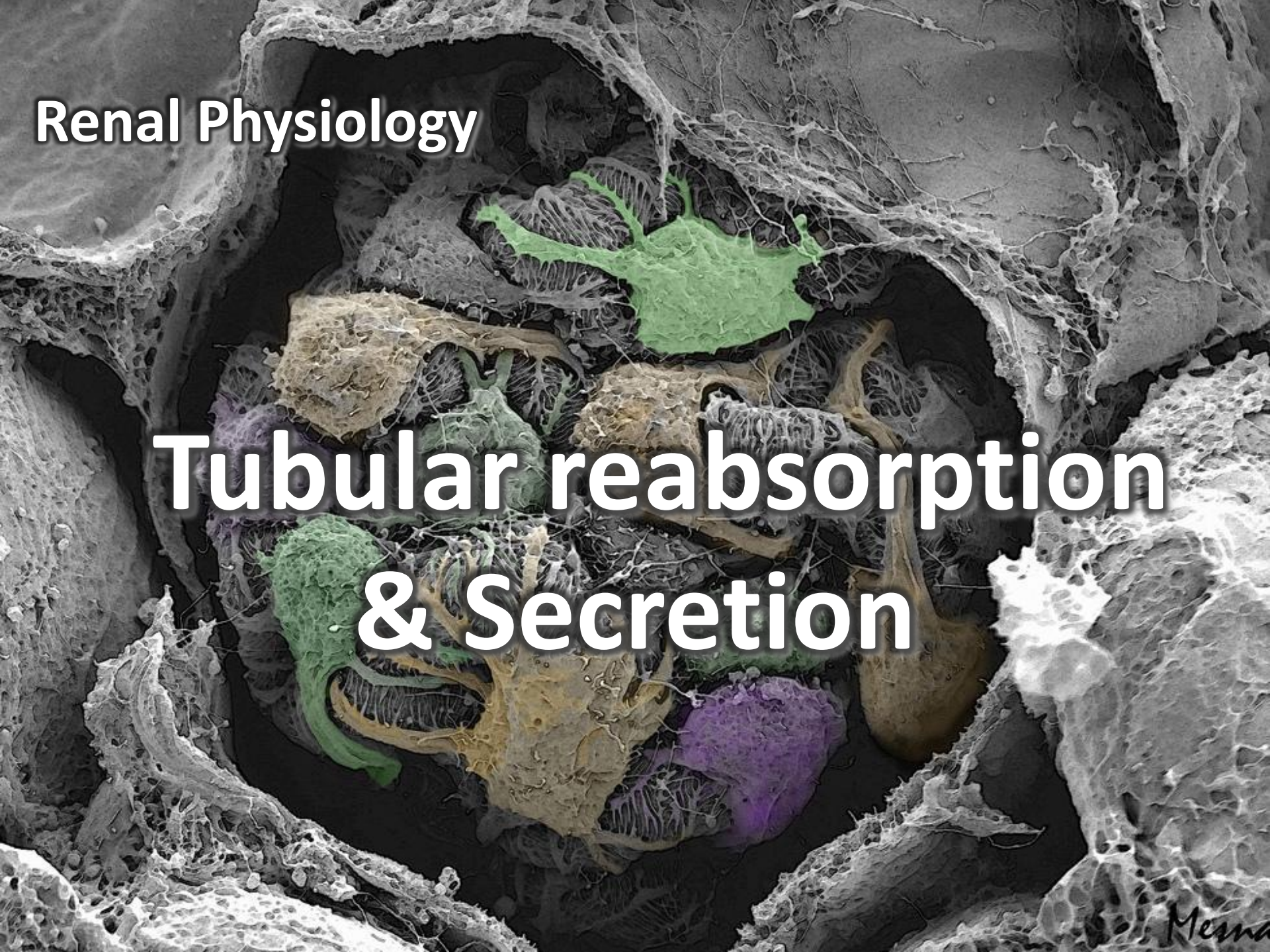
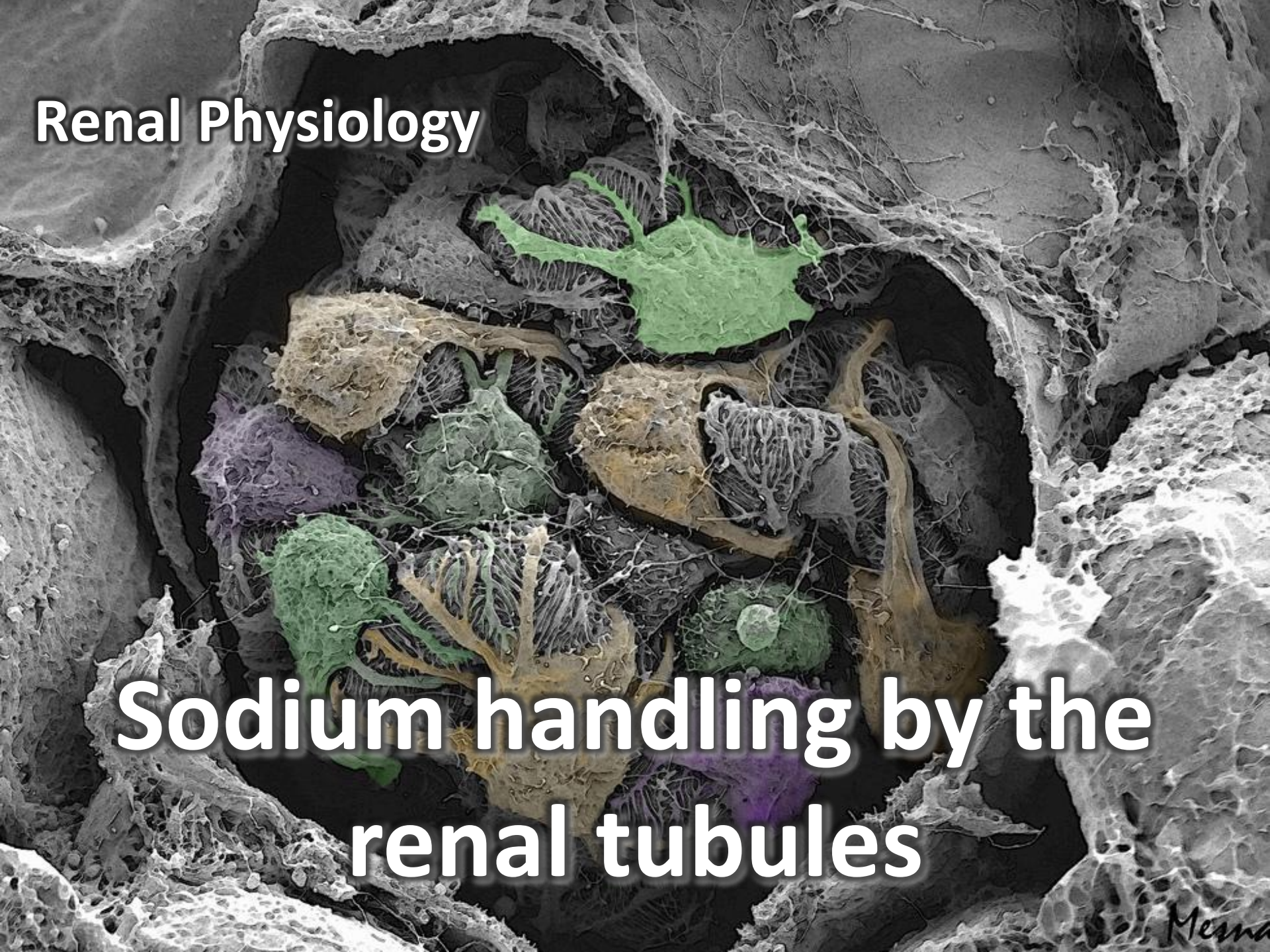

بسم الله الرحمن الرحيم

قَالُوا۟ سُبْحَٰنَكَ لَا عِلْمَ لَنَآ إِلَّا مَا عَلَّمْتَنَآ ۖ إِنَّكَ أَنتَ ٱلْعَلِيمُ ٱلْحَكِيمُ ﴿٣٢﴾


Renal Physiology
Tubular reabsorption
& Secretion


Renal Physiology
Sodium handling by the renal tubules

Mechanisms of Tubular Transport.

- **There are three basic mechanisms:**

1- Active transport.

- **Primary active.**
- **Secondary active:**

Co-transport.

Counter transport.

2- Passive transport.

3- Pinocytosis.

Tubular function

Reabsorption

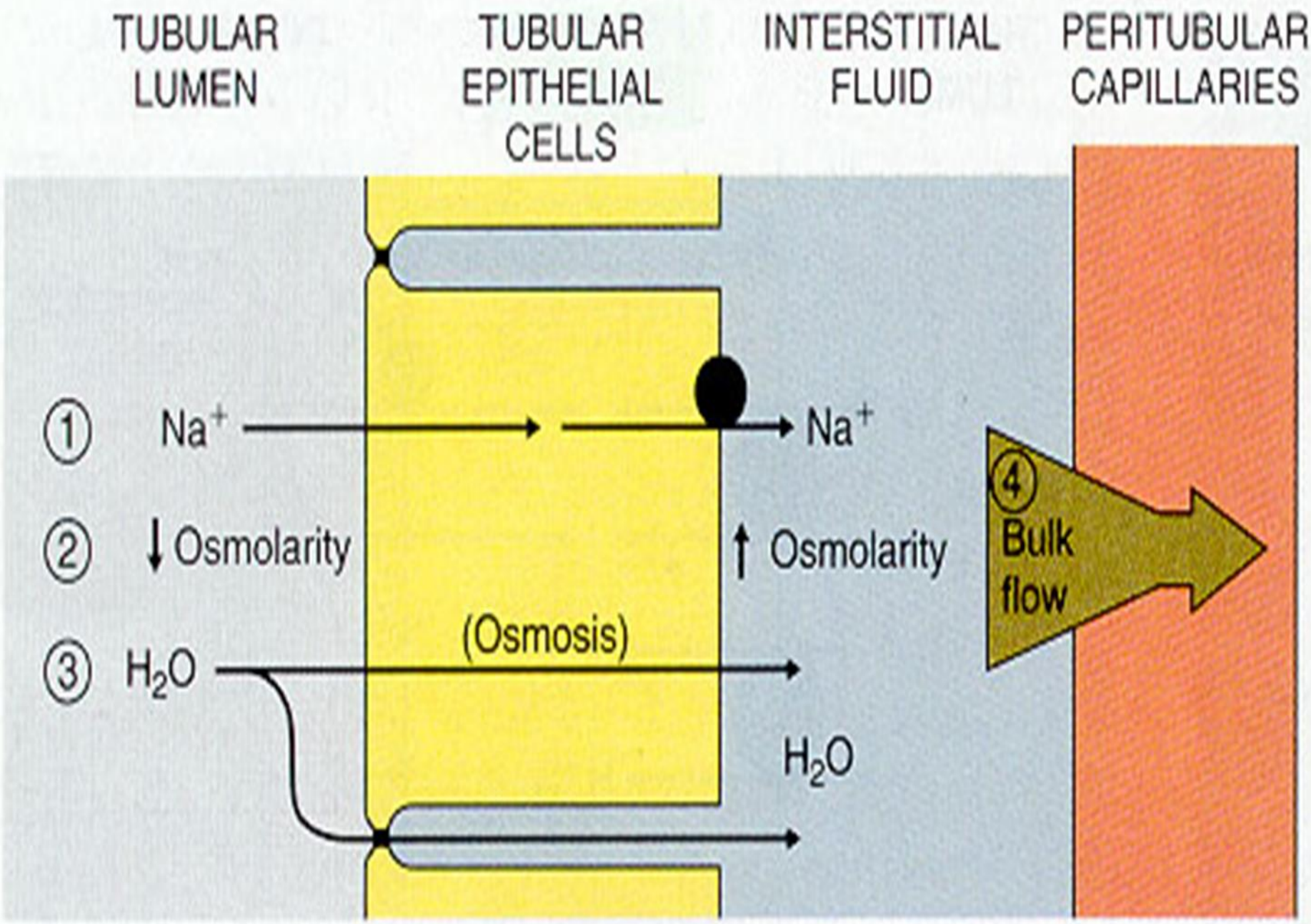
- Moving substances from lumen through renal cells into the blood

Secretion

- Moving substances from blood (peritubular capillary) to the lumen

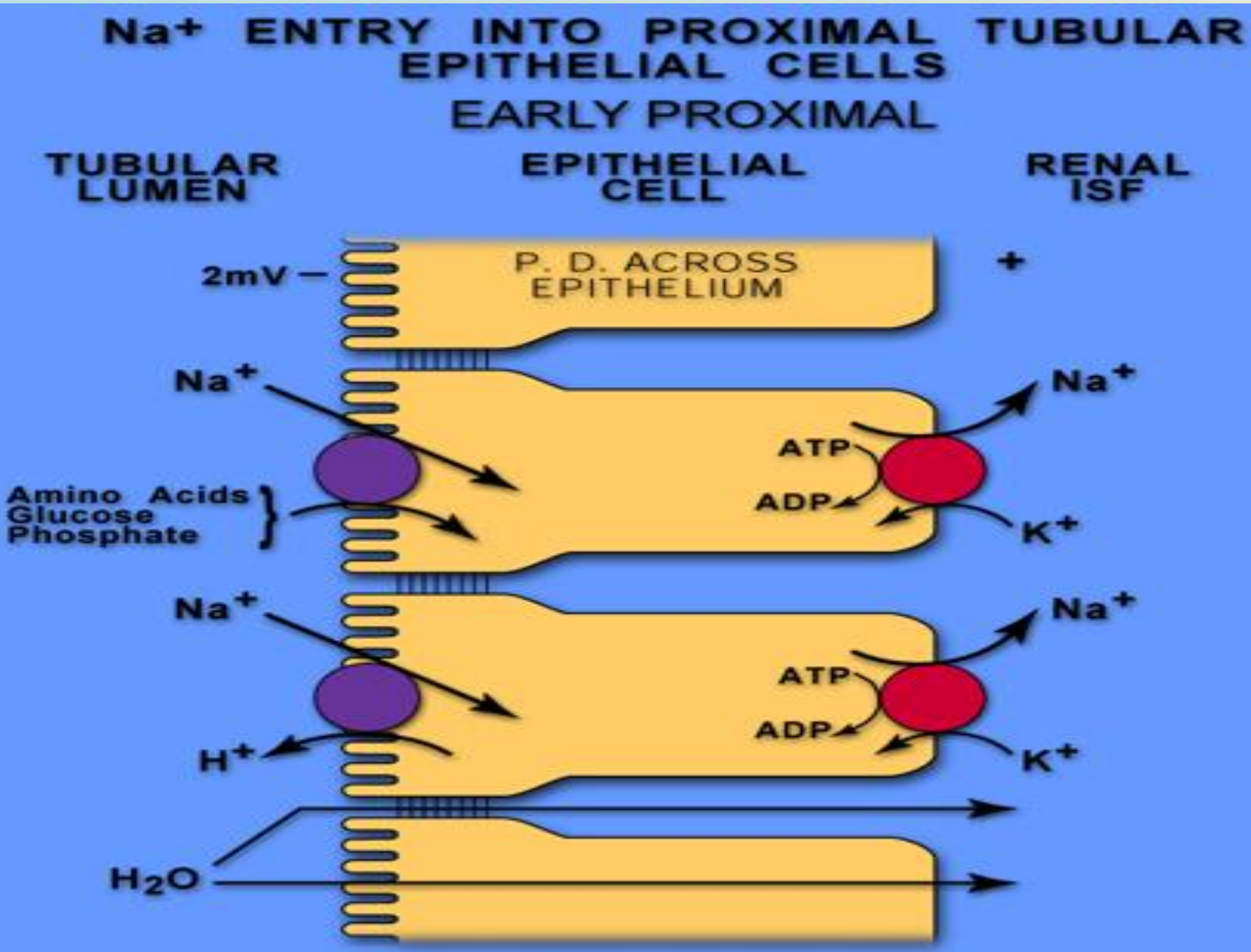
Type of Reabsorption

- Transcellular reabsorption
  (Through the Cells)
  - Primary active transport
  - Secondary active transport
  - Passive transport – Ion channels
- Para cellular reabsorption
  (Between the Cells)


TUBULAR LUMEN
TUBULAR EPITHELIAL CELLS
INTERSTITIAL FLUID
PERITUBULAR CAPILLARIES
① Na^+
Na^+
② ↓ Osmolarity
↑ Osmolarity
(Osmosis)
③ H_2O
H_2O
④ Bulk flow

Primary Active Transport.

- Primary active transport utilizes metabolic energy directly.
- Example: Na^+ reabsorption across PCT.
- At basolateral border:
- Na^+-K^+ ATPase creates negative potential of about -70 mV and low intra cellular Na^+ level.
- At the luminal border:
- Na^+ diffuses from the tubular lumen into the cells according to electrochemical gradient.


Na+ ENTRY INTO PROXIMAL TUBULAR EPITHELIAL CELLS
EARLY PROXIMAL
TUBULAR LUMEN
EPITHELIAL CELL
RENAL ISF
2mV –
P. D. ACROSS EPITHELIUM
+
Na+
Na+
ATP
ADP
K+
Amino Acids
Glucose
Phosphate
Na+
Na+
ATP
ADP
H+
K+
H2O

Secondary Active Transport.

- Does not require energy directly from ATP.
- It utilizes the energy resulting from the work of primary active transport system.
- Cotransport:
- The reabsorption of a substance is linked to the passive reabsorption of another.
- The 2 substances bind to a specific carrier.
- One substance is transported down its gradient and the other against its chemical gradient.

Example

Na^+- glucose co-transport.

At luminal border:

Glucose and Na^+ bind to common carrier SGLT-2.

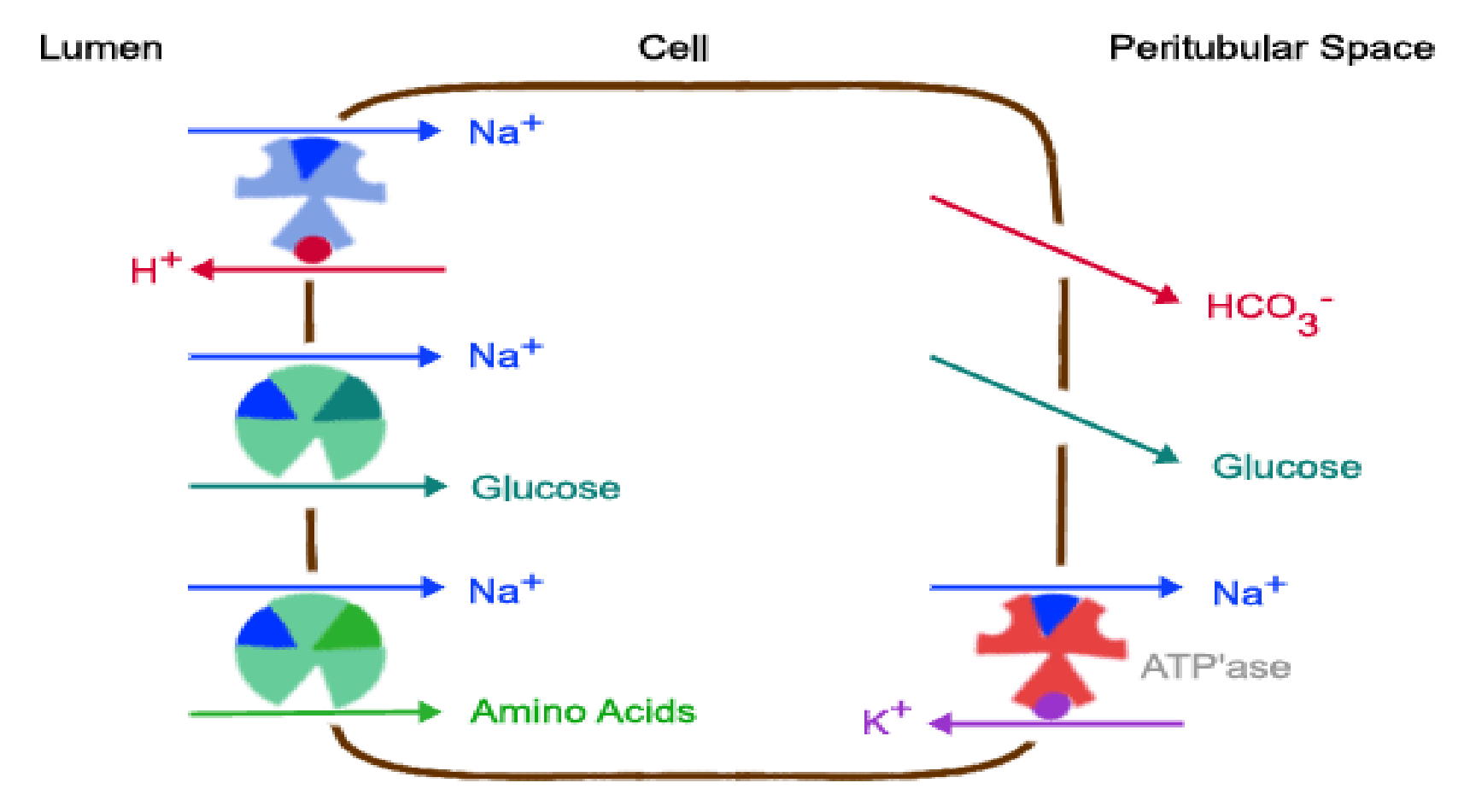
At basolateral border:

Glucose is carried by GLUT-2.

Counter-transport:

Secondary active secretion of H^+ together with Na^+ reabsorption by a Na^+- H^+ counter transport protein in the brush border of the luminal membrane of the proximal convoluted tubule.

Active Transport.



2- Passive Reabsorption:

Chloride:

occurs through paracellular pathway following Na^+ reabsorption which creates negativity inside the tubular lumen.

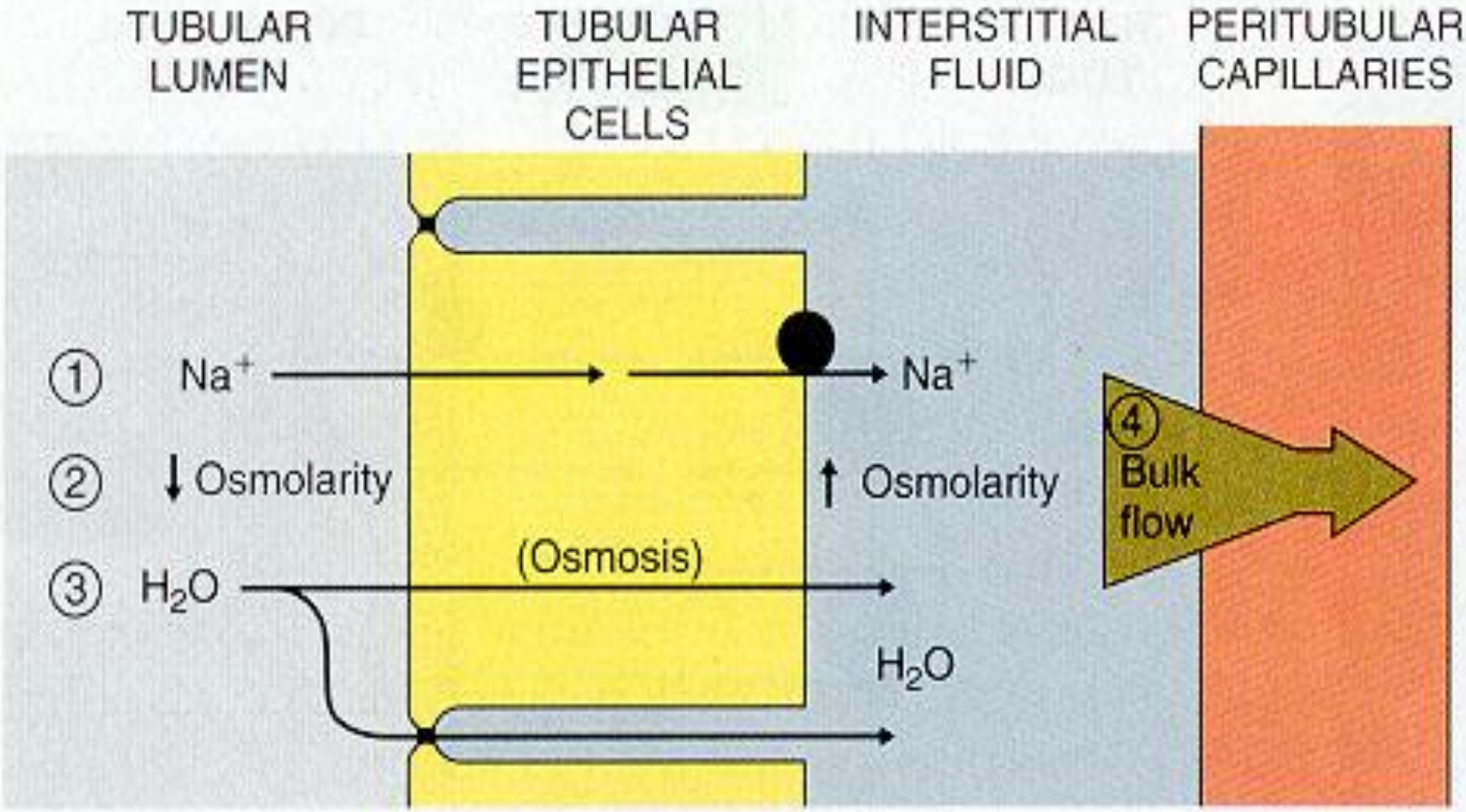
Water (osmosis):

Occurs paracellulary following solute.

Urea:

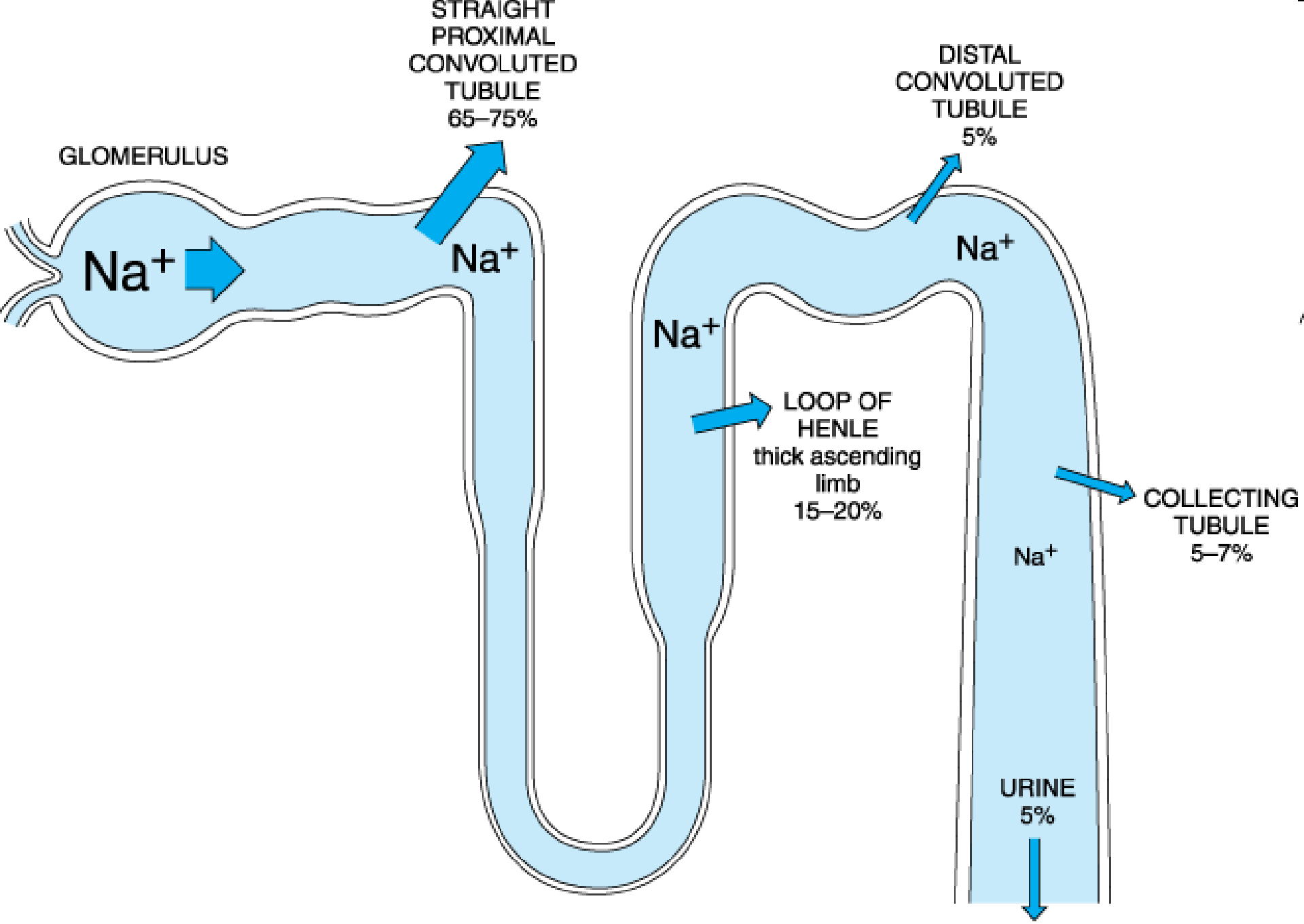
- **H_2O reabsorption leads to urea concentration in the tubular fluid creating a gradient for its absorption, 50% of urea is reabsorbed.**

Passive Water Reabsorption.



Na^+ Handling by Renal Tubule.

- Large amounts of Na^+ are filtered through the glomeruli.
- Na^+ is reabsorbed out of all portions of the tubule except the thin descending limb of loop of Henle.
- 96 - 99% of filtered Na^+ is reabsorbed.
- 90% of the Kidney energy consumption is due to active Na^+ transport which depends on Na^+-K^+ pump.



Reabsorption of Na^+ is coupled with:

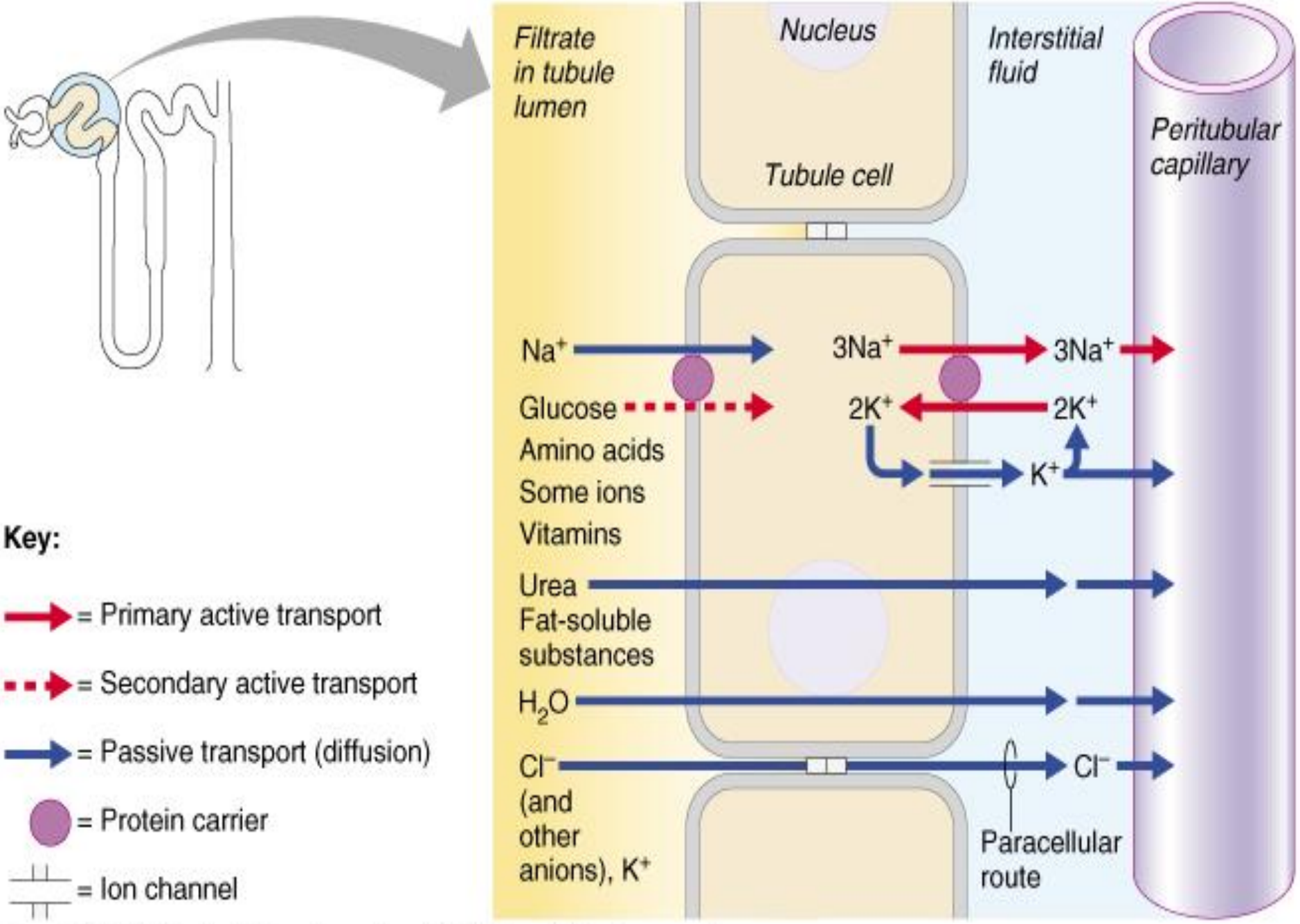
Reabsorption of most solutes by:

Secondary active transport as glucose, amino acids , sulphates, phosphate and organic acids (lactate and citrate) or

Diffusion (Cl^- and urea).

H_2O osmosis.

H^+ & K^+ secretion & HCO_3^- reabsorption



Na^+ Reabsorption in Different Segments

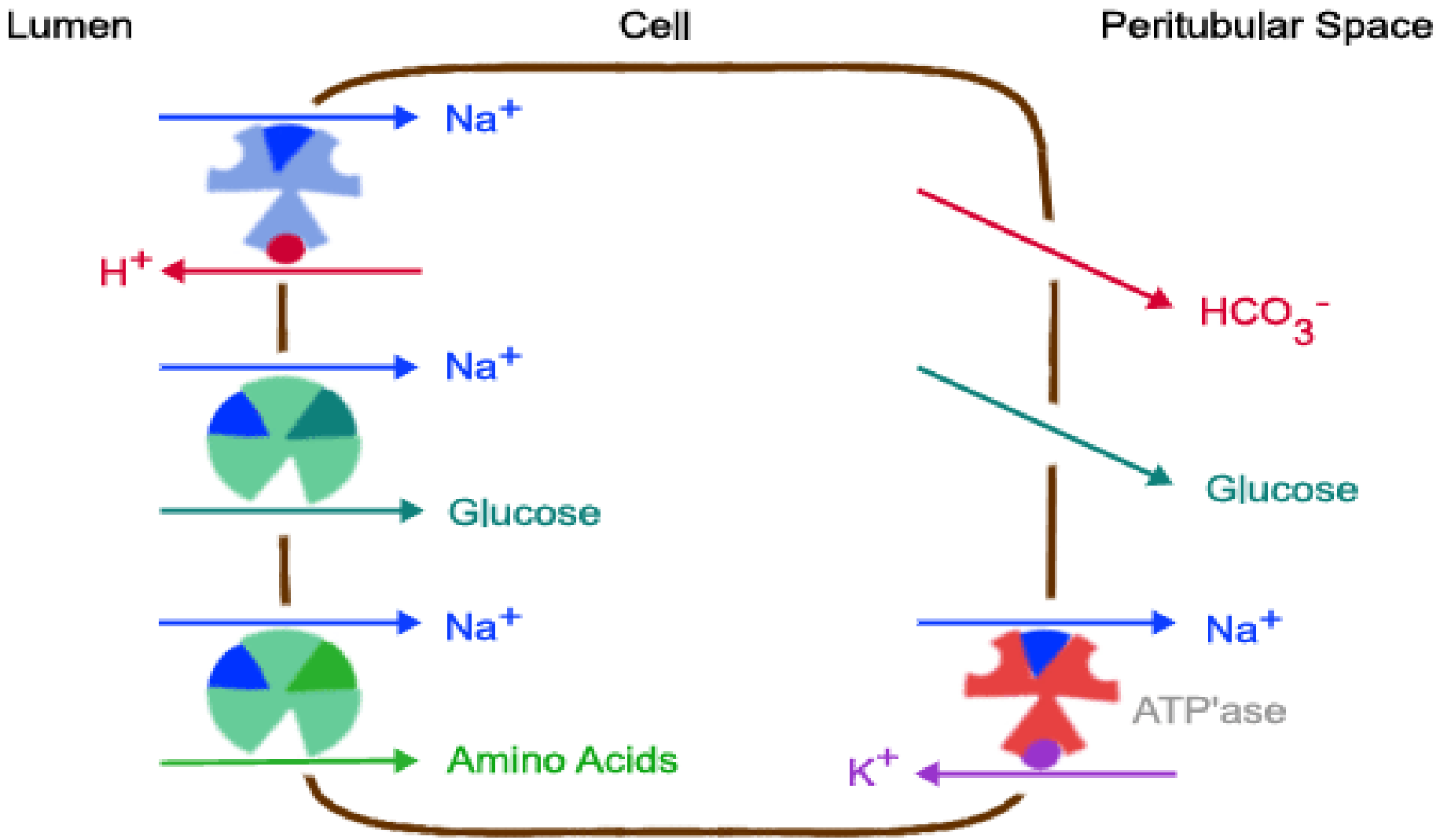
PCT

65% of filtered load.

Although it is an active transport, it has no tubular maximum.

Because the rate of its pumping outside at the basolateral border is greater than the rate of diffusion at luminal border.

Na^+ Reabsorption at PCT



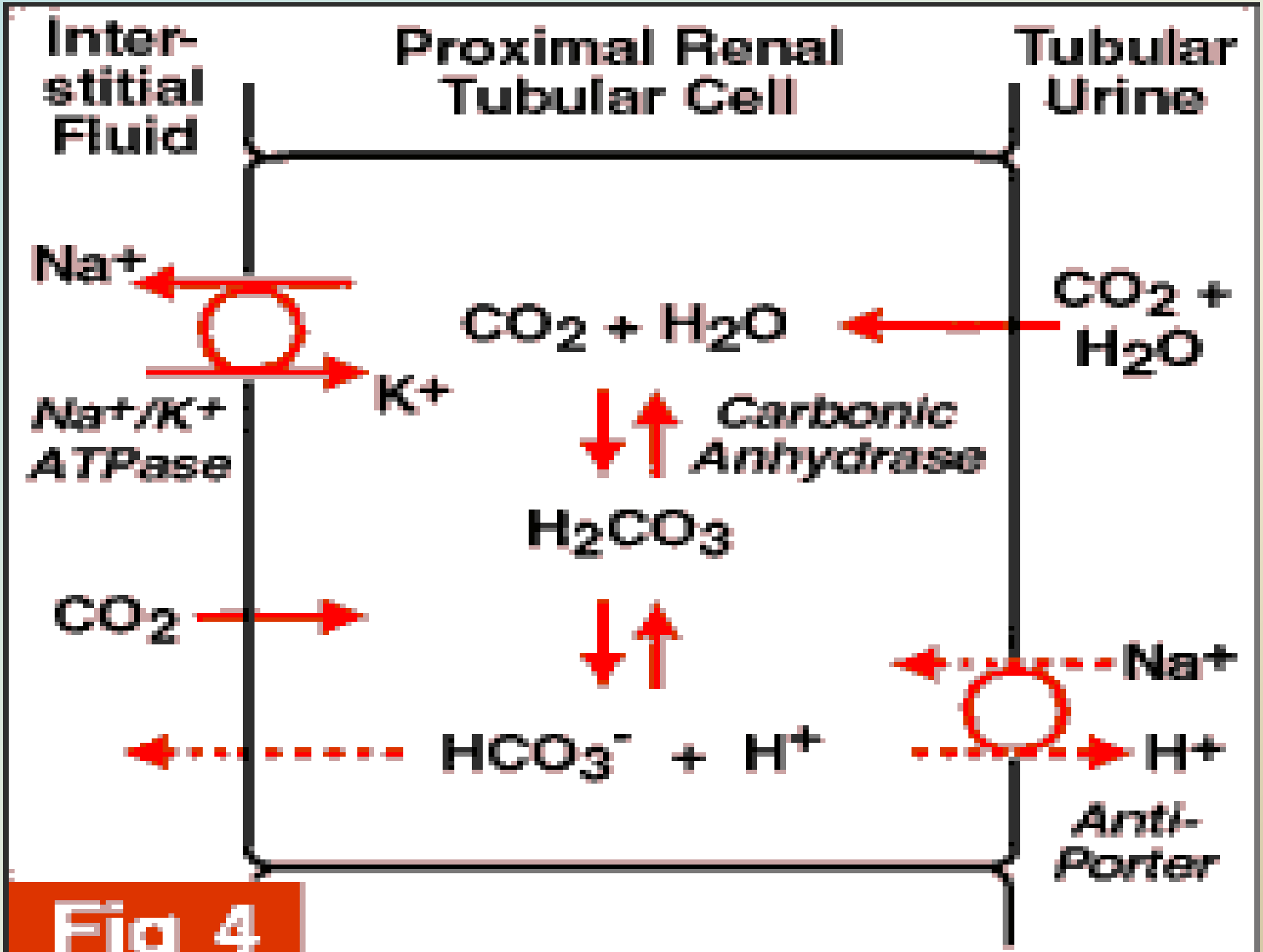
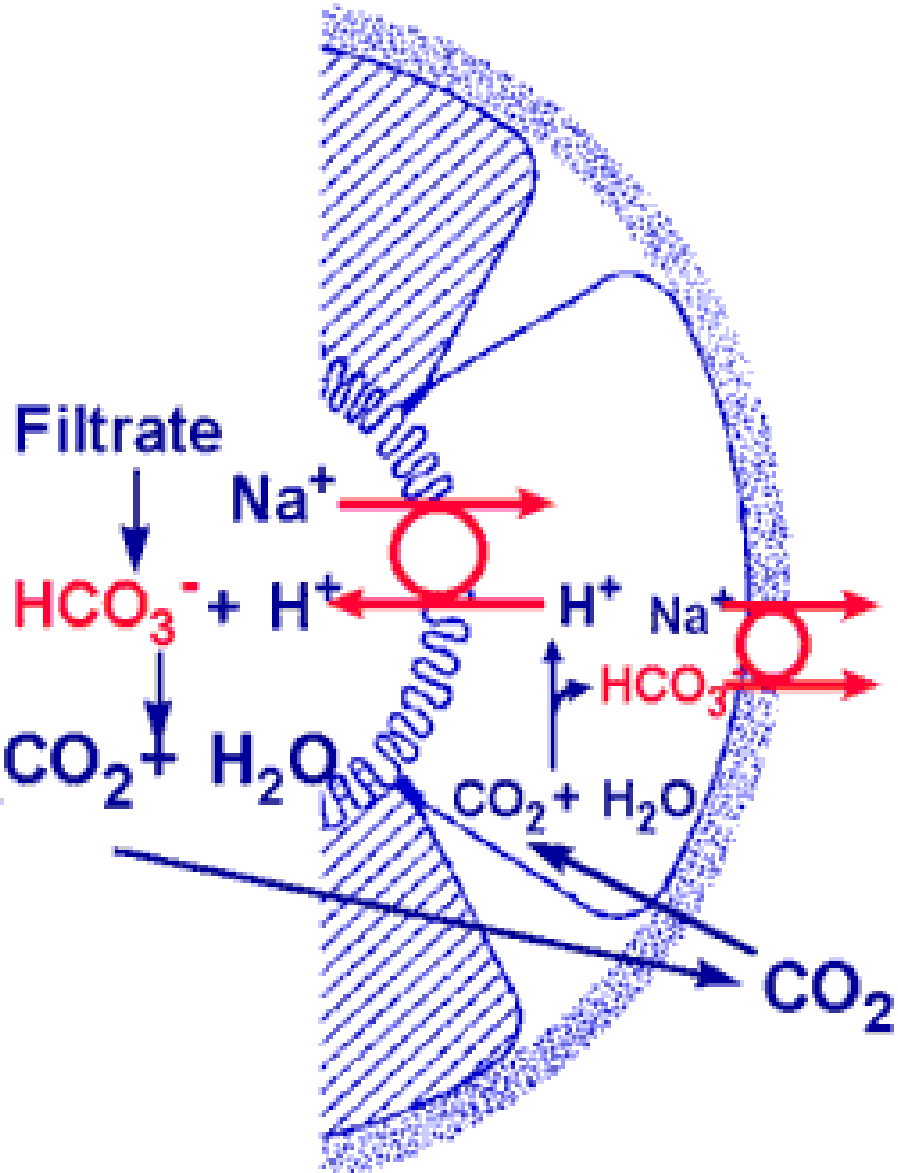
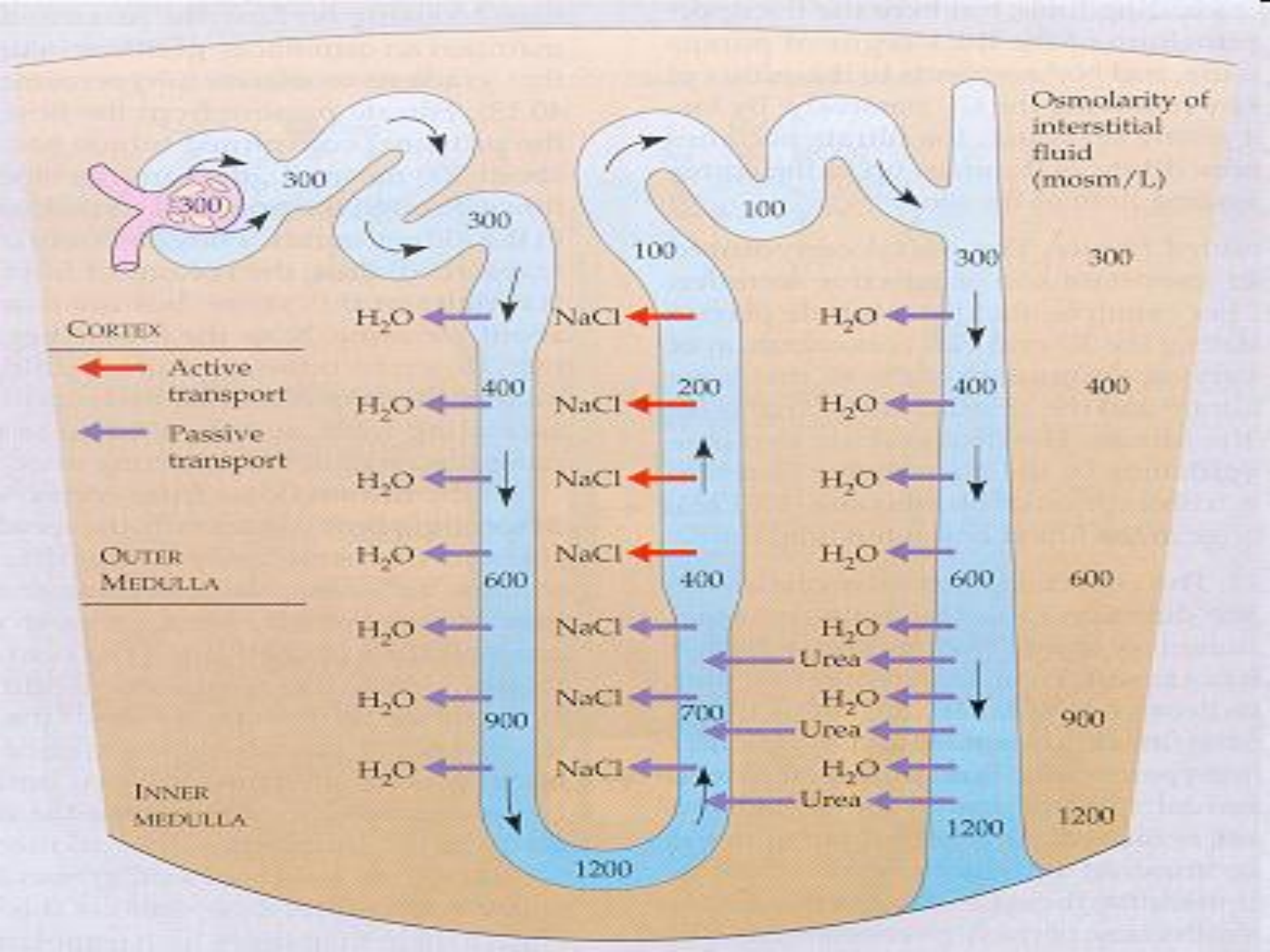

Inter-
stitial
Fluid
Proximal Renal
Tubular Cell
Tubular
Urine
Na+
K+
Na+/K+
ATPase
CO2 + H2O
CO2 +
H2O
Carbonic
Anhydrase
H2CO3
CO2
Na+
HCO3- + H+
H+
Anti-
Porter

Fig 4

BICARBONATE REABSORPTION IN THE PROXIMAL TUBULE

- Filtered HCO_3 is titrated by secreted protons to CO_2 and water.
- Hydration of CO_2 in the cell produces protons for secretion and HCO_3. The HCO_3 is transported into the ISF by a Na-HCO_3 cotransporter in a ratio of 3 HCO_3:1Na.
- Thus one HCO_3 disappears from tubular fluid and another appears in the ISF.
- The net effect is reabsorption of bicarbonate.




Osmolarity of interstitial fluid (mosm/L)
300
300
300
100
100
300
300
400
200
400
400
600
400
600
600
900
700
900
1200
1200
1200
H_2O
NaCl
Urea
Cortex
Active transport
Passive transport
Outer Medulla
Inner Medulla

Loop of Henle

a) Thin descending (permeable to HO_2).

No Na^+ reabsorption as there is no Na^+ transport proteins or channels.

Only H_2O reabsorption.

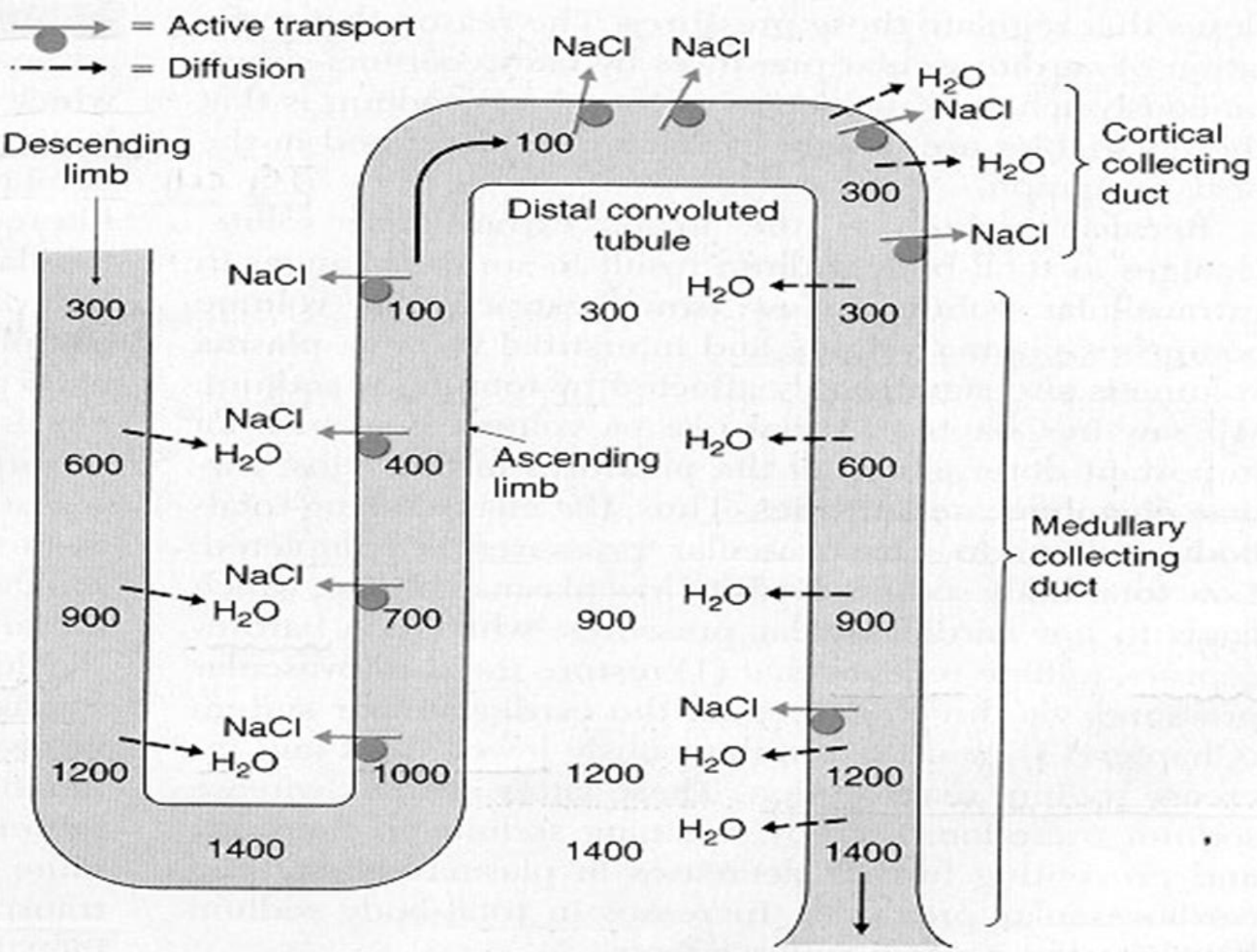
= Concentrating segment

b) Thin ascending (impermeable to HO_2).

Passive reabsorption of NaCl.

Impermeable to H_2O

= diluting segment.


= Active transport
= Diffusion
NaCl
NaCl
H_2O
NaCl
H_2O
NaCl
Cortical collecting duct
Descending limb
100
300
Distal convoluted tubule
NaCl
100
300
H_2O
300
NaCl
H_2O
600
400
Ascending limb
H_2O
600
Medullary collecting duct
NaCl
H_2O
900
700
H_2O
900
NaCl
H_2O
1200
1000
H_2O
1200
H_2O
1400
1400
1400

Thick ascending & early distal

25% of Na^+, K^+& CL^- are reabsorbed by cotransport . (Na^+- K^+- 2 CL^-)

Most of reabsorbed K^+ fluxes back to the lumen via K^+ channels.

This serves 2 purposes:

Ensure sufficient K^+ for the co-transporter.

Results in net positive potential in the lumen that helps paracellular reabsorption of several cations, Na^+, K^+, Ca^{++}& Mg^{++}

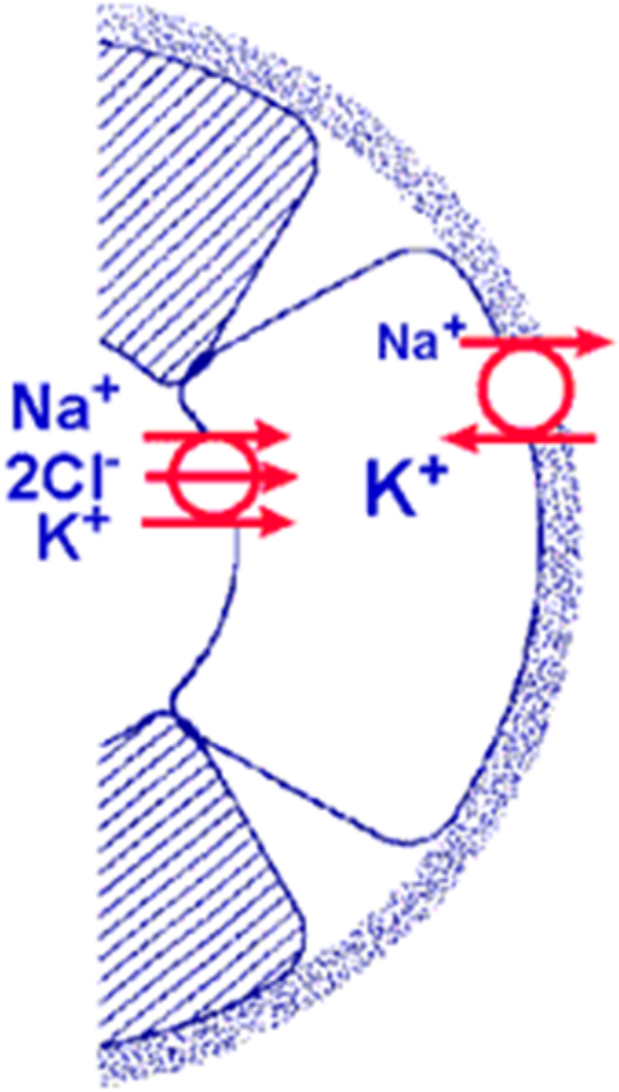
SALT TRANSPORT IN THE THICK ASCENDING LIMB

PRIMARY TRANSPORT MECHANISM:

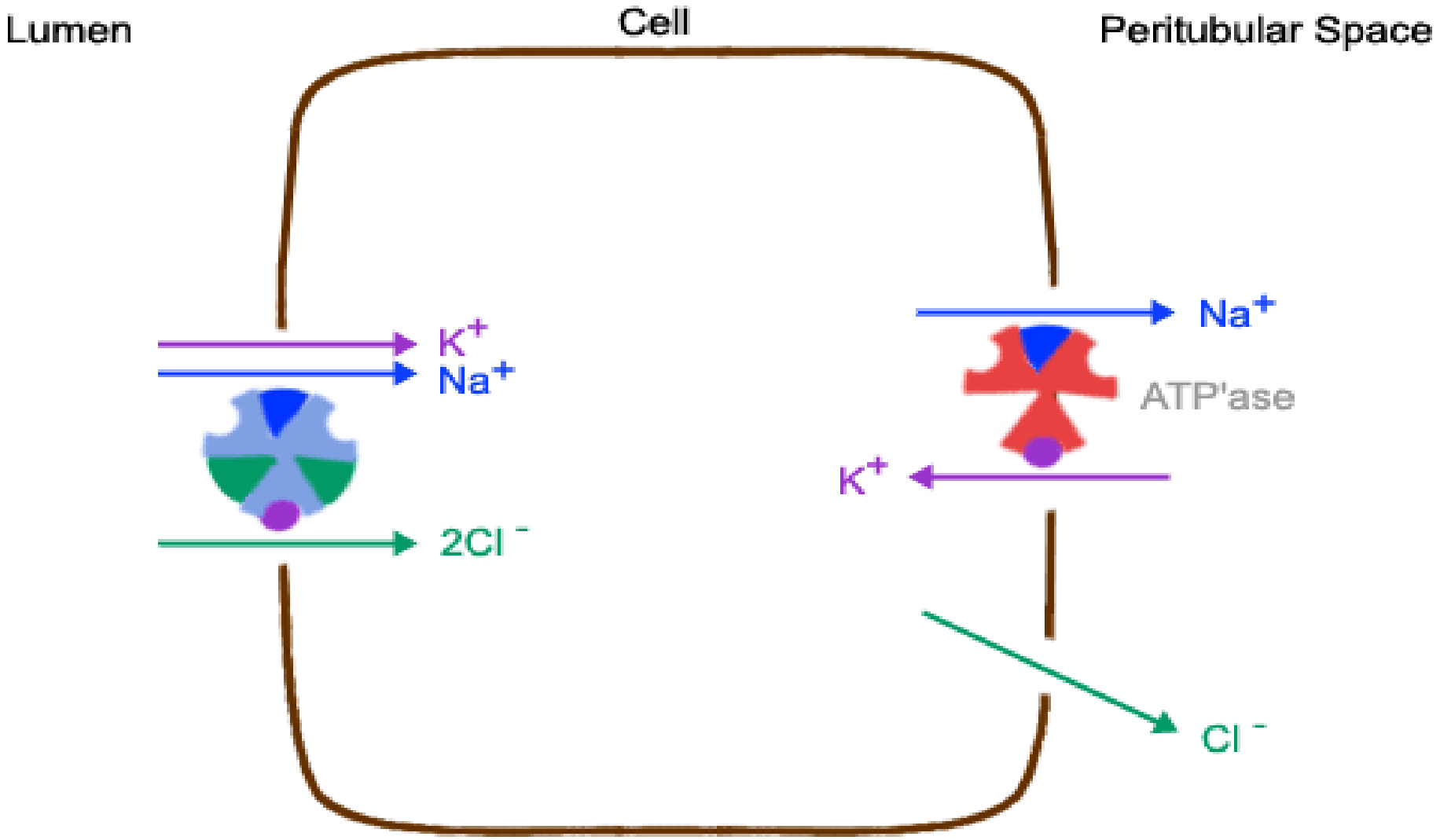
Na-K-ATPase in basolateral membrane.

SECONDARY TRANSPORT SYSTEM:

Na-K-2Cl cotransporter in apical membrane, electrically neutral, driven by Na and Cl gradients.



Thick ascending Loop of Henle.



Bartter's syndrome

Cause

Defect in the Na^+- K^+ -2 CL^- cotransporter in the luminal membrane of the thick ascending limb → loss of Na^+, K^+ ,CL^- and Ca^{++} in urine.

Manifestations:

- **Renal salt wasting.**
- **Volume depletion.**
- **Hypercalcuria.**
- **Hypokalemia.**
- **Metabolic alkalosis.**

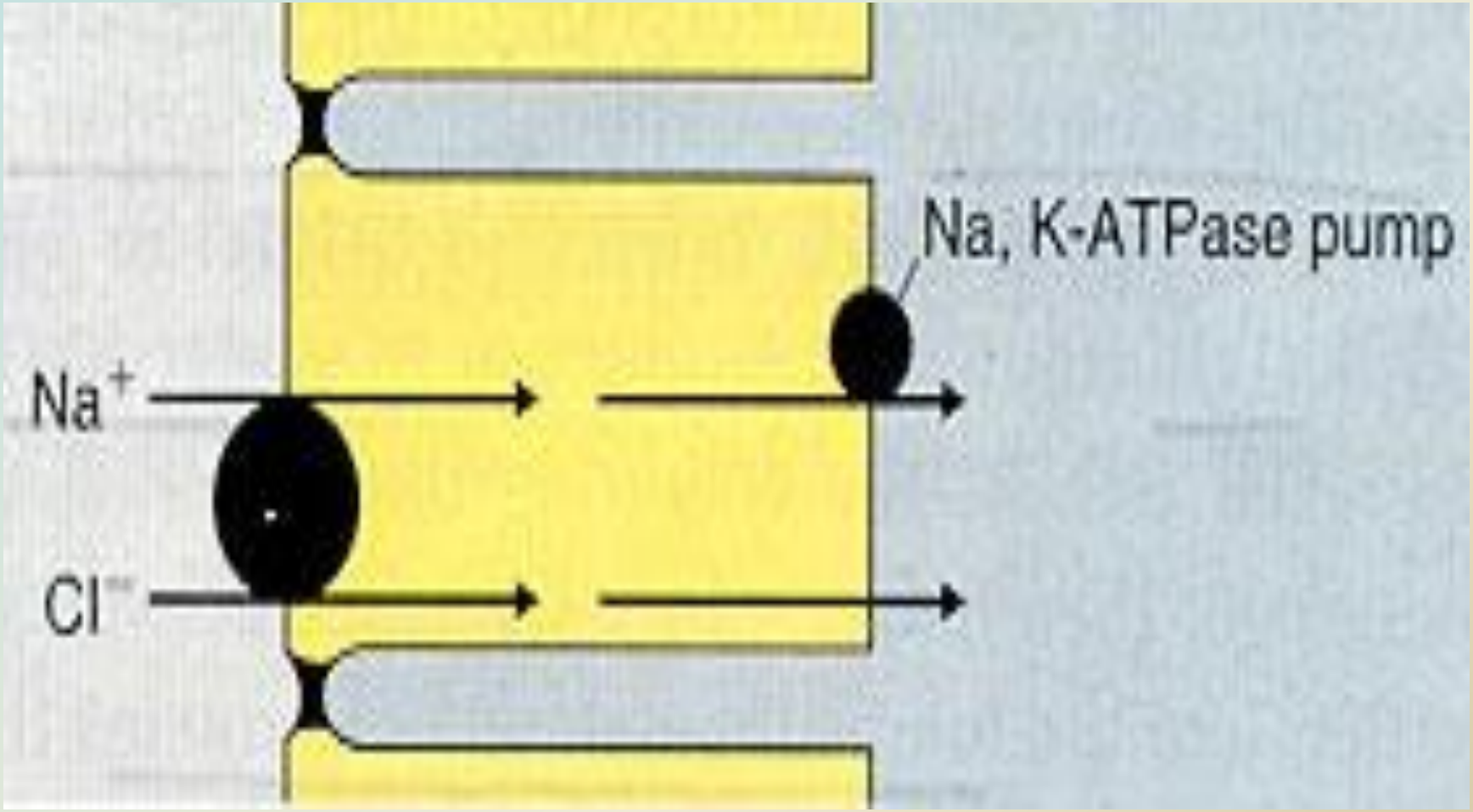
Early distal tubule

Called cortical diluting segment.

Reabsorption of NaCl by Na^+- Cl^- cotransporter.

Impermeable to water, thus the tubular fluid is further diluted.

Early DCT.



Late distal & collecting duct

<10% of Na^+ is reabsorbed at the principle cells as counter transport with K^+ under effect of aldosterone.

Mechanism

Na^+ is extruded via Na^+ -K^+ pump at the basolateral membrane.

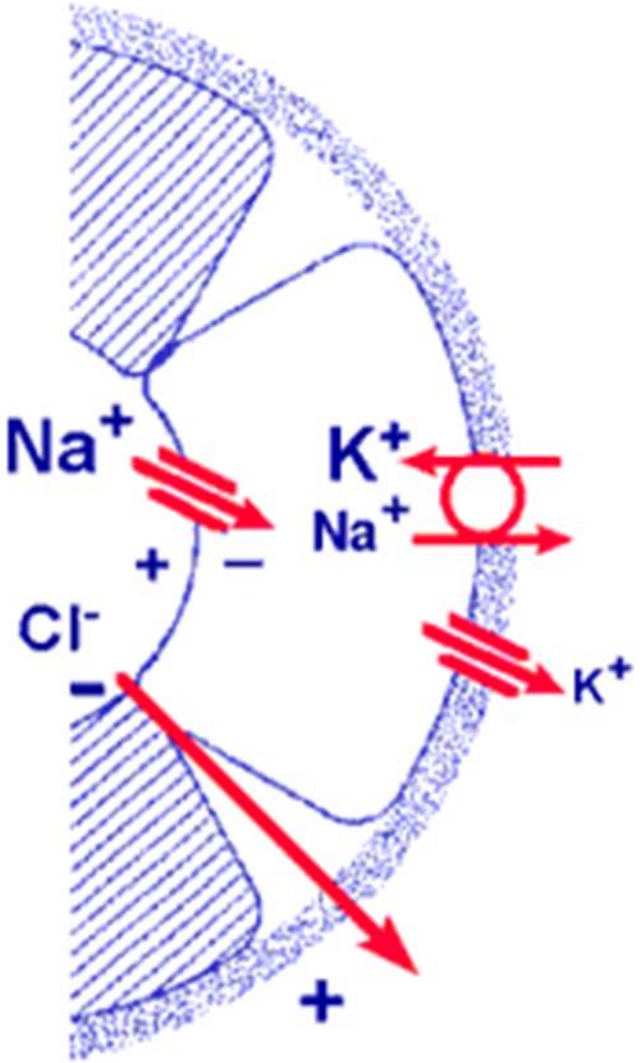
Na^+ diffuses into the principal cell through Na^+ channels at the apical membrane, while K^+ diffuses into the tubular lumen down its concentration gradient.

CL^- accompanies Na^+ paracellularly.

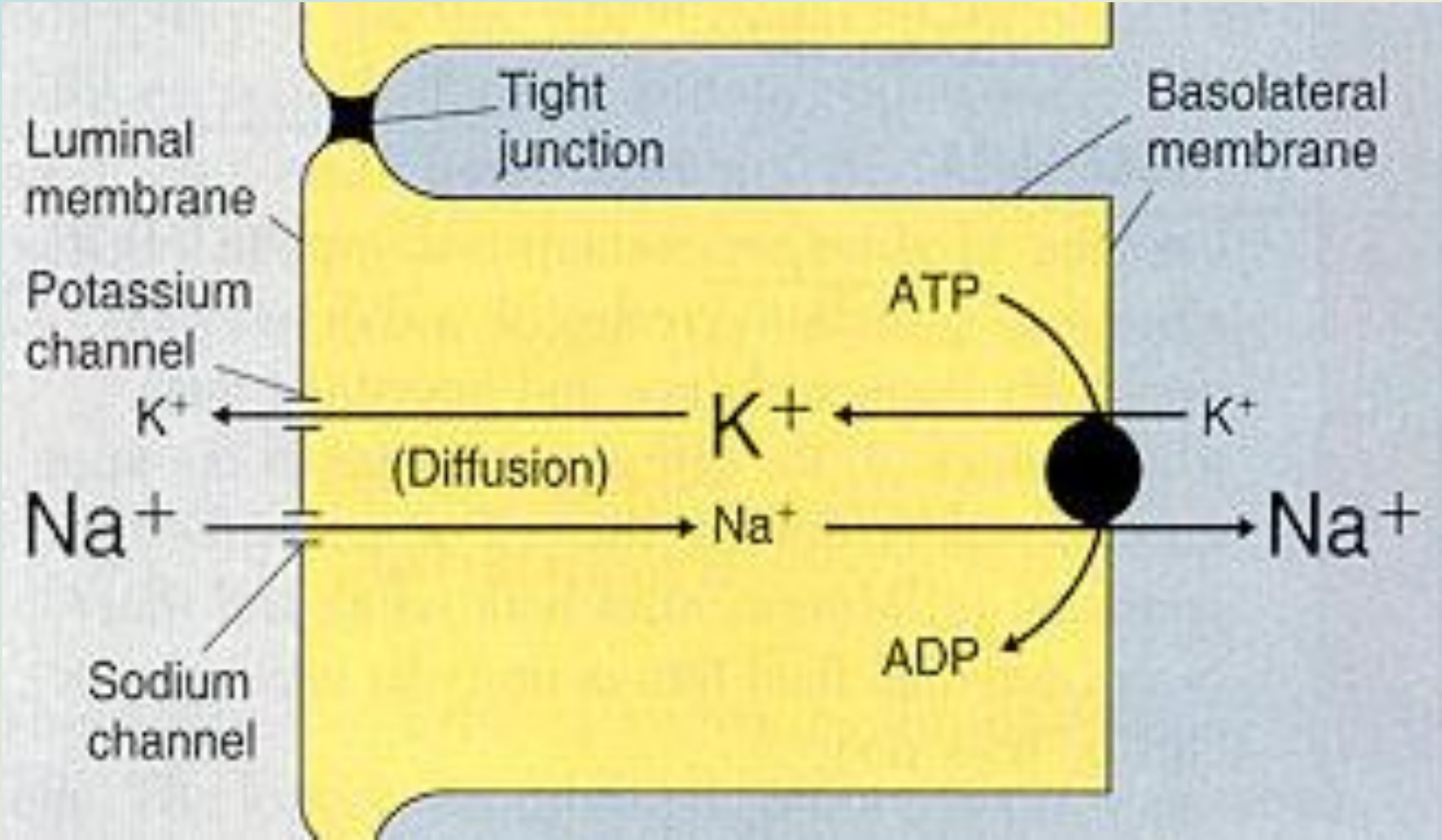
Under the effect of aldosterone

Na REABSORPTION IN THE COLLECTING TUBULE

- Na is reabsorbed by the principal cells in the collecting tubule.
- The primary engine: Na-K ATPase in the basolateral membrane.
- The Na pump in conjunction with K channels establishes an electro-chemical gradient for Na across the apical membrane.
- That gradient drives Na into the cell via a Na channel.
- Na reabsorption here is stimulated by aldosterone.
- Cl reabsorption, via the paracellular pathway, is driven by the lumen-negative electrical gradient.



Late distal and Collecting duct.



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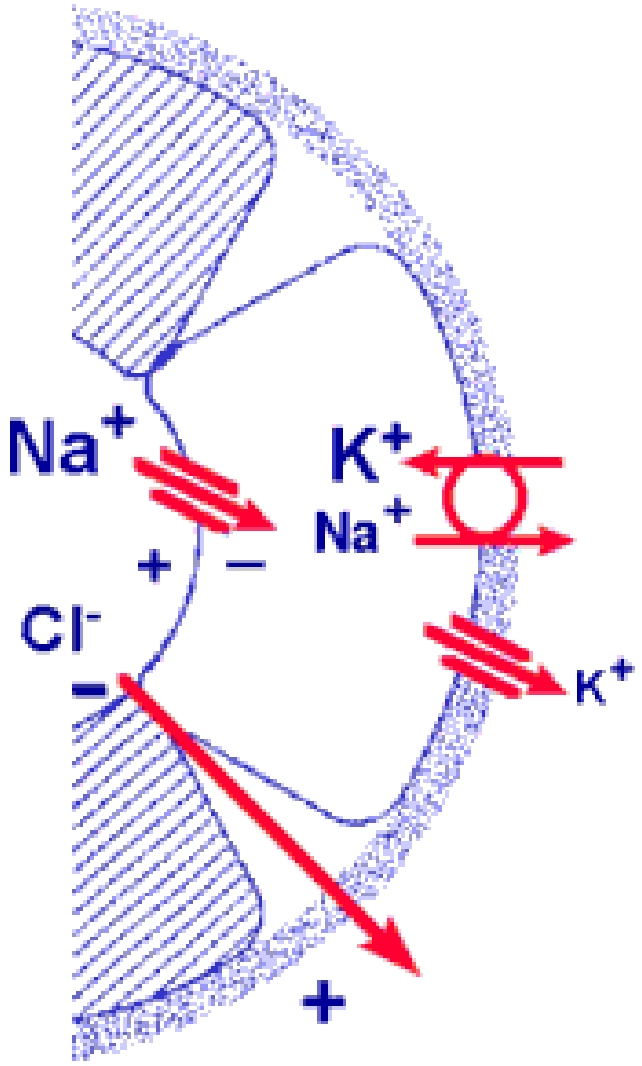
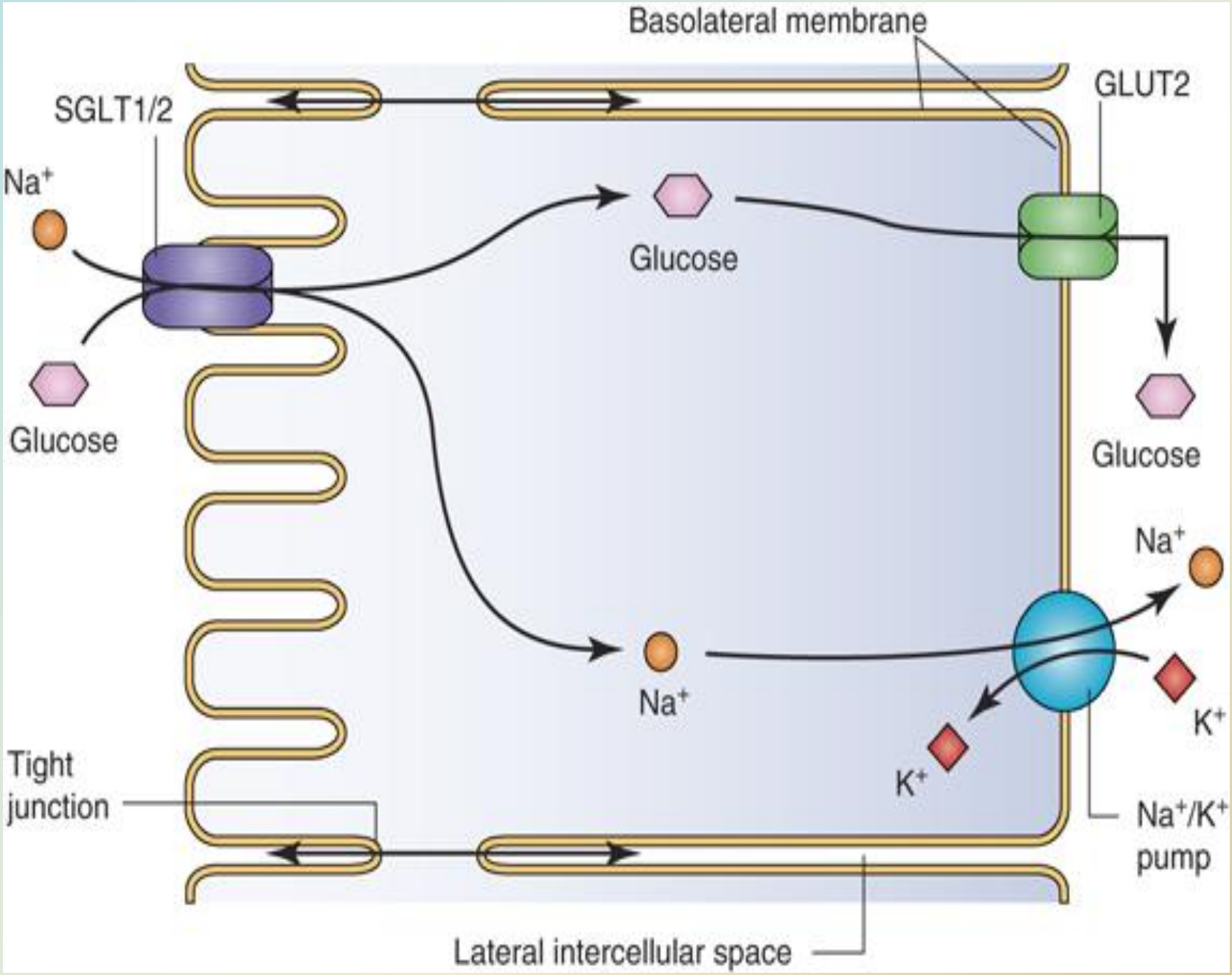



Renal Physiology
Glucose handling by the renal tubules


Basolateral membrane
SGLT1/2
GLUT2
Na+
Glucose
Glucose
Glucose
Na+
Na+
K+
K+
Tight junction
Na+/K+ pump
Lateral intercellular space

Glucose Reabsorption

Normally all filtered glucose is reabsorbed at the early portion of PCT.

Mechanism:

Secondary active transport with $Na.^{+}$

At luminal border

Common carrier with Na^+, SGLT2

Can be blocked by

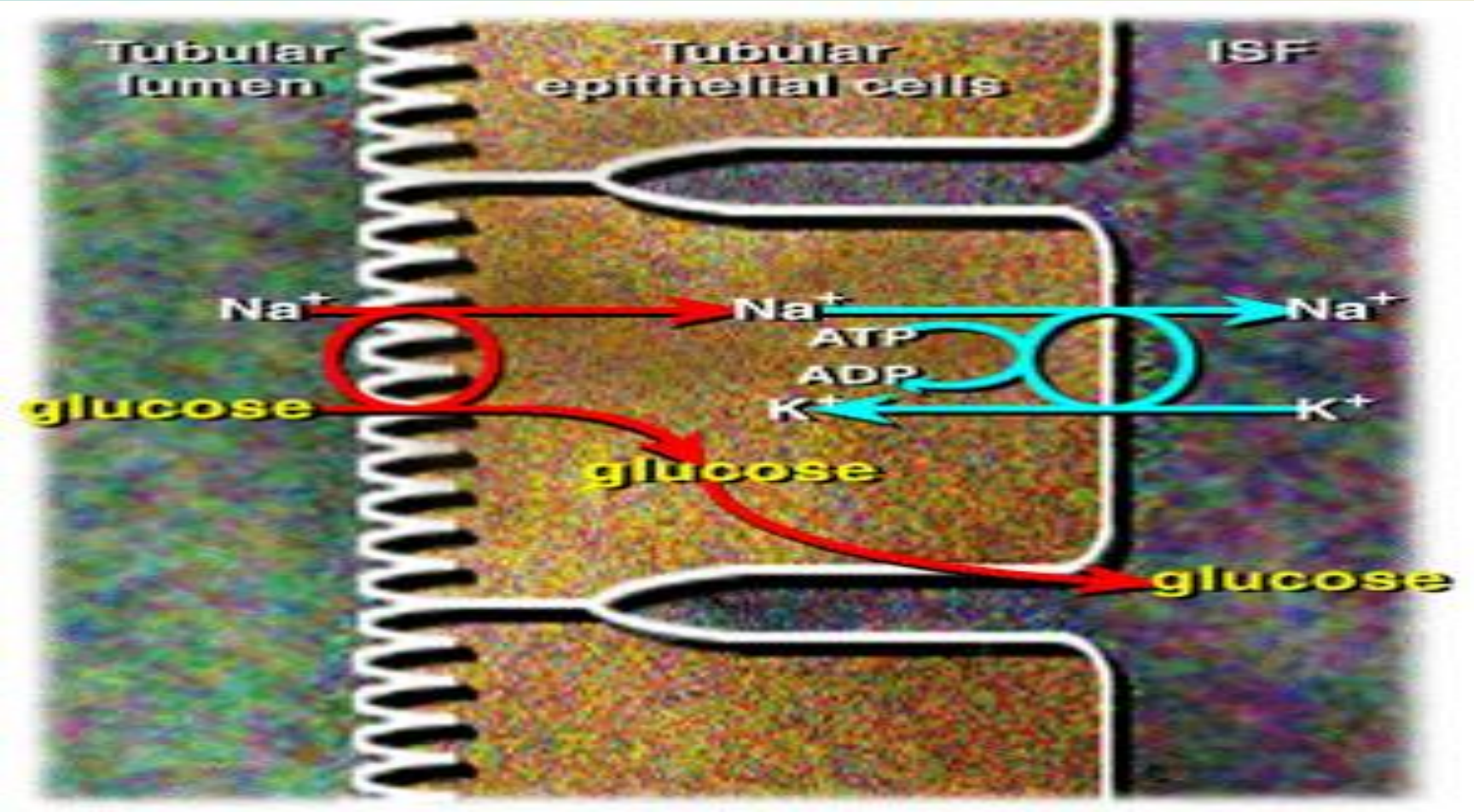
Oubain which blocks Na^+ -K^+ ATPase and

Phlorhizin which competes for the carrier.

At basolateral border

Glucose is carried by facilitated diffusion down chemical gradient by carrier GLUT2.

Secondary active transport of glucose.



Tubular transport maximum for glucose (T_{mG})

Definition:

Maximum amount of glucose in (mg) that can be reabsorbed by renal tubules /min.

Renal threshold for glucose

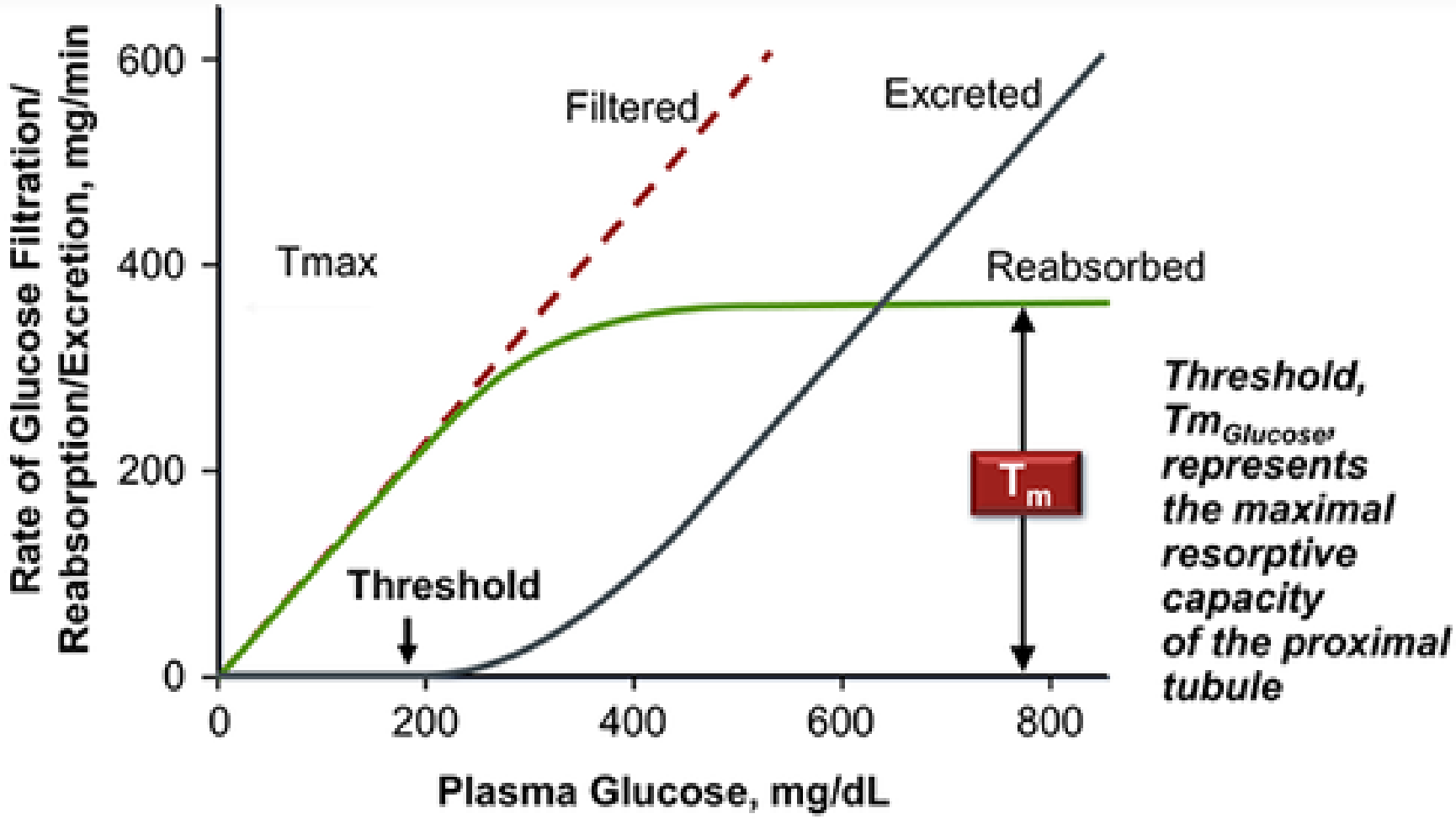
Plasma level at which glucose starts to appear in urine.

Value:

200mg/dL in arterial blood.

180mg/dL in venous blood.

Renal Glucose Handling



Schematic representation of the typical titration curve for renal glucose reabsorption in humans. Silverman M, Turner RJ. *Handbook of Physiology. Section 8: Renal Physiology.* Oxford, UK: Oxford University Press: 1992:2017-2038.[4]

Glycosuria

Excretion of glucose in urine in considerable amounts.

Causes:

Diabetes mellitus,

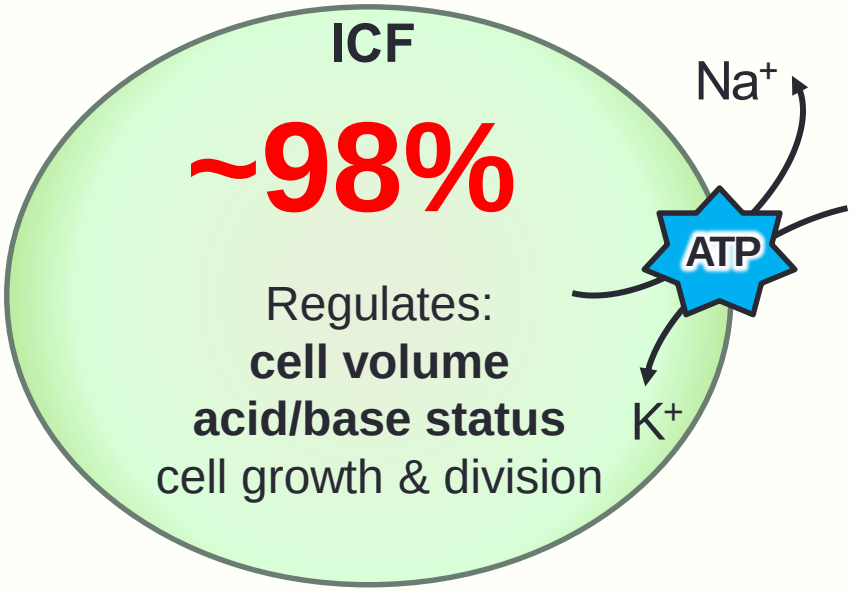
Blood glucose exceeds renal threshold.

Renal glycosuria,

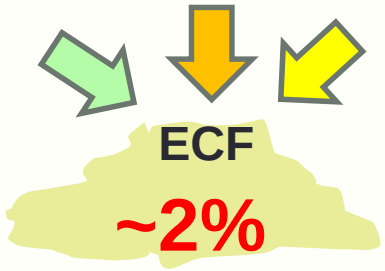
Normal blood glucose but decreased renal threshold below 180 mg%. T_m is markedly decreased in renal glycosuria. Due to congenital defects.


Renal Physiology
Potassium handling by the renal tubules

K^+ is the most abundant cation in the body



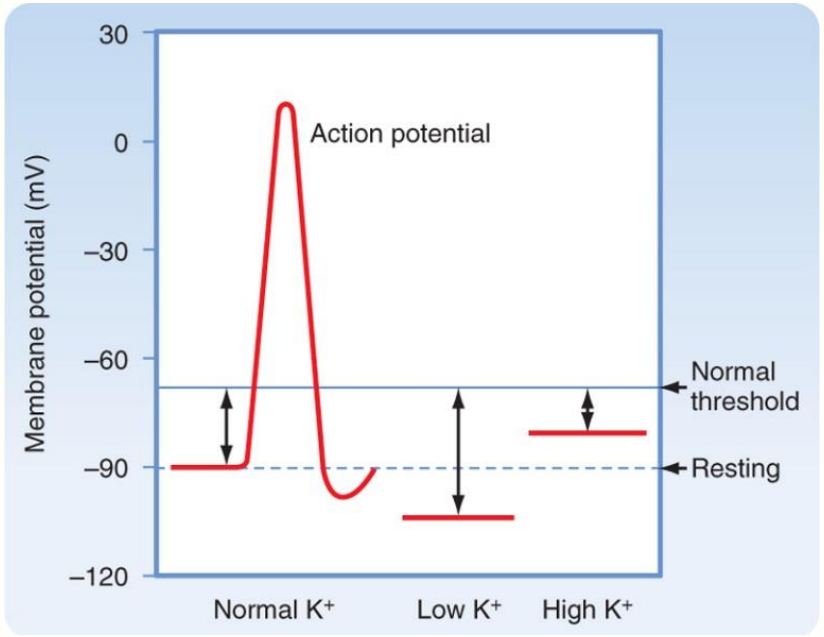
precise control mechanisms



Plasma [K^+] **3.5-4.8 mmol/L**

Regulates:
membrane potentials in excitable cells

- K^+ concentrations in equilibrium → Equal diffusion into and out of cell
- ↓ EC K^+ → ↑ diffusion of K^+ out of cell → cells hyperpolarized
- ↑ EC K^+ → ↓ diffusion of K^+ out of cell → cells partially depolarized



↑ K^+ uptake into the cells is due to:

- **Insulin** ↑ after high K^+ meal.

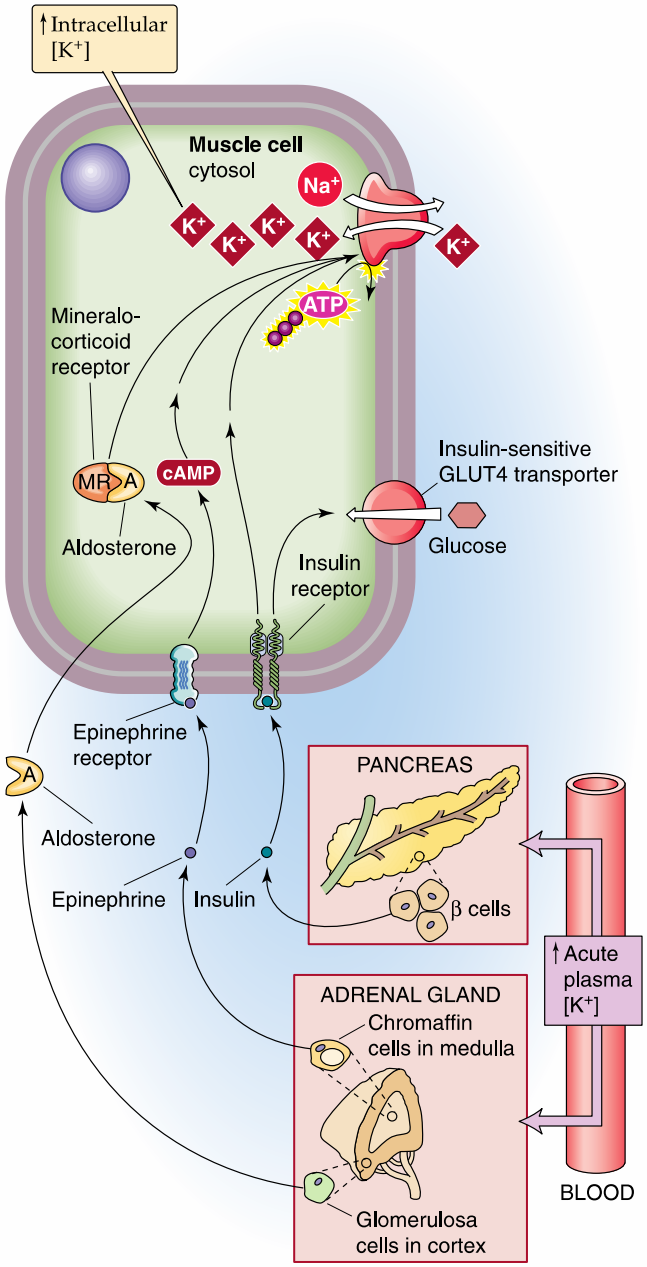
  Insulin + glucose to treat hyperkalaemia.

- **Adrenaline** via β_2 receptors

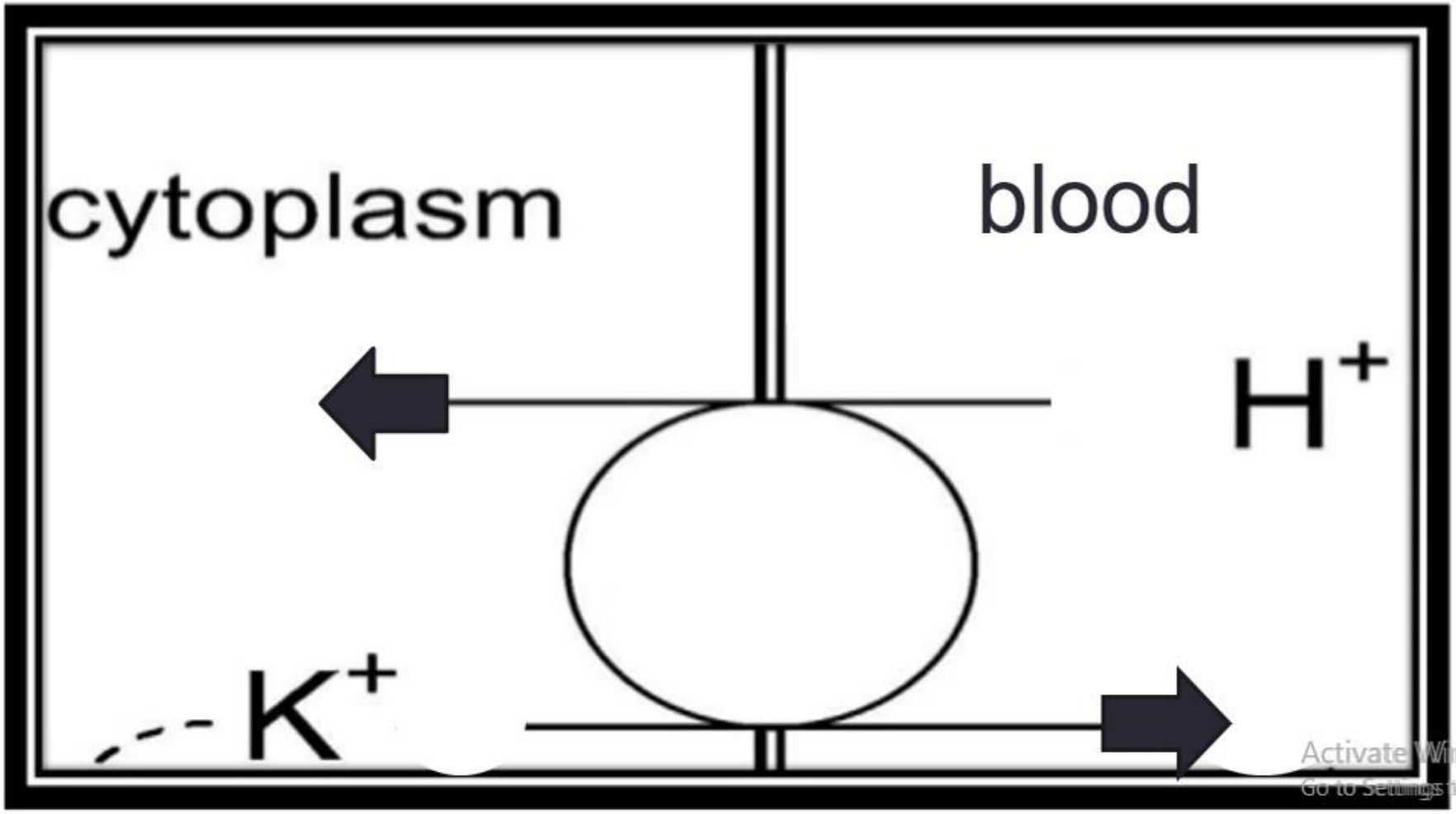
  β blockers ↑ plasma K^+ after a meal or an exercise ☠.

- **Aldosterone**

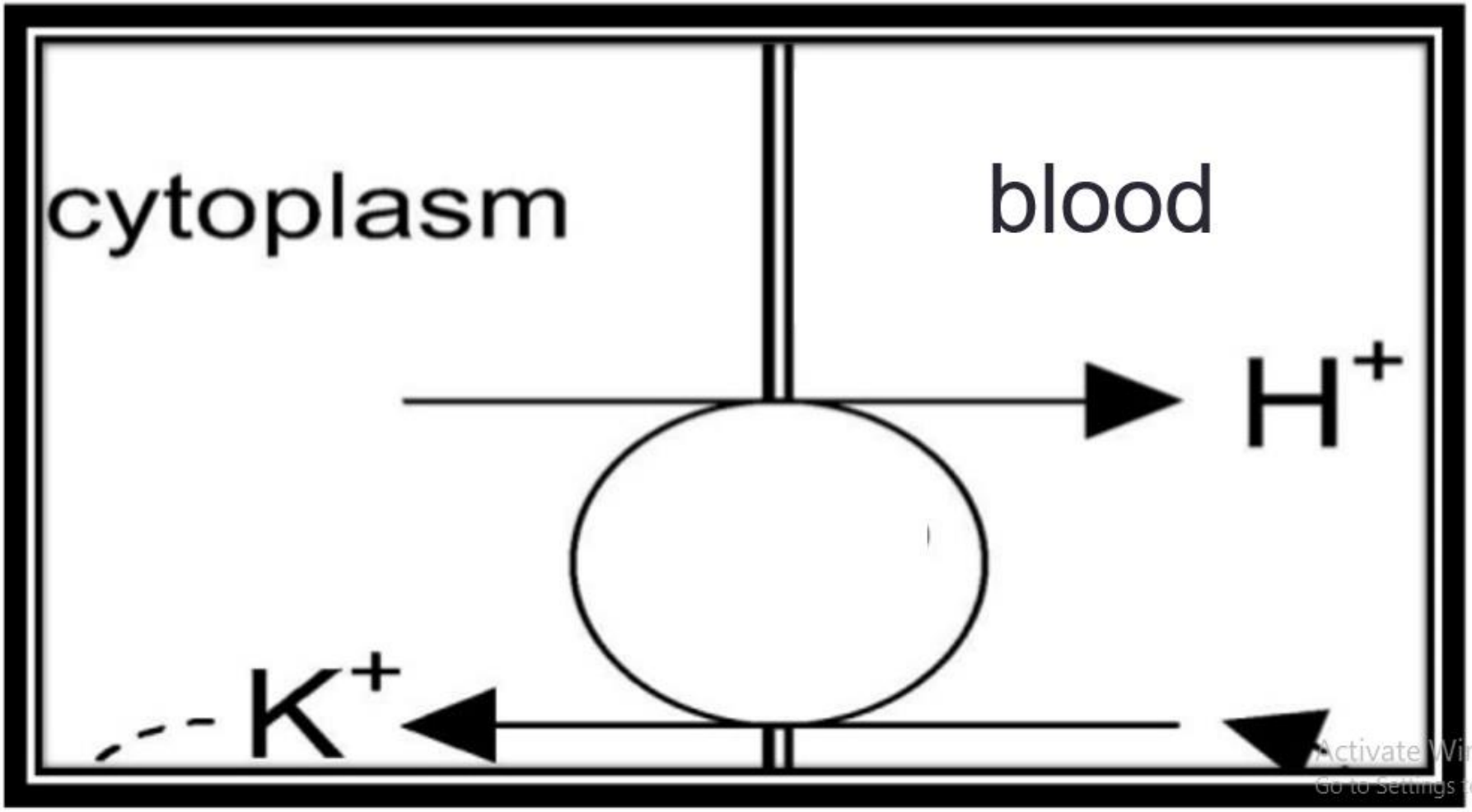
- **Alkalosis** H^+ is "*exchanged*" for extracellular K^+.



During Acidosis

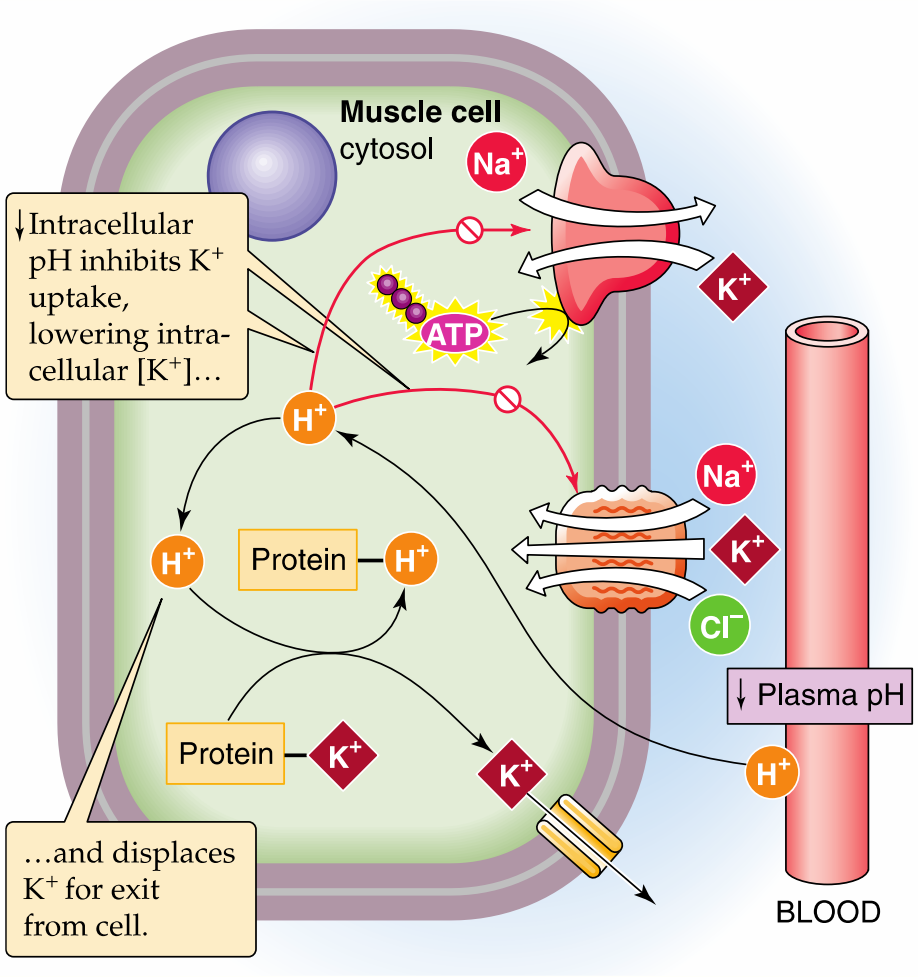


During Alkalosis



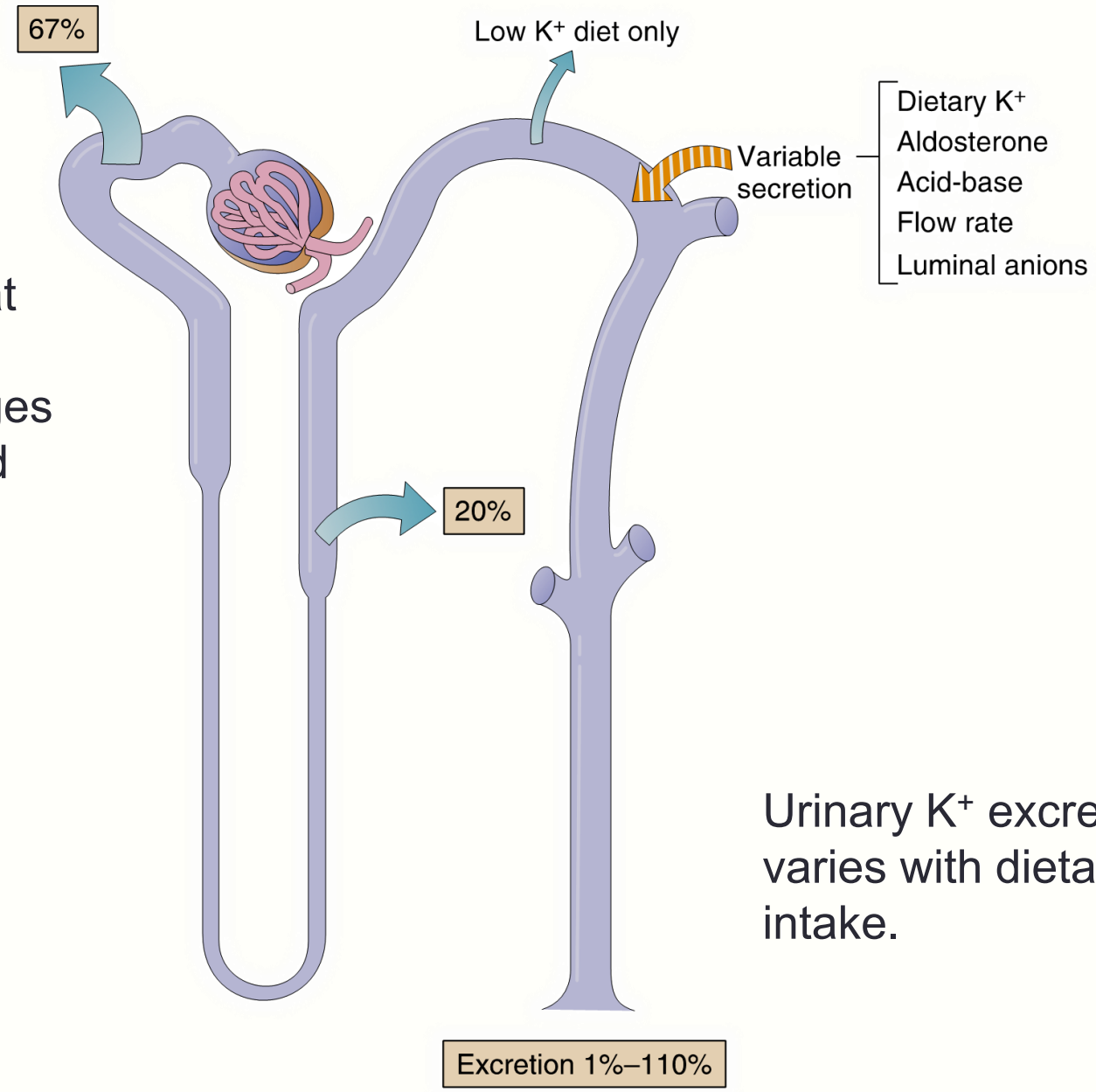
↑ Plasma K^+ levels can be due to:

- **Acidosis:** ICF K^+ is "**<u>exchanged</u>**" for extracellular H^+.
- ↑ **Osmolality** → K^+ moves out secondary to H_2O movement out of cells
- **Exercise** → loss of K^+ from muscles
- **Cell lysis** → release of cellular contents



Renal excretion of potassium

K^+ reabsorption at PCT does not respond to changes in K^+ balance and are not physiologically regulated.



Urinary K^+ excretion varies with dietary K^+ intake.

Major Factors and Hormones Influencing K^+ Excretion

Homeostatic: Keep K^+ Balance Constant

- Plasma $[K^+]$ ($\boxed{\uparrow}$ K^+ excretion)
- Aldosterone ($\boxed{\uparrow}$ K^+ excretion)

Pathophysiological: Displace K^+ Balance

- Flow rate of tubule fluid ($\boxed{\uparrow}$ K^+ excretion)
- Acid-base balance

Plasma [K^+]

Hyperkalaemia stimulates secretion of K^+ within minutes

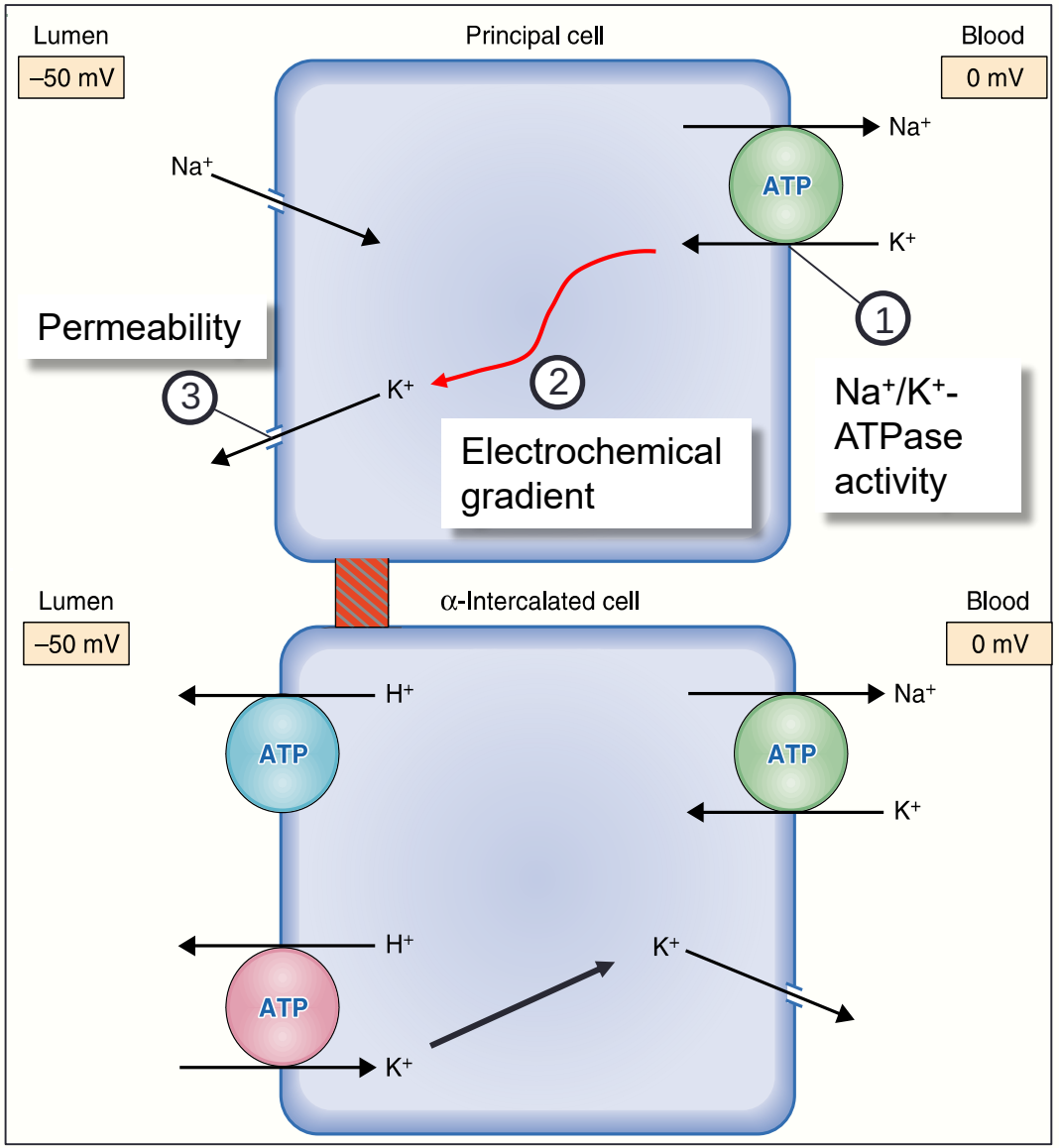
How?

1. Stimulates Na/K-ATPase → ↑ K^+ uptake (*basolateral*) → ↑ electrochemical gradient.

2. ↑ **permeability** to K^+ (*apical*).

3. ↑ **aldosterone** → ↑ secretion of K^+.

Hypokalaemia produces an opposite effect



Aldosterone

↑ K^+ secretion by:

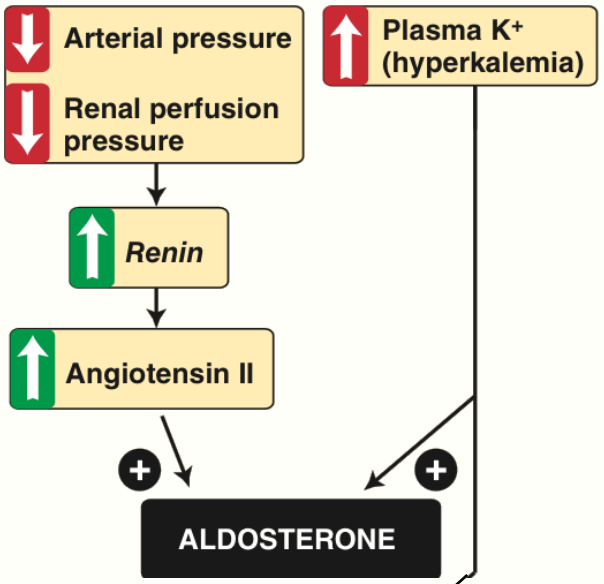
1. ↑ Na/K ATPase → ↑ Na^+ reabsorption → ↑ K^+ secretion.

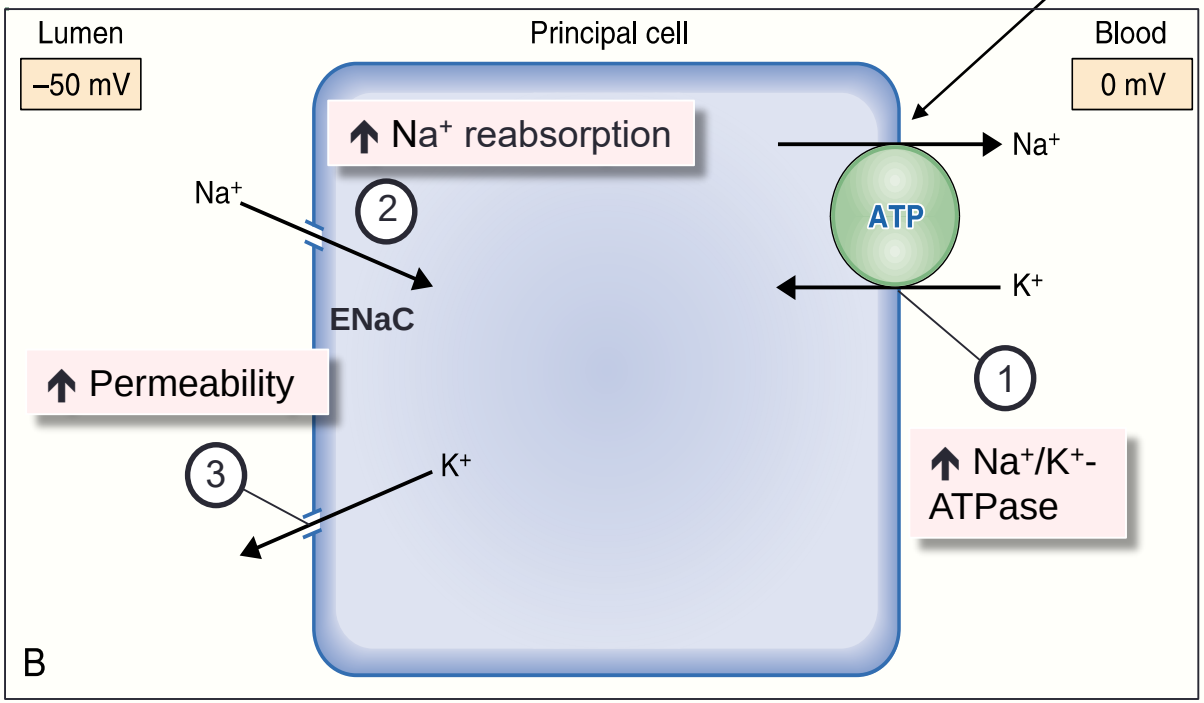
2. ↑ Na+ reabsorption (↑ ENaC) → -ve lumen potential → ↑ K^+ secretion

3. ↑ permeability of apical membrane → ↑ K^+ secretion

Conn's syndrome (↑ aldo) → hypokalaemia

Addison's disease (↓ aldo) → hyperkalaemia

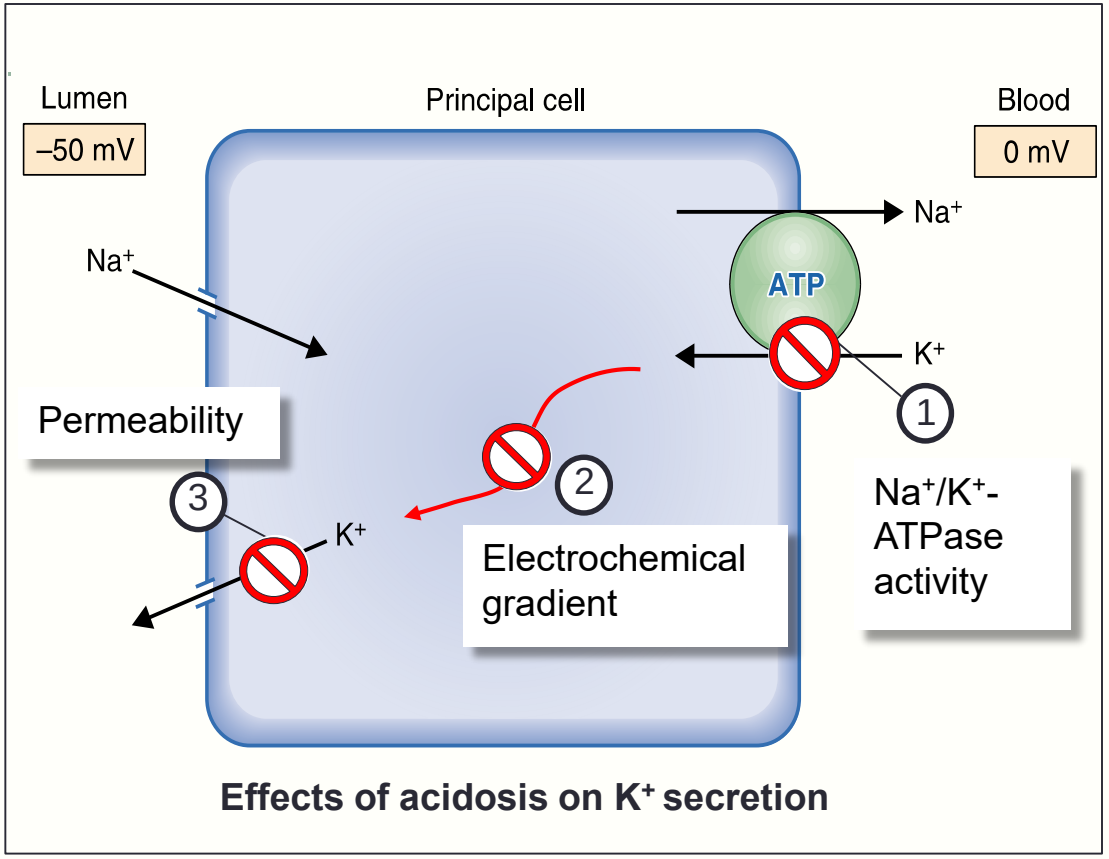




Acid-base balance

Acidosis inhibits K^+ secretion in principal cells by INHIBITING ⊘:

- **Na/K ATPase** → ↓ K^+ uptake from blood → ↓ conc. gradient for K^+ efflux into the lumen.
- **K^+ channels** (*apical*) → ↓ K^+ secretion directly → hyperkalemia.



Effects of acidosis on K^+ secretion

Alkalosis has the opposite effect, promoting K^+ secretion and hypokalemia.


Thank
You!