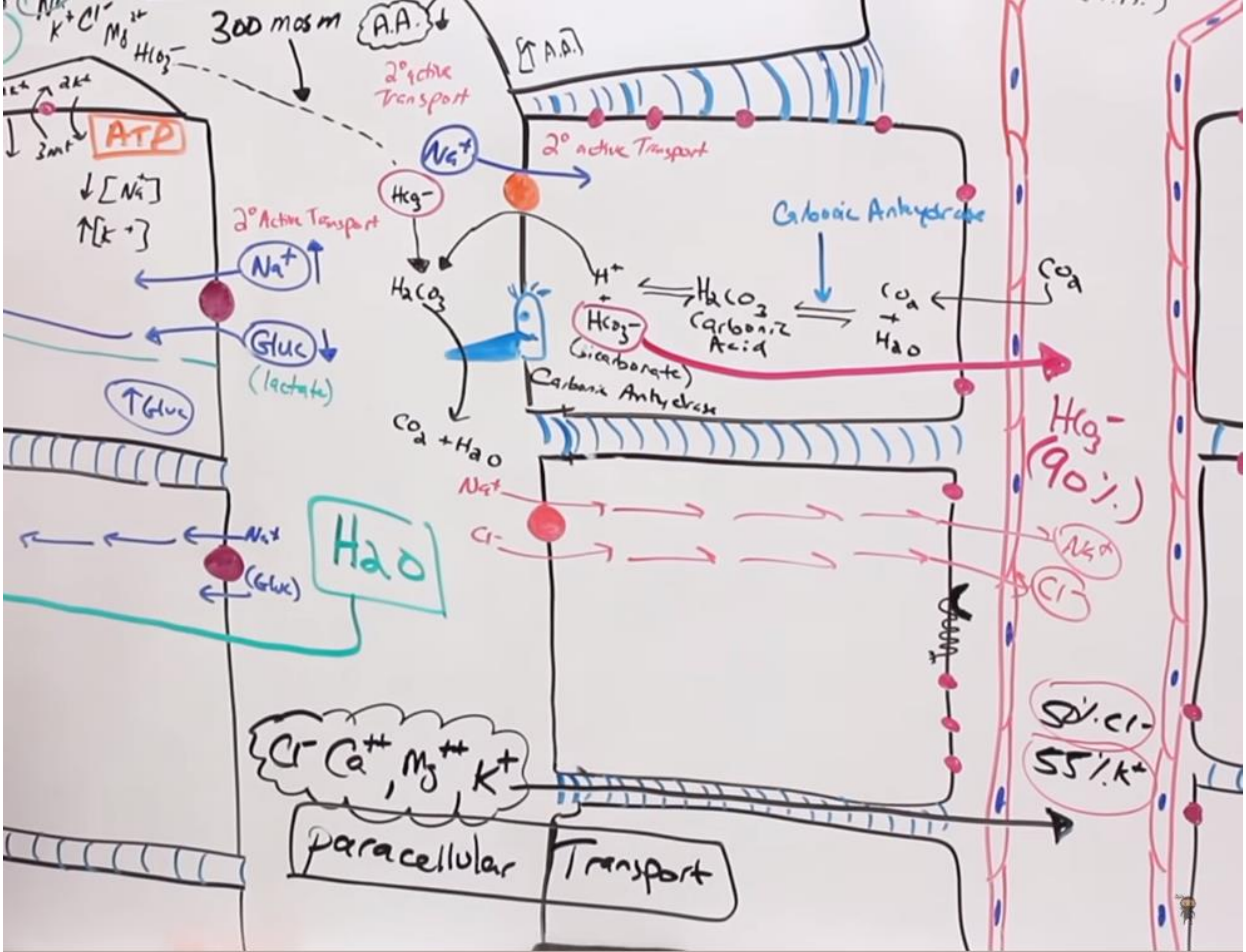


Figure 28-5. Mechanisms by which water, chloride, and urea reabsorption are coupled with sodium reabsorption.

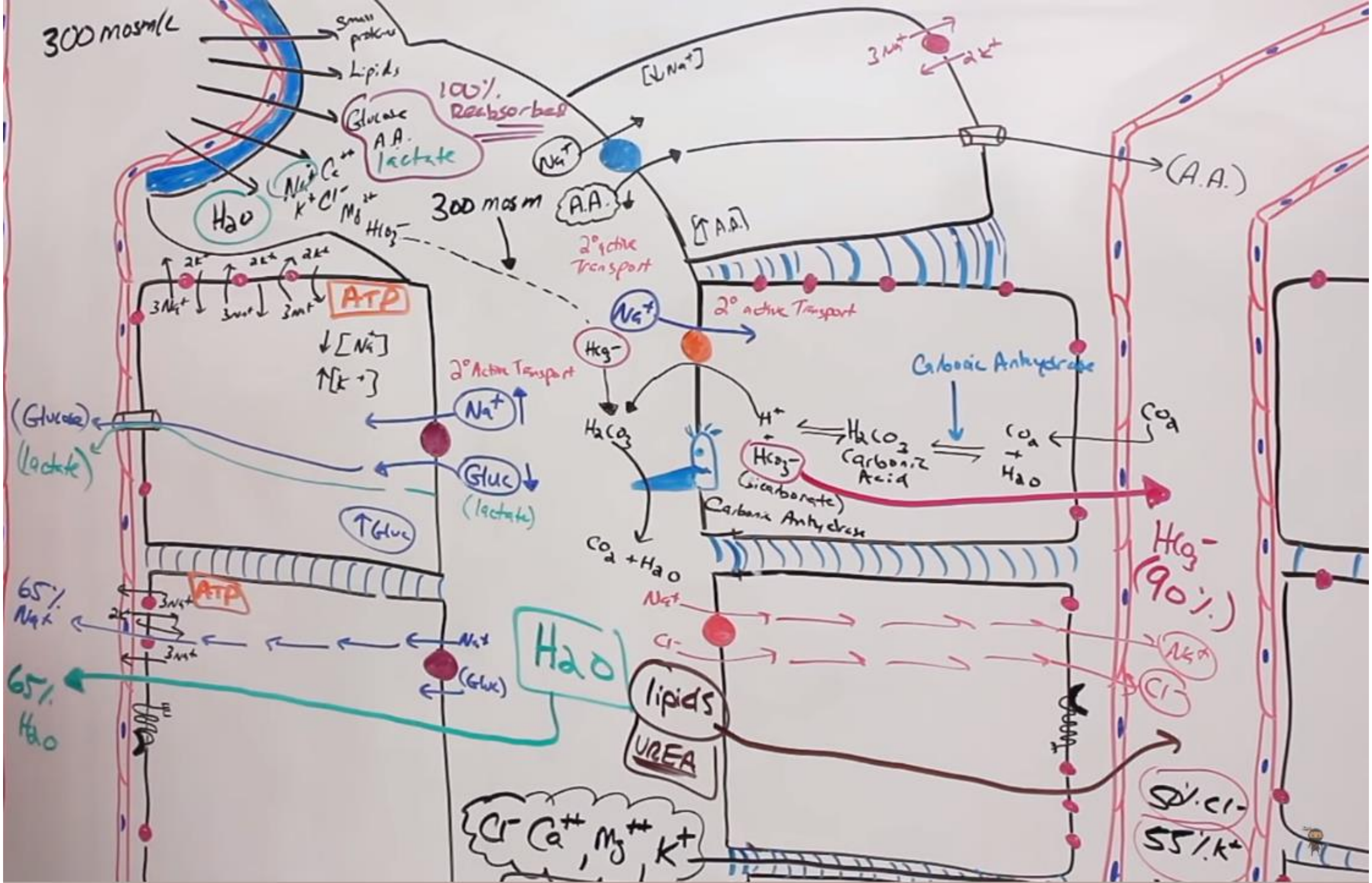
When sodium is reabsorbed through the tubular epithelial cell, negative ions such as chloride are transported along with sodium because of electrical potentials. That is, transport of positively charged sodium ions out of the lumen leaves the inside of the lumen negatively charged, compared with the interstitial fluid. This environment causes chloride ions to diffuse passively through the para-cellular pathway. Additional reabsorption of chloride ions occurs because of a chloride concentration gradient that develops when water is reabsorbed from the tubule by osmosis, thereby concentrating the chloride ions in the tubular lumen. Thus, the active reabsorption of sodium is closely coupled to the passive reabsorption of chloride by way of an electrical potential and a chloride concentration gradient.

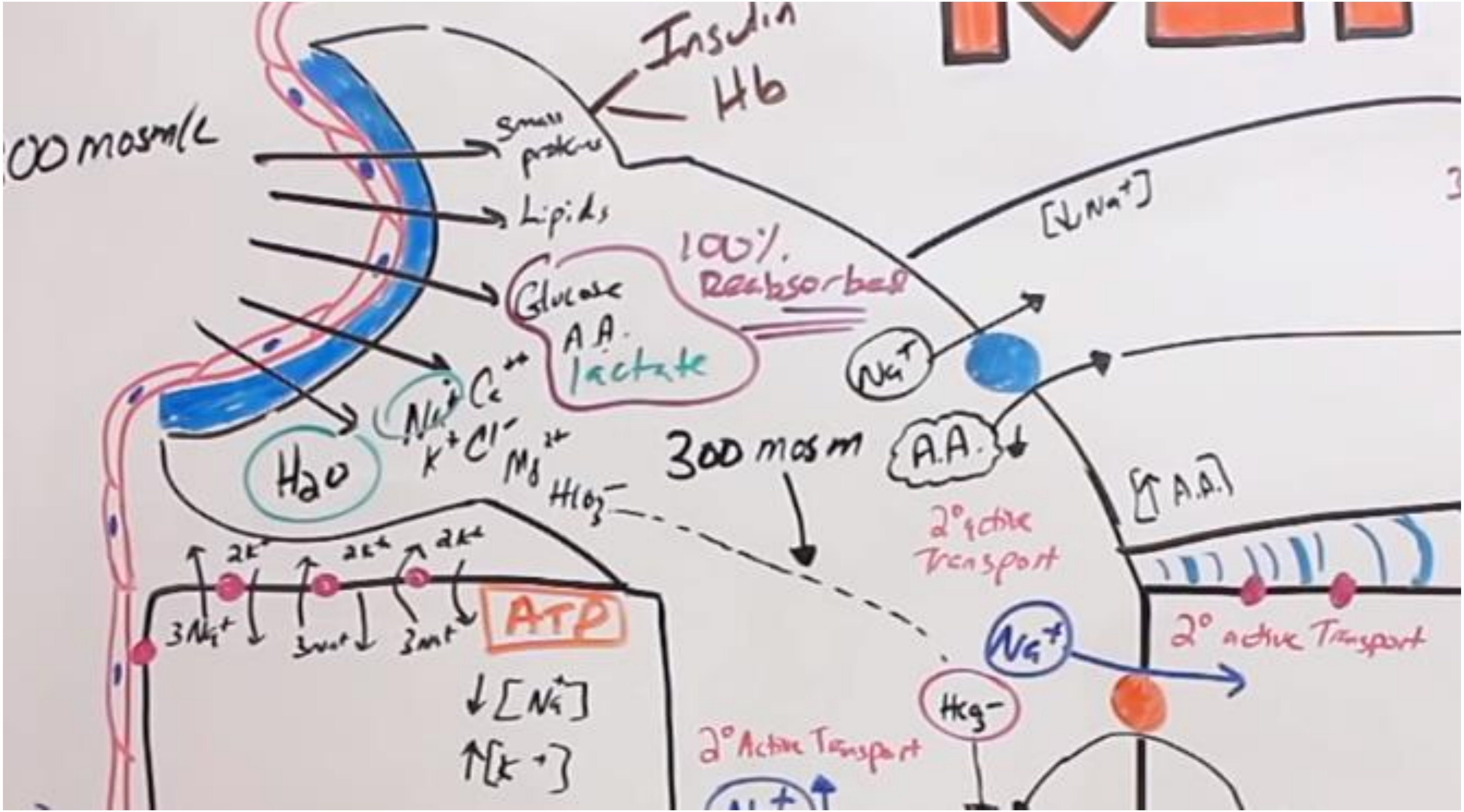
Chloride ions can also be reabsorbed by secondary active transport. The most important of the secondary active transport processes for chloride reabsorption involves co-transport of chloride with sodium across the luminal membrane.

Urea is also passively reabsorbed from the tubule, but to a much lesser extent than chloride ions. As water is reabsorbed from the tubules (by osmosis coupled to sodium reabsorption), urea concentration in the tubular lumen increases. This increase creates a concentration gradient favoring the reabsorption of urea. However, urea does not permeate the tubule as readily as does water. In some parts of the nephron, especially the inner medullary collecting duct, passive urea reabsorption is facilitated by specific urea transporters. Yet, only about one half of the urea that is filtered by the glomerular capillaries is reabsorbed from the tubules. The remainder of the urea passes into the urine, allowing the kidneys to excrete large amounts of this waste product of metabolism. In mammals, more than 90 percent of waste nitrogen, mainly generated in the liver as a product of protein metabolism, is normally excreted by the kidneys as urea.



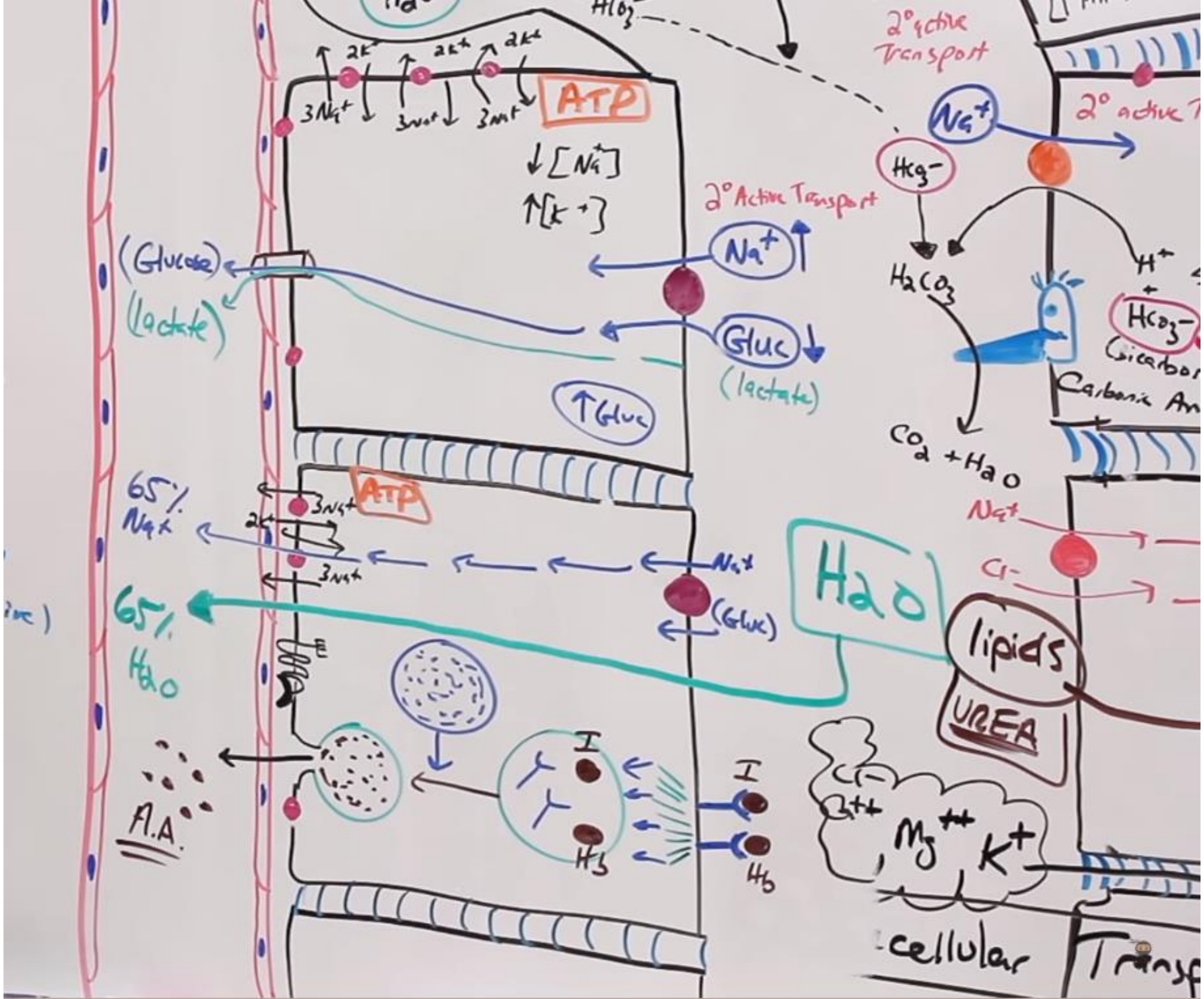
300 mosm
A.A.
A.A.
2° active Transport
ATP
↓[Na+]
↑[K+]
2° Active Transport
Na+
Gluc
(lactate)
↑Gluc
H2O
Na+
(Gluc)
HCO3-
Na+
2° active Transport
Carbonic Anhydrase
H+
H2CO3
H2CO3
Carbonic Acid
CO2
CO2 + H2O
HCO3-
(bicarbonate)
Carbonic Anhydrase
CO2 + H2O
HCO3-
(90%)
Na+
Cl-
Na+
Cl-
50% Cl-
55% K+
Cl- Ca++, Mg++, K+
paracellular Transport


300 mosm/L
Small protein
Lipids
Glucose
A.A.
lactate
100% Reabsorbed
Na^+ Ca^{++}
K^+ Cl^-
Mg^{2+}
HCO_3^-
H_2O
300 mosm
[↓Na^+]
$3Na^+$
$2K^+$
Na^+
A.A.
(A.A.)
[↑A.A.]
2° active Transport
2° active Transport
ATP
↓[Na^+]
↑[K^+]
2° Active Transport
(Glucose)
(lactate)
Gluc
(lactate)
↑Gluc
HCO_3^-
H_2CO_3
$CO_2 + H_2O$
H^+
H_2CO_3
Carbonic Acid
Carbonic Anhydrase
CO_2 + H_2O
CO_2
(bicarbonate)
Carbonic Anhydrase
HCO_3^- (90%)
65% Na^+
65% H_2O
H_2O
lipids
UREA
Na^+
Cl^-
Cl^- Ca^{++}, Mg^{++}, K^+
50% Cl^-
55% K^+

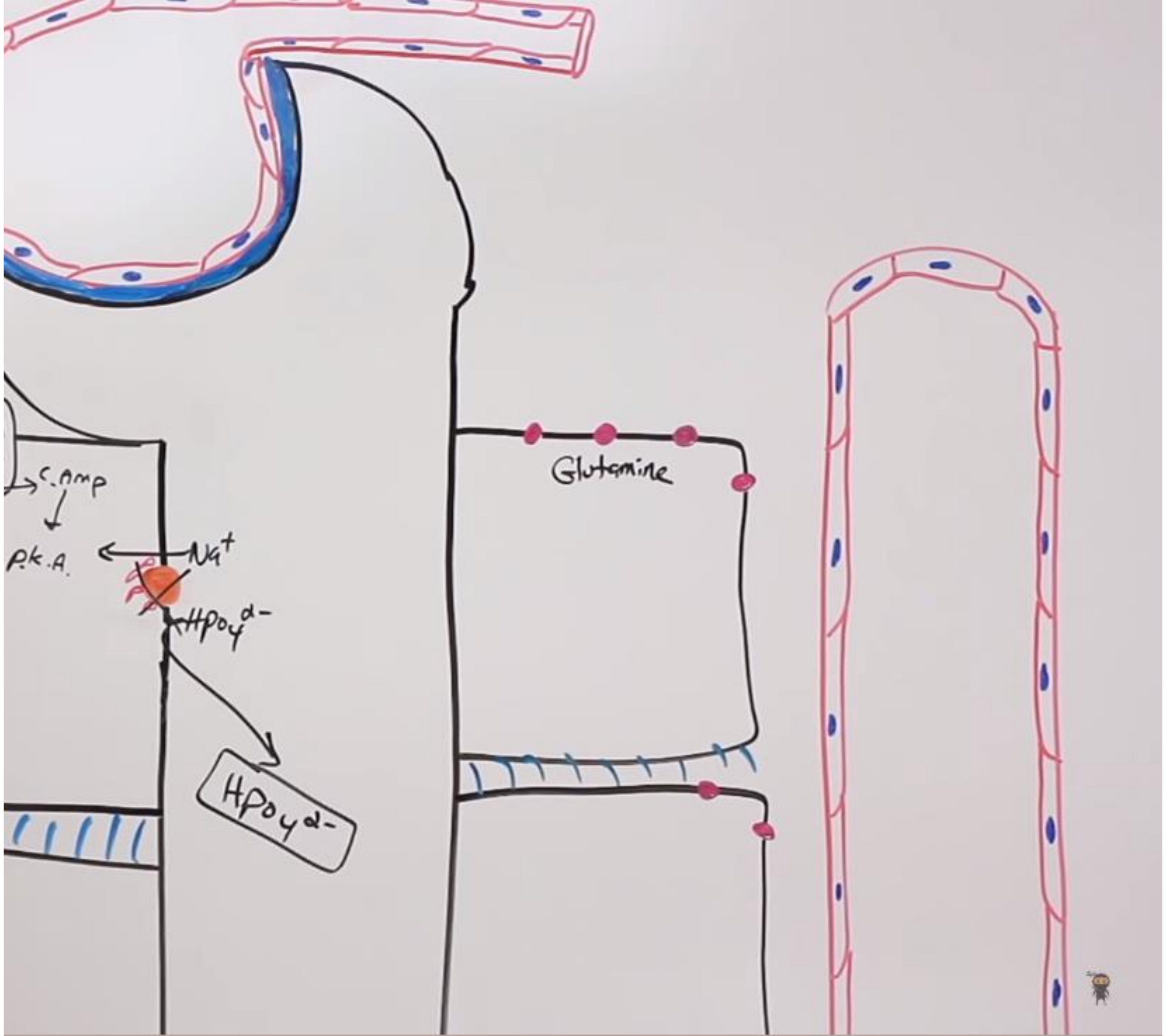


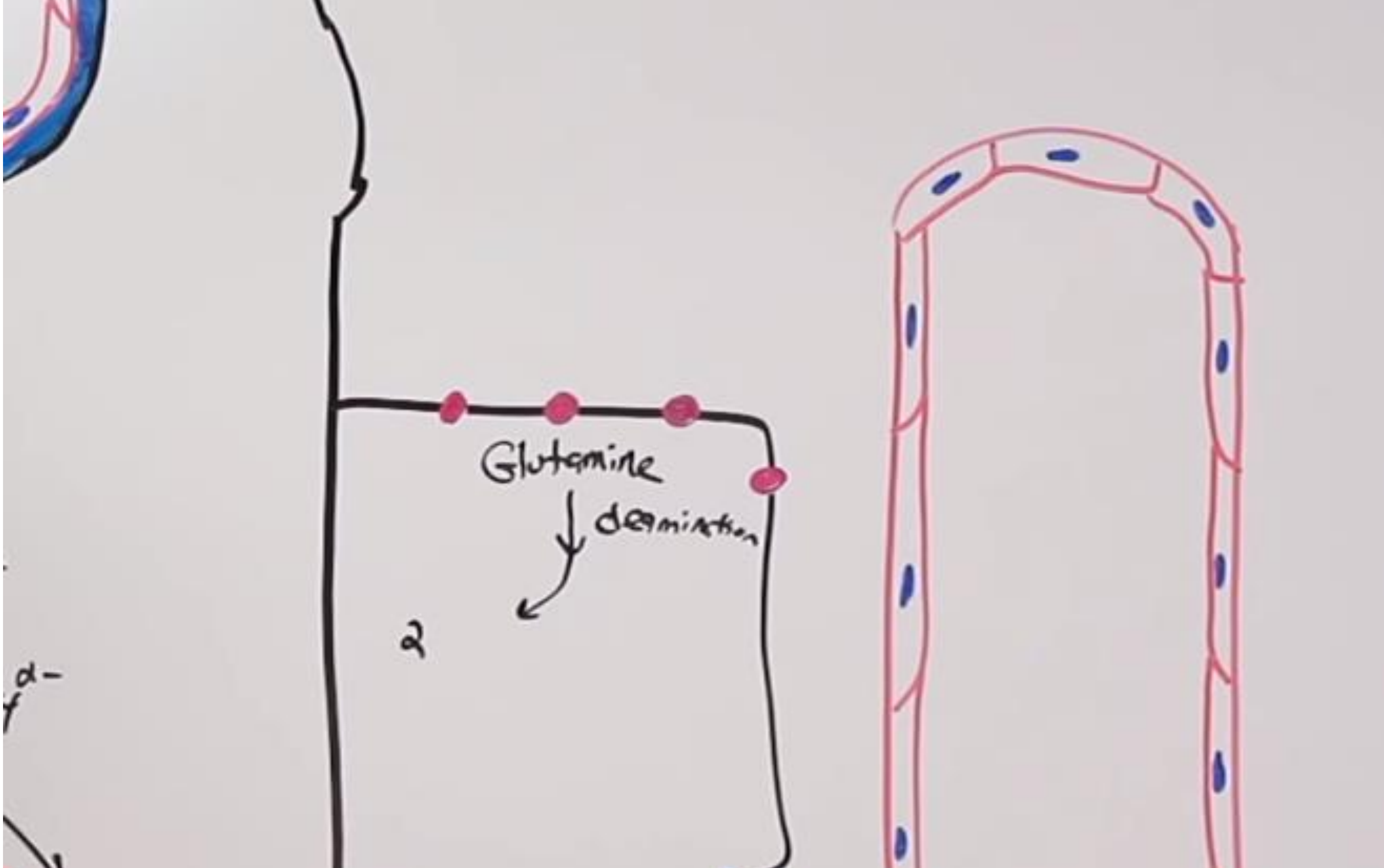
00 mosm/L
Insulin
Hb
Small proteins
Lipids
Glucose
A.A.
lactate
100% Reabsorbed
Na^+
Ca^{2+}
K^+ Cl^-
Mg^{2+}
HCO_3^-
H_2O
300 mosm
[↓ Na^+]
Na^+
A.A.
[↑ A.A.]
2° active Transport
2° active Transport
2° Active Transport
Na^+
Hcg⁻
2K⁺
3Na⁺
ATP
↓[Na^+]
↑[K^+]

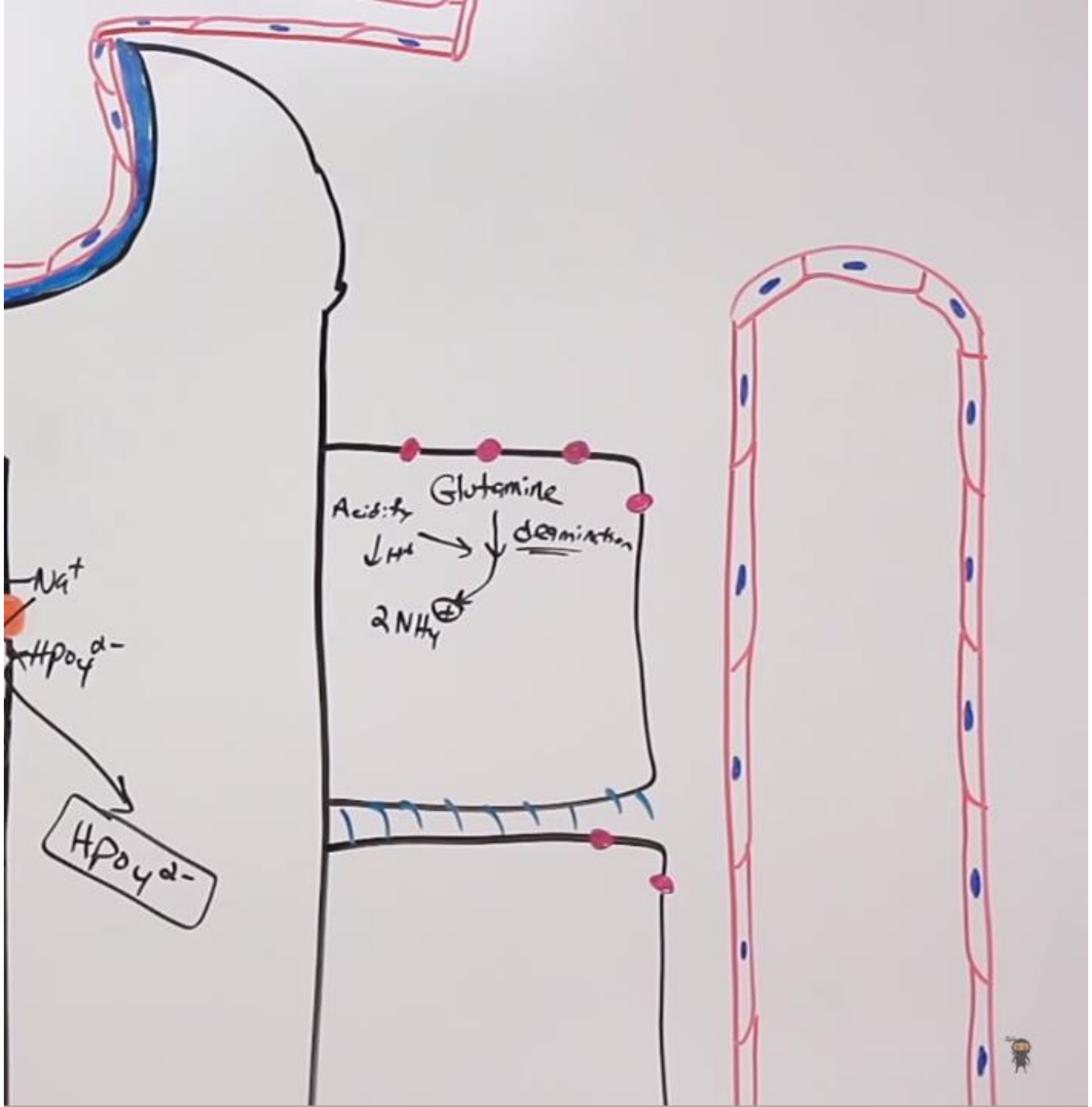
ATP
3Na+
2K+
3Na+
Na+
(Gluc)
I
Hb



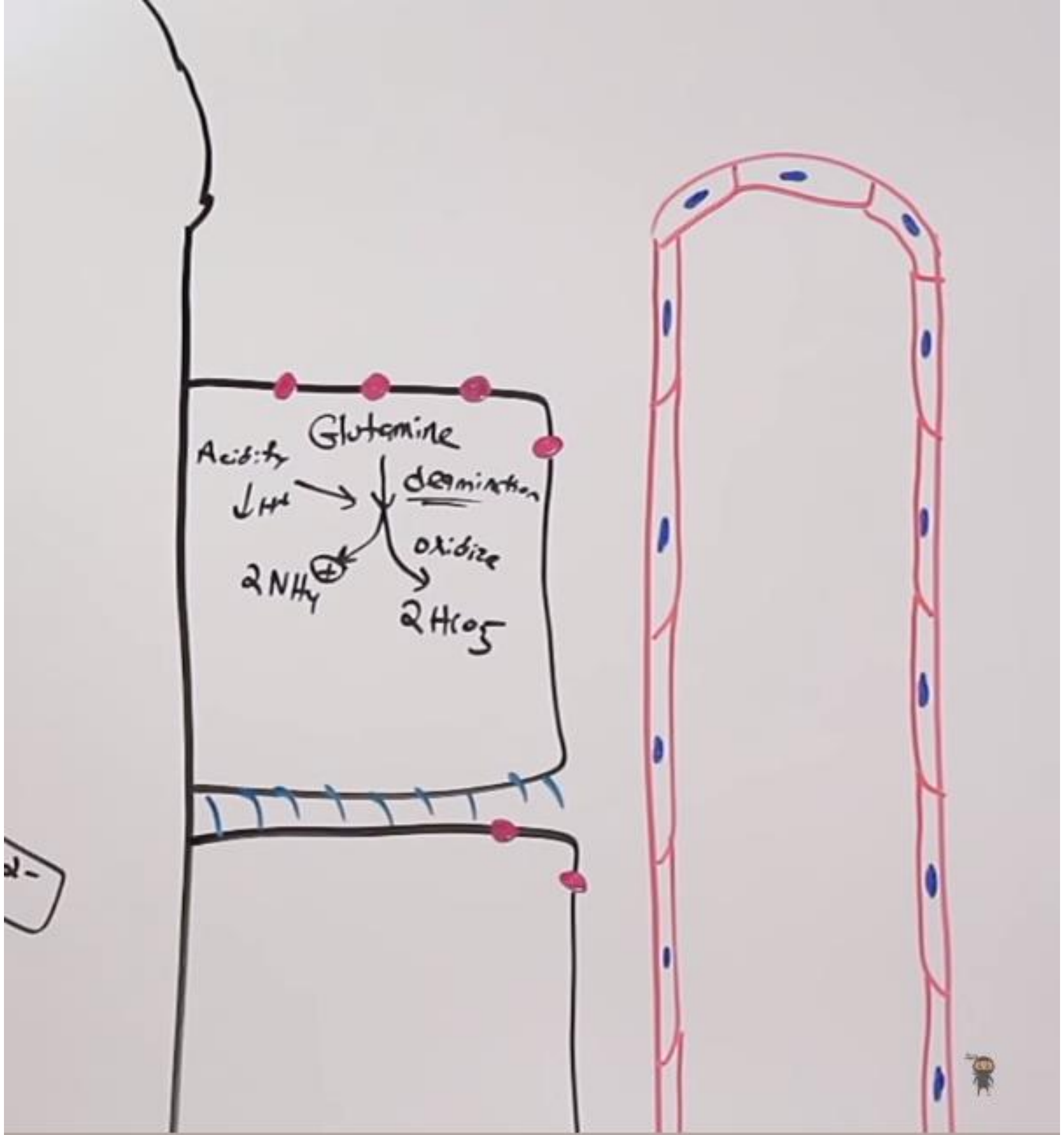
2° active Transport
2° active T
2° Active Transport
ATP
3Na+
2K+
↓[Na+]
↑[K+]
Na+
HCO3-
H2CO3
CO2 + H2O
H+
Carbonic An
(Glucose)
(lactate)
Gluc
↑Gluc
65% Na+
65% H2O
(Gluc)
H2O
lipids
UREA
Cl-
Mg++ K+
I
Hb
A.A.
cellular
Transp

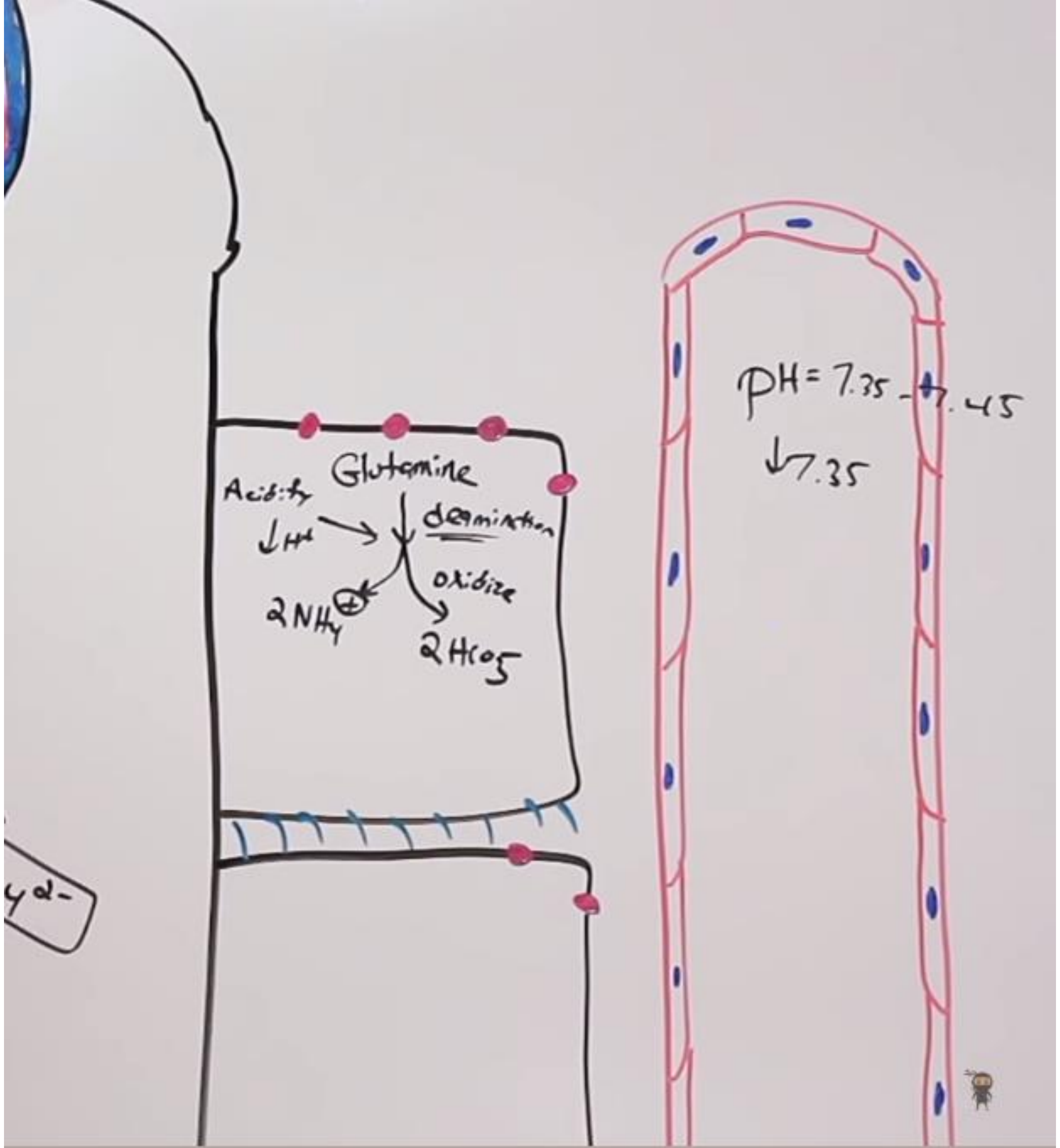

c.AMP
P.K.A.
Na+
HPO4 2-
HPO4 2-
Glutamine


Glutamine
deamination
2

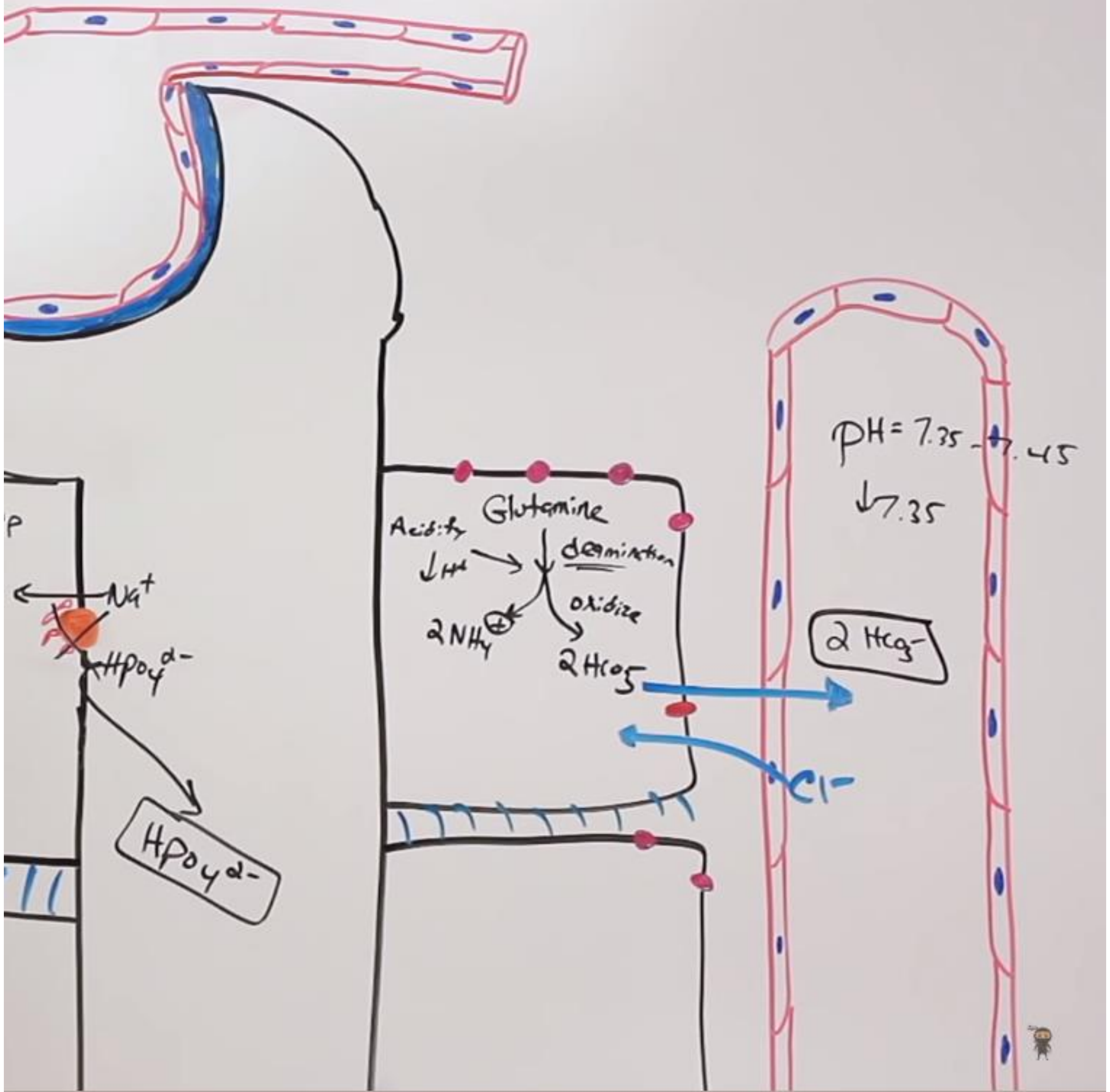


Glutamine
Acidity
↓H+
deamination
2NH4+
Na+
HPO4 2-
HPO4 2-

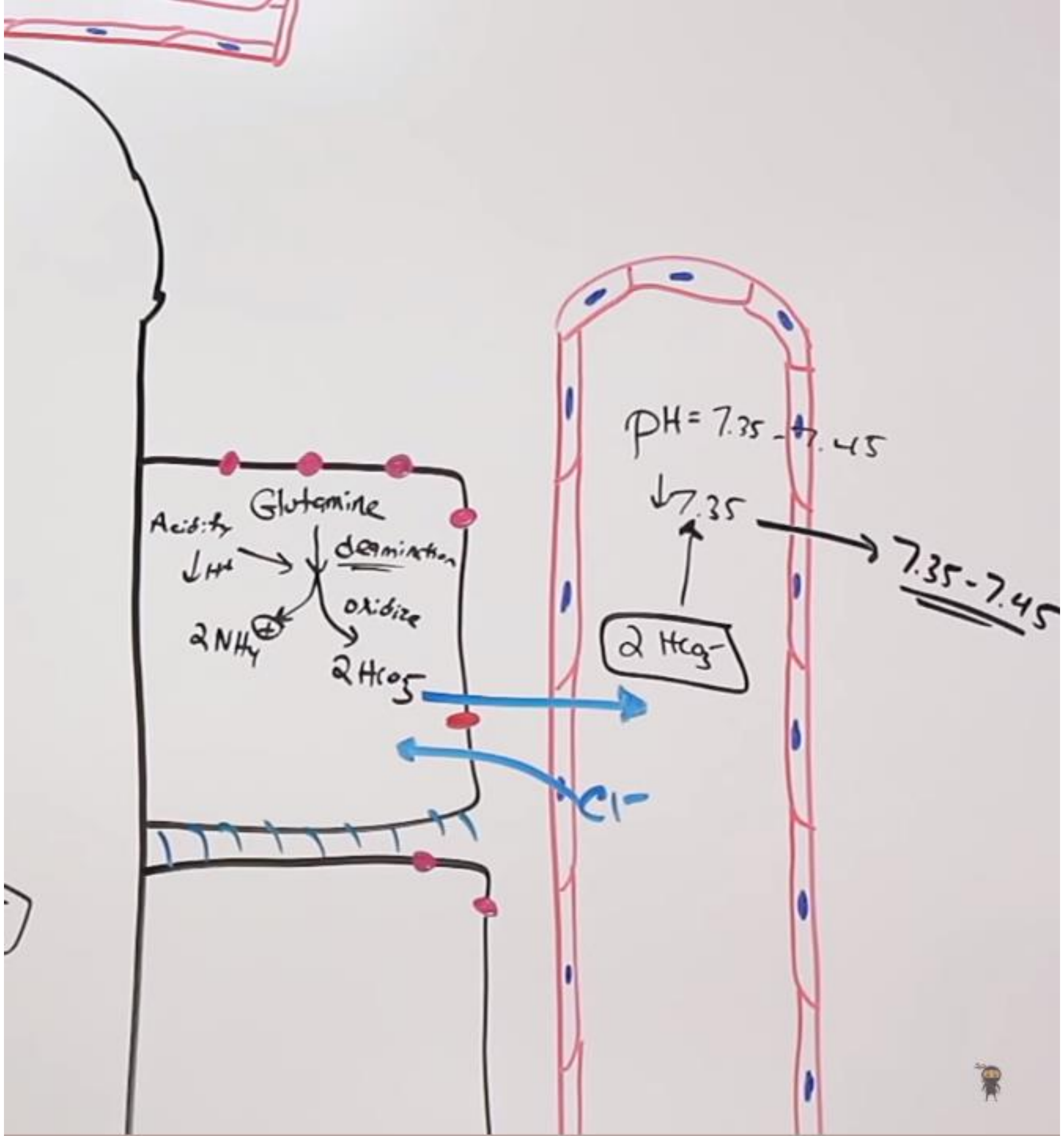

Glutamine
Acidity
deamination
oxidize



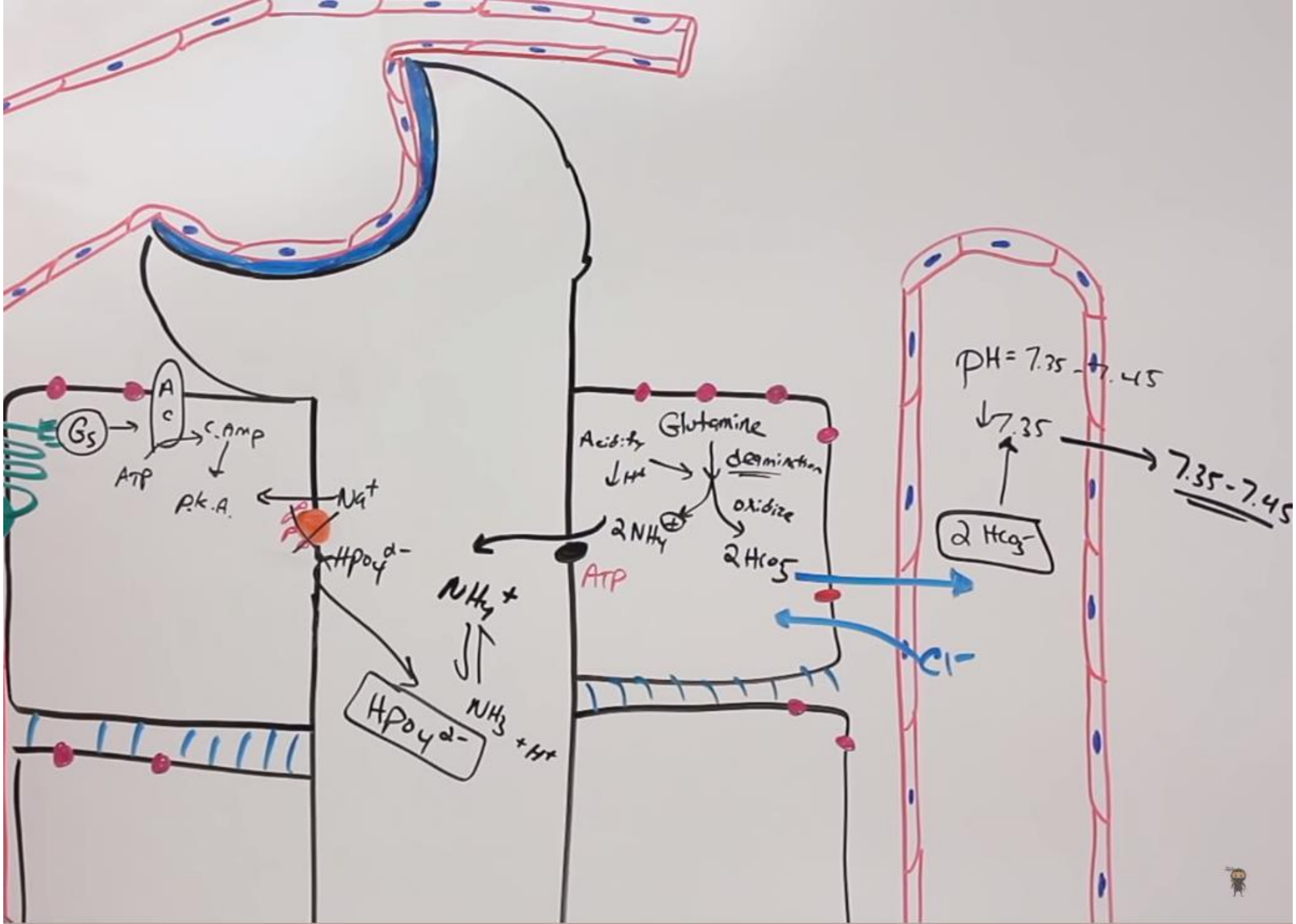
Glutamine
Acidity
↓H+
deamination
oxidize
2NH4+
2HCO3
PH = 7.35 - 7.45
↓7.35



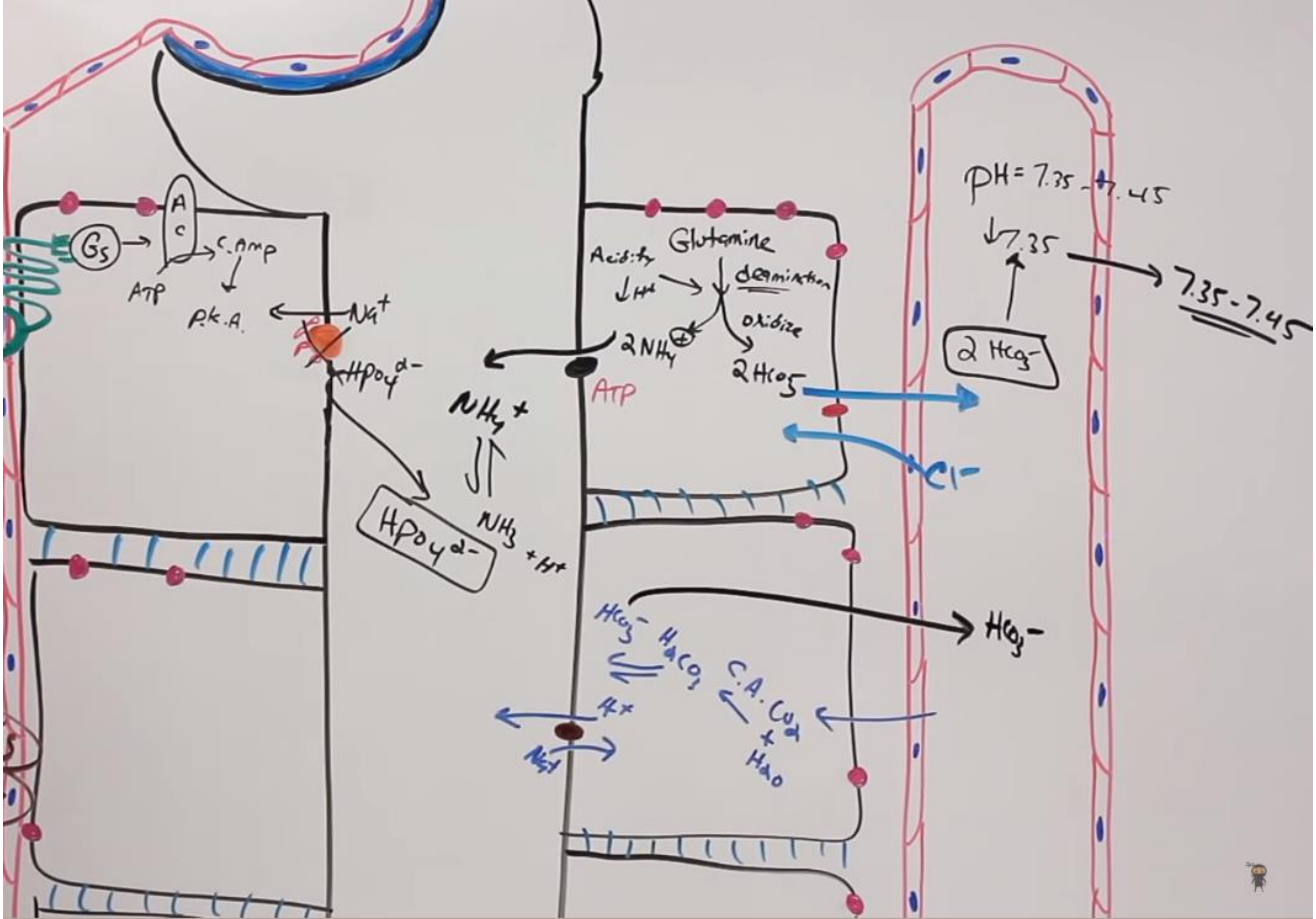
Na+
HPO4 2-
HPO4 2-
Glutamine
Acidity
↓H+
deamination
oxidize
2 NH4+
2 HCO3-
2 HCO3-
Cl-
pH = 7.35 - 7.45
↓7.35



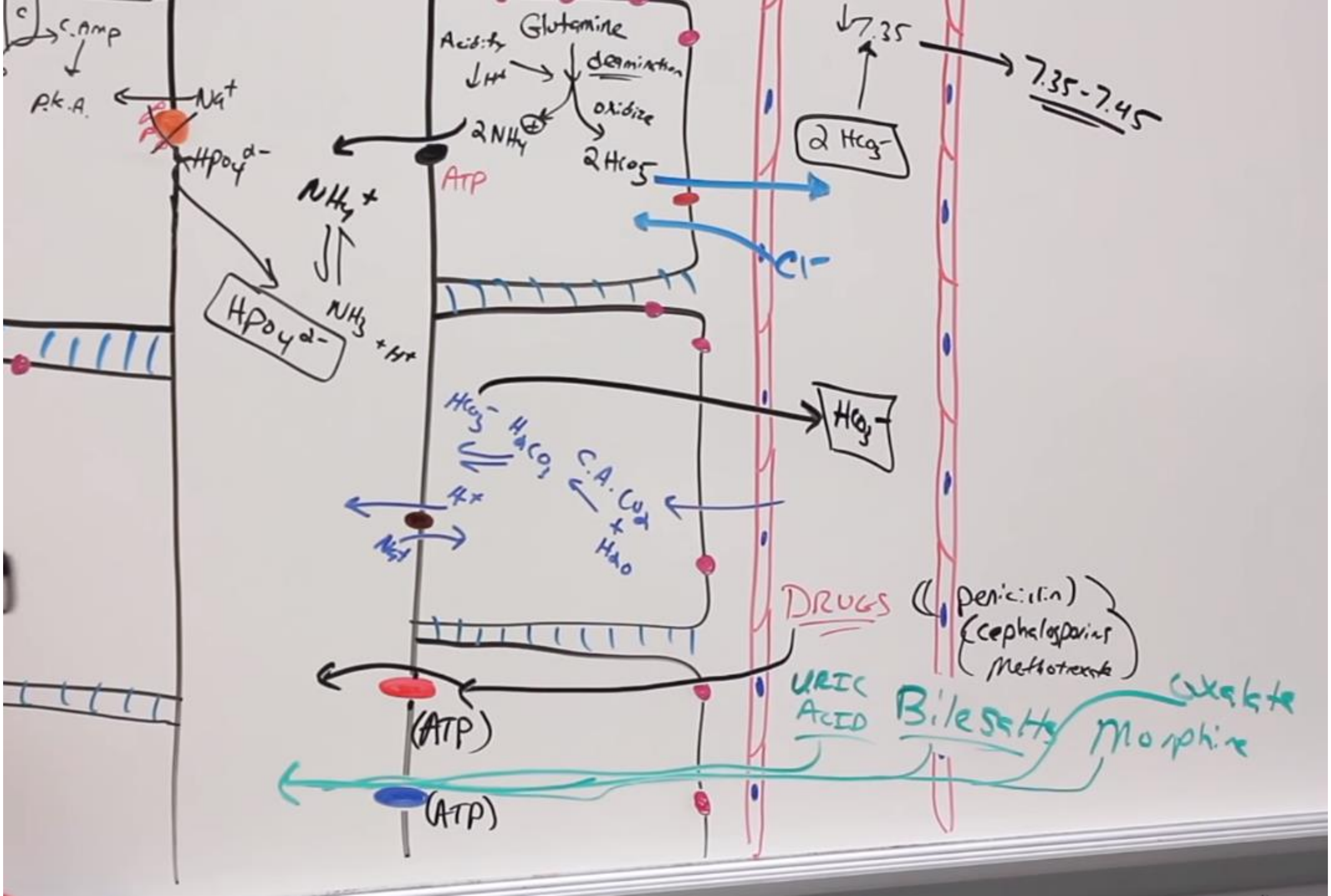
Glutamine
Acidity
↓H+
deamination
oxidize
2NH4+
2HCO3-
Cl-
pH = 7.35 - 7.45
↓7.35
2 HCO3-
7.35-7.45



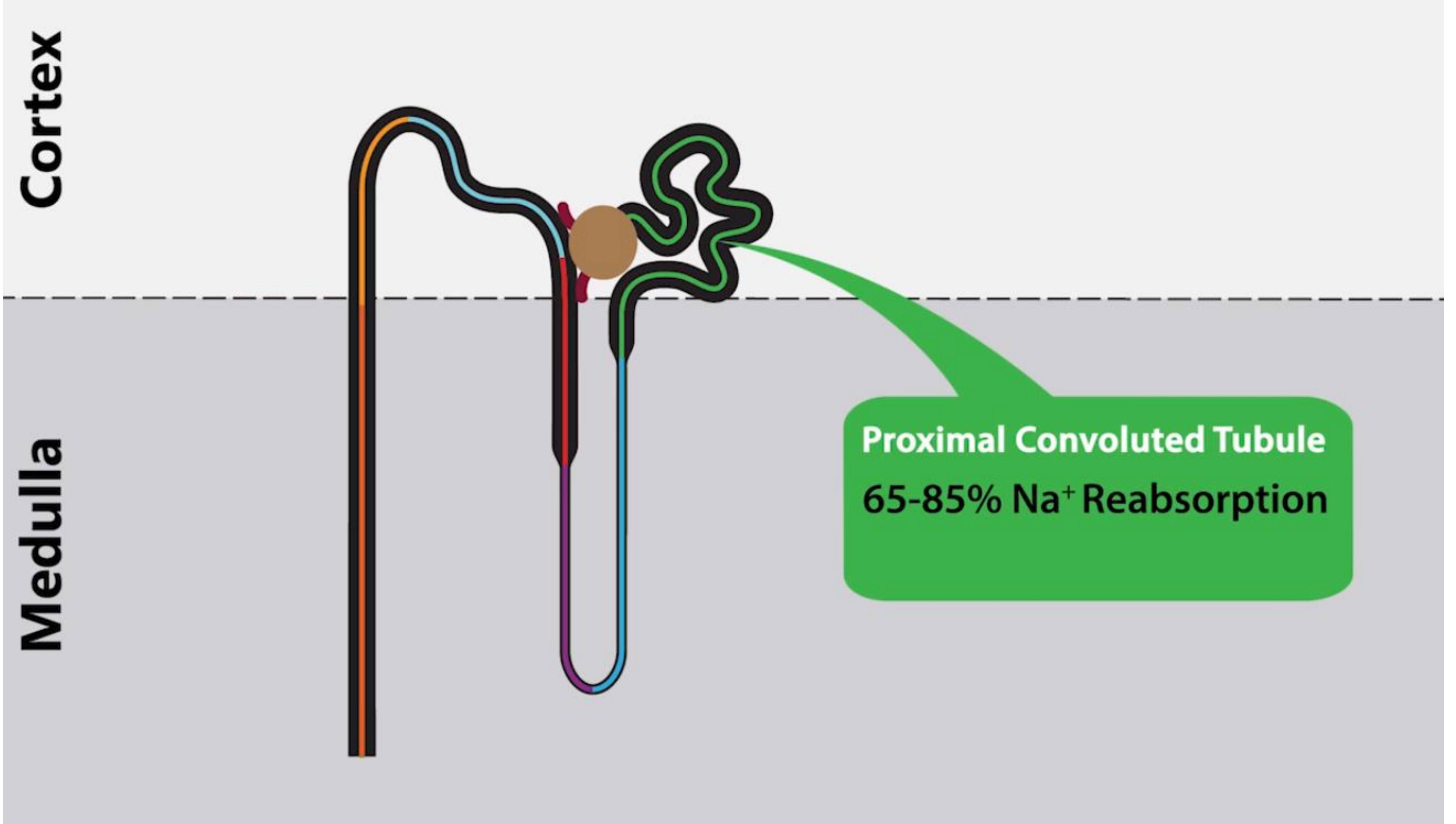
Gs
A
C
ATP
c.AMP
P.K.A.
Na+
HPO4 2-
NH4+
NH3
+H+
HPO4 2-
Acidity
↓H+
Glutamine
deamination
oxidize
2NH4+
2HCO3-
ATP
Cl-
pH = 7.35 - 7.45
↓7.35
2 HCO3-
7.35-7.45

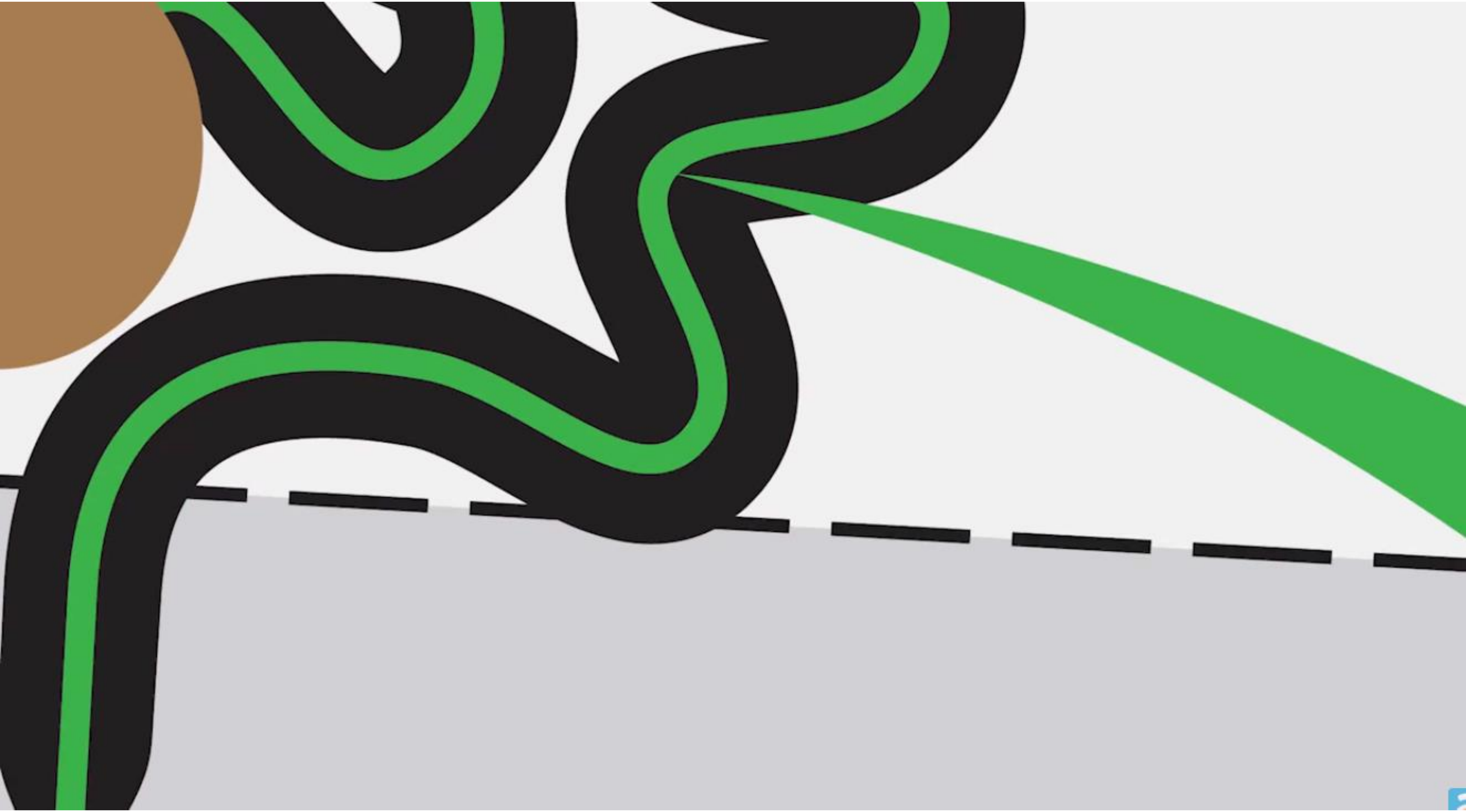


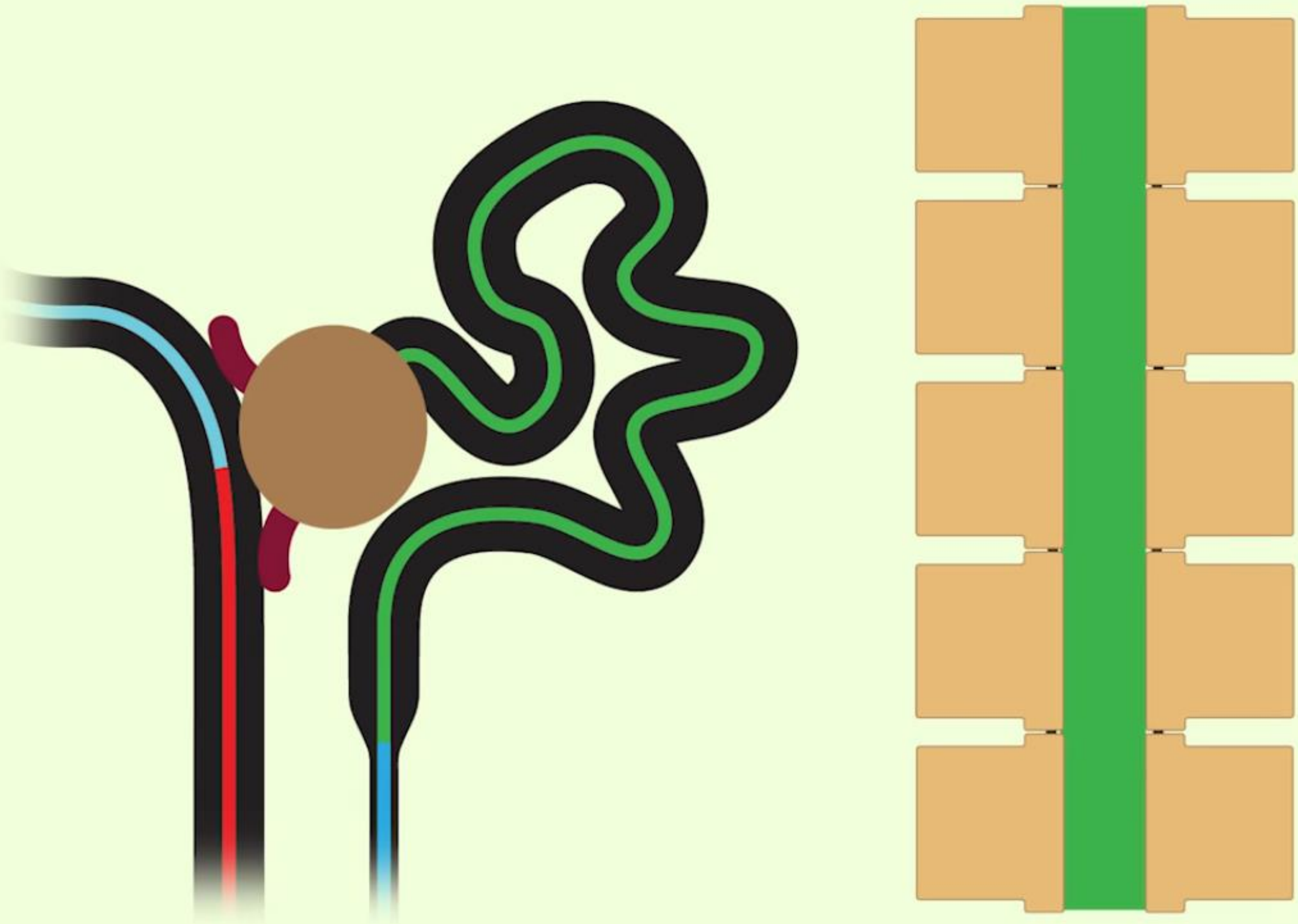
A
C
Gs
c.Amp
ATP
P.K.A.
Na+
HPO4 2-
NH4+
NH3
+H+
HPO4 2-
Glutamine
Acidity
↓H+
deamination
oxidize
2NH4+
2HCO3
ATP
Cl-
pH = 7.35 - 7.45
↓7.35
2 HCO3-
7.35-7.45
HCO3-
HCO3-
H2CO3
C.A.
CO2
+
H2O
H+
Na+

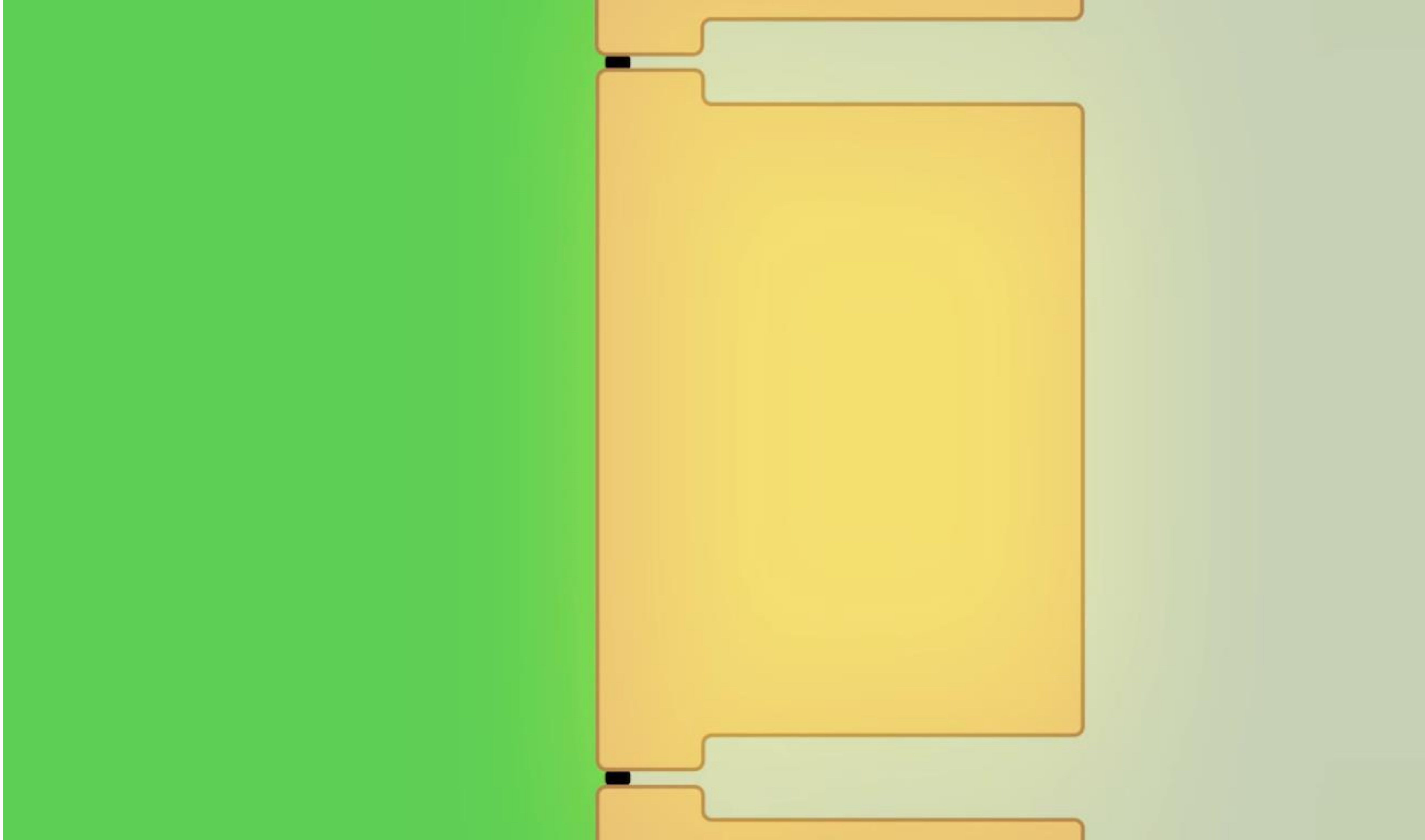


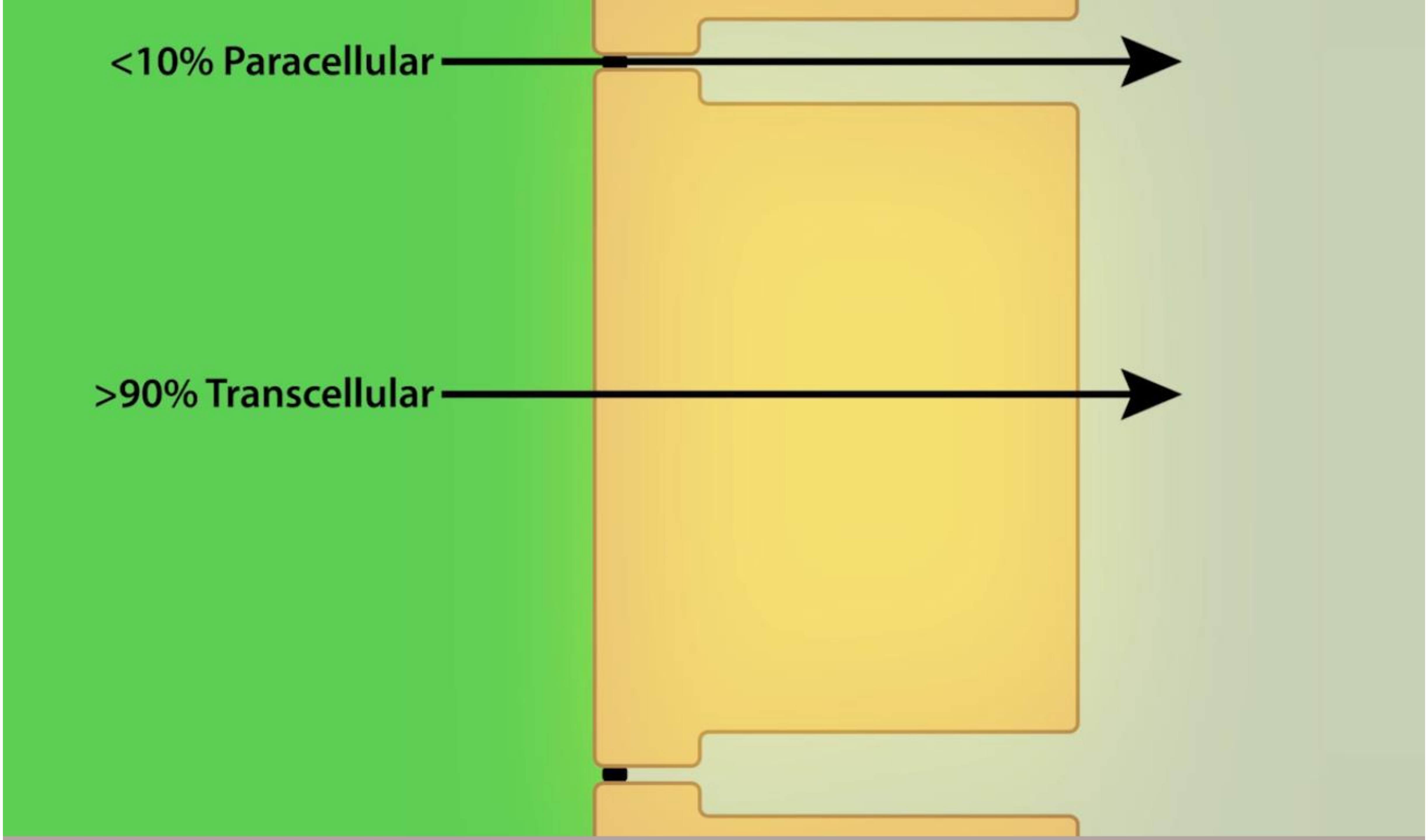
c.Amp
P.K.A.
Na+
HPO4 2-
HPO4 2-
NH4+
NH3 + H+
Acidity
Glutamine
deamination
oxidize
2NH4+
2HCO3
ATP
Cl-
7.35
7.35-7.45
2 HCO3-
HCO3-
HCO3-
H2CO3
C.A.
CO2 + H2O
H+
Na+
DRUGS
penicillin
cephalosporins
Methotrexate
URIC ACID
Bile salts
Oxalate
Morphine
(ATP)
(ATP)


Cortex
Medulla
Proximal Convoluted Tubule
65-85% Na+ Reabsorption

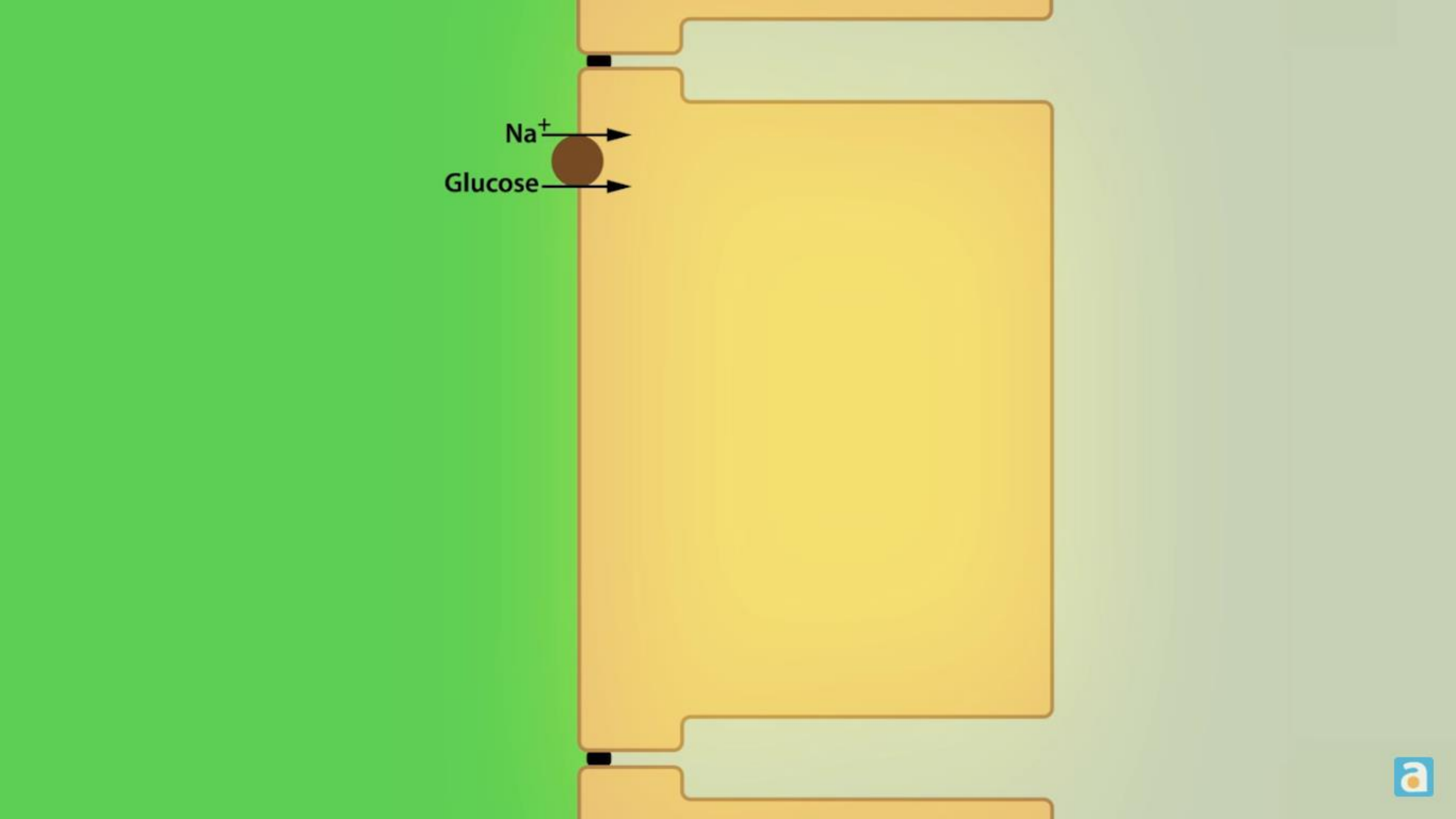


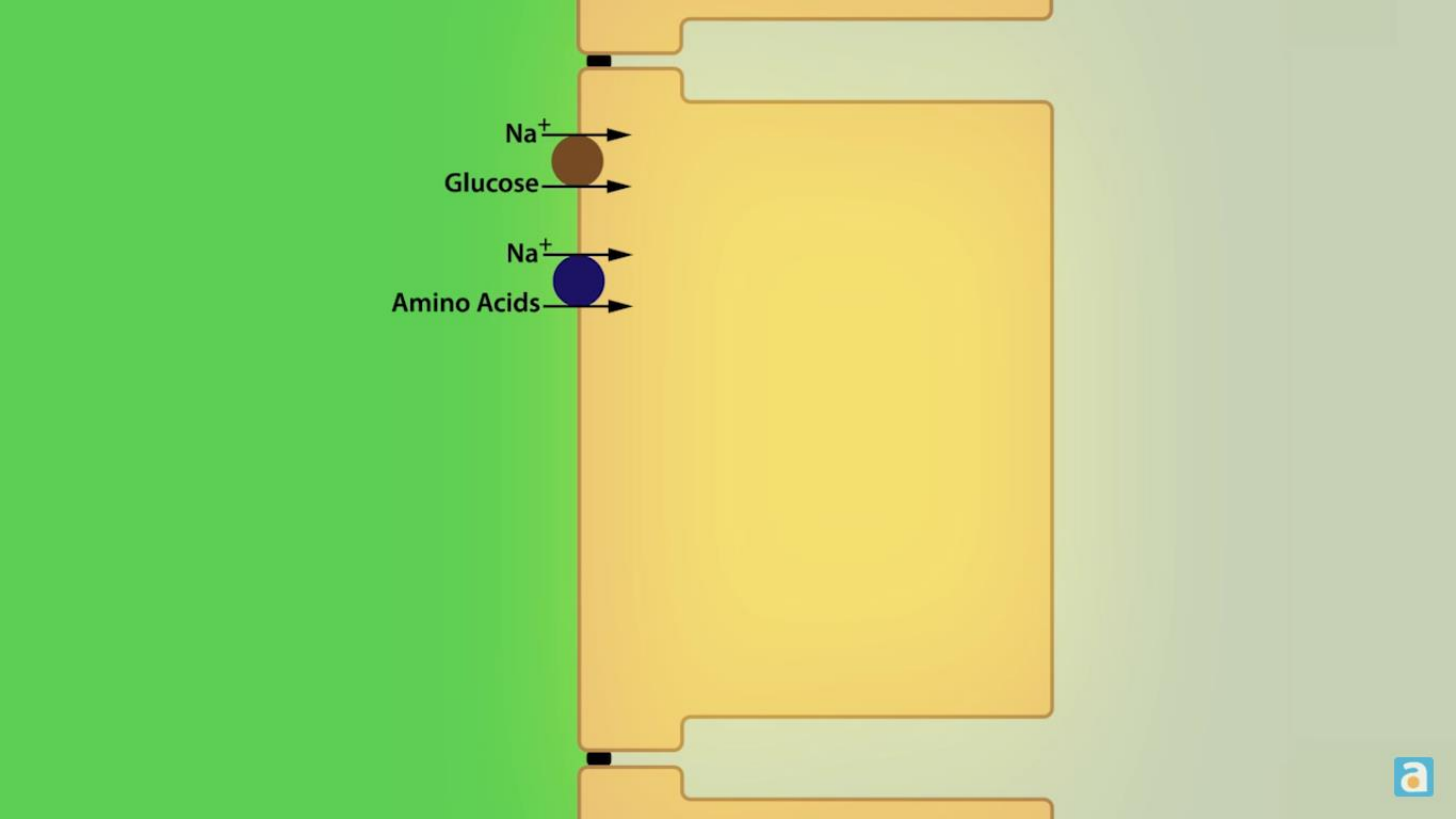


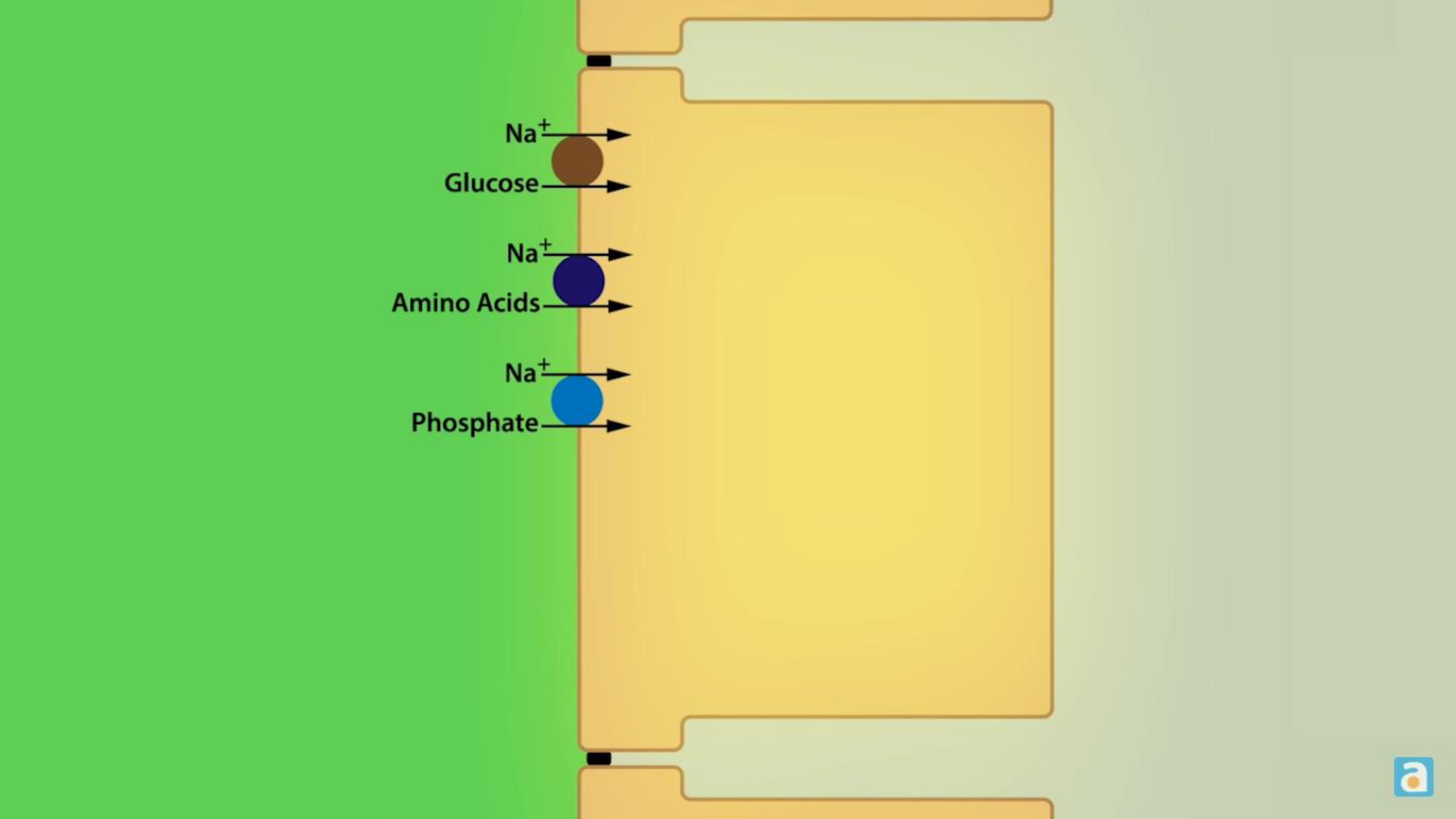




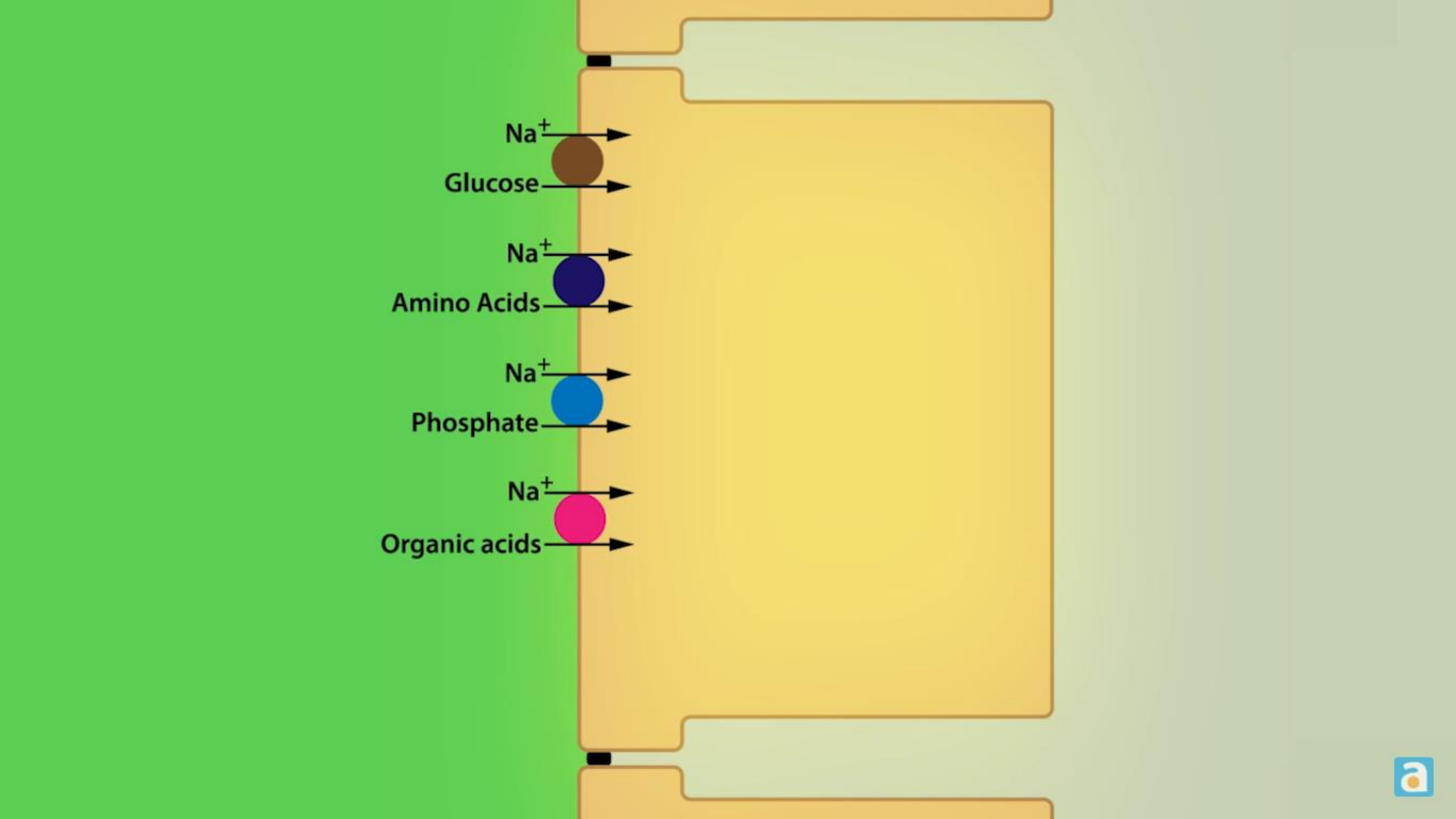
<10% Paracellular
>90% Transcellular


Na+
Glucose

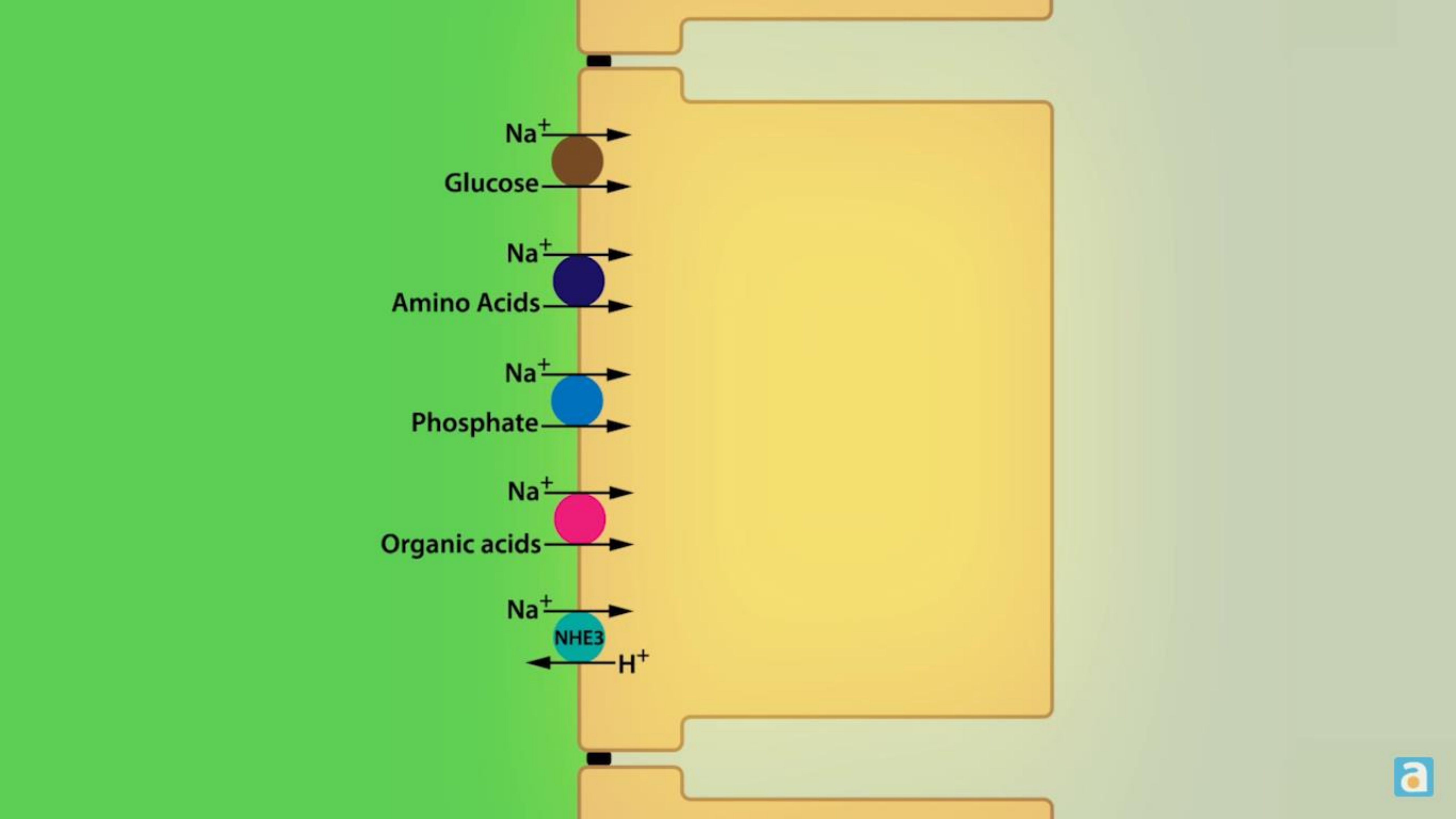

Na+
Glucose
Na+
Amino Acids

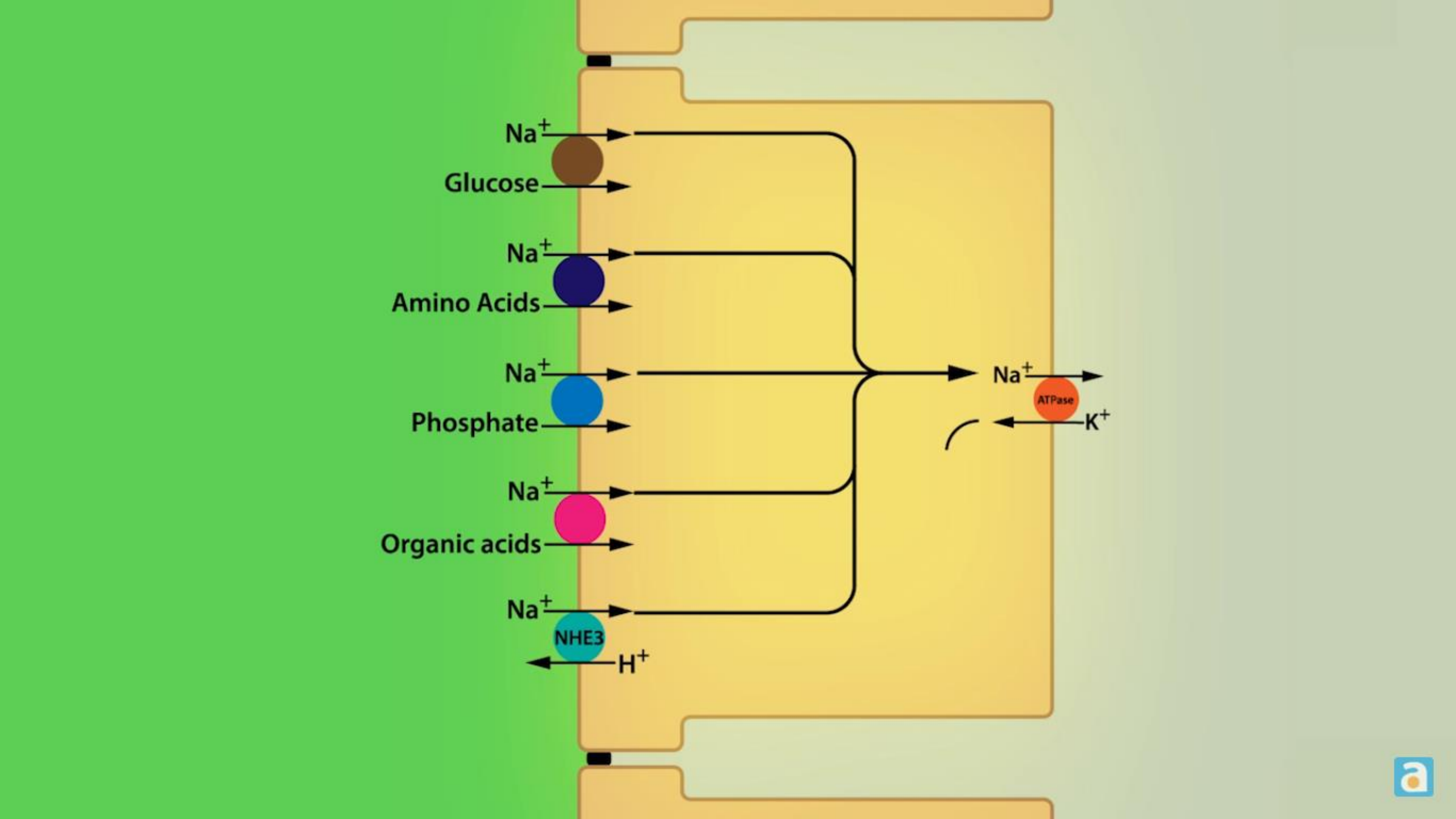


Na^+
Glucose
Na^+
Amino Acids
Na^+
Phosphate

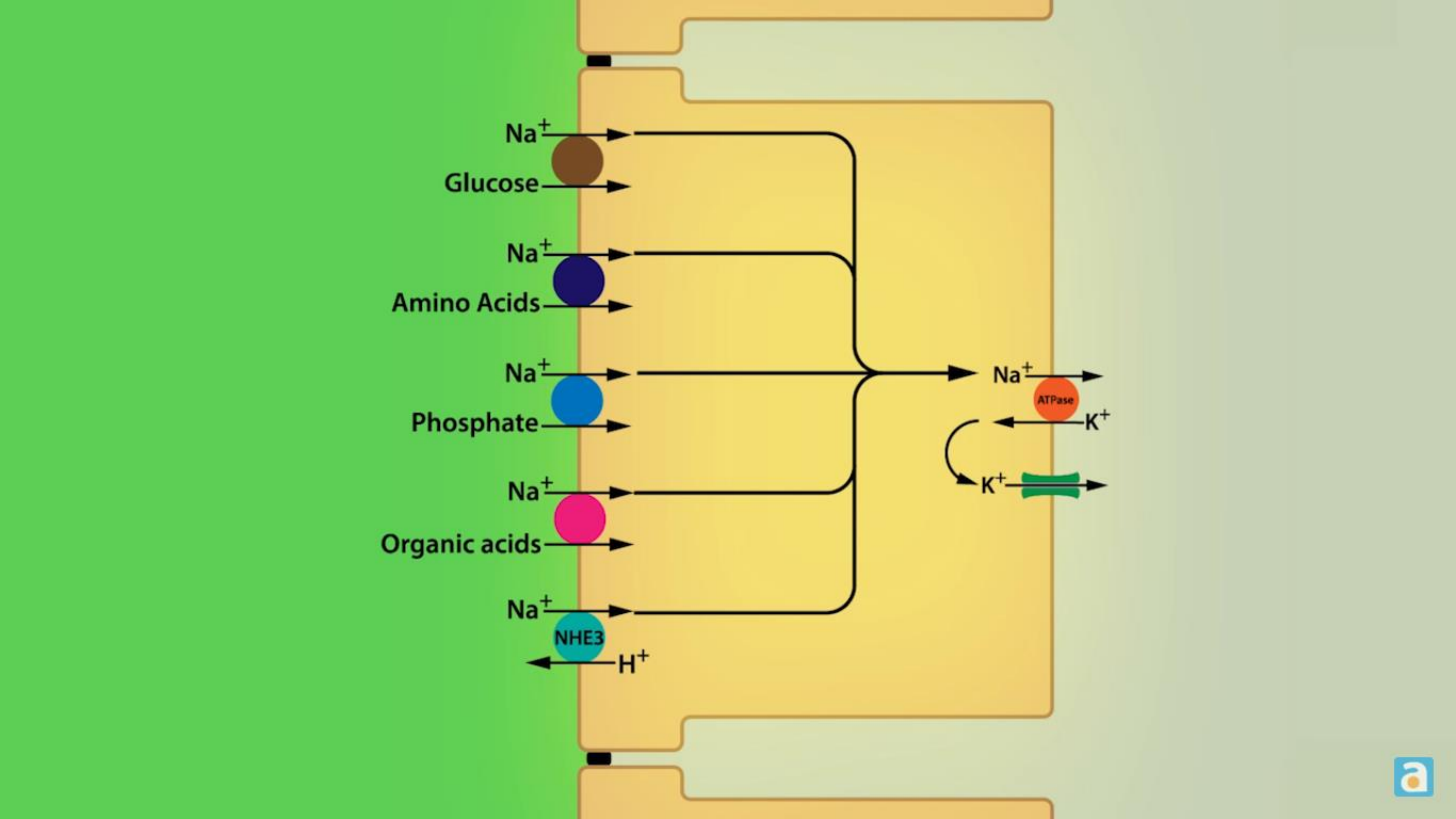


Na+
Glucose
Na+
Amino Acids
Na+
Phosphate
Na+
Organic acids

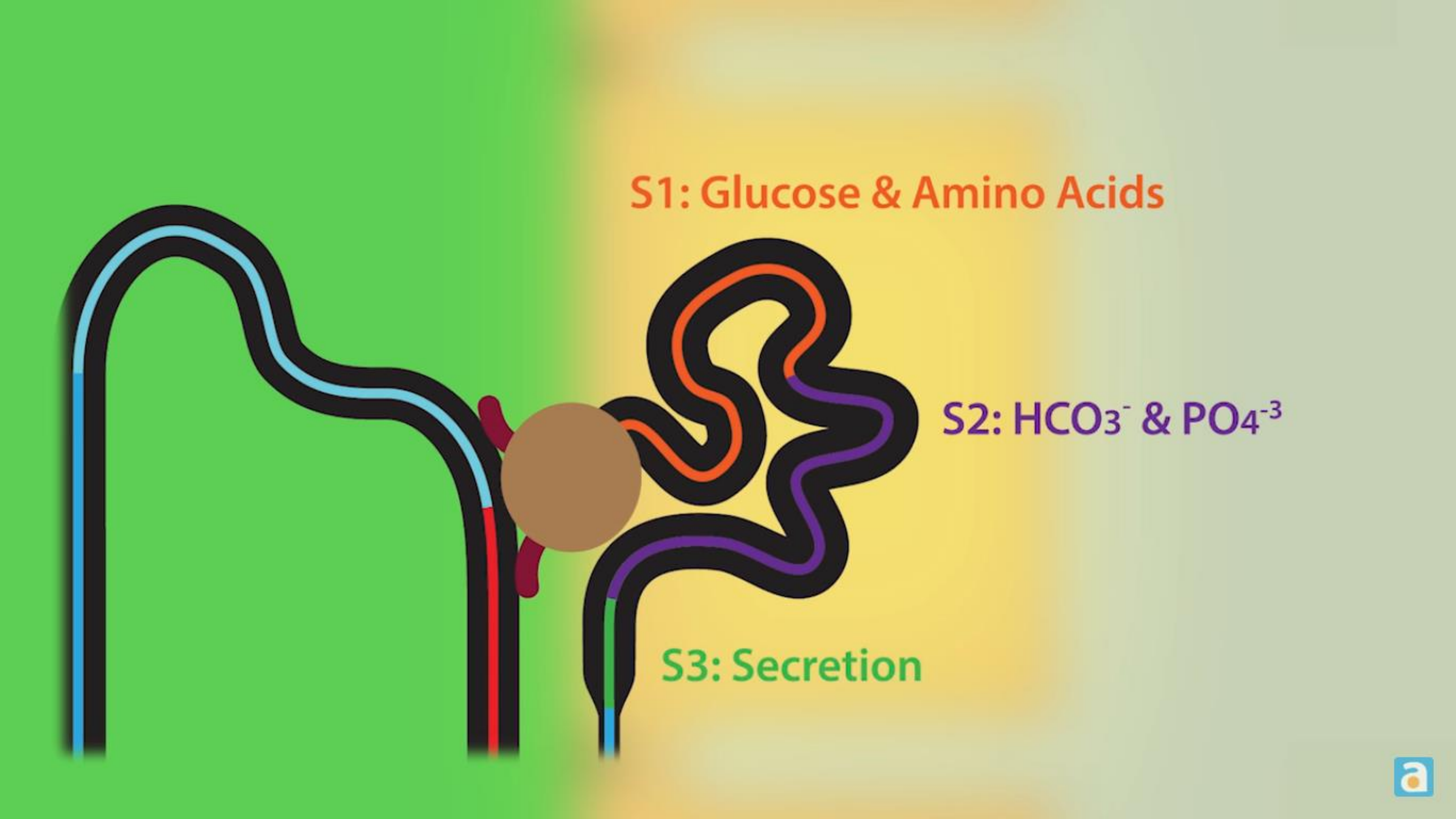

Na+
Glucose
Na+
Amino Acids
Na+
Phosphate
Na+
Organic acids
Na+
NHE3
H+

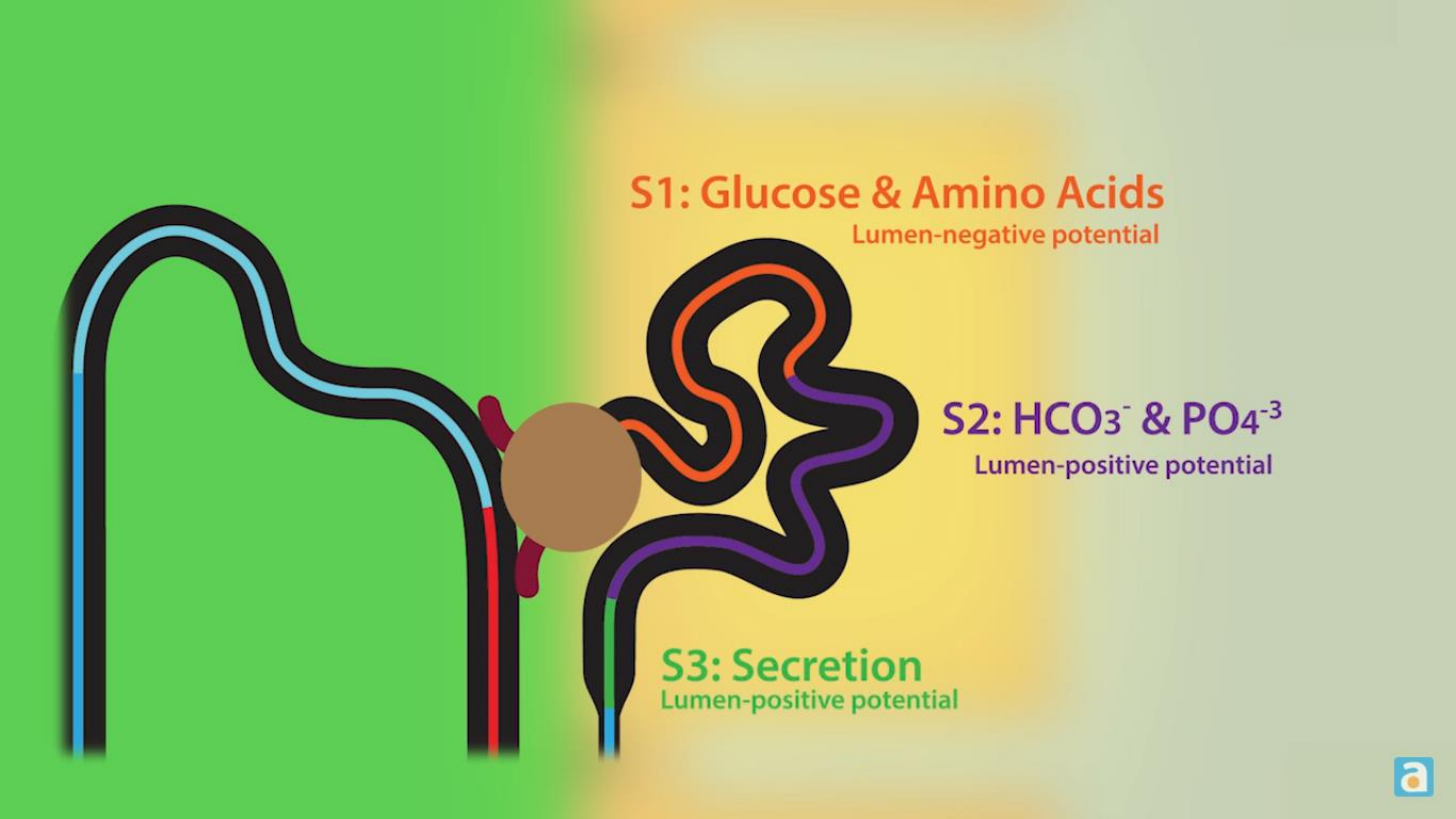


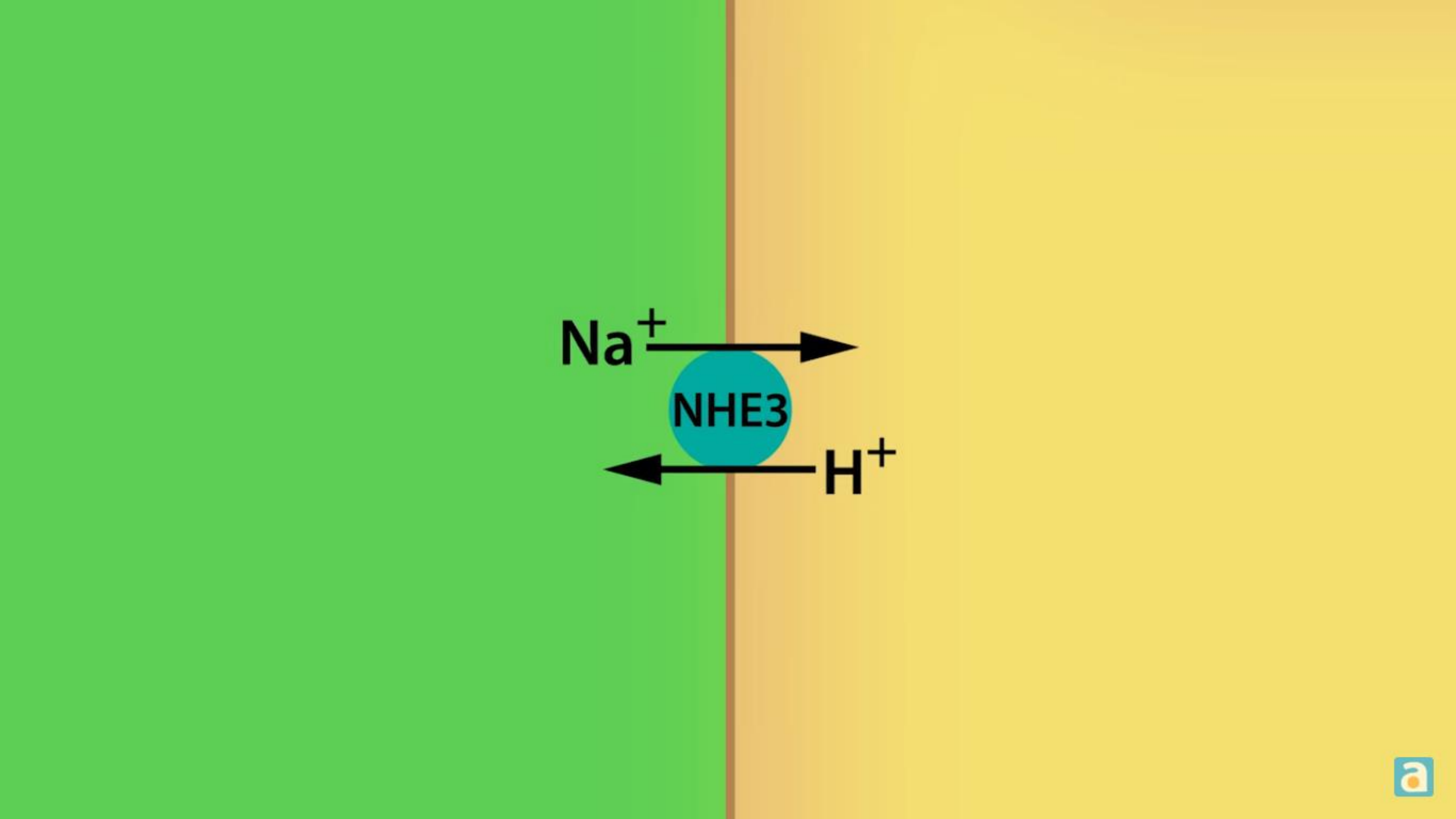
Na+
Glucose
Na+
Amino Acids
Na+
Phosphate
Na+
Organic acids
Na+
NHE3
H+
Na+
ATPase
K+



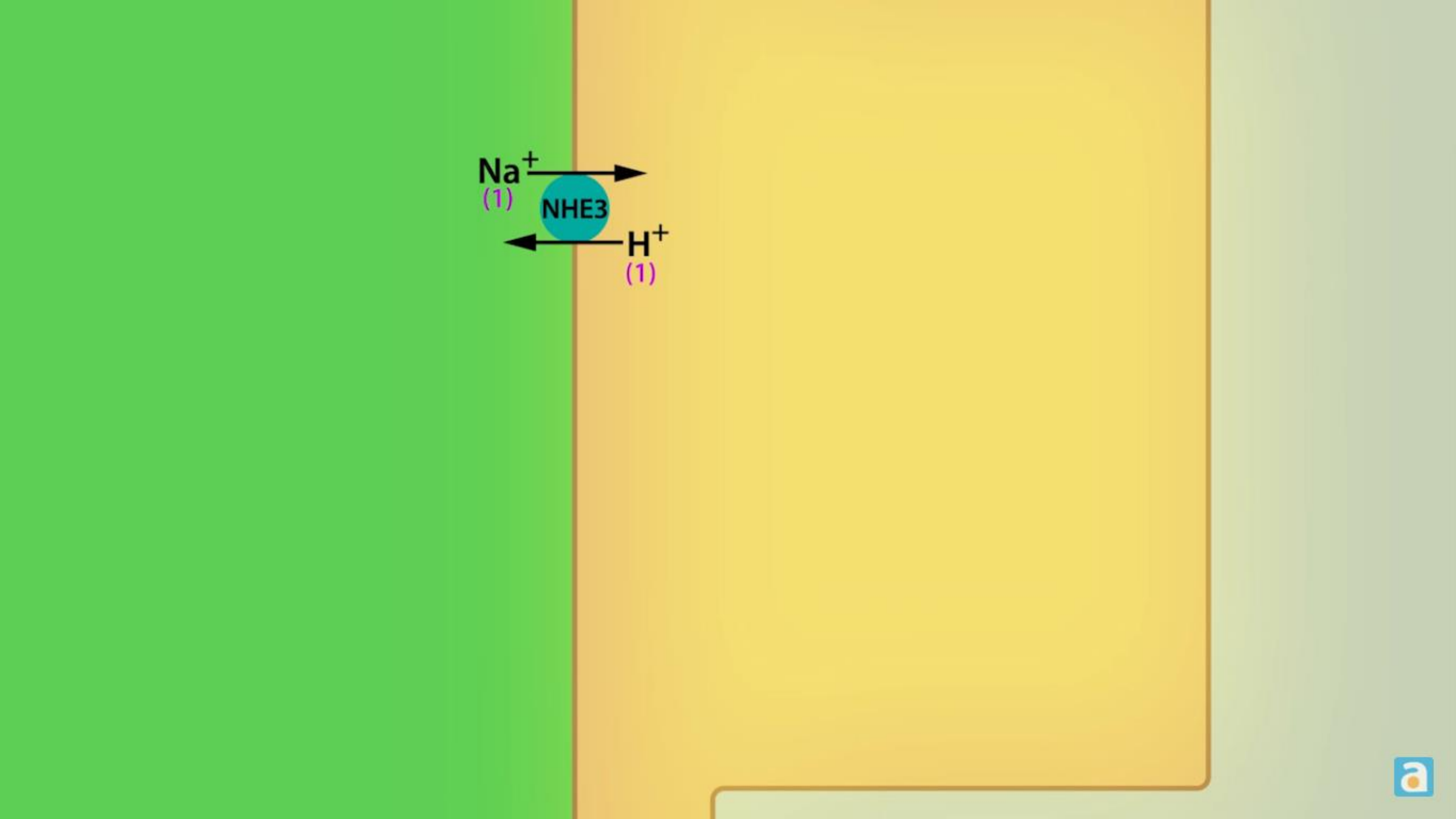
Na+
Glucose
Na+
Amino Acids
Na+
Phosphate
Na+
Organic acids
Na+
NHE3
H+
Na+
ATPase
K+
K+


S1: Glucose & Amino Acids
S2: HCO_3^- & PO_4^{-3}
S3: Secretion

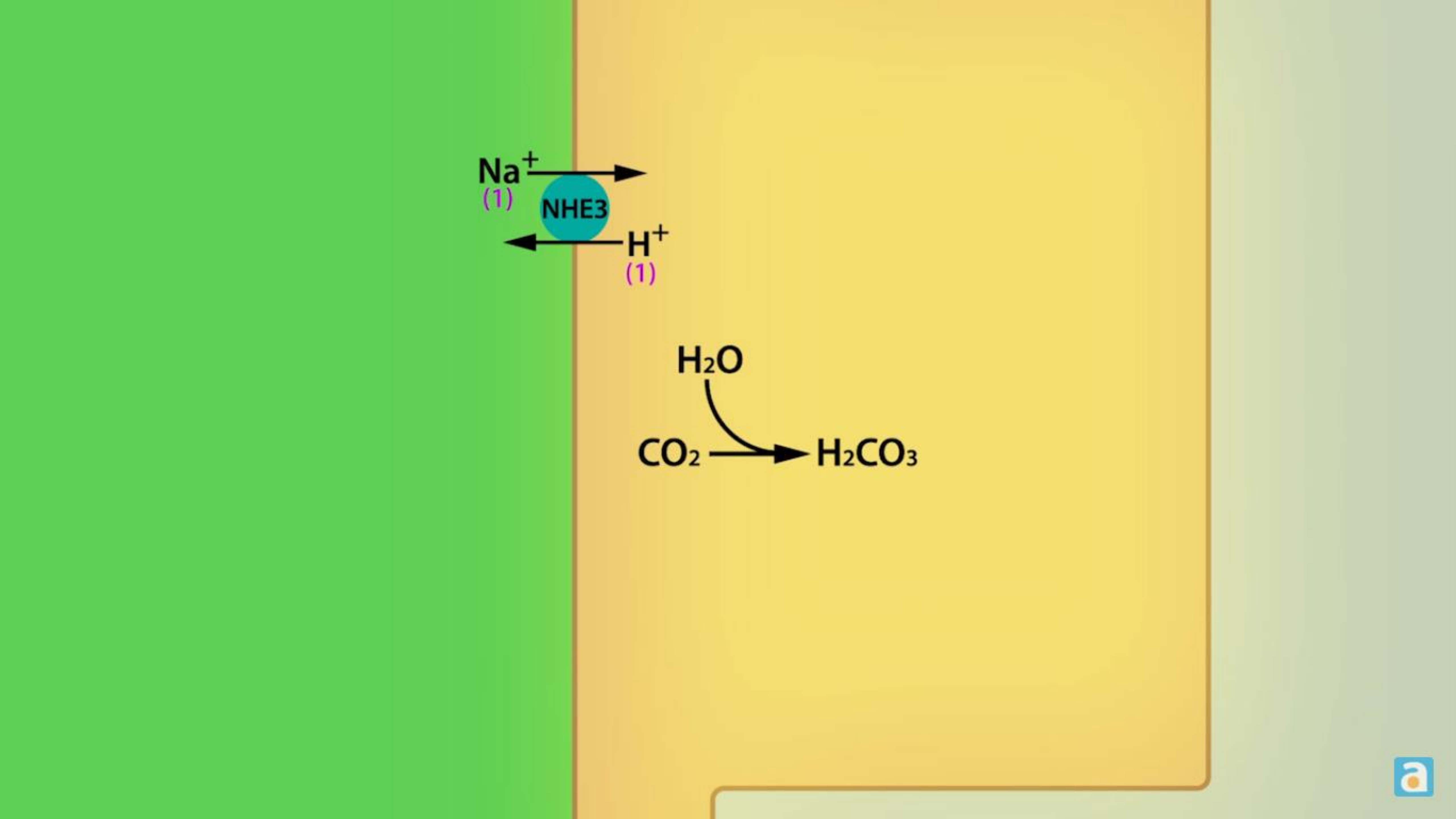

S1: Glucose & Amino Acids
Lumen-negative potential
S2: HCO_3^- & PO_4^{-3}
Lumen-positive potential
S3: Secretion
Lumen-positive potential



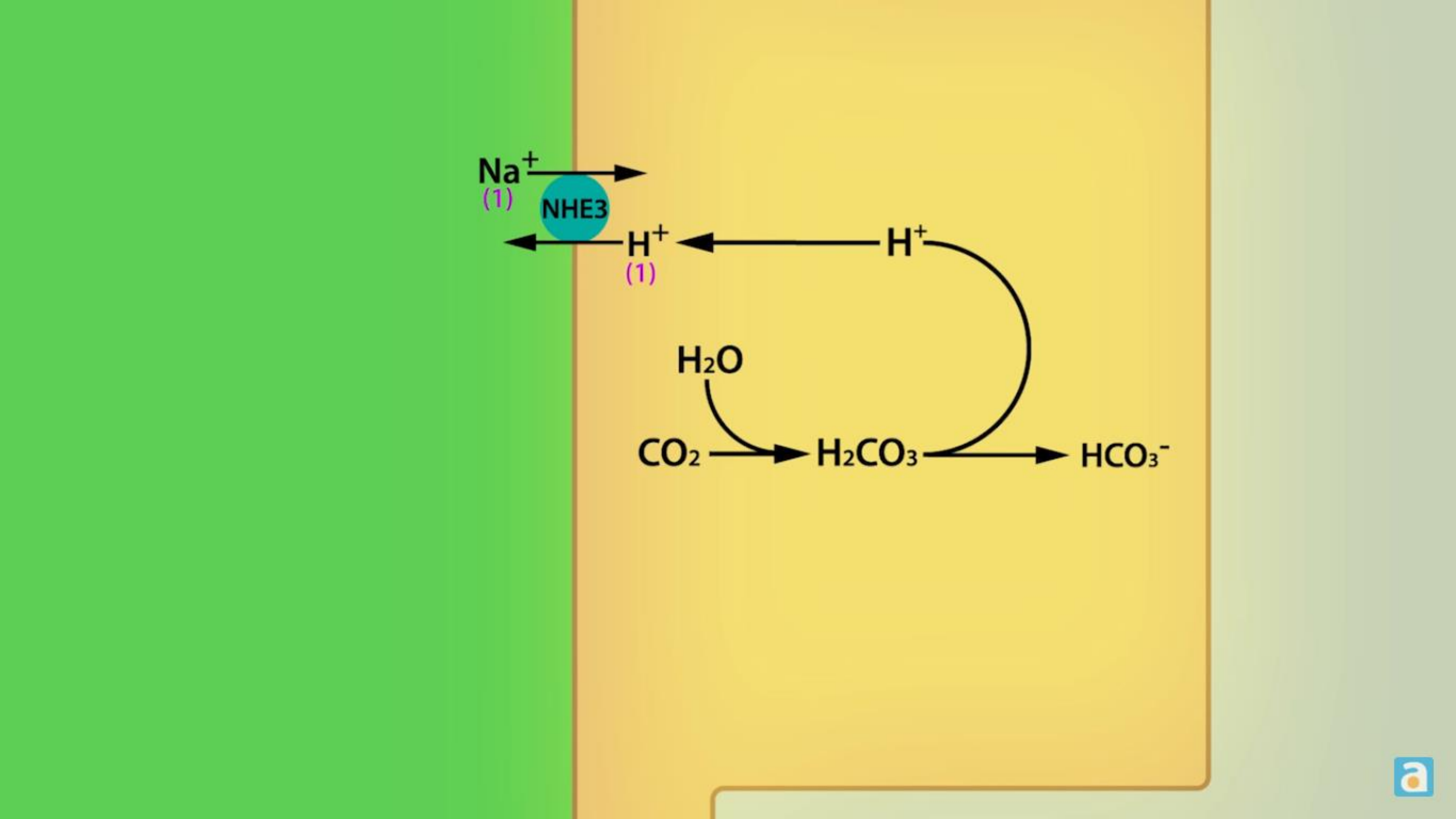
Na^+
NHE3
H^+

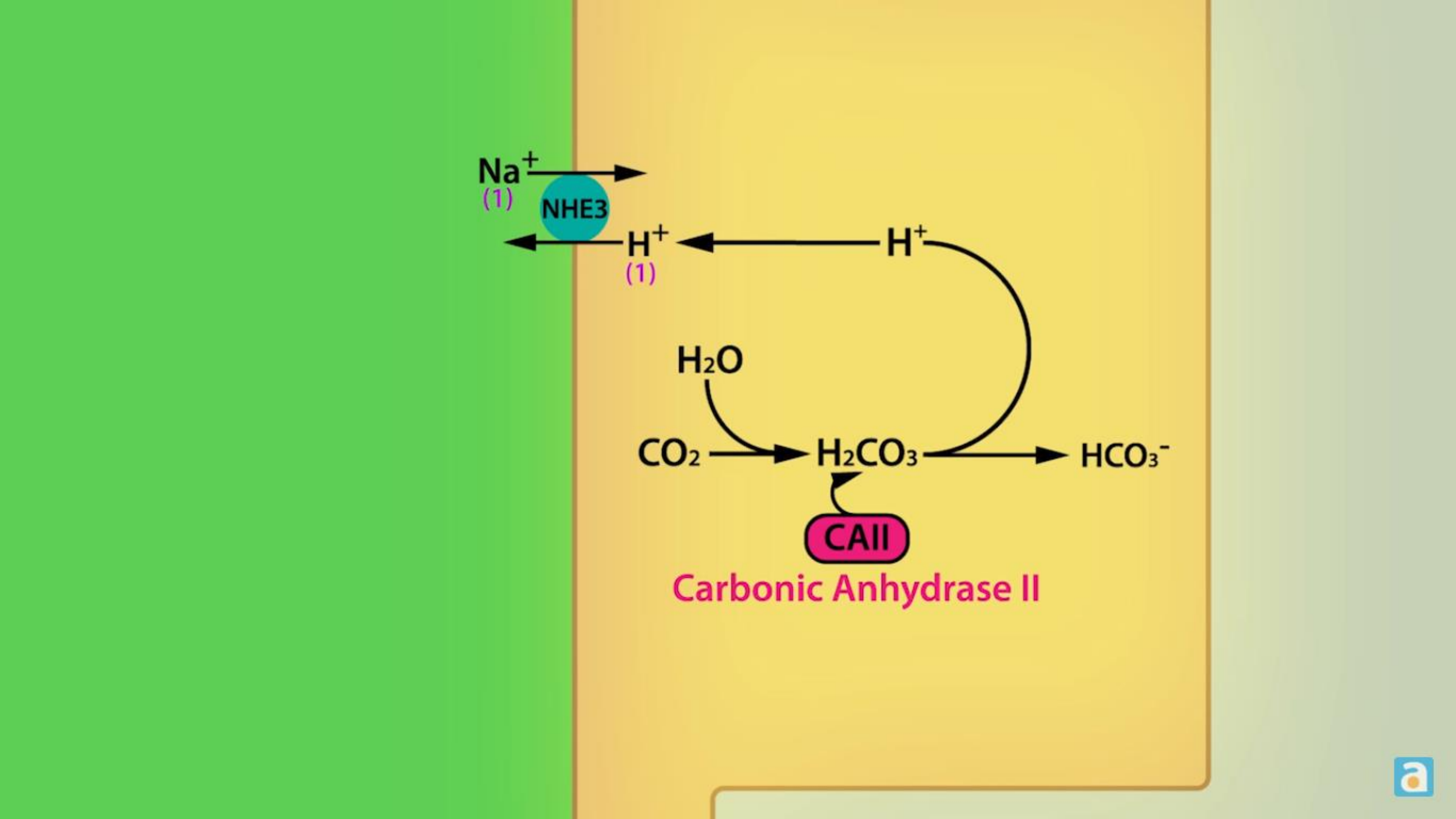


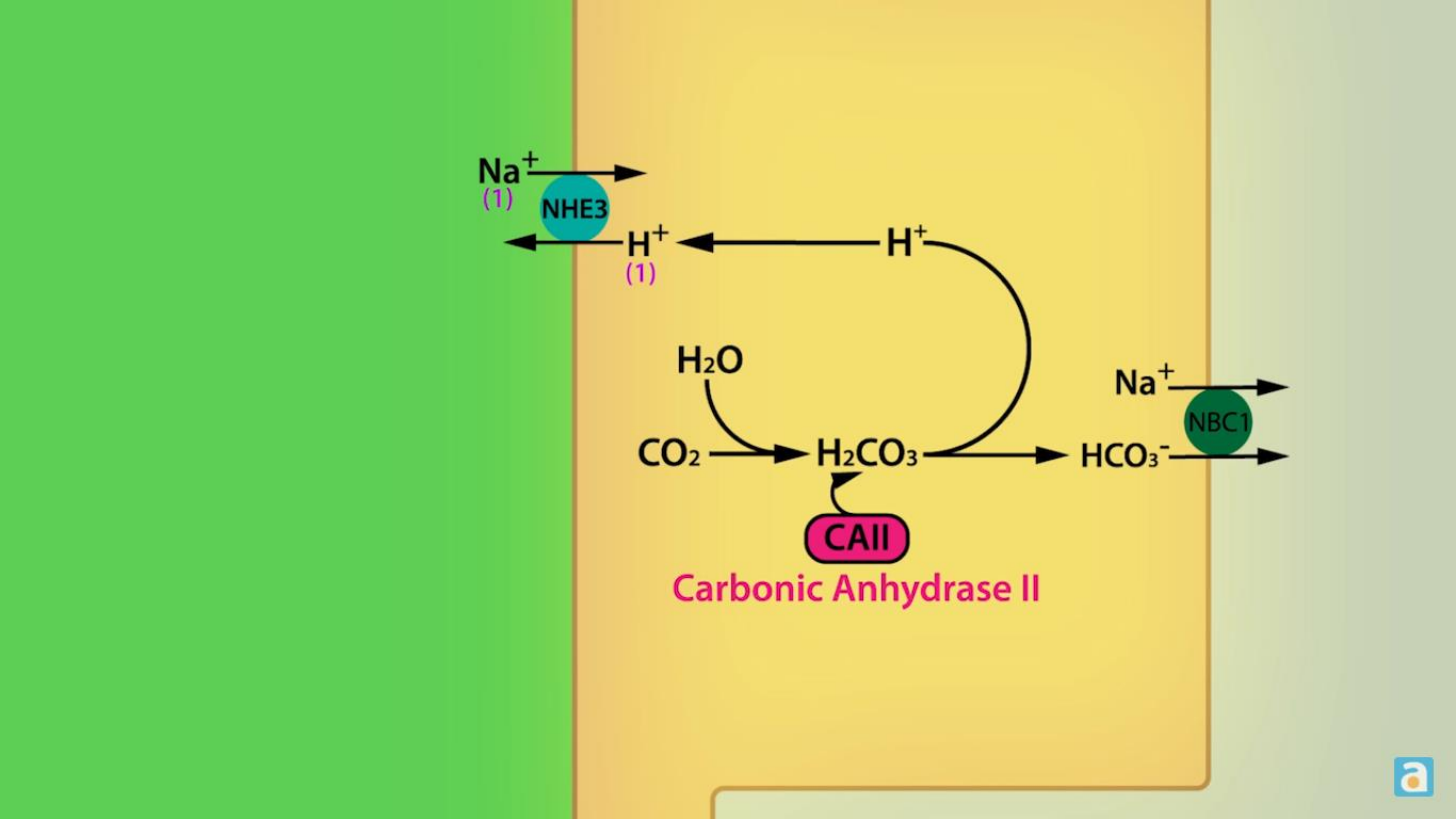
Na+
(1)
NHE3
H+
(1)

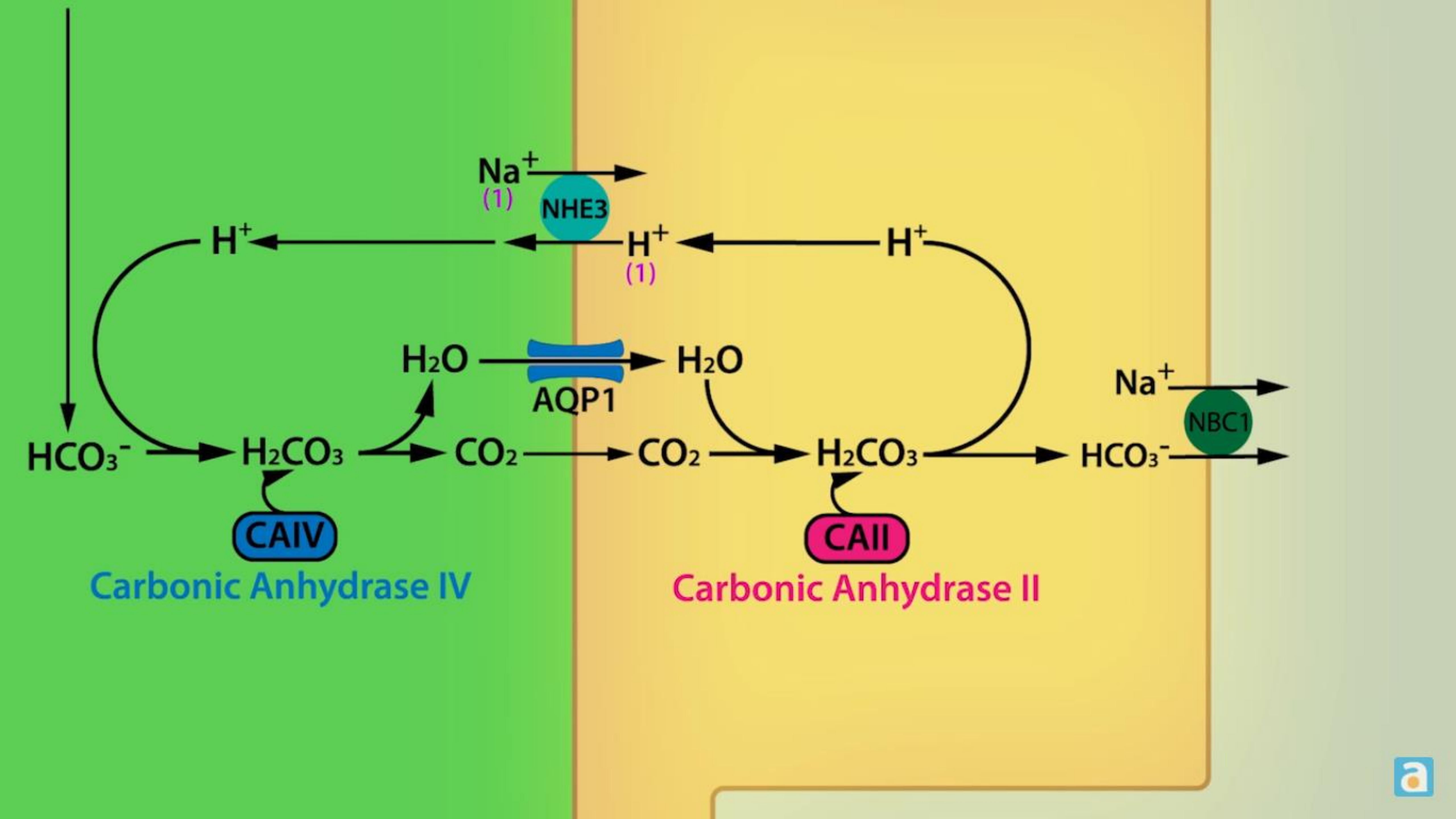


Na+
(1)
NHE3
H+
(1)
H2O
CO2
H2CO3

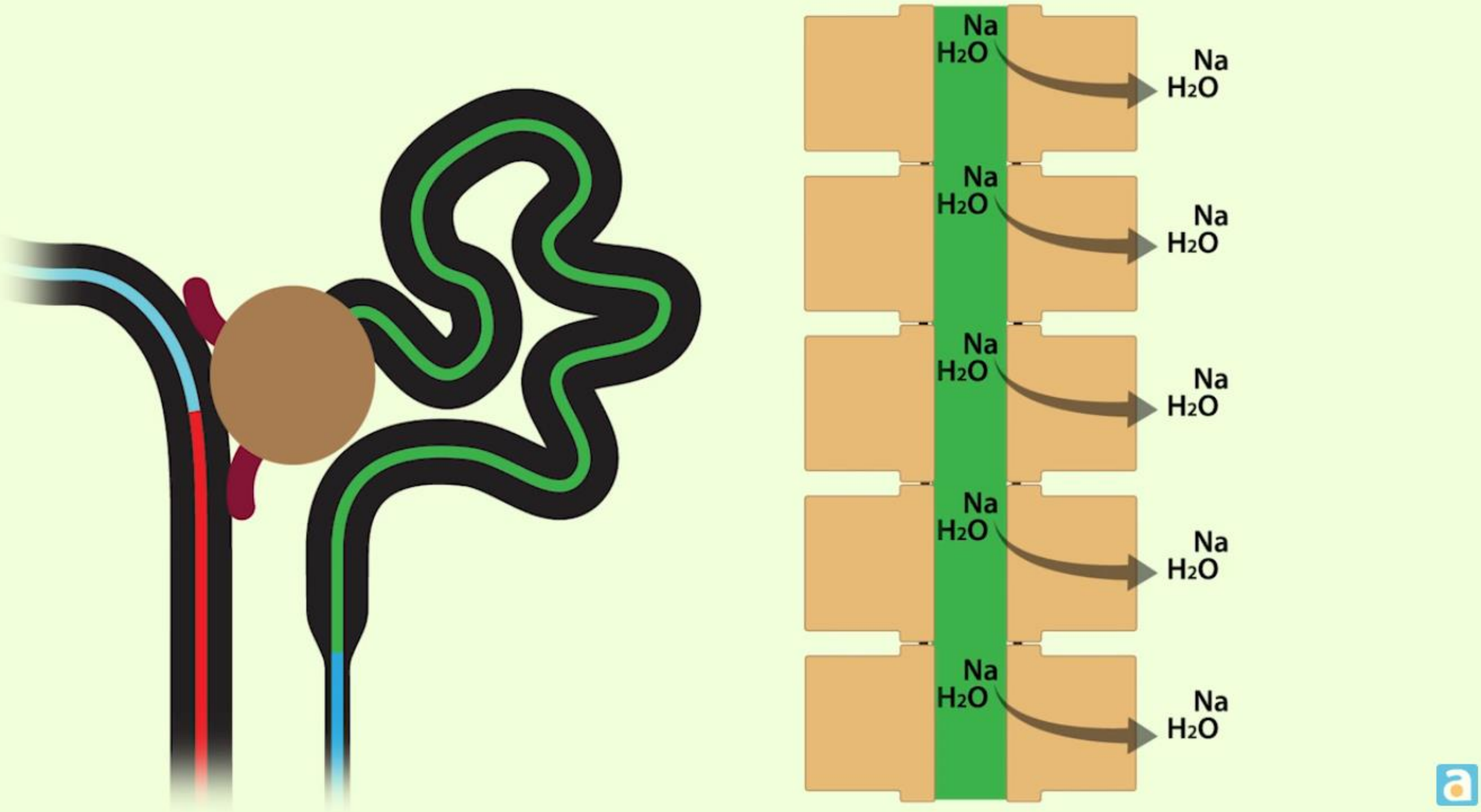

Na+
(1)
NHE3
H+
(1)
H+
H2O
CO2
H2CO3
HCO3-

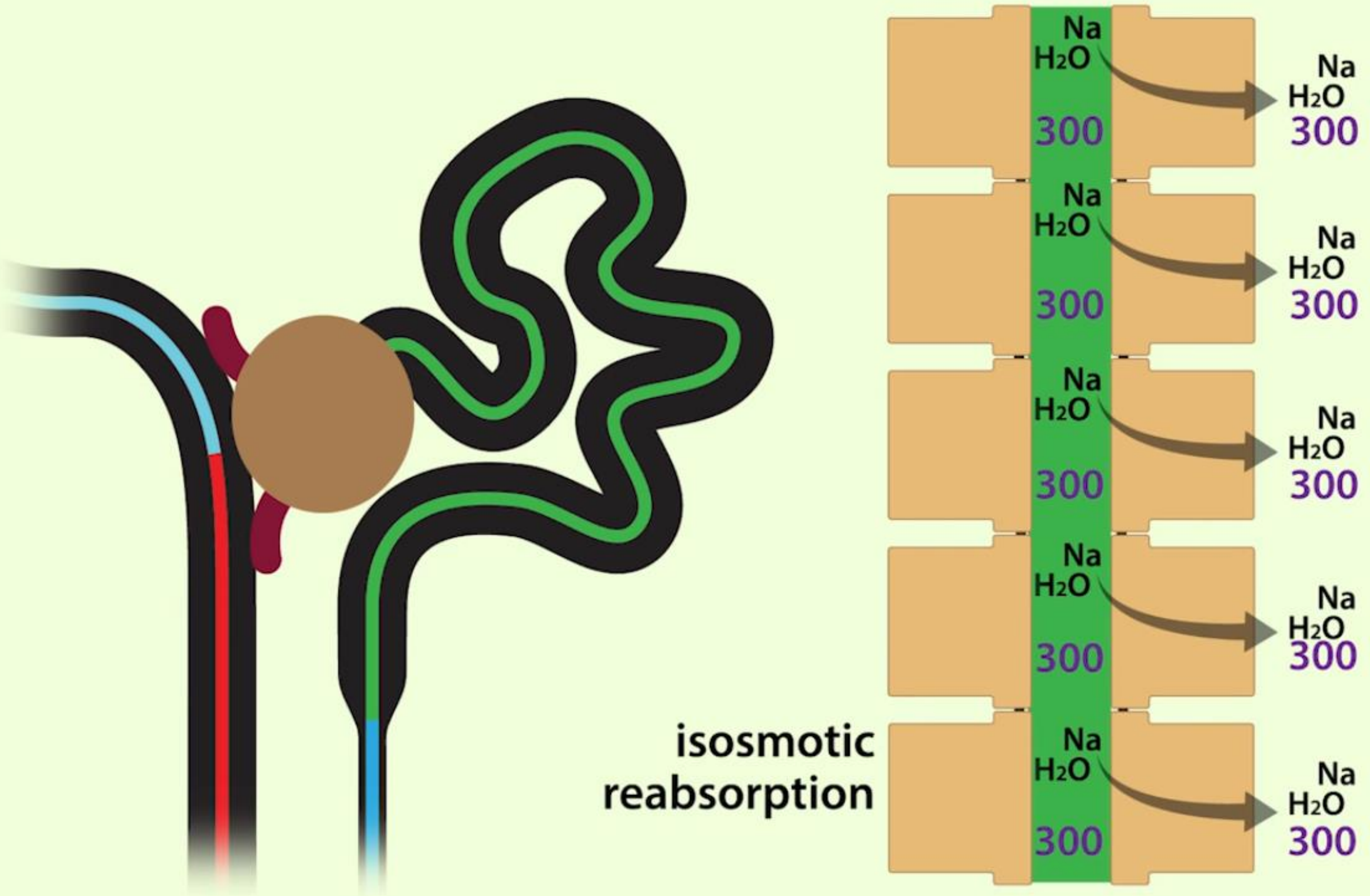

Na+
(1)
NHE3
H+
(1)
H+
H2O
CO2
H2CO3
HCO3-
CAII
Carbonic Anhydrase II

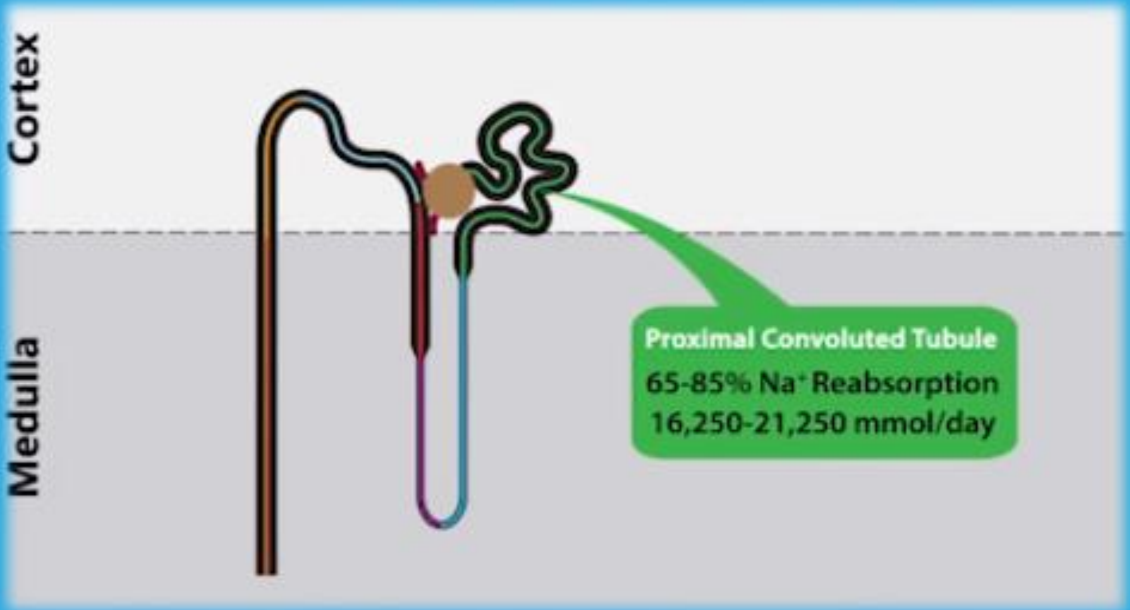

Na+
(1)
NHE3
H+
(1)
H+
H2O
CO2
H2CO3
HCO3-
Na+
NBC1
CAII
Carbonic Anhydrase II



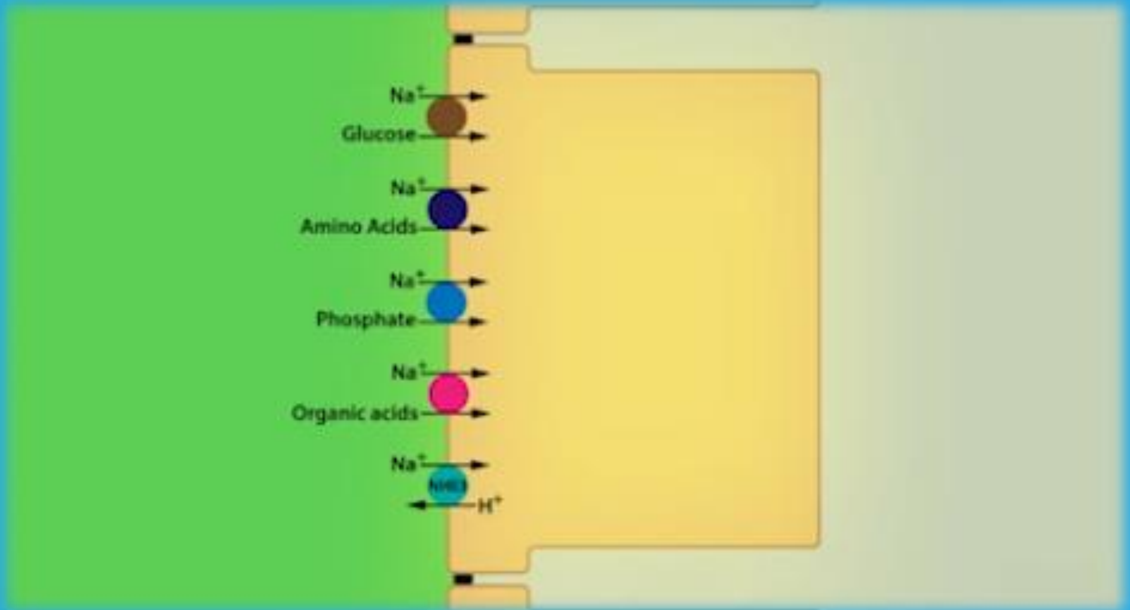
Na+
(1)
NHE3
H+
H+
(1)
H+
H2O
H2O
AQP1
Na+
NBC1
HCO3-
H2CO3
CO2
CO2
H2CO3
HCO3-
CAIV
Carbonic Anhydrase IV
CAII
Carbonic Anhydrase II


Na
H2O
Na
H2O
Na
H2O
Na
H2O
Na
H2O
Na
H2O
Na
H2O
Na
H2O
Na
H2O
Na
H2O

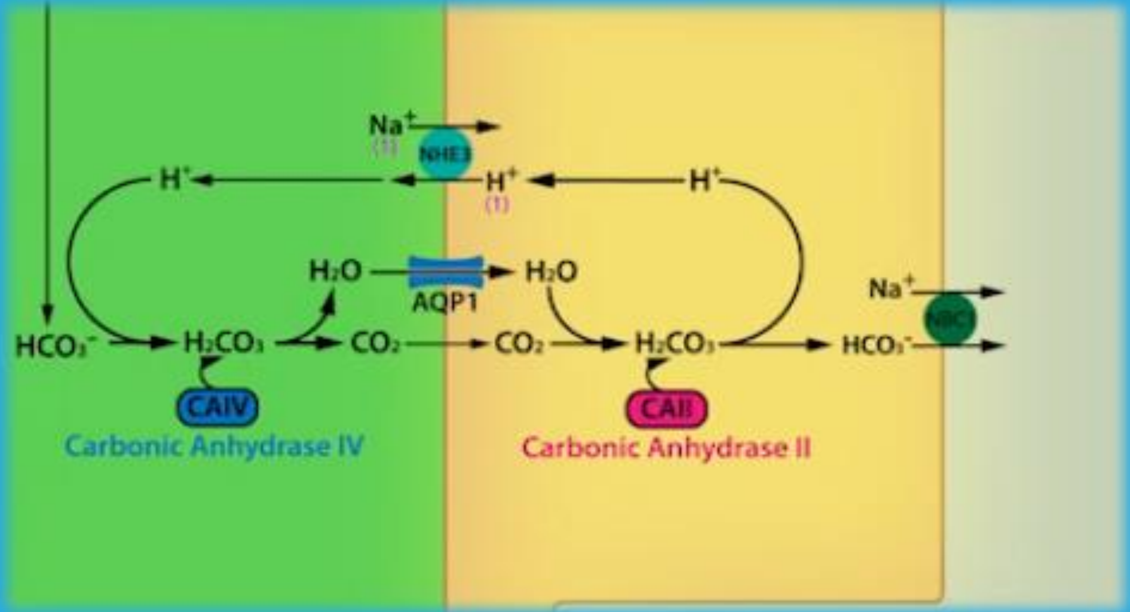

isosmotic
reabsorption
Na
H2O
300
Na
H2O
300
Na
H2O
300
Na
H2O
300
Na
H2O
300
Na
H2O
300
Na
H2O
300
Na
H2O
300
Na
H2O
300
Na
H2O
300



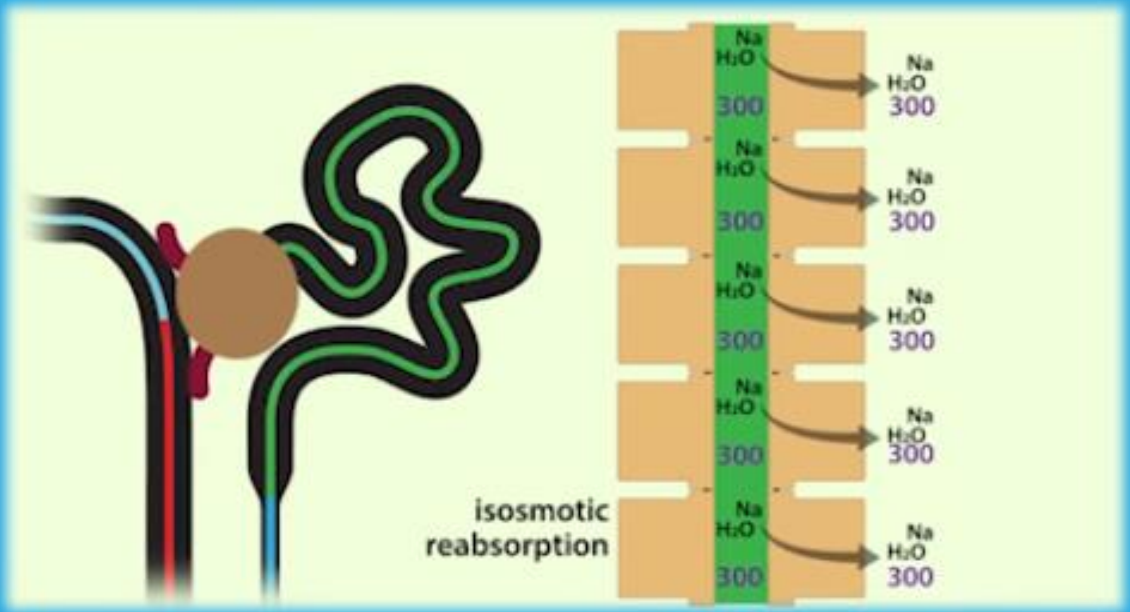
Cortex
Medulla
Proximal Convoluted Tubule
65-85% Na⁺ Reabsorption
16,250-21,250 mmol/day



Na⁺
Glucose
Na⁺
Amino Acids
Na⁺
Phosphate
Na⁺
Organic acids
Na⁺
H⁺



Na⁺
NHE3
H⁺
H⁺
H⁺
H₂O
AQP1
H₂O
Na⁺
HCO₃⁻
H₂CO₃
CO₂
CO₂
H₂CO₃
HCO₃⁻
CAIV
Carbonic Anhydrase IV
CAII
Carbonic Anhydrase II



Na
H₂O
300
isosmotic
reabsorption

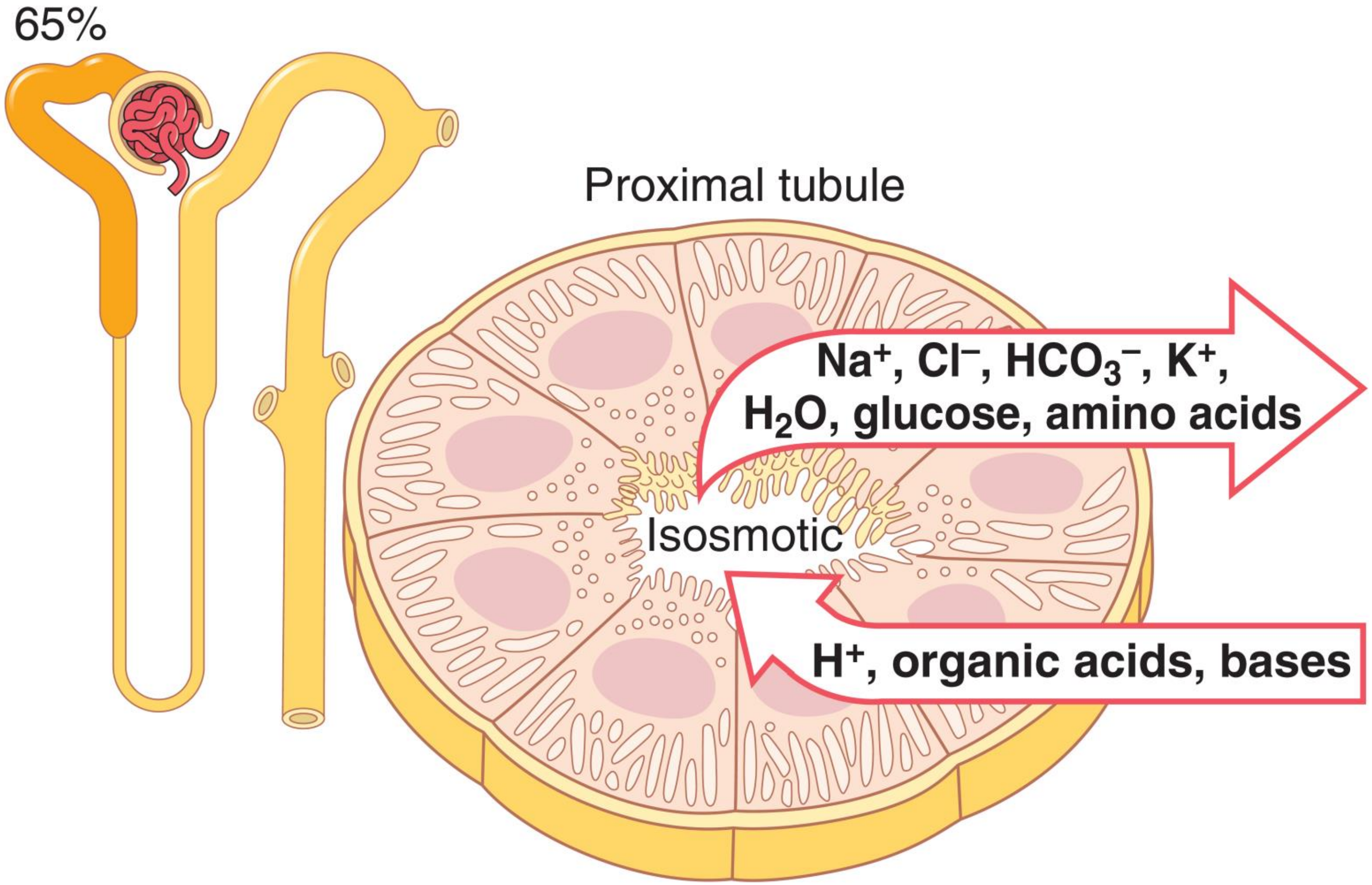
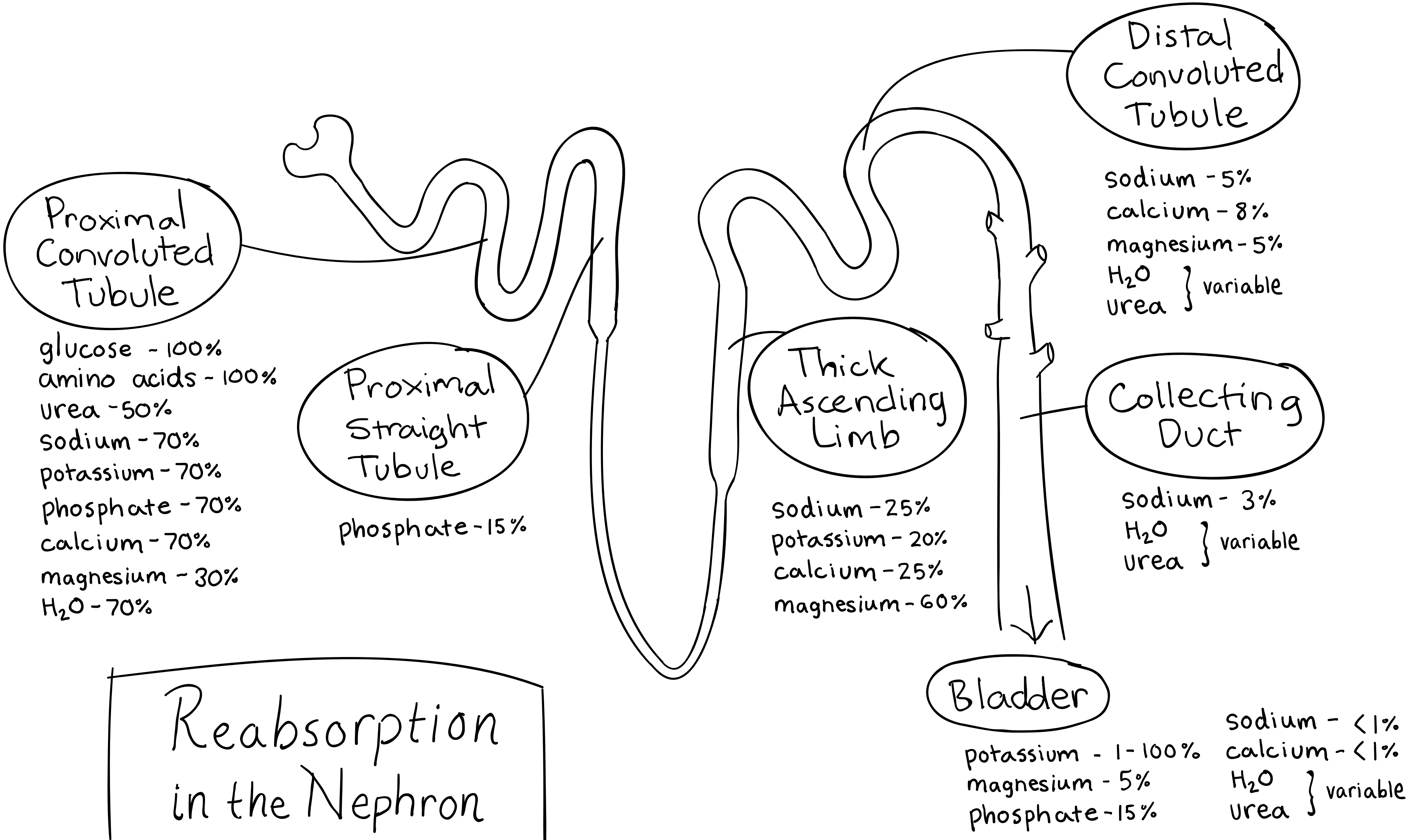
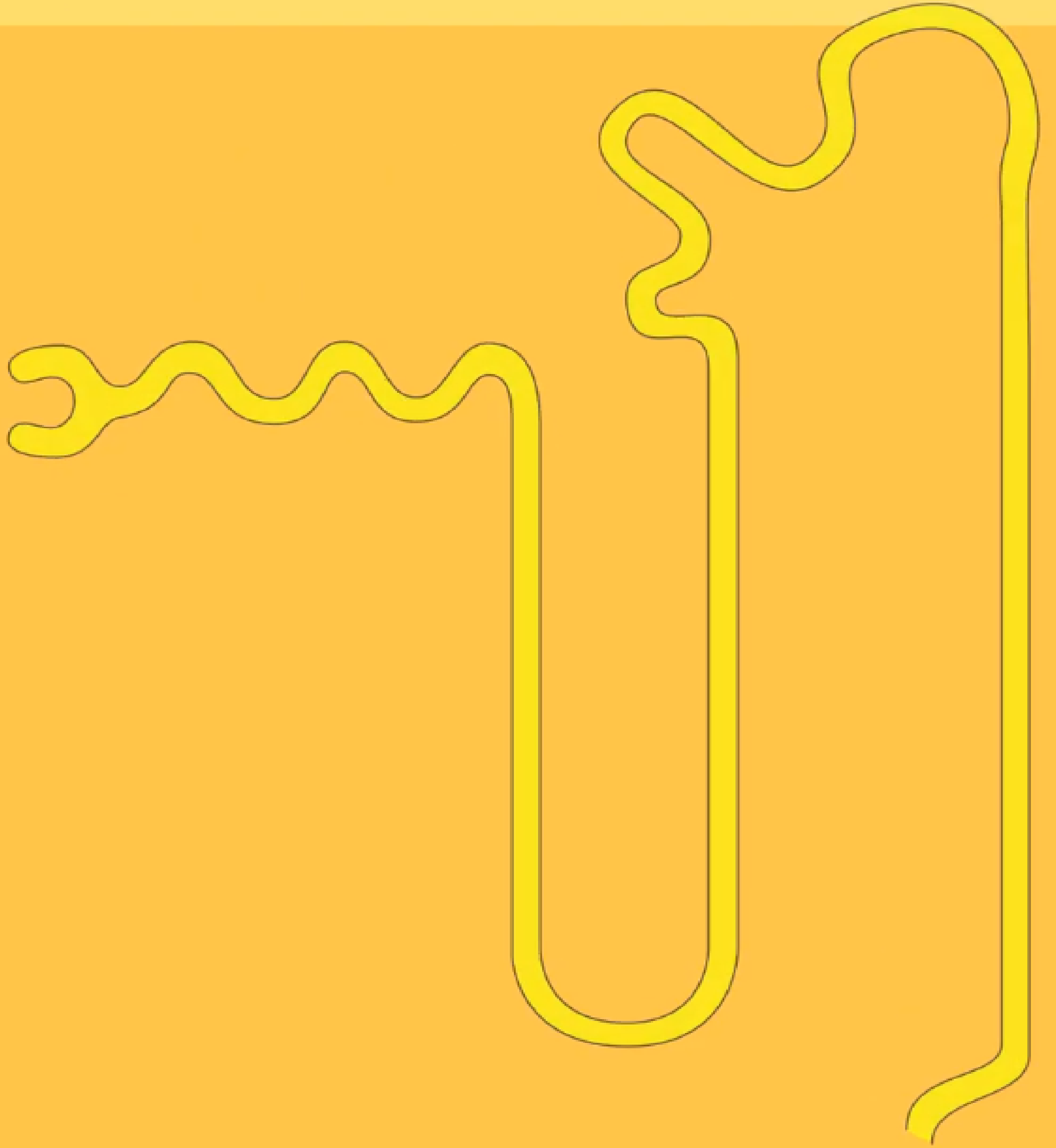
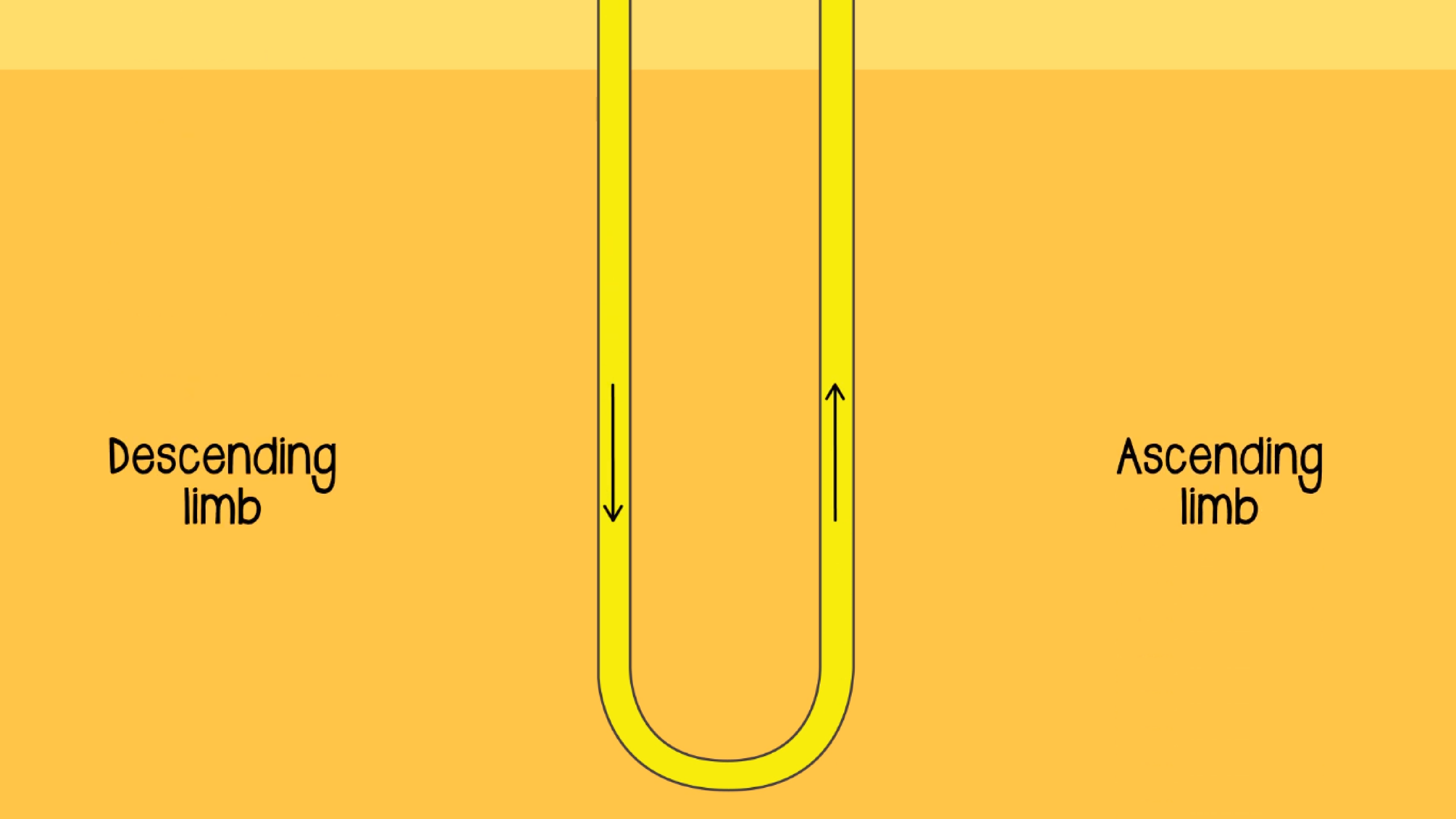


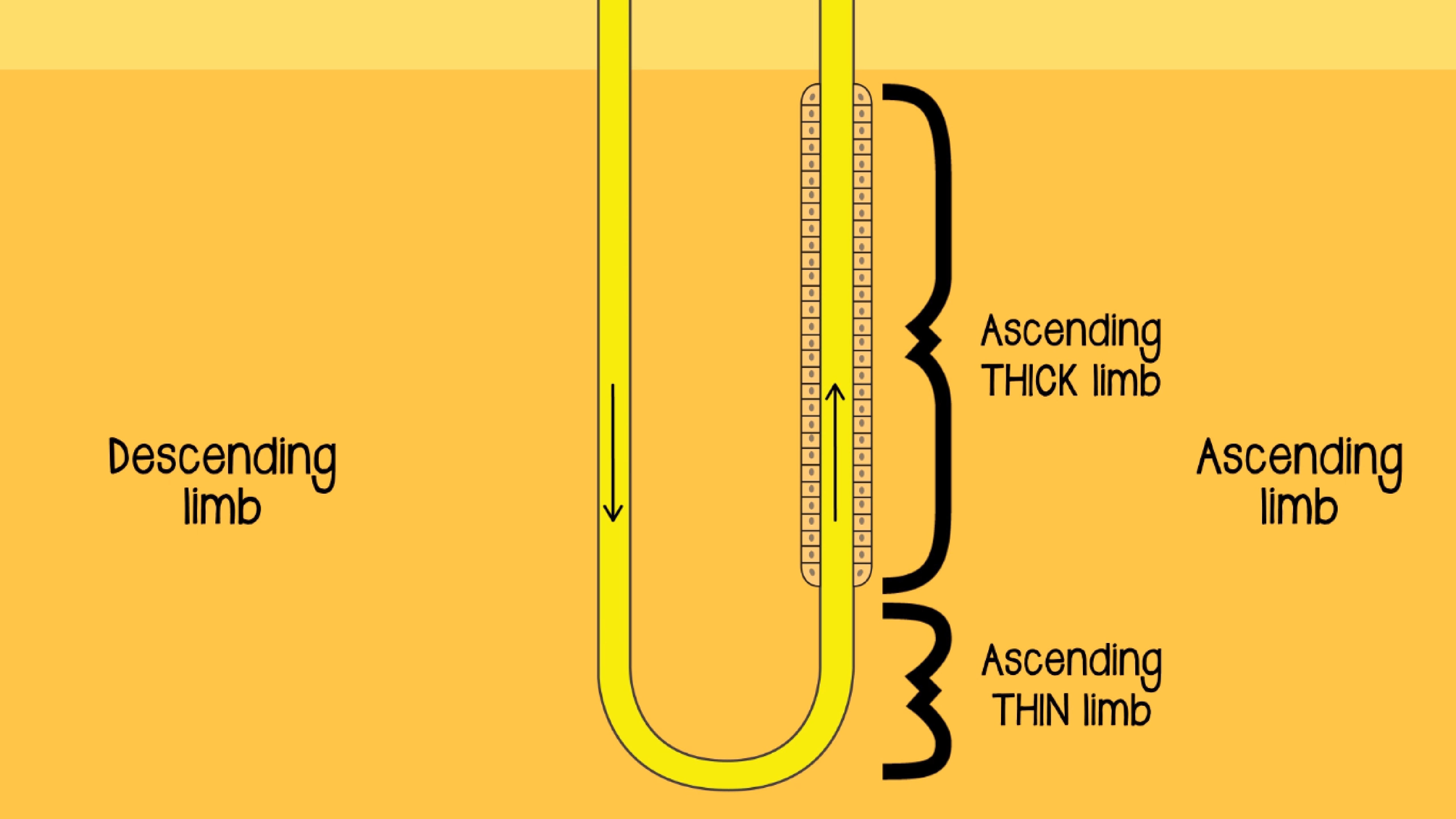
Figure 28-6. Cellular ultrastructure and primary transport characteristics of the proximal tubule. The proximal tubules reabsorb about 65 percent of the filtered sodium, chloride, bicarbonate, and potassium and essentially all the filtered glucose and amino acids. The proximal tubules also secrete organic acids, bases, and hydrogen ions into the tubular lumen.

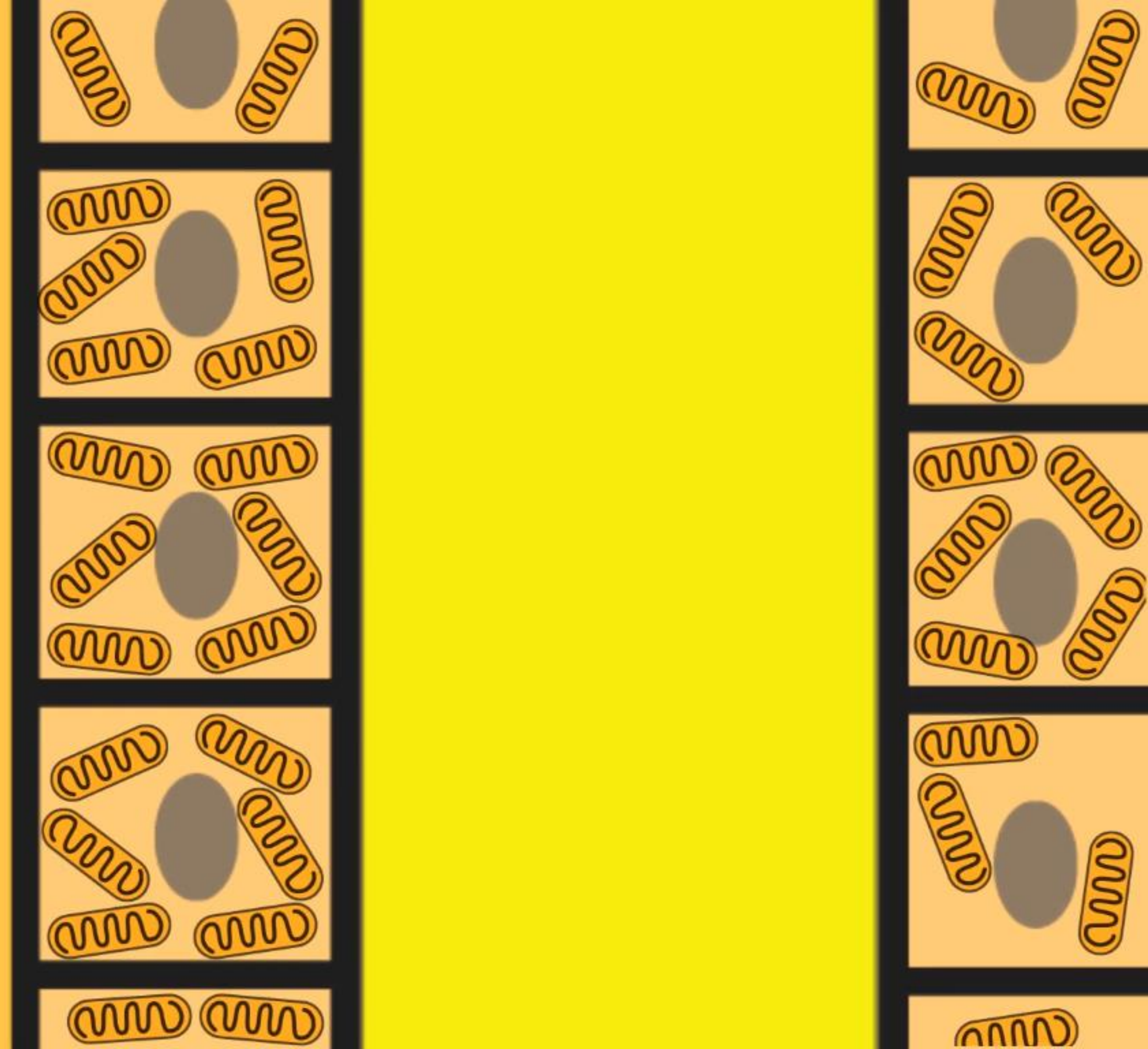
Reabsorption in the Nephron

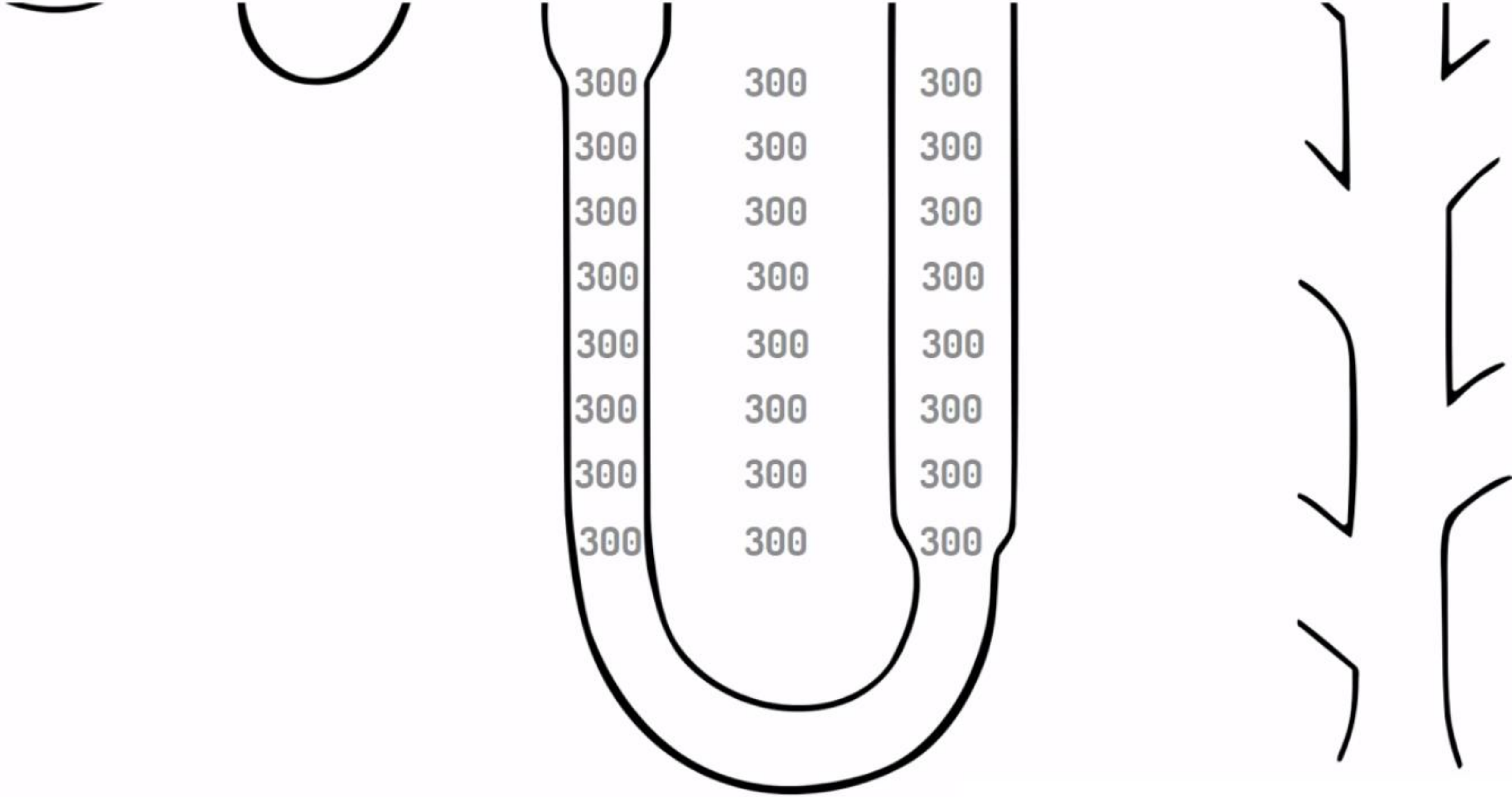


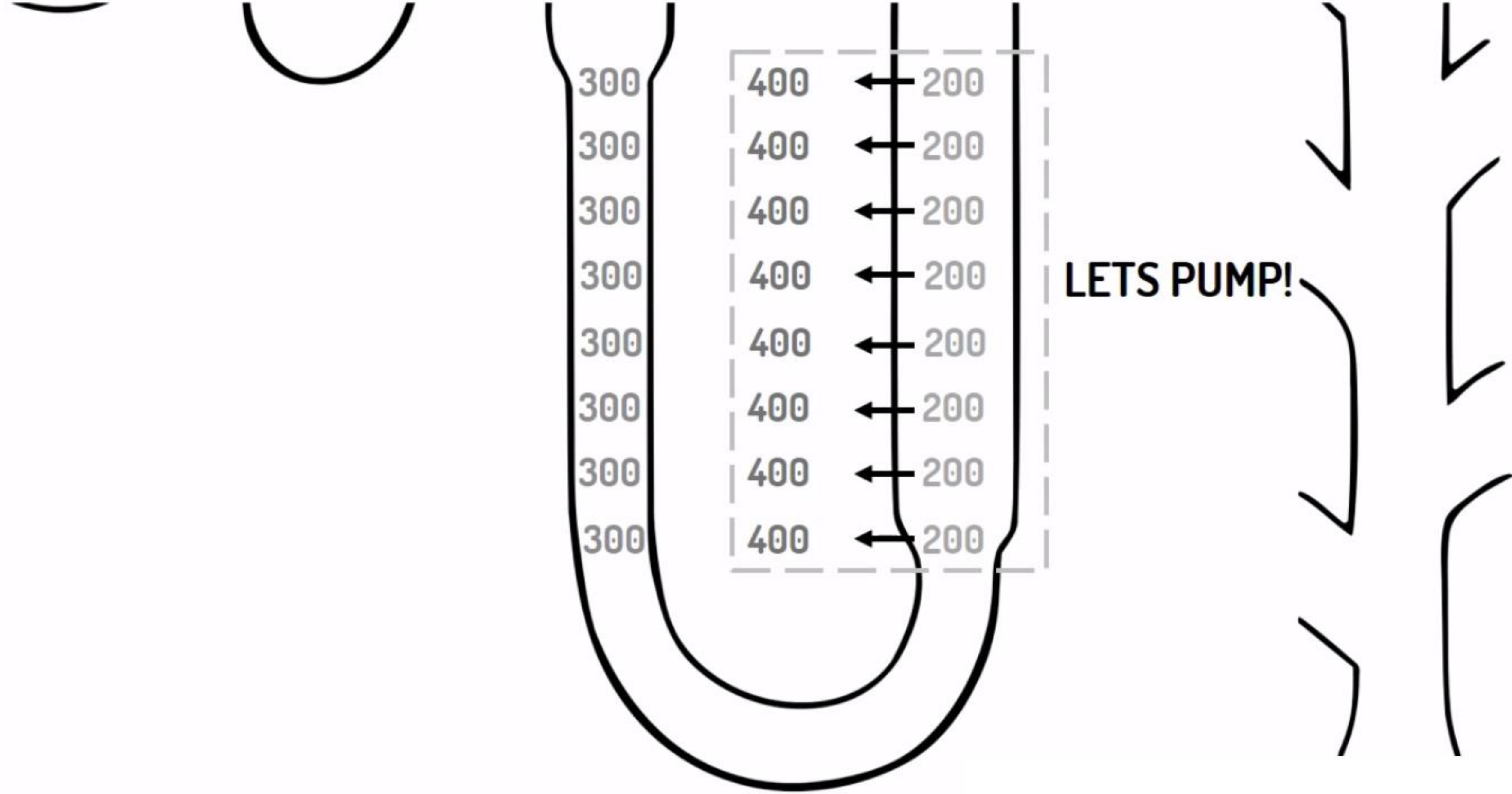


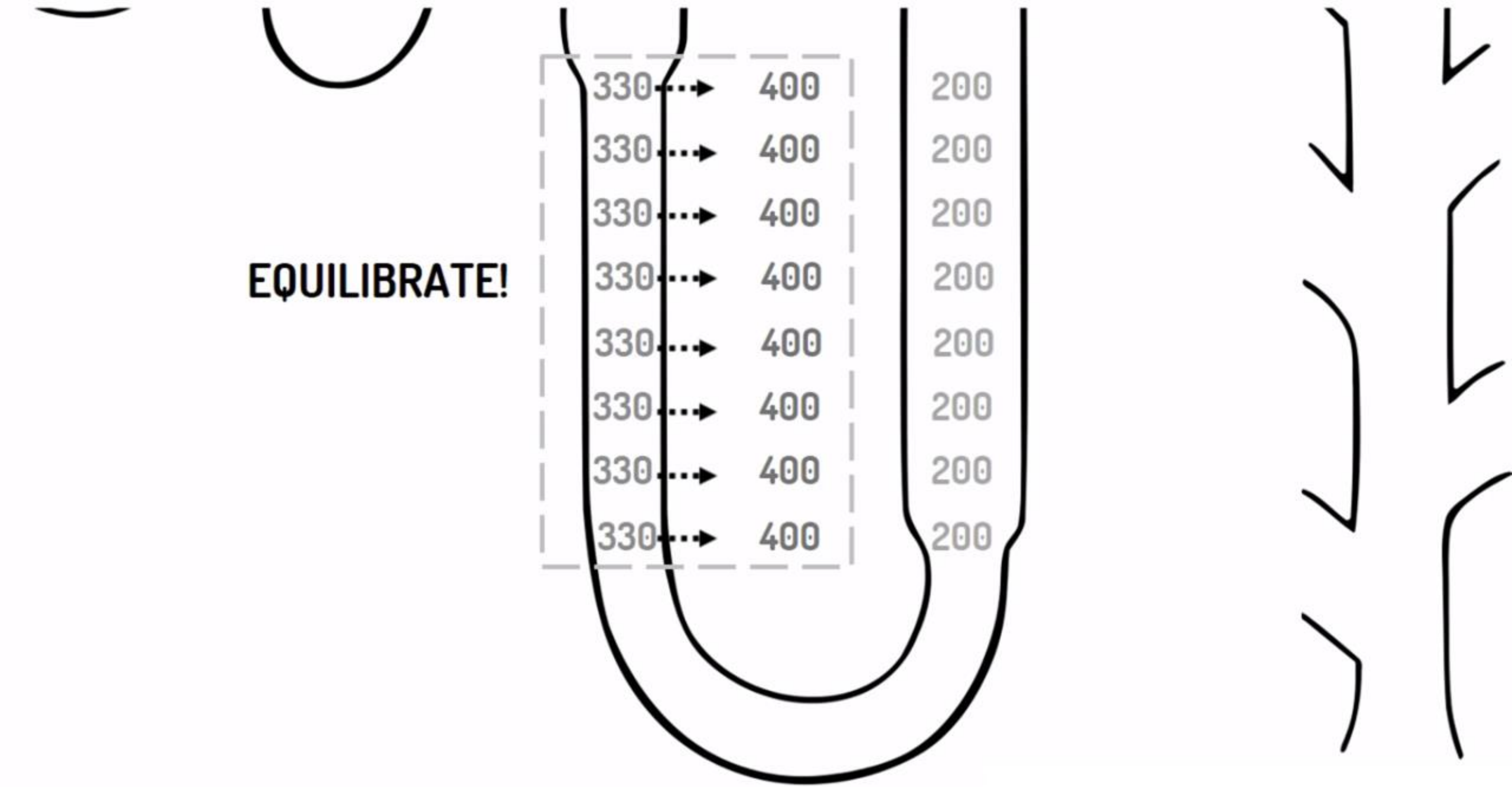

Descending limb
Ascending limb


Descending limb
Ascending THICK limb
Ascending limb
Ascending THIN limb

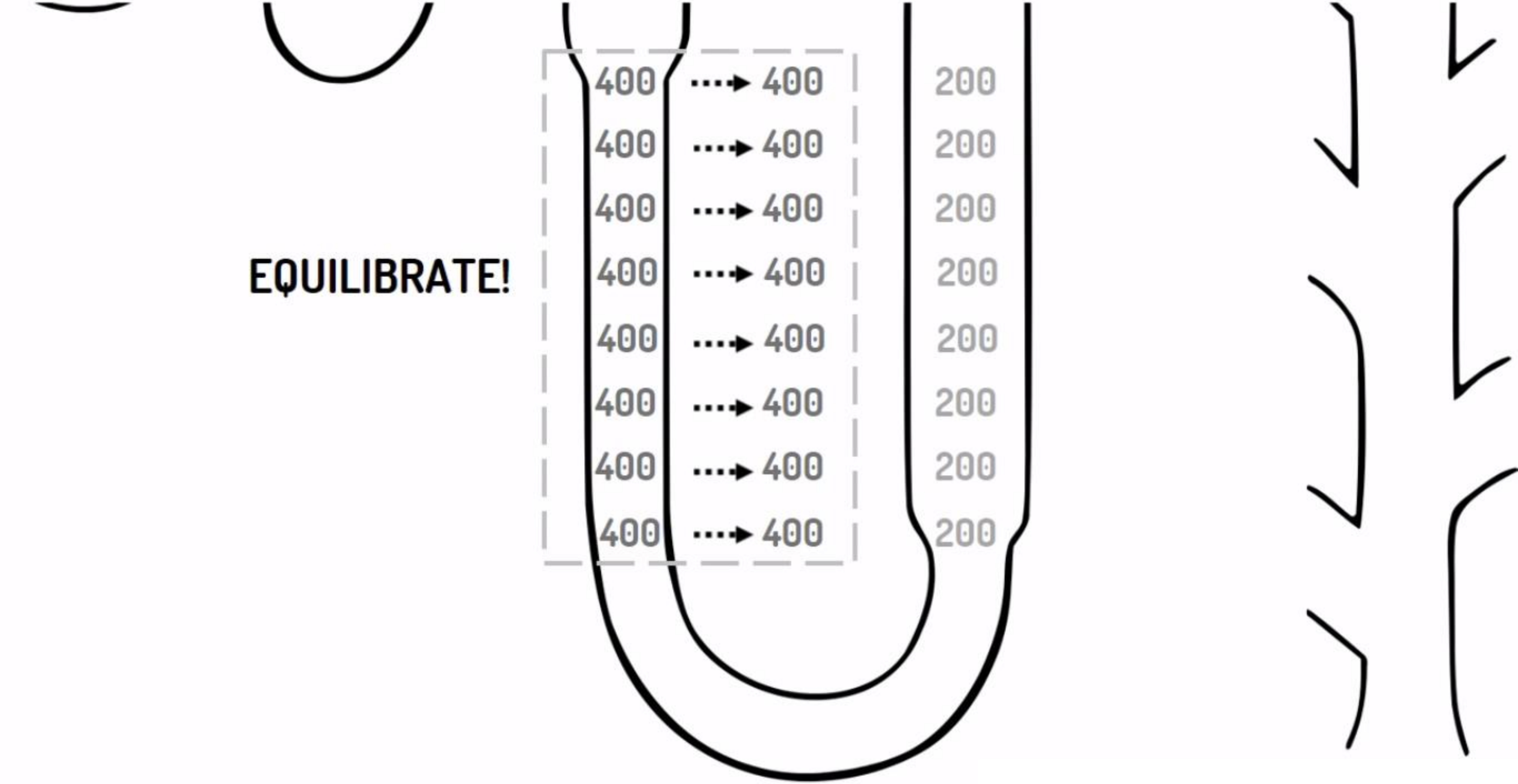


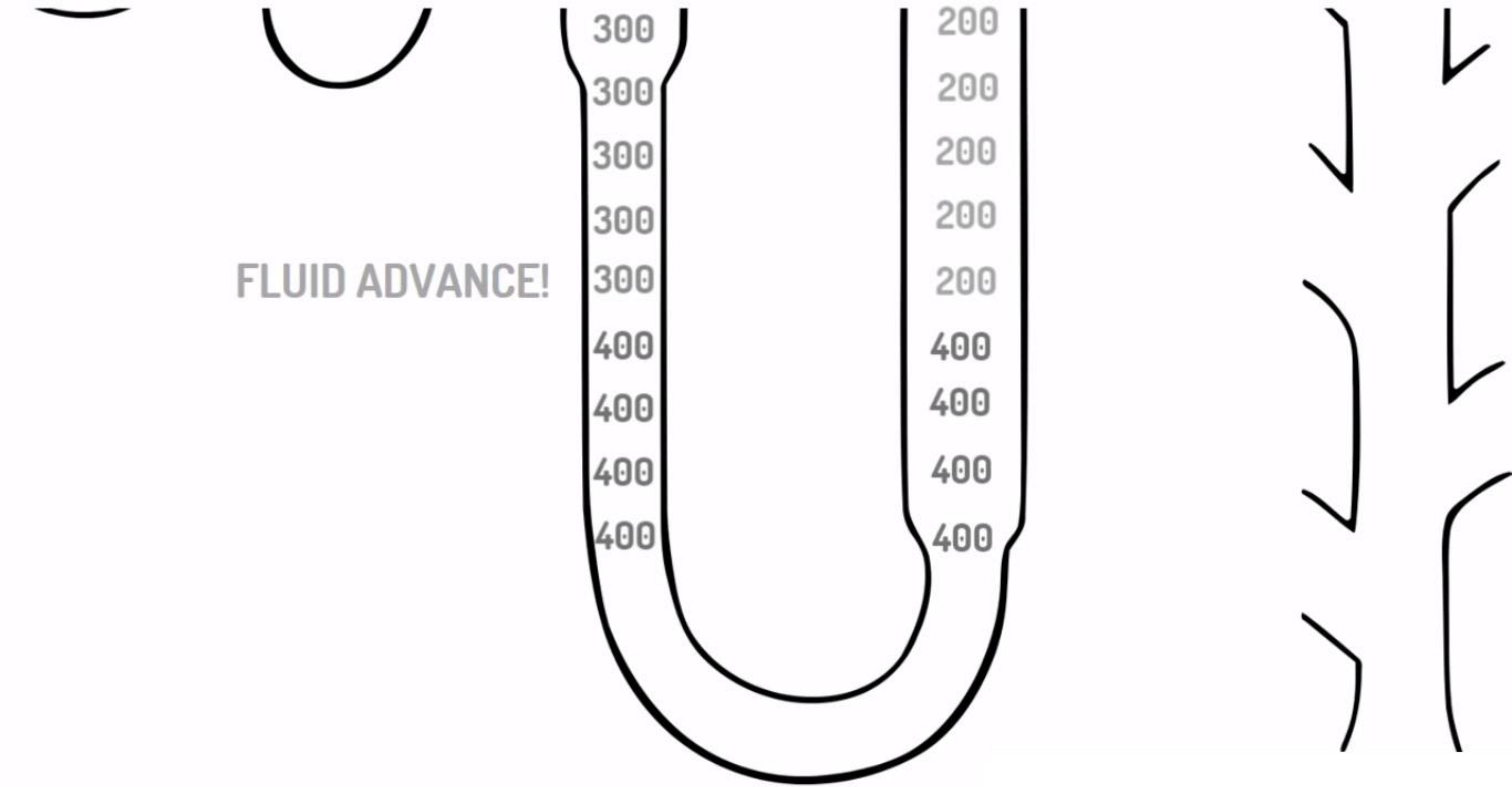

300 300 300
300 300 300
300 300 300
300 300 300
300 300 300
300 300 300
300 300 300
300 300 300


300
300
300
300
300
300
300
300
400
400
400
400
400
400
400
400
200
200
200
200
200
200
200
200
LETS PUMP!


EQUILIBRATE!
330 400 200
330 400 200
330 400 200
330 400 200
330 400 200
330 400 200
330 400 200
330 400 200

EQUILIBRATE!





FLUID ADVANCE!
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300
300
300
300
400
400
400
400
200
200
200
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200
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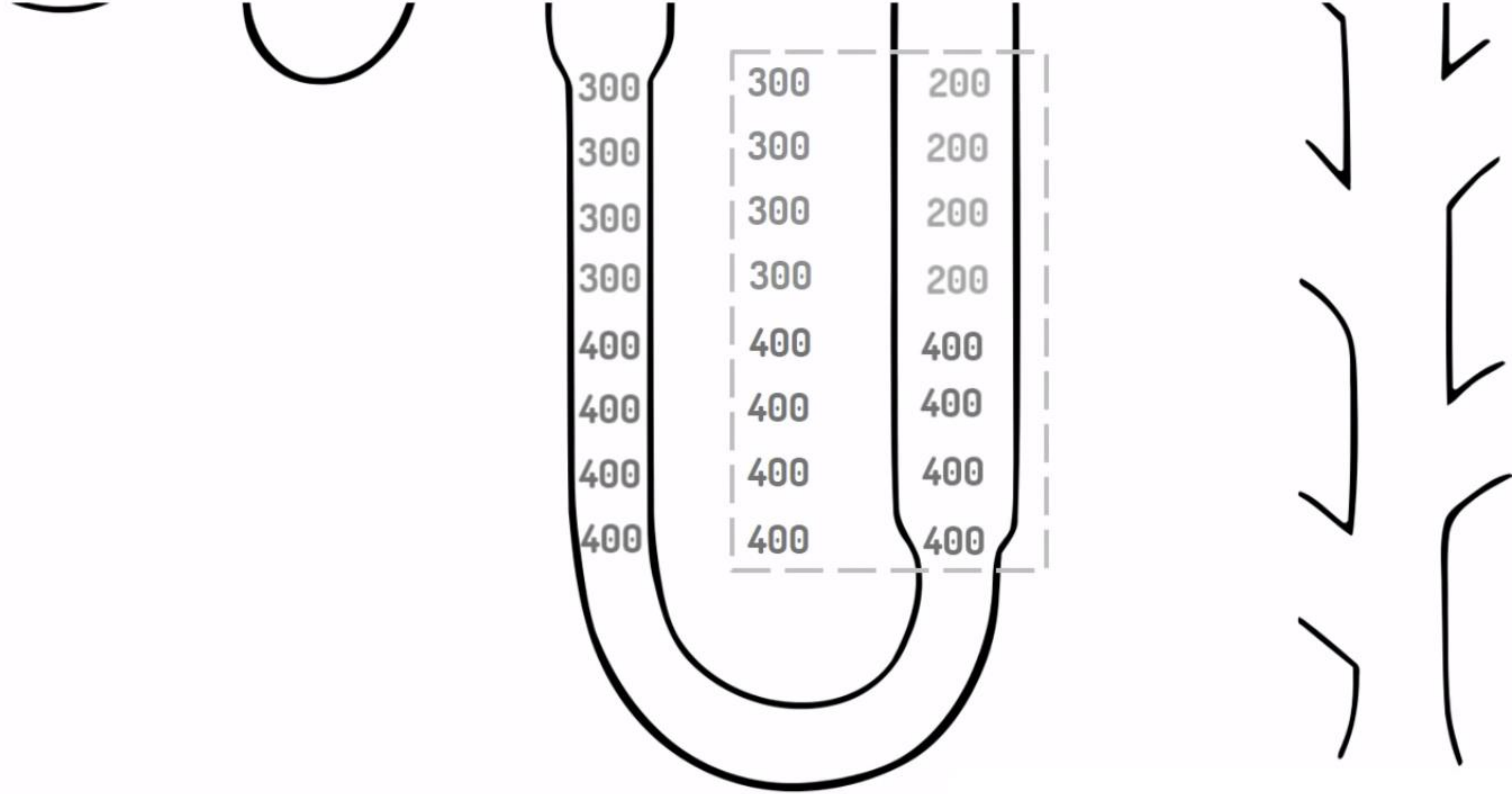
400
400


300
300
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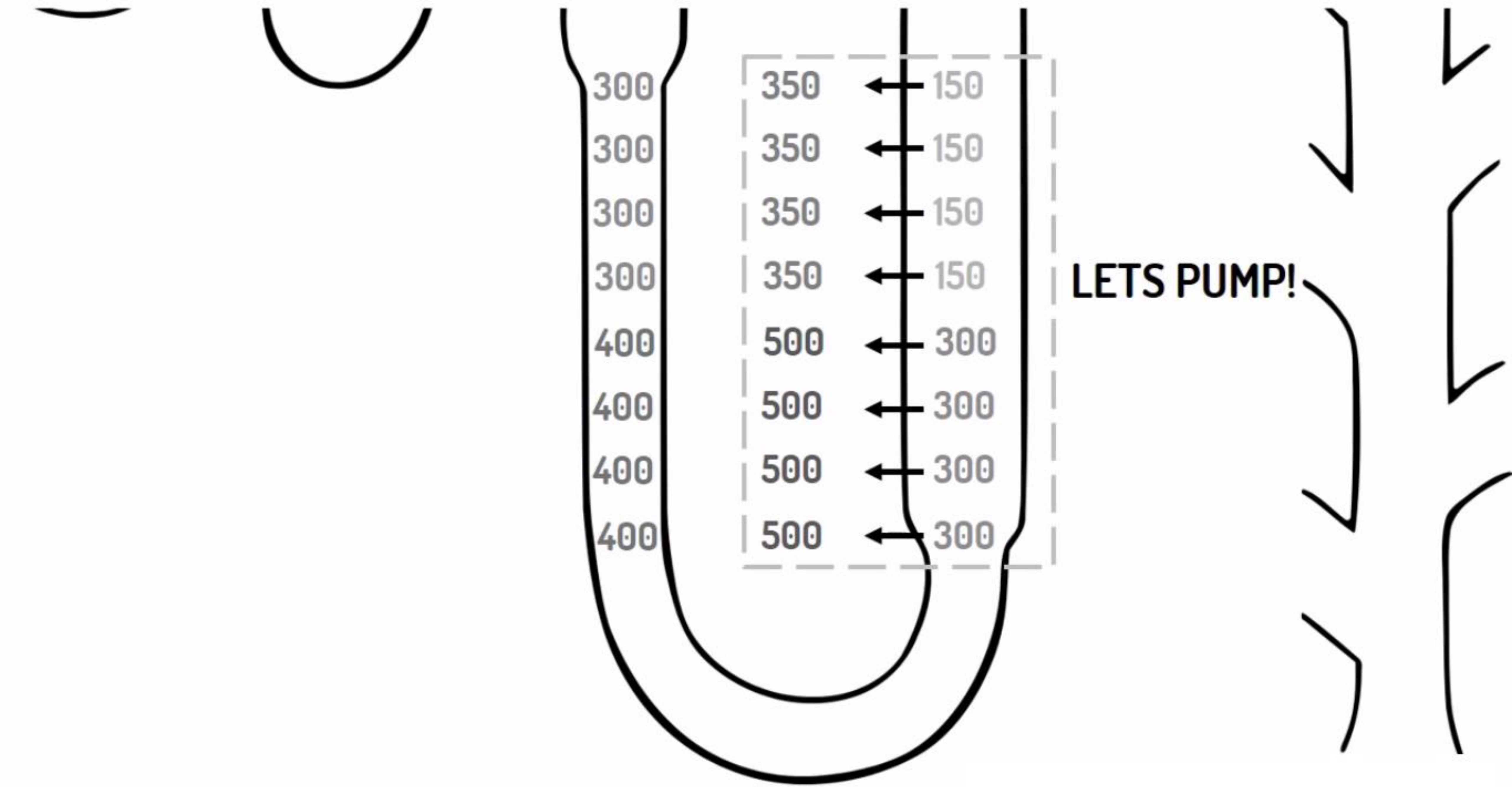
400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300
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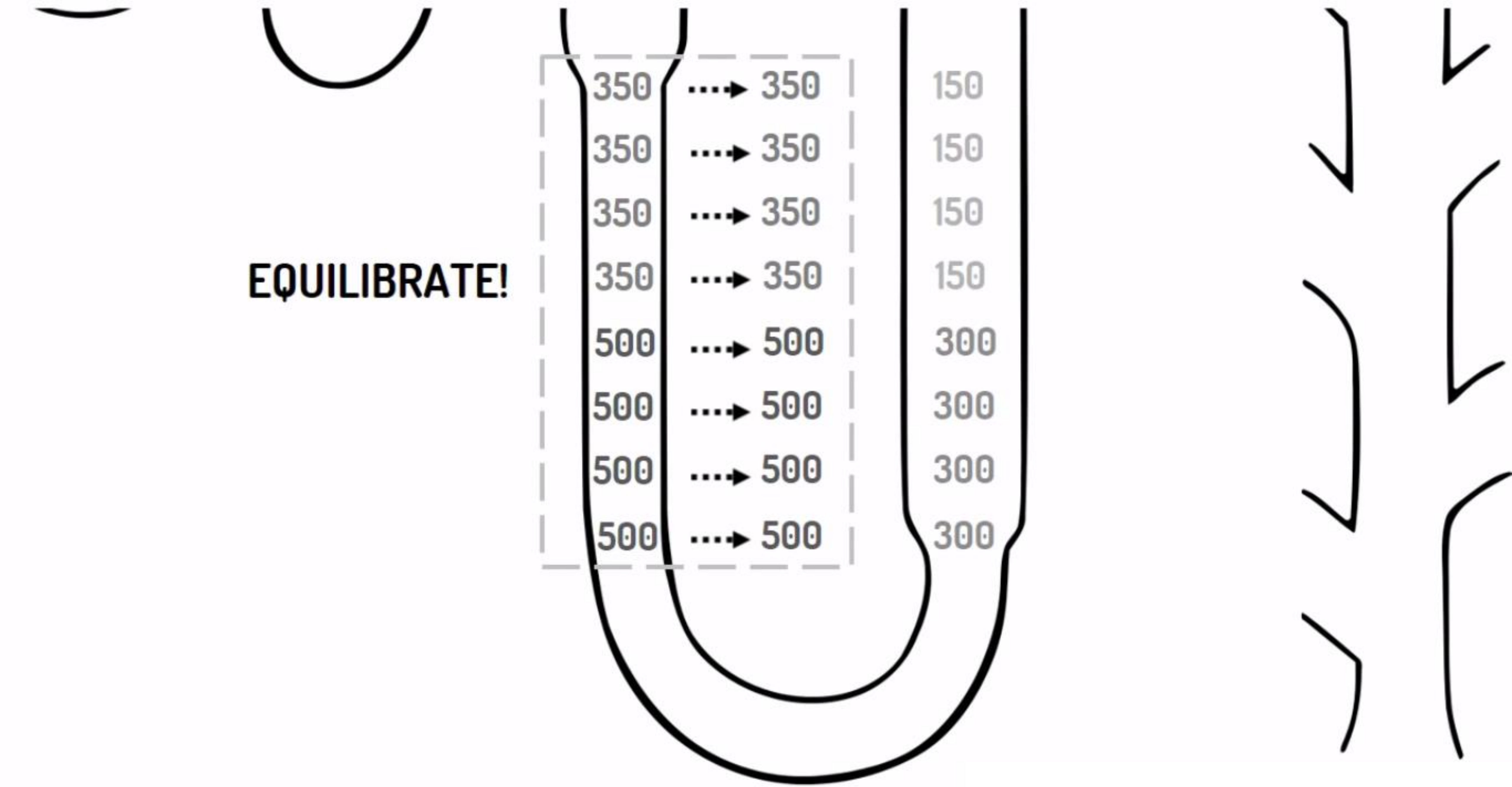
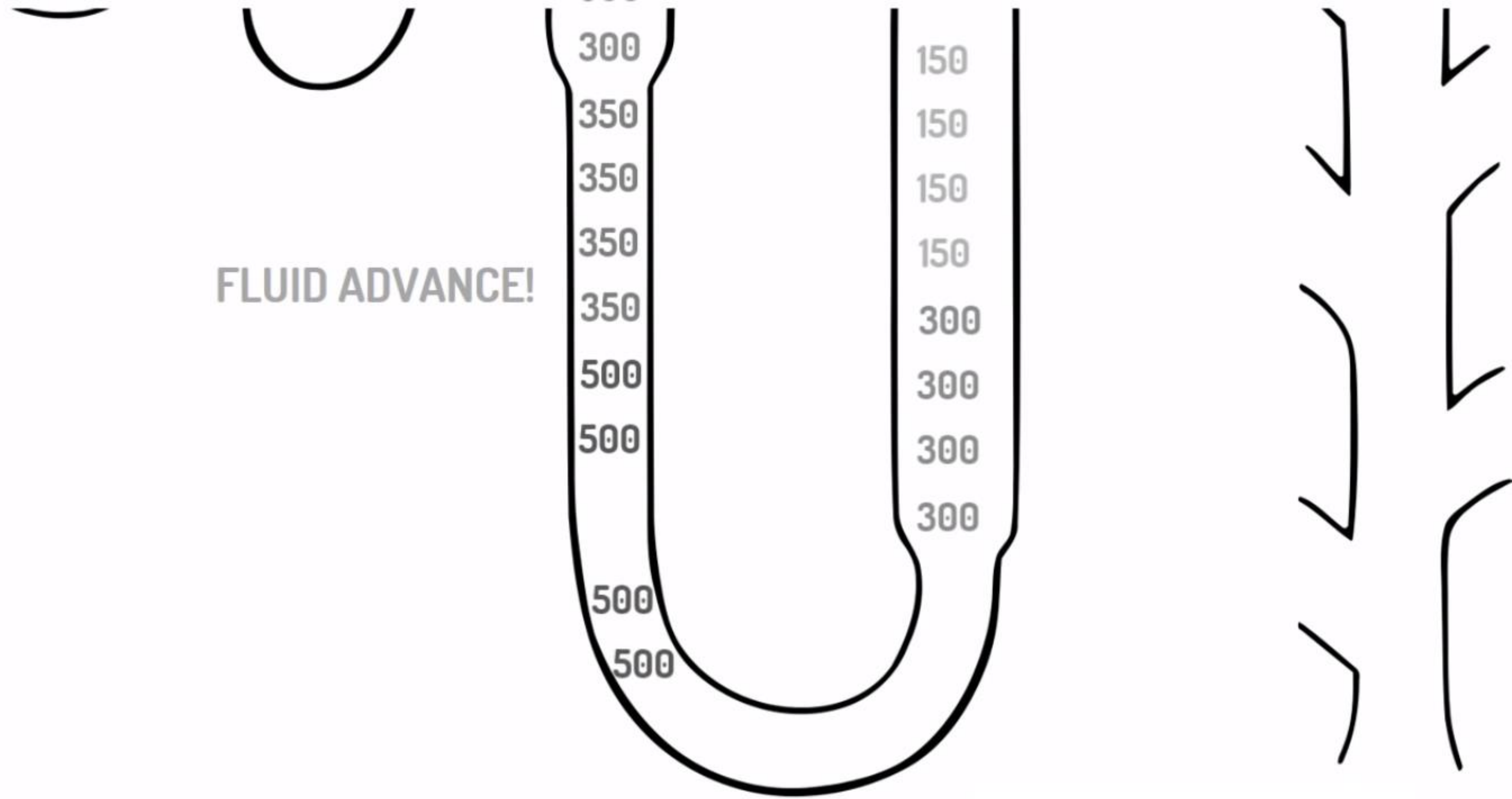
400
400
400
400
350
350
350
350
500
500
500
500
150
150
150
150
300
300
300
300
LETS PUMP!



EQUILIBRATE!
350 → 350 150
350 → 350 150
350 → 350 150
350 → 350 150
500 → 500 300
500 → 500 300
500 → 500 300
500 → 500 300


FLUID ADVANCE!
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350
350
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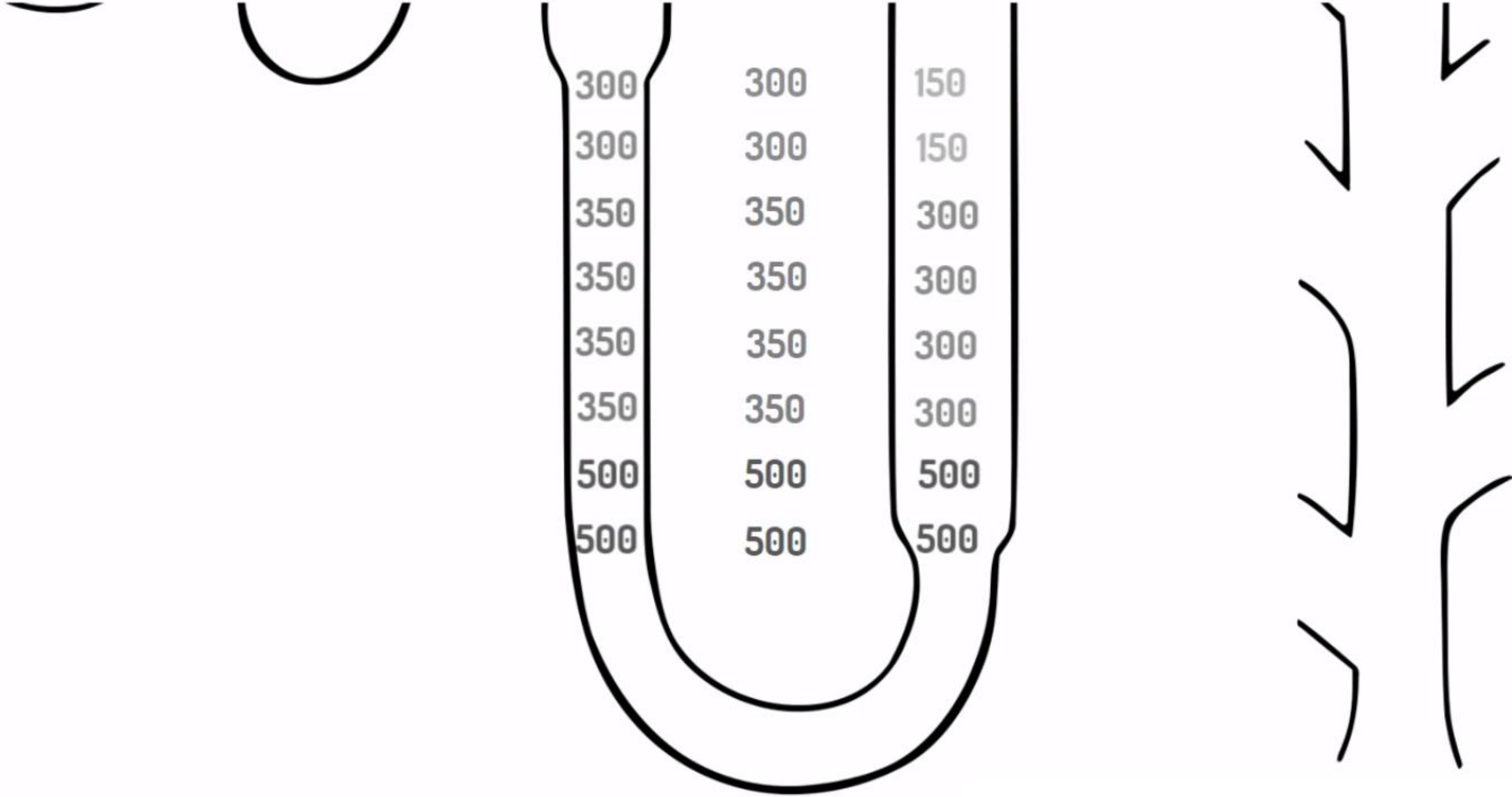
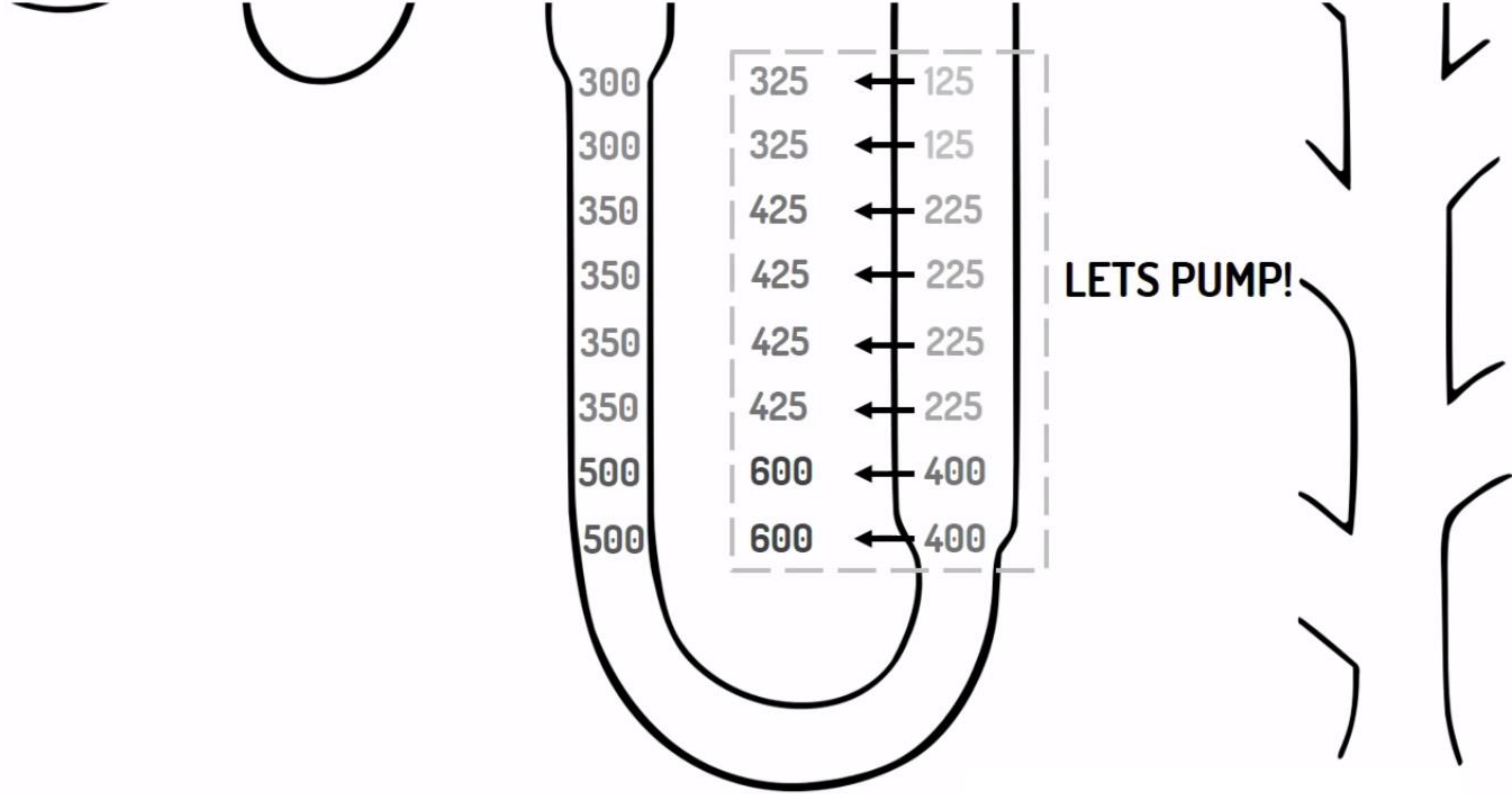
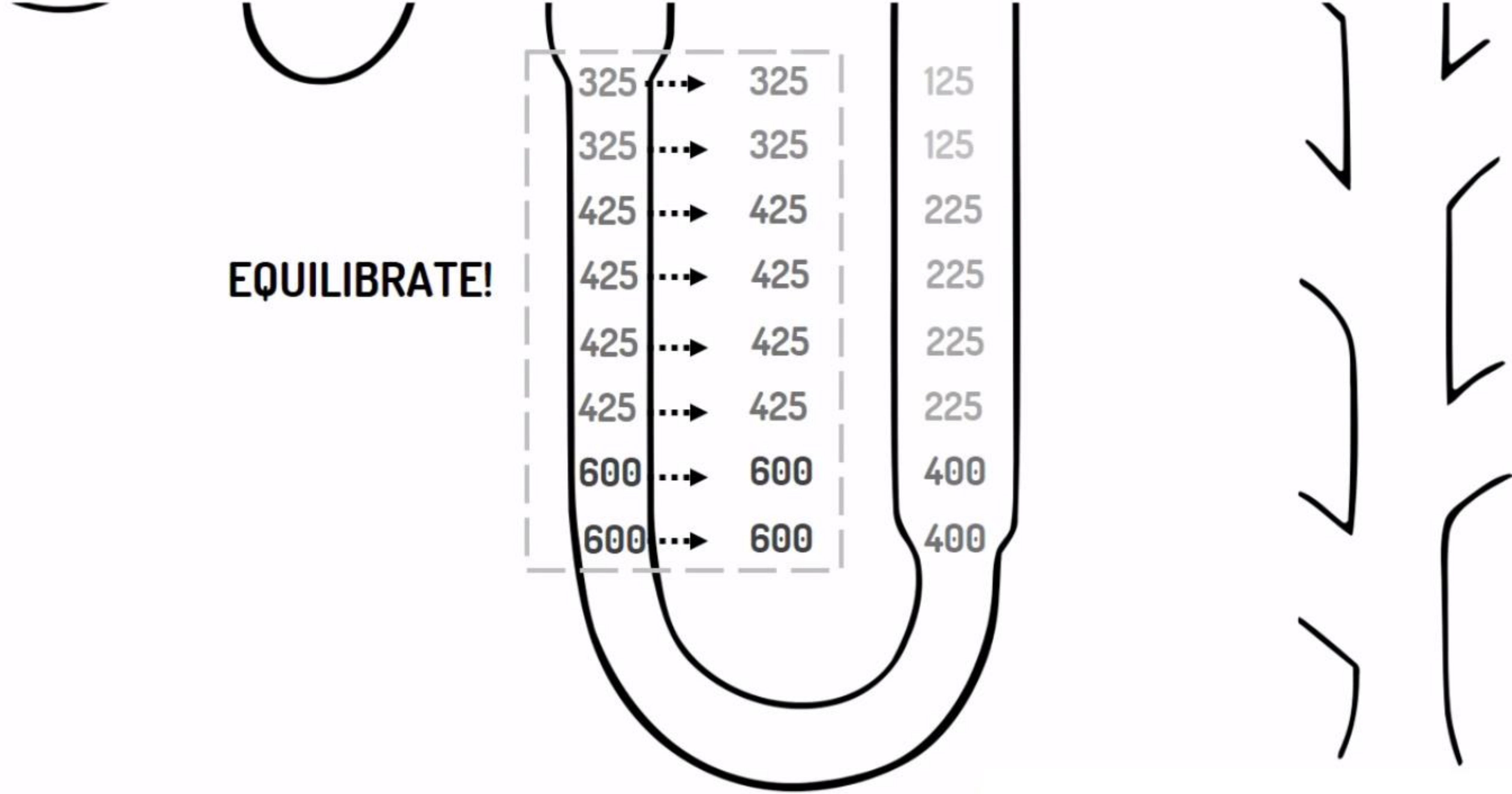
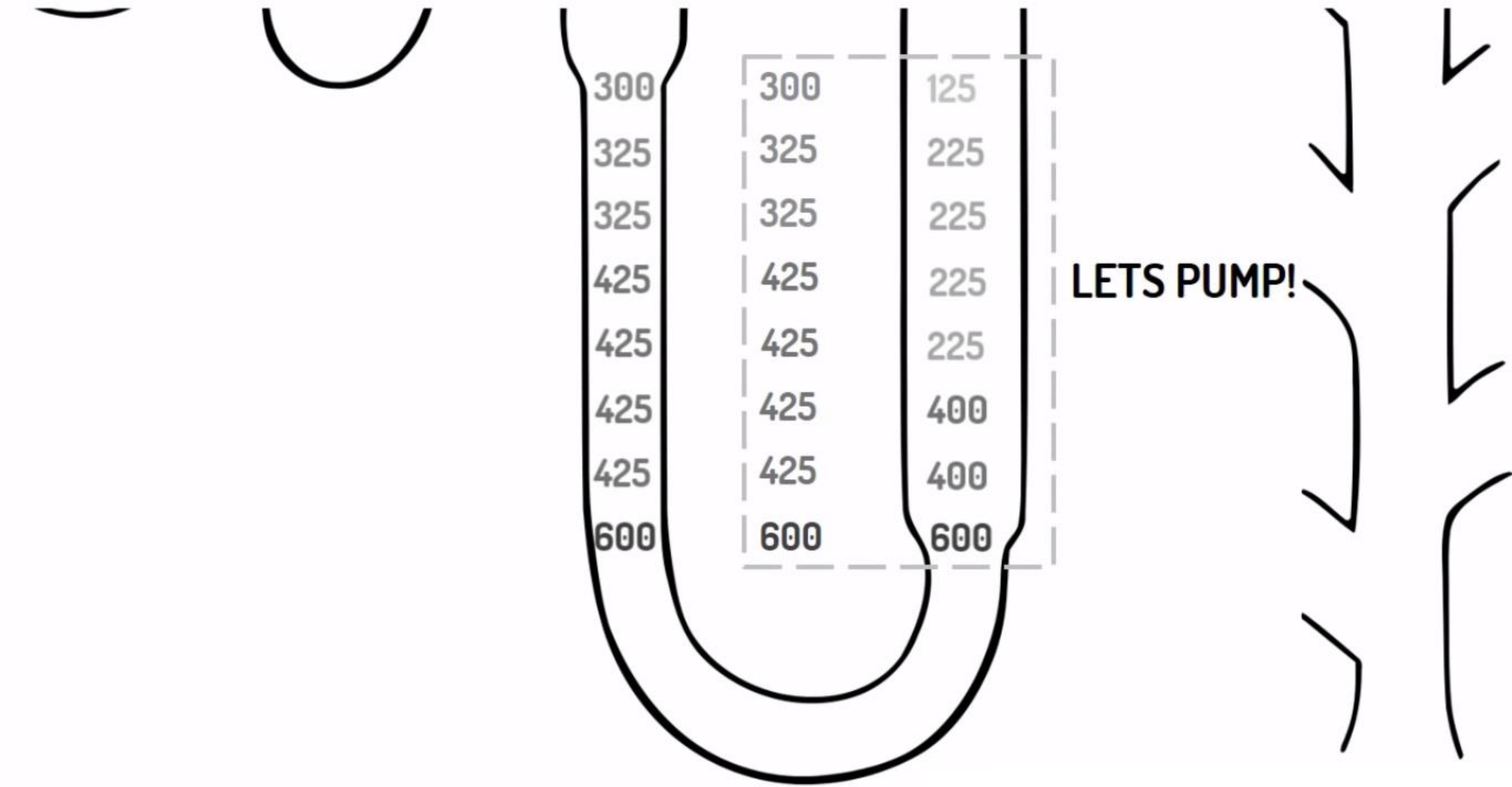
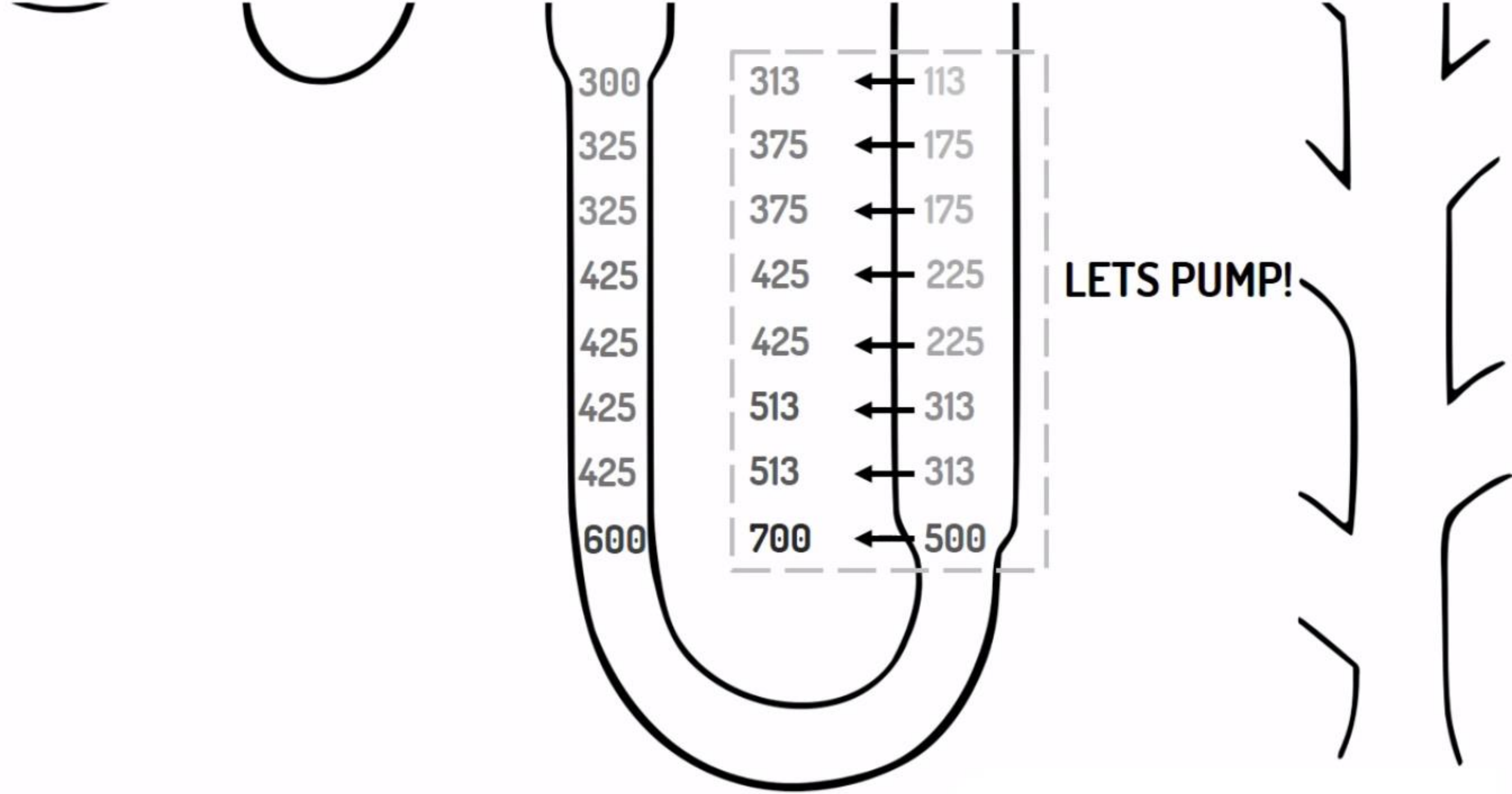
500
500
500
500
150
150
150
150
300
300
300
300

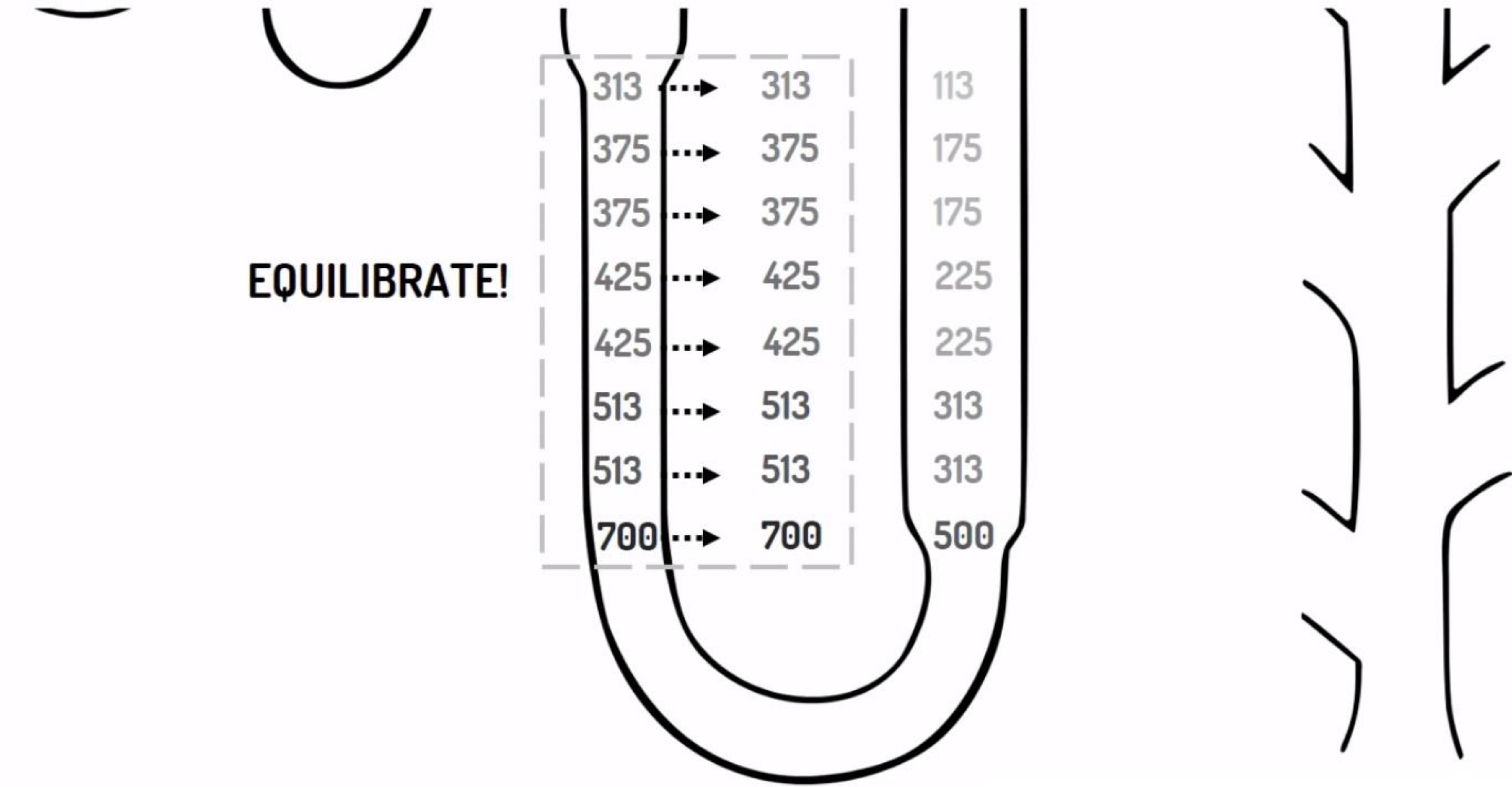

300
300
150
300
300
150
350
350
300
350
350
300
350
350
300
350
350
300
500
500
500
500
500
500


300
300
350
350
350
350
500
500
325
325
425
425
425
425
600
600
125
125
225
225
225
225
400
400
LETS PUMP!

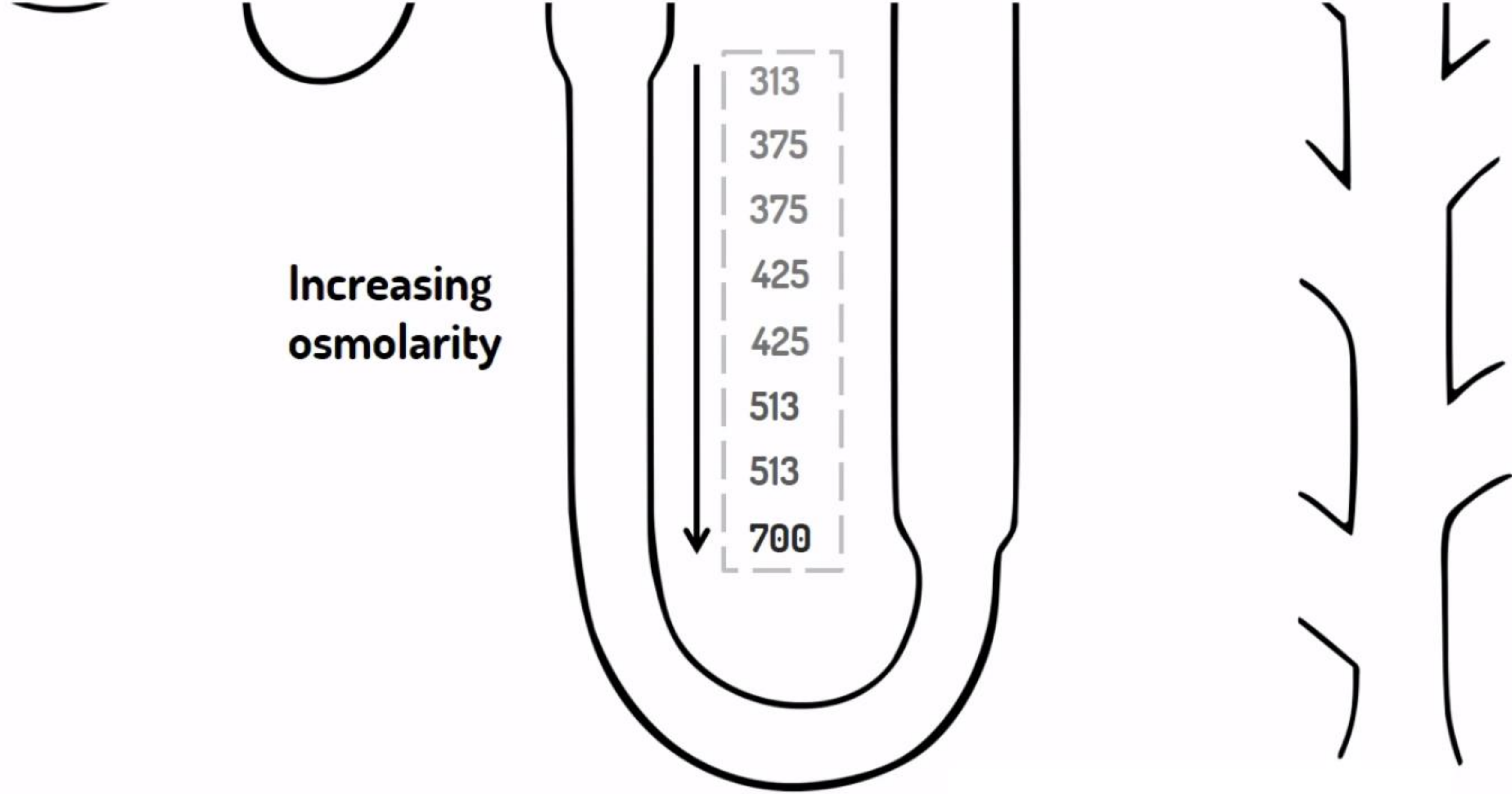

EQUILIBRATE!
325 325 125
325 325 125
425 425 225
425 425 225
425 425 225
425 425 225
600 600 400
600 600 400


300
325
325
425
425
425
425
600
300
325
325
425
425
425
425
600
125
225
225
225
225
400
400
600
LETS PUMP!

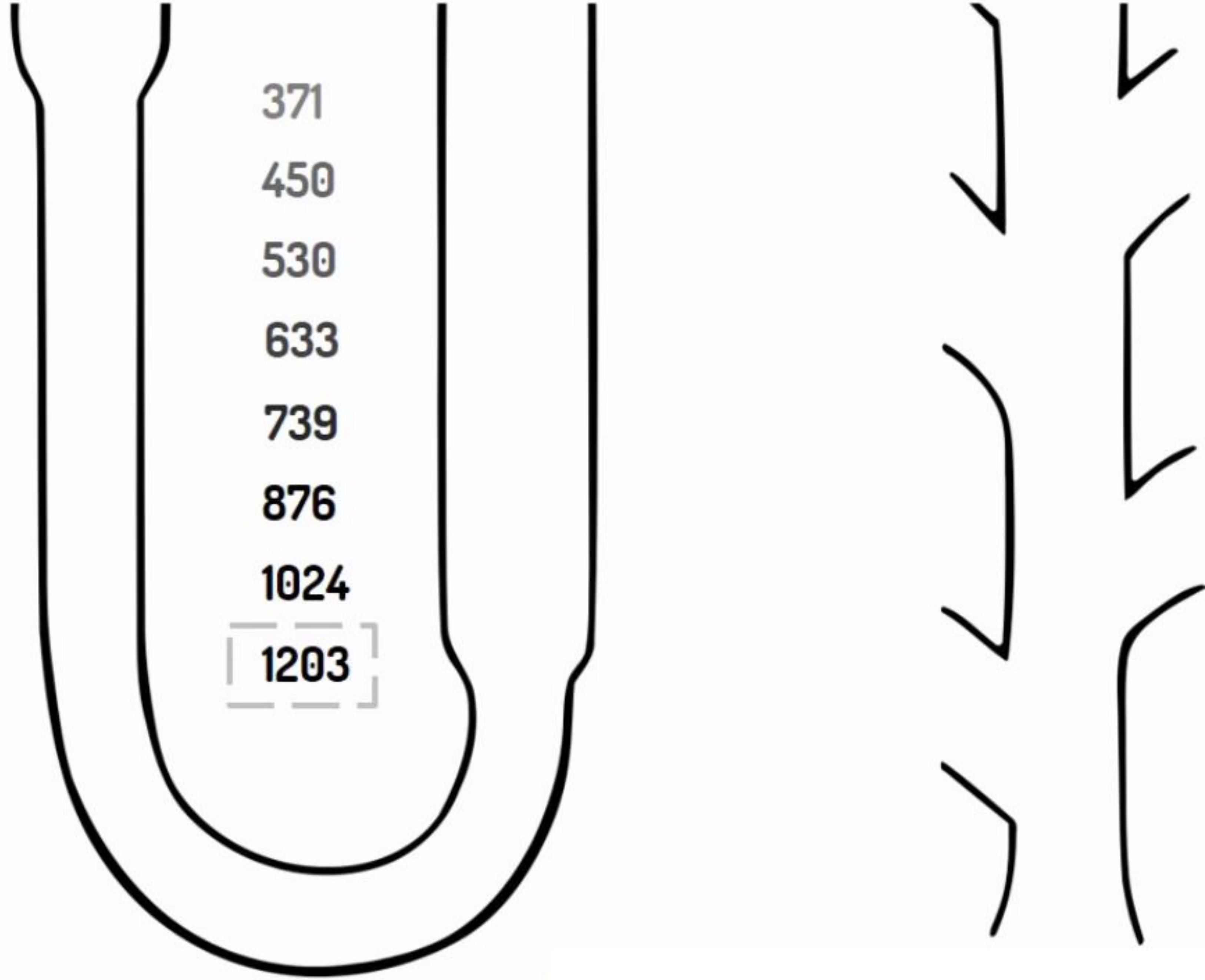

300
325
325
425
425
425
425
600
313
375
375
425
425
513
513
700
113
175
175
225
225
313
313
500
LETS PUMP!



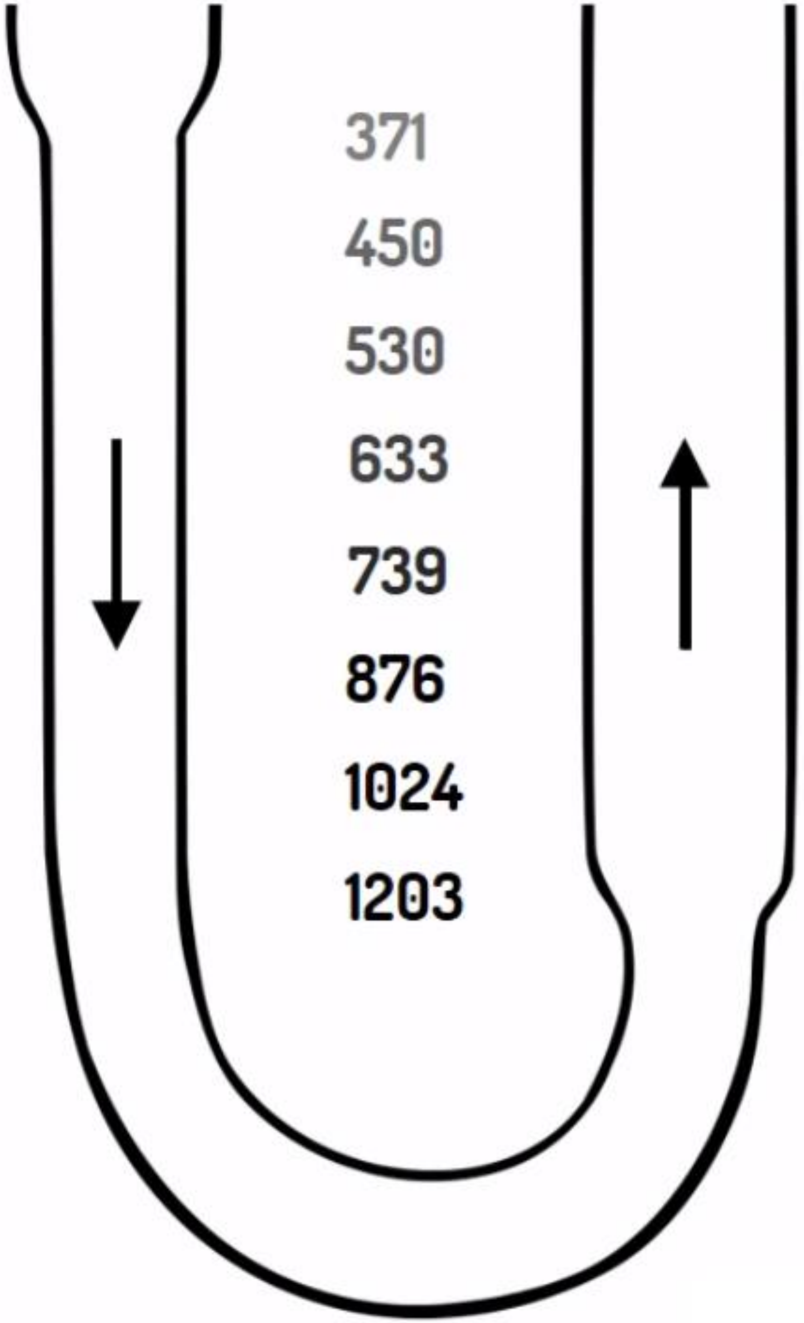
EQUILIBRATE!
313 313 113
375 375 175
375 375 175
425 425 225
425 425 225
513 513 313
513 513 313
700 700 500

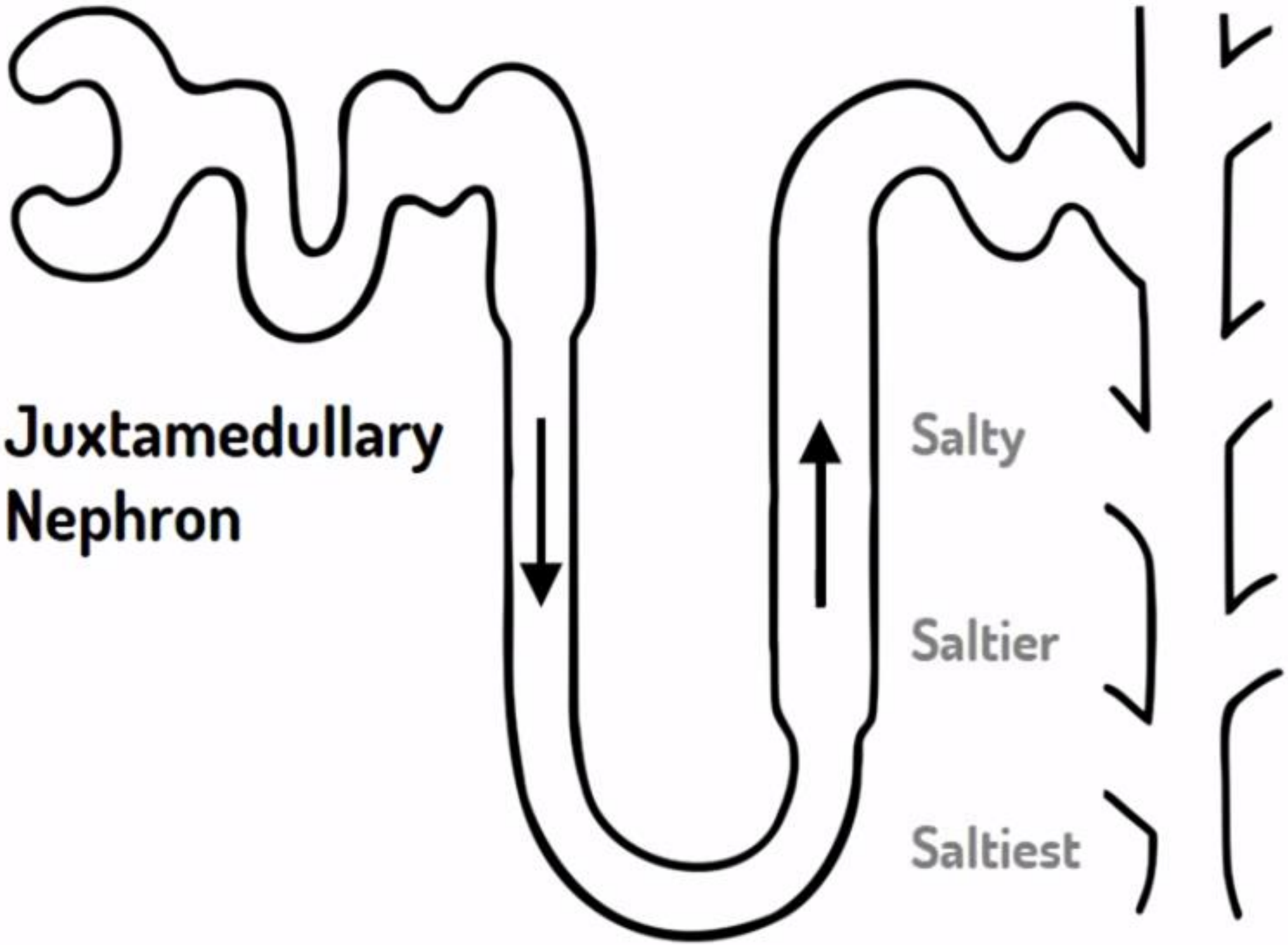

Increasing
osmolarity
313
375
375
425
425
513
513
700

Countercurrent Multiplication

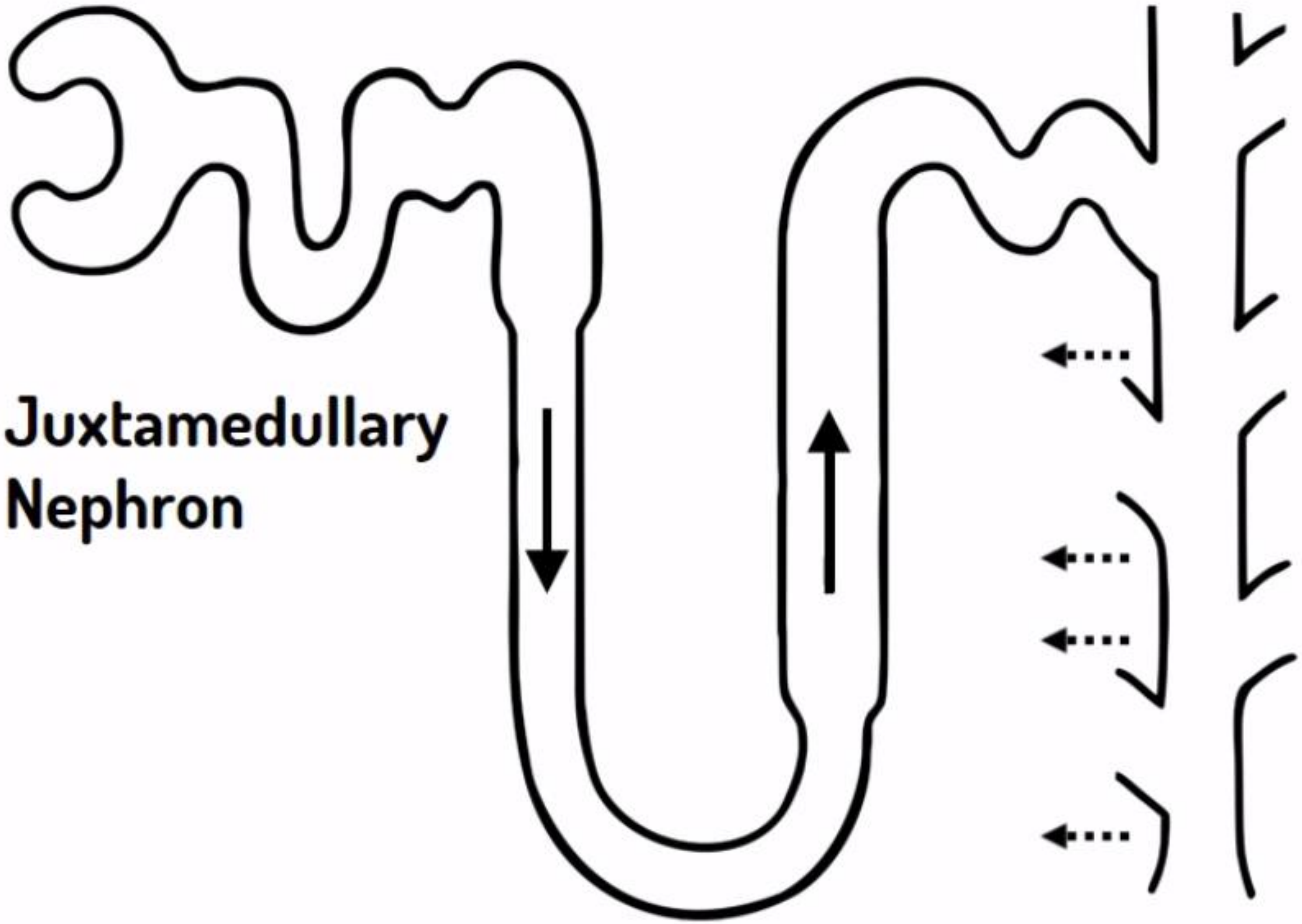


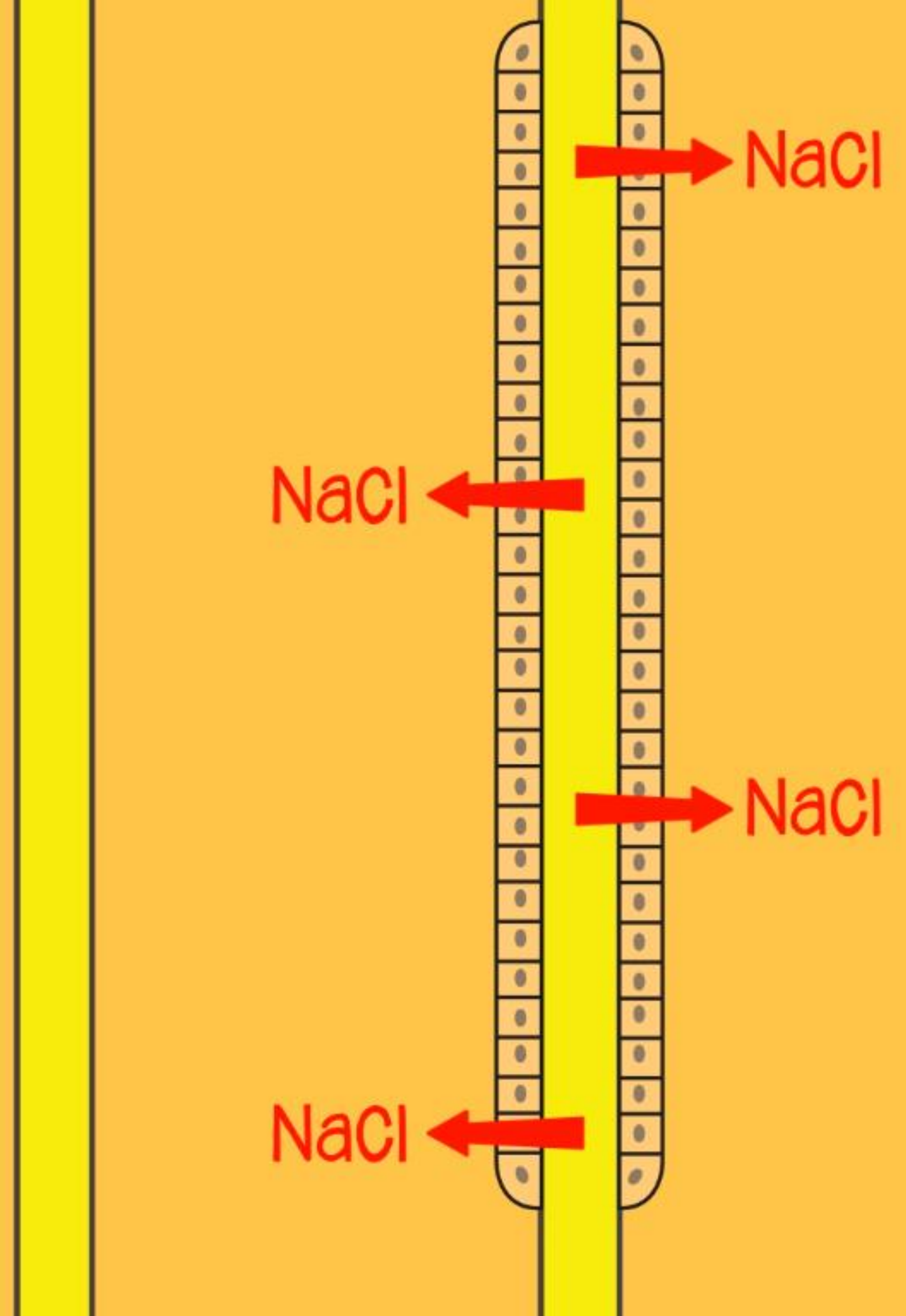
Countercurrent Multiplication

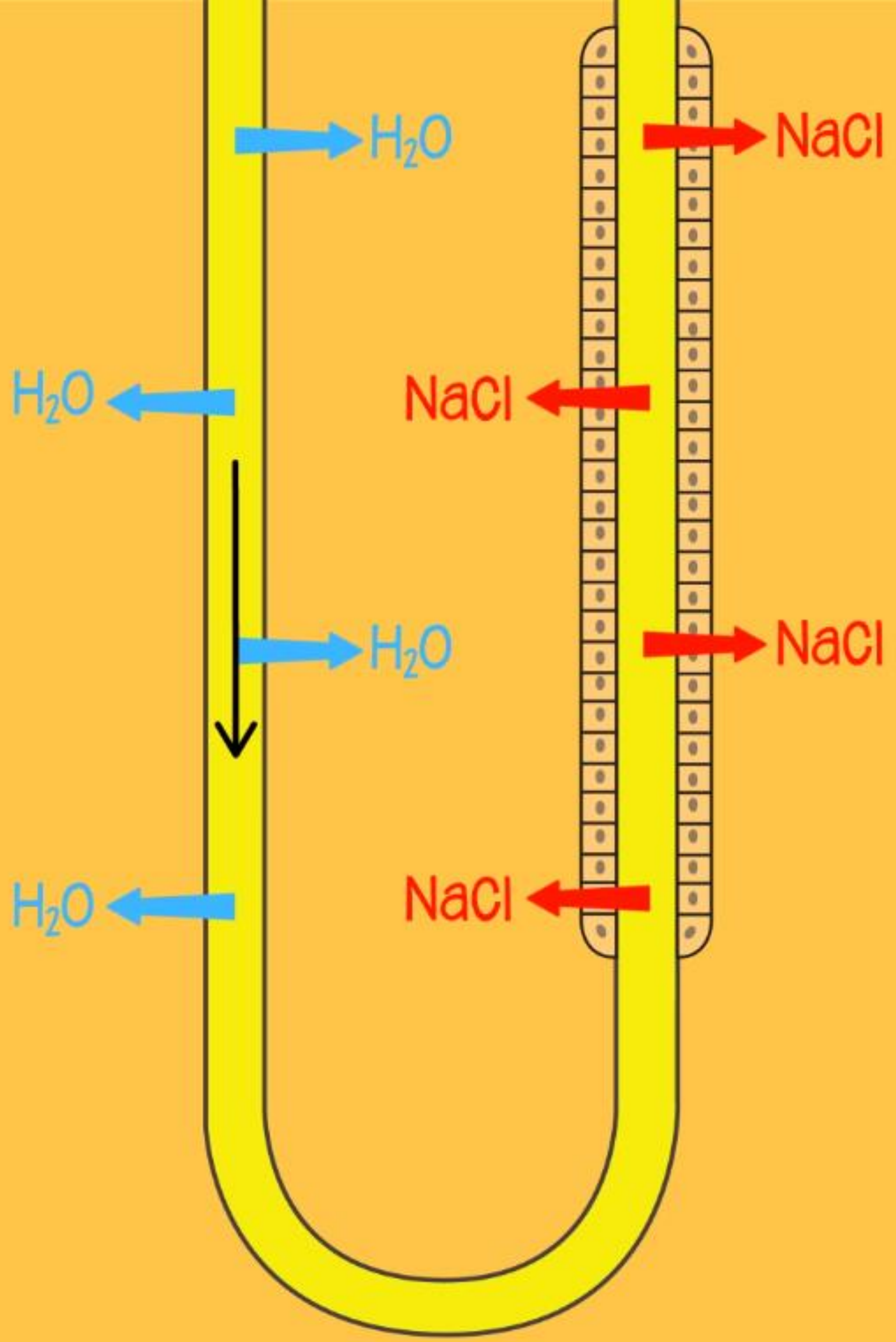


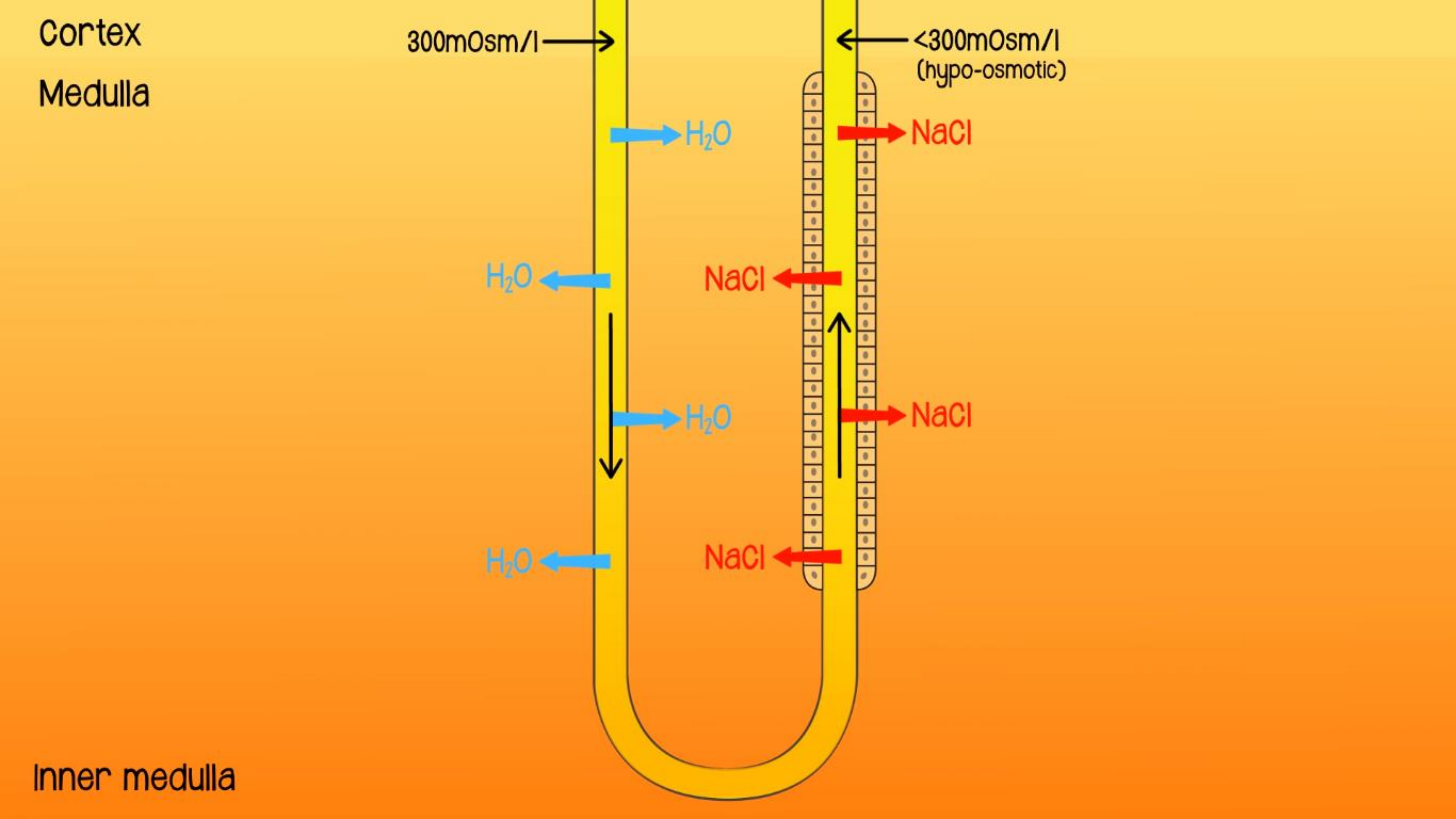

Juxtamedullary
Nephron
Salty
Saltier
Saltiest

Juxtamedullary
Nephron

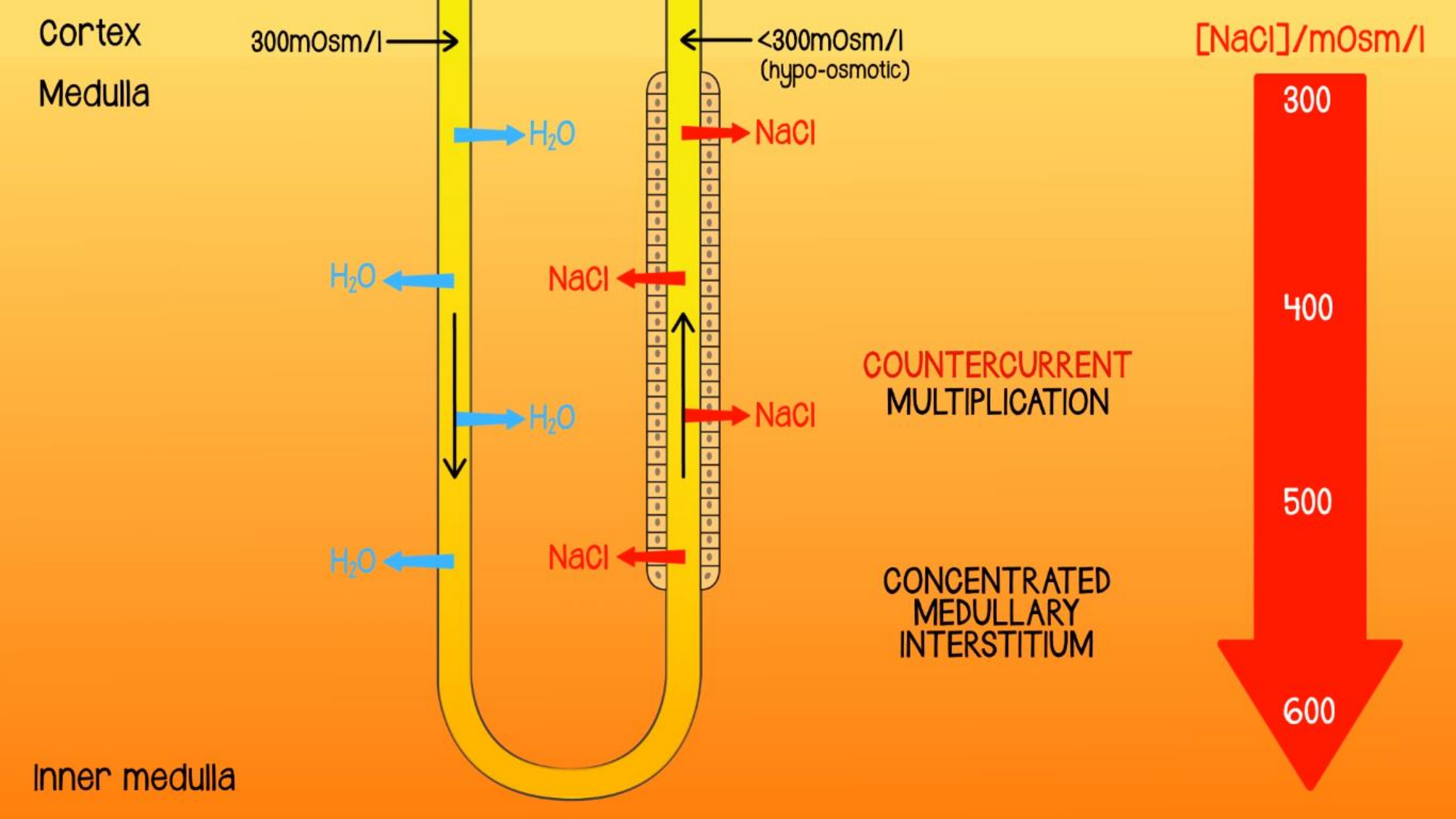



NaCl
NaCl
NaCl
NaCl

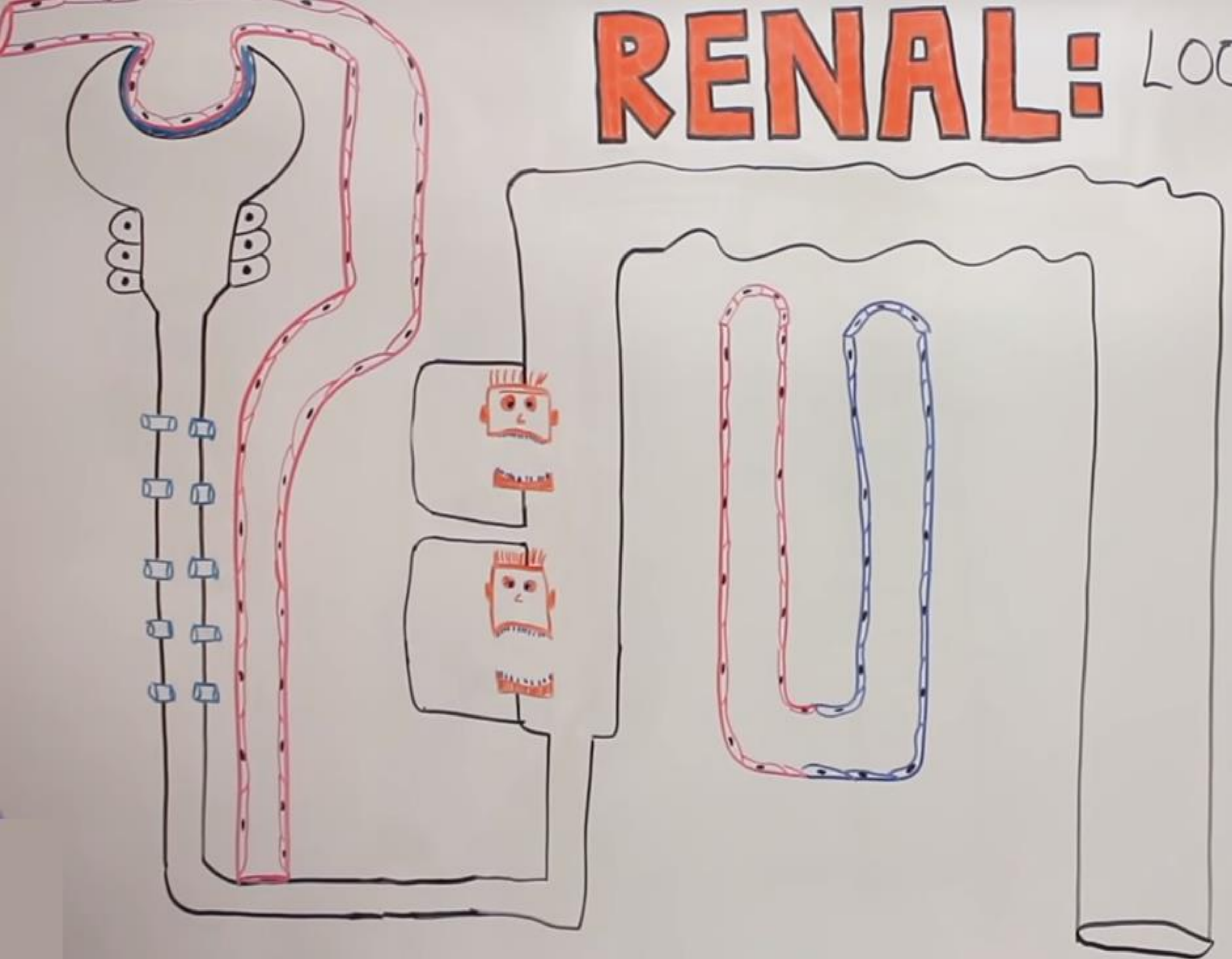

H2O
NaCl
H2O
NaCl
H2O
NaCl
H2O
NaCl

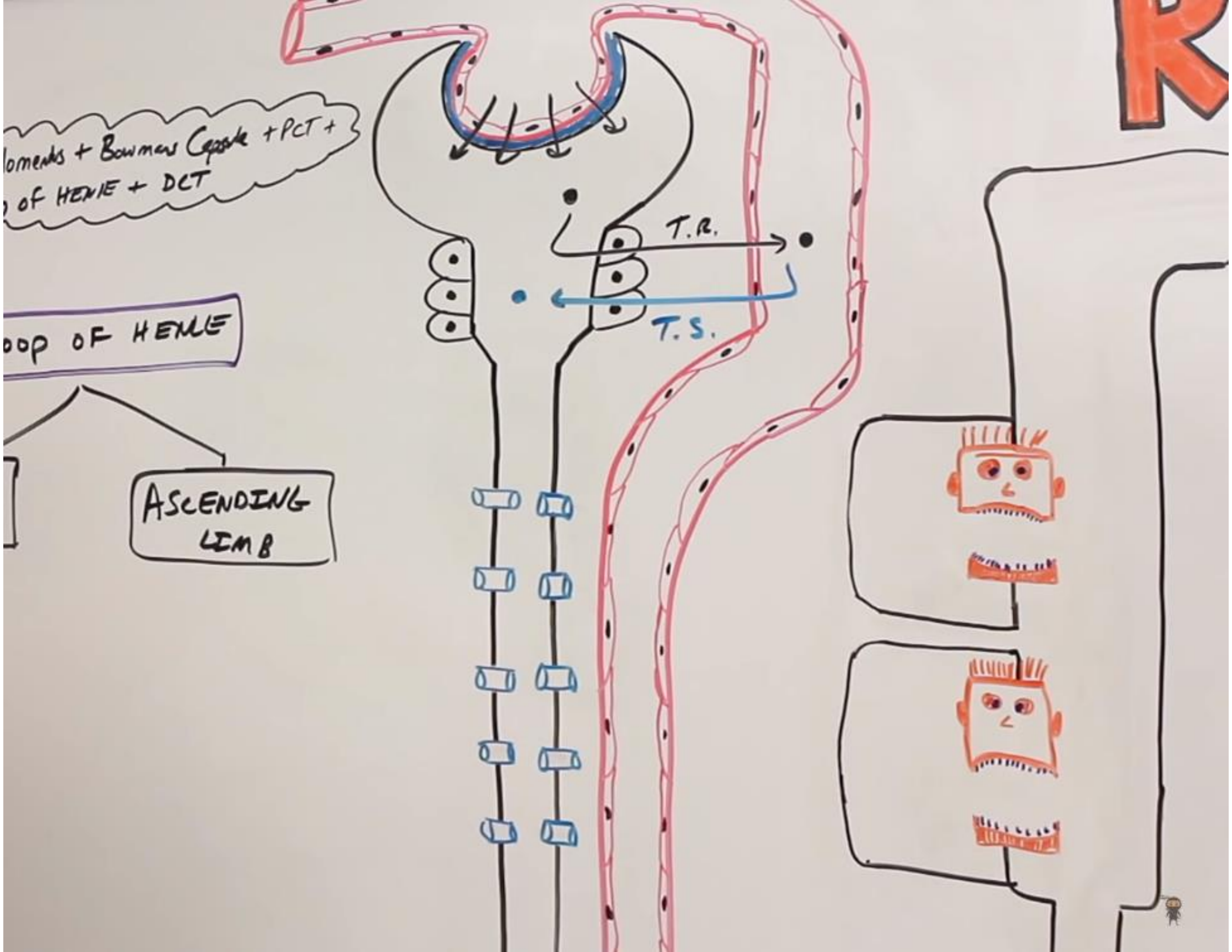


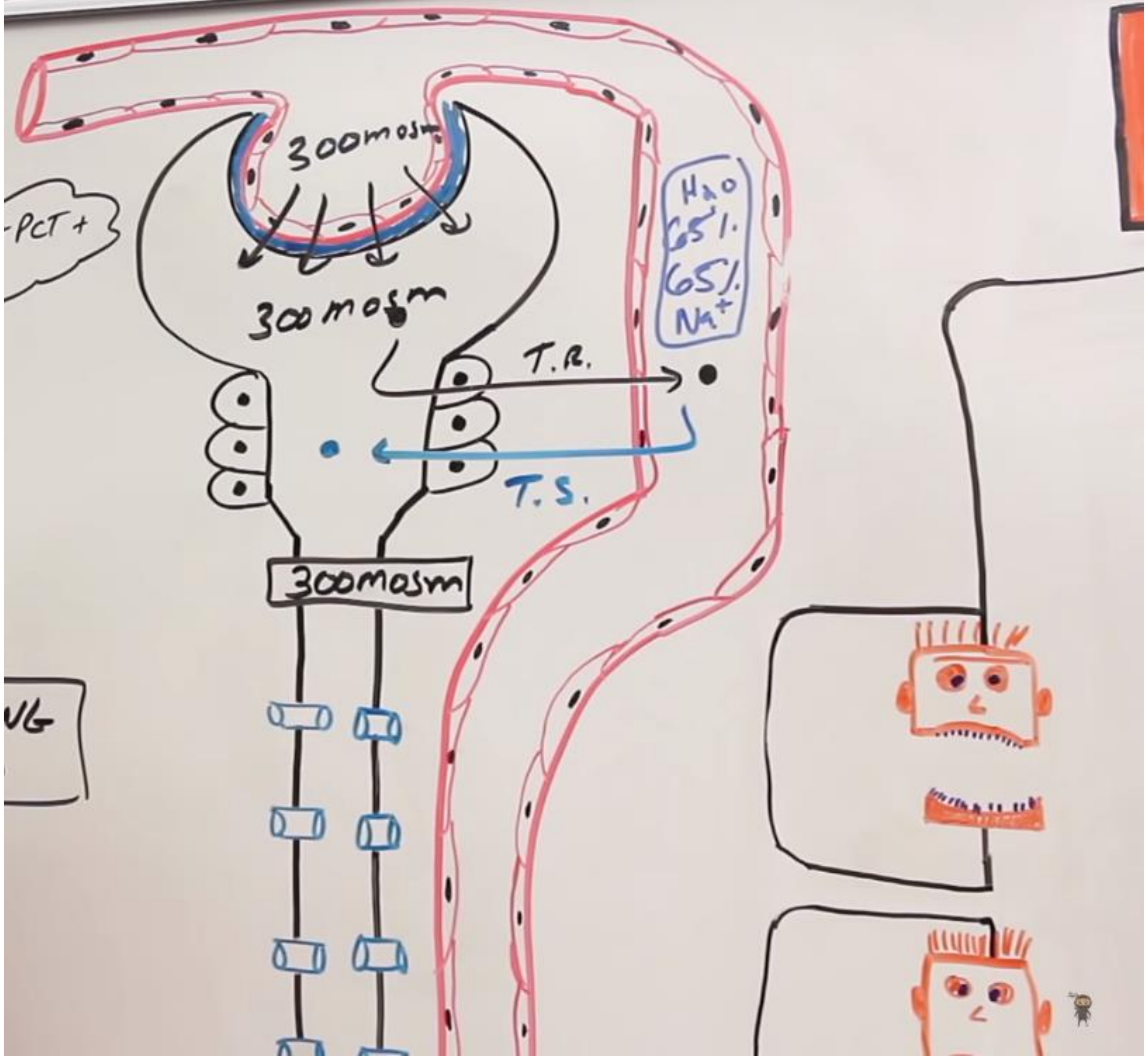
Cortex
Medulla
300mOsm/l
<300mOsm/l
(hypo-osmotic)
H2O
NaCl
H2O
NaCl
H2O
NaCl
H2O
NaCl
Inner medulla


Cortex
Medulla
300mOsm/l
<300mOsm/l
(hypo-osmotic)
[NaCl]/mOsm/l
300
H_2O
NaCl
H_2O
NaCl
400
COUNTERCURRENT
MULTIPLICATION
H_2O
NaCl
500
H_2O
NaCl
CONCENTRATED
MEDULLARY
INTERSTITIUM
600
Inner medulla

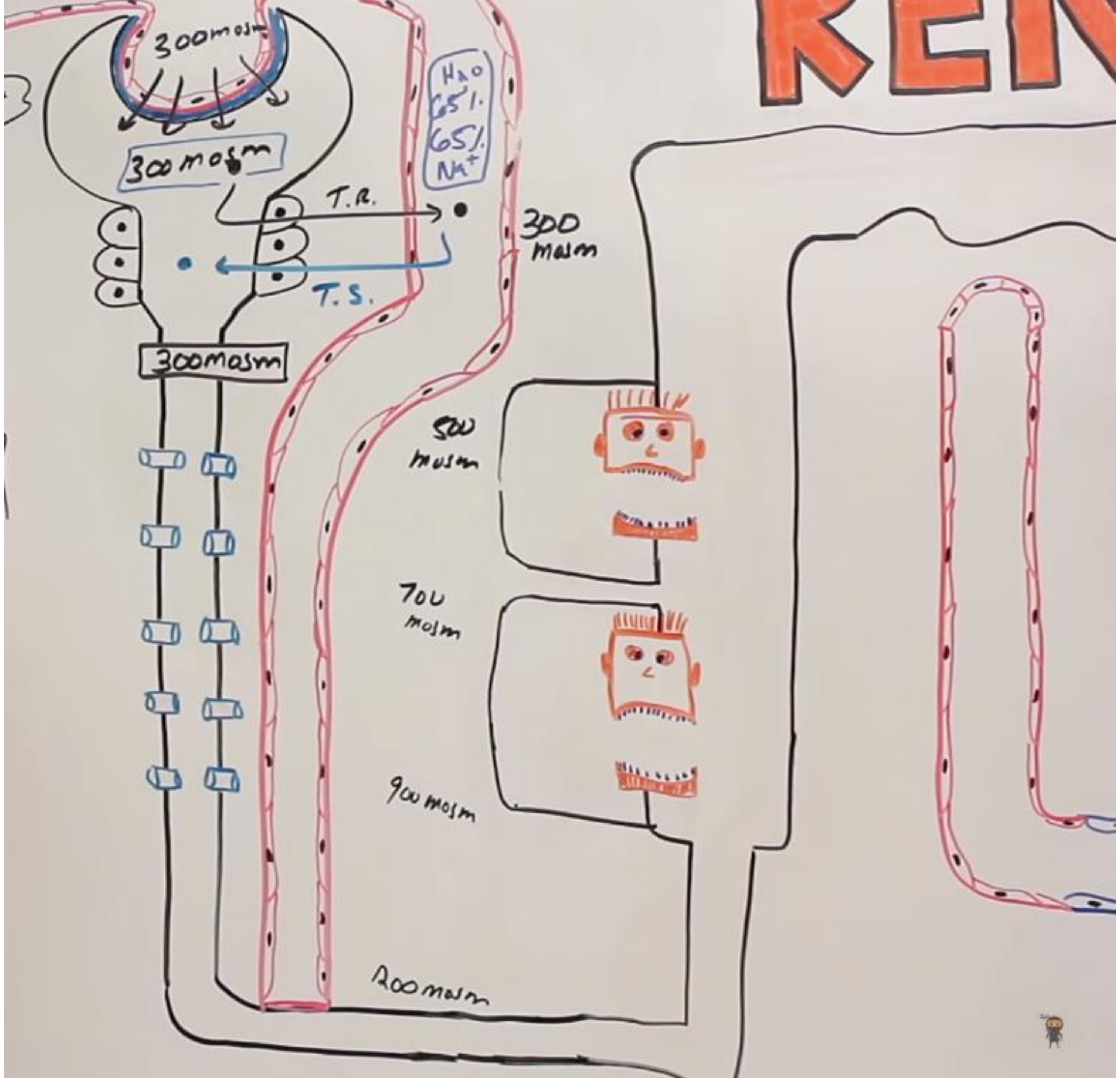
RENAL: LOOP OF HENLE



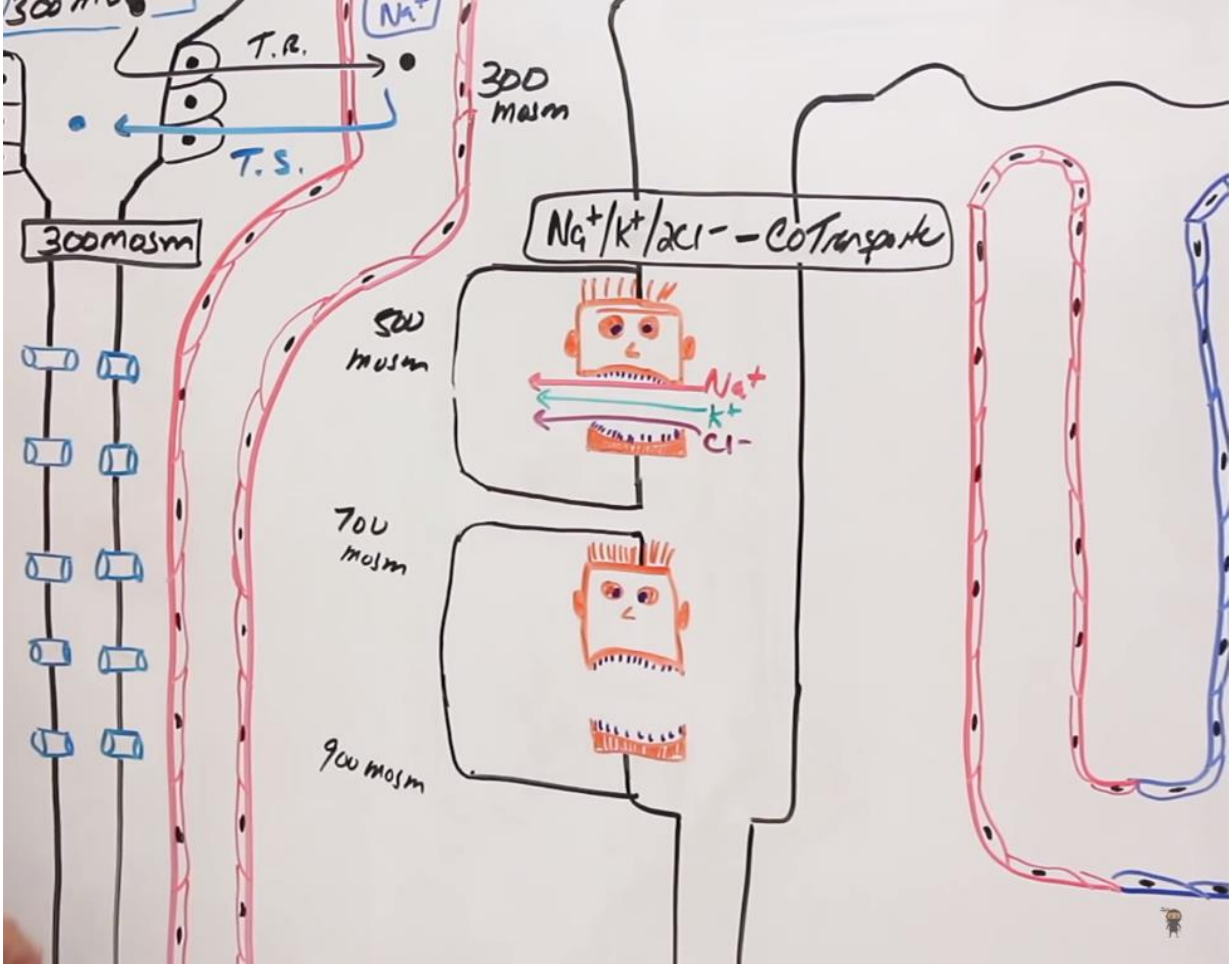

lomerulus + Bowman Capsule + PCT +
of HENLE + DCT
T.R.
T.S.
oop OF HENLE
ASCENDING LIMB



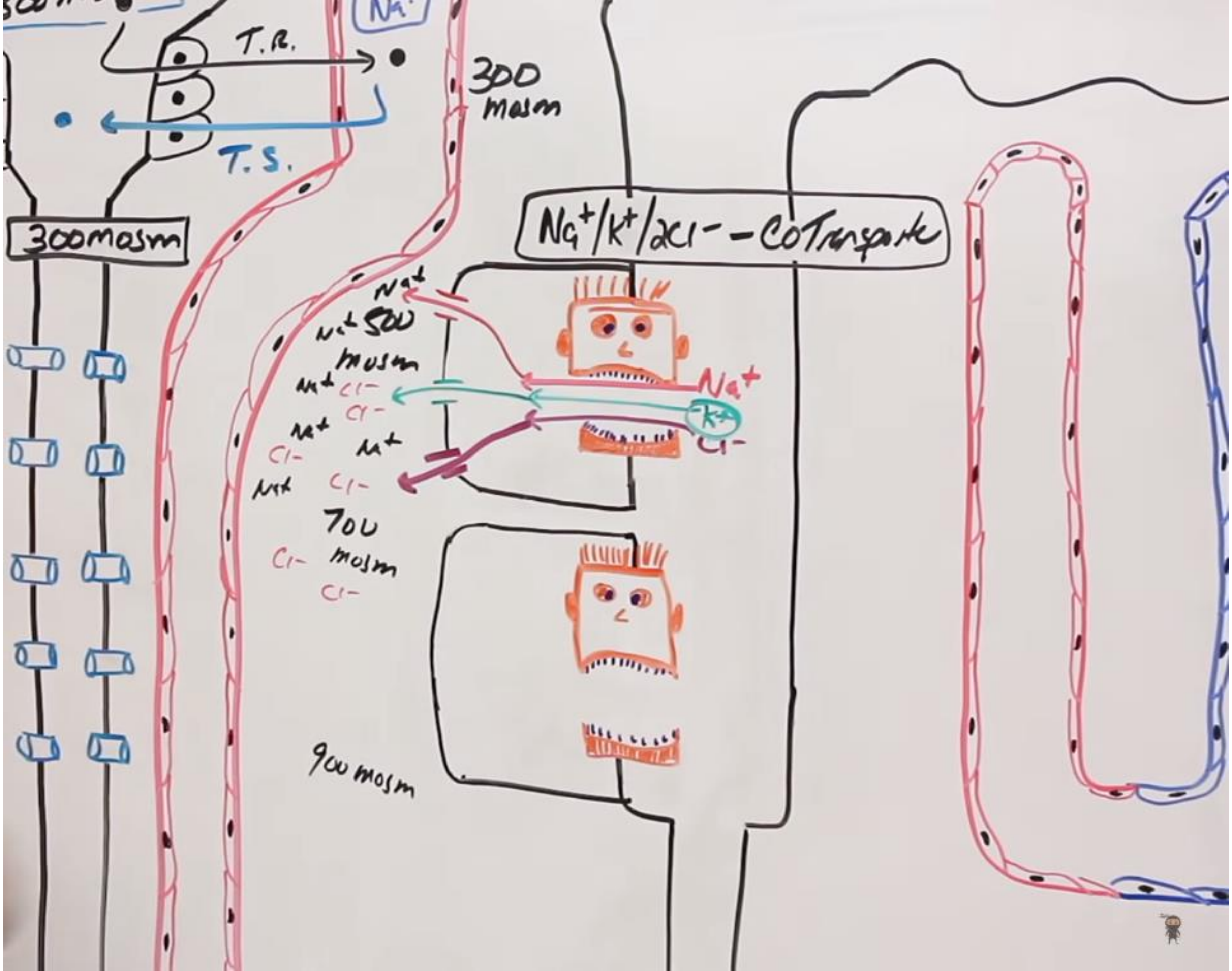
300mosm
PCT +
300mosm
T.R.
H_2O
65%
65%
Na^+
T.S.
300mosm
NG



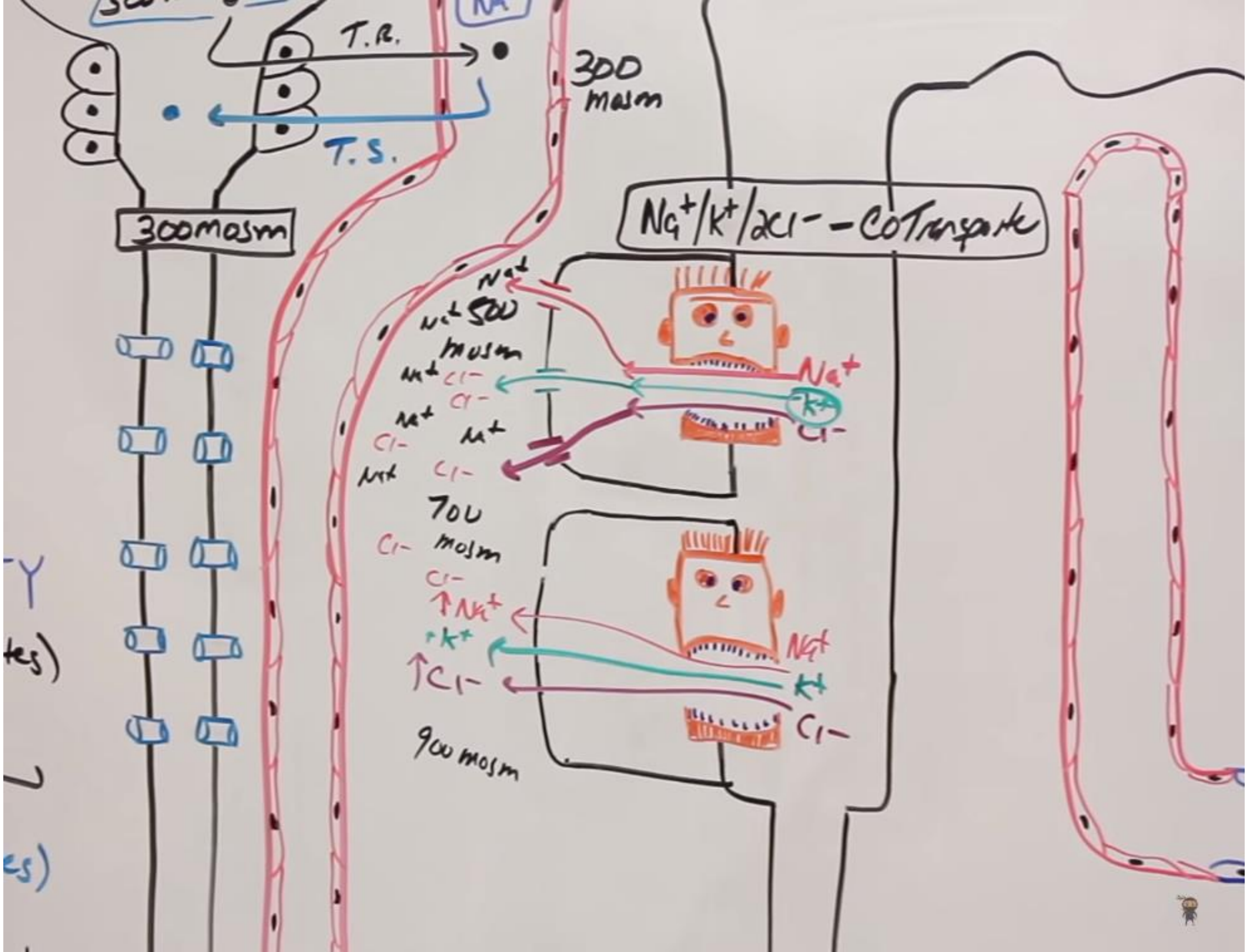
REN
300mosm
300mosm
T.R.
T.S.
H_2O 65%
65% Na^+
300 mosm
300mosm
500 mosm
700 mosm
900 mosm
1200 mosm

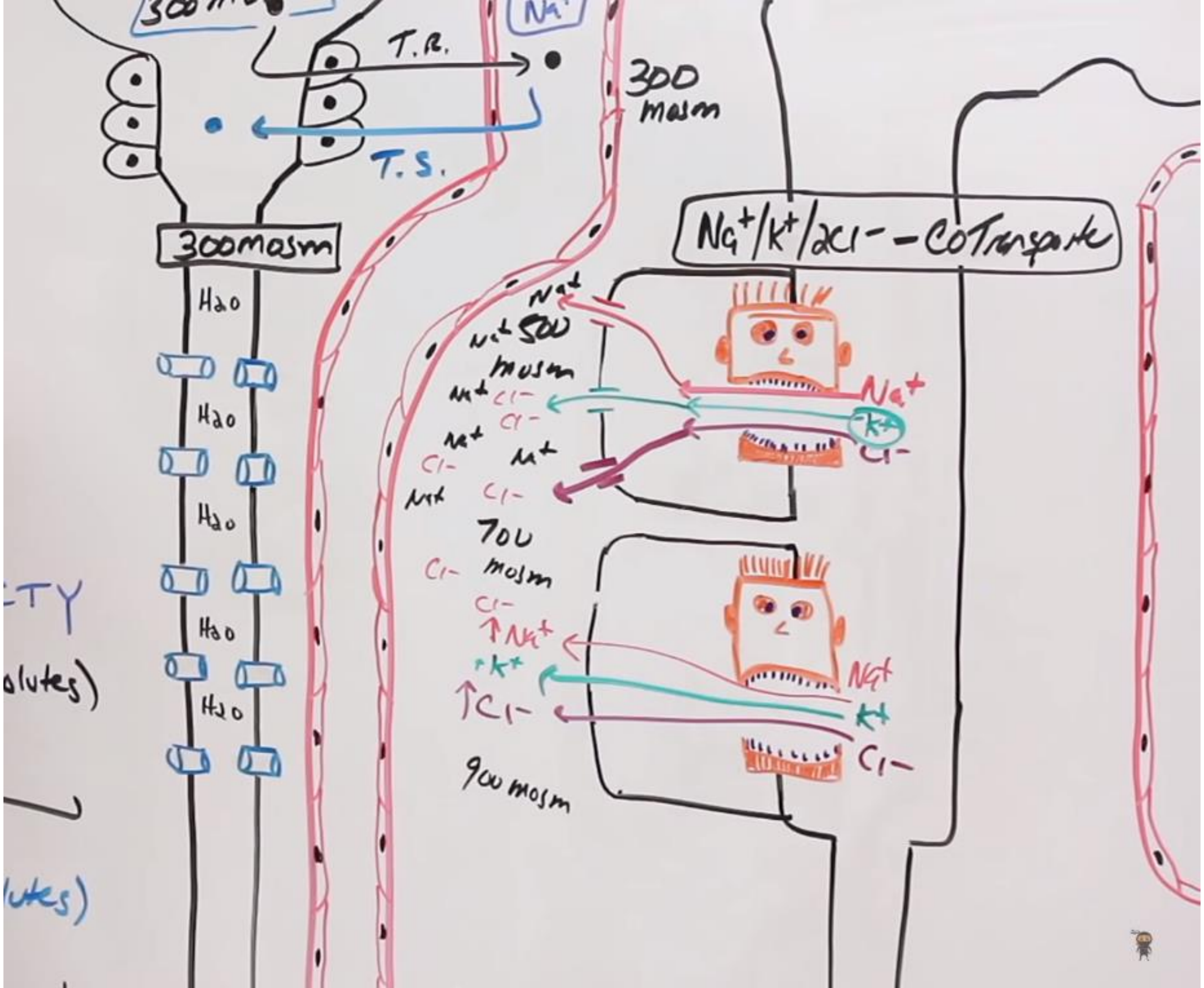


T.R.
T.S.
300 mosm
300mosm
Na+/K+/2Cl- - CoTransport
500 mosm
Na+
K+
Cl-
700 mosm
900 mosm

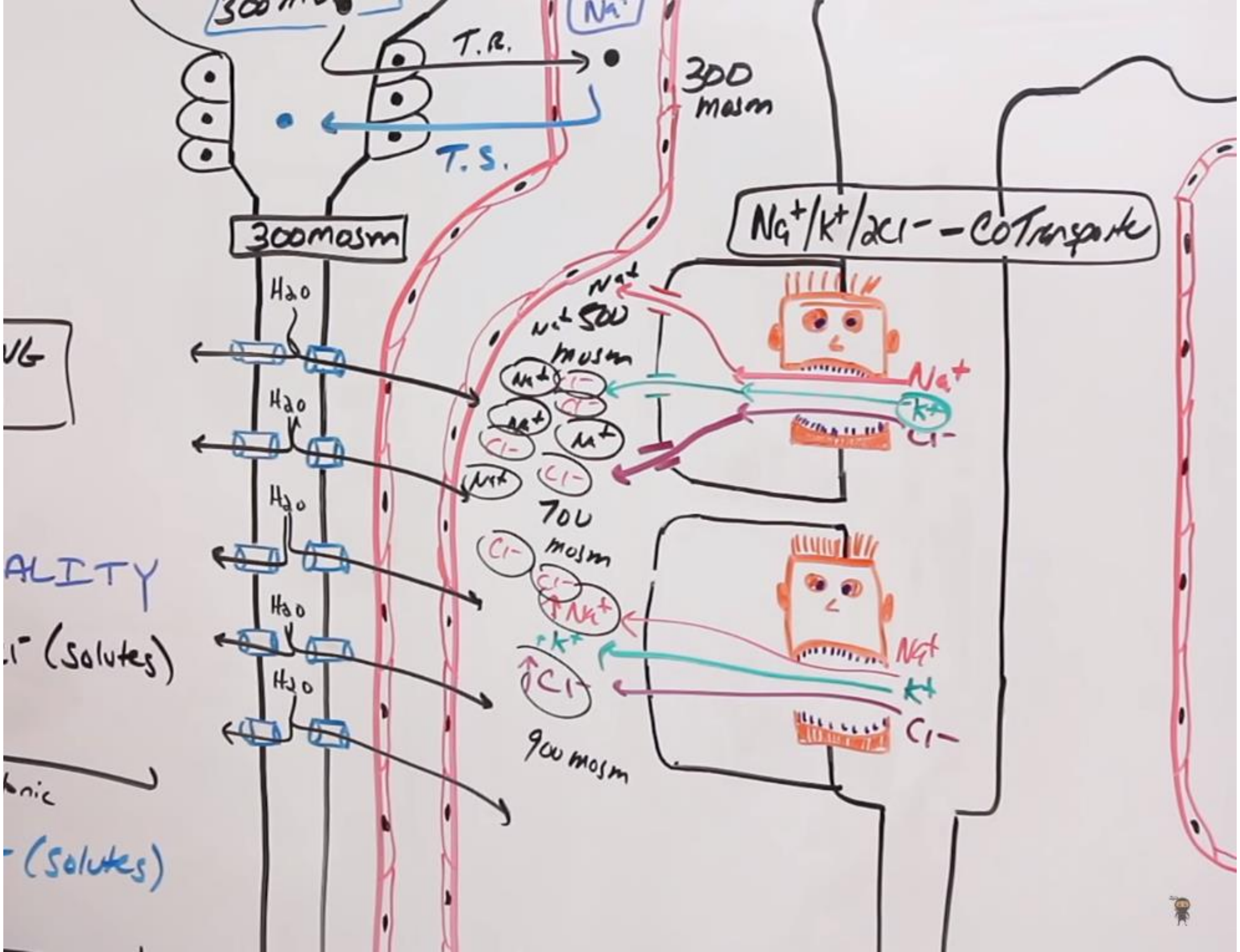


T.R.
T.S.
300 mosm
300mosm
Na+/K+/2Cl- - CoTransporter
500 mosm
700 mosm
900 mosm
Na+
K+
Cl-

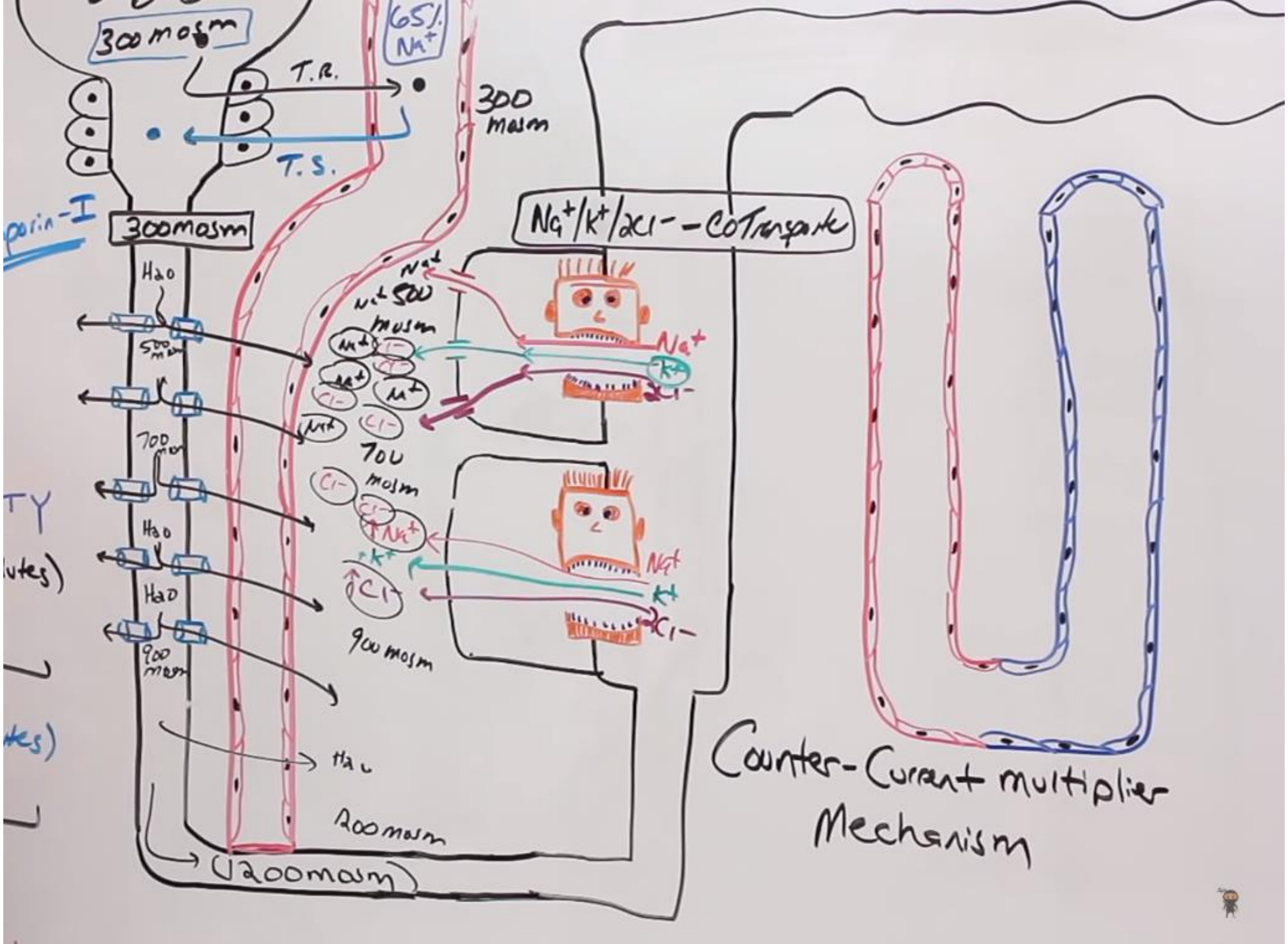

T.R.
T.S.
300mosm
300
mosm
Na+/K+/2Cl- -CoTransporter
Na+
Na+ 500
mosm
Na+
Cl-
Cl-
Na+
Cl-
Na+
Na+
Cl-
Na+
K+
Cl-
700
mosm
Cl-
Cl-
↑Na+
↑K+
↑Cl-
Na+
K+
Cl-
900 mosm

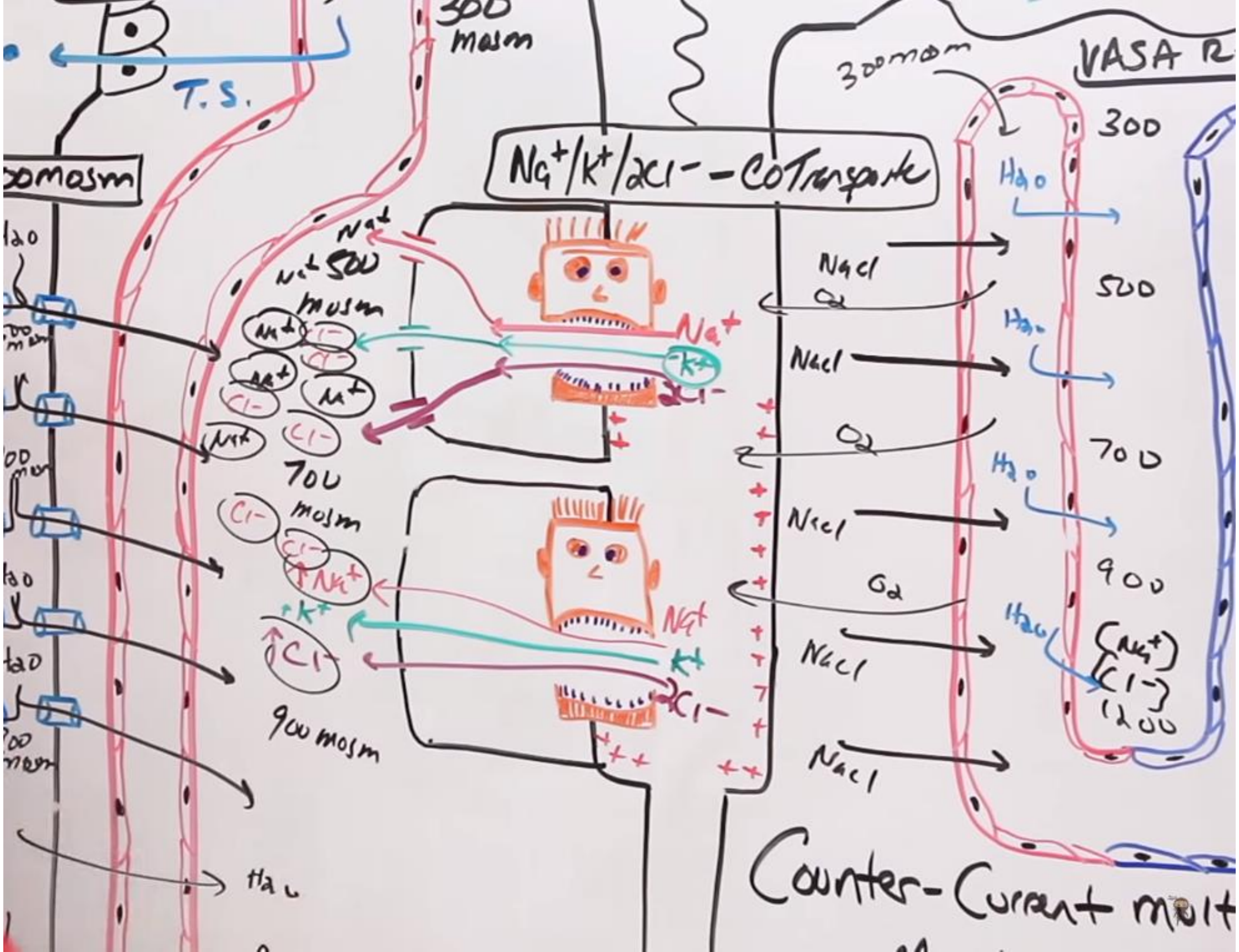


T.R.
T.S.
300 mosm
300mosm
H2O
Na+/K+/2Cl- - CoTransporter
Na+ 500 mosm
700 mosm
900 mosm
Na+
K+
Cl-

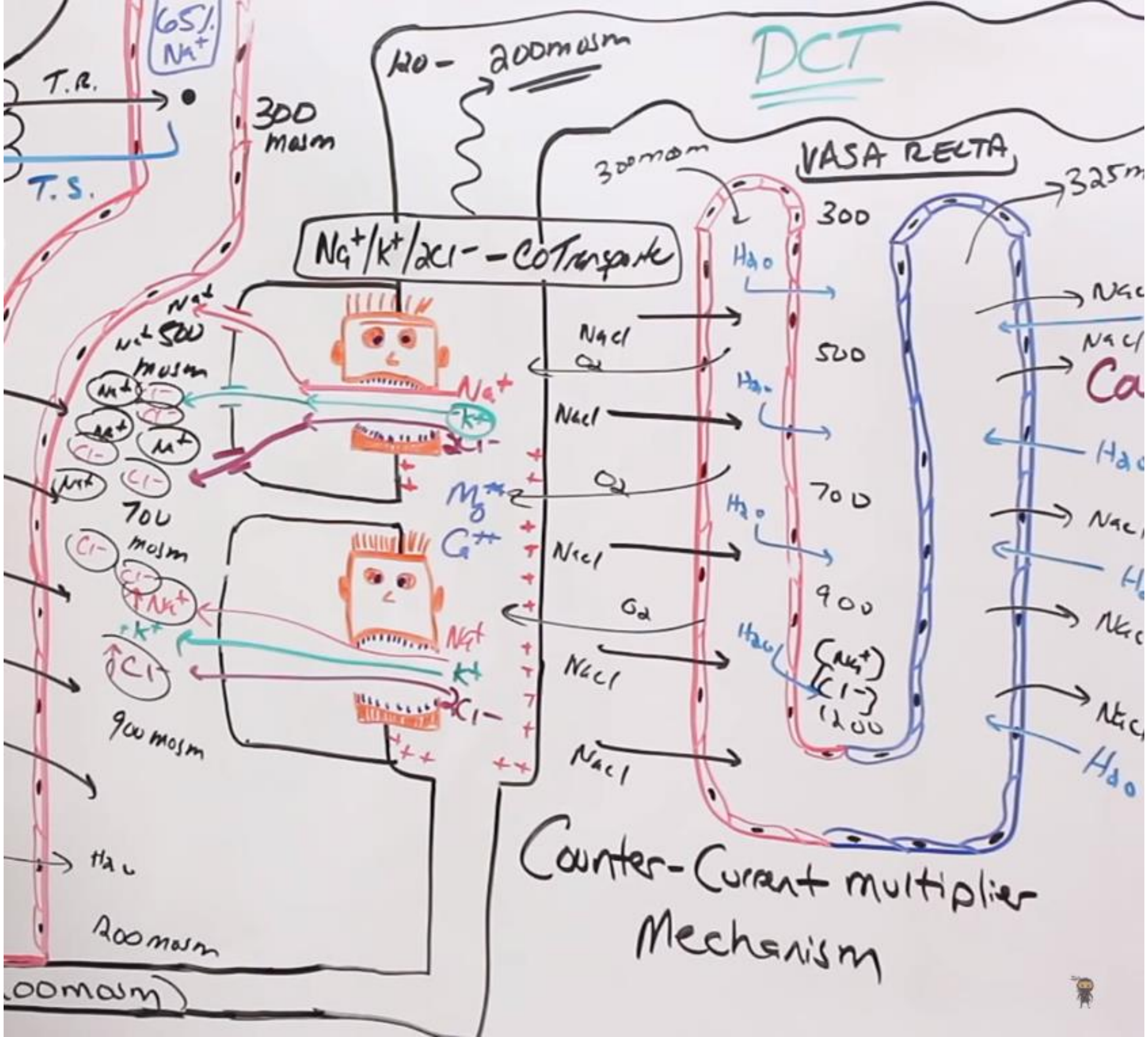


T.R.
300 mosm
T.S.
300mosm
Na+/K+/2Cl- - CoTransporte
H2O
H2O
H2O
H2O
H2O
500 mosm
700 mosm
900 mosm
Na+
K+
Cl-
ALITY
(solutes)
(solutes)

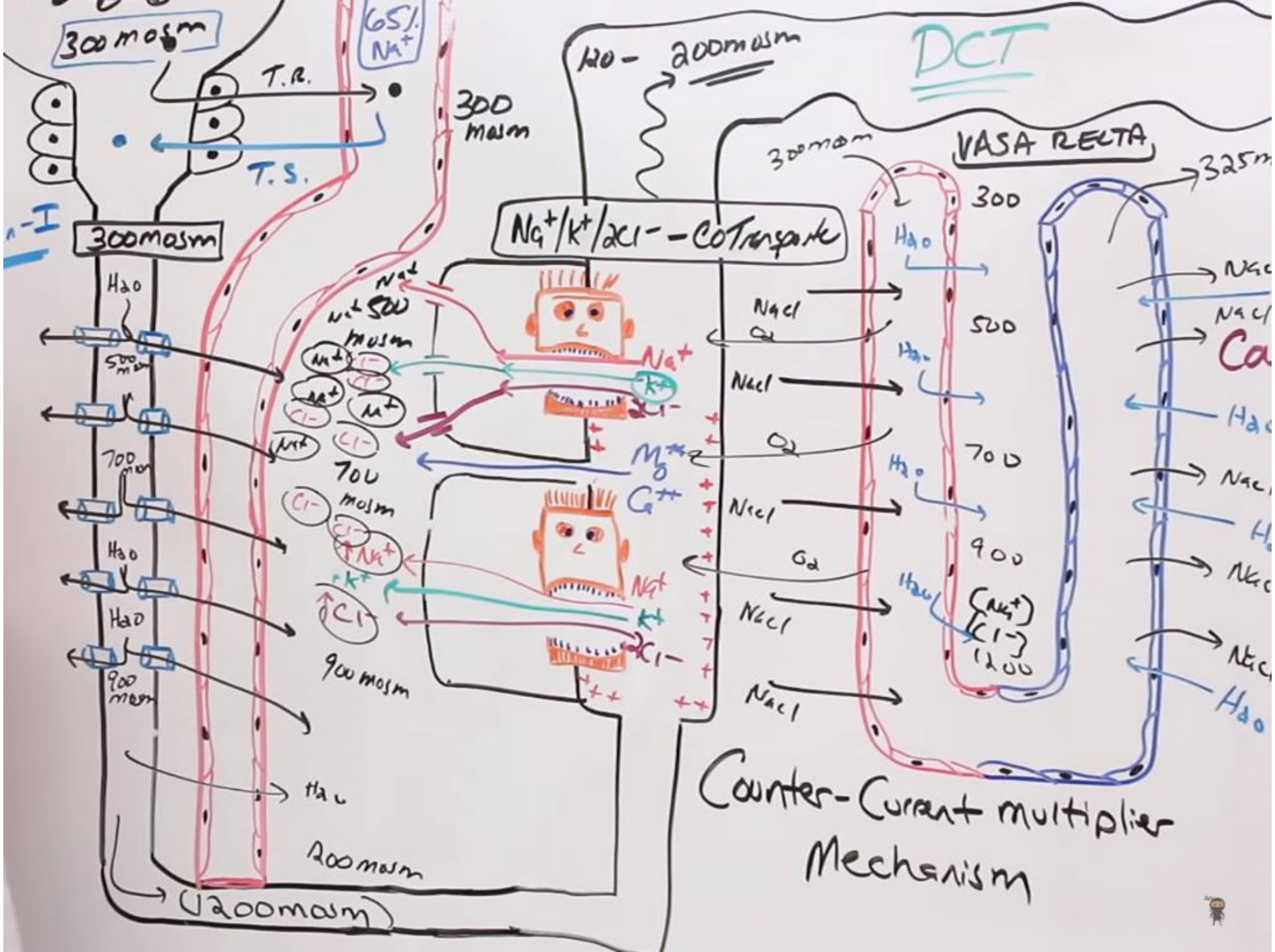

300 mosm
T.R.
T.S.
65% Na+
300 mosm
porin-I
300 mosm
Na+/K+/2Cl- - CoTransporter
H2O
500 mosm
700 mosm
900 mosm
700 mosm
900 mosm
1200 mosm
Counter-Current multiplier Mechanism



300 mosm
T.S.
Na+/K+/2Cl- -CoTransporte
VASA R
300mosm
300
500
700
900
1200
NaCl
O2
H2O
Na+
K+
Cl-
Na+ 500 mosm
700 mosm
900 mosm
Counter-Current mult



65% Na+
T.R.
T.S.
300 mosm
H2O
200mosm
DCT
VASA RECTA
300mosm
325m
Na+/K+/2Cl- - CoTransporter
Na+
Na+ 500 mosm
700 mosm
900 mosm
200 mosm
200mosm
Na+
K+
Cl-
Mg++
Ca++
NaCl
O2
H2O
300
500
700
900
[Na+]
[Cl-]
1200
Counter-Current multiplier Mechanism


300mosm
T.R.
T.S.
65% Na+
300 mosm
300mosm
H2O - 200mosm
DCT
VASA RECTA
Na+/K+/2Cl- - CoTransporter
500 mosm
700 mosm
900 mosm
200mosm
(1200mosm)
300
500
700
900
1200
Counter-Current multiplier
Mechanism

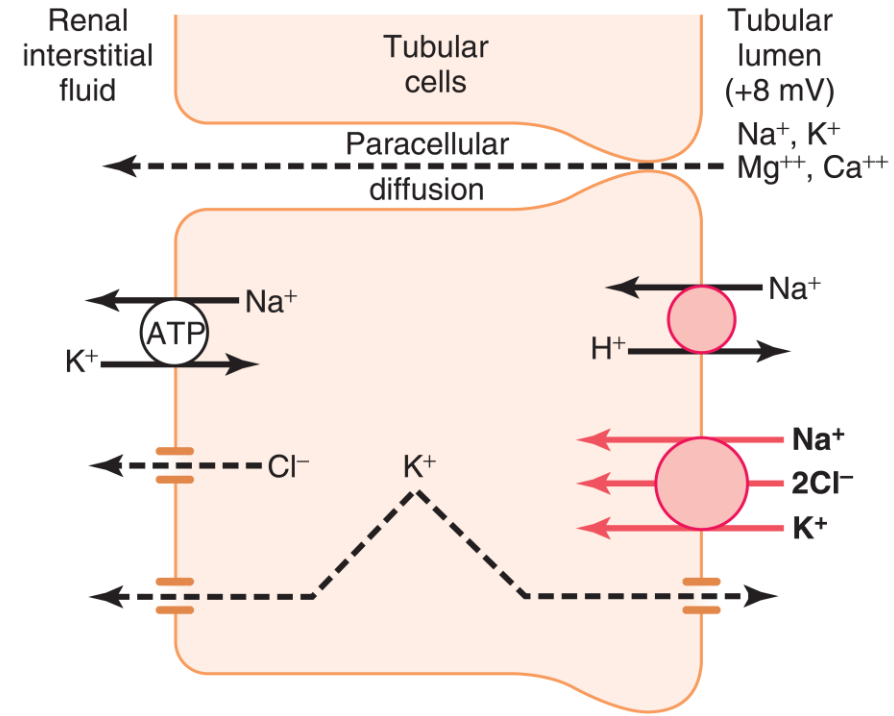


Figure 28-9. Mechanisms of sodium, chloride, and potassium transport in the thick ascending loop of Henle. The sodium-potassium ATPase pump in the basolateral cell membrane maintains a low intracellular sodium concentration and a negative electrical potential in the cell. The 1-sodium, 2-chloride, 1-potassium co-transporter in the luminal membrane transports these three ions from the tubular lumen into the cells, using the potential energy released by diffusion of sodium down an electrochemical gradient into the cells. Sodium is also transported into the tubular cell by sodium-hydrogen counter-transport. The positive charge (+8 mV) of the tubular lumen relative to the interstitial fluid forces cations such as Mg^{++} and Ca^{++} to diffuse from the lumen to the interstitial fluid via the paracellular pathway.

There is also significant paracellular reabsorption of cations, such as Mg++, Ca++, Na+, and K+, in the thick ascending limb as a result of the slight positive charge of the tubular lumen relative to the interstitial fluid. Although the 1-sodium, 2-chloride, 1-potassium co-transporter moves equal amounts of cations and anions into the cell, there is a slight backleak of potassium ions into the lumen, creating a positive charge of about +8 millivolts in the tubular lumen. This positive charge forces cations such as Mg++ and Ca++ to diffuse from the tubular lumen through the paracellular space and into the interstitial fluid.

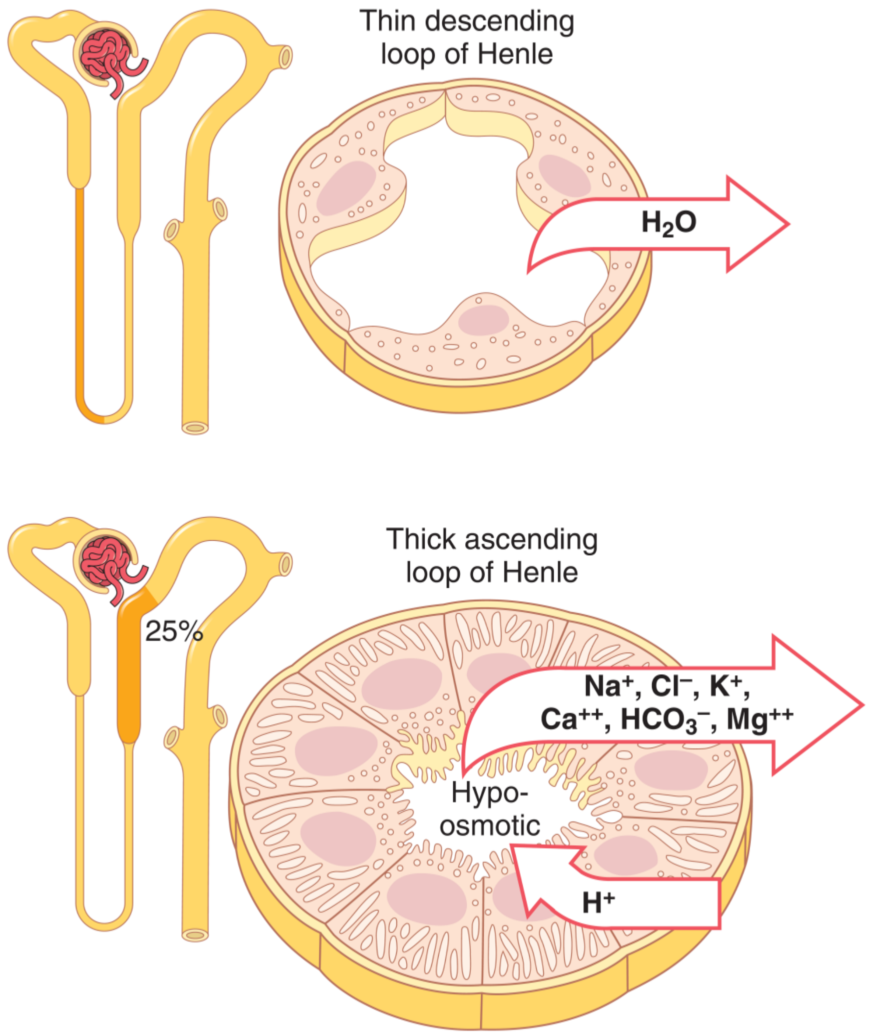
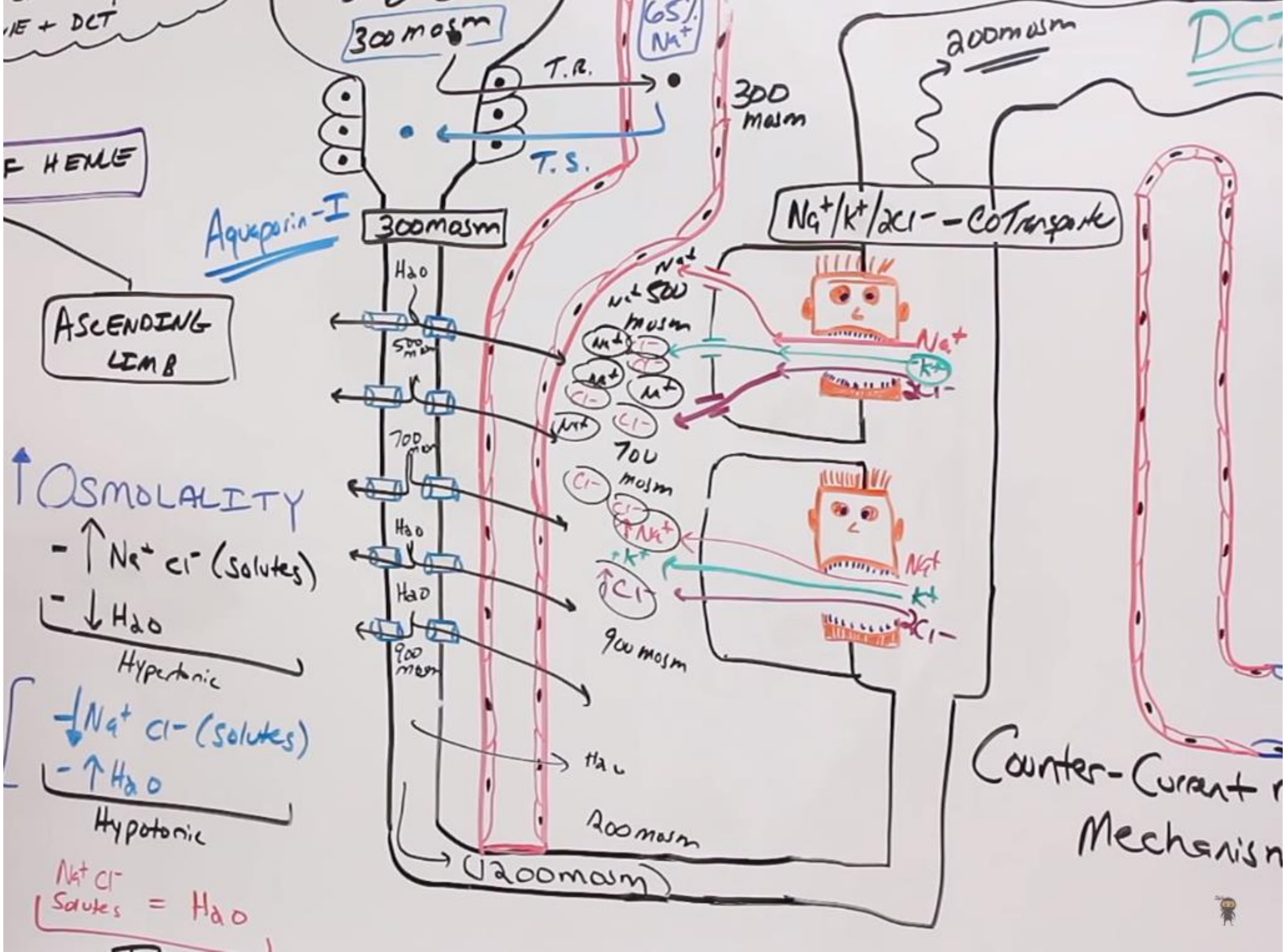
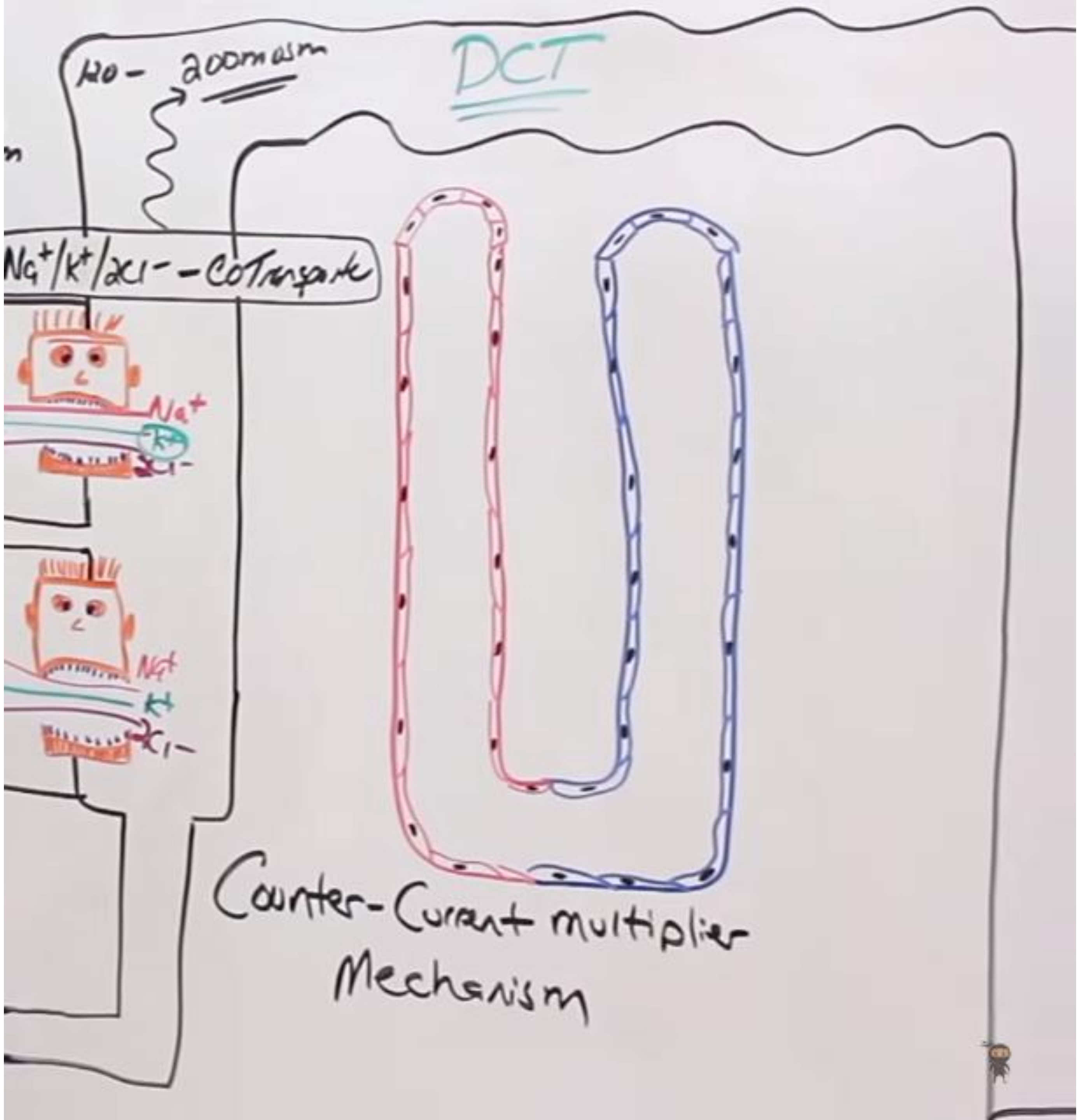
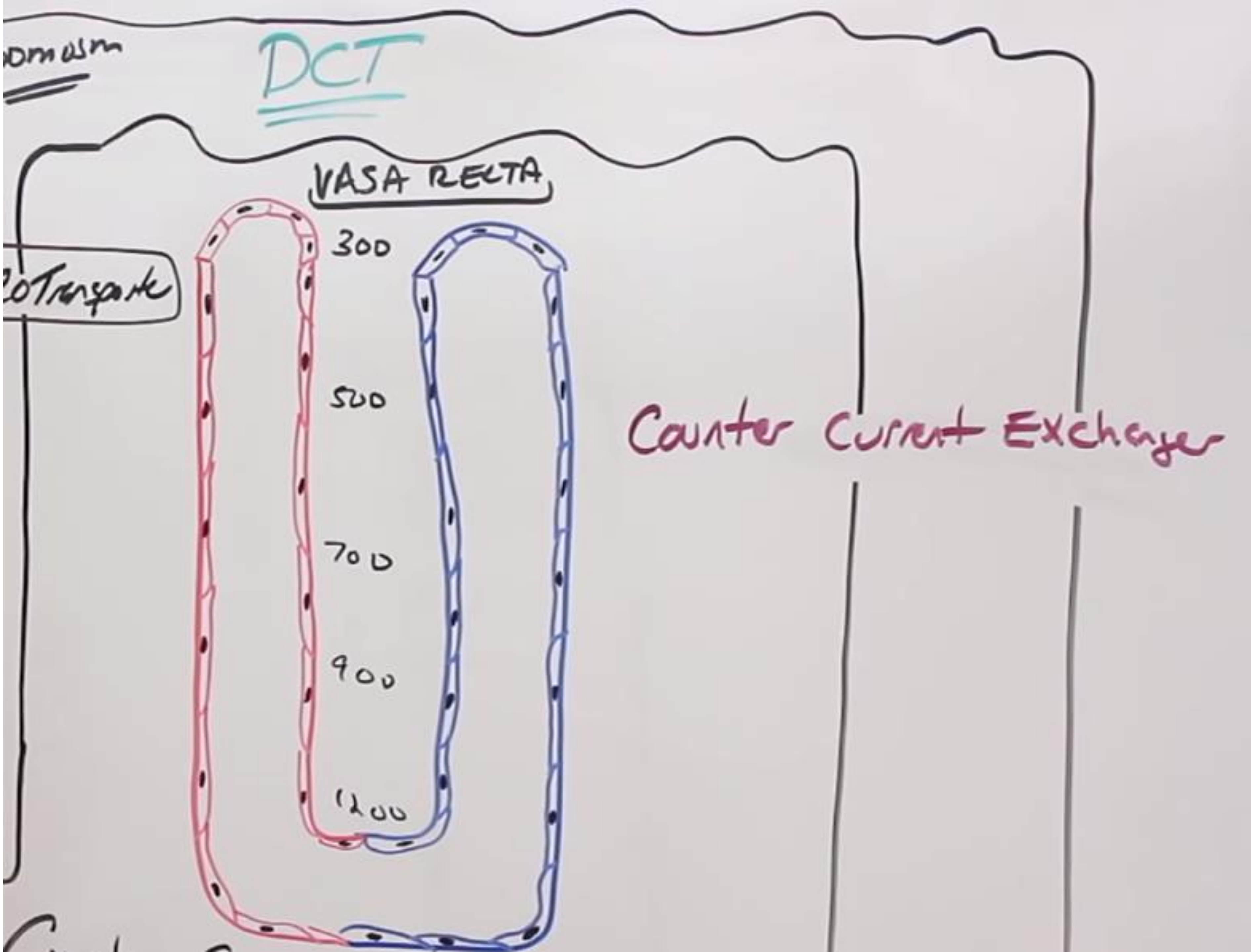


Figure 28-8. Cellular ultrastructure and transport characteristics of the thin descending loop of Henle (*top*) and the thick ascending segment of the loop of Henle (*bottom*). The descending part of the thin segment of the loop of Henle is highly permeable to water and moderately permeable to most solutes but has few mitochondria and little or no active reabsorption. The thick ascending limb of the loop of Henle reabsorbs about 25 percent of the filtered loads of sodium, chloride, and potassium, as well as large amounts of calcium, bicarbonate, and magnesium. This segment also secretes hydrogen ions into the tubular lumen.

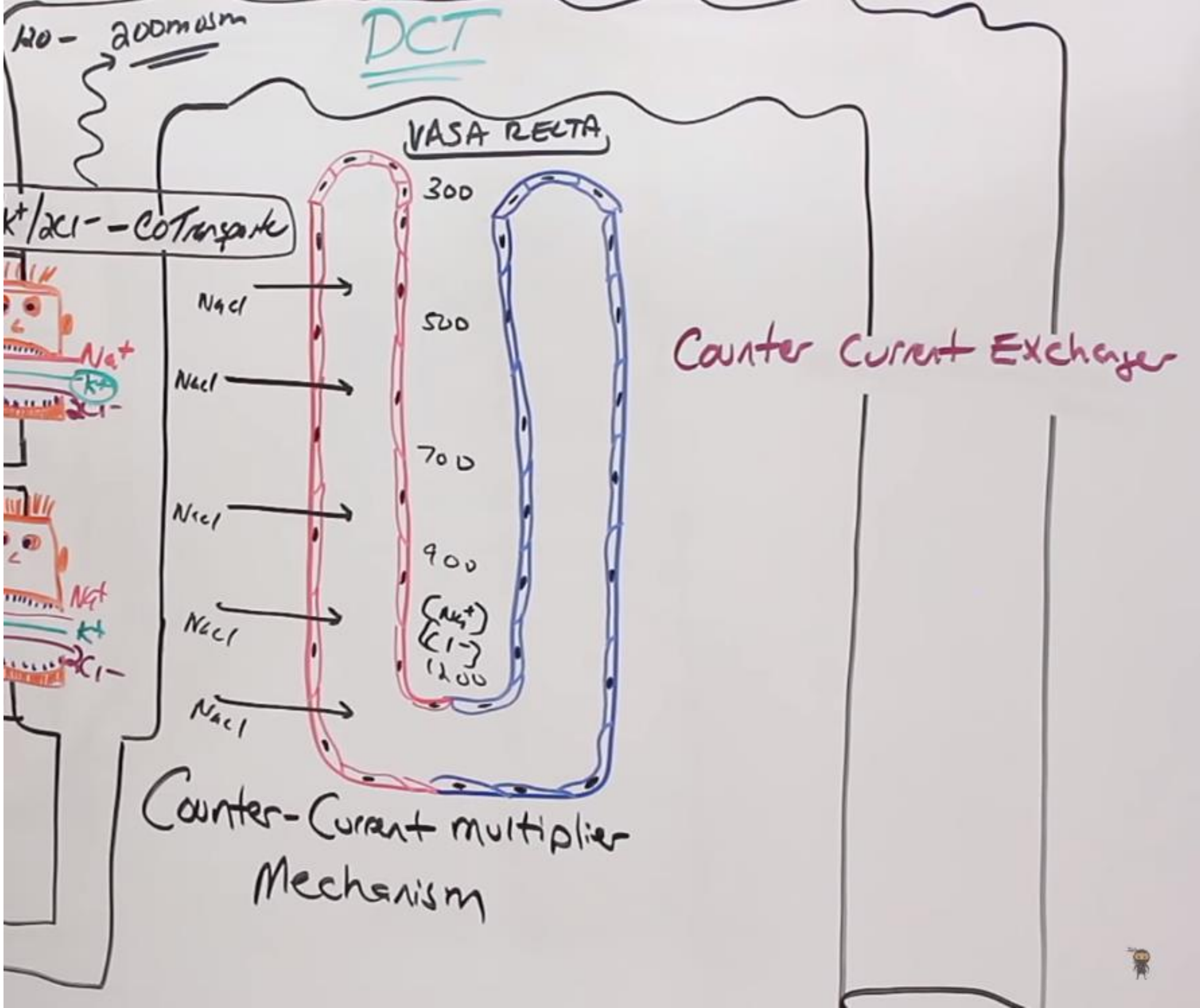


...IE + DCT
...F HENLE
ASCENDING LIMB
300 mosm
T.R.
T.S.
65% Na+
300 mosm
200 mosm
DCT
Aquaporin-I
300 mosm
H_2O
500 mosm
700 mosm
900 mosm
Na+ 500 mosm
700 mosm
900 mosm
1200 mosm
200 mosm
Na+/K+/2Cl- - CoTransporter
Na+
K+
Cl-
↑ Osmolality
- ↑ Na+ Cl- (solutes)
- ↓ H_2O
Hypertonic
- ↓ Na+ Cl- (solutes)
- ↑ H_2O
Hypotonic
Na+ Cl- Solutes = H_2O
Counter-Current Mechanism

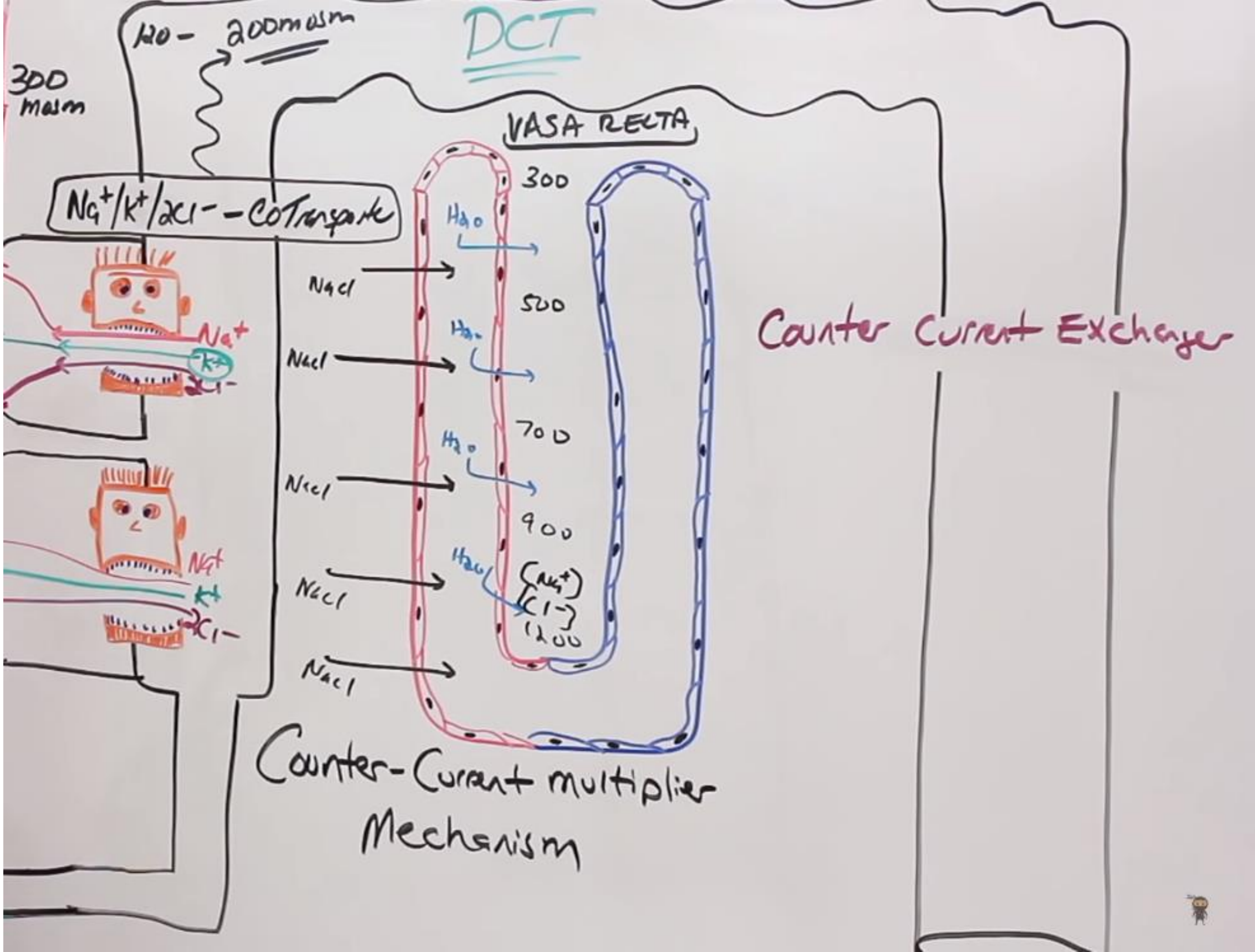

H2O - 200mosm
DCT
Na+/K+/2Cl- - CoTransport
Na+
K+
2Cl-
Na+
K+
2Cl-
Counter-Curant multiplier
Mechanism



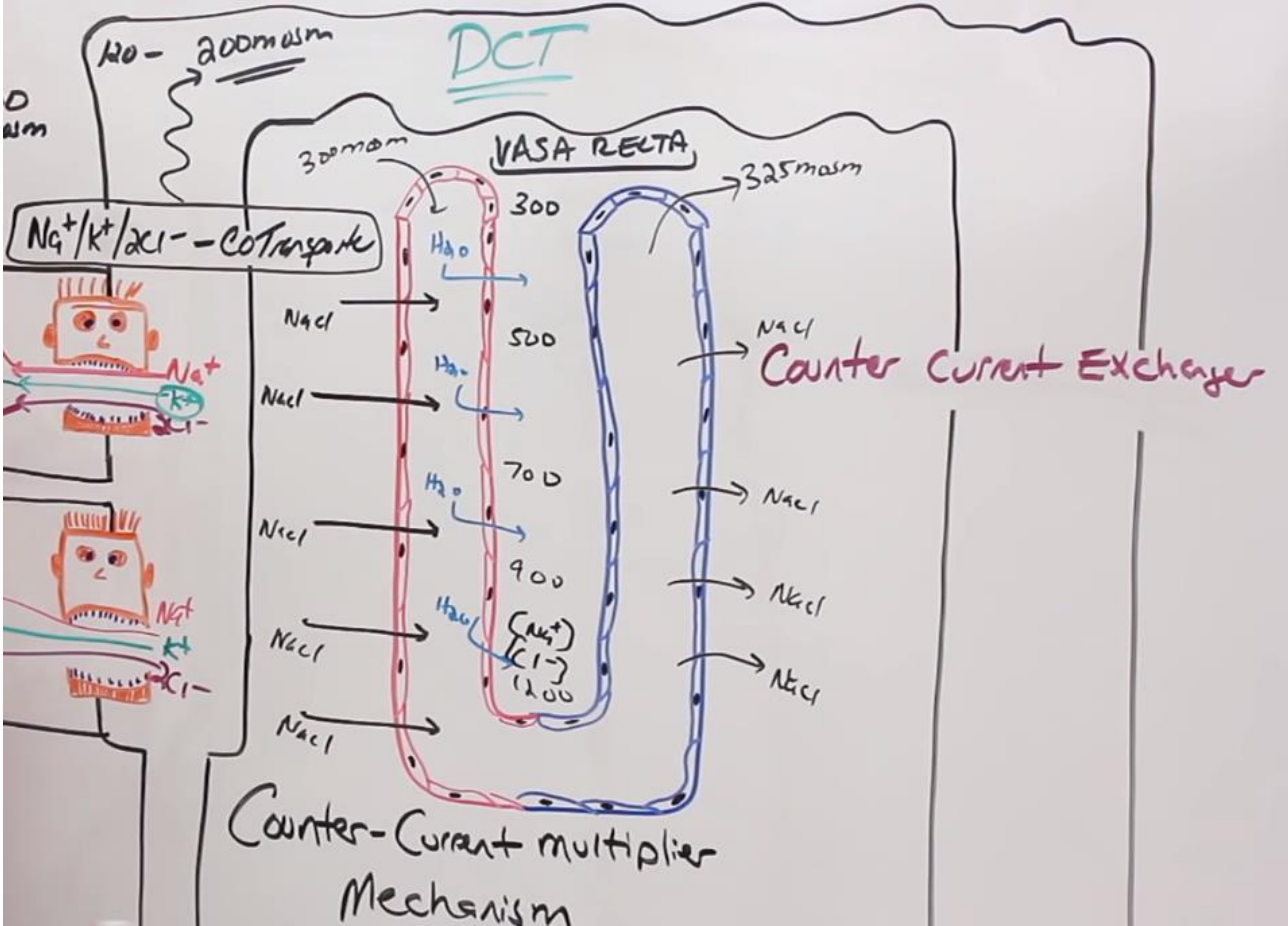
DCT
VASA RECTA
300
500
700
900
1200
Counter Current Exchanger



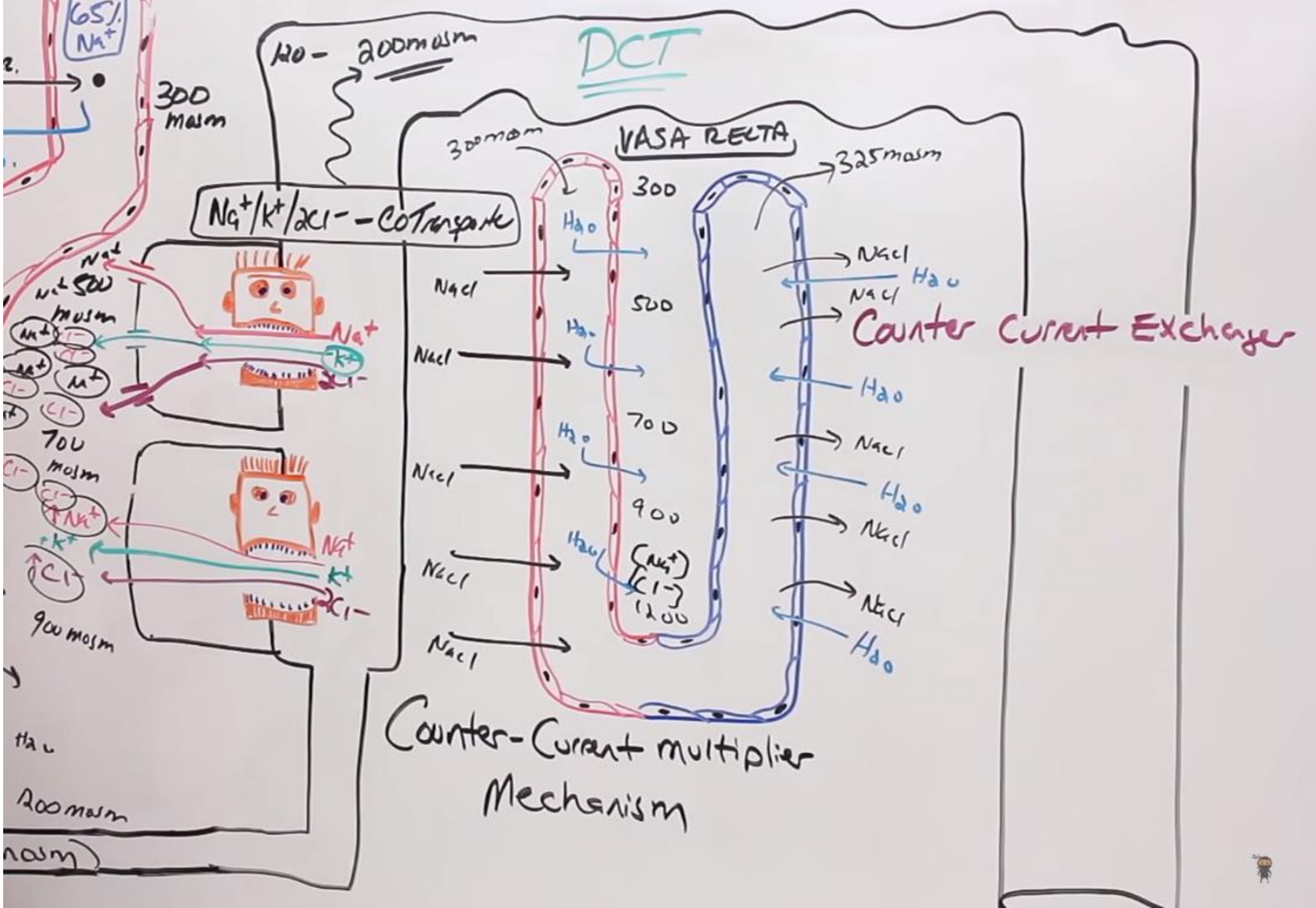
H2O - 200mosm
DCT
VASA RECTA
K+/2Cl- - CoTransport
300
NaCl
500
NaCl
Na+
K+
Cl-
700
NaCl
900
NaCl
Na+
K+
Cl-
Na+
Cl-
1200
NaCl
Counter Current Exchanger
Counter-Current multiplier
Mechanism



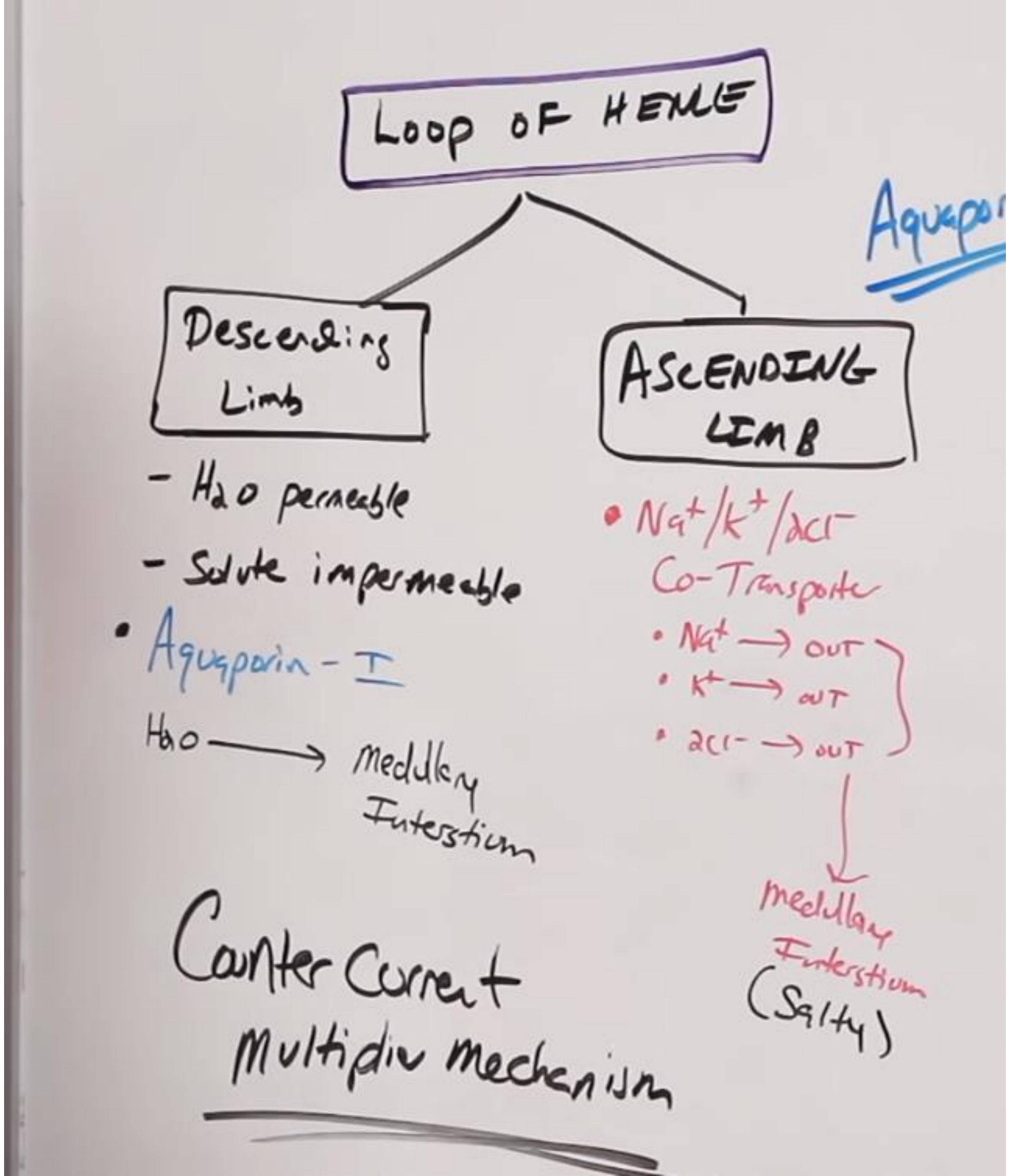
DCT
120- 200mosm
300 mosm
VASA RECTA
Na+/K+/2Cl- - CoTransporter
NaCl
H2O
300
500
700
900
[Na+]
[Cl-]
1200
Na+
K+
2Cl-
Counter Current Exchanger
Counter-Current multiplier Mechanism



DCT
H2O - 200mosm
VASA RECTA
300mosm
325mosm
Na+/K+/2Cl- - CoTransporter
300
500
700
900
1200
H2O
NaCl
Na+
K+
2Cl-
Counter Current Exchanger
Counter-Current multiplier Mechanism



DCT
200mosm
300 mosm
VASA RECTA
300mosm
325mosm
Na+/K+/2Cl- -CoTransporter
300
500
700
900
1200
NaCl
H2O
Na+
K+
Cl-
500 mosm
700 mosm
900 mosm
Counter Current Exchanger
Counter-Current multiplier Mechanism
65% Na+
200mosm

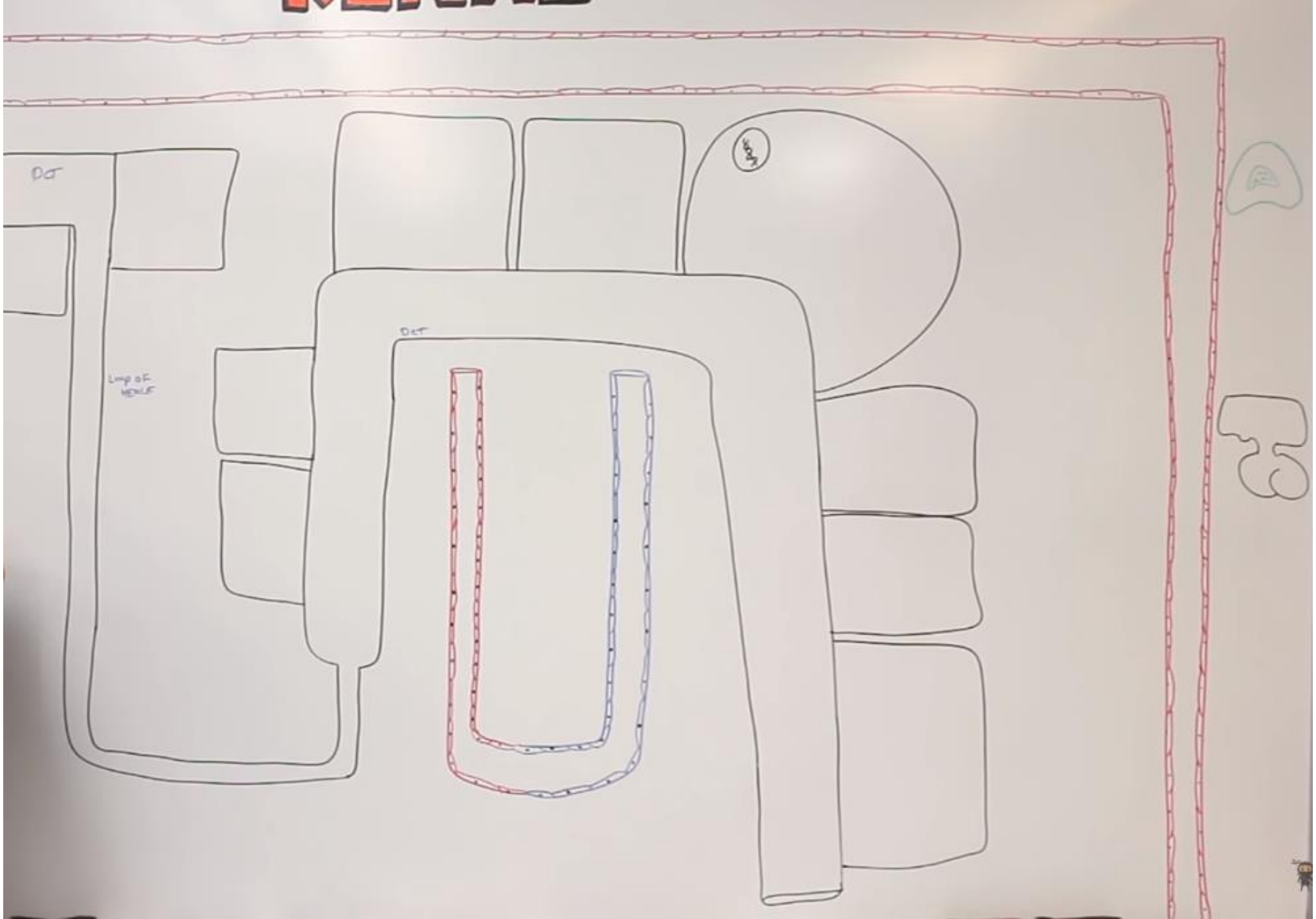

LOOP OF HENLE
Descending Limb
- H2O permeable
- Solute impermeable
• Aquaporin - I
H2O → medullary Interstium
Counter Current
Multiplier Mechanism
ASCENDING LIMB
• Na+/K+/2Cl- Co-Transporter
• Na+ → OUT
• K+ → OUT
• 2Cl- → OUT
medullary Interstium
(Salty)
Aquapor

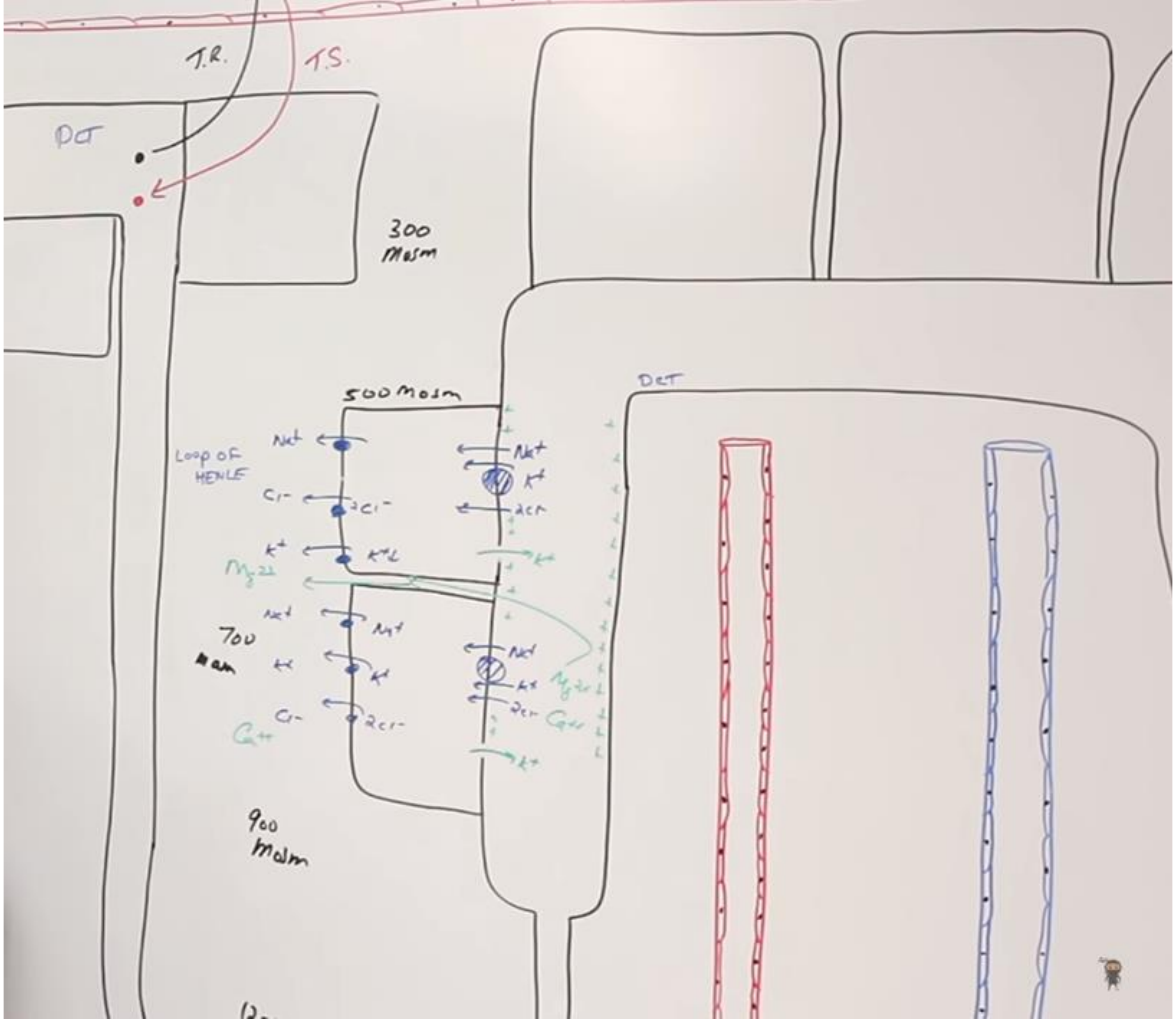
Urinary system lecture 3/ part 2

Process of urine Formation

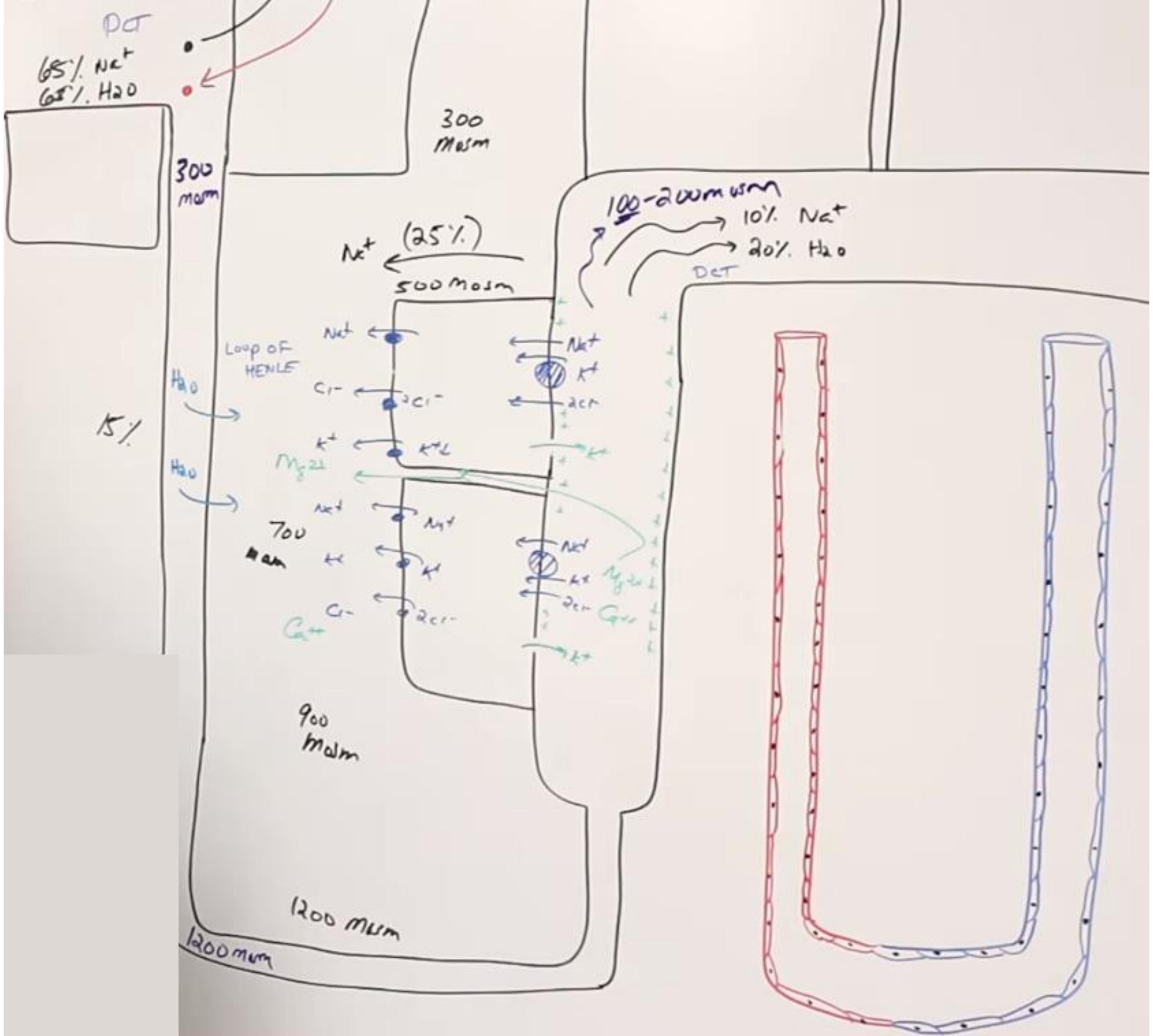
Abdallah Wasel Hattab

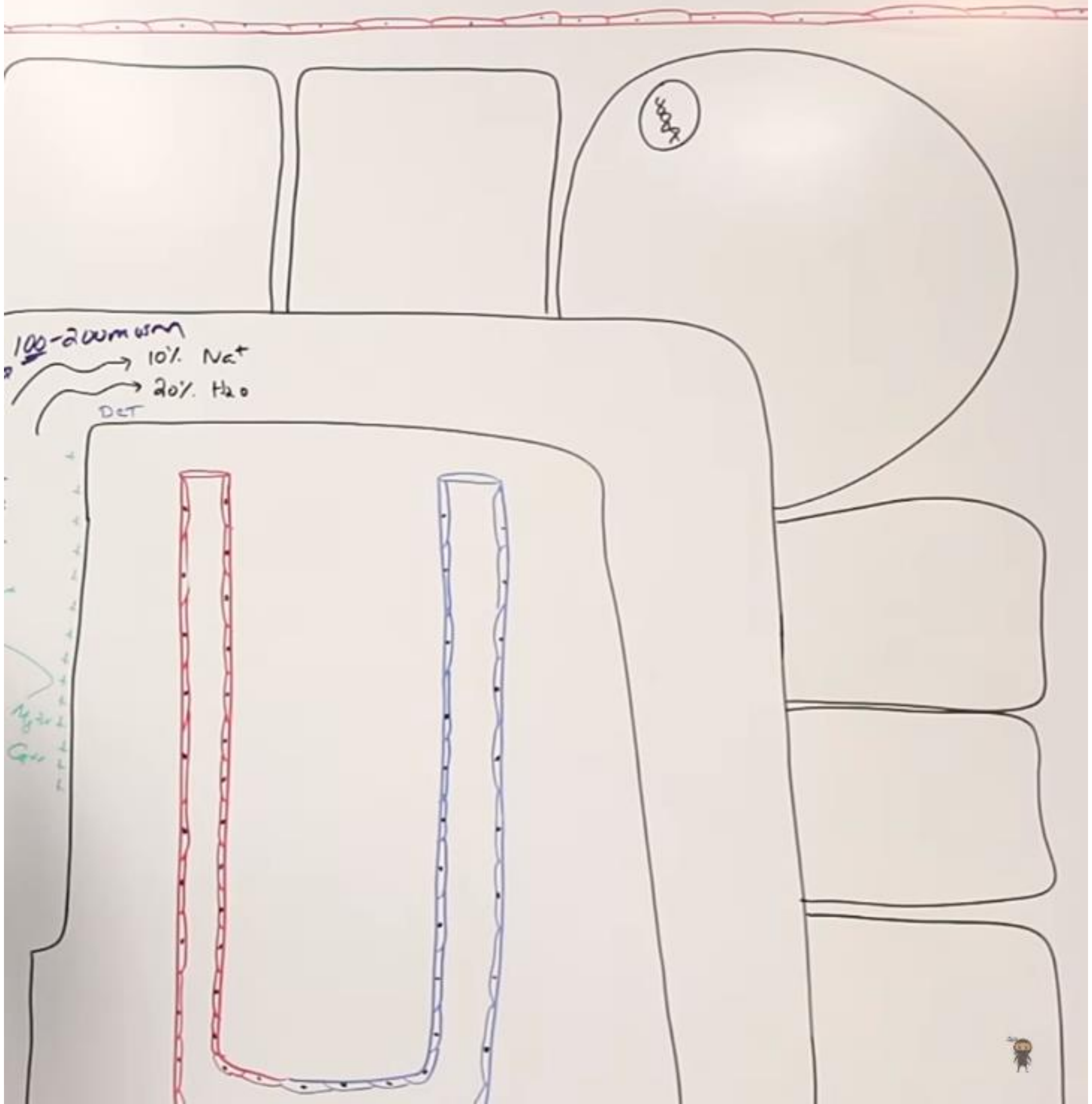
lecture 10

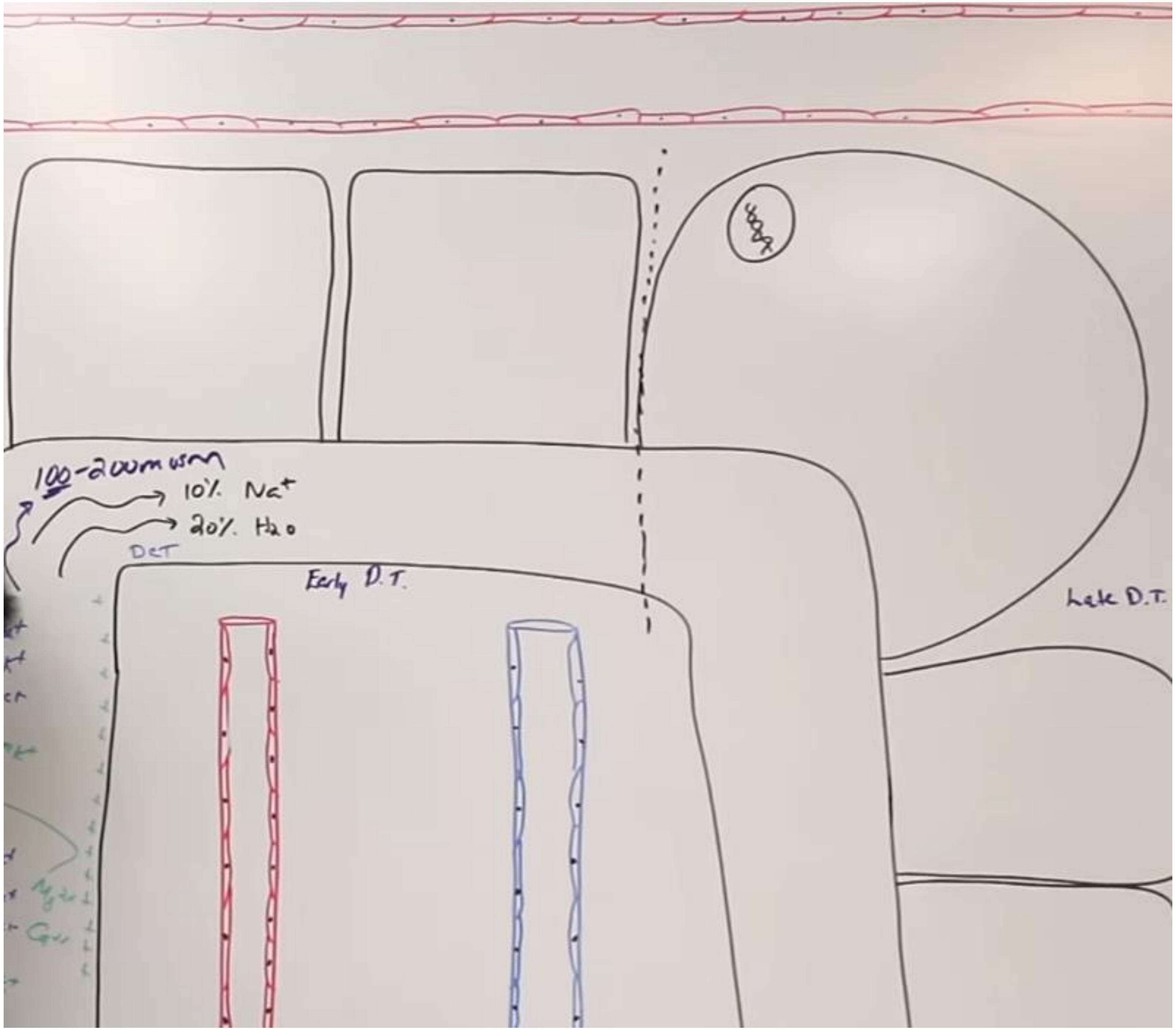

DCT
Loop of
Henle
DCT



T.R.
T.S.
DCT
300 mOsm
500 mOsm
LOOP OF HENLE
Na+
Cl-
2Cl-
K+
Mg2+
700
900 mOsm
Ca++
DCT

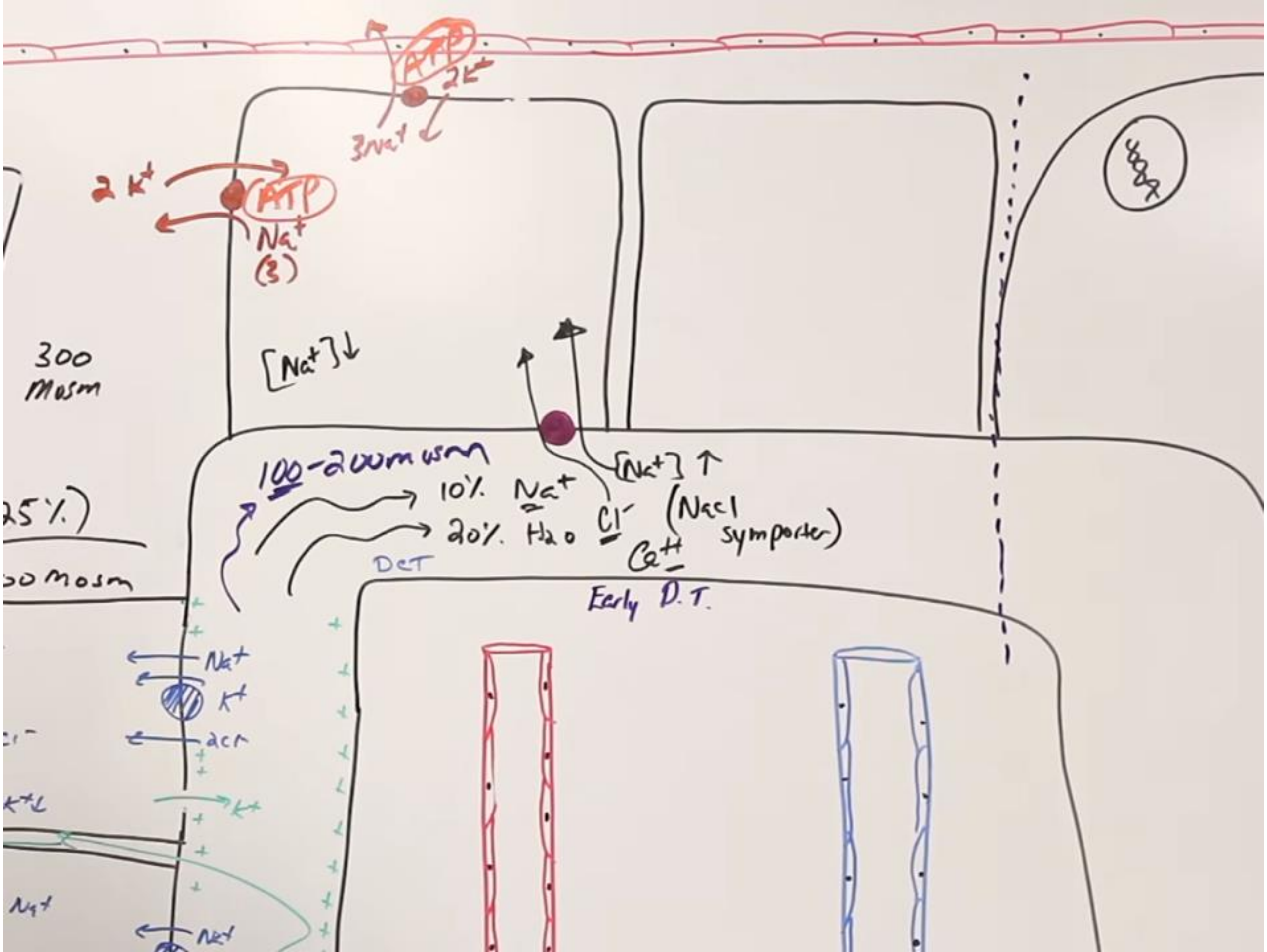

PCT
65% Na+
65% H2O
300 Mosm
300 mosm
Na+
(25%)
500 mosm
100-200 mosm
10% Na+
20% H2O
DCT
Loop of HENLE
H2O
H2O
15%
Na+
Cl-
2Cl-
K+
K+
Mg2+
Na+
K+
2Cl-
700 mosm
Ca++
900 mosm
1200 mosm
1200 mosm


100-200mosm
10% Na+
20% H2O
DCT

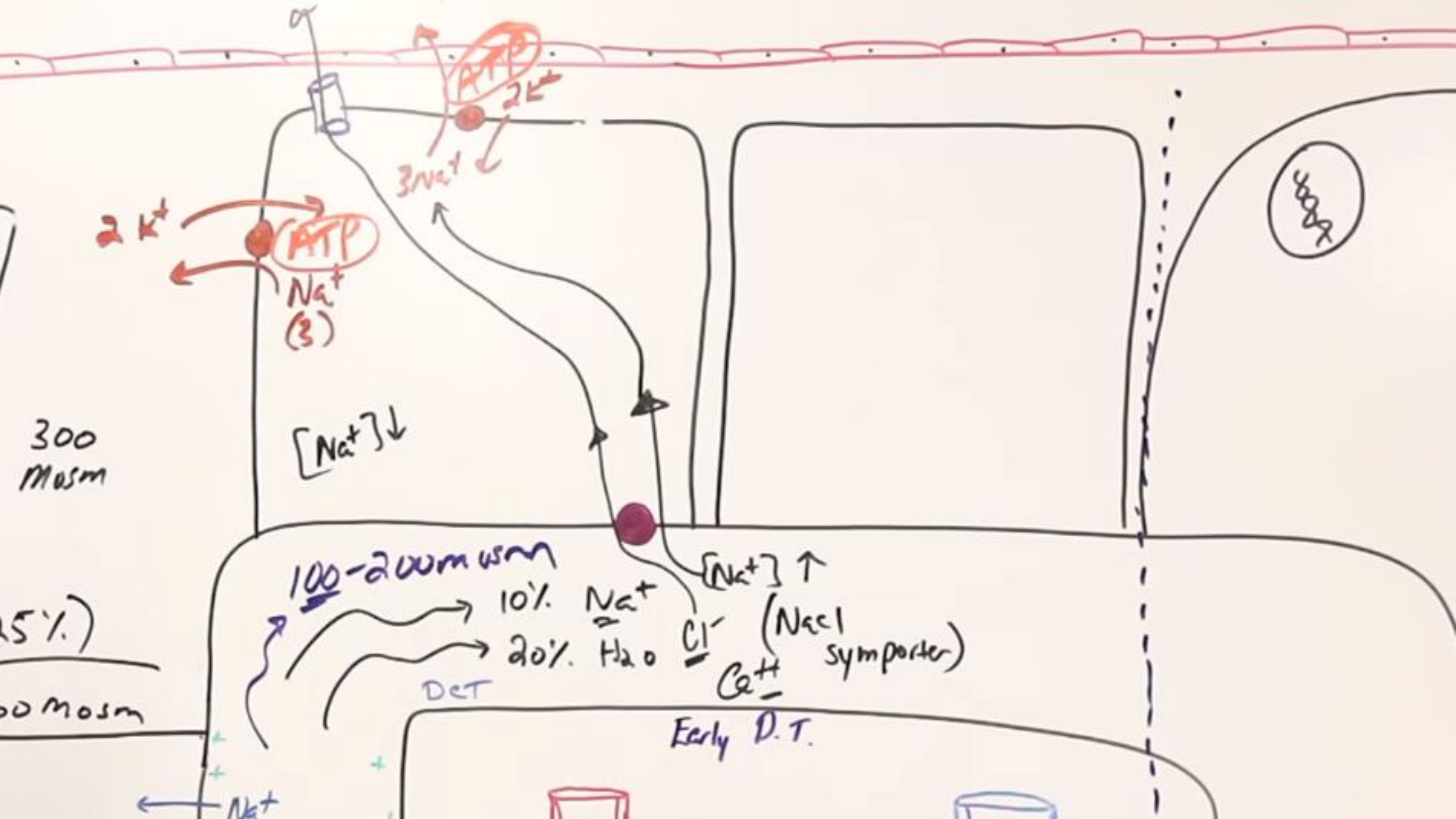


100-200mosm
10% Na+
20% H2O
DCT
Early D.T.
Late D.T.

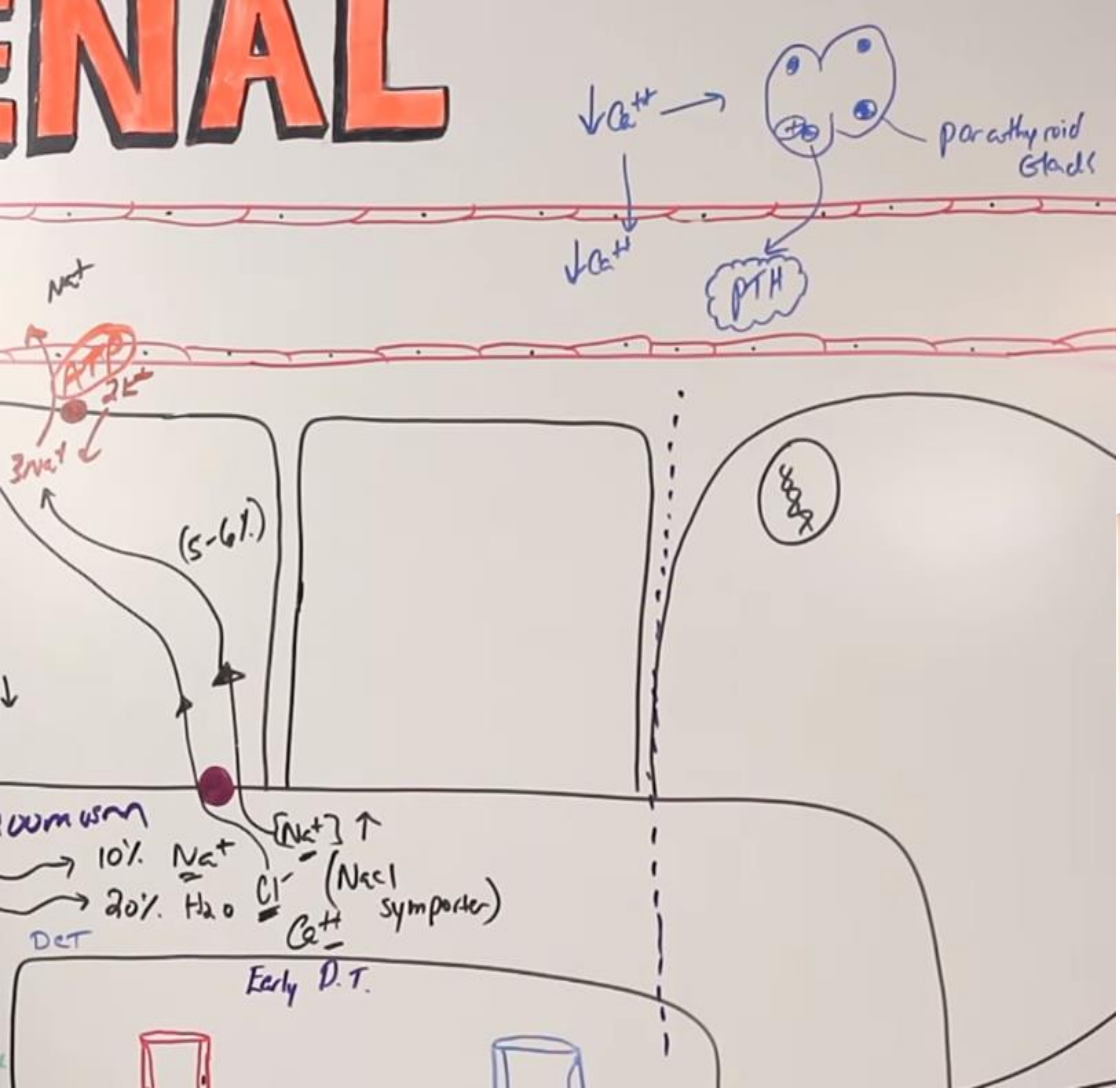
T.S.
ATP
2K+
3Na+
2 K+
ATP
Na+ (3)
300 Mosm
100-200mosm
10% Na+
20% H2O
DCT
(25%)
Na+
500 mosm
Early D.T.
Na+
K+
2Cl-
K+
Na+



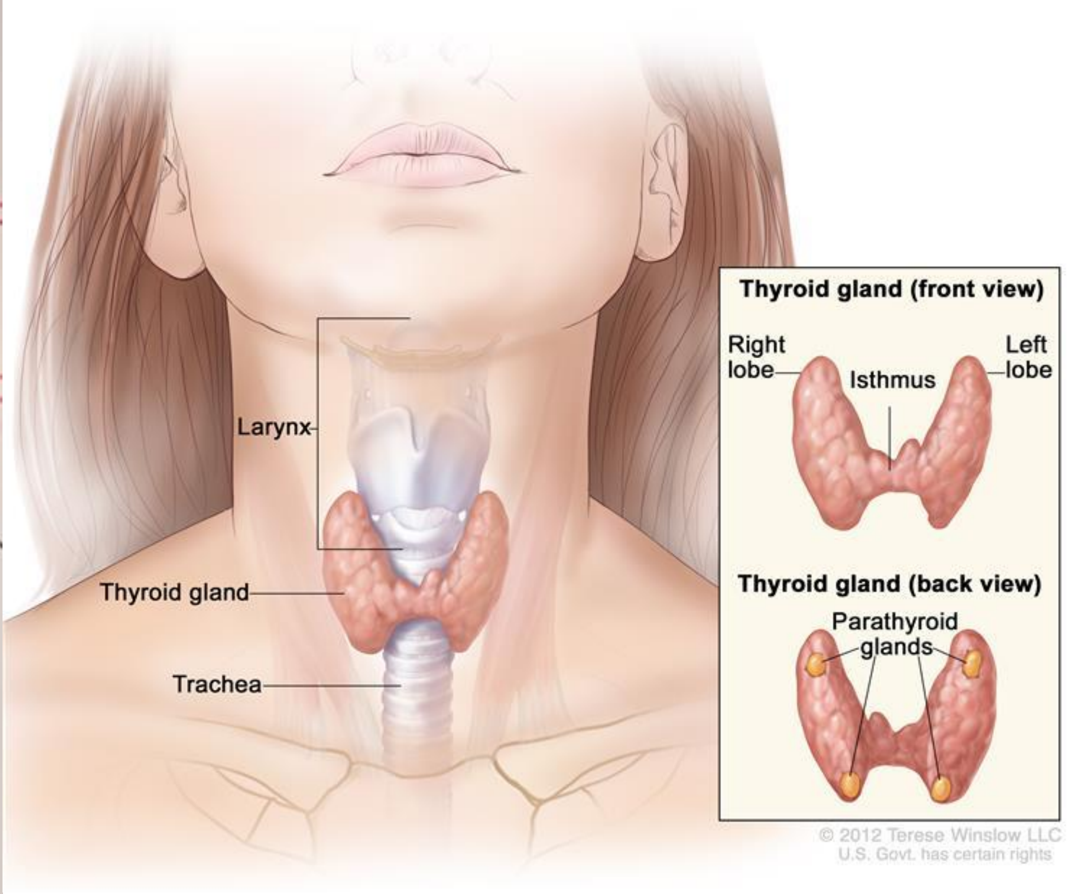
ATP
2K+
3Na+
2K+
ATP
Na+
(3)
300
Mosm
[Na+]↓
[Na+]↑
100-200mosm
10% Na+
20% H2O
Cl-
Ca++
(NaCl
symporter)
DCT
Early D.T.
25%
Na+
K+
2Cl-
K+
Na+
Na+

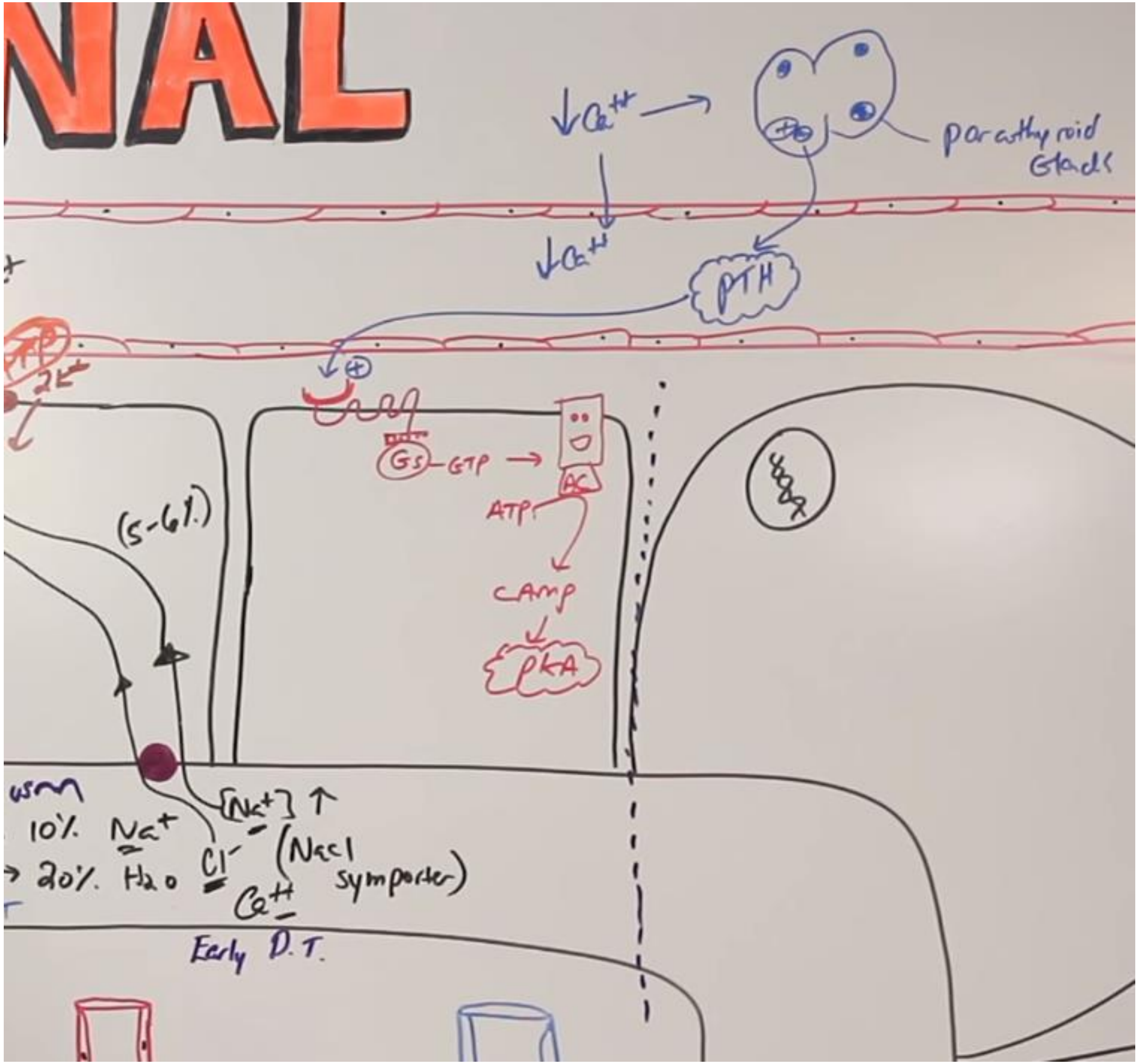


ATP
2K+
3Na+
2 K+
ATP
Na+
(3)
300
Mosm
[Na+]↓
100-200mosm
10% Na+
20% H2O
Cl-
[Na+]↑
(NaCl
symporter)
Ca++
DCT
Early D.T.
Na+

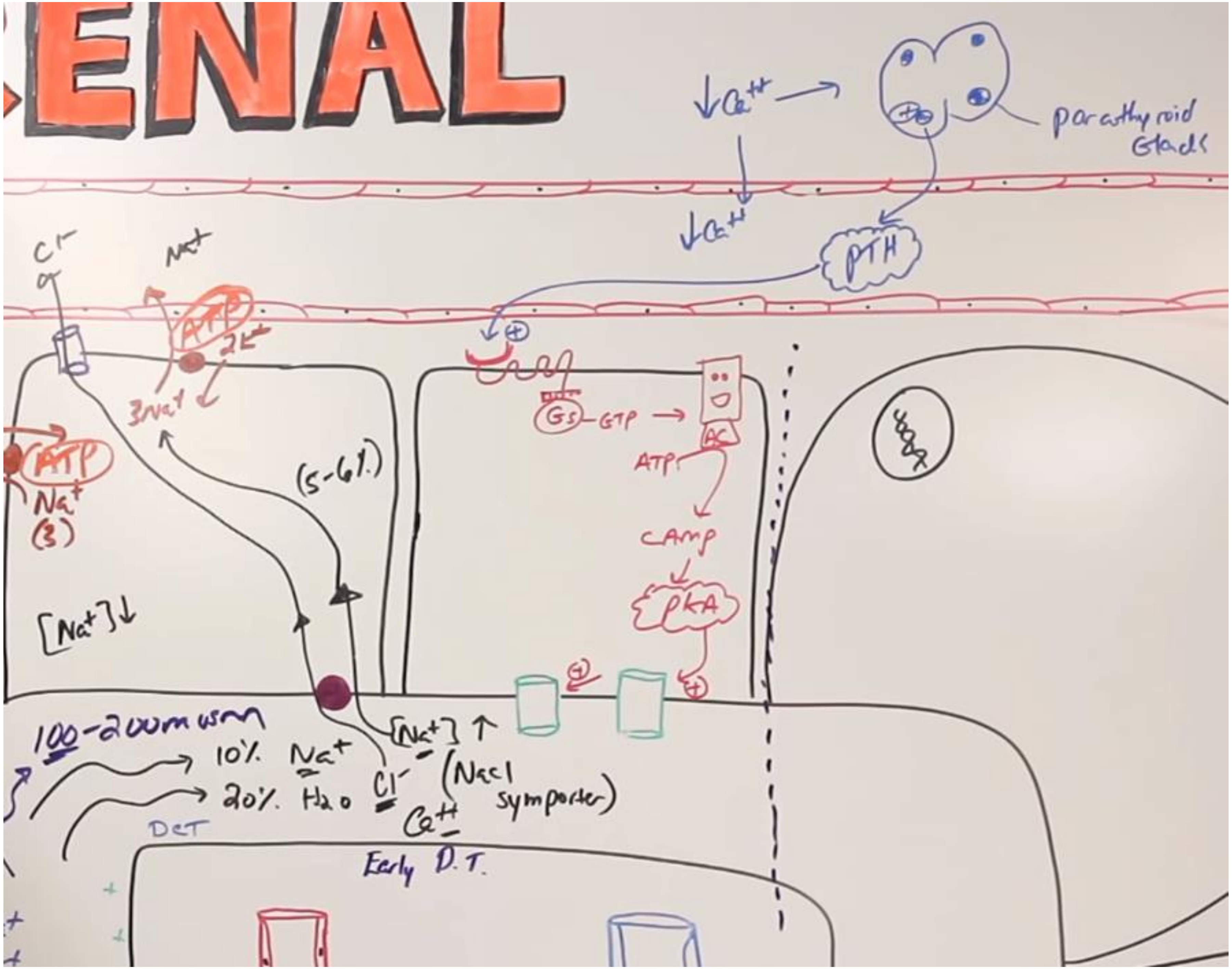


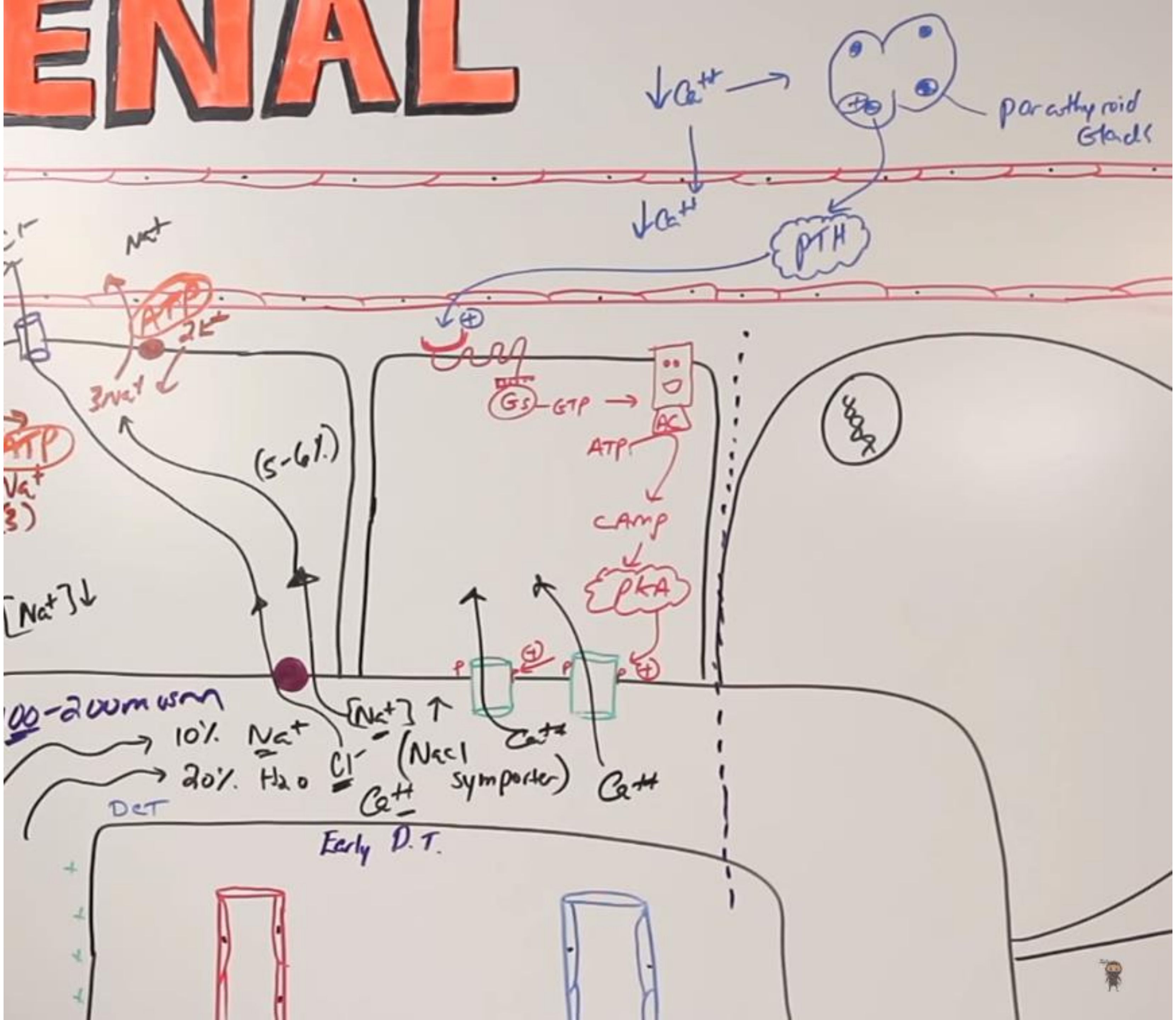
Anatomy of the Thyroid and Parathyroid Glands

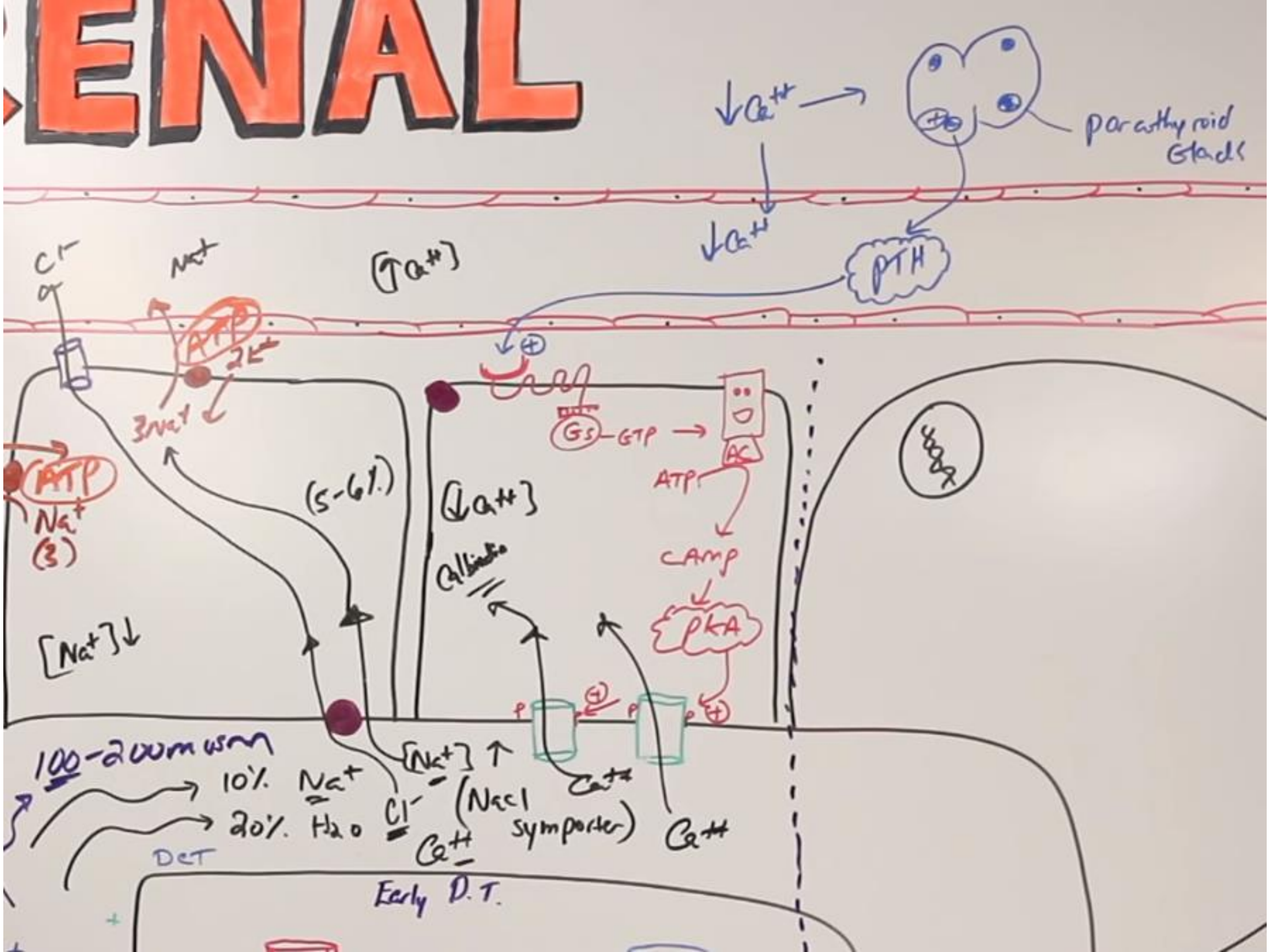




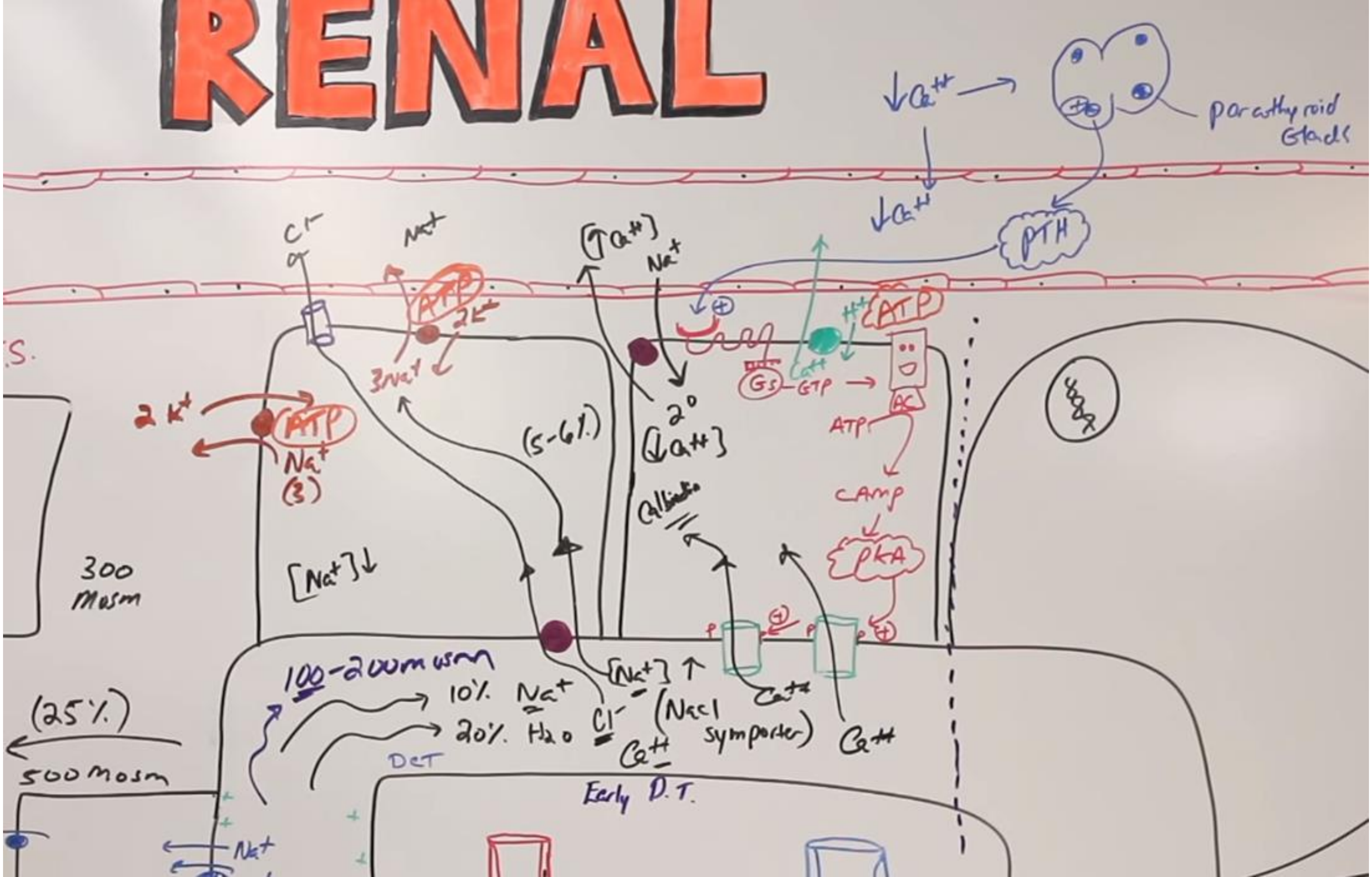
NAL
↓Ca++
parathyroid Glands
↓Ca++
PTH
Gs-GTP
AC
ATP
cAMP
PKA
(5-6%)
[Na+] ↑
10% Na+
20% H2O
Cl-
(NaCl symporter)
Ca++
Early D.T.

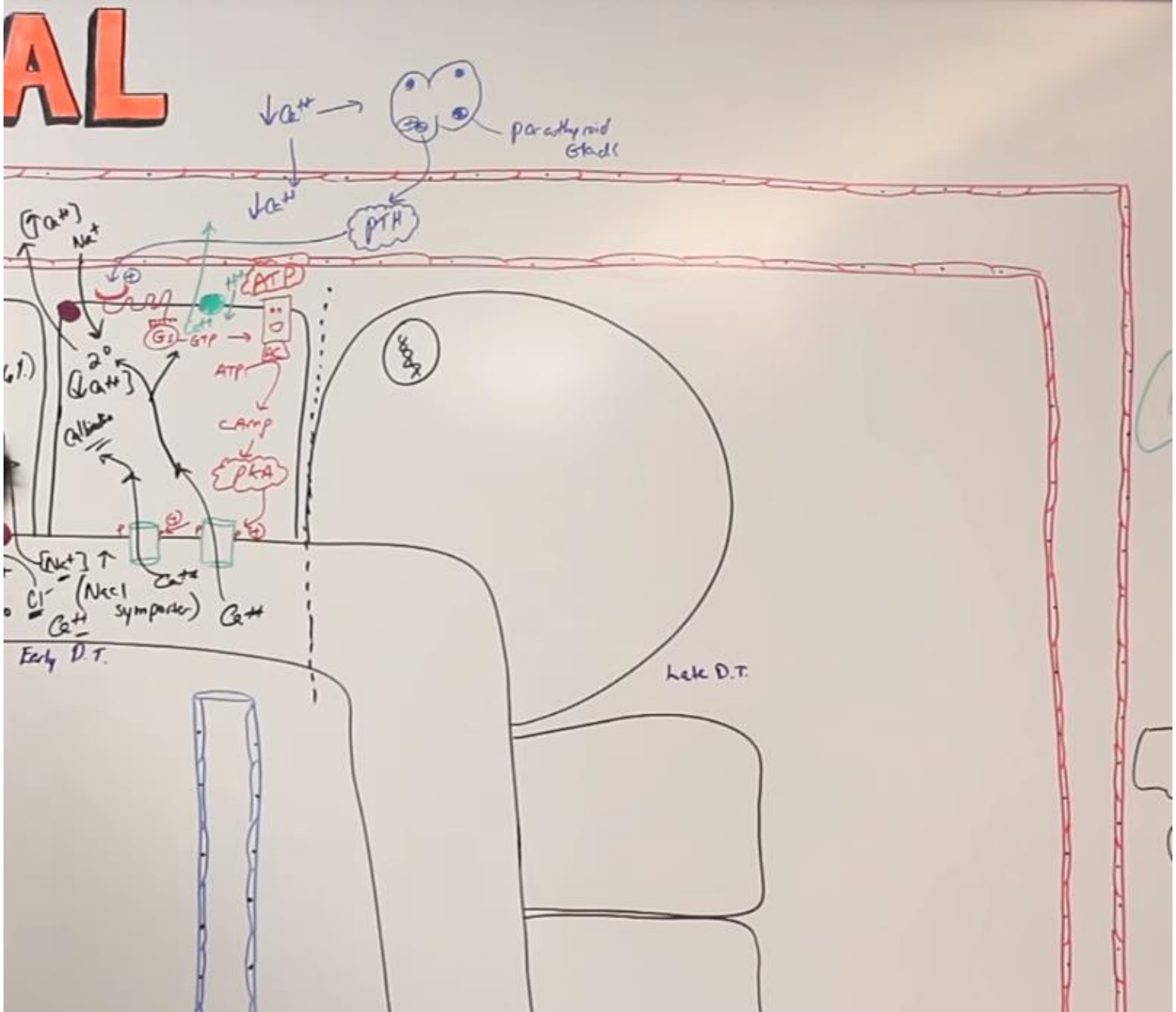

ENAL
↓Ca++
parathyroid Glands
↓Ca++
PTH
Cl⁻
Na⁺
ATP
2K⁺
3Na⁺
Gs
GTP
AC
ATP
cAMP
PKA
ATP
Na⁺ (3)
(5-6%)
[Na⁺]↓
[Na⁺]↑
100-200mosm
10% Na⁺
20% H2O
Cl⁻
Ca++
(NaCl symporter)
DCT
Early D.T.


ENAL
↓Ca++
parathyroid Glands
↓Ca++
PTH
Na+
ATP
2K+
3Na+
ATP
Na+
(5-6%)
Gs
GTP
AC
ATP
cAMP
PKA
[Na+]↓
[Na+] ↑
100-200mosm
10% Na+
20% H2O
Cl-
(NaCl symporter)
Ca++
Ca++
Ca++
DCT
Early D.T.

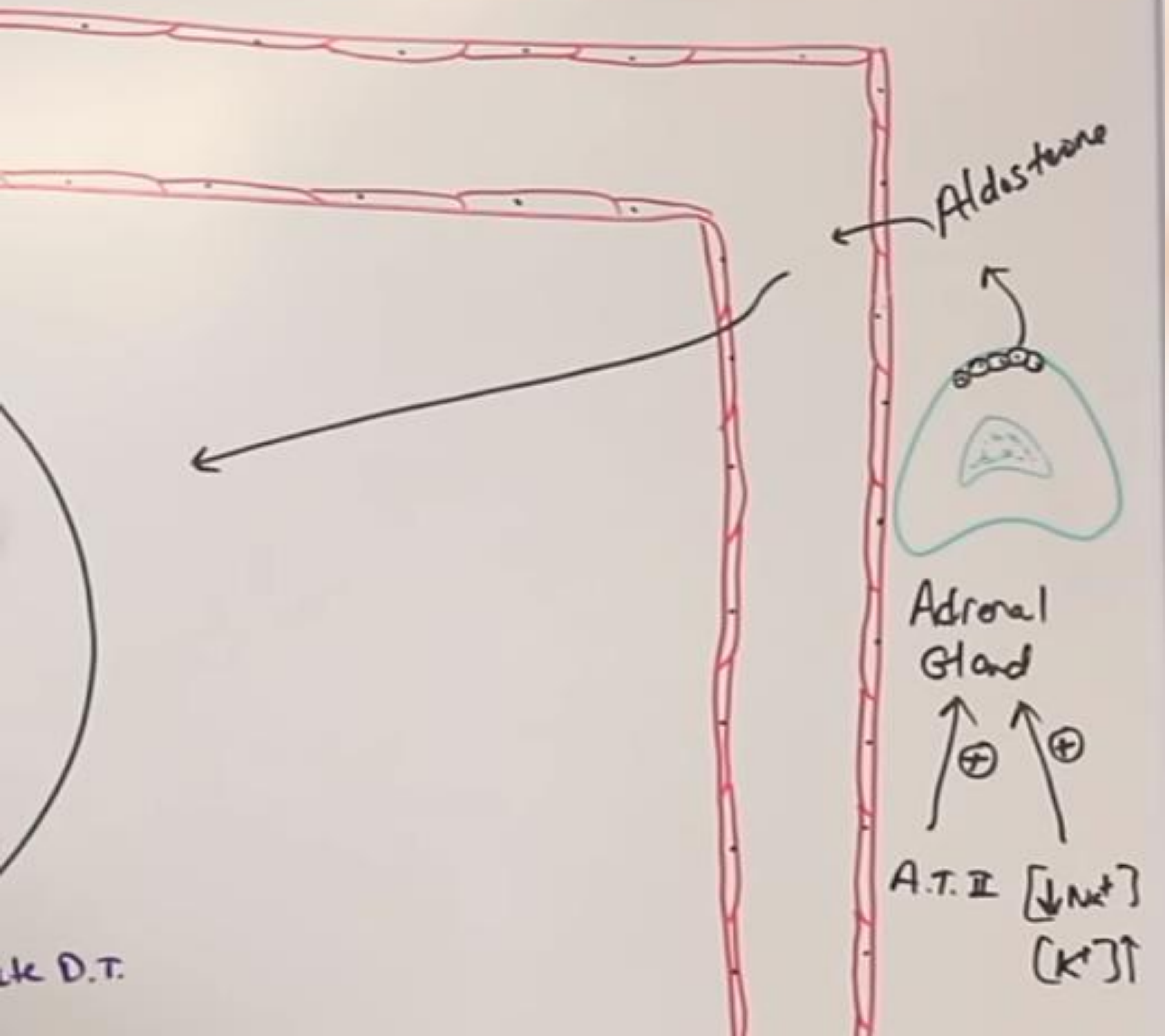


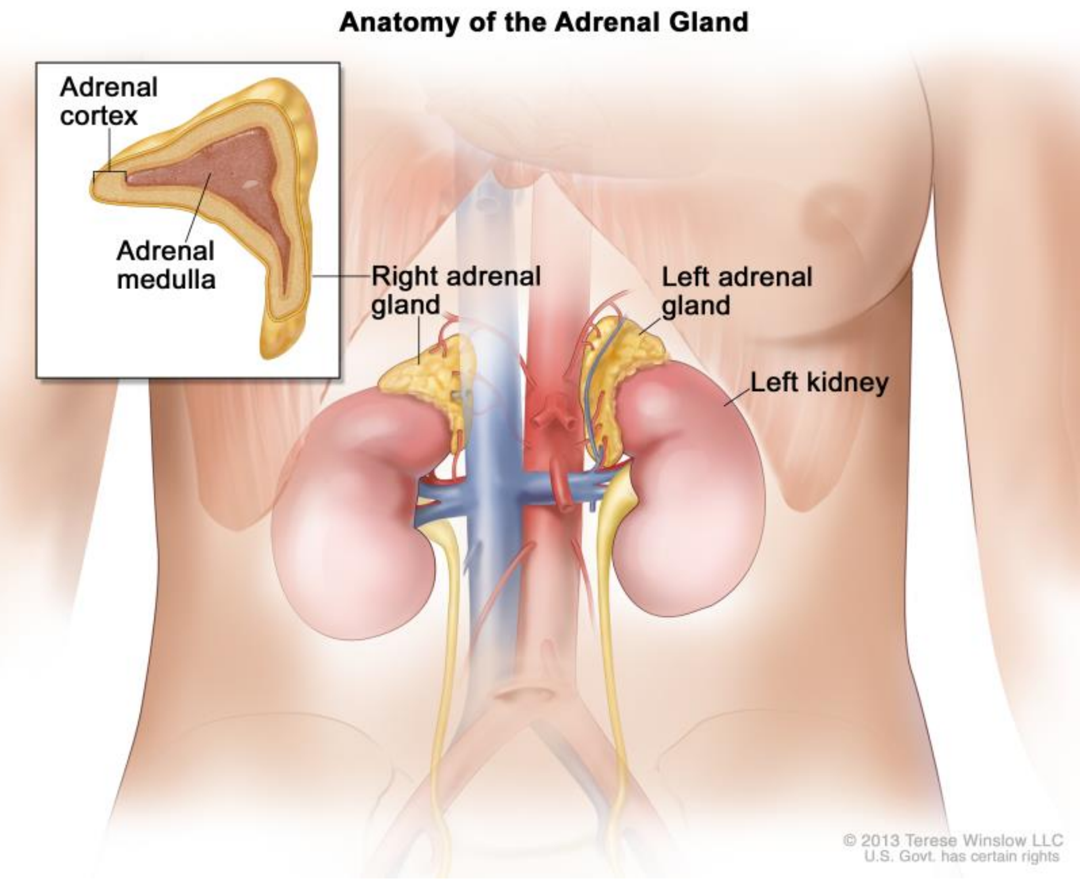
ENAL
↓Ca++
parathyroid Glands
↓Ca++
PTH
Cl⁻
Na+
[↑Ca++]
ATP
2K+
3Na+
ATP
Na+
(3)
(5-6%)
[↓Ca++]
Calbindin
Gs
GTP
AC
ATP
cAMP
PKA
[Na+]↓
100-200mosm
10% Na+
20% H2O
Cl⁻
[Na+]↑
(NaCl symporter)
Ca++
Ca++
Ca++
DCT
Early D.T.


RENAL
↓Ca++
↓Ca++
parathyroid Glands
PTH
Cl⁻
Na+
ATP
2K+
3Na+
[↑Ca++]
Na+
2°
[↓Ca++]
(5-6%)
Gs
GTP
ATP
AC
cAMP
PKA
H+
ATP
2K+
ATP
Na+
(3)
300
Mosm
[Na+]↓
Calbindin
100-200mosm
10% Na+
20% H2O
Cl⁻
Ca++
[Na+] ↑
(NaCl
symporter)
Ca++
Ca++
(25%)
500mosm
DCT
Early D.T.
Na+



AL
↓Ca++
parathyroid Glands
↓Ca++
PTH
[↑Ca++]
Na+
ATP
GTP
AC
ATP
cAMP
PKA
2° [↓Ca++]
Calbindin
[Na+] ↑
Cl-
(NaCl symporter)
Ca++
Early D.T.
Late D.T.


Aldosterone
Adrenal Gland
A.T.II
[↓Na+]
[K+]↑
D.T.


Anatomy of the Adrenal Gland
Adrenal cortex
Adrenal medulla
Right adrenal gland
Left adrenal gland
Left kidney
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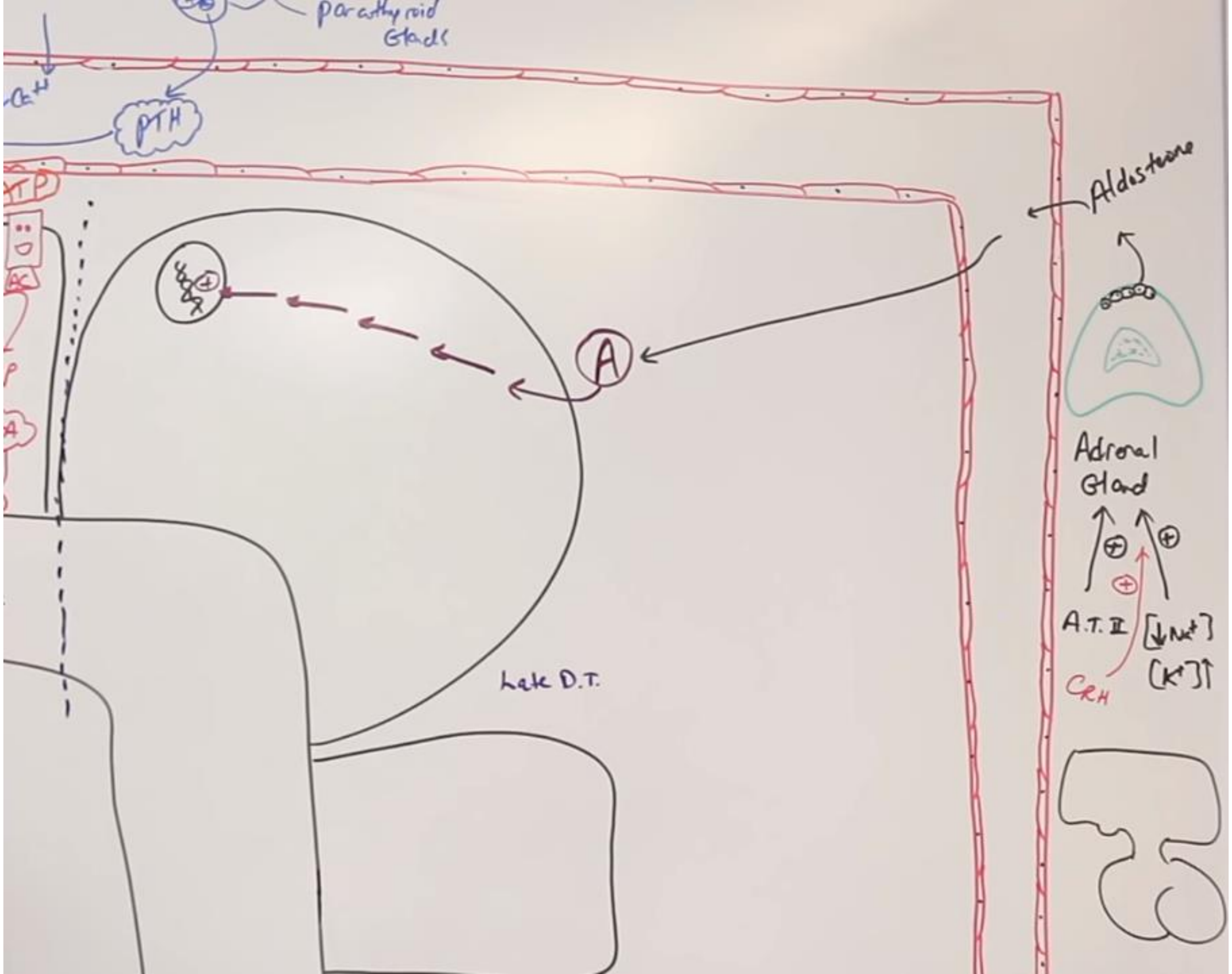
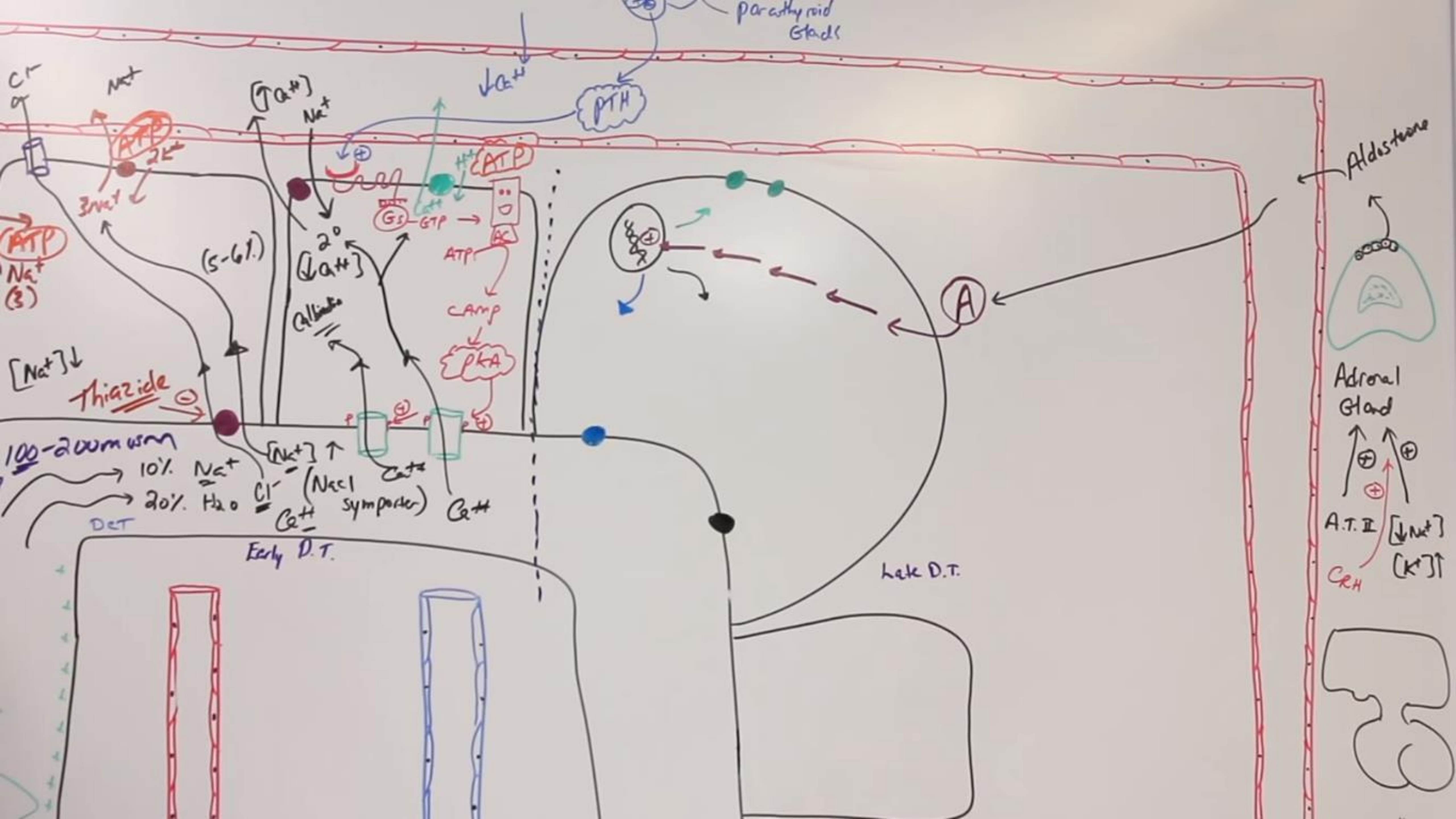
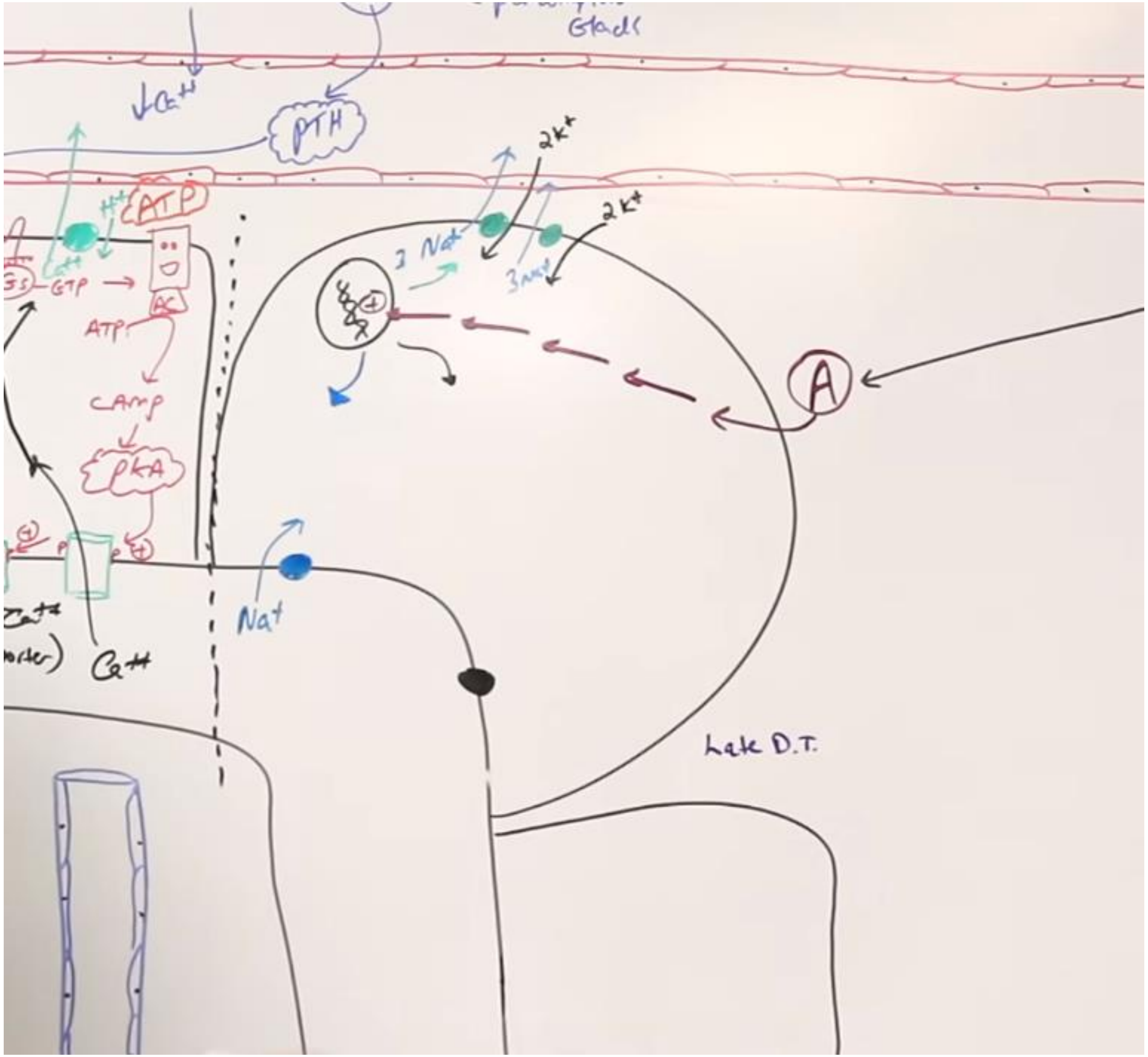
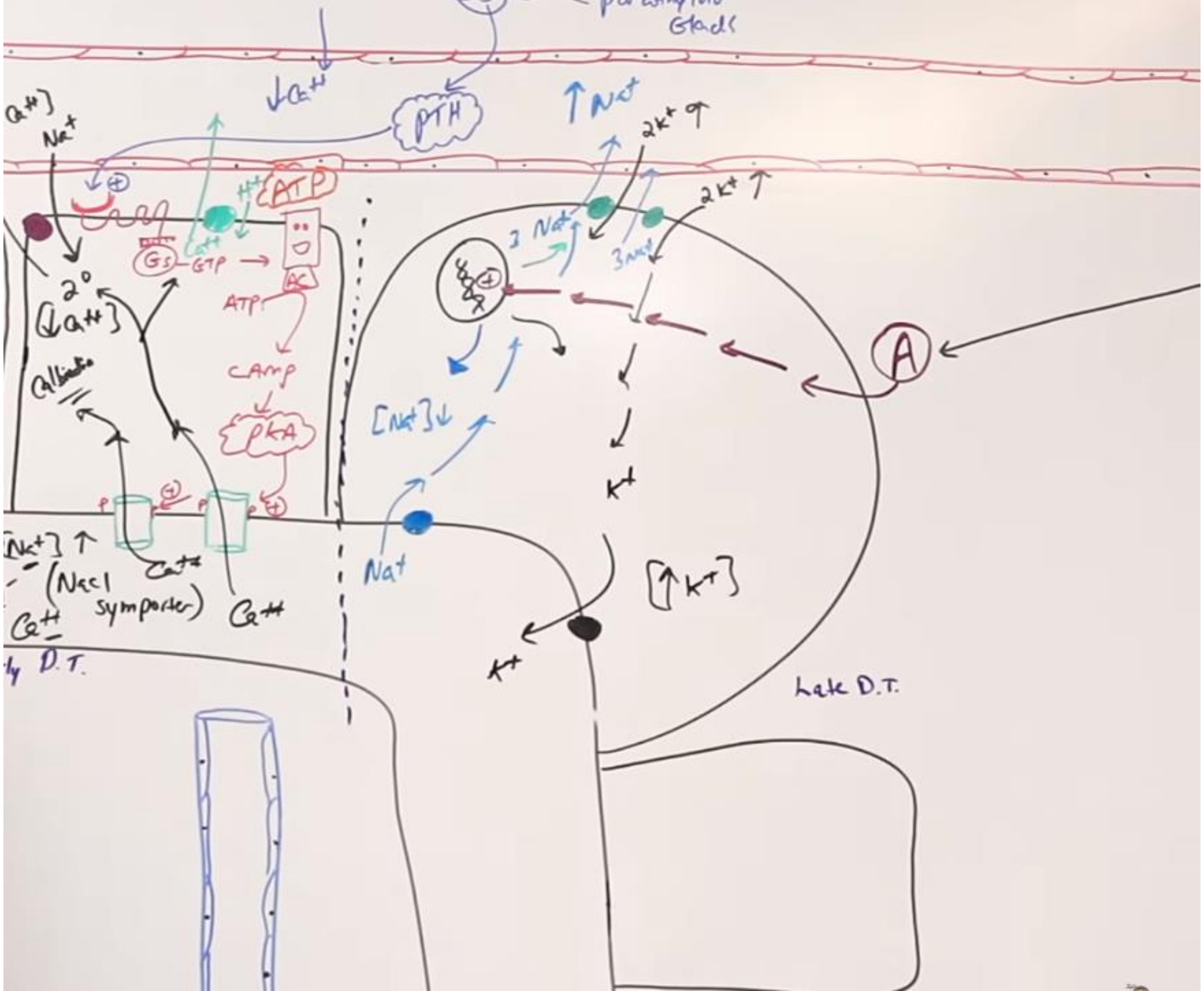

parathyroid Glands
PTH
Aldosterone
A
Adrenal Gland
A.T. II
[↓Na+]
[K+]↑
Late D.T.



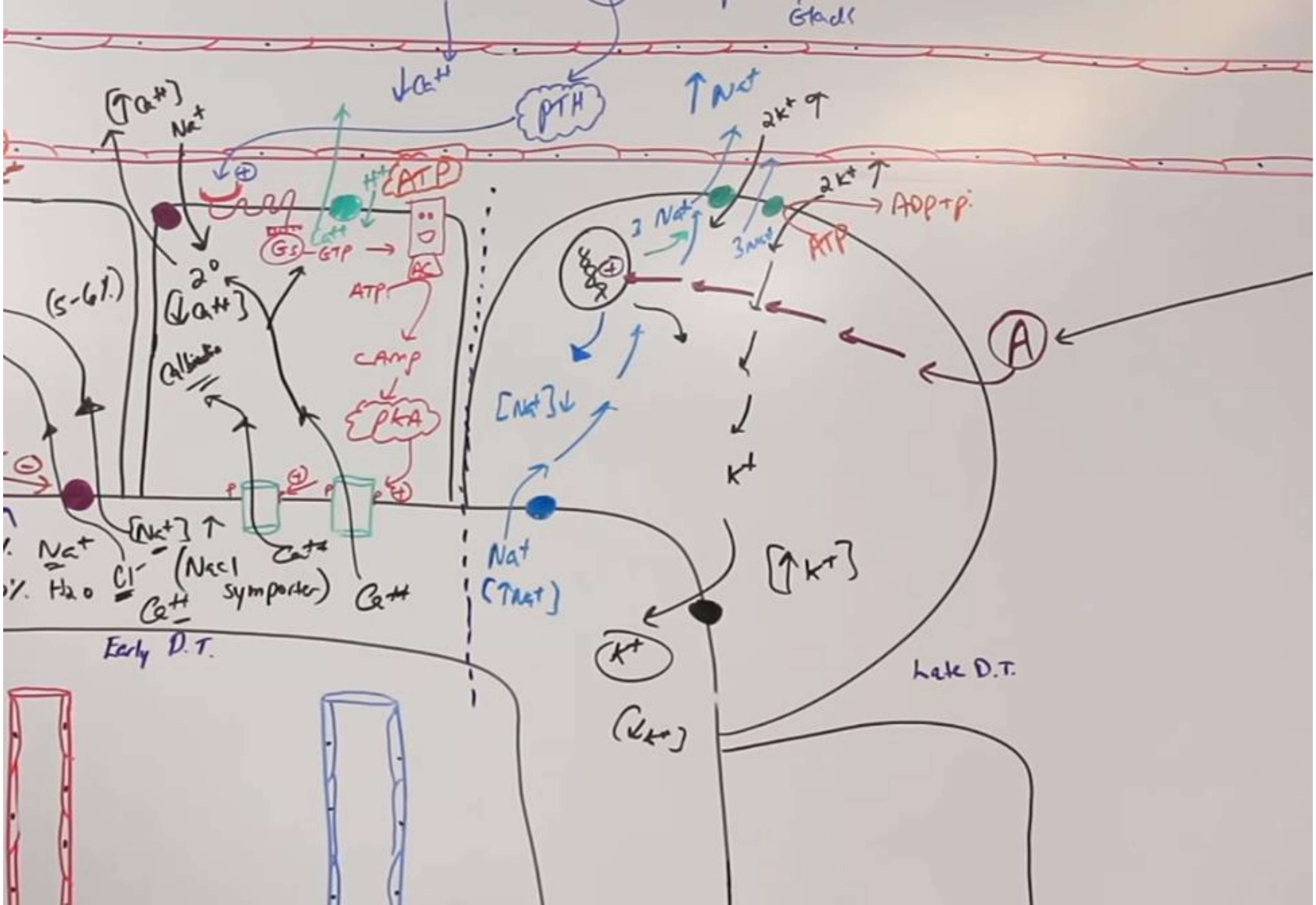
parathyroid Glands
PTH
Aldosterone
Adrenal Gland
A.T. II
[↓Na+]
[K+]↑
CRH
Thiazide
[Na+]↓
100-200mosm
10% Na+
20% H2O
DCT
Early D.T.
Late D.T.
(5-6%)
(NaCl symporter)
Calbindin
Gs
GTP
ATP
cAMP
PKA
ATP
3Na+
2K+
Na+
Cl-
Ca++
[Ca++]
2° [↓Ca++]
[Na+]↑

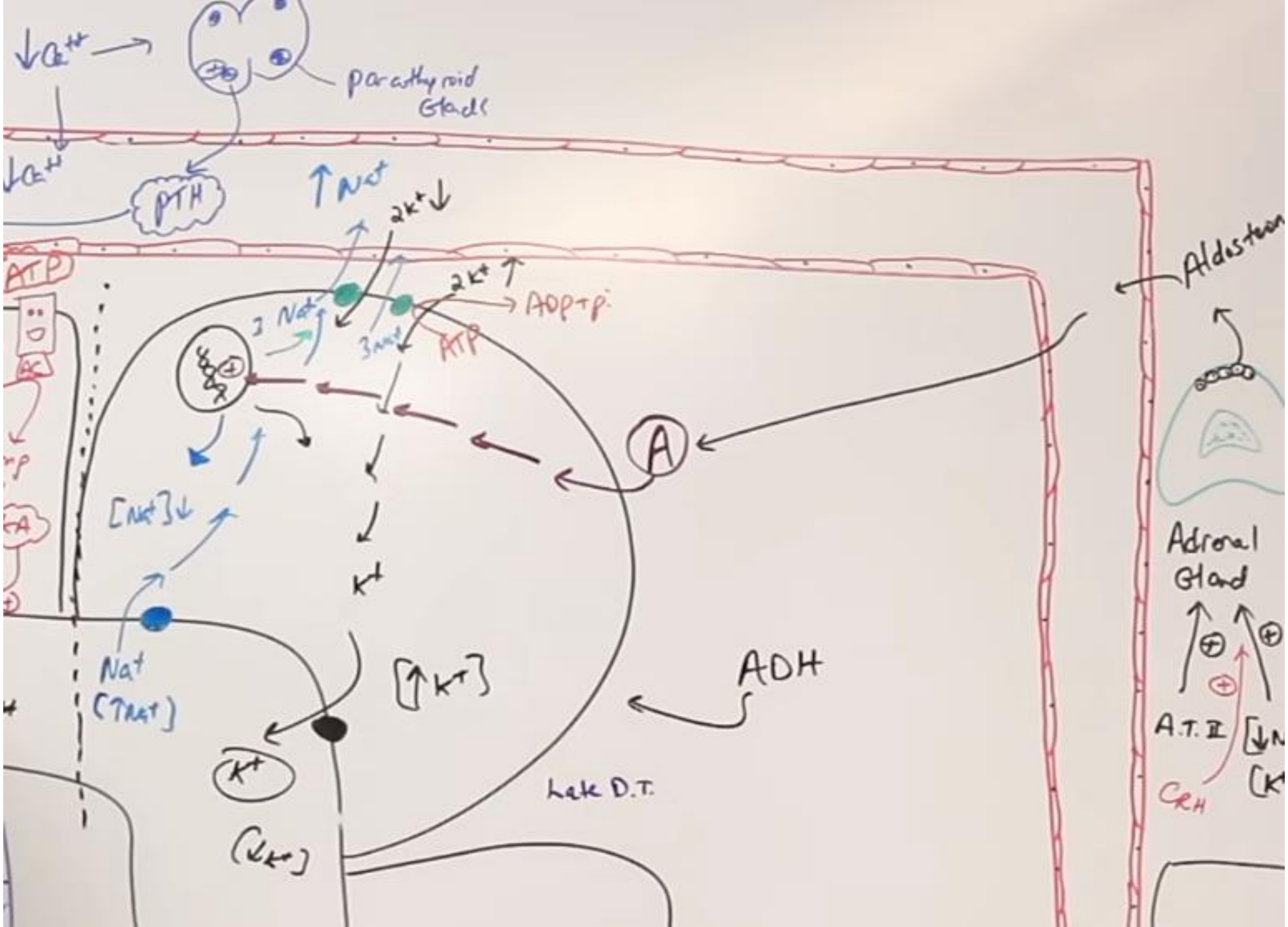


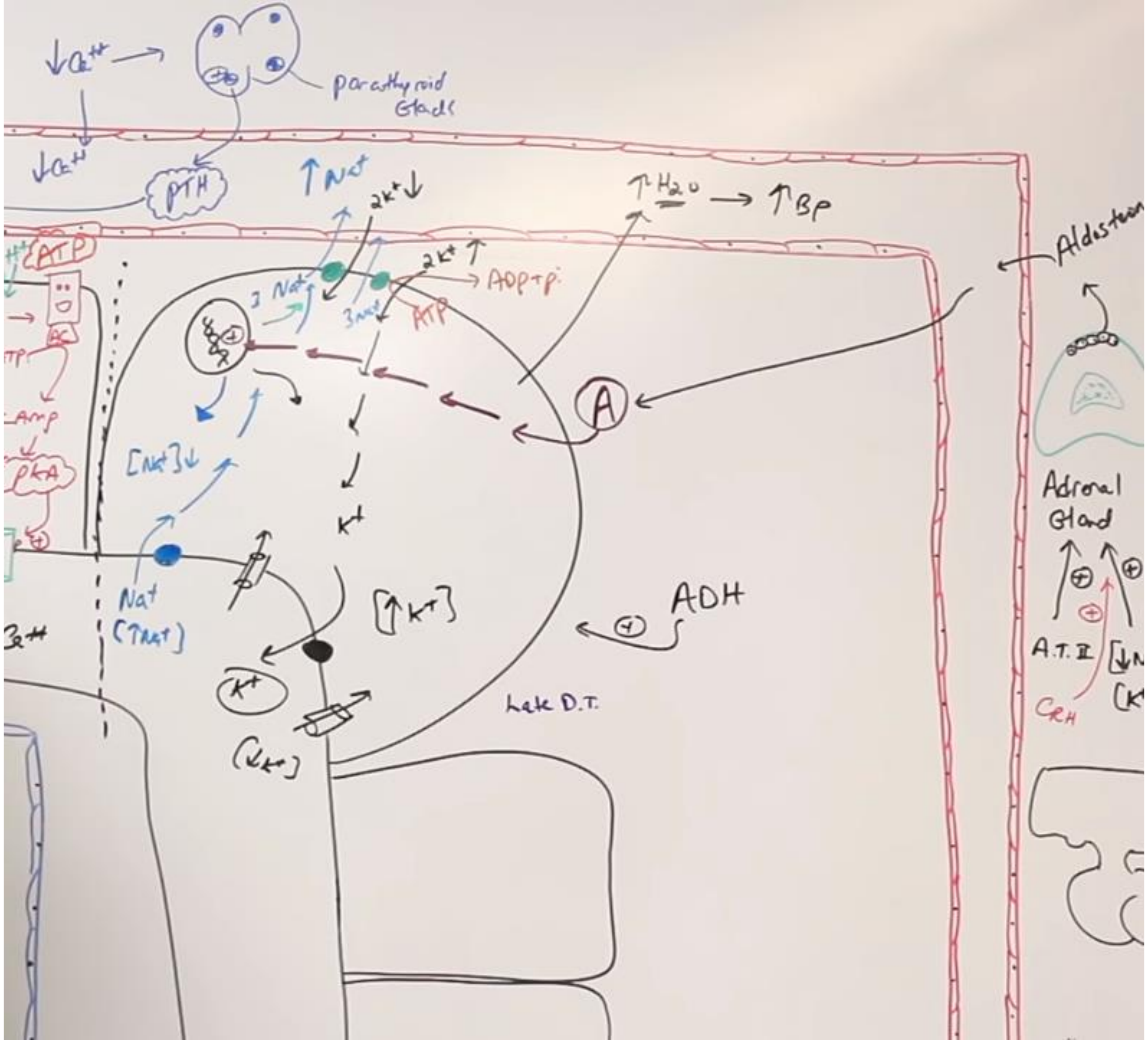
Glads
Ca++
PTH
ATP
H+
Ca++
GS
GTP
AC
ATP
cAMP
PKA
2K+
3 Na+
2K+
3Na+
A
Na+
Ca++
Ca++
Late D.T.



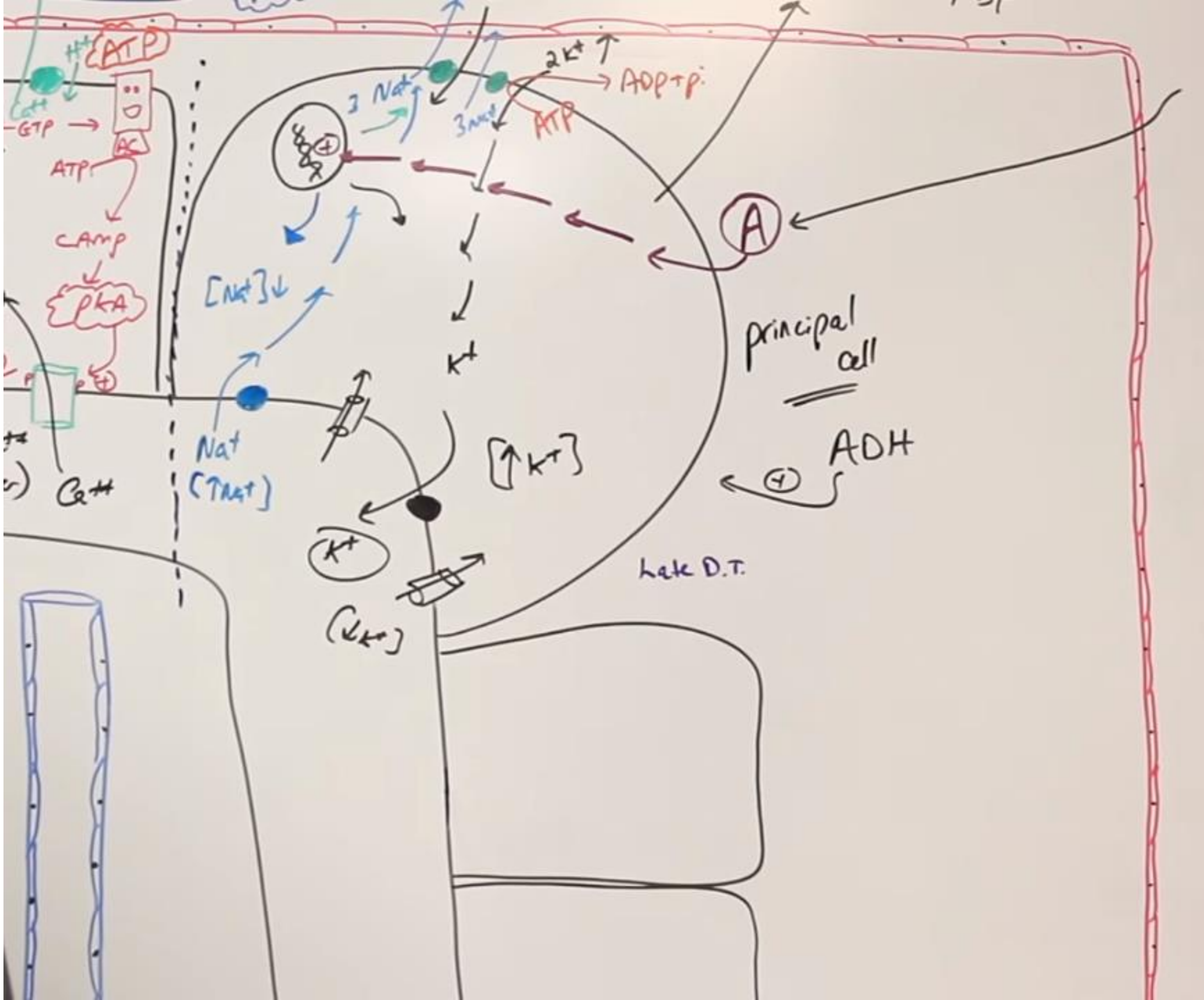
Glands
PTH
ATP
Gs
GTP
AC
cAMP
PKA
2°
[↓Ca++]
[Na+] ↑
(NaCl symporter)
Ca++
D.T.
3 Na+
[Na+]↓
Na+
K+
[↑K+]
A
Late D.T.

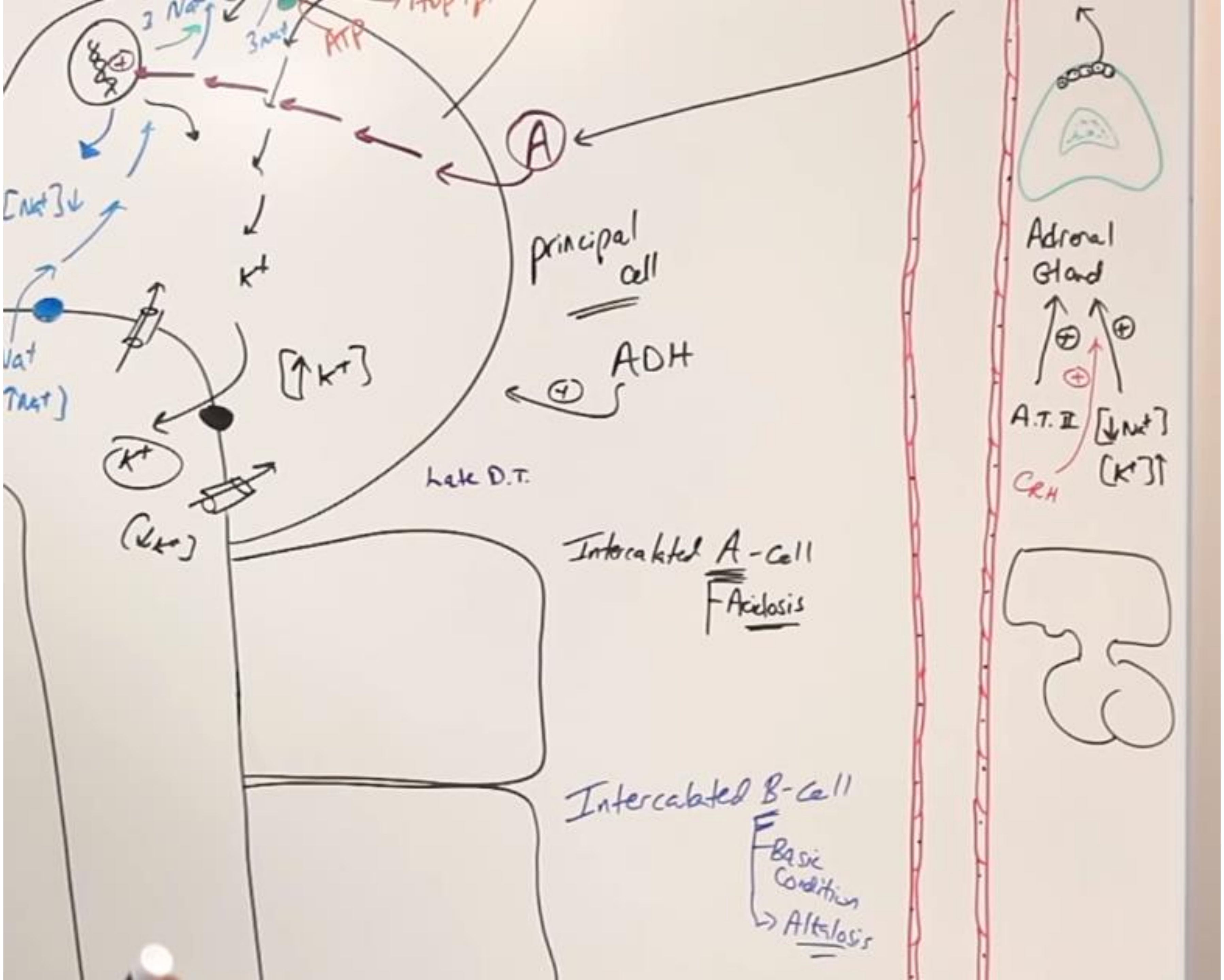

PTH
↑Na+
2K+
ADP+Pi
ATP
3 Na+
[↑Ca++]
Na+
H+
Gs
GTP
AC
ATP
cAMP
PKA
2°
[↓Ca++]
(5-6%)
Calbindin
[Na+]↓
A
K+
[↑K+]
[Na+] ↑
Cl-
(NaCl symporter)
Ca++
Na+
[↑Na+]
(↓K+)
Early D.T.
Late D.T.


parathyroid Glands
PTH
Aldosterone
ATP
ADP+pi
A
ADH
Adrenal Gland
A.T. II
Late D.T.

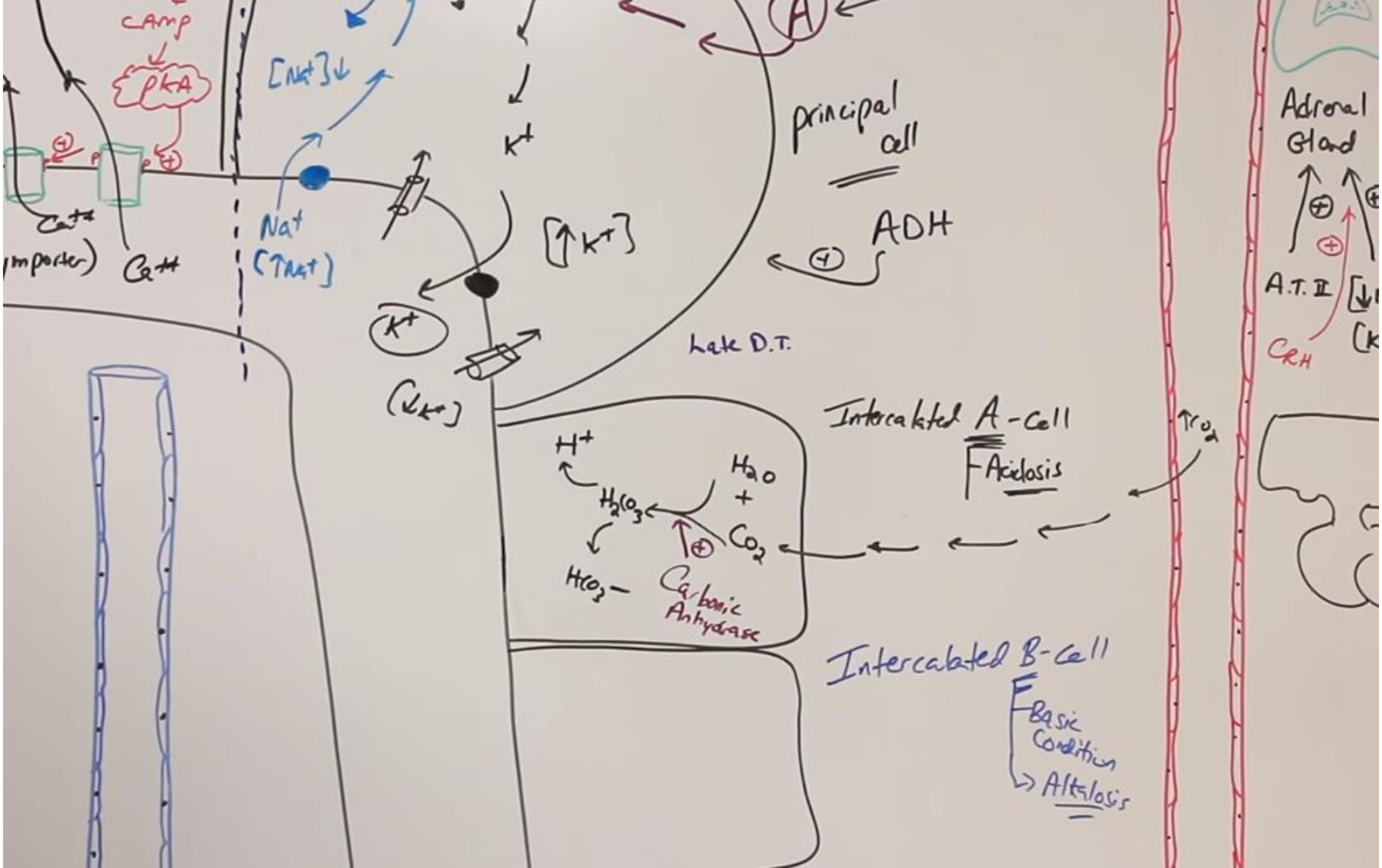


parathyroid Glands
PTH
ATP
AC
cAmp
PKA
↑Na+
2K+
3 Na+
ADP+Pi
ATP
↑H2O → ↑BP
Aldosterone
A
[Na+]↓
K+
[↑K+]
Na+
[↑Na+]
K+
[↓K+]
ADH
Late D.T.
Adrenal Gland
A.T. II
CRH

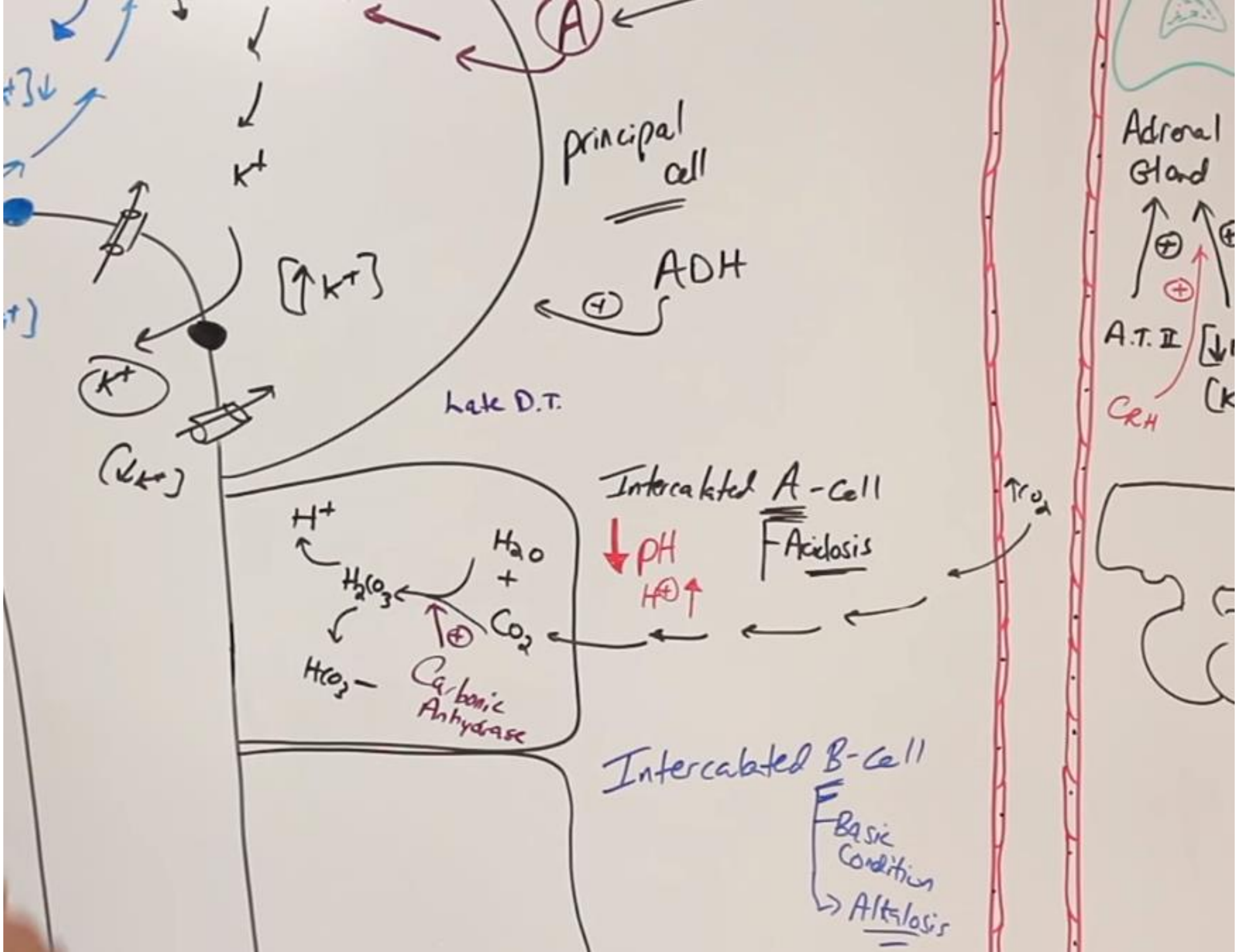

ATP
GTP
AC
ATP
cAMP
PKA
3 Na+
3 Na+
2K+
ADP+Pi
ATP
A
[Na+]↓
K+
principal cell
ADH
Na+
[↑Na+]
[↑K+]
K+
[↓K+]
Ca++
Late D.T.



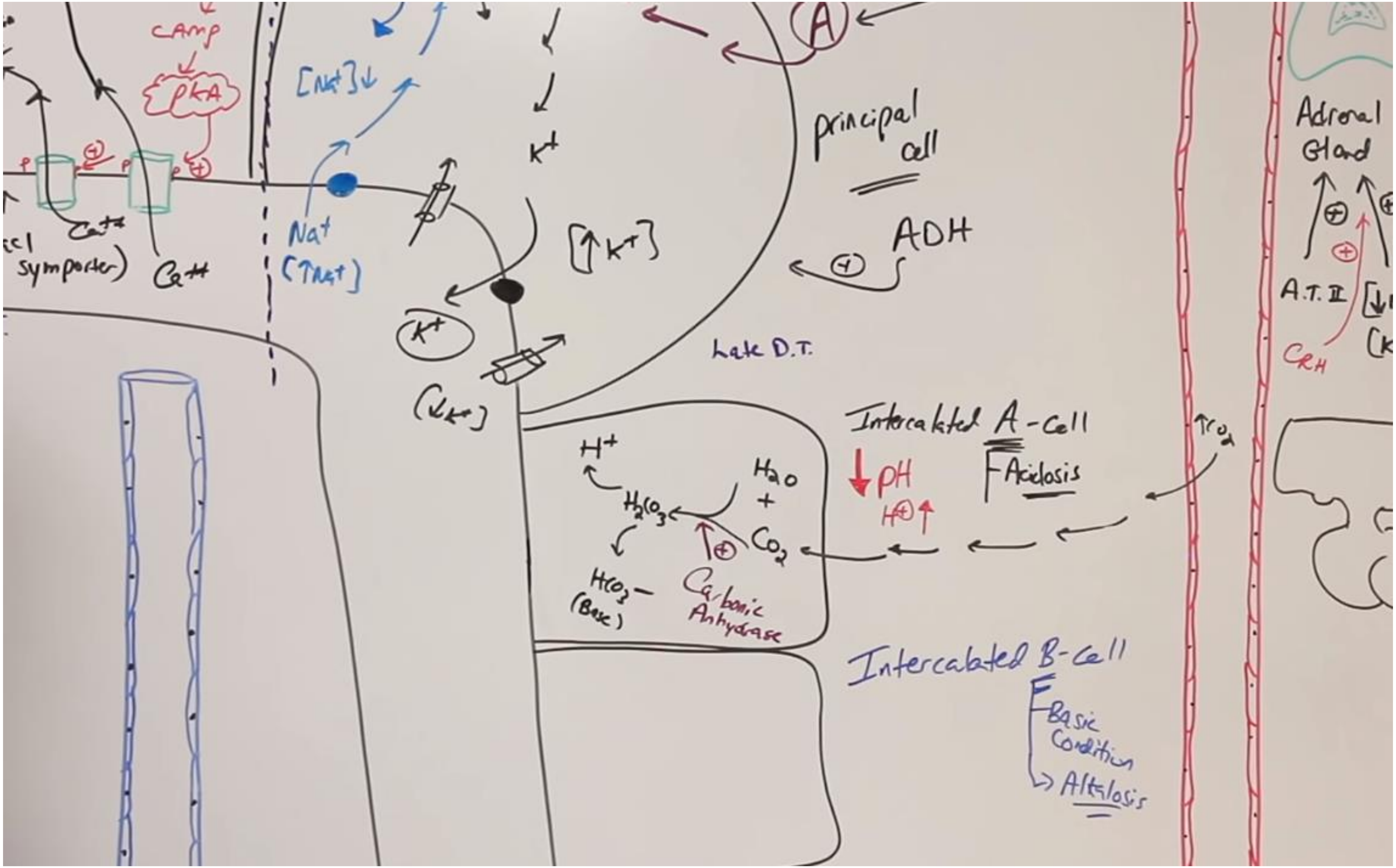
ATP
[Na+]↓
Na+
K+
[↑K+]
K+
principal cell
ADH
Late D.T.
Intercalated A-cell
Acidosis
Intercalated B-cell
Basic Condition
Alkalosis
A
Adrenal Gland
A.T. II
[↓Na+]
[K+]↑
CRH

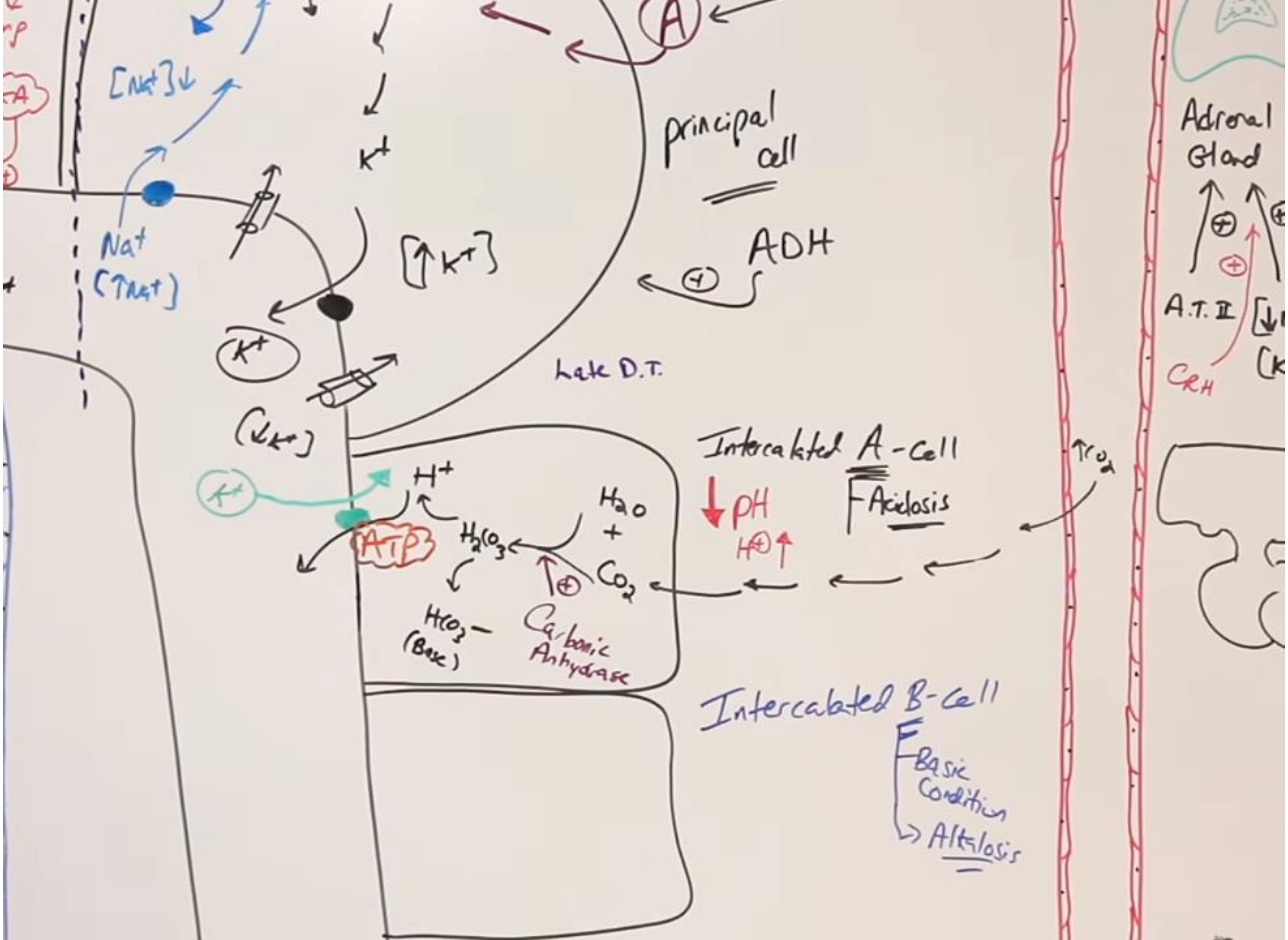


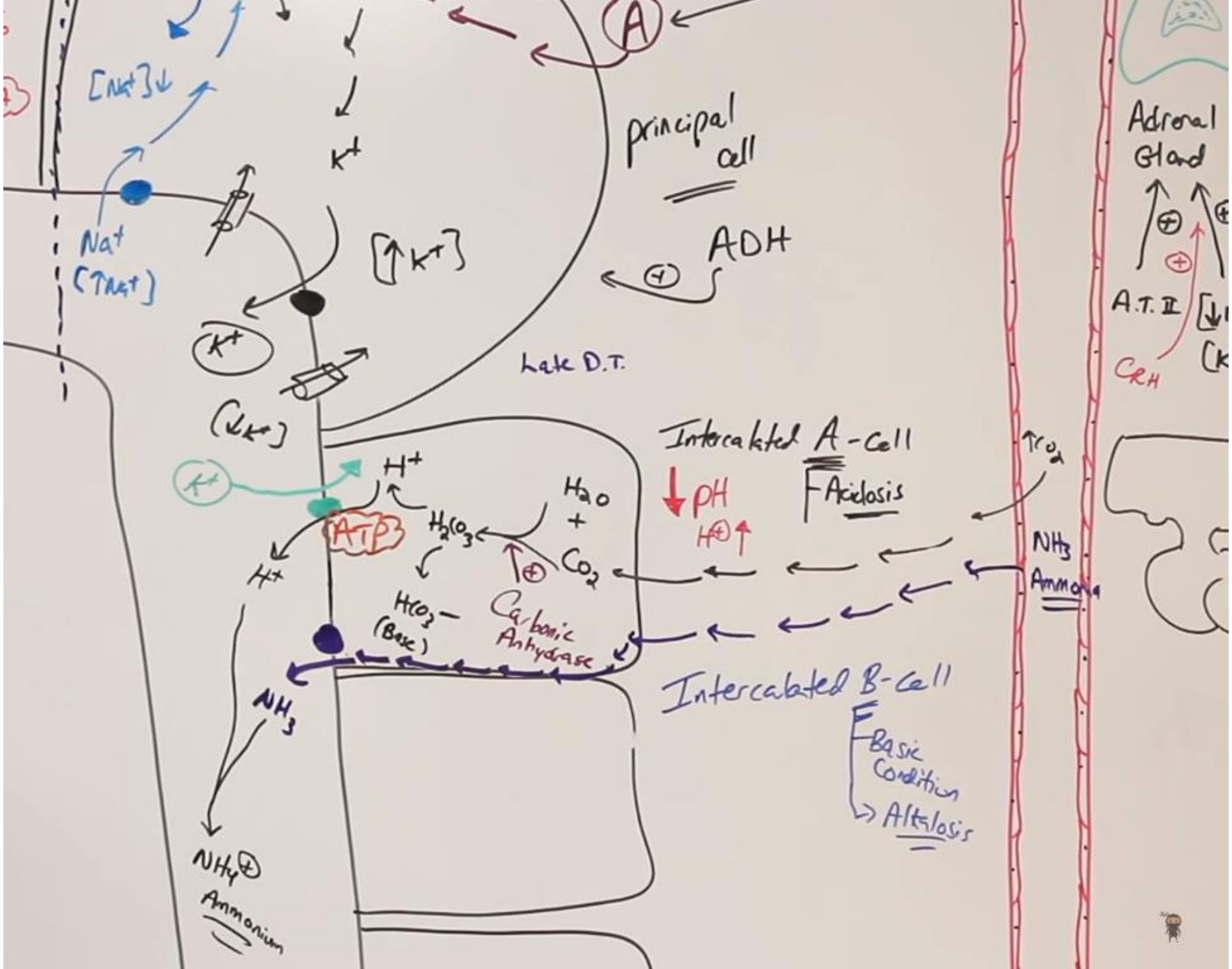
cAMP
PKA
[Na+]↓
K+
principal cell
ADH
[↑K+]
Ca++
Na+
(↑Na+]
ymporter)
Ca++
K+
(↓K+]
Late D.T.
Intercalated A-Cell
Acidosis
H+
H2O
+
H2CO3
CO2
HCO3 −
Carbonic Anhydrase
↑CO2
Intercalated B-Cell
Basic Condition
Alkalosis
Adrenal Gland
A.T. II
CRH



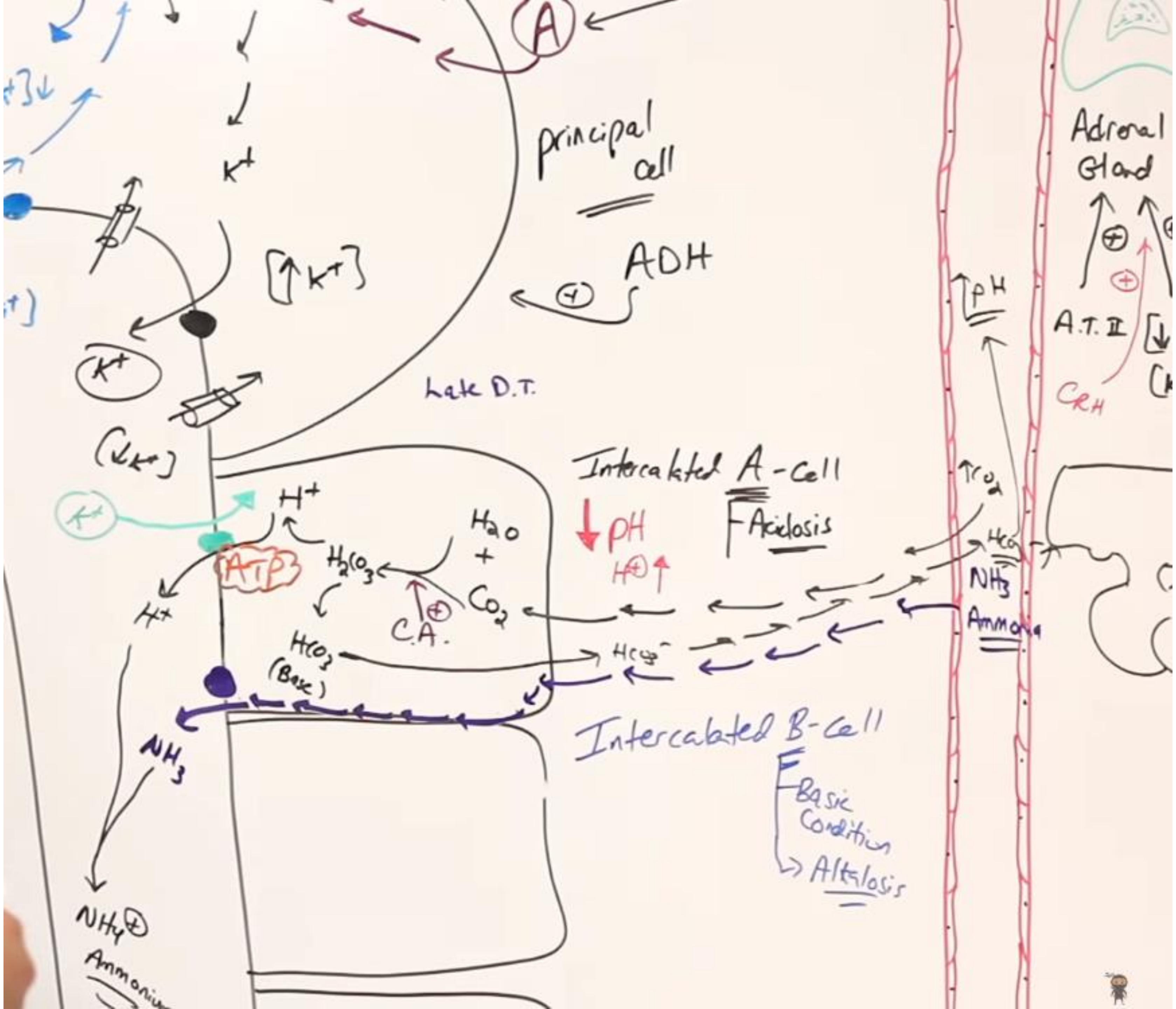
A
principal cell
ADH
K+
[↑K+]
K+
[↓K+]
Late D.T.
Intercalated A-cell
Acidosis
↓pH
H+ ↑
H+
H2O
+
CO2
H2CO3
HCO3−
Carbonic Anhydrase
Intercalated B-cell
Basic Condition
Alkalosis
Adrenal Gland
A.T. II
CRH


cAMP
PKA
[Na+]↓
Na+
(↑Na+)
symporter)
Ca++
K+
[↑K+]
(↓K+]
principal cell
ADH
Late D.T.
Intercalated A-Cell
Acidosis
↓pH
H+↑
H+
H2O
+
CO2
H2CO3
HCO3−
(Base)
Carbonic Anhydrase
Intercalated B-Cell
Basic Condition
Alkalosis
Adrenal Gland
A.T. II
CRH

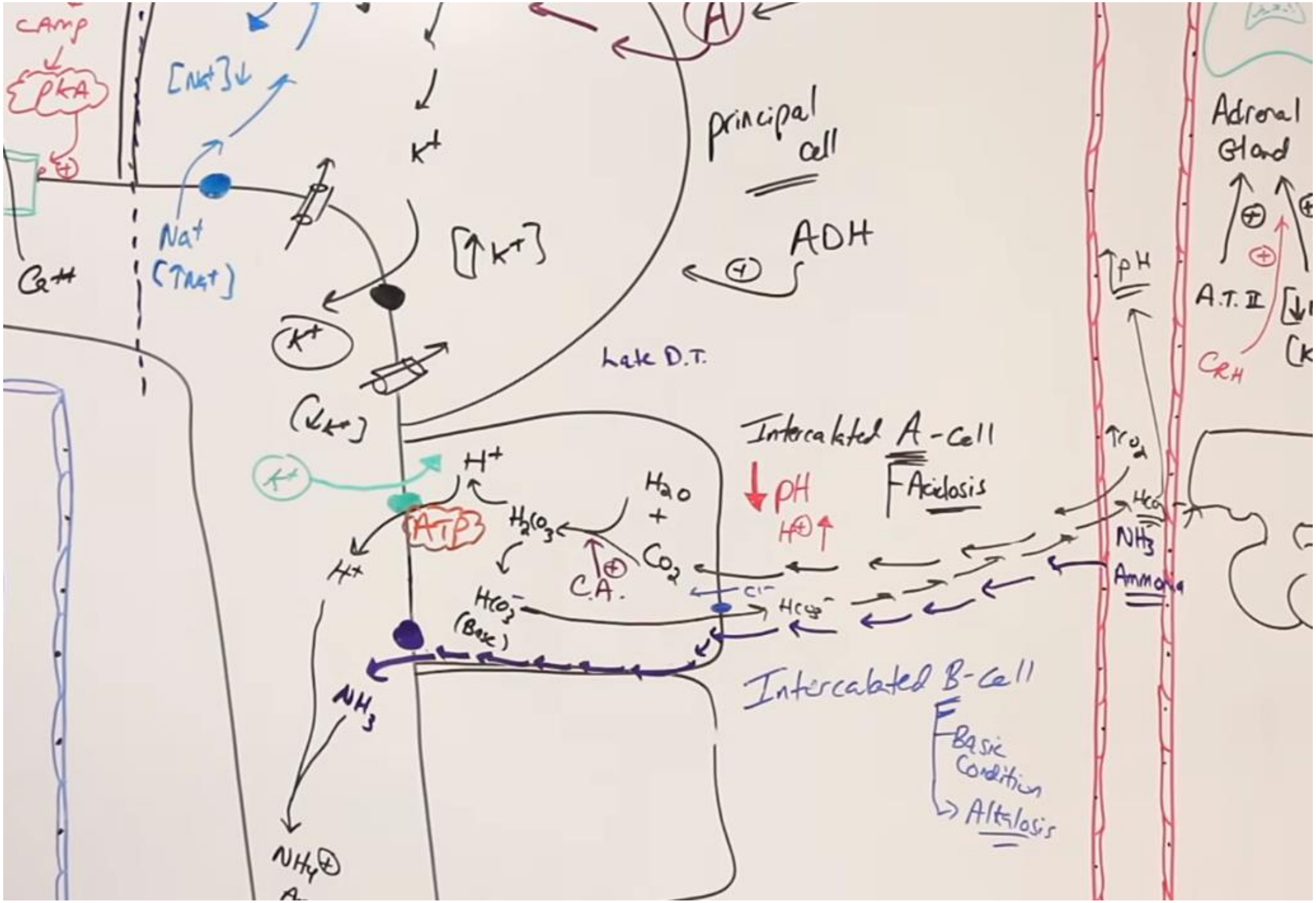

[Na+]↓
K+
Na+
(↑Na+)
[↑K+]
K+
(↓K+]
principal cell
ADH
Late D.T.
H+
H2O
+
CO2
H2CO3
ATP
HCO3−
(Base)
Carbonic Anhydrase
Intercalated A-cell
↓pH
H+↑
Acidosis
↑CO2
Intercalated B-cell
Basic Condition
Alkalosis
Adrenal Gland
A.T. II
CRH



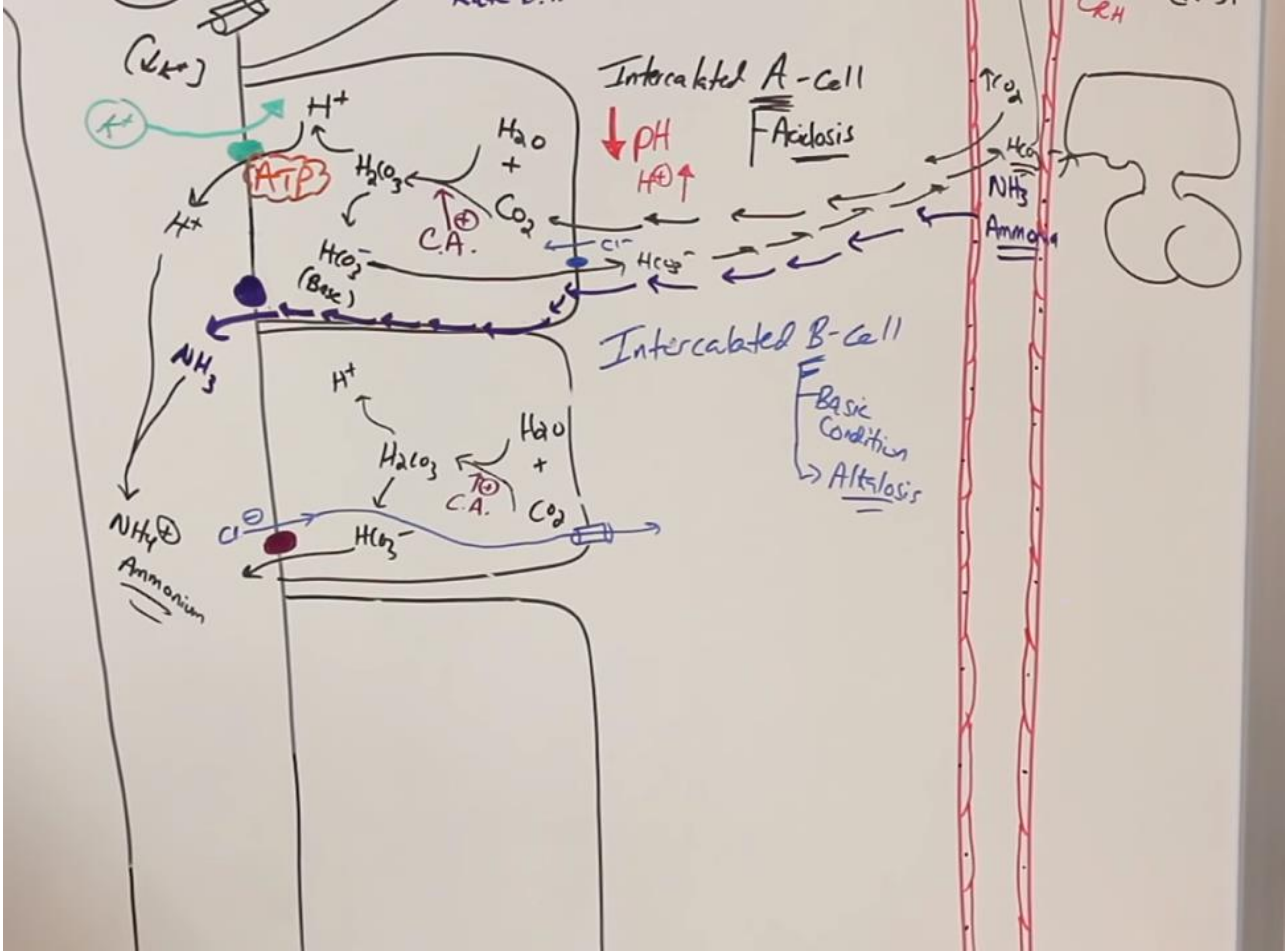
A
[Na+]↓
Na+
(↑Na+)
K+
[↑K+]
K+
(↓K+)
principal cell
ADH
Adrenal Gland
A.T. II
CRH
Late D.T.
Intercalated A-cell
↓pH
H+↑
Acidosis
H+
H2O
+
CO2
H2CO3
ATP
H+
HCO3−
(Base)
Carbonic Anhydrase
NH3
Ammonia
NH3
NH4+
Ammonium
Intercalated B-cell
Basic Condition
Alkalosis



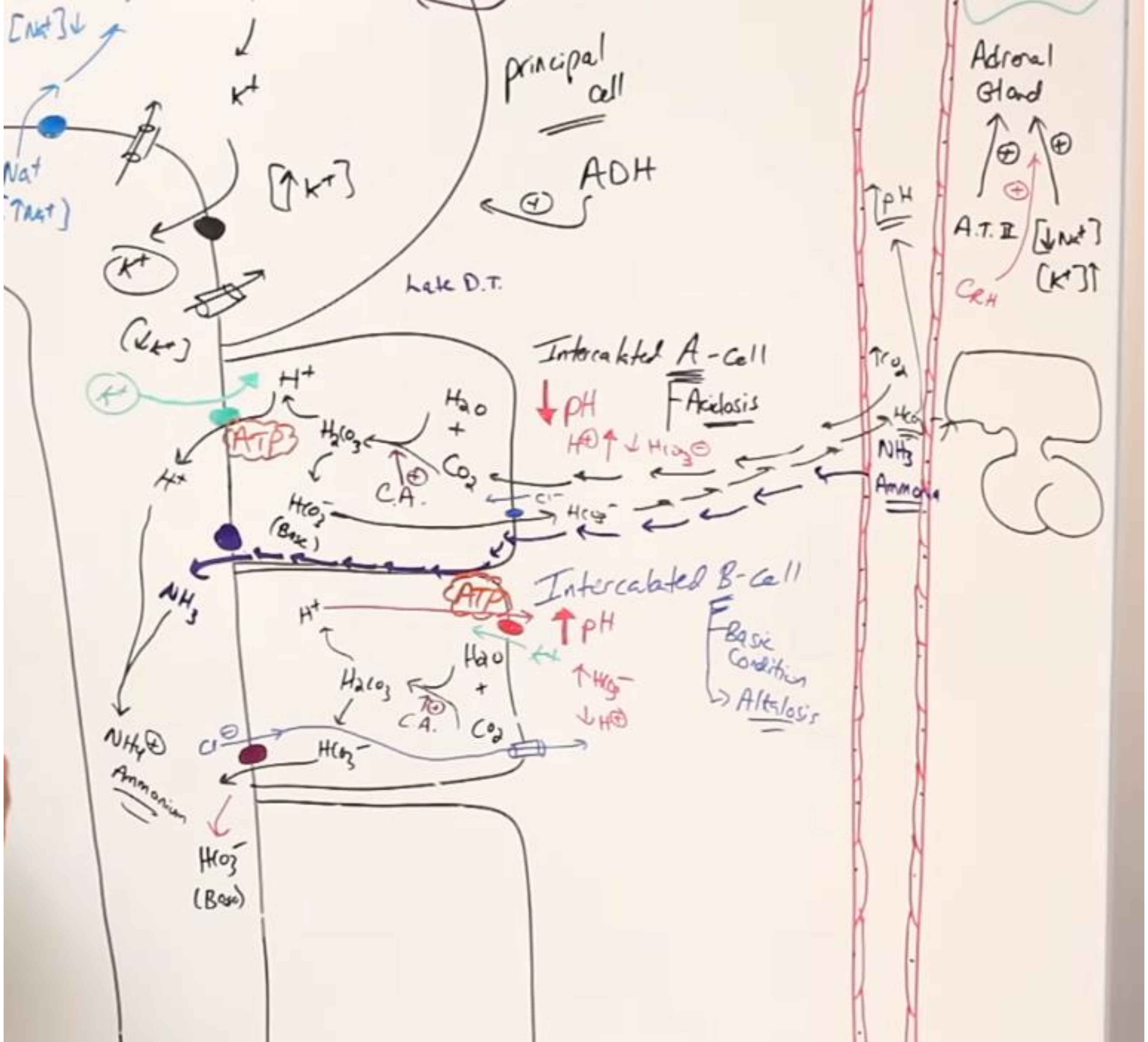
A
principal cell
ADH
K^+
[↑K^+]
K^+
(↓K^+)
Late D.T.
Intercalated A-Cell
Acidosis
↓pH
H⊕↑
H^+
H_2O +
CO_2
H_2CO_3
C.A.
ATP
HCO_3 (Base)
NH_3
NH_4⊕ Ammonium
Intercalated B-cell
Basic Condition
Alkalosis
↑pH
CO_2
NH_3
Ammonia
Adrenal Gland
A.T.II
CRH



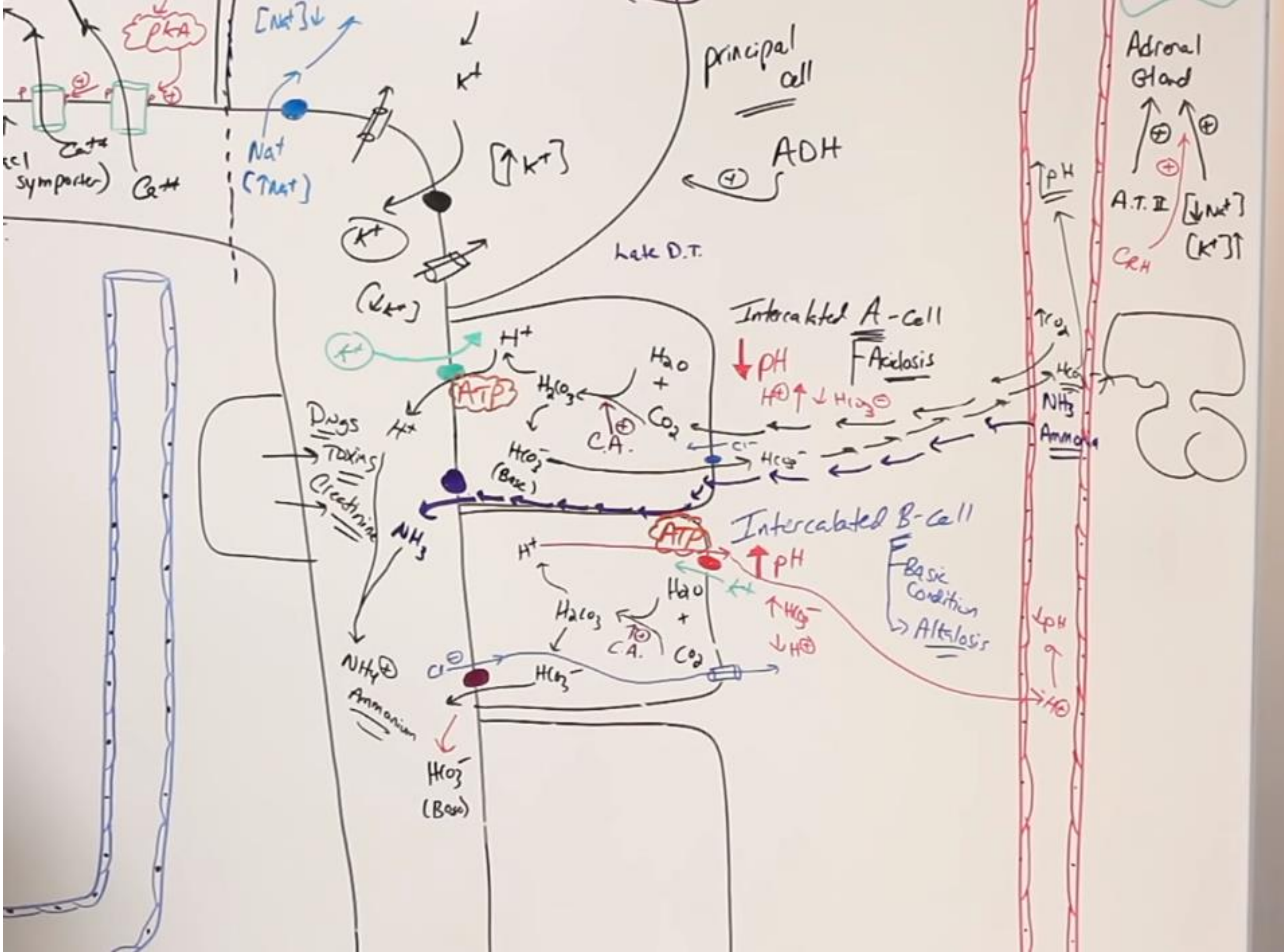
cAMP
PKA
[Na+]↓
Na+
[↑Na+]
Ca++
K+
[↑K+]
K+
[↓K+]
principal cell
ADH
Late D.T.
Intercalated A-Cell
Acidosis
↓pH
H+ ↑
H+
H2O
+
CO2
H2CO3
C.A.
HCO3-
(Base)
ATP
Cl-
NH3
NH4+
Intercalated B-Cell
Basic Condition
Alkalosis
↑pH
↑CO2
Ammonia
Adrenal Gland
A.T. II

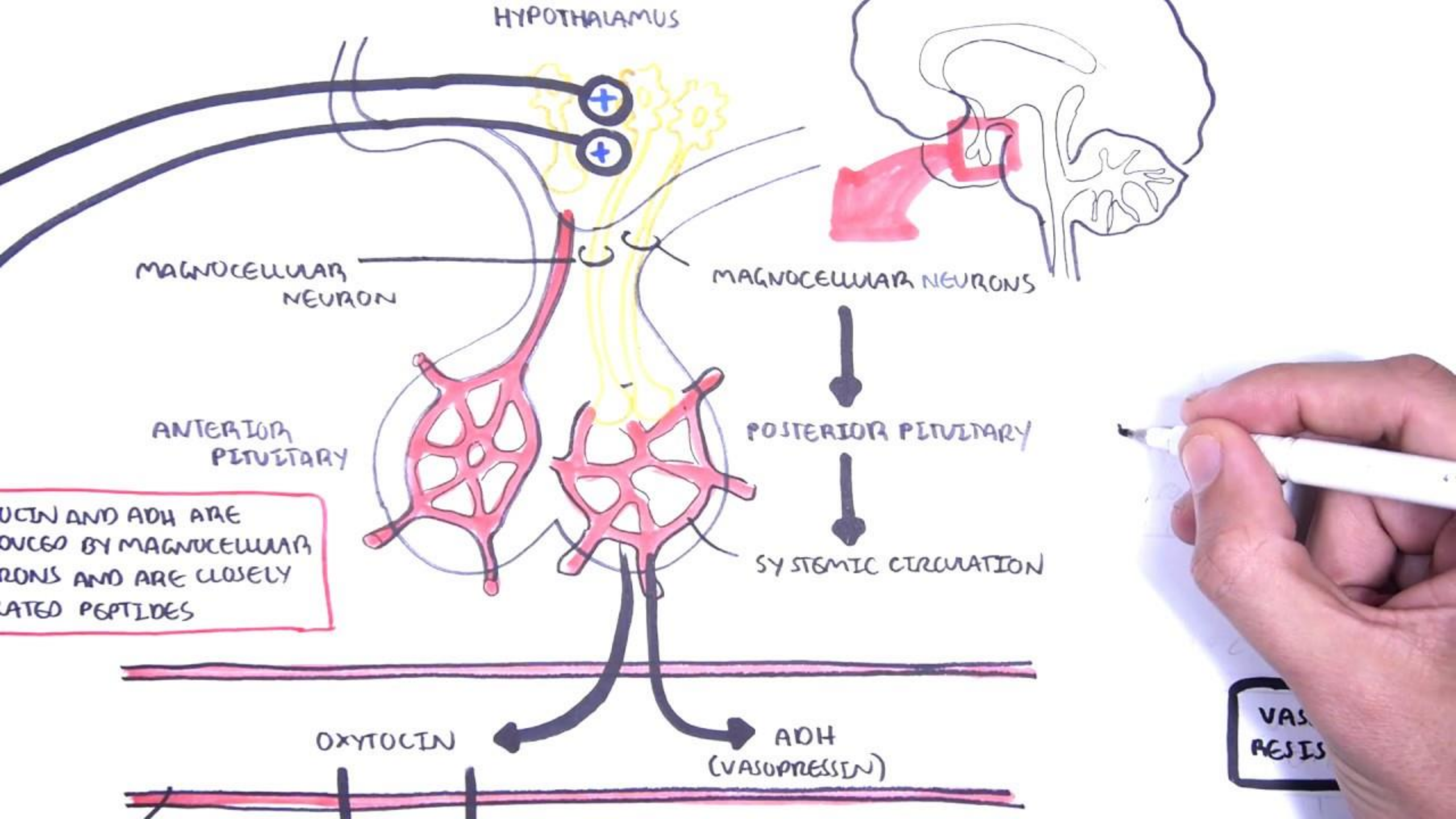


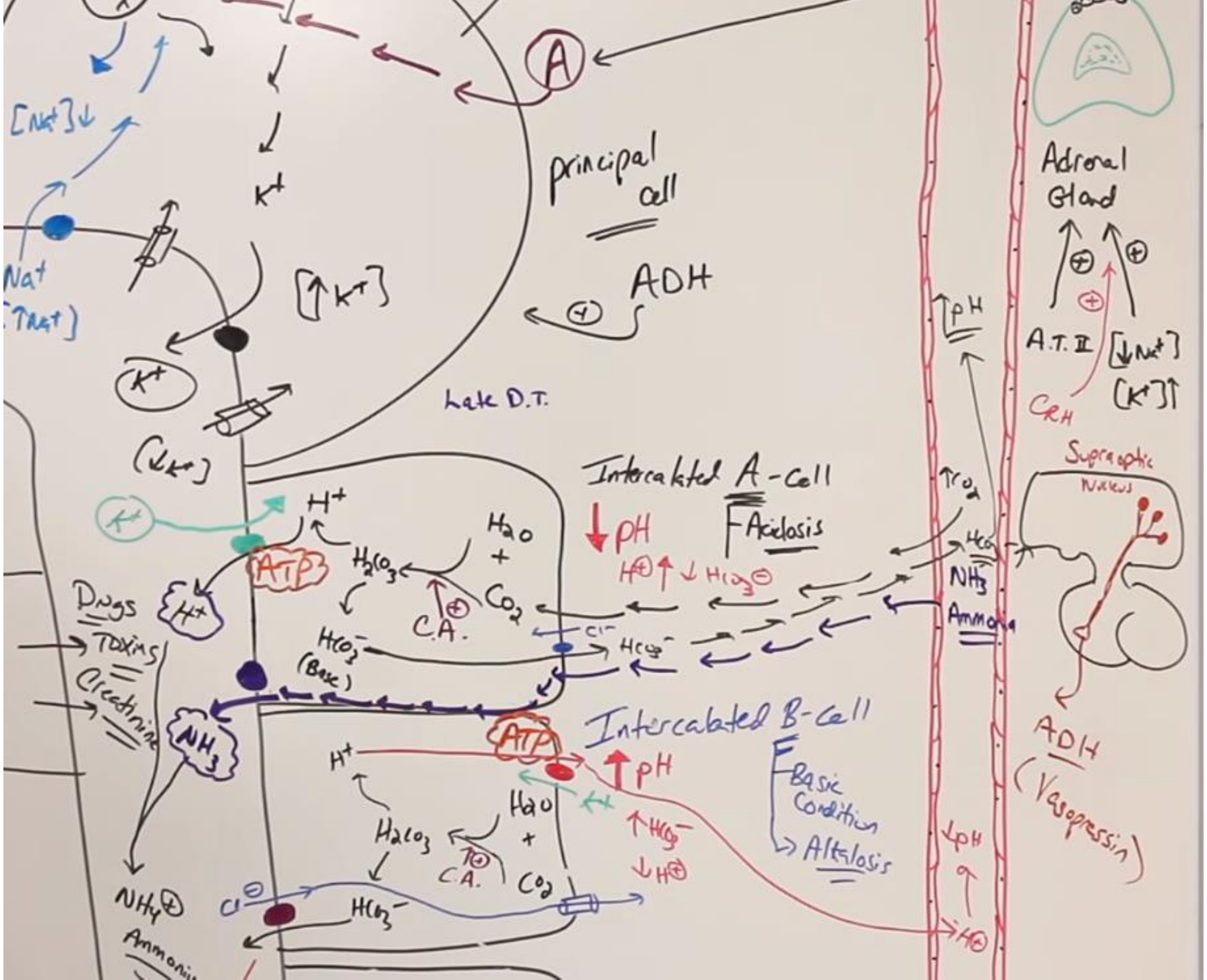
Intercalated A-Cell
pH
Acidosis
H+
H2O
+
CO2
H2CO3
C.A.
HCO3-
(Base)
ATP
K+
Cl-
NH3
Ammonia
NH4+
Ammonium
Intercalated B-Cell
Basic
Condition
Alkalosis

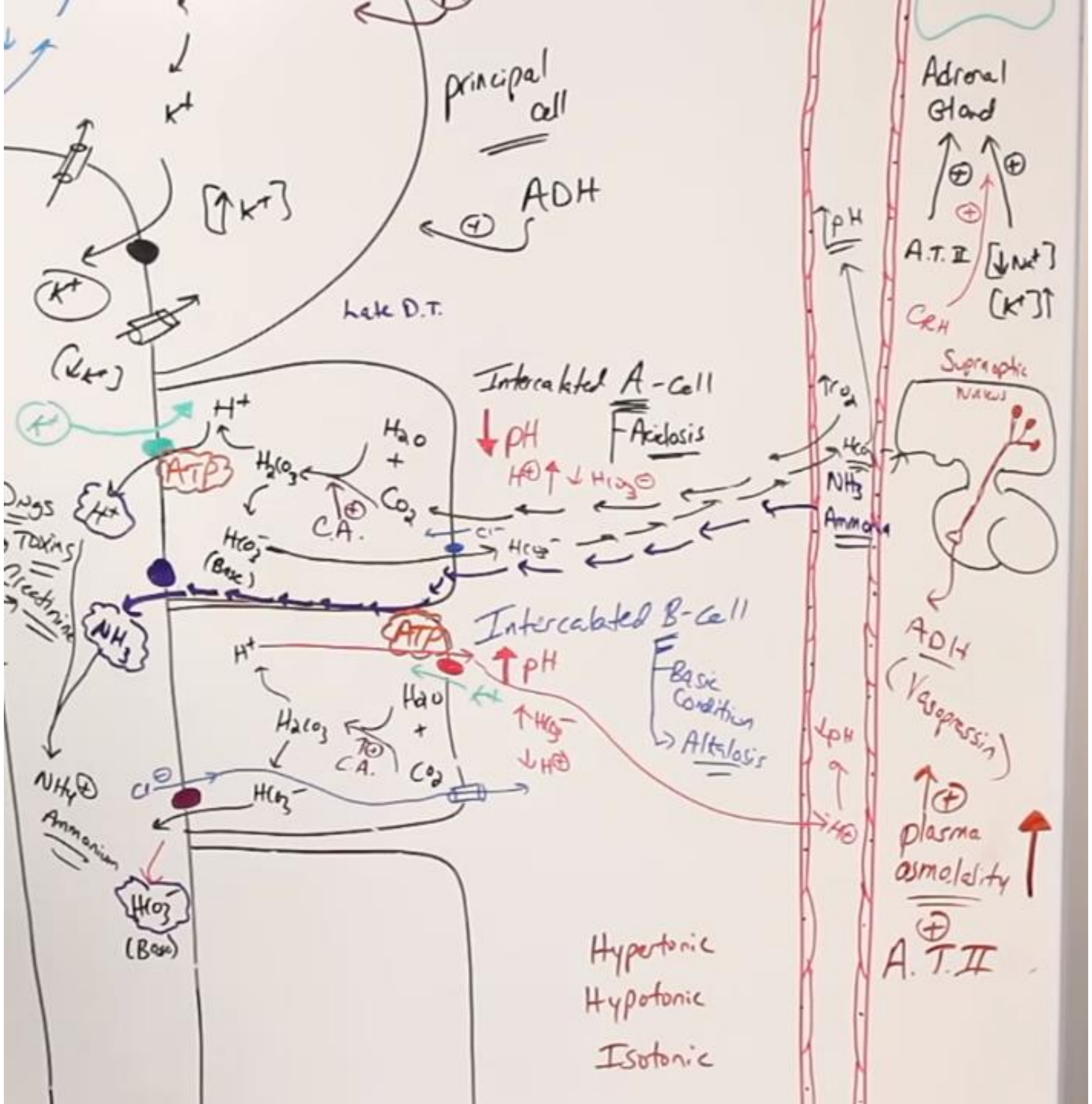


principal cell
ADH
Late D.T.
Intercalated A-cell
↓pH
Acidosis
Intercalated B-cell
↑pH
Basic Condition
Alkalosis
Adrenal Gland
A.T. II
CRH
NH3
Ammonia
NH4+
Ammonium
HCO3- (Base)
ATP
C.A.

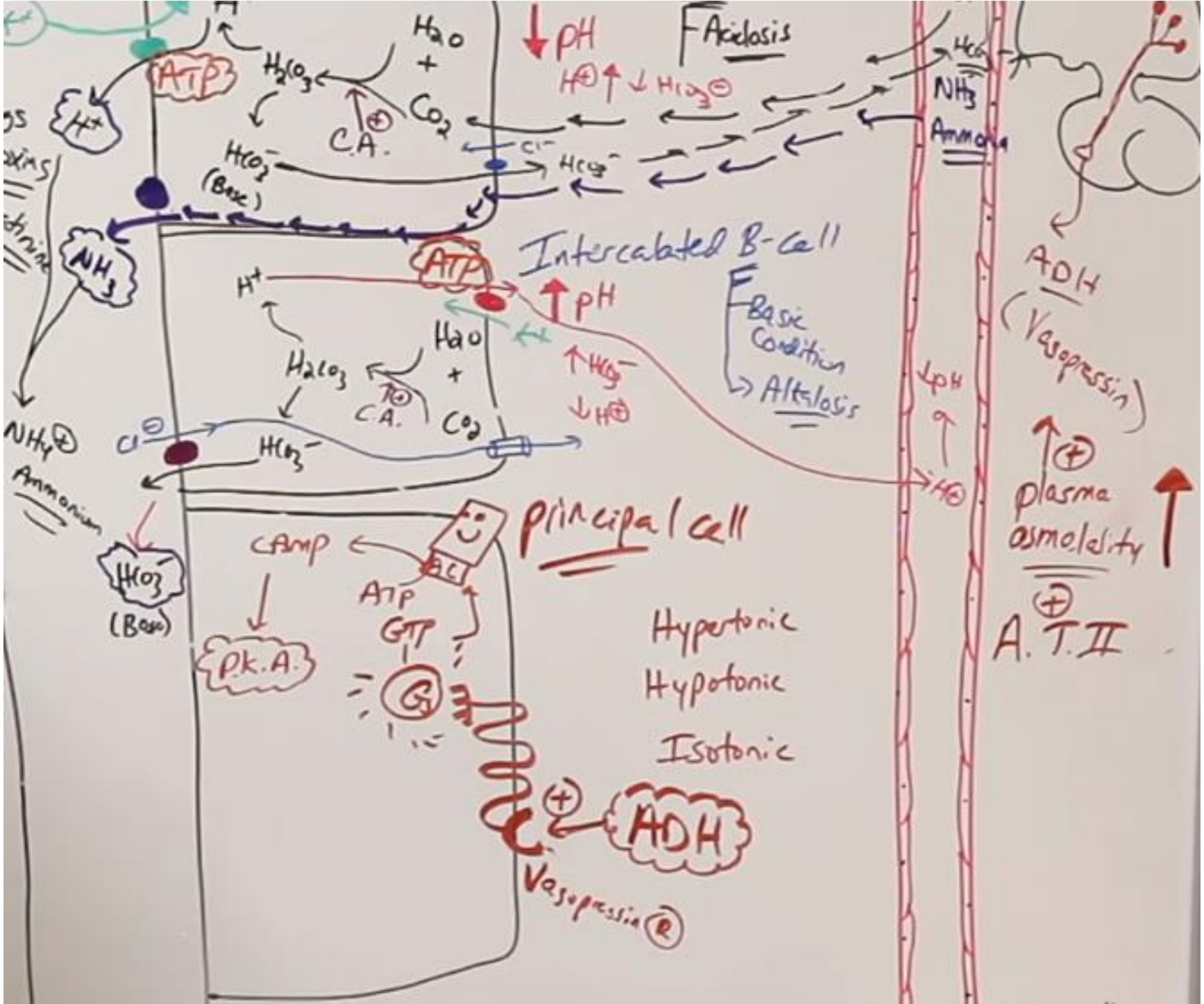

PKA
[Na+]↓
K+
principal cell
ADH
symporter)
Ca++
Na+
[↑K+]
K+
Late D.T.
Intercalated A-Cell
Acidosis
↓pH
H+ ↑ ↓ HCO3−
H+
ATP
H2CO3
H2O
+
CO2
C.A.
HCO3−
(Base)
Cl−
Drugs
Toxins
Creatinine
NH3
NH4+
Ammonia
HCO3−
(Base)
Intercalated B-Cell
↑pH
Basic Condition
Alkalosis
↑HCO3−
↓H+
↑pH
NH3
Ammonia
Adrenal Gland
A.T. II
[↓Na+]
[K+]↑
↓pH


HYPOTHALAMUS
MAGNOCELLULAR NEURON
MAGNOCELLULAR NEURONS
ANTERIOR PITUITARY
POSTERIOR PITUITARY
SYSTEMIC CIRCULATION
UCIN AND ADH ARE
DUCED BY MAGNOCELLULAR
RONS AND ARE CLOSELY
LATED PEPTIDES
OXYTOCIN
ADH
(VASOPRESSIN)
VAS
RESIS

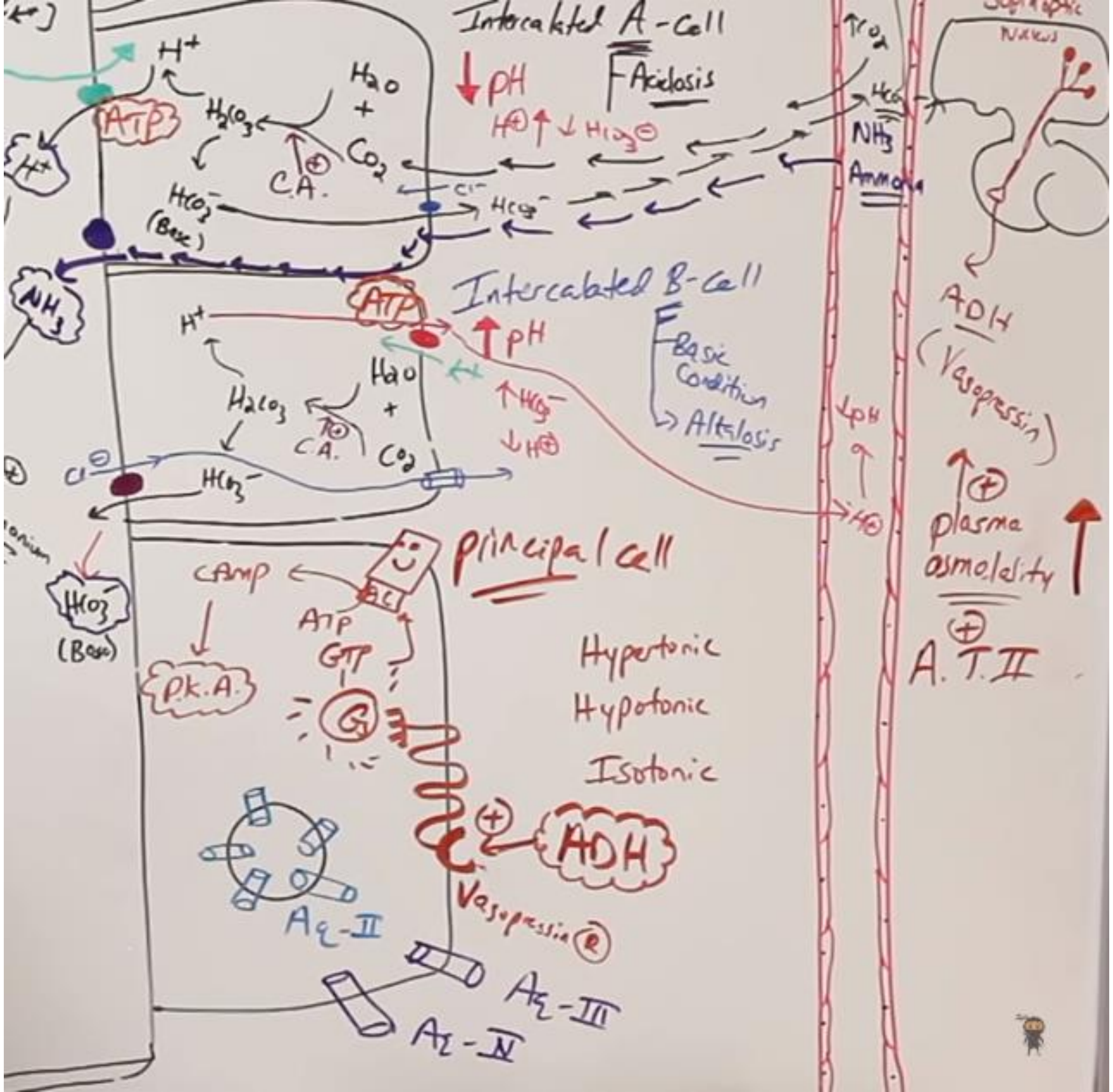

A
principal cell
ADH
[Na+]↓
Na+
K+
[↑K+]
(↓K+)
Late D.T.
Intercalated A-Cell
↓pH
Acidosis
H+↑ ↓HCO3−
H+
H2O
+
CO2
H2CO3
C.A.
HCO3−
(Base)
Cl−
ATP
Drugs
Toxins
Creatinine
NH3
NH4+
Ammonia
Intercalated B-Cell
↑pH
Basic Condition
Alkalosis
↑HCO3−
↓H+
↑pH
↑CO2
HCO3−
NH3
Ammonia
↓pH
Adrenal Gland
A.T. II
[↓Na+]
[K+]↑
CRH
Supraoptic Nucleus
ADH
(Vasopressin)



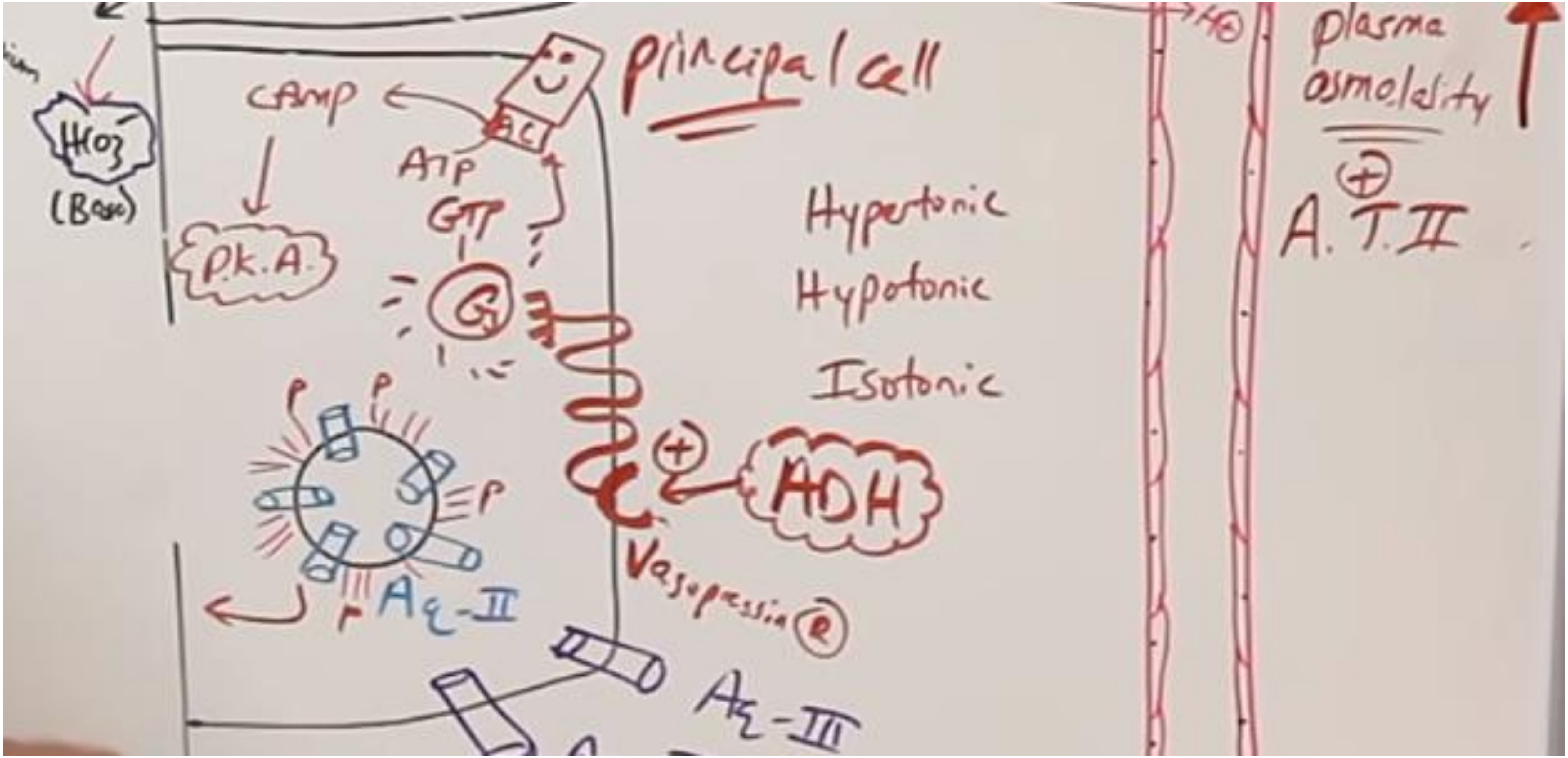
principal cell
ADH
$[\uparrow K^+]$
K^+
$[\downarrow K^+]$
Late D.T.
Intercalated A-Cell
↓pH
Acidosis
H^+↑ ↓HCO_3^-
H_2O + CO_2
H_2CO_3
C.A.
HCO_3^- (Base)
ATP
Drugs
Toxins
Creatinine
NH_3
Ammonia
Intercalated B-Cell
↑pH
Basic Condition
Alkalosis
↑HCO_3^-
↓H^+
NH_4^+
Ammonium
HCO_3^- (Base)
Adrenal Gland
A.T.II
$[\downarrow Na^+]$
$[K^+]\uparrow$
CRH
Supraoptic Nucleus
ADH (Vasopressin)
↑ plasma osmolality
A.T.II
Hypertonic
Hypotonic
Isotonic



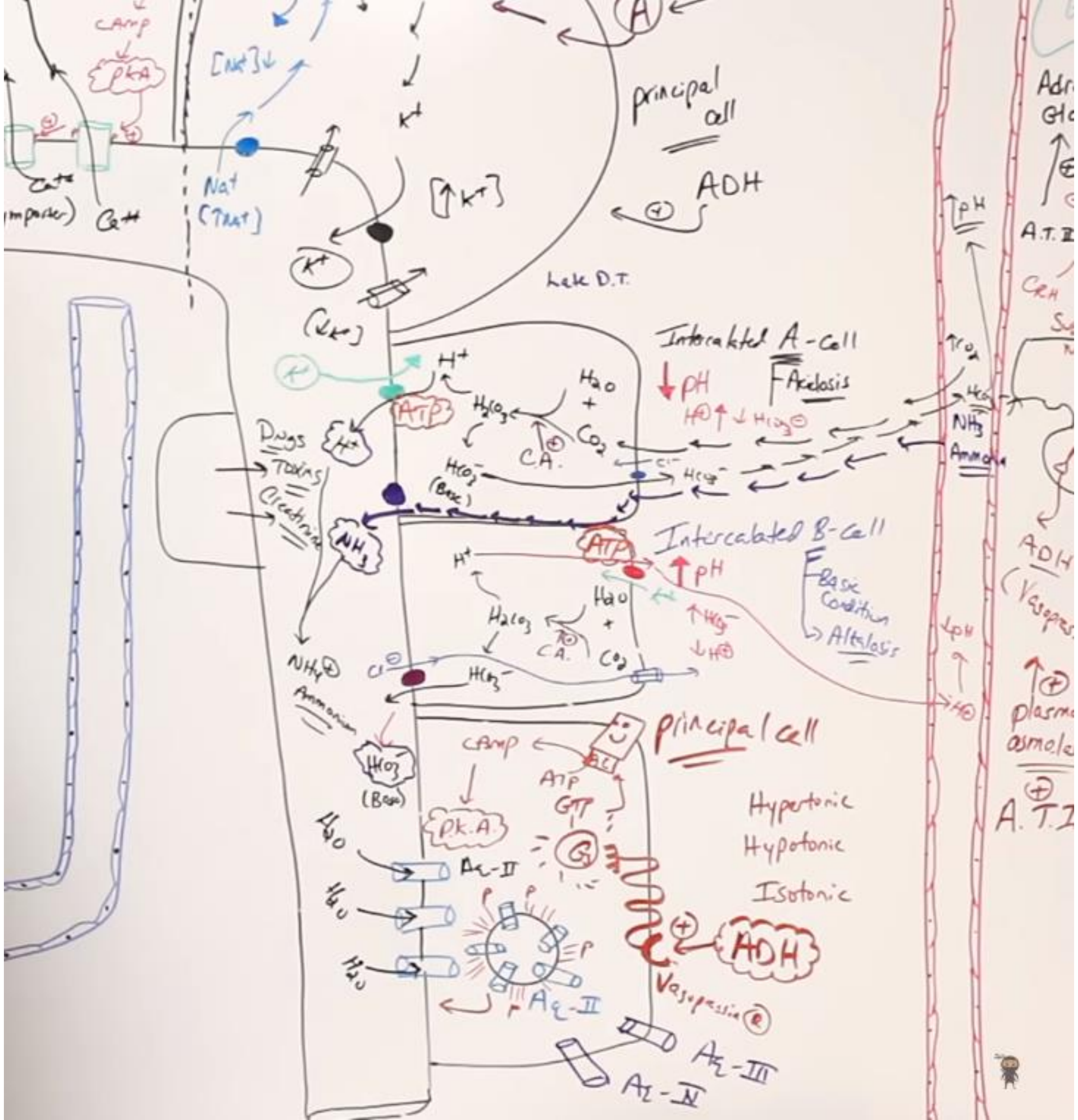
↓pH
Acidosis
H⊕ ↑ ↓ HCO3⊖
H2O
+
CO2
H2CO3
C.A.
HCO3⁻
(Base)
ATP
H+
Cl⁻
HCO3⁻
NH3
Ammonia
NH4⊕
Ammonium
HCO3⁻
(Base)
Intercalated B-cell
↑pH
Basic Condition
Alkalosis
↑HCO3⁻
↓H⊕
principal cell
cAMP
ATP
GTP
AC
G
P.K.A.
ADH
Vasopressin ®
Hypertonic
Hypotonic
Isotonic
ADH
(Vasopressin)
plasma osmolality
A.T.II

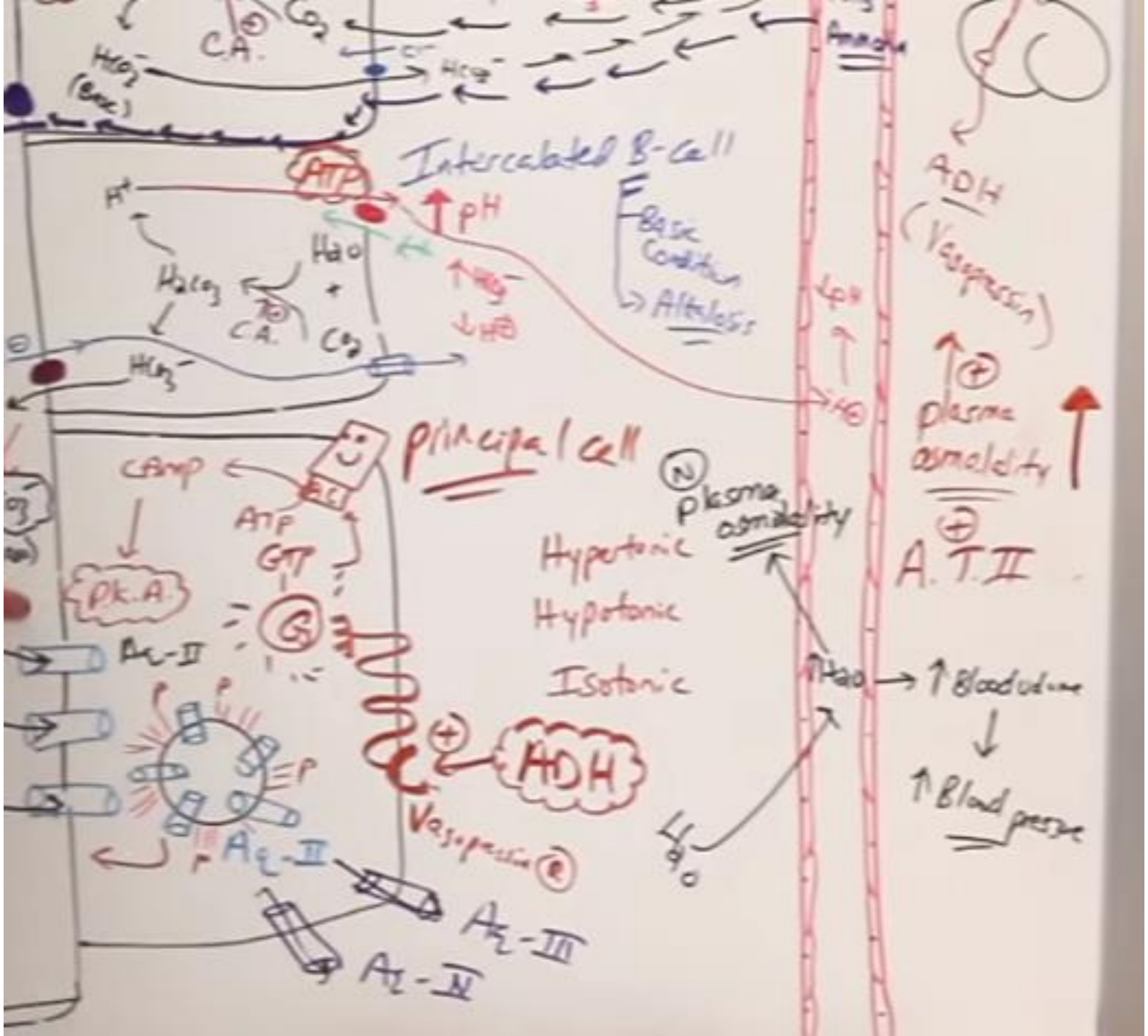


Intercalated A-Cell
↓pH
Acidosis
ATP
H2CO3
H2O
CO2
C.A.
HCO3- (Base)
NH3
Ammonia
Intercalated B-Cell
↑pH
Basic Condition
Alkalosis
principal cell
cAMP
P.K.A.
ATP
GTP
HCO3- (Base)
Hypertonic
Hypotonic
Isotonic
ADH
Vasopressin Ⓡ
Aq-II
Aq-III
Aq-IV
ADH (Vasopressin)
plasma osmolality
A.T.II

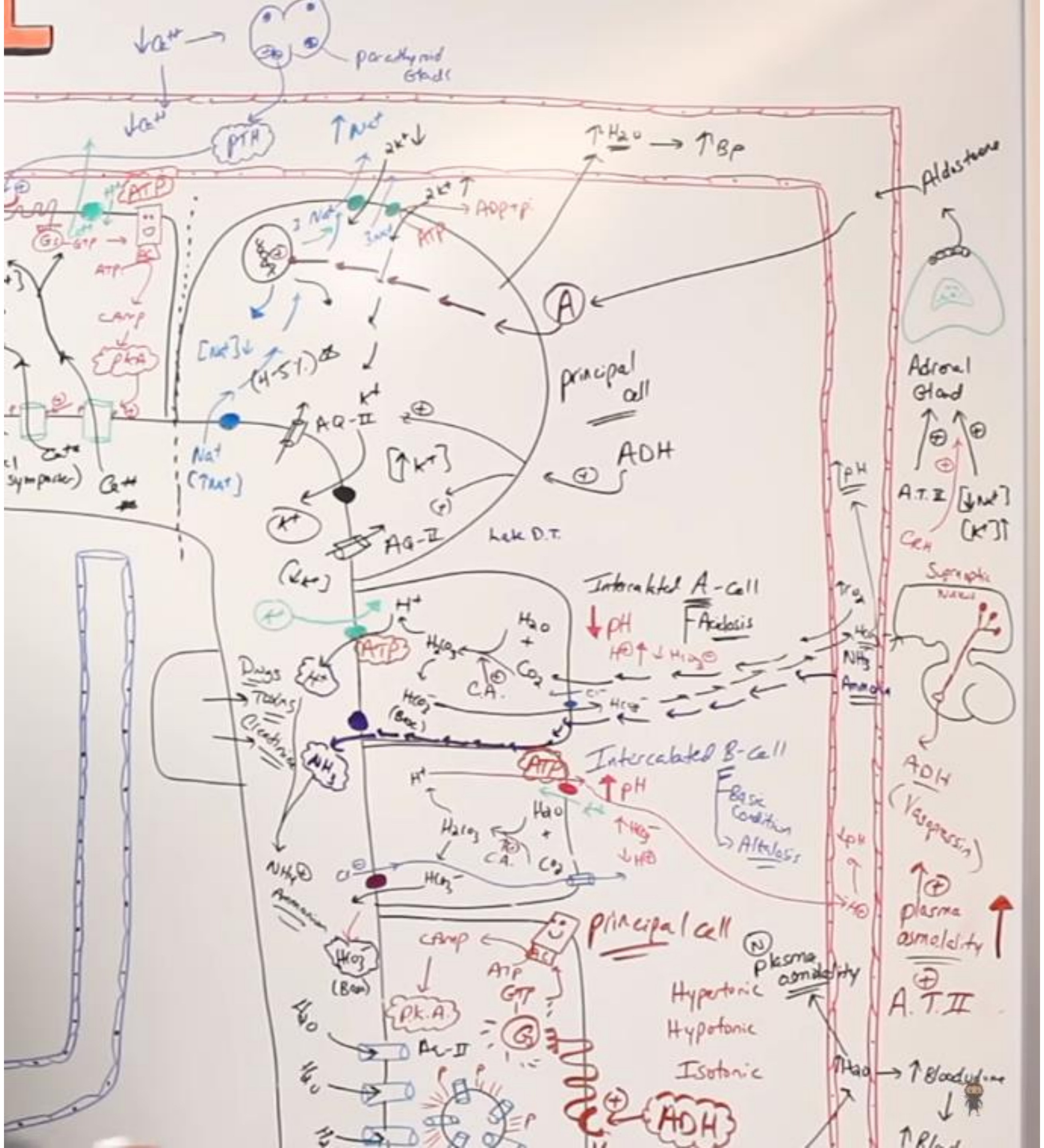


principal cell
cAMP
AC
ATP
GTP
G
P.K.A.
HCO_3^-
(Base)
P
Aq-II
ADH
Vasopressin R
Aq-III
Hypertonic
Hypotonic
Isotonic
plasma osmolality
A.T.II

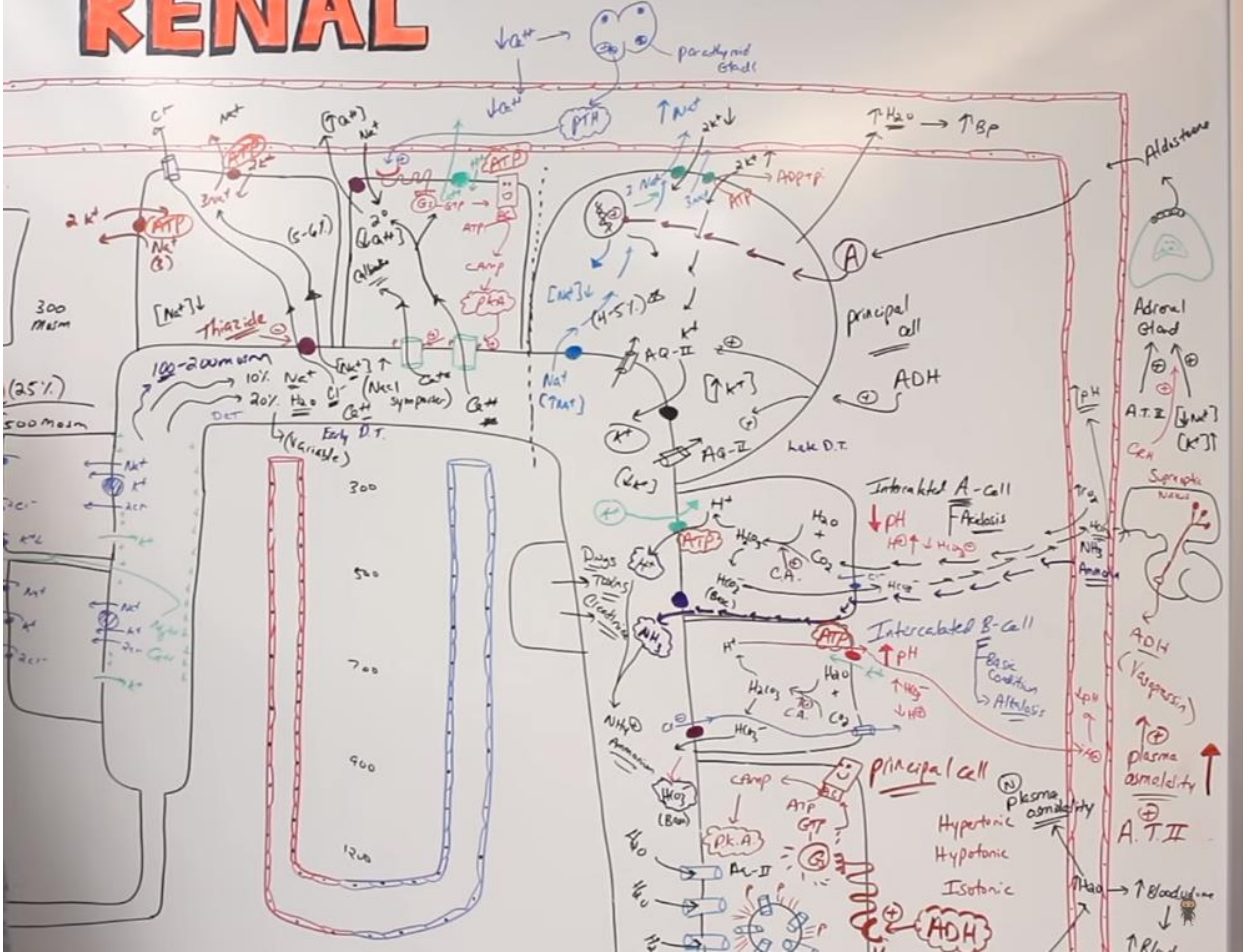

cAMP
PKA
Ca++
Na+
[Na+]↓
K+
[↑K+]
principal cell
ADH
Late D.T.
Intercalated A-cell
↓pH
Acidosis
H+
H2O
+
CO2
H2CO3
C.A.
HCO3-
(Base)
ATP
Drugs
Toxins
Creatinine
NH3
Ammonia
Intercalated B-cell
↑pH
Basic Condition
Alkalosis
NH4+
Principal cell
Hypertonic
Hypotonic
Isotonic
GTP
Aq-II
Aq-III
Aq-IV
Vasopressin
A.T.II
plasma osmolality

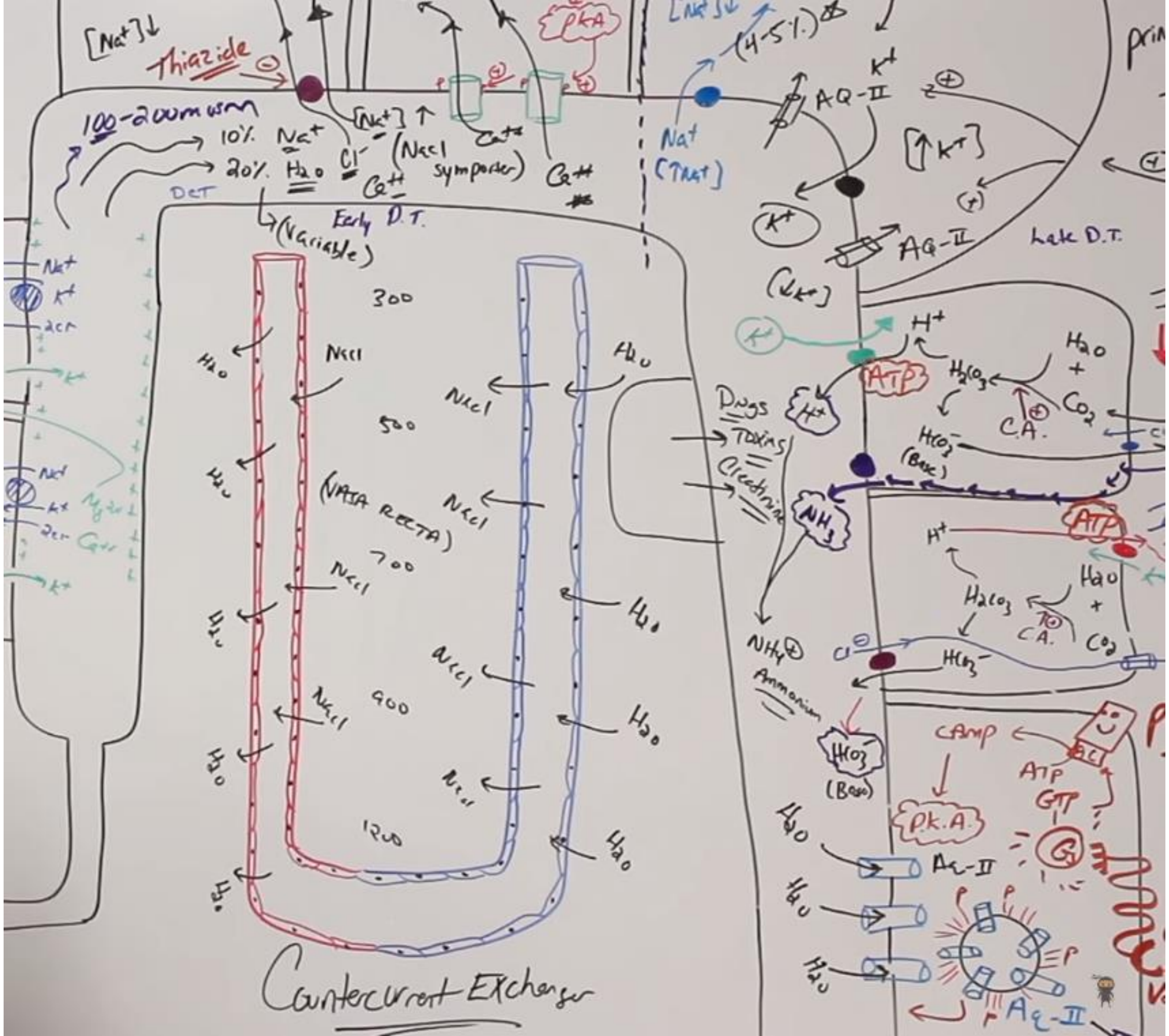


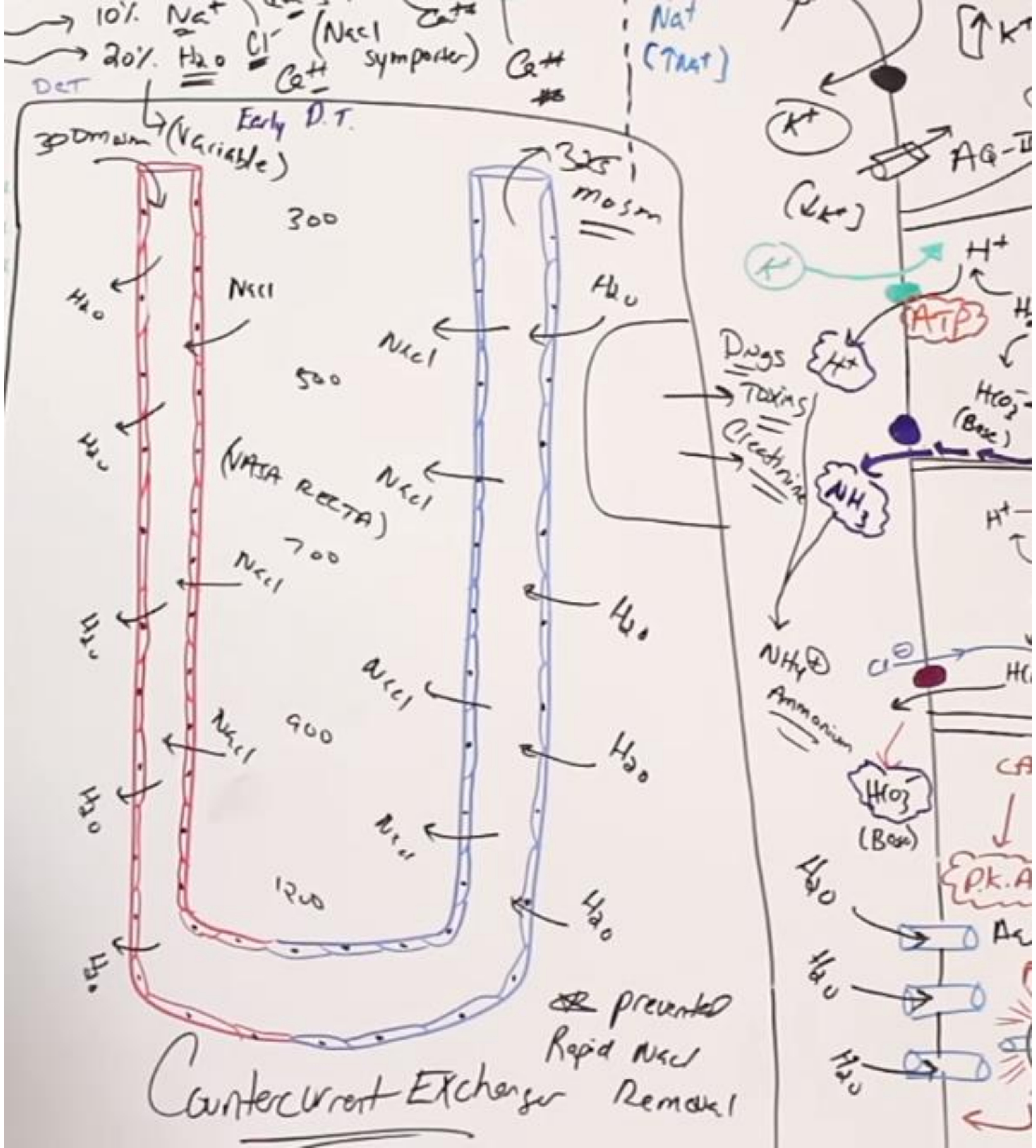
C.A.
Intercalated B-cell
ATP
pH
Base Condition
Alkalosis
C.A.
principal cell
cAMP
ATP
GTP
PK.A.
ADH
Vasopressin
Hypertonic
Hypotonic
Isotonic
plasma osmolality
ADH
(Vasopressin)
plasma osmolality
A.T.II
Blood volume
Blood pressure



parathyroid Glands
PTH
ATP
cAMP
PKA
principal cell
ADH
Aldosterone
Adrenal Gland
A.T.II
Late D.T.
Intercalated A-cell
Acidosis
Intercalated B-cell
Basic Condition
Alkalosis
ADH (Vasopressin)
plasma osmolality
Principal cell
Hypertonic
Hypotonic
Isotonic


RENAL
parathyroid gland
PTH
Aldosterone
Adrenal Gland
300 mosm
Thiazide
Early D.T.
Late D.T.
principal cell
ADH
Intercalated A-cell
Acidosis
Intercalated B-cell
Basic Condition
Alkalosis
Drugs
Toxins
Creatinine
Principal cell
plasma osmolality
Hypertonic
Hypotonic
Isotonic
ADH (Vasopressin)
plasma osmolality
A.T.II
cAMP
ATP
300
500
700
900
1200


[Na+]↓
Thiazide
PKA
(4-5%)
K+
AQ-II
100-200 mosm
10% Na+
20% H2O
Cl-
(NaCl symporter)
Ca++
[Na+]↑
DCT
Early D.T.
(Variable)
Na+
[↑K+]
(↓K+]
Late D.T.
300
500
700
900
1200
NaCl
H2O
(VASA RECTA)
Drugs
Toxins
Creatinine
H+
H2CO3
H2O + CO2
C.A.
HCO3- (Base)
ATP
NH3
NH4+
Ammonium
cAMP
P.K.A.
GTP
AC
Aq-II
Countercurrent Exchanger



10% Na+
20% H2O
Cl-
(NaCl symporter)
Ca++
DCT
Early D.T.
300 mosm (variable)
325 mosm
300
500
700
900
1200
NaCl
H2O
(VASA RECTA)
prevented Rapid NaCl Removal
Countercurrent Exchanger
Na+ (TRAT)
K+
AQ-II
ATP
H+
Drugs
Toxins
Creatinine
HCO3- (Base)
NH3
NH4+ Ammonium
Cl-
HCO3- (Base)
P.K.A

Antidiuretic Hormone

ADH has three actions on the renal tubule.
(1) It increases the water permeability of the principal cells of the late distal tubule and collecting ducts.
(2) It increases the activity of the Na+-K+-2Cl– cotransporter of the thick ascending limb, thereby enhancing countercurrent multiplication and the size of the corticopapillary osmotic gradient.
(3) It increases urea permeability in the inner medul-lary collecting ducts (but not in the cortical or outer medullary collecting ducts), enhancing urea recycling and the size of the corticopapillary osmotic gradient.

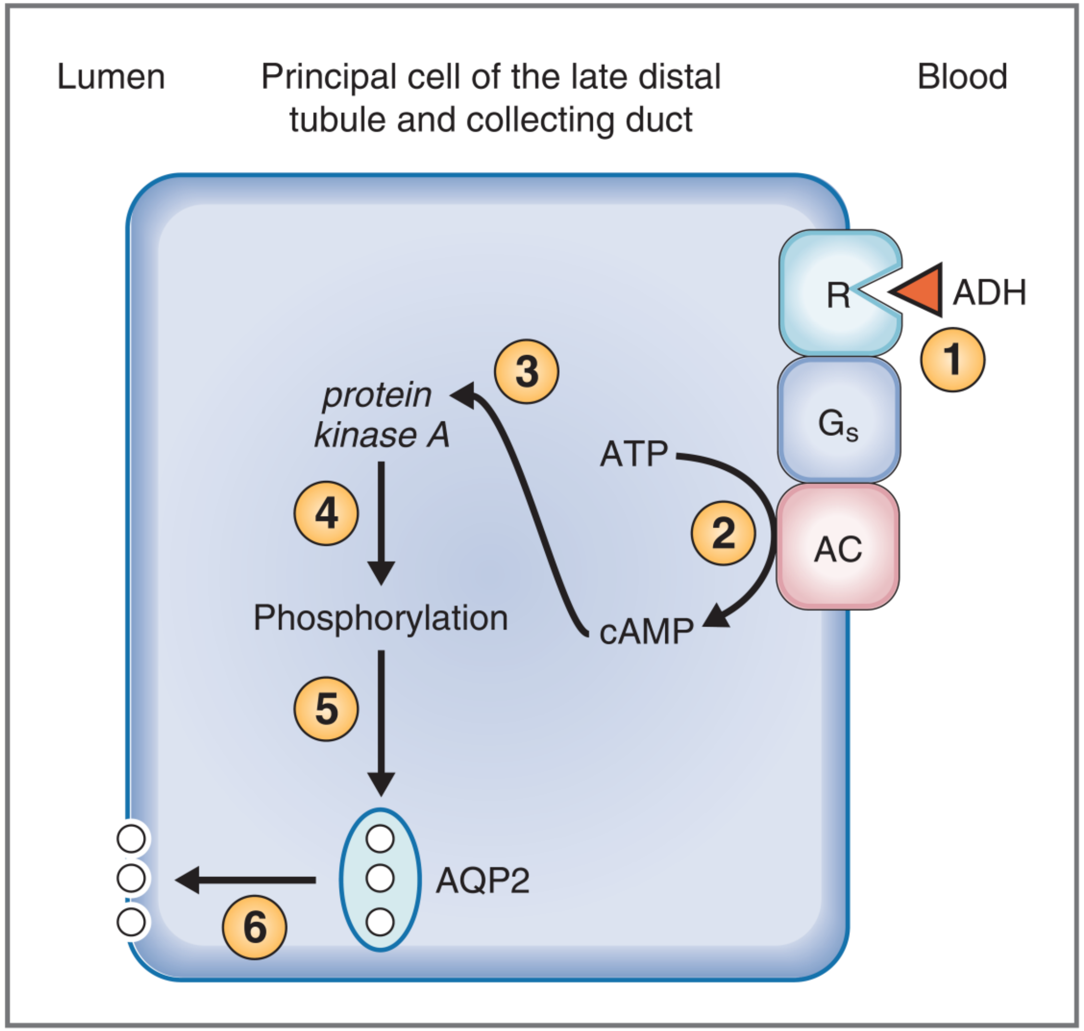


Fig. 6.41 Cellular mechanism of action of antidiuretic hormone in the principal cell of the late distal tubule and collecting duct. See the text for an explanation of the circled numbers. *AC,* Adenylyl cyclase; *ADH,* antidiuretic hormone; *AQP2,* aquaporin 2; *ATP,* adenosine triphosphate; *cAMP,* cyclic adenosine monophosphate, or cyclic AMP; G_s, stimulatory G protein; *R,* V_2 receptor.

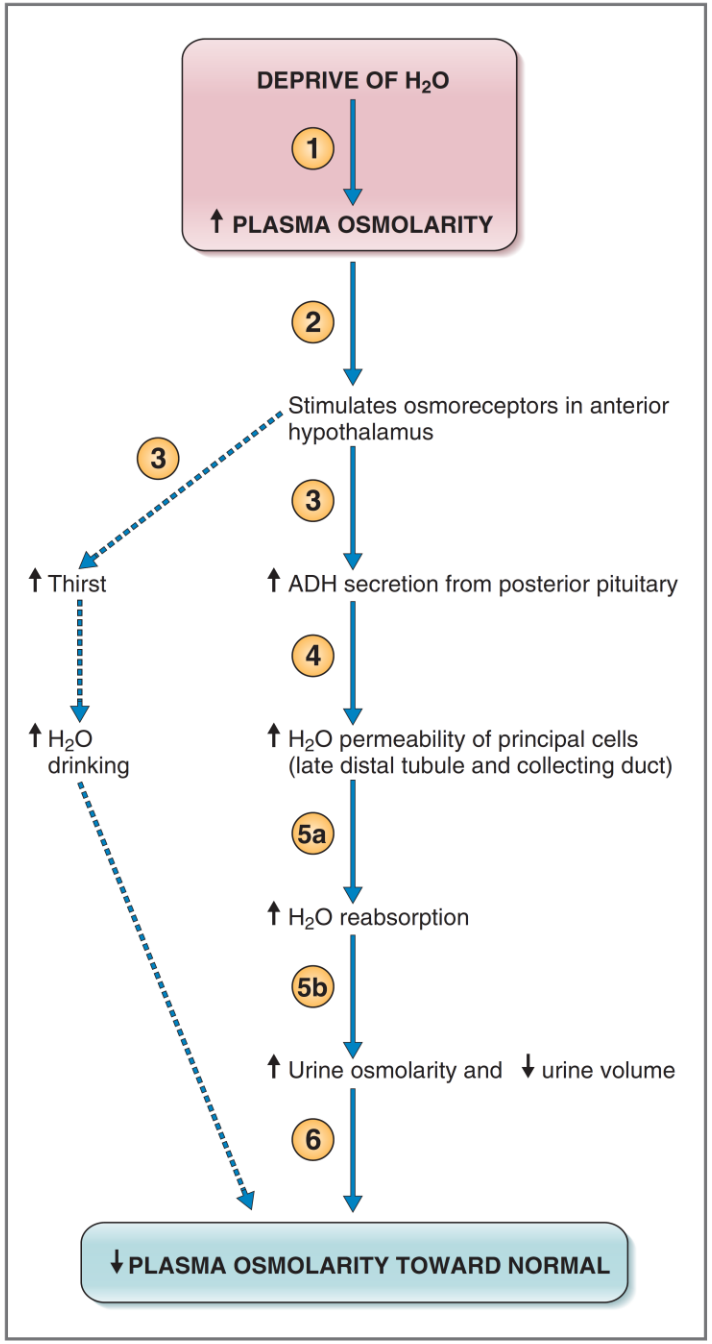


Fig. 6.36 Responses to water deprivation. See the text for an explanation of the circled numbers. *ADH,* Antidiuretic hormone.

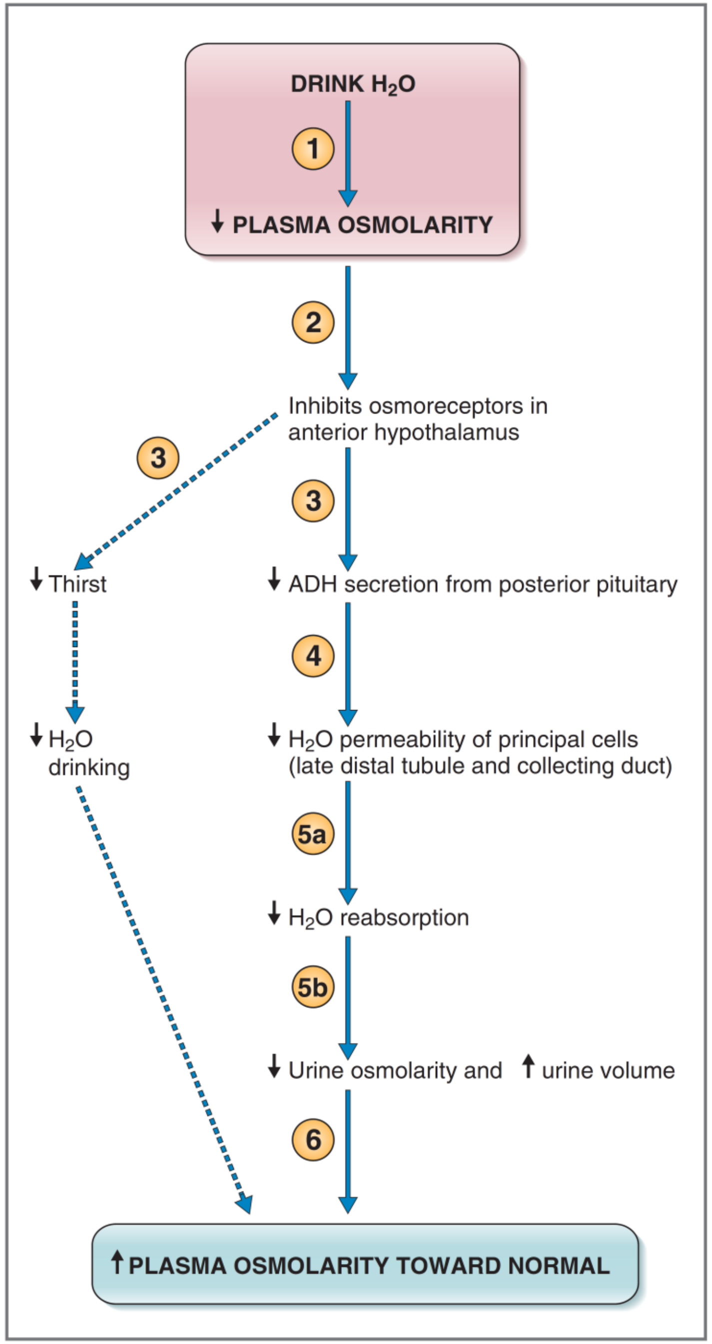
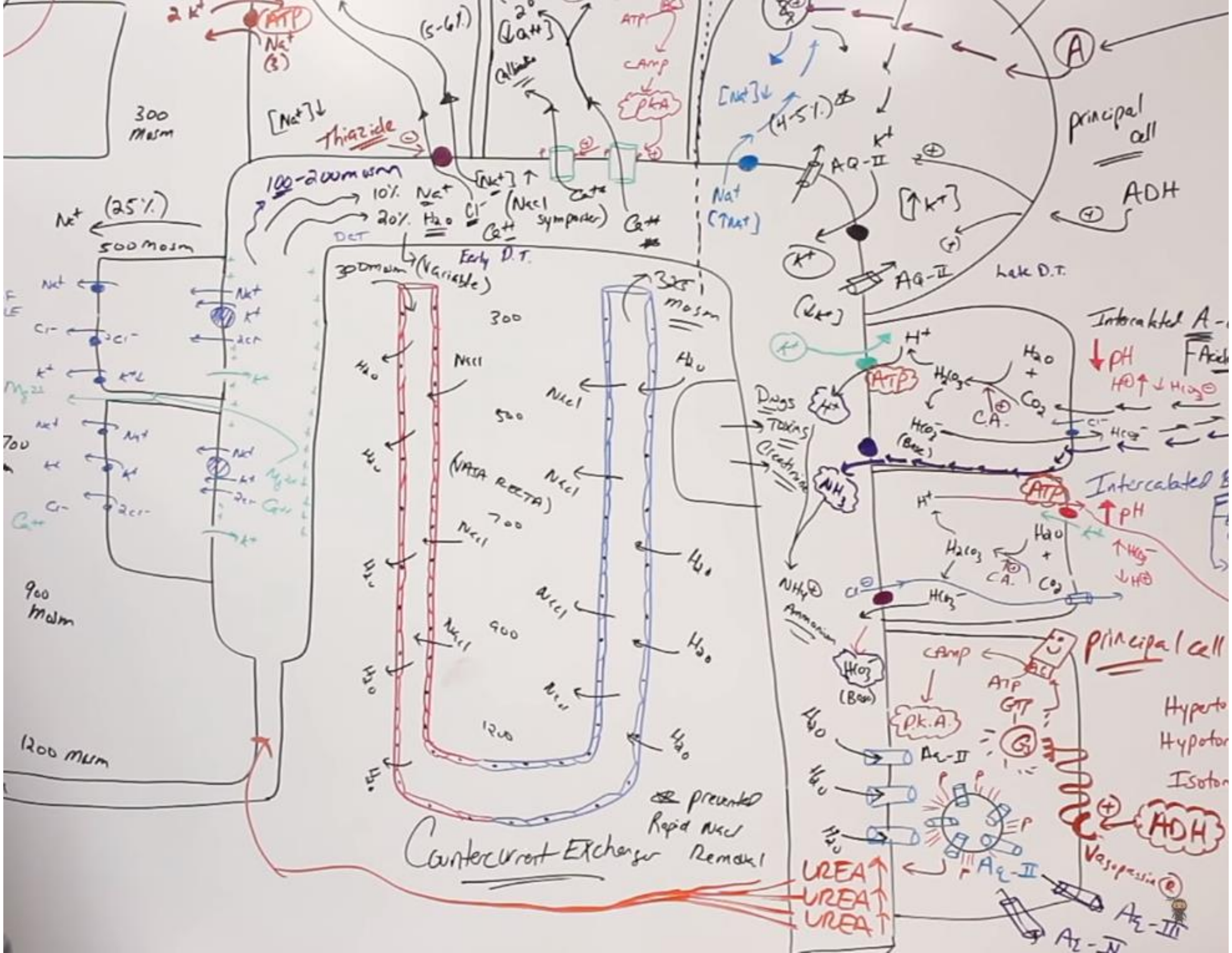
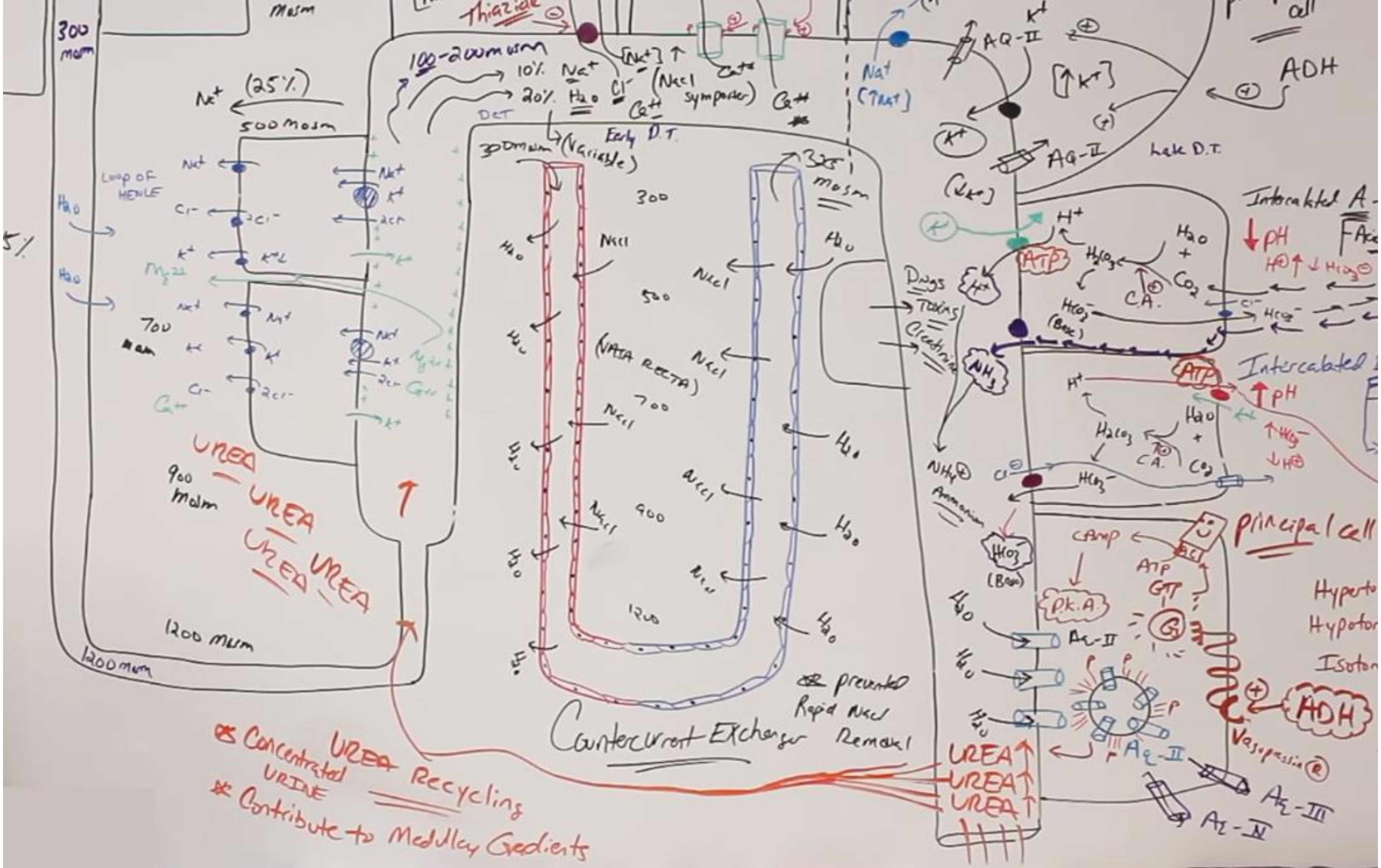


Fig. 6.37 Responses to water drinking. See the text for an explanation of the *circled numbers. ADH,* Antidiuretic hormone.


300 Mosm
Thiazide
[Na+]↓
100-200 mosm
10% Na+
20% H2O
(NaCl symporter)
Early D.T.
Na+ (25%)
500 mosm
900 Mosm
1200 Mosm
300 mosm (Variable)
300
500
700
900
1200
NaCl
H2O
(VASA RECTA)
325 mosm
Countercurrent Exchanger
prevented Rapid NaCl Removal
cAMP
PKA
[Na+]↓
(4-5%)
Na+ (↑Na+)
AQ-II
[↑K+]
Late D.T.
principal cell
ADH
Intercalated A
↓pH
H2CO3
H2O
CO2
C.A.
HCO3- (Base)
Drugs
Toxins
Creatinine
NH3
NH4+ Ammonium
Intercalated B
↑pH
HCO3 (Base)
principal cell
cAMP
P.K.A.
ATP
GTP
Aq-II
Aq-III
Aq-IV
ADH
Vasopressin
UREA
UREA
UREA

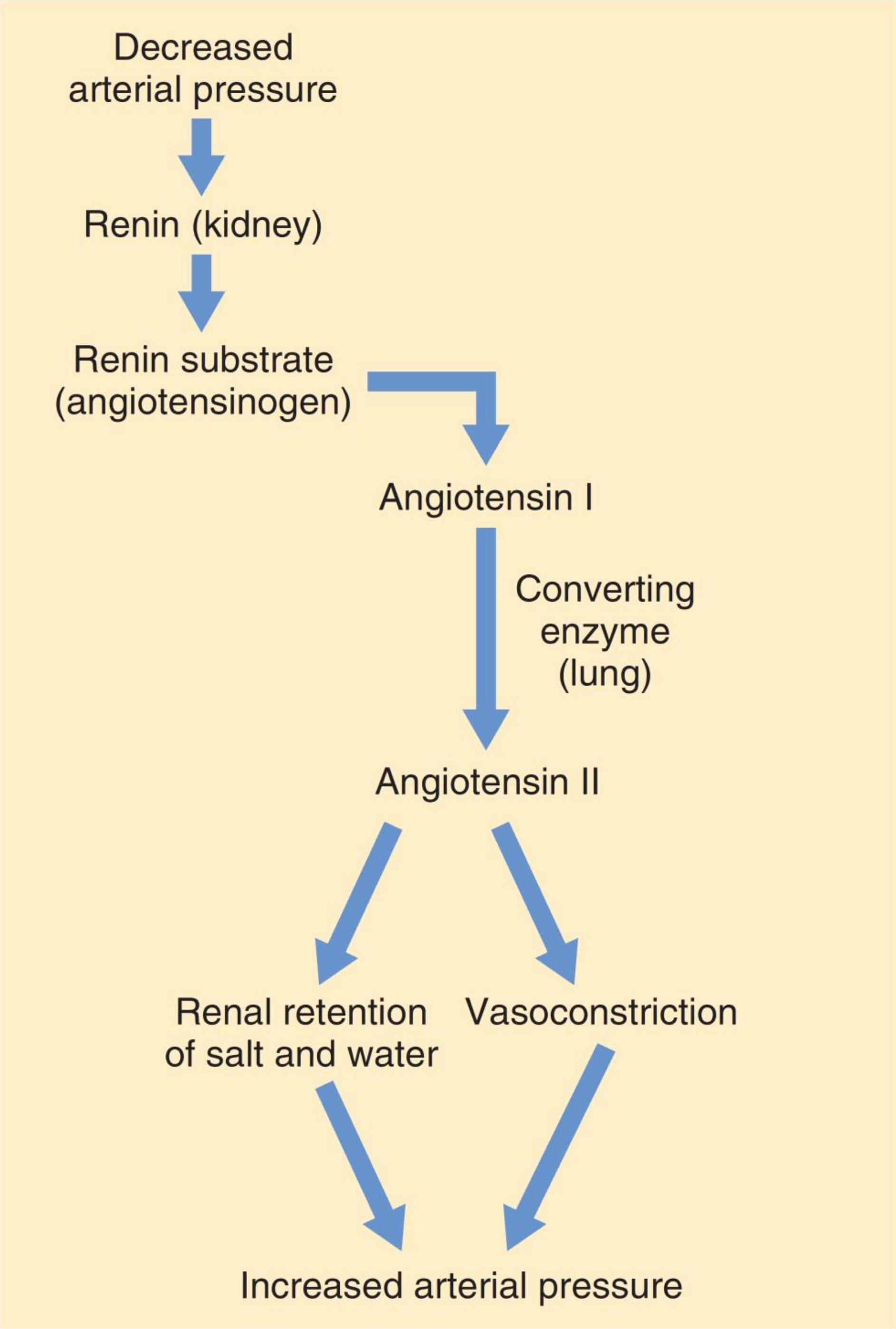


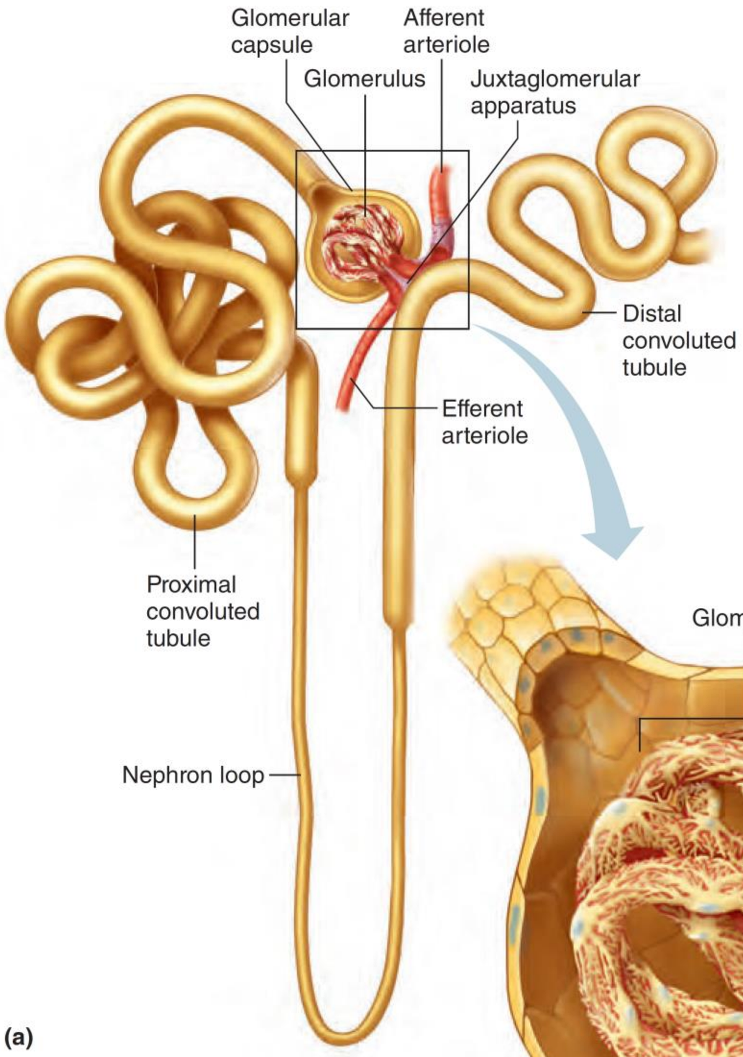
300 mosm
Thiazide
100-200 mosm
10% Na+
20% H2O
Cl-
(NaCl symporter)
Ca++
Early D.T.
Na+ (25%)
500 mosm
Loop of Henle
700 mosm
900 mosm
1200 mosm
1200 mosm
UREA
UREA
UREA
UREA
300 mosm (Variable)
325 mosm
300
500
700
900
1200
NaCl
H2O
(VASA RECTA)
Countercurrent Exchanger
prevents Rapid NaCl Removal
* Concentrated URINE
* Contribute to Medullary Gradients
UREA Recycling
UREA
UREA
UREA
AQ-II
AQ-II
Late D.T.
ADH
Intercalated A
↓pH
Intercalated B
↑pH
ATP
C.A.
H2CO3
HCO3- (Base)
NH3
NH4+ Ammonium
Drugs
Toxins
Creatinine
Principal cell
cAMP
ATP
GTP
G
P.K.A.
Aq-II
Aq-III
Aq-IV
ADH
Vasopressin
Hypertonic
Hypotonic
Isotonic

Renin-angiotensin-aldosterone system.

Renin is synthesized and stored in an inactive form called prorenin in the juxtaglomerular cells (JG cells) of the kidneys. The JG cells are modified smooth muscle cells located mainly in the walls of the afferent arterioles immediately proximal to the glomeruli. When the arterial pressure falls, intrinsic reactions in the kidneys cause many of the prorenin molecules in the JG cells to split and release renin. Most of the renin enters the renal blood and then passes out of the kidneys to circulate throughout the entire body. However, small amounts of the renin do remain in the local fluids of the kidne and initiate several intrarenal functions.

The renin- angiotensin-aldosterone system is activated in response to decreased arterial pressure (i.e., decreased renal perfusion pressure). angiotensin II stimulates Na+ reabsorption in the proximal tubule (Na+-H+ exchange), and aldosterone stimulates Na+ reabsorption in the late distal tubule and the collecting duct.





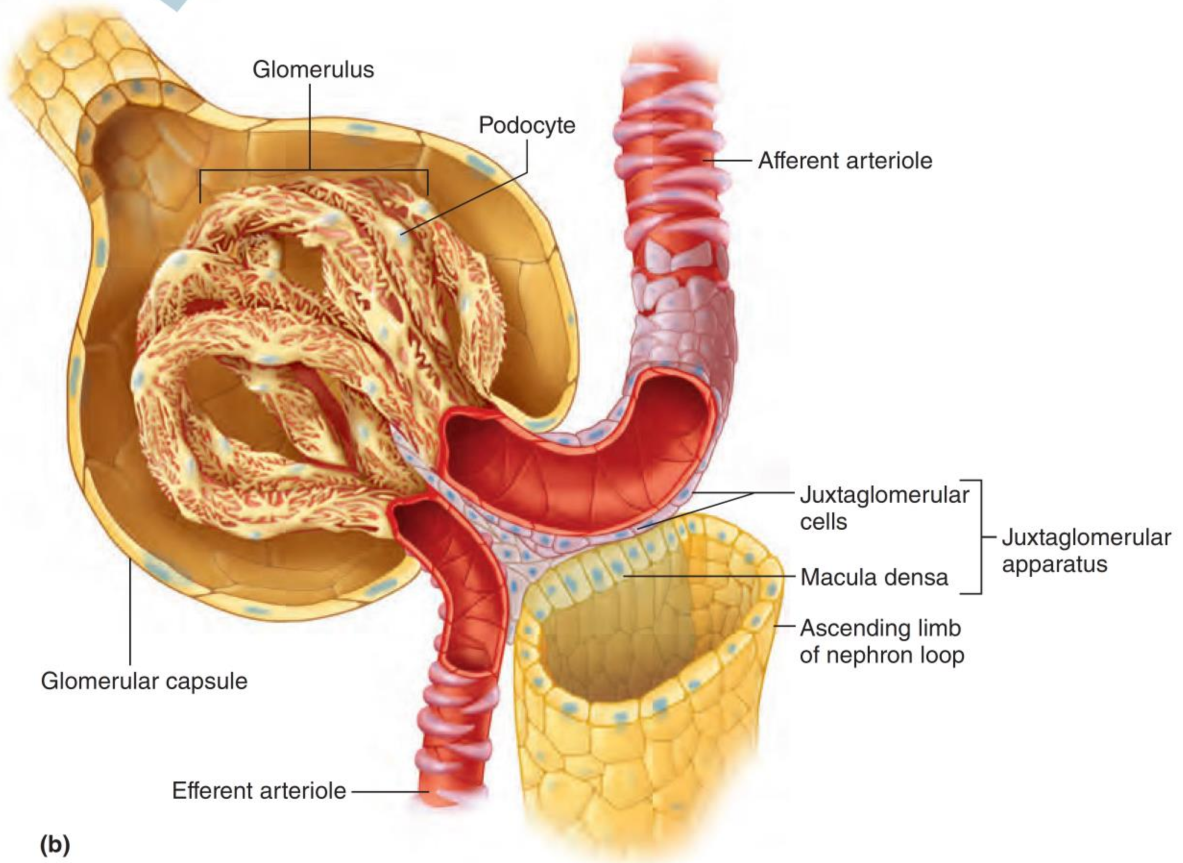
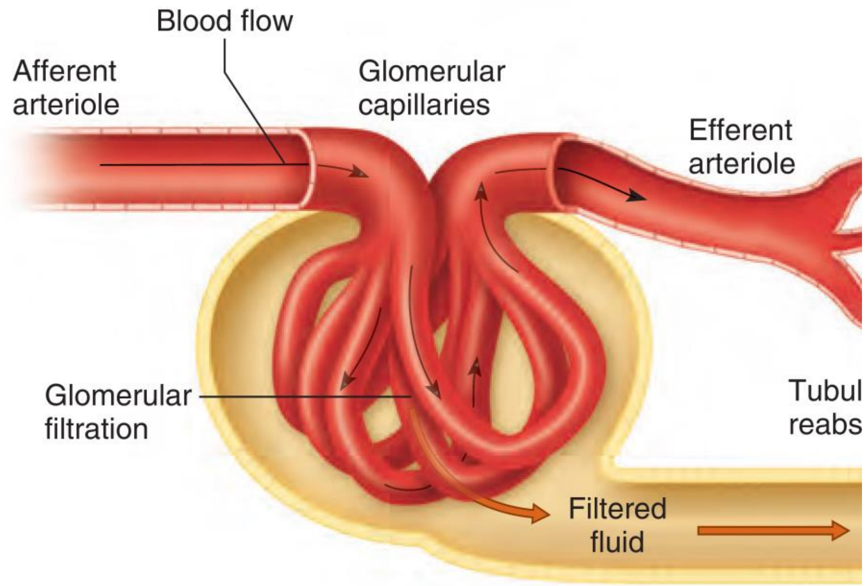


FIGURE 17.8 Juxtaglomerular apparatus. (**a**) Location of the juxtaglomerular apparatus. (**b**) Enlargement of a section of the juxtaglomerular apparatus, which consists of the macula densa and the juxtaglomerular cells.



Another mechanism to control filtration rate involves the enzyme renin. Juxtaglomerular cells secrete renin in response to three types of stimuli: (1) when special cells in the afferent arteriole sense a drop in blood pressure; (2) in response to sympathetic stimulation; and (3) when the macula densa senses decreased numbers of chloride, potassium, and sodium ions reaching the end of the ascending limb of the nephron loop. Once in the bloodstream, renin reacts with the plasma protein angiotensinogen to form angiotensin I. A second enzyme (angiotensin-converting enzyme, or ACE) in the lungs and in plasma quickly converts angiotensin I to angiotensin II.

Angiotensin II carries out a number of actions that help maintain sodium balance, water balance, and blood pressure. Angiotensin II vasoconstricts the efferent arteriole, which causes blood to back up into the glomerulus, raising filtration pressure. This important action helps minimize the decrease in glomerular filtration rate when systemic blood pressure is low. Angiotensin II has a major effect on the kidneys by stimulating secretion of the adrenal hormone aldosterone, which stimulates tubular reabsorption of sodium.

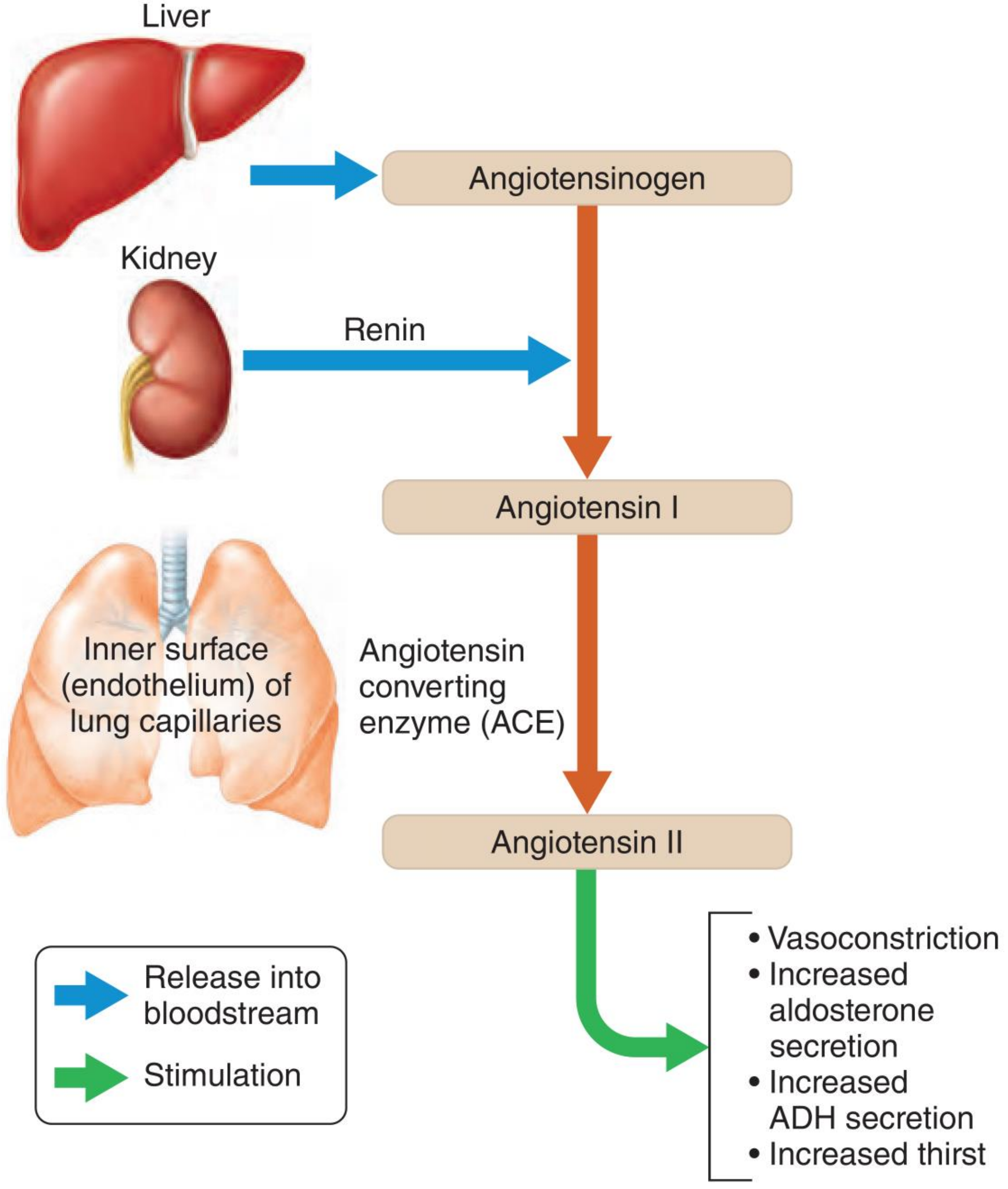


FIGURE 17.12 The formation of angiotensin II in the bloodstream involves several organs and results in multiple actions that conserve sodium and water.

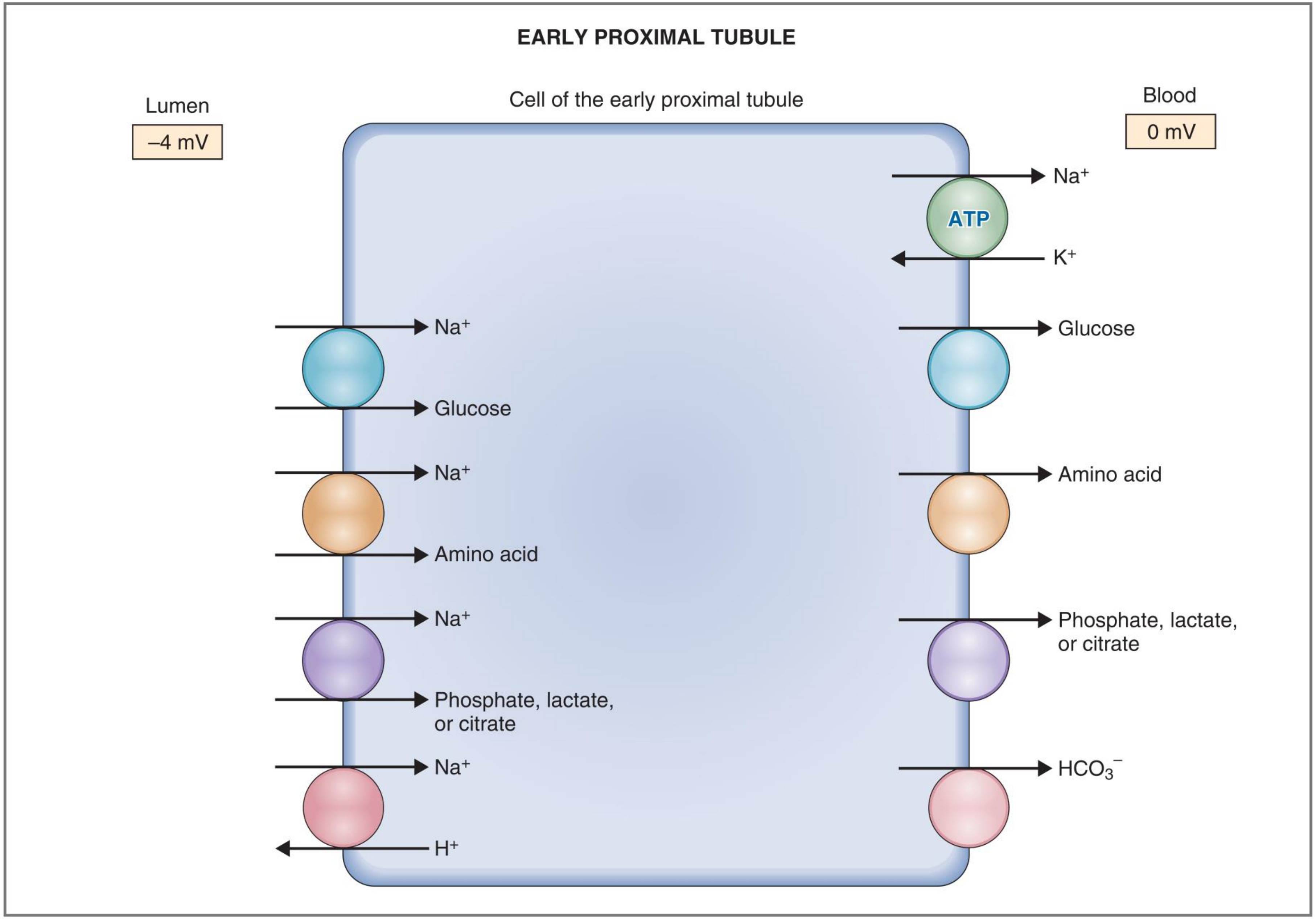


Fig. 6.20 Cellular mechanisms of Na^+ reabsorption in the early proximal tubule. The transepithelial potential difference is the difference between the potential in the lumen and the potential in blood, –4 mV. *ATP,* Adenosine triphosphate.

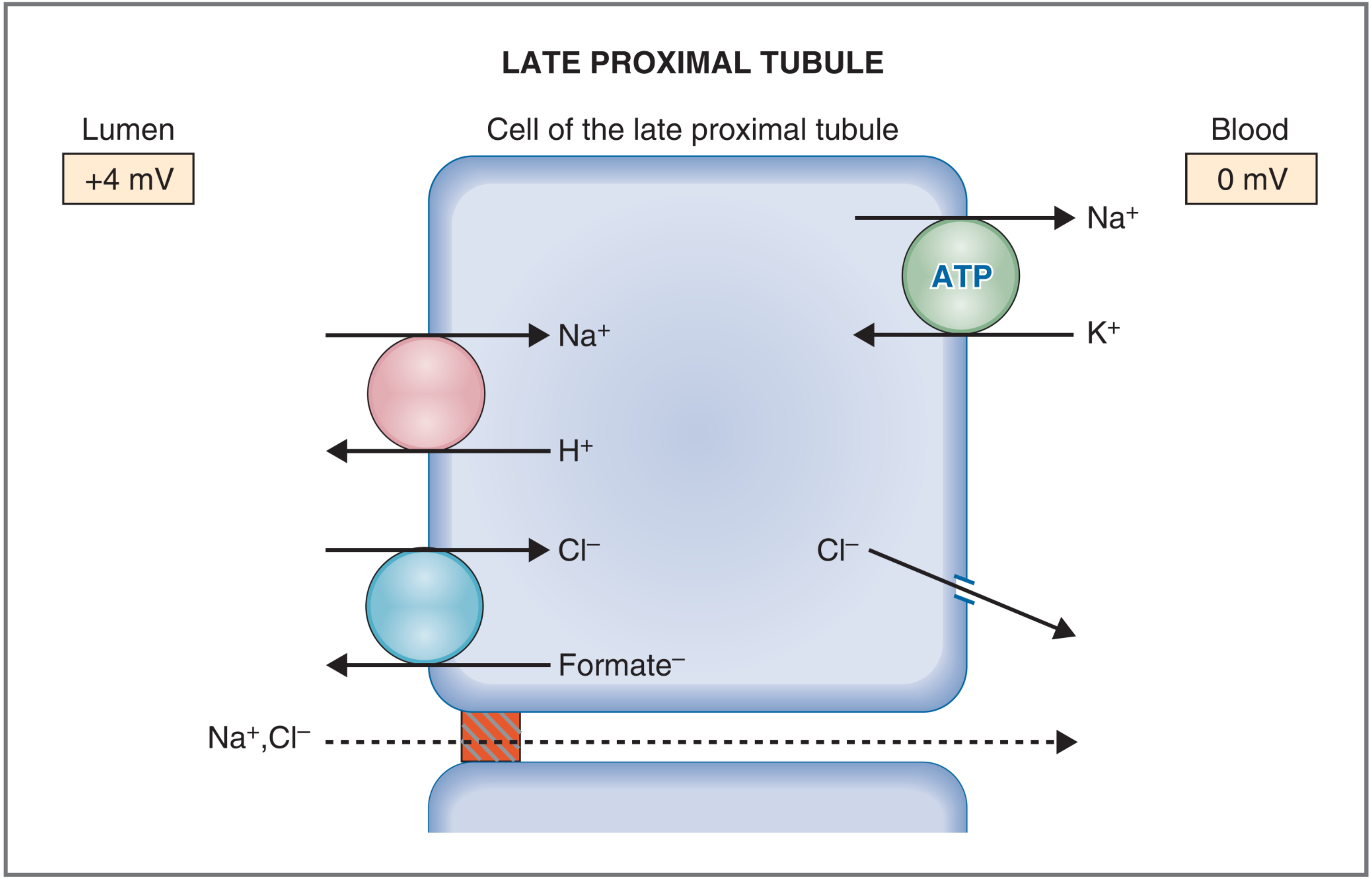


Fig. 6.21 Cellular mechanisms of Na^+ reabsorption in the late proximal tubule. The transepithelial potential difference is +4 mV. *ATP,* Adenosine triphosphate.

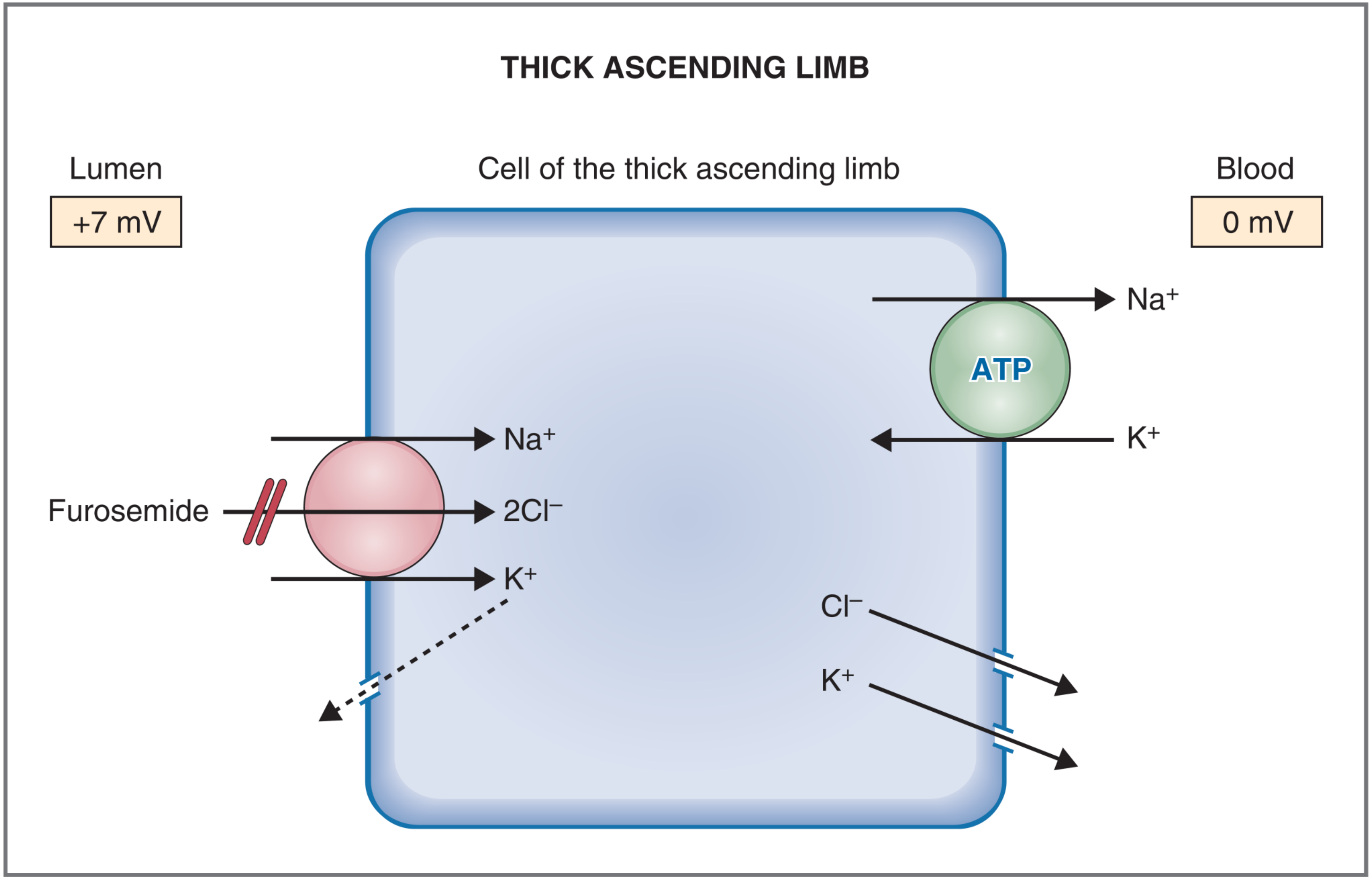


Fig. 6.25 Cellular mechanism of Na+ reabsorption in the thick ascending limb of the loop of Henle. The transepithelial potential difference is +7 mV. *ATP,* Adenosine triphosphate.

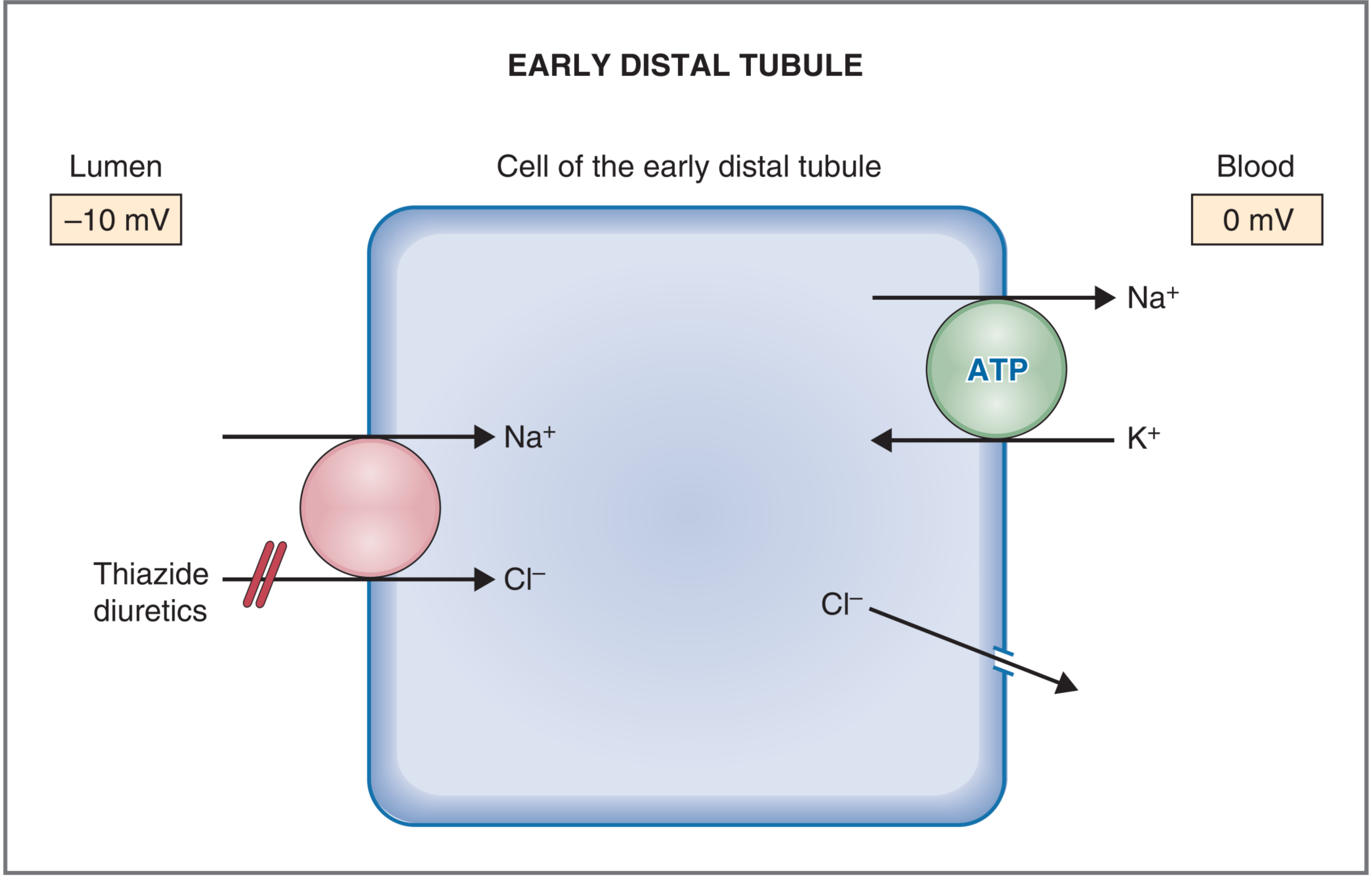


Fig. 6.26 Cellular mechanism of Na^+ reabsorption in the early distal tubule. The trans-epithelial potential difference is –10 mV. *ATP,* Adenosine triphosphate.

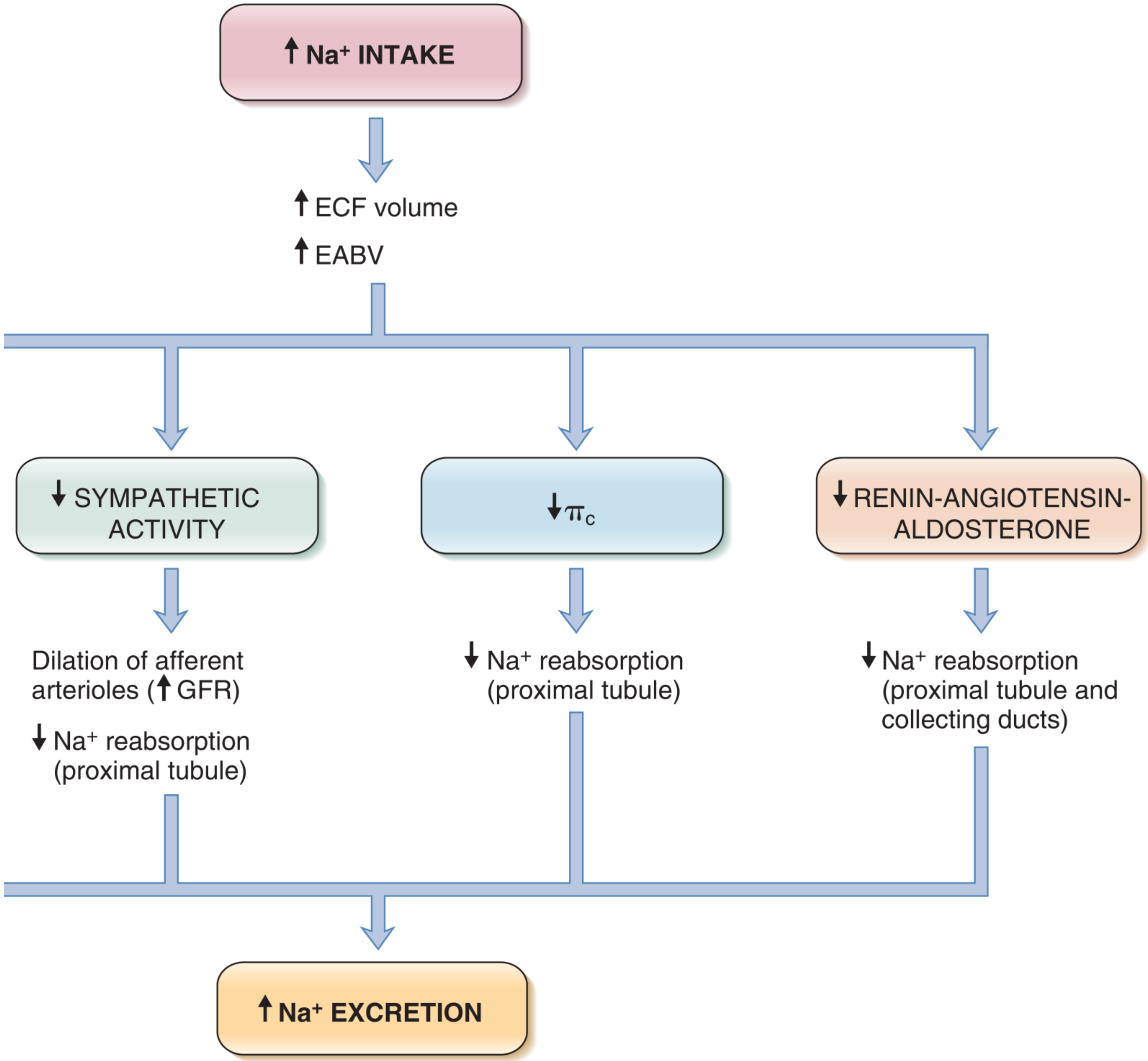

↑ Na+ INTAKE
↑ ECF volume
↑ EABV
↓ SYMPATHETIC ACTIVITY
↓ π_c
↓ RENIN-ANGIOTENSIN-ALDOSTERONE
Dilation of afferent arterioles (↑ GFR)
↓ Na+ reabsorption (proximal tubule)
↓ Na+ reabsorption (proximal tubule)
↓ Na+ reabsorption (proximal tubule and collecting ducts)
↑ Na+ EXCRETION

TABLE 6.7 Summary of the Functions of the Major Nephron Segments

Segment/Cell Type	Major Functions	Cellular Mechanisms	Hormone Actions
Early Proximal Tubule	Isosmotic reabsorption of solute and water	Na^+-glucose, Na^+-amino acid, Na^+-phosphate cotransport Na^+-H^+ exchange	PTH inhibits Na^+-phosphate cotransport Angiotensin II stimulates Na^+-H^+ exchange
Late Proximal Tubule	Isosmotic reabsorption of solute and water	NaCl reabsorption driven by Cl^- gradient	—
Thick Ascending Limb of the Loop of Henle	Reabsorption of NaCl without water Dilution of tubular fluid Single effect of countercurrent multiplication Reabsorption of Ca^{2+} and Mg^{2+} driven by lumen-positive potential	Na^+-K^+-$2Cl^-$ cotransport	ADH stimulates Na^+-K^+-$2Cl^-$ cotransport
Early Distal Tubule	Reabsorption of NaCl without water Dilution of tubular fluid	Na^+-Cl^- cotransport	PTH stimulates Ca^{2+} reabsorption
Late Distal Tubule and Collecting Ducts (principal cells)	Reabsorption of NaCl K^+ secretion Variable water reabsorption	Na^+ channels (ENaC) K^+ channels AQP2 water channels	Aldosterone stimulates Na^+ reabsorption Aldosterone stimulates K^+ secretion ADH stimulates water reabsorption
Late Distal Tubule and Collecting Ducts (α-intercalated cells)	Reabsorption of K^+ Secretion of H^+	H^+-K^+ ATPase H^+ ATPase	— Aldosterone simulates H^+ secretion

ADH, Antidiuretic hormone; *PTH*, parathyroid hormone; *ENaC*, epithelial Na^+ channels; *AQP2*, aquaporin 2.

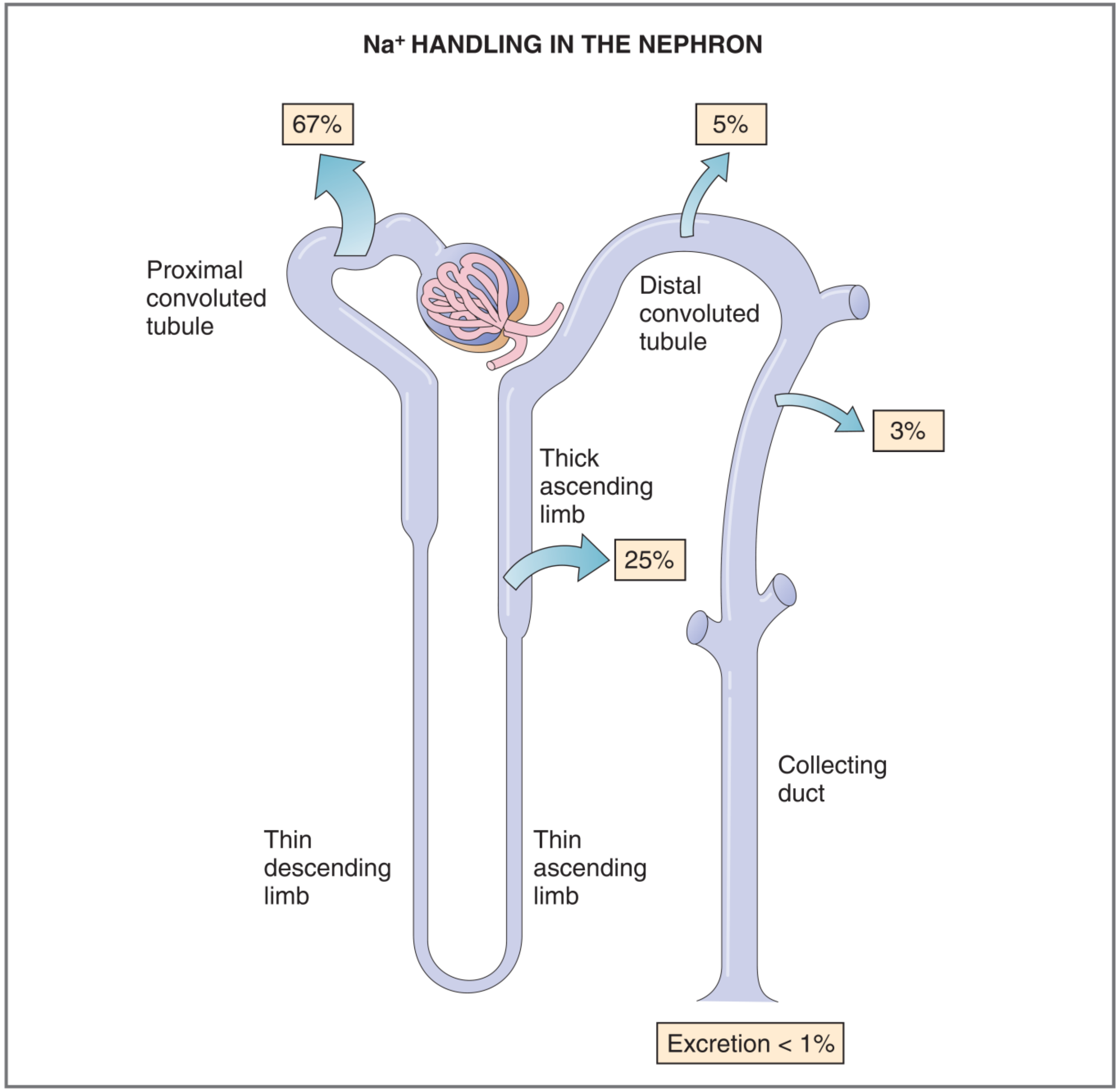


Fig. 6.19 Na^+ handling in the nephron. *Arrows* show locations of Na^+ reabsorption; numbers are percentages of the filtered load reabsorbed or excreted.

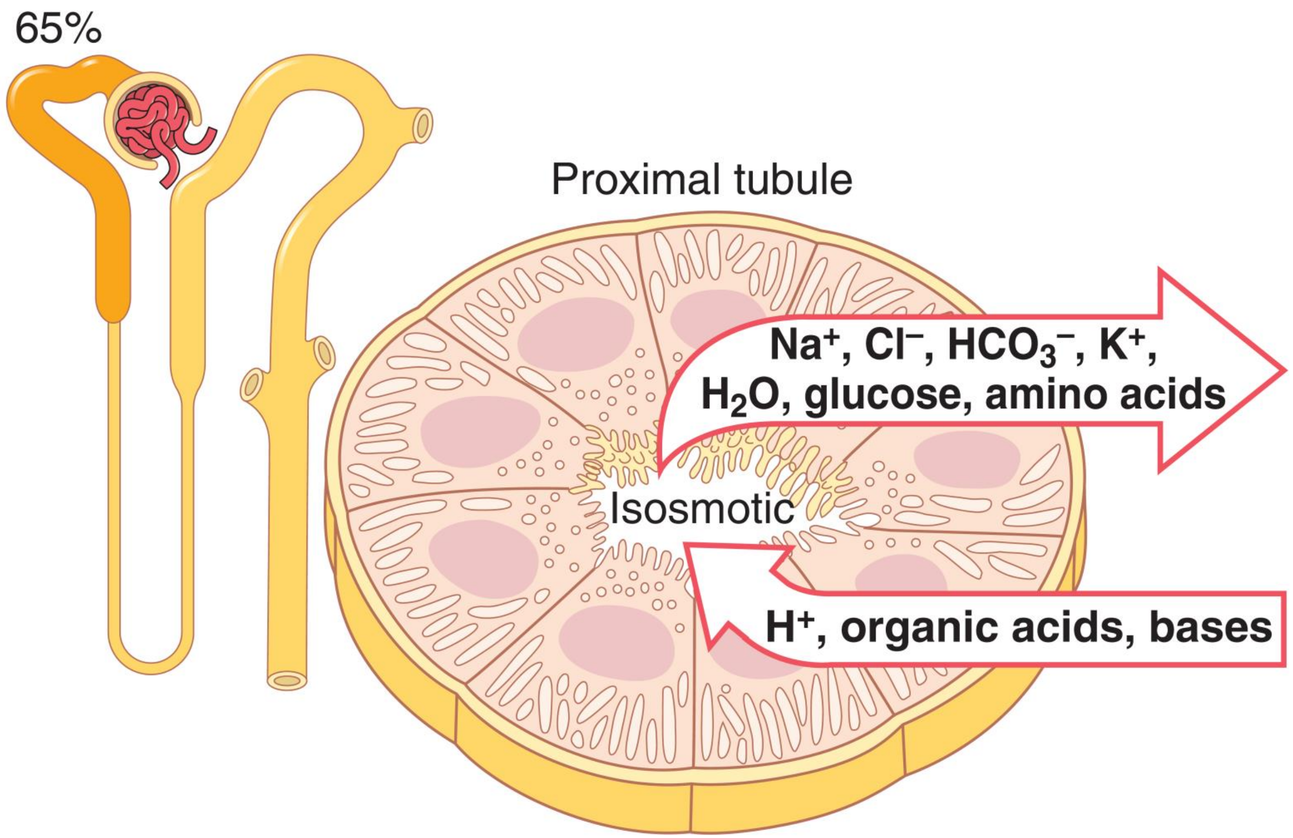


Figure 28-6. Cellular ultrastructure and primary transport characteristics of the proximal tubule. The proximal tubules reabsorb about 65 percent of the filtered sodium, chloride, bicarbonate, and potassium and essentially all the filtered glucose and amino acids. The proximal tubules also secrete organic acids, bases, and hydrogen ions into the tubular lumen.

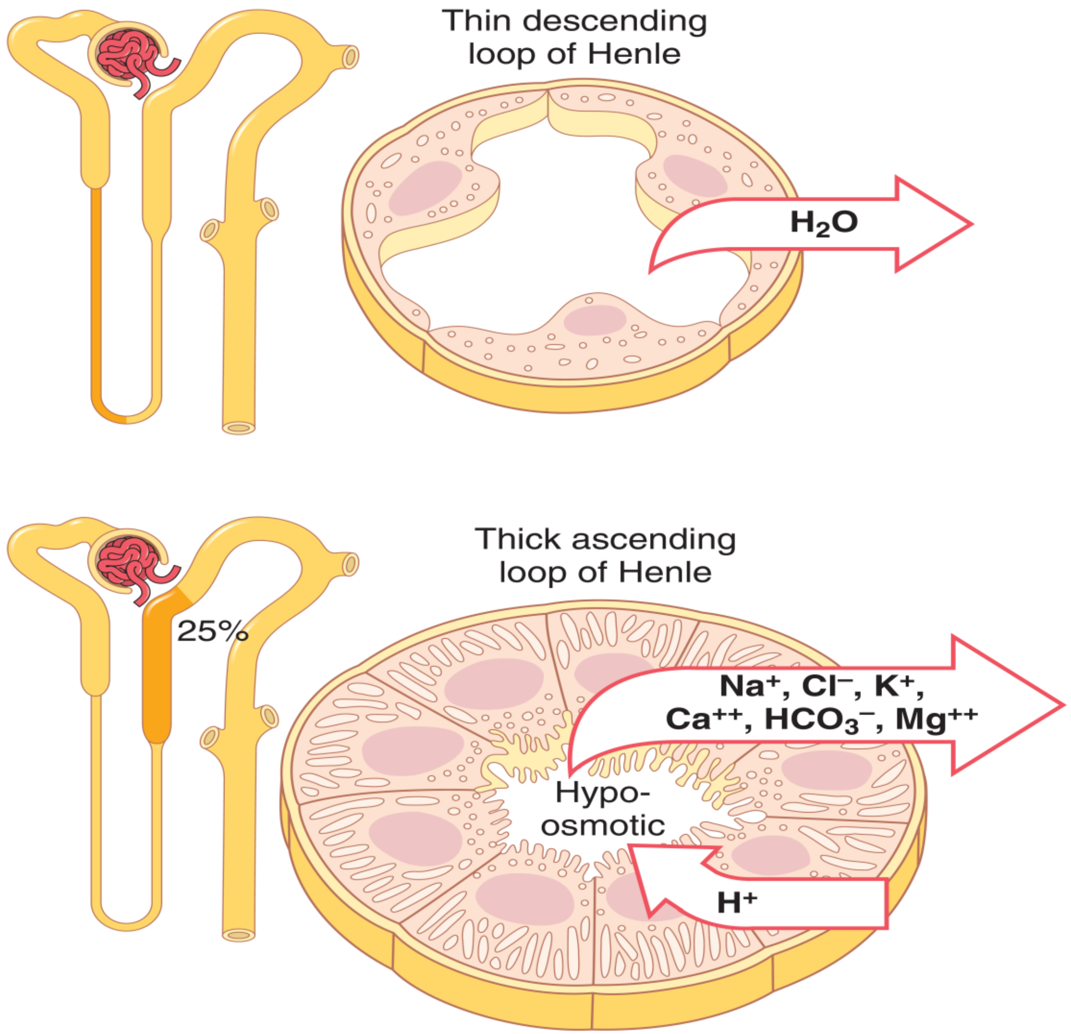


Figure 28-8. Cellular ultrastructure and transport characteristics of the thin descending loop of Henle (*top*) and the thick ascending segment of the loop of Henle (*bottom*). The descending part of the thin segment of the loop of Henle is highly permeable to water and moderately permeable to most solutes but has few mitochondria and little or no active reabsorption. The thick ascending limb of the loop of Henle reabsorbs about 25 percent of the filtered loads of sodium, chloride, and potassium, as well as large amounts of calcium, bicarbonate, and magnesium. This segment also secretes hydrogen ions into the tubular lumen.

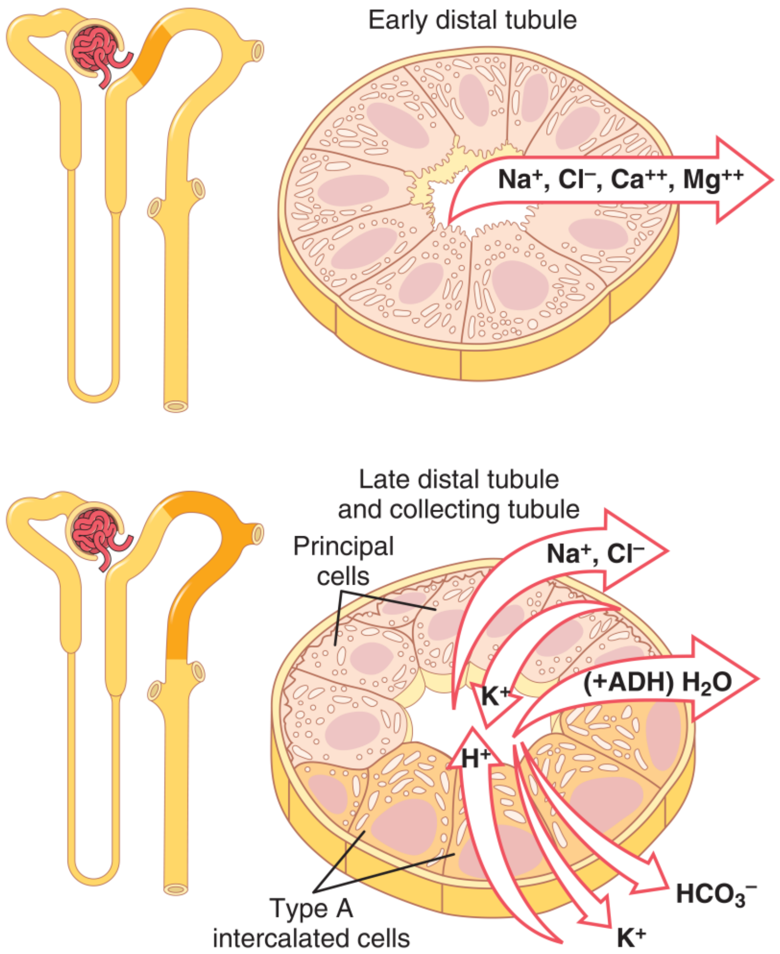


Figure 28-11. Cellular ultrastructure and transport characteristics of the early distal tubule and the late distal tubule and collecting tubule. The early distal tubule has many of the same characteristics as the thick ascending loop of Henle and reabsorbs sodium, chloride, calcium, and magnesium but is virtually impermeable to water and urea. The late distal tubules and cortical collecting tubules are composed of two distinct cell types, the *principal cells* and the *intercalated cells*. The principal cells reabsorb sodium from the lumen and secrete potassium ions into the lumen. Type A intercalated cells reabsorb potassium and bicarbonate ions from the lumen and secrete hydrogen ions into the lumen. The reabsorption of water from this tubular segment is controlled by the concentration of *antidiuretic hormone*.

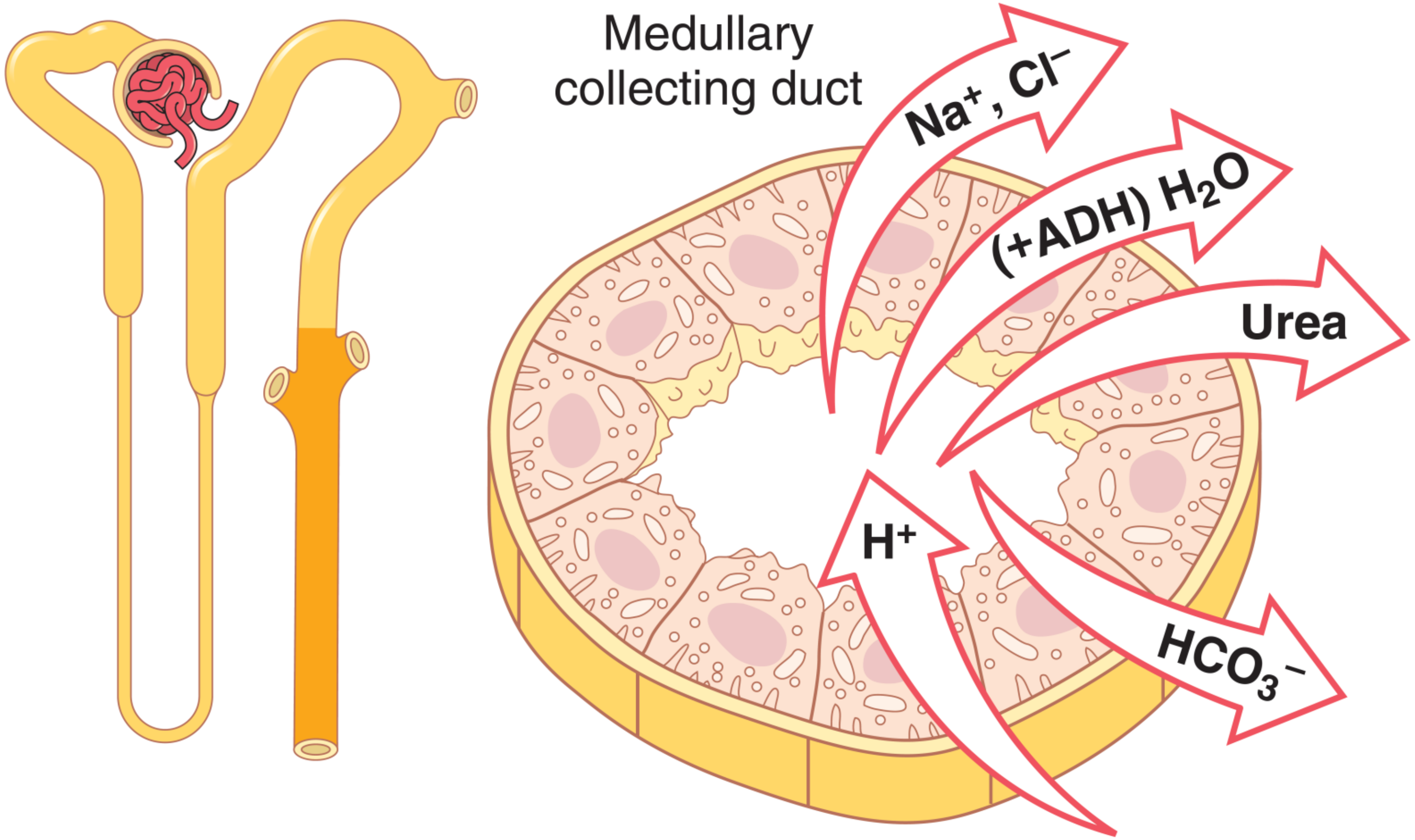


Figure 28-14. Cellular ultrastructure and transport characteristics of the medullary collecting duct. The medullary collecting ducts actively reabsorb sodium and secrete hydrogen ions and are permeable to urea, which is reabsorbed in these tubular segments. The reabsorption of water in medullary collecting ducts is controlled by the concentration of antidiuretic hormone.

Reabsorption and secretion along different tubular segments

1-Proximal convoluted tubules (PCT):

<u>I-Reabsorption of:</u>

A- 67 % of filtered sodium, water.

K and Calcium

Most of HCO_3^-

And slightly less load of filtered chloride.

B-All filtered glucose and amino – acids in early PCT.

C-In first half of PCT ,Na+ is reabsorped by CO transport with glucose and amino acids. In second half Na+ is reabsorbed with CL ion because its concentration increases due to water Reabsorption. The tubular fluid remains iso –osmolar along the PCT.

II-Secretion of:

a-Organic acids and bases which result from metabolism

e.g bile salts and oxalates. b-Secretes catecholamines and some drugs e.g pencillin.

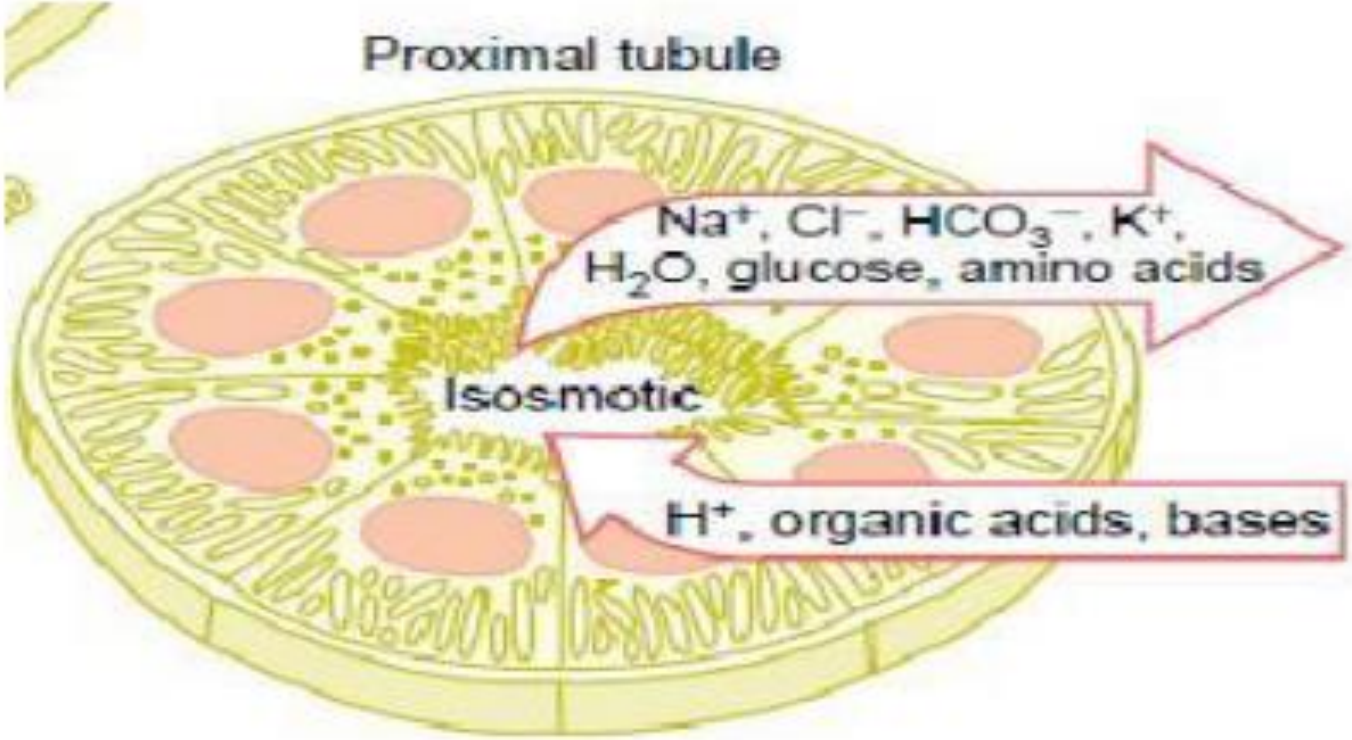


Figure (18): Transport characteristics of the proximal tubule.

2-The loop of Henle:

a-Thin descending segment.

- Formed of simple epithelial lining.
- Allow simple diffusion of H2O and solutes.
- Highly permeable to H2O but moderetaly permeable to solutes.
- 10 % of filtered water is reabsorbed in this part so osmolarity is too much increased by the end of this segment.
- The descending limb of loops of Henle receive isotonic fluid from the proximal convoluted tubules.
- Their walls are highly permeable to H2O and less permeable to NaCl so water diffuses freely from tubular lumen outwards by the high osmolarity of medullary interstatium.
- **Net result:**

Tubular fluid become hypertonic and this hypertonicity increases gradually as it moves downward. Maximal hypertonicity occurs at its bend reaching in humans to about 1200-1400 milliosmols.

b-Thin ascending segment.

- Less absorptive capacity for solutes.
- Na^+ is absorbed passively after CL^- Reabsorption.
- It is impermeable to water.

c-Thick ascending segment.

- It is thick epithelium with signs of activity.
- Reabsorption of:
  27 % of filtered Na^+
  20 % of filtered K^+
  27 % of filtered Ca^{+2}
- The luminal cell membrane contains Na^+ - K^+ - 2 CL transporter.
- It is impereabile to water so osmolarity decreases due to Reabsorption of Na^+ and K^+ and Ca^{+2} to become hypotonic (having osmolarity of 100 – 200 milliosmoles) on reaching the distal convoluted tubules

3-The distal convoluted tubules:

It consists of

a-The early diluting segment.

Has the same characters as thick ascending limb of loop of Henle

b-Late distal tubule and cortical collecting tubule.

They have the same characters and contain two types of cells.

1-The principal cells.

Responsible for K+ secretion

2-The intercalated cells.

Secretes H+ and reabsorbs K+ in case of K+ depletion.

Characters of both segments

1-Reabsorbes sodium and secretes K+ under influence of aldosterone hormone.

2-Secretes H+ via primary active transport by H+ pump ,that can transport H+ against gradients up to 1000 folds.

3-Water Reabsorption under the influence of ADH.

4-Impermeable to urea.

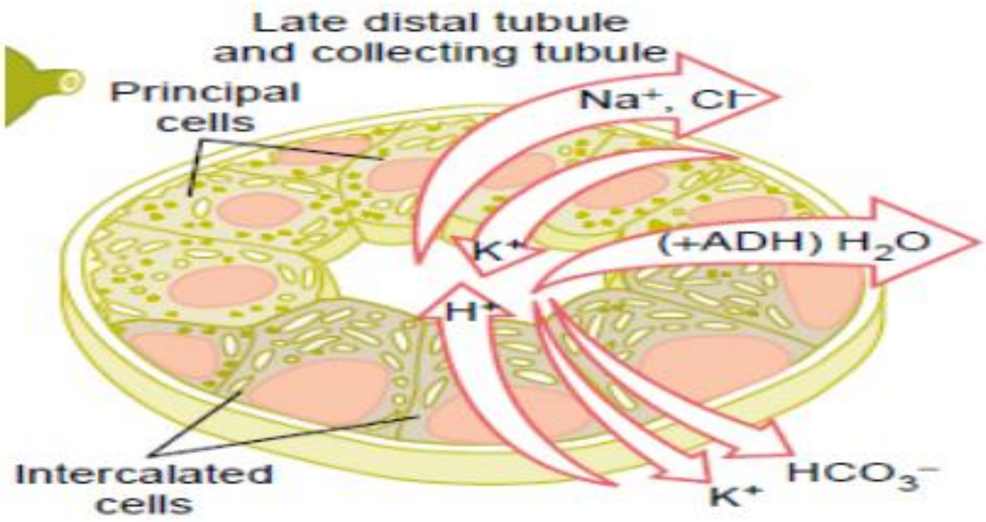


Figure (20): Transport characteristics of the late distal tubule and collecting tubule.

4-Medullary collecting duct.

It has the same characters as distal nephron except it is permeable to urea and ADH increases this permeability.

<u>The transport via distal tubules differ from proximal tubule in the following.</u>

A-Proximal tubules has a large capacity so reabsorb large quantities of salt and water,

while distal tubules has a smaller capacity, it can reabsorb 9% of filtered sodium and 19 % of filtered water.

B-Na^+ and H_2O Reabsorption are closely coupled in proximal tubules because H_2O permeability is high ,while in the distal tubules as H_2O permeability is variable and low so Na^+ and H_2O Reabsorption may be uncoupled.

The ability of the kidney to dilute or concentrate urine

The mechanism:

In order to excrete concentrated urine ,the kidney has to increase water Reabsorption by the collecting tubules.

This process needs 2 factors.

1-The action of ADH to open water intracellular channels.

2-High and stable osmotic gradient in the area surrounding the collecting tubules to maintain high rate of water movement according to osmotic gradient through opened channels.

This can be done only by a special mechanism in the renal medulla called Counter current mechanism.

Steps needed for creation of osmotic gradient.

1-Increaded solute load in the renal medulla by:

a-Active Na+ Reabsorption in the thick ascending limb of loop of Henle followed by passive movement of other solutes e.g CL- and HCO3 .

b-Active Na+ Reabsorption by the collecting tubules.

c-Passive urea Reabsorption by the collecting tubules.(solvent drag*****)

2-Creation of Osmotic gradient by Counter current system.

Definition of counter current system: It is a system characterized by the presence of:

- U shaped tube with its 2 limbs close to each other.
- Continuous counter current stream.
- A source of energy.

All these characters are found in the loop of Henle as:

- It consists of U shaped tube with 2 limbs are close to each other.
- The tubular fluid flows in the 2 limbs in a counter current stream.
- The source of energy is the active Na+ - K + pump of the thick ascending limb of loop of Henle.
- The loop of Henle acts as a counter current multiplier which multiply the tonicity of the medullary interstitium about 5 times (from 300m.osm/L at the outer medulla to 1400m.osm/L at the renal papilla).

To understand how the counter current can create an osmotic gradient we have to imagine that this process can occur in successive steps beginning from position Zero as follow:

- **Position Zero:**

We imaging that fluid entering and leaving loop of Henle is Iso-Osmotic with fluid flowing out of proximal tubule = 300 mOsm / L.

Steps:

<u>Ascending limb:</u>

is impermeable to water but permeable to solutes, thus its main function is removal of solutes.

Na Cl is transferred to medullary interstitium (M.I) passively in thin part and actively in the thick part.

As the ascending limb is impermeable to water, so tubular fluid inside he ascending limb is hypotonic to M.I (it's 200 m osm/ L less than M.I at any transverse level) so fluid leaving the ascending limb is hypotonic (100 m osm/L).

This results in:

1- Hypertonic medullary interstitum

in a longitudinal direction from 300 (outer medulla) – 1400 m osm/ L (inner medulla).

The tonicity is multiplied about 5 times.

2- Hypotonic fluid leaves medulla:

at any transverse level, the osmolarity is 200 m osm/L less than M.I.

Descending limb:

is impermeable to Na Cl but permeable to water thus its main function is water removal.

The hypertonic M.I produced by the ascending limb will absorb water from descending limb till the fluid in the descending limb becomes isotonic with M.I at any transverse level.

The end of descending limb at renal papilla is 1400 m osm/L.

Preservation of osmotic gradient

(the role of vasa recta as a counter current exchanger):

The preservation of osmotic gradient is very important because any osmotic gradient in the medullary tissue could be washed out by the medullary blood flow.

However the blood supply to the medulla (vasa recta) has some characters that help to maintain the solute load and prevent the washout of the osmotic gradient in the medullary tissue.

Vasa recta is a loop of peritubular capillaries, which run close to and parallel to the loop of Henle.

<u>It is characterized by.</u>

a-U shaped loop of capillaries.

b-Counter current blood flow.

c-High permeability to water and electrolytes.

d- Low blood flow (0.25 ml / gm tissue / min)

The role of vasa recta in the counter current mechanism is to exchange the Nacl and urea between its 2 limbs so as to keep them in the medullary interstitial fluid as follow:

- 1-In descending limb of vasa recta water flow out and Nacl flows inside due to increased osmolarity of medullary ISF as blood moves deep in the medulla.
- 2-In ascending limb ,and as osmolarity decreases gradually toward the cortex H_2O moves again to inside the ascending limb ,while Nacl and urea moves out in the medullary interstatium.

-The net result of the above 2 points osmolarity is kept constant in the medullary interstatium.

-The function of vasa recta as a counter current exchanger is to maintain renal medullary hyperosmolority through:

- 1-Trapping of solutes (Nacl and urea) in renal medulla.
- 2-removing excess water from medullary interstitium **By:**

Walls of vasa recta are highly permeable so allowing passive diffusion of water and solutes

In their descending limbs: The solutes diffuse (Nacl and urea) from medullary interstatium into the vessel because its concentration is higher than blood so diffuses according to concentration gradient into vasa recta.

At the same time water diffuses out into medullary interstitiatium because Osmolority of Medullary interstatium exceeds that of blood .

Net result:

Blood become gradually concentrated as it moves downward until an osmotic pressure of 1200 mOsm at the tip.

In ascending limb:

Solutes diffuses from blood into the medullary interstatium as osmolarity in the interstatium gradually decrease.

H_2O moves from interstatium to the blood again.

NaCl and urea moves out of the ascending limb to the Medullary interstatium.

Net result:

The blood flows out of the medulla carries no solutes but only a small amount of excess water, which is absorbed by the renal tubules in the medulla, thus Osmolority is kept constant in medullary interstatium.

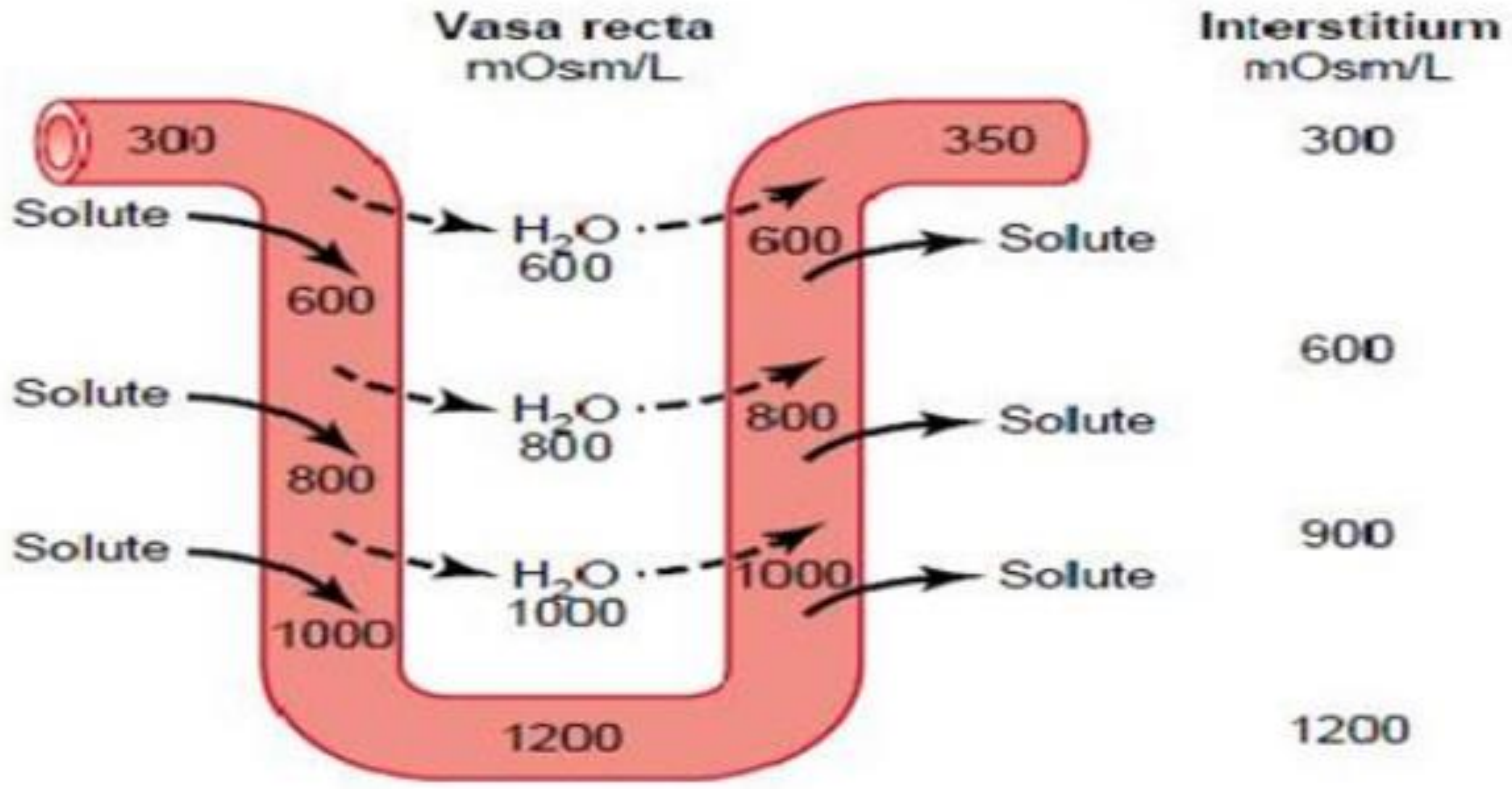


Figure (22): vasa recta as a counter current exchanger.

Role of urea in urine concentration

Urea plays an important role in the concentrating ability of the kidney.

It shares in 45-50% of osmolarity of M.I.

This can be explained by the following steps:

- **Step (1)**

Concentration of urea in the tubular fluid increases gradually as most renal tubules are impermeable to urea (ascending limb of L.H, DCT, cortical CD and outer medullaryCD),while water and other solutes are absorbed in large amounts along renal tubules.

❖Step (2)

Concentration of urea reach its maximum level in the late collecting duct (inner medullary collecting duct)which is highly permeable to urea in the presence of (ADH), so urea is passively reabsorbed according to concentration gradient.

❖Step (3)

Absorption of urea in this segment adds much to the osmolarity of lower medulla, which in turn increases the rate of H_2O Reabsorption by descending limb of loop of Henle so increasing NacL concentration in the tubular fluid that reach ascending limb. Urea diffuses from M.I. to the thin ascending limb and to the descending limb of L.H till reaches inner medullary collecting duct to be reabsorbed again by ADH which is known as **urea trapping** or **urea cycling.**

❖ Step (4)

When NaCL rich fluid reach the ascending limb which is permeable to NaCL, passive NaCL Reabsorption occurs increasing the solute load in the renal medulla.

Role of ADH in formation of concentrated urine

ADH plays a key role in urine concentration by:

1- Increase CD permeability to water along osmotic gradient of M.I.

2- Increase urea reabsorbtion passively from inner medullary CD.

3- V.C of the efferent arteriole which lead to:

a- increase osmolarity of M.I. by decrease washing out of solutes from it.

b- Increase the filtered load of Na+ leading to increase Na+ reaching to ascending limb of L.H. and more removal of Na+ from ascending limb to M.I adding to the hypertyonicity of M.I.

General functions of the kidney:-

❖**Homeostatic function:-**

It is the most important function. The kidney plays the major role in homeostasis. The kidney regulates volume, ionic composition and H+ concentration of the plasma.

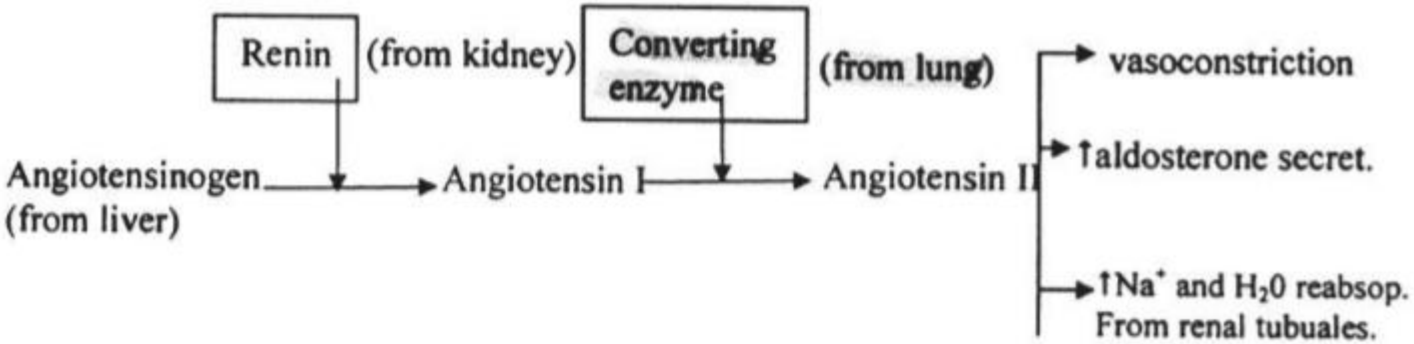
The kidney performs this important function through urine formation.

❖**Secretory function (endocrinal function):**

it produces:-

1. Renin

- It is secreted from the JG cells.
- It has an important role in the regulation of arterial blood pressure.



Factors that increase renin secretion:-

1. ↓ NaCl concentration in the tubular fluid >> stimulation of macula densa cells >> ↑ JG to secrete renin.
2. ↓ Blood pressure in the afferent arteriole >> ↑ JG cells to secrete renin (JG cells act as intra renal baroreceptors).
3. Sympathetic stimulation >> direct stimulation of JG cells

2_Erythropoietin:

It regulates RBCs production from bone marrow.

It is secreted in response to hypoxia.

Renal Handling of Sodium

Functions of sodium in the body are:

1. Keeping volumes of both extracellular fluid & blood constant → maintains normal ABP.
2. Formation of resting membrane potential, action potential & conduction of nerve impulse.
3. Skeletal & smooth muscle contraction by releasing Ca++ from sarcoplasmic reticulum.
4. Controlling release of many vital substances in body as renin & Aldosterone.
5. Bone formation.

Na+ reabsorption

- Na+ reabsorption is associated with transport of many other substances as H_2O, H^+, glucose, amino acids, Cl^-, HCO_3^- , and K^+.

Renal handling of Na+:

1) Na+ reabsorption in PCT (70%).

- About 70% of Na+ load is reabsorbed in PCT.

❖At the luminal border:

Na+ is transported from lumen to inside cells by facilitated diffusion under effect of:

1. Concentration gradient.

2. Electrical gradient (in lumen – 3 mv & inside cell – 70 mv).

- This is helped by large surface area of brush border of PCT & by presence of carriers.

❖At baso-lateral border:

Na+ crosses to interstitium fluid by active pump against its electrochemical gradient by Na+- K+ ATPase activity (for each 3 Na+ pumped out only 2K+ ions are carried in).

- After entering the cell K+ ions diffuses back again to the interstitium helped by concentration gradient & high permeability of cell membrane → maintain the intracellular negativity in relation to luminal fluid → ↑ Na+ entry to the cell (help the facilitated diffusion).

This reabsorption result in:

1- Reabsorption of 70% of water

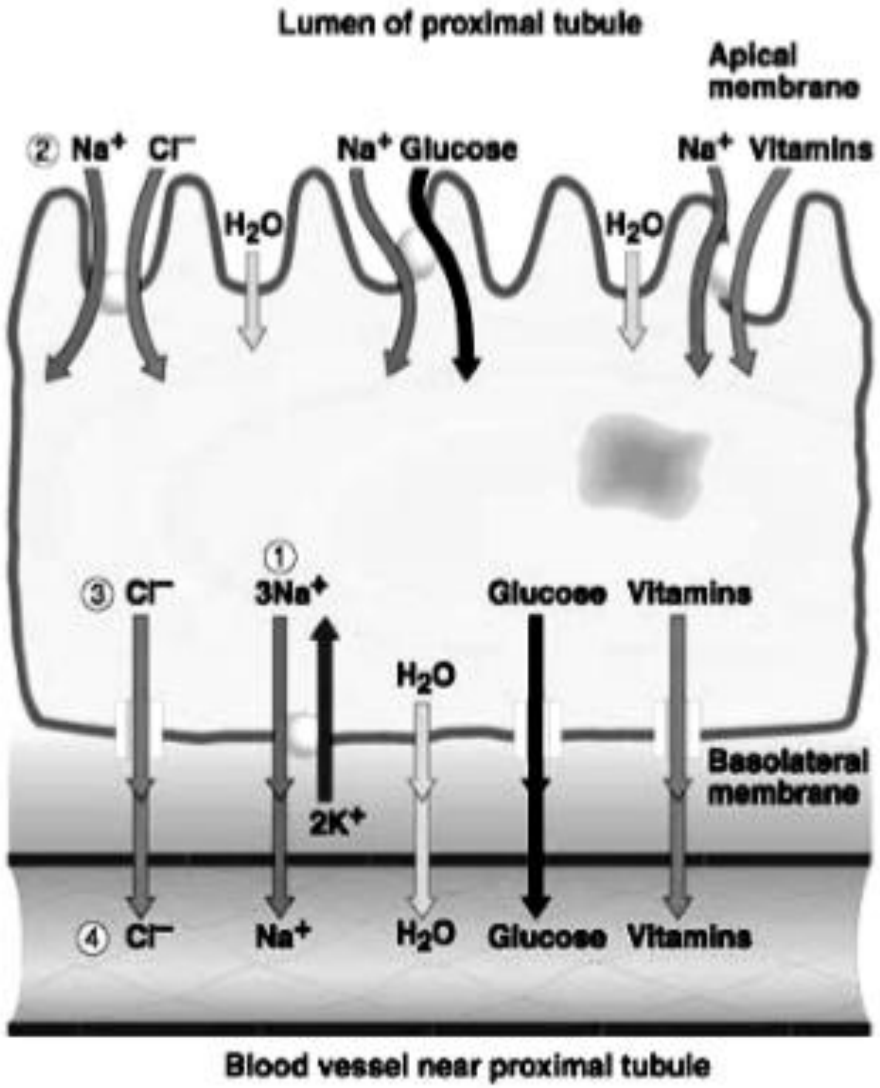
"obligatory water reabsorption" because of the high osmolality created by Na^+ reabsorption.

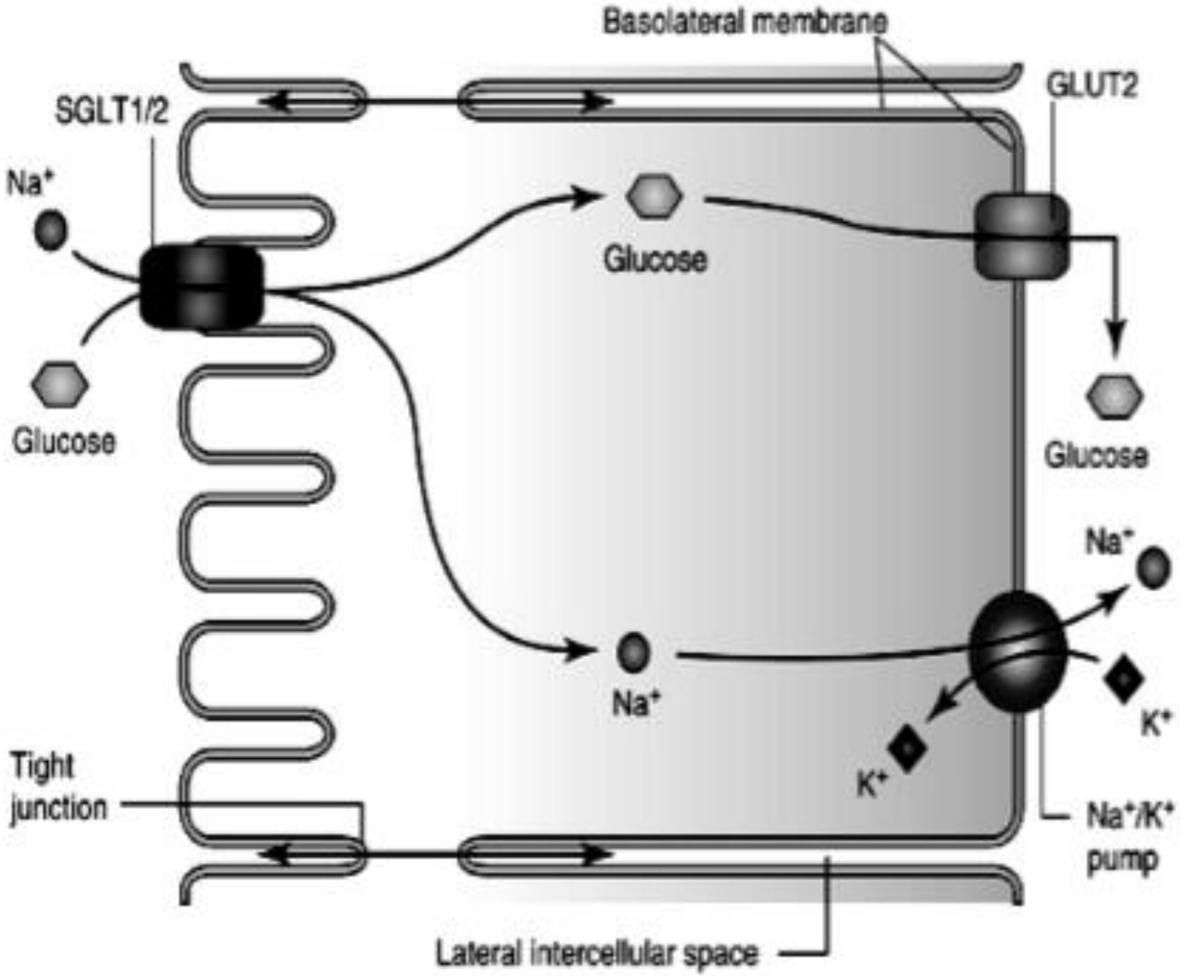
2- Active co-transport transport

of glucose, amino acids, HCO_3^- & other organic acids (these substance are carried by same carrier of Na^+).

3- Passive diffusion

of Cl^- (in 2nd half of PCT due to ↑Cl^- concentration).





Na^+ reabsorption in PCT

2) Na+ reabsorption in the loop of Henle (20%)

- **Thin descending part:**

The only part in the nephron in which Na+ is not reabsorbed (also this part is freely permeable to H_2O → hypertonic tubular fluid).

- **Thin ascending part:**

passive reabsorption of Na+.

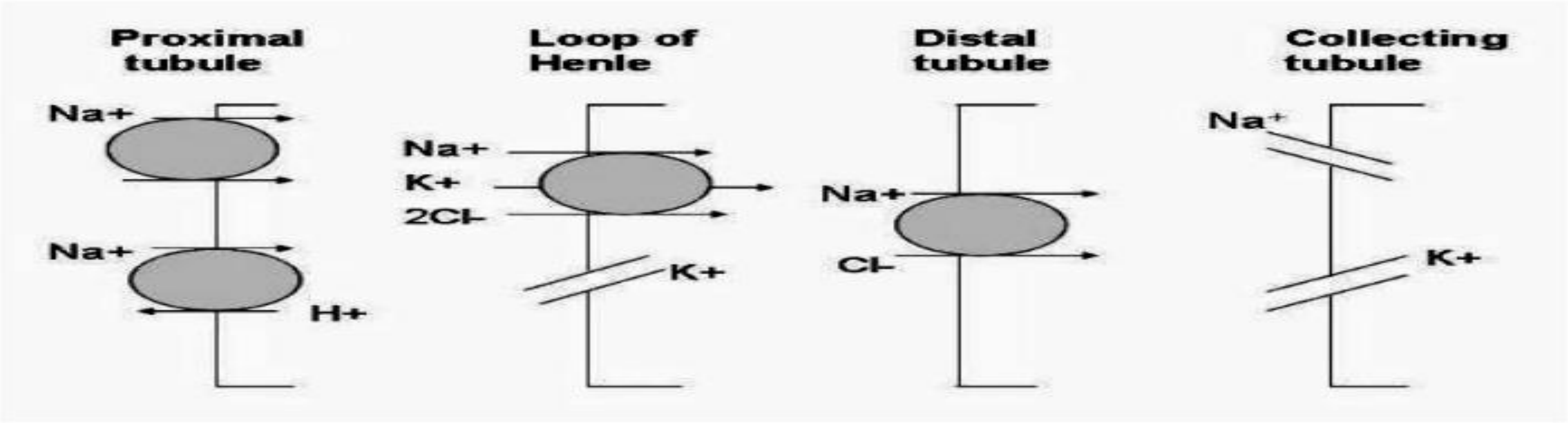
- **Thick ascending part:**

active reabsorbtion of 20% of Na+ by co-transport protein carrier (1Na+, 2 Cl- & 1K+) mechanism

(also this part is poorly permeable to water→ fluid leaving this thick part is hypotonic).

3) Na+ reabsorption in the distal convoluting & collecting tubules (10%)

- 10% of Na+ is actively reabsorbed, in exchange with H+ or K+ by the help of Aldosterone hormone.
- NB: Na+ reabsorption is active along the nephron except in thin ascending part of loop of Henle.



Na^+ reabsorption in renal tubules

Factors controlling Na+ reabsorption:

The amount of Na+ excreted per day may be as low as 1mEq/day to as high as 400mEq/day.

The factors controlling are:

1- Amount of NaCL intake per day: increase intake → increase Na+ reabsorption & excretion (& vice versa).

2- Hormonal factors:

- Aldosterone: Acts mainly on principal cells of DCT & collecting ducts → increase Na+ reabsorption in exchange with K+ & H+.
- Glucocorticoids : -Weak Aldosterone like action on sodium reabsorption → Na+ & water retention & decrease Na+ excretion in urine.
- Sex hormones (estrogens): Salt retention effect, so contraceptive pills that contain oestrogen → oedema in prolonged use.
- PGE2: Increase Na+ excretion in urine (naturesis)

• This by inhibiting Na+ K+, ATPase & by increase intracellular Ca++, which inhibit Na+ transport across the channels.

• Endothelins causes naturesis by increasing PGE2.

- Atrial naturetic peptide (ANP): Decrease Na+ reabsorption & increase excretion

3- Glomerulo-tubular balance:

- Increase GFR ⟶ increase tubular load of any substance ⟶ increase its reabsorption to prevent overloading of the distal tubules with these solutes.

4- Effect of ABP:

- Increase ABP above 180mmHg ⟶ increase Na+ excretion & urine output "pressure diuresis".

5- Diuretics:

✓ Osmotic diuretics as mannitol⟶ Decrease Na+ reabsorption from PCT

✓ Loop diuretics (Lasix) ⟶ Decrease Na+ reabsorption from Henle's loop

✓Aldactone ⟶ Decrease Aldosterone ⟶ Decrease Na+ reabsorption from DCT.

Events that occur inside PCT

1- 70% of Na+ load is reabsorbed.

2- 70% of water load is reabsorbed = obligatory water reabsorption .

3- Co-transport of K+, glucose, amino acids & other organic acids at the 1st half of PCT.

4- Absorption of CL- & secretion of H+ ions in the 2nd half of PCT.

5- Reabsorption & synthesis of $NaHCO_3$

6- Remaining tubular fluid is isotonic (300mosmol) but slightly acidic ($pH<7.35$).

Counter current system

⇐ اتجاه مرور الدم يكون عكس اتجاه مرور السائل

⇐ السائل في ال Descinding Limb بيكون نازل

بنفس الوقت الدم في ال vasa recta بيكون طالع

A) PCT

1) Sodium passes: via

• From Lumen → tubular Cell ⇒ passive transport

2) A.A + glucoses via

From Lumen → tubular cell ⇒ Secondary active transport

→ without Sodium in Filtrate, No glucose no A.A

67% Na, Ca, Chlorid + bicarbonate + glucose + A.A

* زي ما امتص ملح امتص ماء

* the Fluid in PCT is isosmotic

▶ Subject : .... / /

Descending limb of loop of Henle

Fluid in Descending limb of loop of Henle is Hyperosmolar

~~Fluid in ascending limb is~~

- Counter current multiplayer

→ سائل نازل وسائل طالع في التواء هنلي

→ multiplayer : ← يعني بتضاعف ال osmolarity :

* increase gradually in descending limb
* Decrease gradually in ascending limb

DCT مقسومة لجزئين
الاول نفس وظيفة
ascending Limb

DCT مقسومة لنصين

الأول نفس وظيفة ascending Limb
يعني فيها :
K, Na, Ca, 2Cl
pump

الثاني :
بتطرد الملح من
السائل و بتخففه
ماء ↑ ملح ↓

السائل يخرج من Loop of Henle : isosmotic تقريبا

ADH : لما يطلع بخلي يؤدي إلى خروج Concentrated urine

↳ DCT + Medullary collecting duct بروح على

بعمل على فتح قناة ~~تمر الما~~ يمر الماء منها

Aquaporines . بنسمي هاي القنوات

Aqua → water

porines ↳ pores that the water cross ~~through~~ through them.

• All of the tubules are impermeable to uria except Medullary collecting duct

⇒ uria concentration in medullary collecting duct is high

يعدين فجأة بتفتح قناة وبتنتقل من :
collecting duct to interstitial fluid by simple diffusion
Medullary من منطقة ال
interstitial
Hanging بتكون filtrate اليوريا لما تخرج من

S T A R S N O T E B O O K

Special type of simple diffusion:

Solvent drag → اليوريا بتهرب وبتأخذ معها الماء

Medullary collecting duct is permeable to uria.
reabsorbtion of uria بتعمل

~~Hanging~~: uria يعمل حالة يطلع بكون بمشي
hanging in Medullary interstitial
thin ascending limb of loop of Henle لعند ما يوصل بعدين
tubular Filtrate في وتنزلها active secretion بتصيرلها

الفرق بين

Difference between water reabsorbtion in: الفرق بين

1) PCT:

الماء يكون مرافق للملح

- H_2O reabsorbtion is coubled with Na reabsorbtion (obligatory water reabsorbtion with Na)

2) DCT: under effect of ADH

→ Facultative: حسب الحاجة

→ if ADH is secreted: concentrated urine + H_2O reabsorb

↳ no secretion: diluted urine

Scanned with CamScanner

⇐ المريض الذي & يخرج ADH بمسيرله :

Diabetes insipidus السكري الكاذب

• لو ما في ADH ← ما يتم انتاج Aquaporin 1
← يؤدي إلى انتاج : very diluting urine

~~العلاقة~~

• العلاقة بين السائل في Loop of Henle والدم

counter current : في vasa recta

※ ال peritubular capillary بتعمل نفس عمل Loop of Henle

When Descending limb of loop of Henle causes reabsorbtion of water

ال peri tubular cappillary بتعمل نفس الشي بتعمل على اخراج الماء إلى Medullary interstitial

وبتدخل ملح

→ Counter Current exchanger

مشان أعمل concentrated urine بحتاج :

1) Counter current multiplier : (Loop of Henle فقط)

2) Counter current exchanger : (vasa recta)

3) uria cycle : all of segments of nephron is impermeable to uria exept Medullary CD

الـ uria بتمشي بالـ Hanging Medullary interstitial

بوصل بتكسير : actively secreted in Loop of Henle

4) ADH : leading to aquaporine 1 , which uria + H_2O ق enters through it