Western

UNIVERSITY · CANADA

Tutorial 14
Sections 009/010

TA: Greydon Gilmore
Physiology 2130
Jan 21st, 2020

Your TA reminding you…

- 3rd Peerwise assignment (1.5%)
  - Post 2 MC questions: due Feb 12th @ midnight
  - Answer 5 MC questions: due Feb 14th @ midnight
- 3rd Quiz (1%)
  - Opens: Feb 24th @ 4pm
  - Closes: Feb 25th @ 4pm
- 3rd Midterm (15%)
  - When: Feb 28th @ 6pm-7pm

Midterm #2 Results

	.id	N	overall	sd	se	ci
1	<NA>	587	74.64072	17.94863	0.7408191	1.454984

- 17 students with 100%

Today

- Group work activities
- Learning Catalytics Question
- Renal Physiology

Group Work

Sandra has been referred to a nephrology clinic due to the pain she has been experiencing in her lower back, which may be related to a problem with her kidneys. The following is her blood work and urinalysis results:

[Sodium]plasma = 8 mg/L

[Potassium]plasma = 2 mg/L

[Creatinine]plasma = 2 mg/L

[Glucose]plasma = 15 mg/L

[Magnesium]plasma = 20 mg/L

[Sodium]urine = 10 mg/L

[Potassium]urine = 12 mg/L

[Creatinine]urine = 120 mg/L

[Glucose]urine = 0 mg/L

[Magnesium]urine = 15 mg/L

Urine volume = 2.5 L/day

1. **Calculate Sandra's GFR.**
2. **What is the filtered load of sodium?**
3. **What is the filtered load of glucose?**
4. **What is the filtered load of magnesium?**
5. **What is the renal handling for potassium?**

Calculate the net filtration pressure if the forces are determined as the following:

Hydrostatic pressure of Bowman's capsule = 35 mmHg

Hydrostatic pressure of Glomerular capillaries = 60 mmHg

Colloid osmotic pressure of Bowman's capsule = 5 mmHg

Colloid osmotic pressure of Glomerular capillaries = 25 mmHg

Based on the calculation you have made, knowing that normal net filtration pressure is 10 mmHg, is this person filtering a normal volume, less or more volume of fluid per day?

Think of and discuss analogies that could help to understand renal physiology.

- ie. symporters are like Ferris wheels when the passengers get on, the Ferris wheel turns.
- post the analogy to Learning catalytics

Learning Catalytic Question

Sandra has been referred to a nephrology clinic due to the pain she has been experiencing in her lower back, which may be related to a problem with her kidneys. The following is her blood work and urinalysis results (Page 259):

1. **Calculate Sandra's GFR.**

$$GFR = \frac{[creatine]_{urine} * total\ urine\ volume}{[creatine]_{plasma}} = \frac{120\ mg/L * 2.5\ L/day}{2\ mg/L} = 150\ L/day$$

2. **What is the filtered load of sodium?**

$$Filtered\ Load_{Na} = [sodium]_{plasma} * GFR = 8\ mg/L * 150\ L/day = 1200\ mg/day$$

3. **What is the filtered load of glucose?**

$$Filtered\ Load_{Glucose} = [glucose]_{plasma} * GFR = 15\ mg/L * 150\ L/day = 2250\ mg/day$$

4. **What is the filtered load of magnesium?**

$$Filtered\ Load_{Mg} = [\text{magnesium}]_{plasma} * GFR = 20\ mg/L * 150\ L/day = 3000\ mg/day$$

5. **What is the renal handling for potassium?**

$$Filtered\ Load_{K} = [\text{potassium}]_{plasma} * GFR = 2\ mg/L * 150\ L/day = 300\ mg/day$$

$$Rate\ of\ Excretion_{K} = [\text{potassium}]_{urine} * total\ urine\ volume = 12\ mg/L * 2.5\ L/day = 30\ mg/day$$

$$\%\ Reabsorption = \frac{filtered\ load_{K} - rate\ of\ excretion_{K}}{filtered\ load_{K}} * 100 = \frac{300\ mg/day - 30\ mg/day}{300\ mg/day} * 100 = 90\%$$

Calculate the net filtration pressure if the forces are determined as the following:

Hydrostatic pressure of Bowman's capsule = 35 mmHg

Hydrostatic pressure of Glomerular capillaries = 60 mmHg

Colloid osmotic pressure of Bowman's capsule = 5 mmHg

Colloid osmotic pressure of Glomerular capillaries = 25 mmHg

$$NFP = (P_{GC} + \pi_{BC}) - (P_{BC} + \pi_{GC}) = (60\ mmHg + 5\ mmHg) - (35\ mmHg + 25\ mmHg) = 5\ mmHg$$

Based on the calculation you have made, knowing that normal net filtration pressure is 10 mmHg, is this person filtering a normal volume, less or more volume of fluid per day?

Since it is less than normal, this person would filter less fluid per day than a healthy individual.

Renal Physiology

Chapter 8: Dr. Woods

An individual suffers from kidney failure, which leads to development of a disease. Their symptoms are likely linked to …

A. Build up of waste
B. Inability to produce new glucose
C. Inability to produce hormones
D. Severe ion imbalance

An individual suffers from kidney failure, which leads to development of a disease. Their symptoms are likely linked to …

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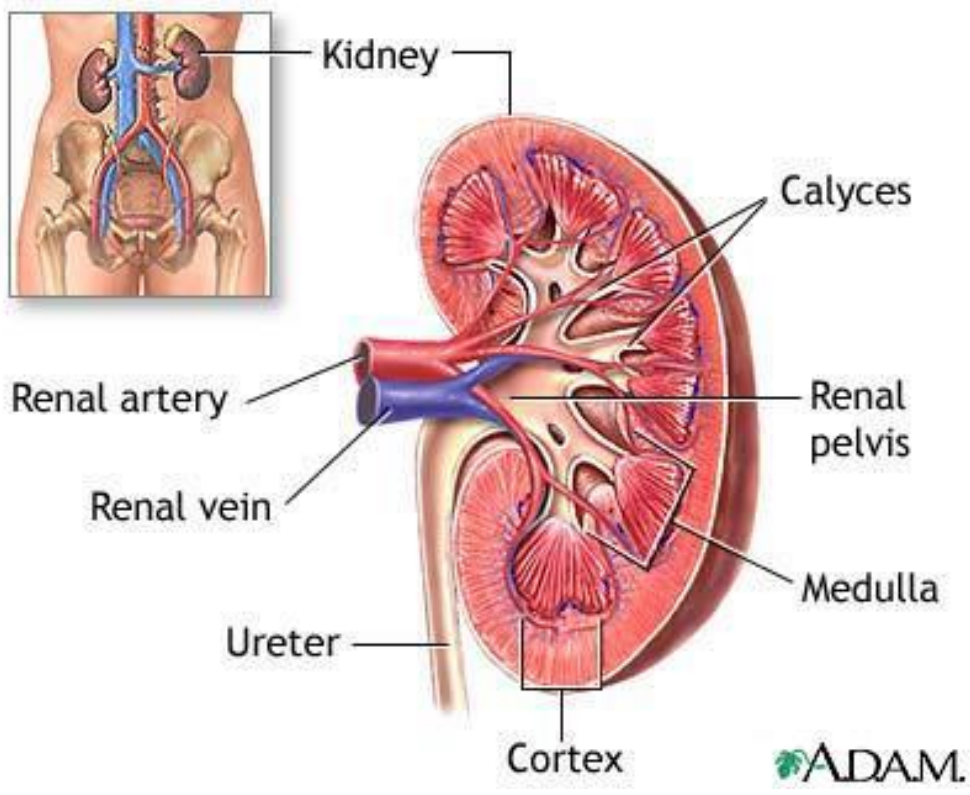
Kidney Functions

1. Regulation of ECF volume and blood pressure
2. Regulation of osmolarity
3. Maintain ion balance
4. Maintenance of body pH
5. Excretion of wastes
6. Production of hormones
7. Gluconeogenesis

The kidneys most important role is to regulate salt and water balance, not to remove waste

Kidney Anatomy

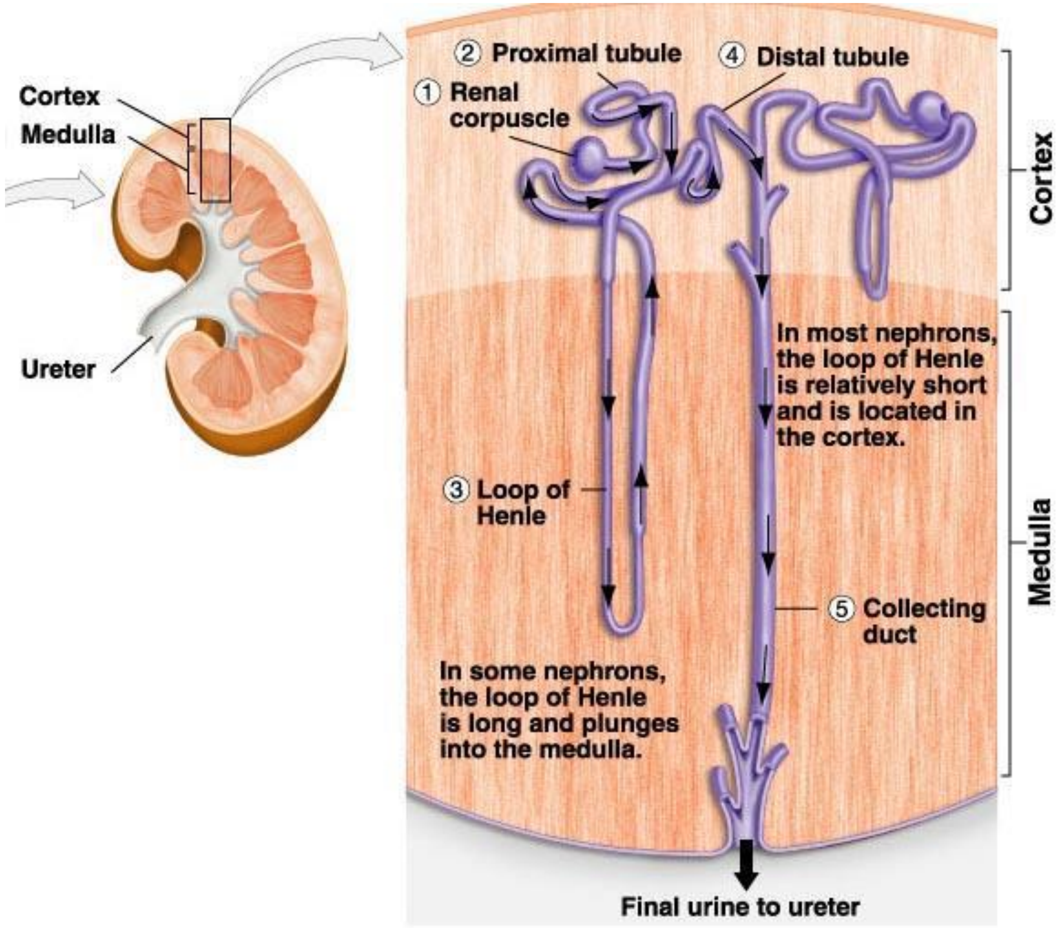
- Two kidneys that sit posterior and outside of abdominal cavity (i.e. retroperitoneal)
- Cortex = outer portion
- Medulla = inner portion
- Fluid collected into minor calyces → major calyces → renal pelvis → ureter
- Renal artery carries blood to kidneys
- Renal vein carries blood away from kidneys



Nephron

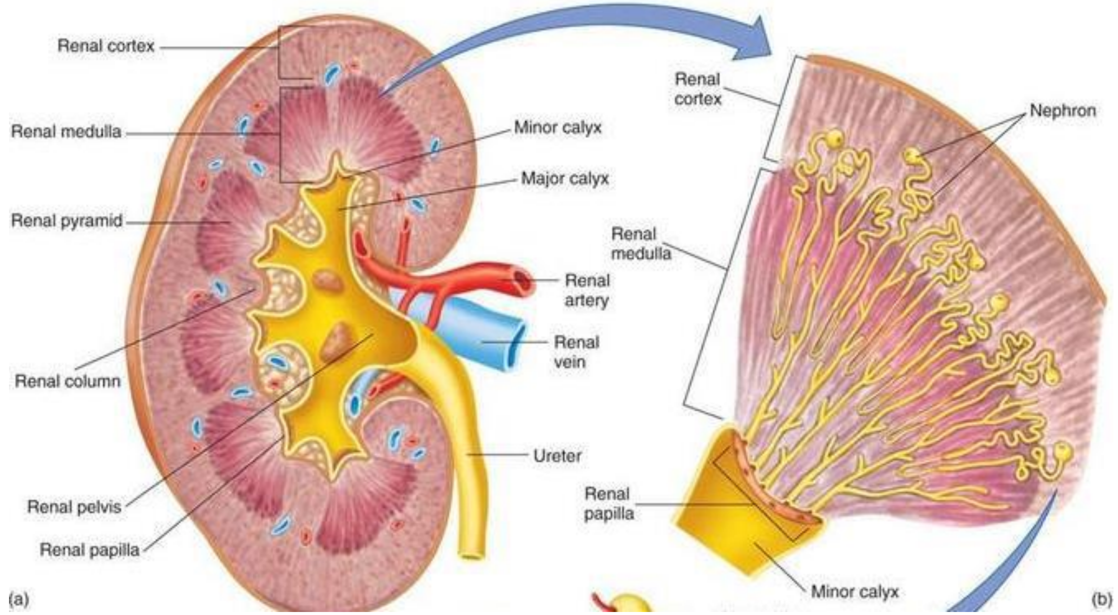
- Functional unit of kidney
- ~1 million per kidney
- Two major components:

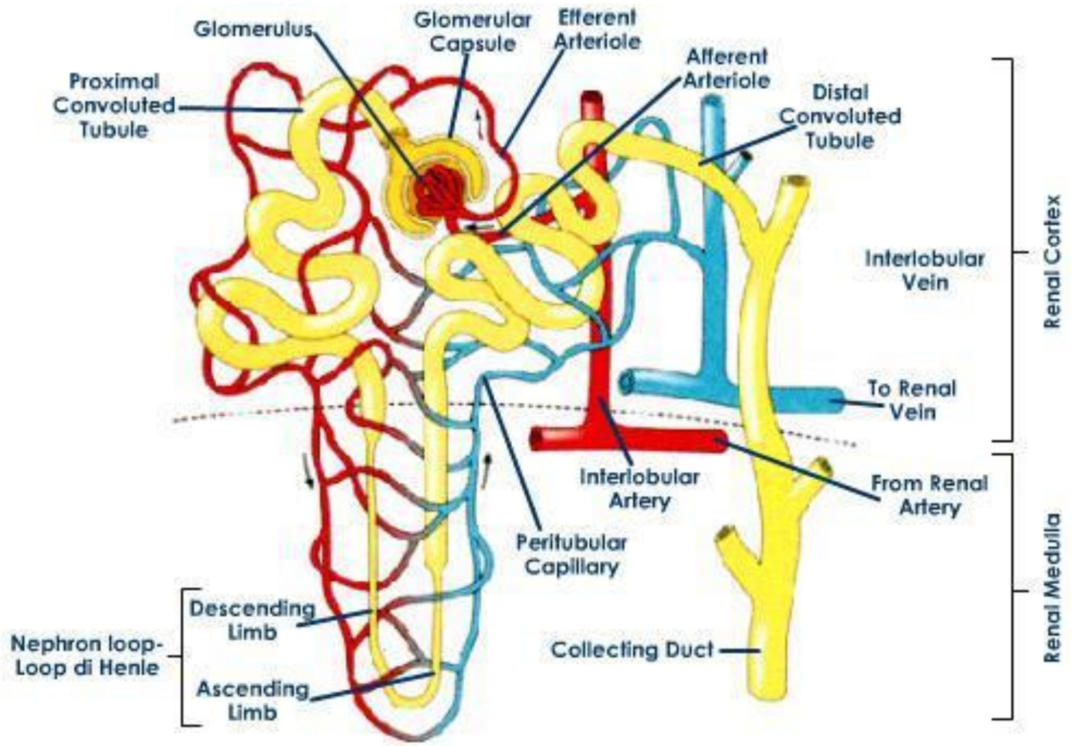
1. Renal corpuscle:
   - ➢ Contains glomerulus and Bowman's capsule
   - ➢ Where filtration occurs
2. Tubule
   - ➢ Proximal tubule → descending limb of loop of Henle → ascending limb of loop of Henle → distal convoluted tubule
   - ➢ Where reabsorption and secretion occur



Nephron Organization In The Kidney

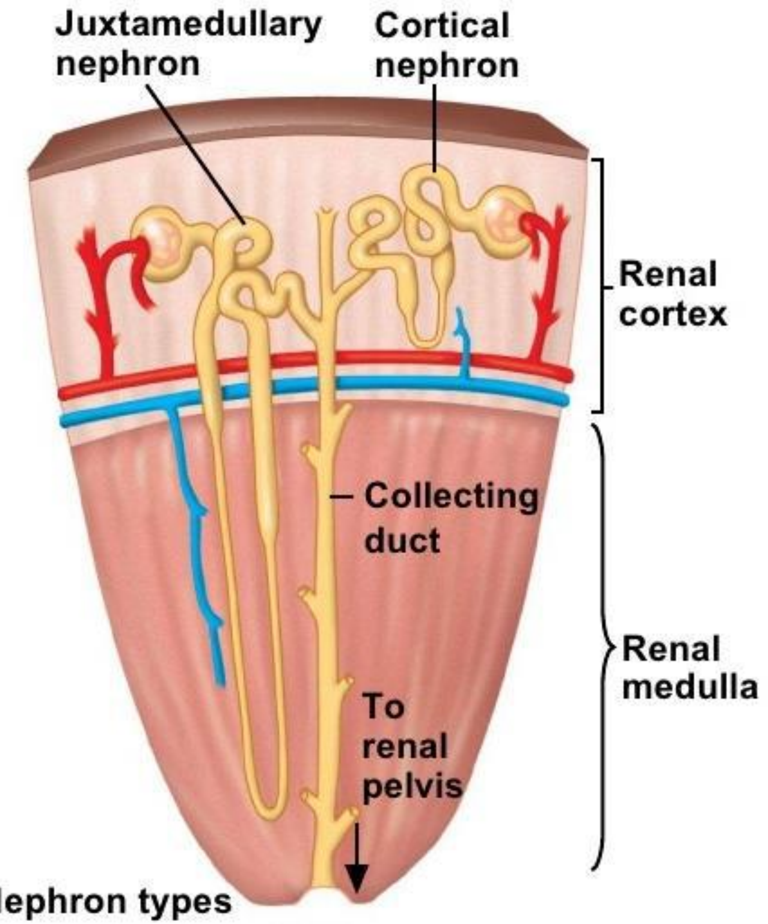
- Renal corpuscle located in cortex
- Loop of Henle projects into and out of renal medulla
- 4-5 nephrons share a collecting duct
- Collecting ducts drain into minor calyx
- In 3D, the ascending limb is found near the glomerulus





Types of Nephrons

	Juxamedullary Nephron	Cortical Nephron
# in Kidney	Few	Many
Ability to concentrate urine	Good	Bad
Ability to filter blood	Good	Good
Location of Corpuscle in Cortex	Low	High
Loop of Henle	Long	Short
Capillaries	Vasa recta	Peritubular



(c) Nephron types

If blood is detected in a patient's urine, you can conclude that:

A. There is damage to the glomerulus that lead to abnormal filtration
B. There is damage to the glomerulus that lead to abnormal reabsorption
C. There is damage to the collecting duct that lead to abnormal reabsorption
D. There is damage to the colleting duct that lead to abnormal secretion

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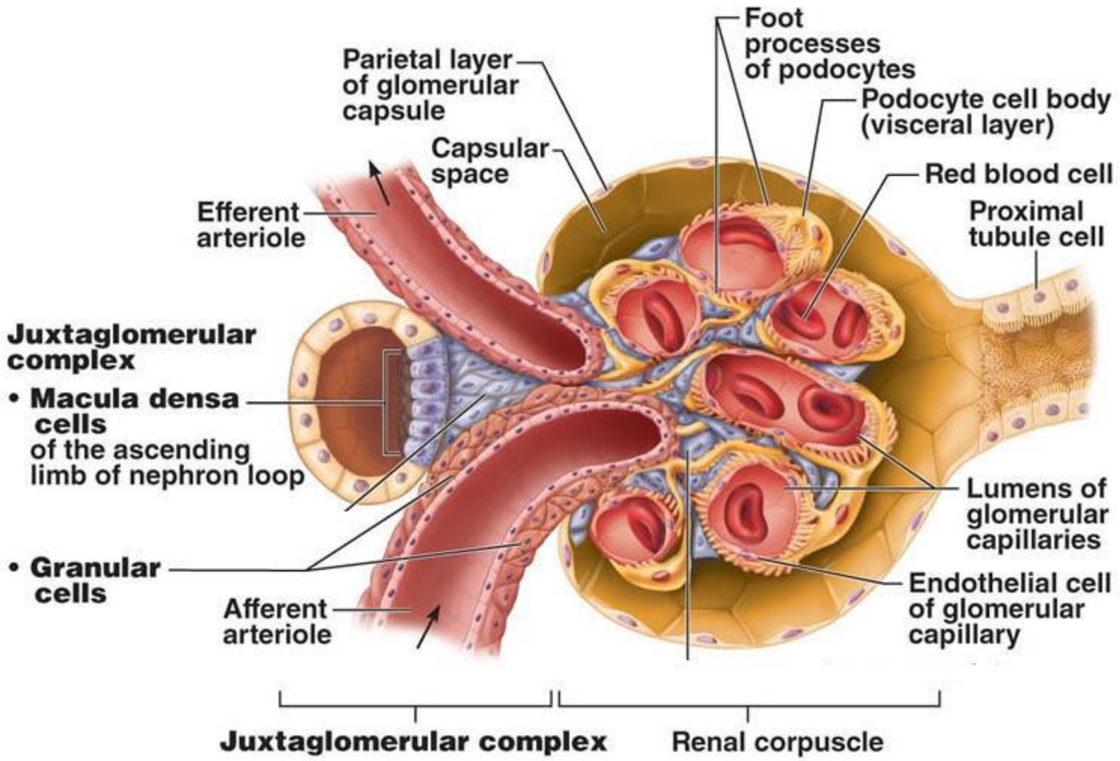
C. There is damage to the collecting duct that lead to abnormal reabsorption

D. There is damage to the colleting duct that lead to abnormal secretion

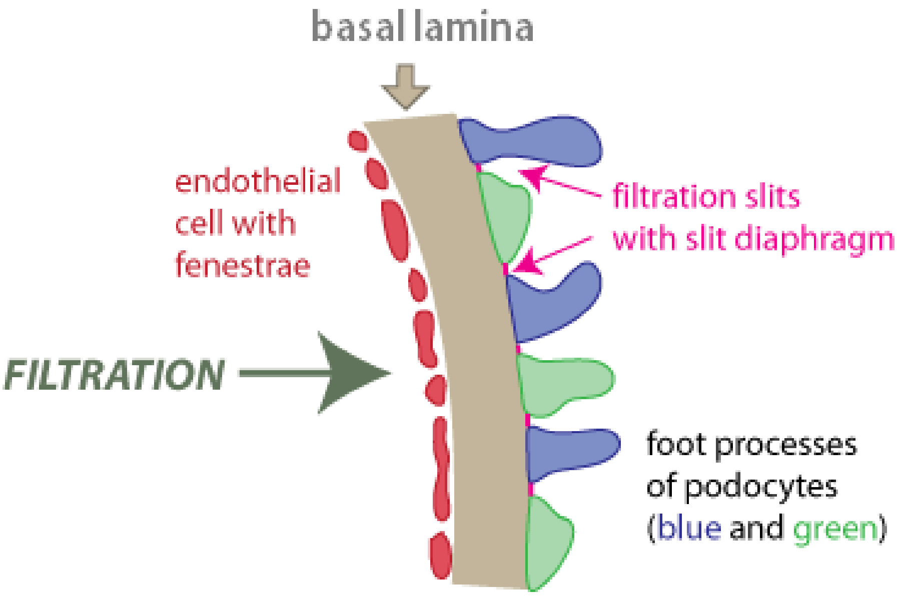
Renal Corpuscle

- Glomerulus: Group of fenestrated capillaries
- Fenestrations allow passage of many substances (ions, water, etc.) into Bowman's space (except red/white blood cells)
- Cells of Bowman's capsule (outer layer) are simple squamous epithelial cells
- Cells of Bowman's capsule (inner layer) are called podocytes
- Cells of glomerular capillaries are called endothelial cells
- Endothelial cells are fused with podocytes by basal lamina



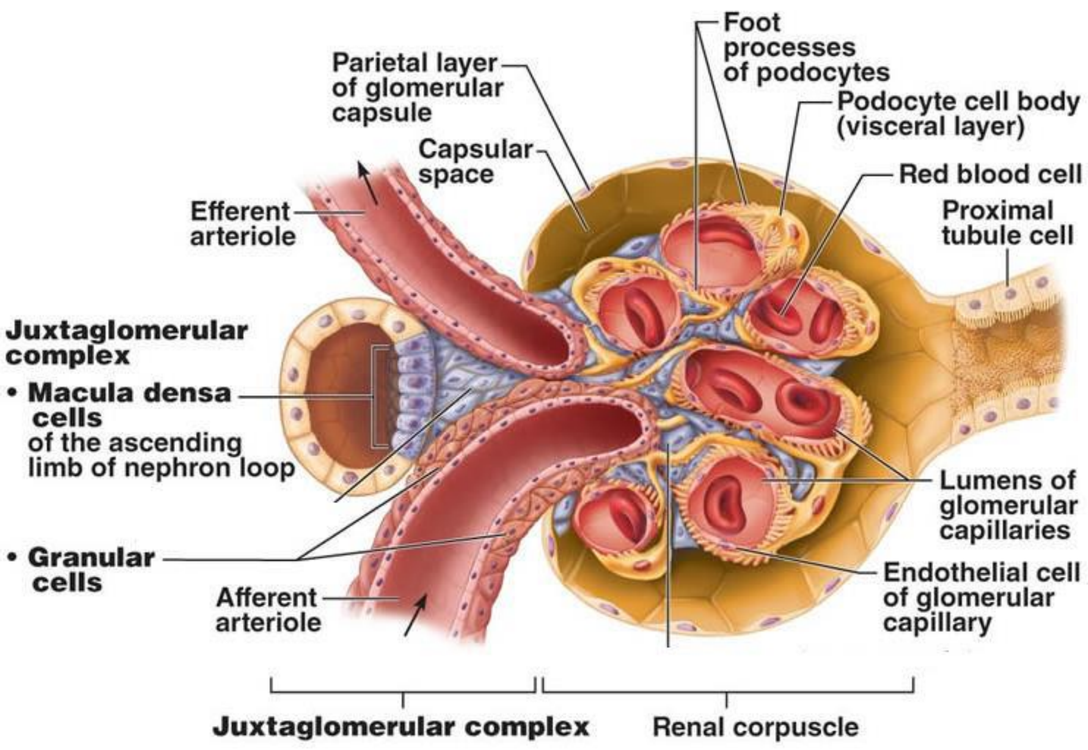
Barriers to Filtration

1. Size of glomerular gaps/fenestrations
2. Gaps in basal lamina
3. Space between podocytes



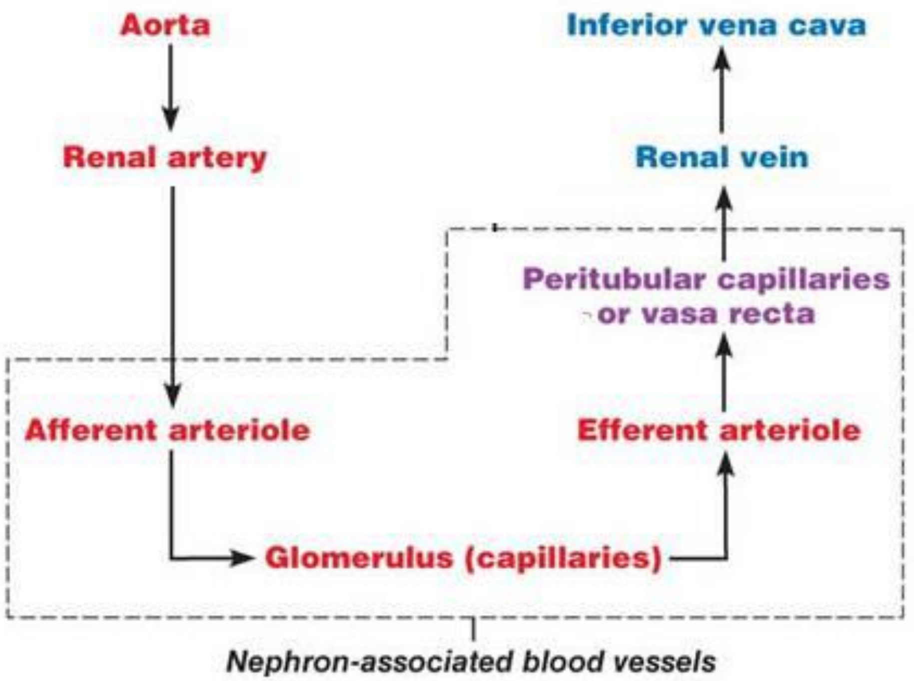
Juxtaglomerular Apparatus (JGA)

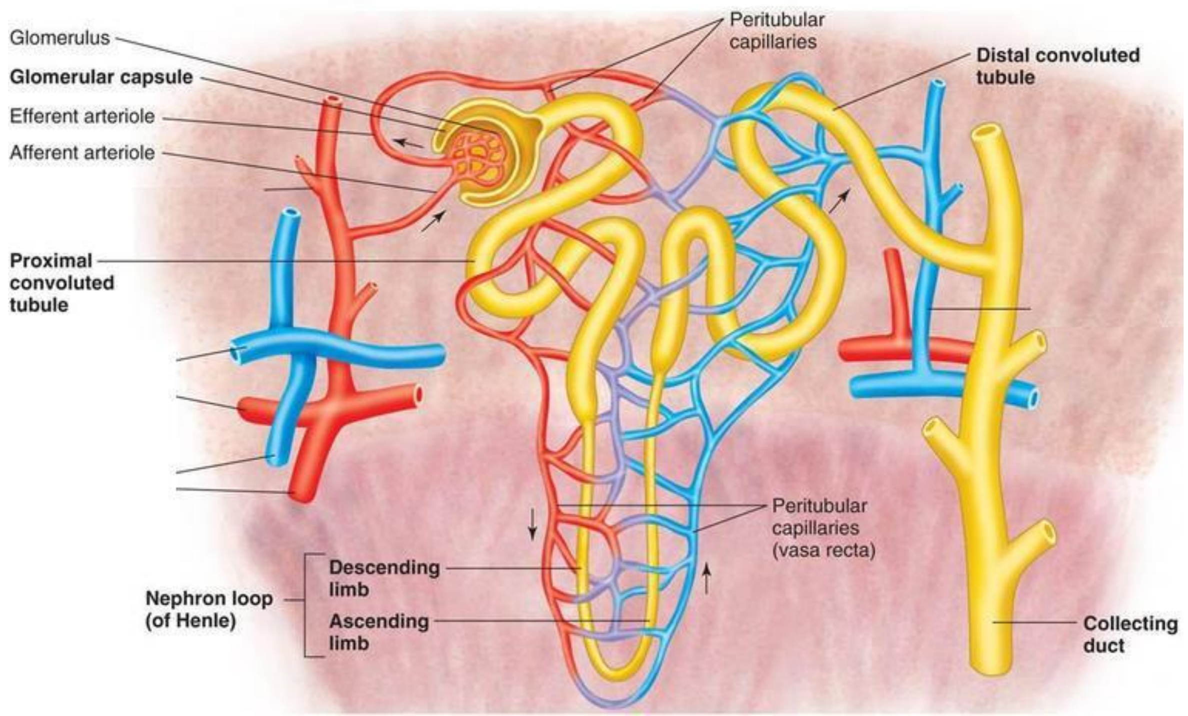
- Structure formed by late ascending loop of Henle passing between afferent and efferent arteriole near renal corpuscle
- Specialized cells of ascending limb called macula densa cells
  - ➢Detect [Na^+] and [Cl^-] in filtrate
- Specialized cells on arteriole called granular cells
  - ➢Produce renin



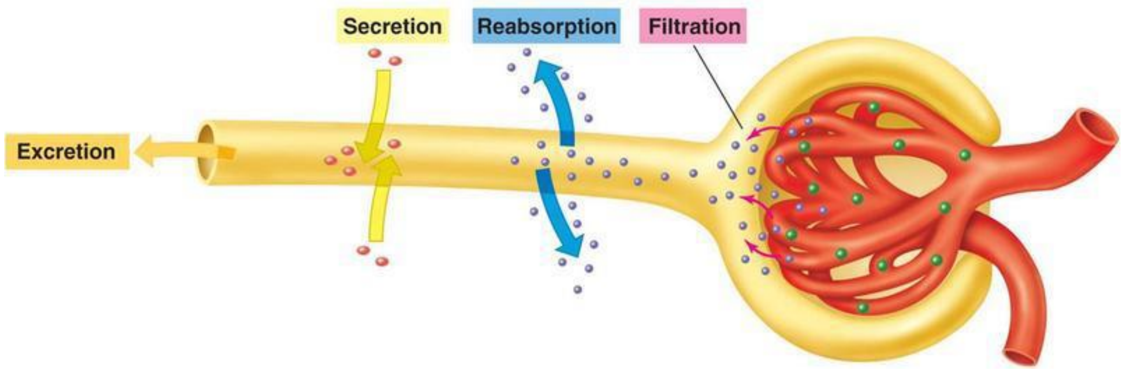
Blood Flow In Kidneys

- Receives 20% of cardiac output





3 Key Processes



	Filtration	Reabsorption	Secretion
Where does it occur?	Renal Corpuscle	Tubule	Tubule
From _____ to _____.	From glomerular capillaries to Bowman's space	From lumen of tubule to surrounding capillaries (peritubular/ vasa recta)	From surrounding capillaries (peritubular/vasa recta) to lumen of tubule
Overall	Blood → Pre-urine (filtrate)	Removes from filtrate (e.g. body wants to keep)	Adds to filtrate (e.g. body wants to remove as waste)

Glomerular Filtration

- Of all the blood that arrives at kidney, only 20% is filtered
- Net filtration pressure (NFP): Sum of forces that affect filtration
  - NFP > 0: filtration
  - NFP ≤ 0: no filtration

	Hydrostatic Pressure of Glomerular Capillaries	Colloid Osmotic Pressure of Glomerular Capillaries	Hydrostatic Pressure of Bowman's Capsule	Colloid Osmotic Pressure of Bowman's Capsule
Abbreviation	P_{GC}	π_{GC}	P_{BC}	π_{BC}
Caused by	Blood flowing into glomerulus	Presence of proteins in glomerulus	Filtrate remaining in Bowman's space	Presence of proteins in Bowman's space
Filtration	Promotes	Inhibits	Inhibits	Promotes
mmHg	55	30	15	0

NFP Calculation

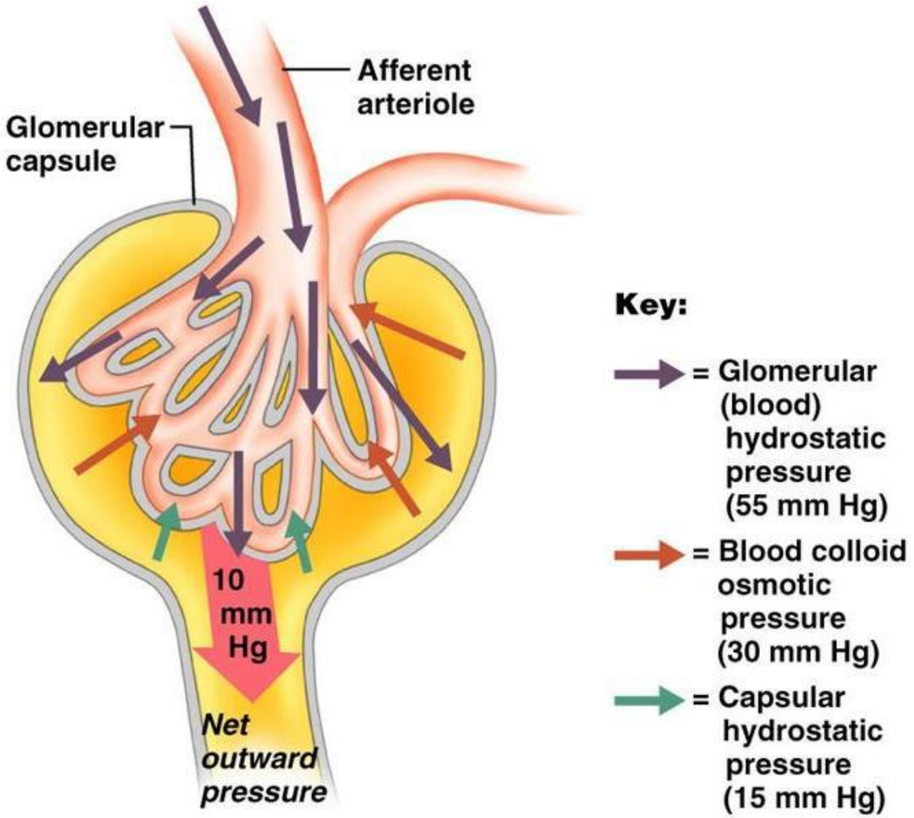
- NFP = Promotes Filtration – Inhibits Filtration

$$= (P_{GC} + \pi_{BC}) - (P_{BC} + \pi_{GC})$$

$$= (55 + 0) - (15 + 30)$$

$$= 10 \text{ mmHg}$$

	P_{GC}	π_{GC}	P_{BC}	π_{BC}
Filtration	Promotes	Inhibits	Inhibits	Promotes
mmHg	55	30	15	0



Will filtration occur if: P_{GC} = 20 mmHg, P_{BC} = 20 mmHg, π_{GC} = 15 mmHg, π_{BC} = 5 mmHg,

A. No, because NFP = -10 mmHg
B. Yes, because NFP = +10mmHg
C. No, because NFP = -20mmHg
D. Yes, because NFP = +20mmHg

Will filtration occur if: P_{GC} = 20 mmHg, P_{BC} = 20 mmHg, π_{GC} = 15 mmHg, π_{BC} = 5 mmHg,

A. No, because NFP = -10 mmHg
B. Yes, because NFP = +10mmHg
C. No, because NFP = -20mmHg
D. Yes, because NFP = +20mmHg

$$NFP = (P_{GC} + \pi_{BC}) - (P_{BC} + \pi_{GC}) = (20 + 5) - (20 + 15) = -10 \text{ mmHg}$$

Glomerular Filtration Rate (GFR)

- Volume of fluid filtered per day by the kidneys
- Normal: 180 L/day
- Important to maintain a constant GFR throughout the day
- Affected by:
  1. Net Filtration Pressure (NFP)
     - Mostly affected by renal blood flow and pressure (P_{GC})
  2. Filtration Coefficient
     - Mostly affected by podocytes and basal lamina

GFR Regulation: Myogenic Response

↑ Arterial blood pressure

↓

↑ Afferent arteriolar blood pressure

↓

↑ Afferent arteriole stretches

↓

↑ Sensing by stretch sensitive ion channels (opening)

↓

↑ Depolarization of smooth muscle open voltage-gated Ca^{2+} channels

↓

↑ Smooth muscles of afferent arteriole contraction

↓

↑ Vasoconstriction

↓

↓ Blood flow in glomerulus

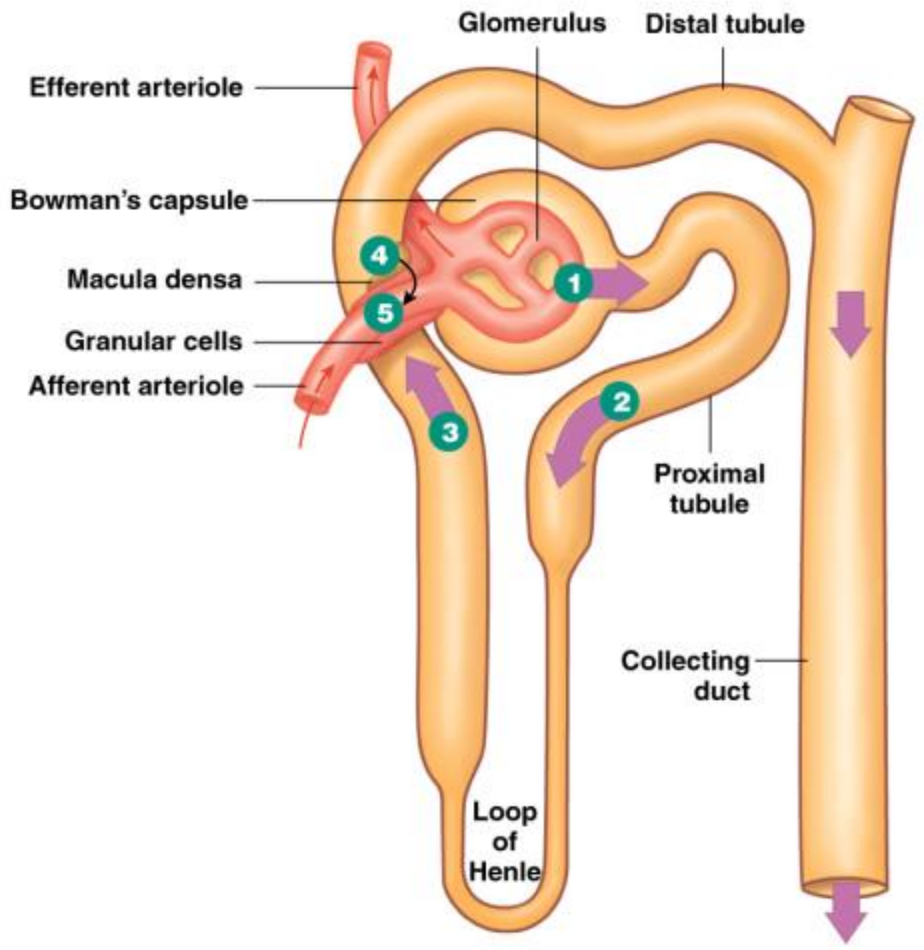
GFR Regulation: Tubuloglomerular feedback

1. GFR increases.
2. Flow through tubule increases.
3. Flow past macula densa increases.
4. Paracrine from macula densa to afferent arteriole
5. Afferent arteriole constricts.

Resistance in afferent arteriole increases.

Hydrostatic pressure in glomerulus decreases.

GFR decreases.



GFR Regulation: Overview

- Both the myogenic response and tubuloglomerular response are used to increase and decrease GFR
- Their combined goal is to mediate a constant GFR throughout the day

	Afferent Arteriole		Efferent Arteriole	
Smooth Muscle	**Dilate**	**Constrict**	**Dilate**	**Constrict**
GFR	⬆	⬇	⬇	⬆

Measurement of GFR

- In order to measure GFR, you want to choose a substance that is excreted, but not reabsorbed
- Bad substances: glucose, ions, water
- Best substance: creatinine
- Rate of creatinine excretion from the body is equivalent to GFR
- GFR (L/day) = ([Creatinine]$_{urine}$ x Urine/day) / [Creatinine]$_{plasma}$

= (90 mg/L x 2 L/day) / (1 mg/L)

= 180 L/day

Renal Handling

- GFR can be used to calculate renal handling (i.e. what they kidney did to the substance from the plasma)
- Filtered Load of X = $[X]_{plasma}$ x GFR
- Reminder: Normal GFR = 180 L/day or 125 mg/min

Can you fill out this table?

Substance	Concentration (in plasma)	Filtered Load	Amount Excreted	% Excreted	% Reabsorbed
Sodium	3.5 g/L		3.2 g		
Glucose	1.0 g/L		0 g		
Urea	0.31 g/L		28 g		

Renal Handling

Example: Urea

- Filtered Load of Urea = $[\text{Urea}]_{plasma}$ x GFR = 0.31 x 180

  = 56 g/day

- % Excreted = (Amount Excreted/Filtered Load) x 100% = (28/56) x 100%

  = 50 %

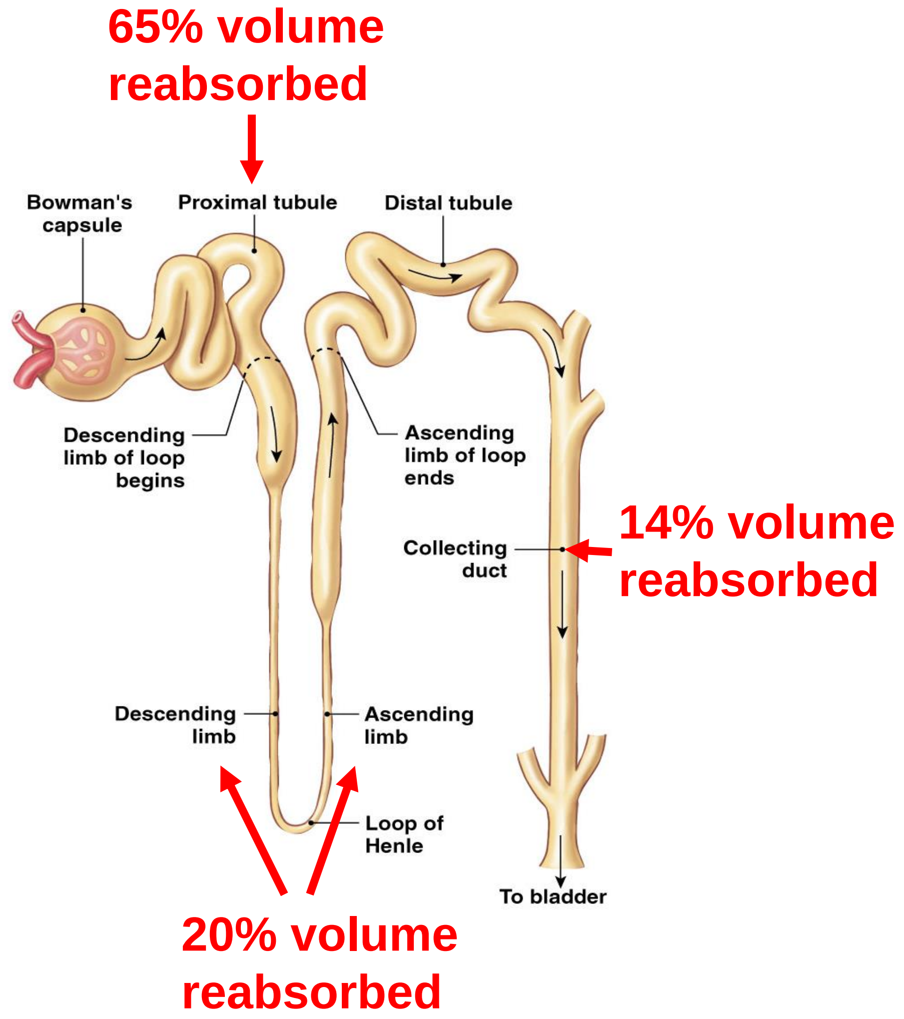
- % Reabsorbed = 100 -% Excreted = 100 –50

  = 50%

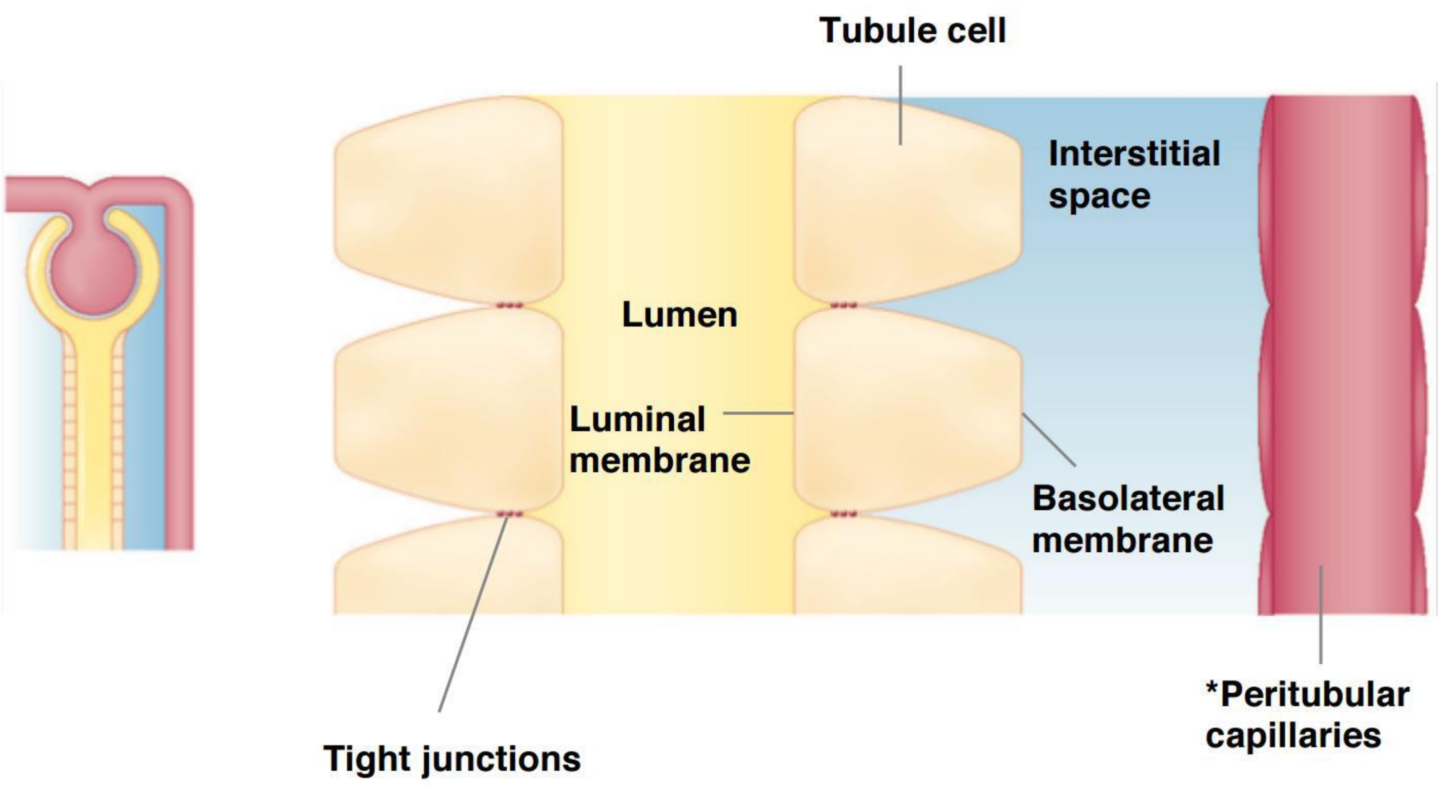
Substance	Concentration (in plasma)	Filtered Load	Amount Excreted	% Excreted	% Reabsorbed
Sodium	3.5 g/L	630 g/day	3.2 g	0.5%	99.5%
Glucose	1.0 g/L	180 g/day	0 g	0%	100%
Urea	0.31 g/L	56 g/day	28 g	50%	50%

Reabsorption Along The Tubule

Segment of Tubule	Substances	Hormone Regulation	Percent
Proximal Tubule	Glucose, amino acids, H_2O, Na^+, K^+, Cl^-	Yes	65%
Descending Limb of LOH	H_2O, minimal Na^+	No	20 %
Ascending Limb of LOH	Na^+, K^+, Cl^-	No	
Distal Tubule	Na^+, K^+, Cl^- , Ca^{2+}	Yes	14%
Collecting Duct	H_2O, Na^+	Yes	



Cells of the Tubule



Cells of the Tubule

Reabsorption

Transcellular:

- Two-step process
- Moves through luminal, then basolateral membrane

Paracellular:

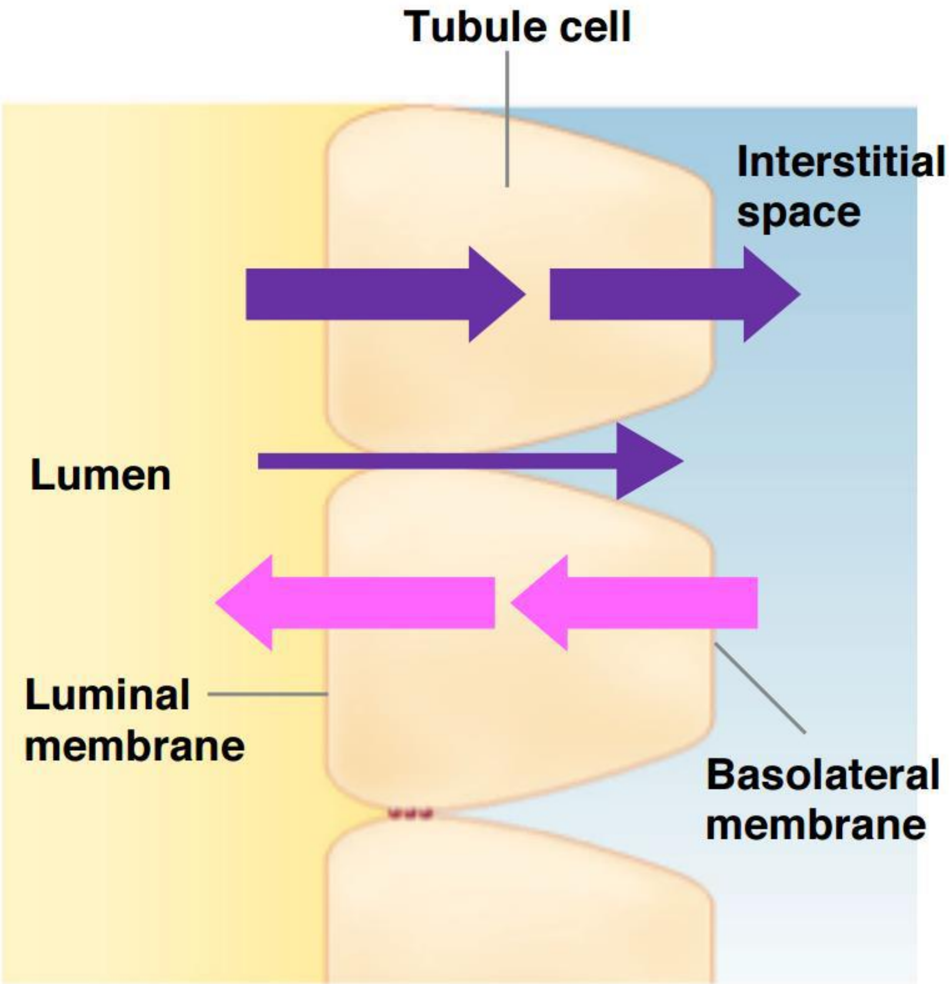
- One-step process
- In between tubule cells

Secretion

Always Transcellular:

- Moves through basolateral, then luminal membrane

No Paracellular



Transport Mechanisms

Chapter 8: Dr. Woods

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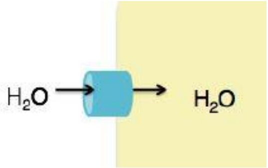
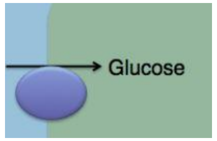
Review of Transport Mechanisms

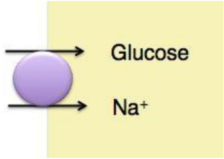
- Channels: Passive diffusion through a protein pore in membrane (ex: aquaporin)



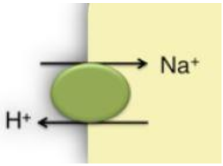
- Transporters: Carries molecule across membrane
  - Uniporters: Move a single molecule across membrane (ex: glucose uniporter)



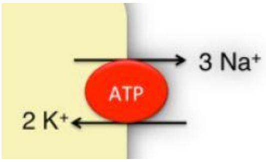
  - Symporters: Moves two molecules in the same direction across membrane. At least one molecule must move down its concentration gradient (ex: Na+/glucose symporter)

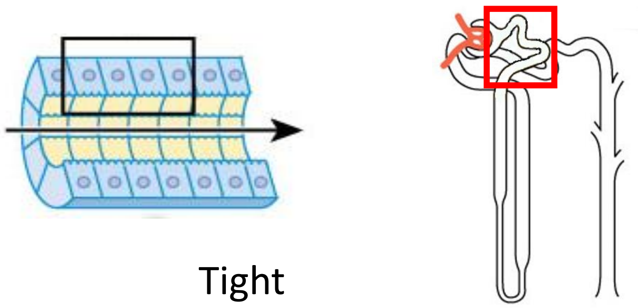


  - Antiporters: Moves two molecules in opposite directions across membrane. At least one molecule must move down its concentration gradient (ex: Na^+/H^+ antiporter)



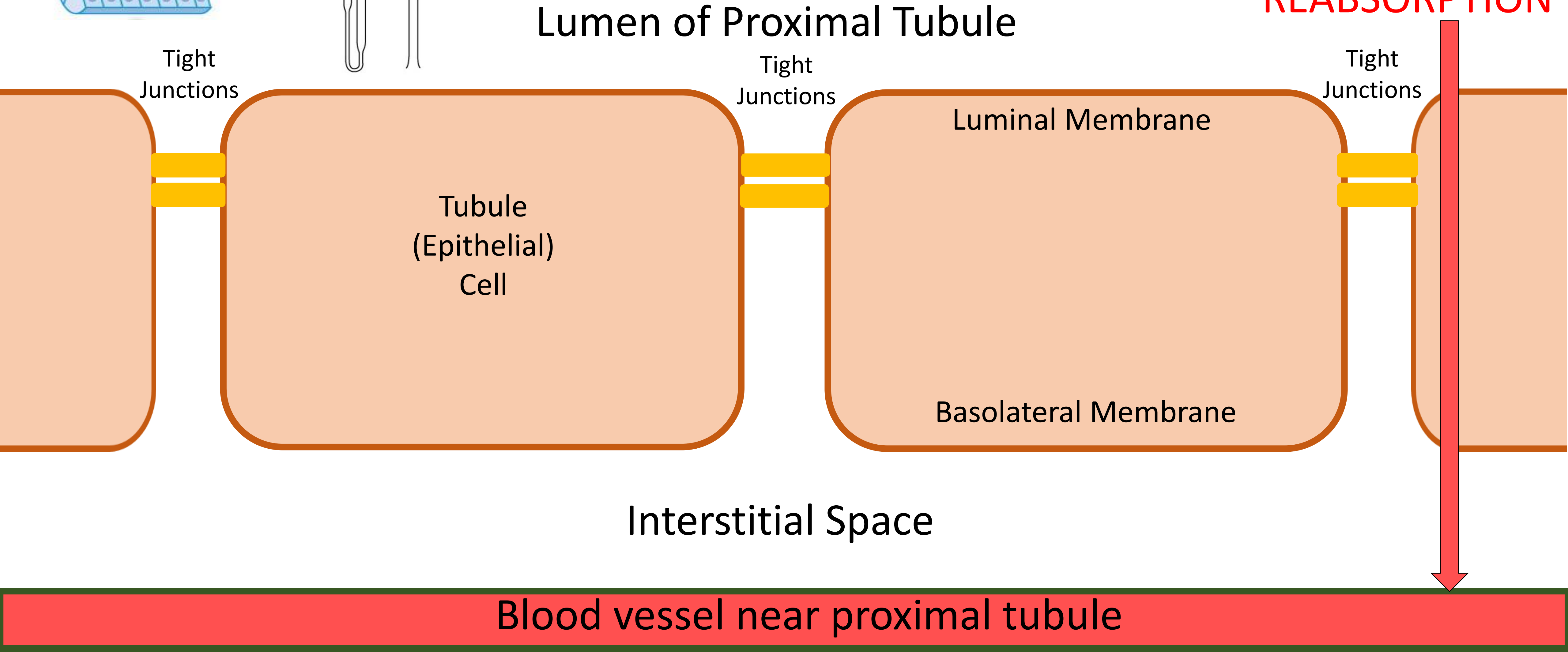
- Primary Active Transporters: Require ATP to move molecules against their concentration gradients (ex: Na^+/K^+ ATPase)



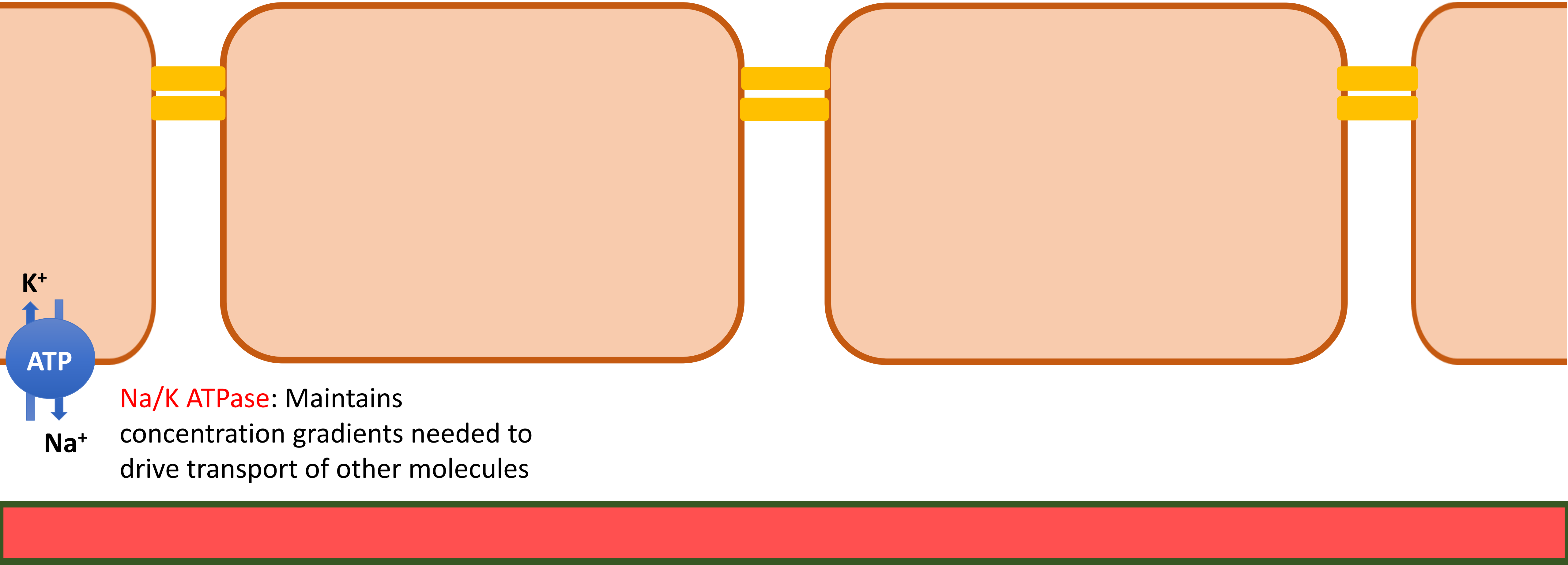


Proximal Tubule

Overall Goal:
REABSORPTION



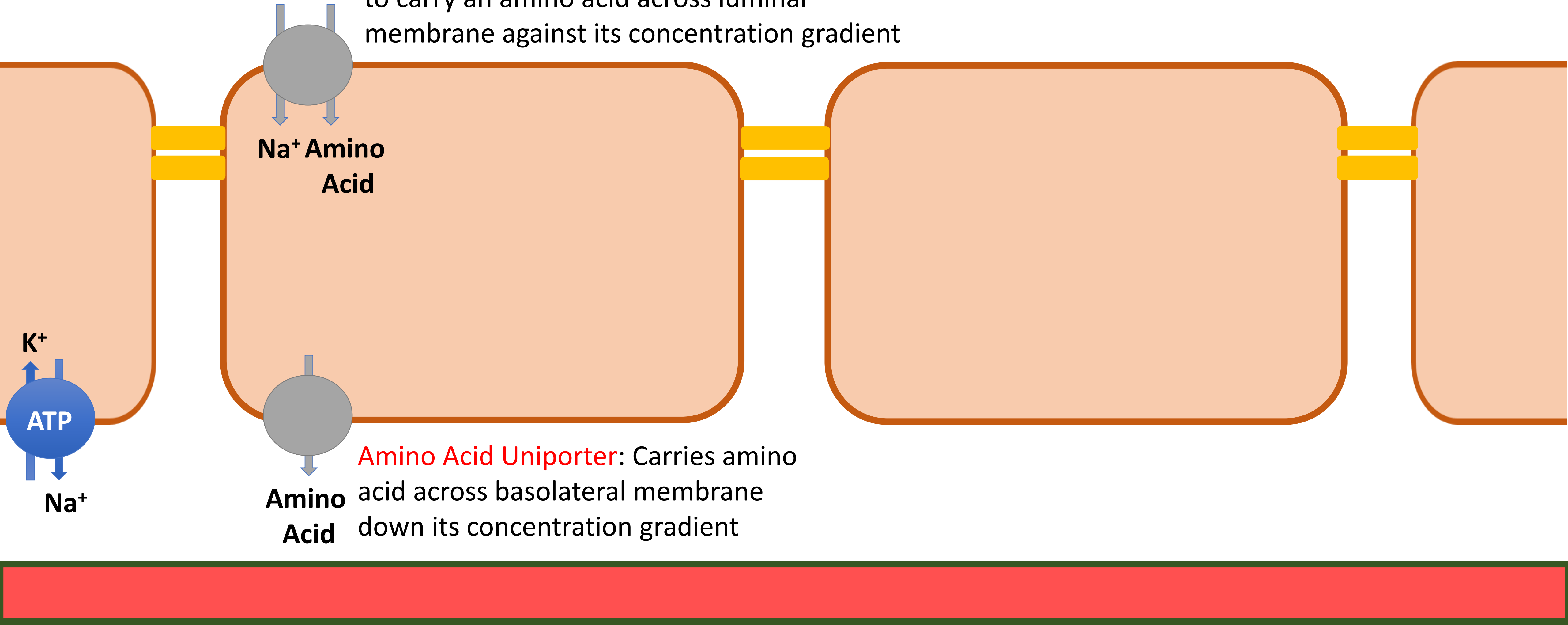
Sodium Potassium Pump



Na/K ATPase: Maintains concentration gradients needed to drive transport of other molecules

Reabsorbing Amino Acids

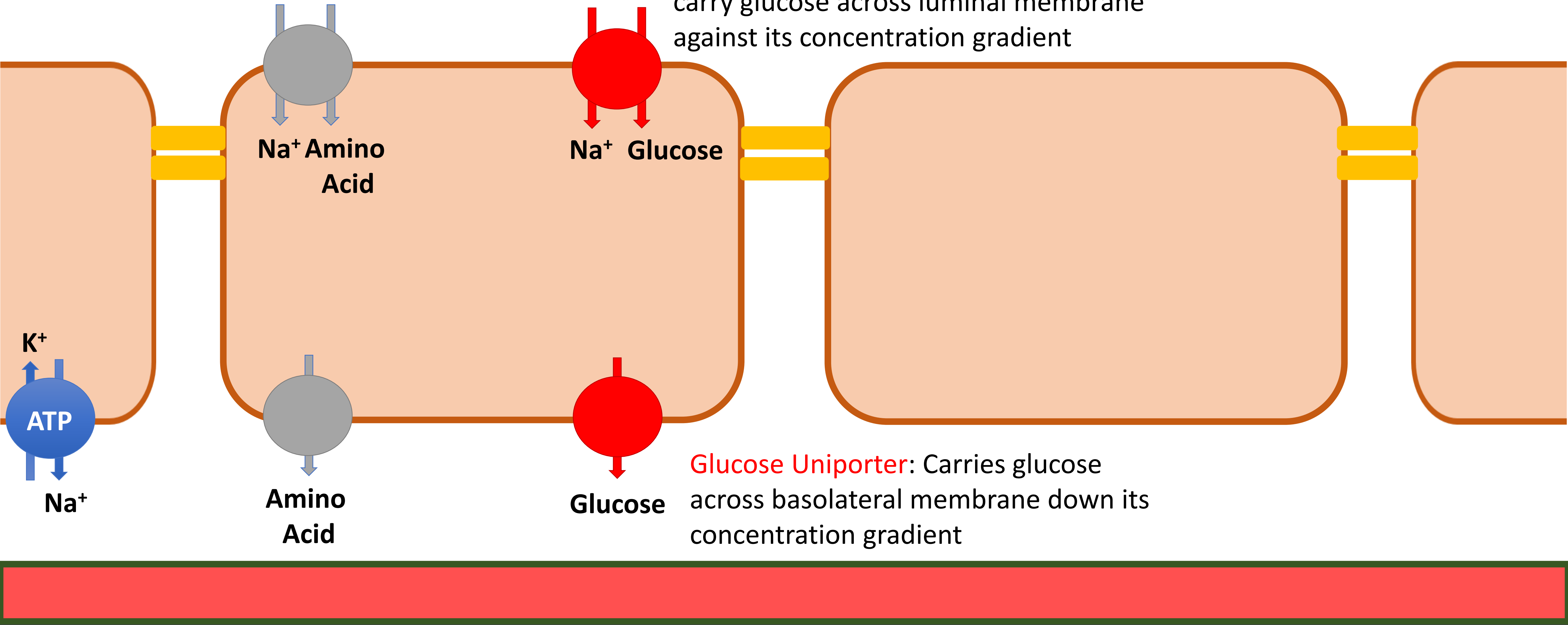
Na^+/Amino Acid Symporter: Uses Na^+ gradient to carry an amino acid across luminal membrane against its concentration gradient



Amino Acid Uniporter: Carries amino acid across basolateral membrane down its concentration gradient

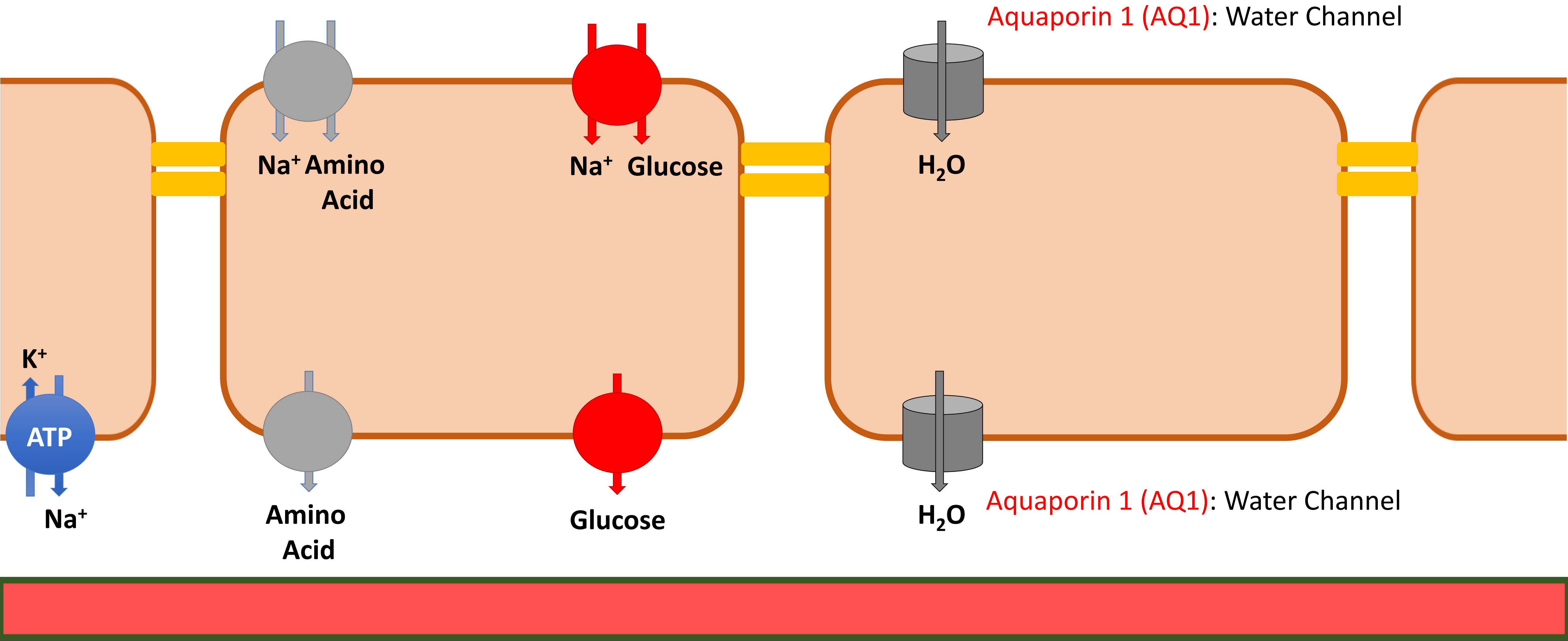
Reabsorbing Glucose (100%)

Na⁺/Glucose Symporter: Uses Na^+ gradient to carry glucose across luminal membrane against its concentration gradient

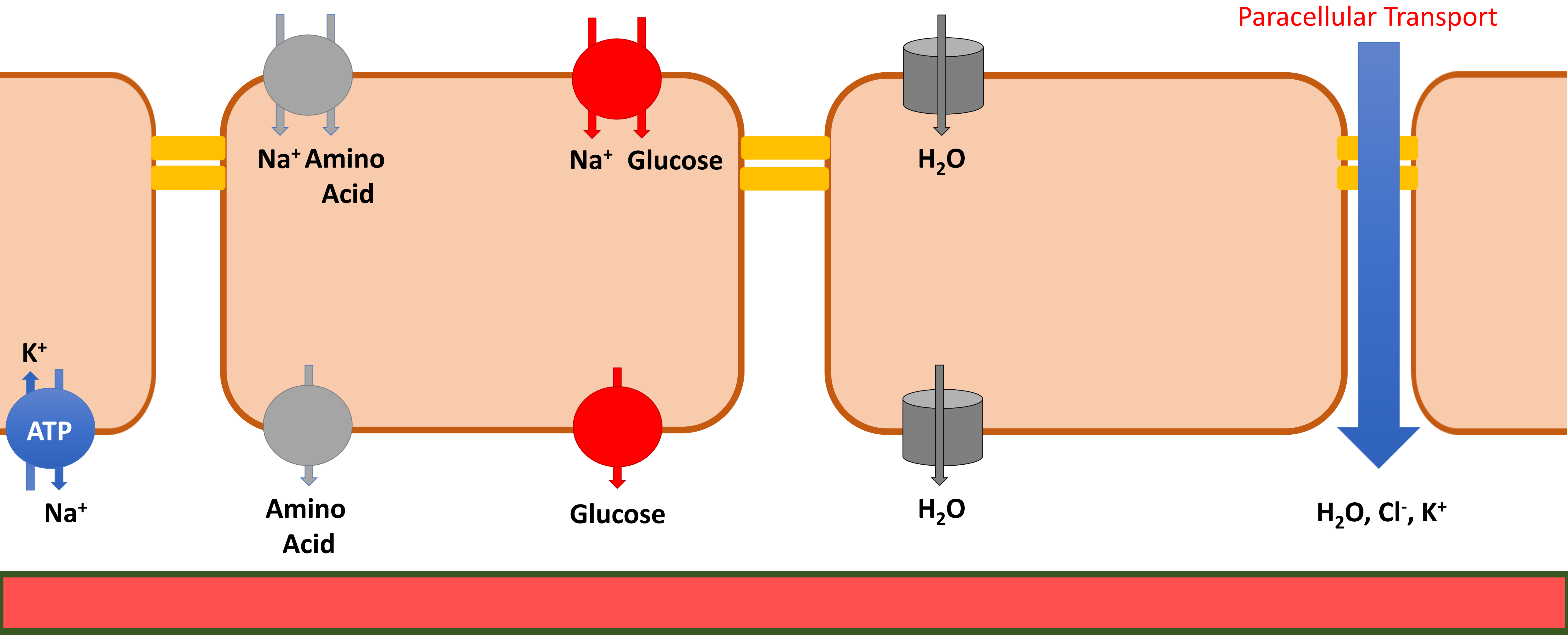


Glucose Uniporter: Carries glucose across basolateral membrane down its concentration gradient

Reabsorbing Water

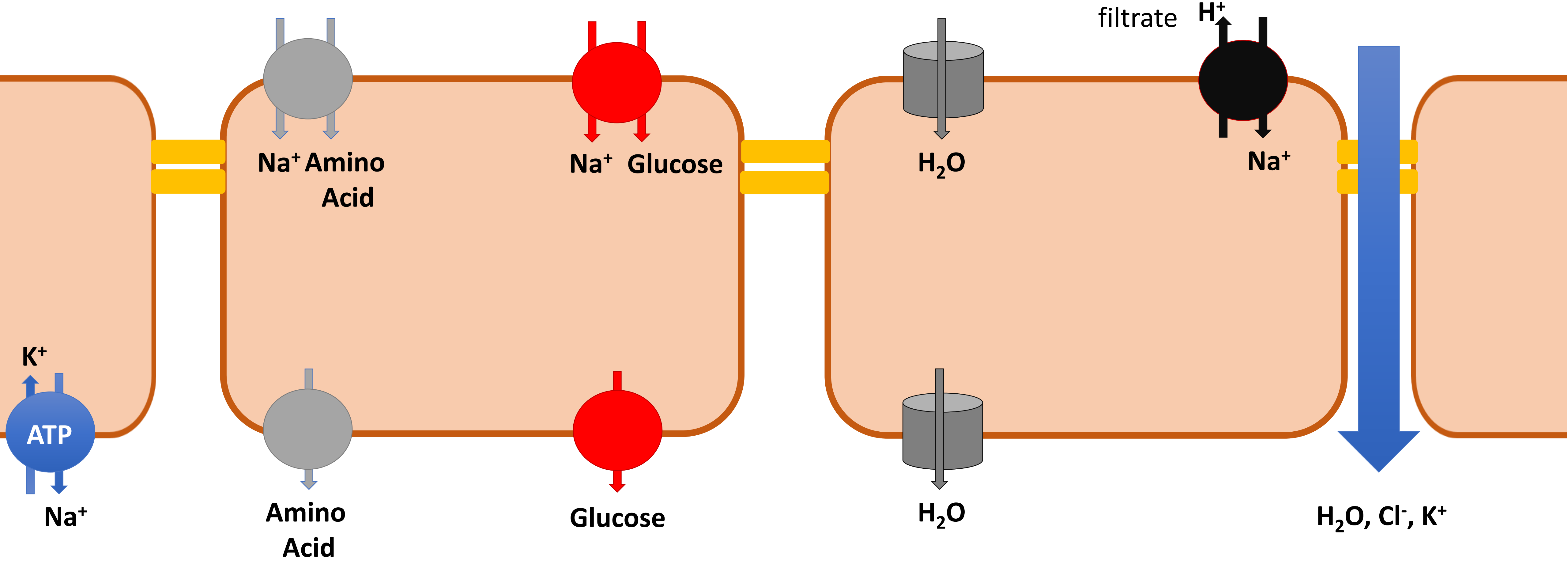


Reabsorbing Ions and More Water

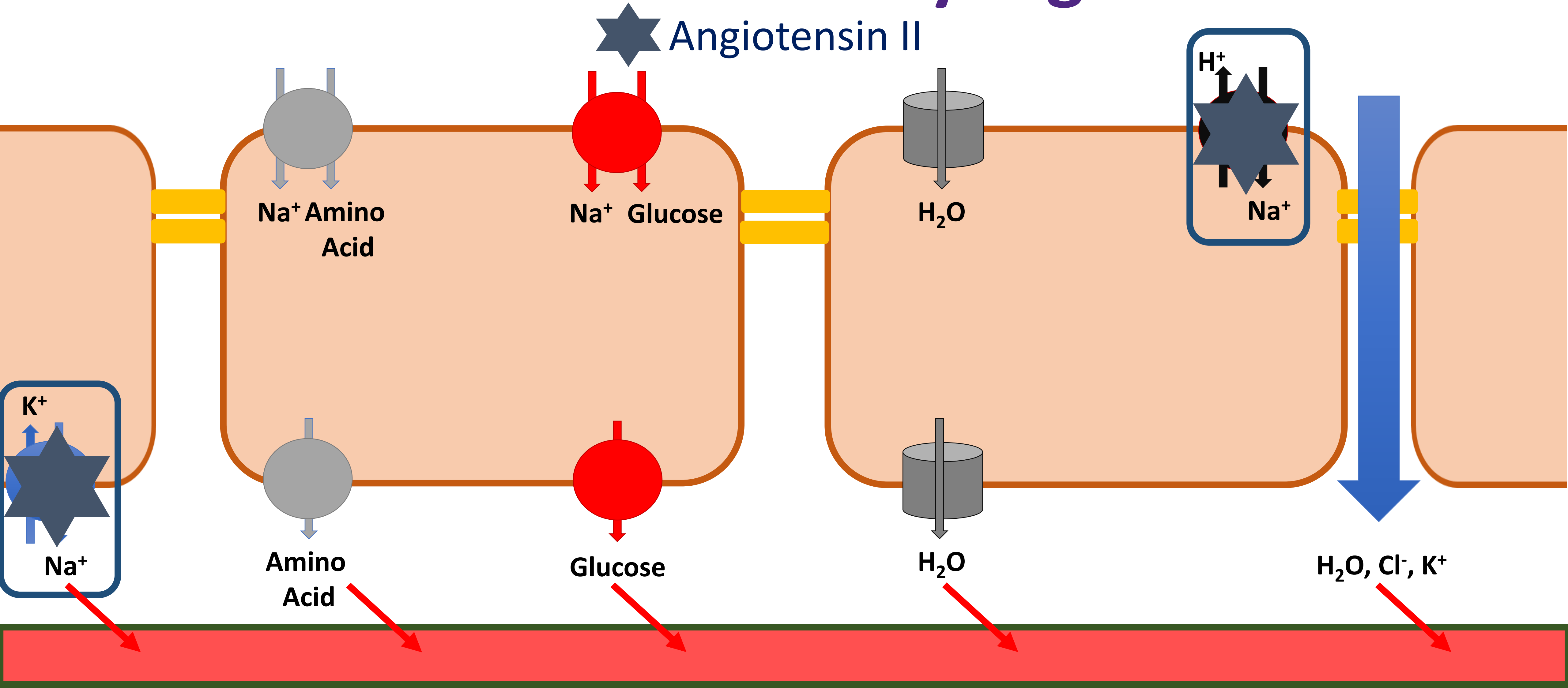


Regulating pH of filtrate/urine

Na/H+Antiporter/Exchanger: Uses Na gradient to carry H+ across luminal membrane into filtrate



Which are hormonally regulated?



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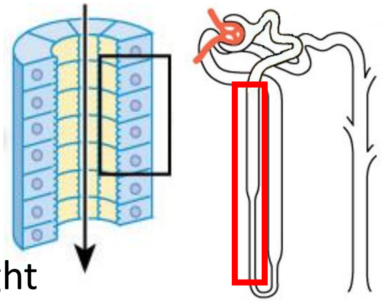
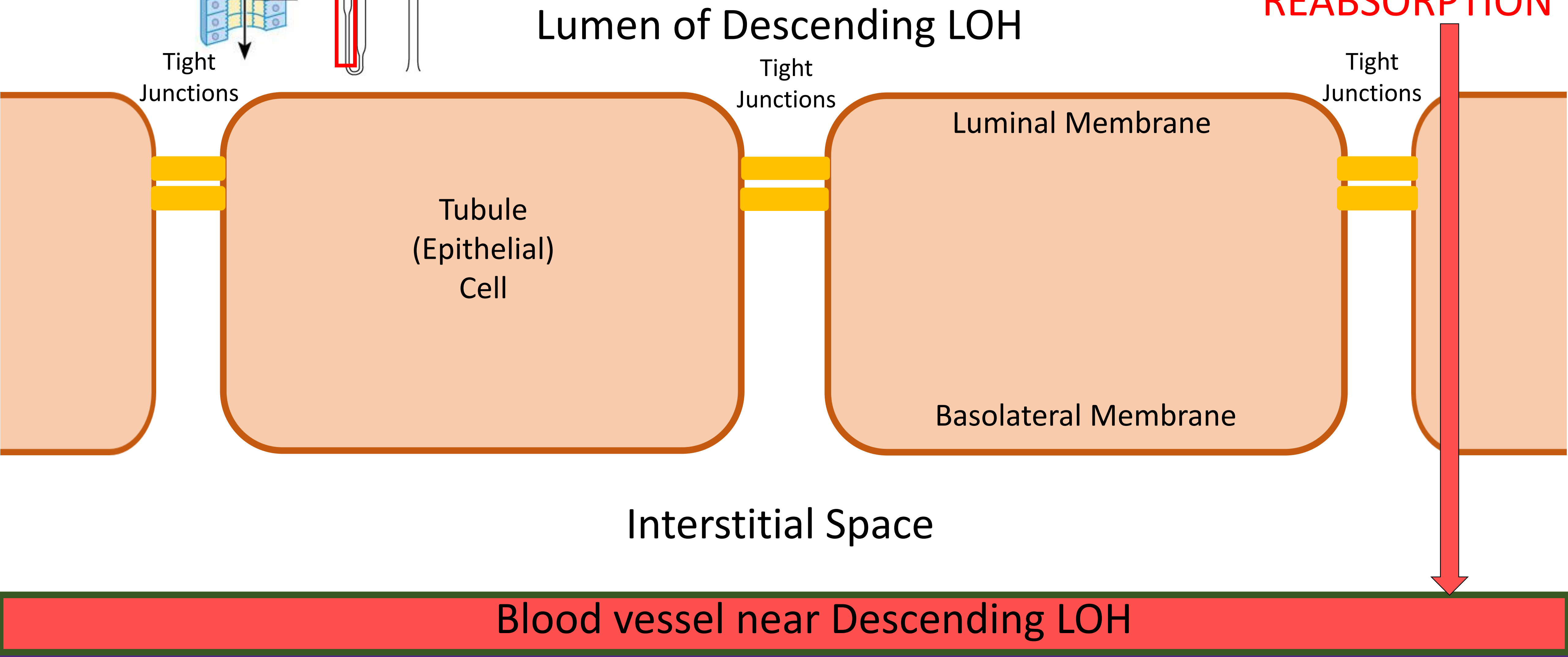
Descending LOH

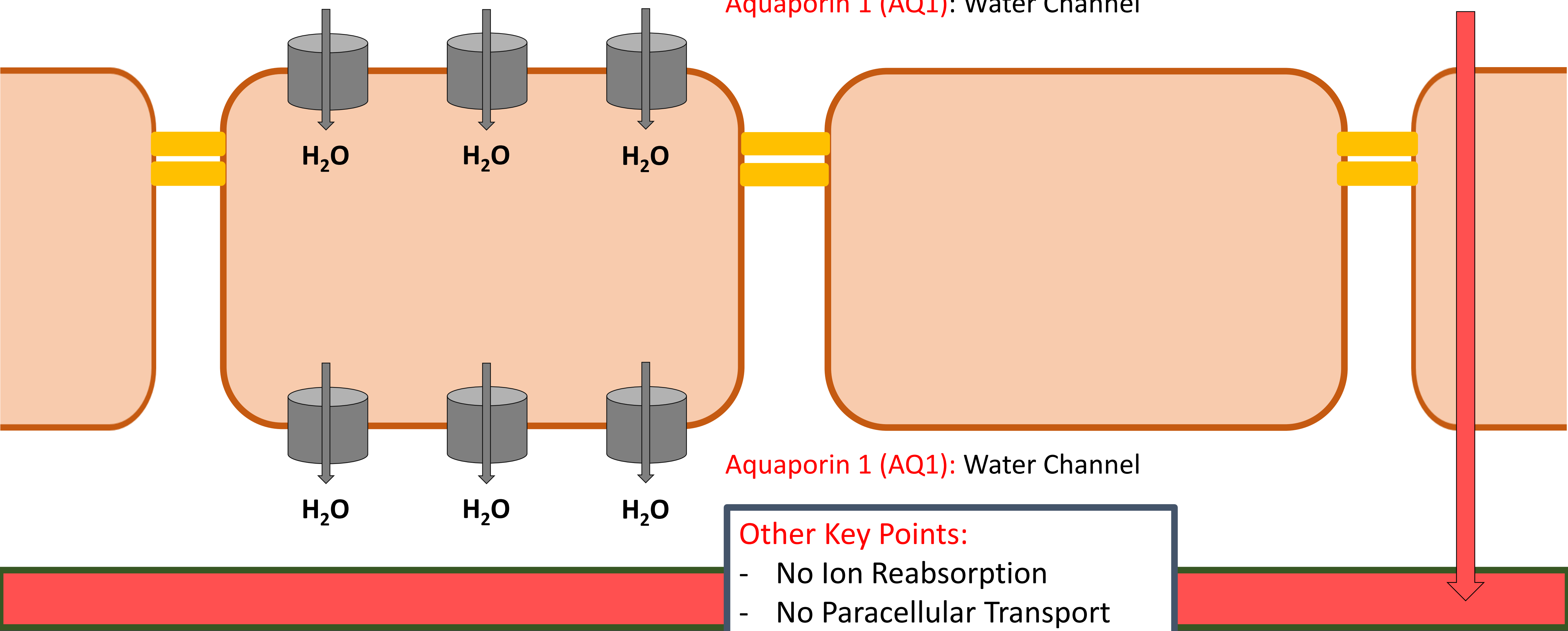


Overall Goal: REABSORPTION



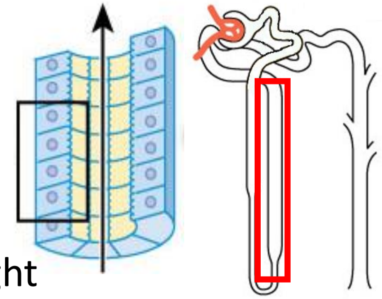
Descending LOH

Overall Goal: REABSORPTION

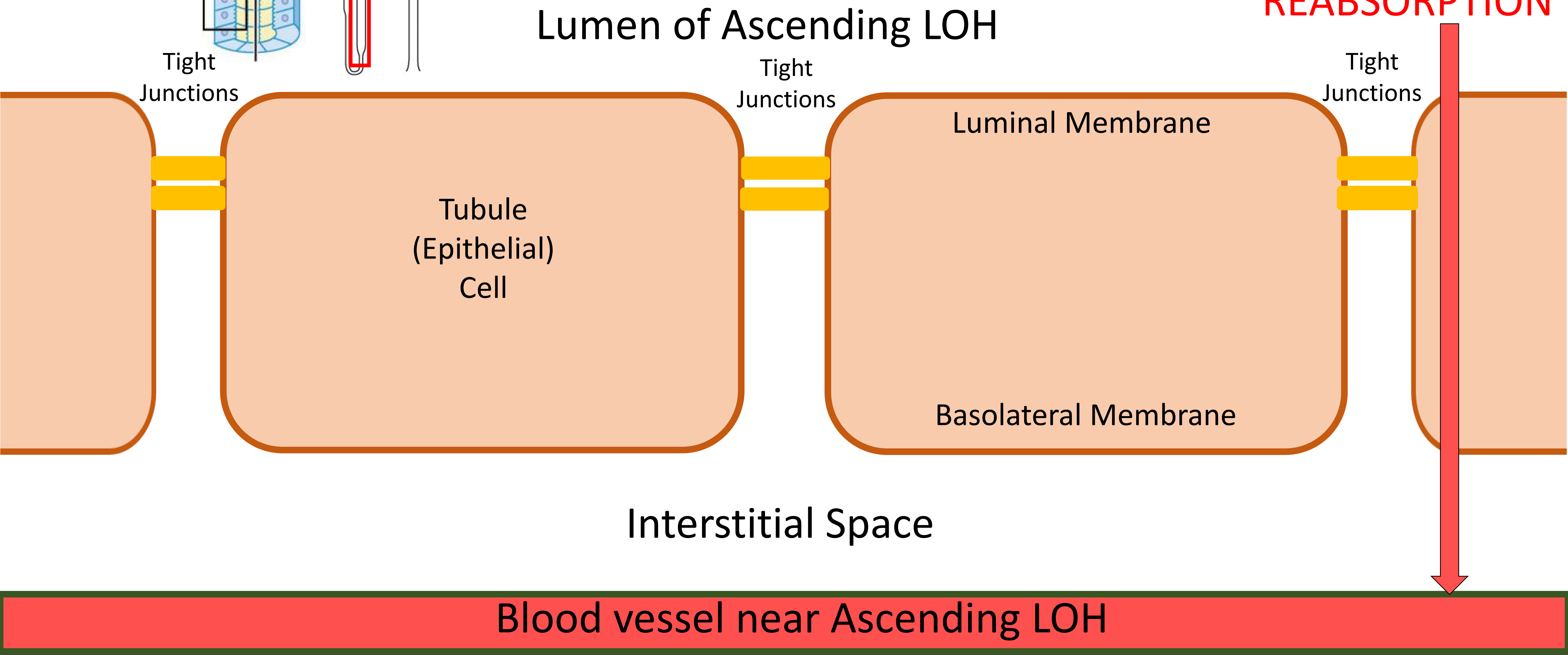


Other Key Points:
- No Ion Reabsorption
- No Paracellular Transport
- No Hormonal Regulation

Ascending LOH

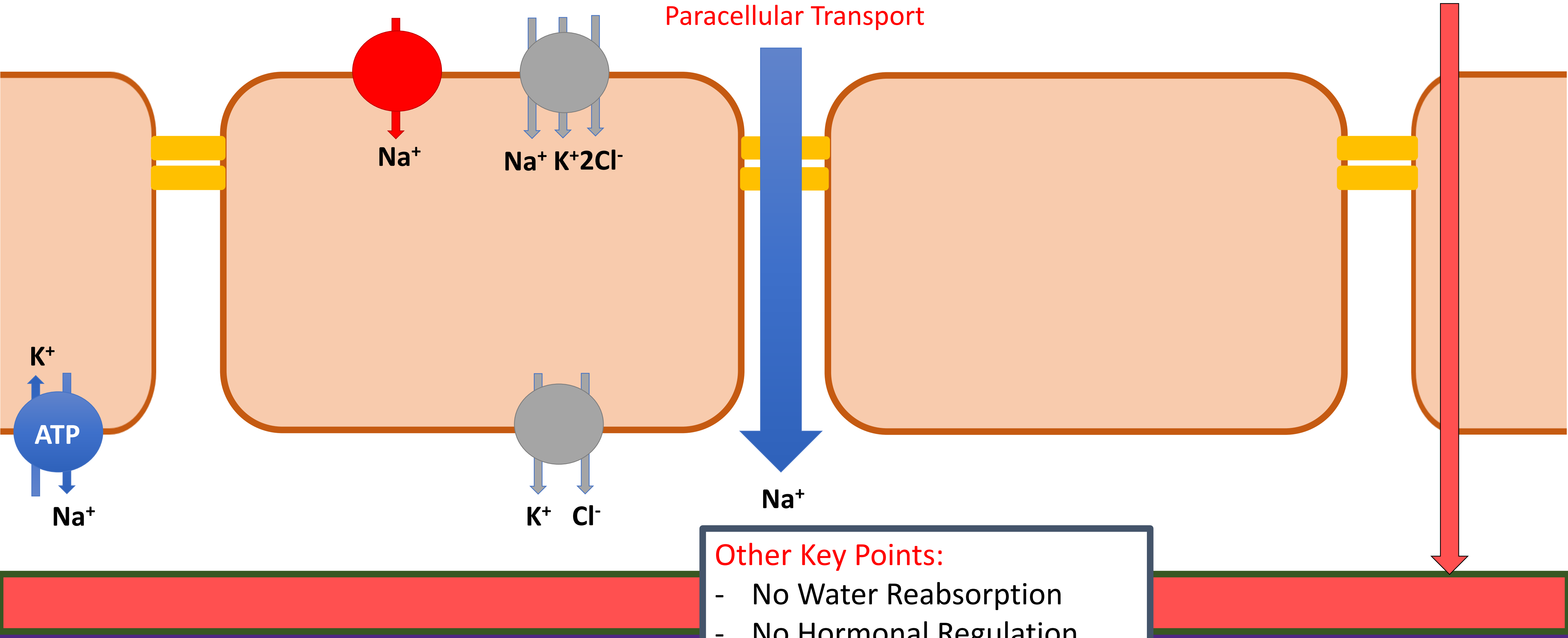


Overall Goal:
REABSORPTION



Ascending LOH

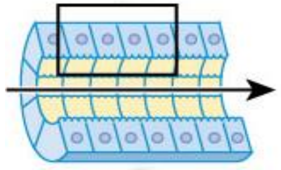
Overall Goal:
REABSORPTION

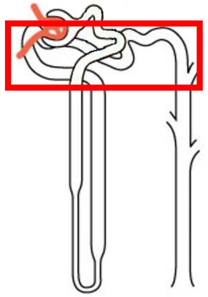


Other Key Points:

- No Water Reabsorption
- No Hormonal Regulation

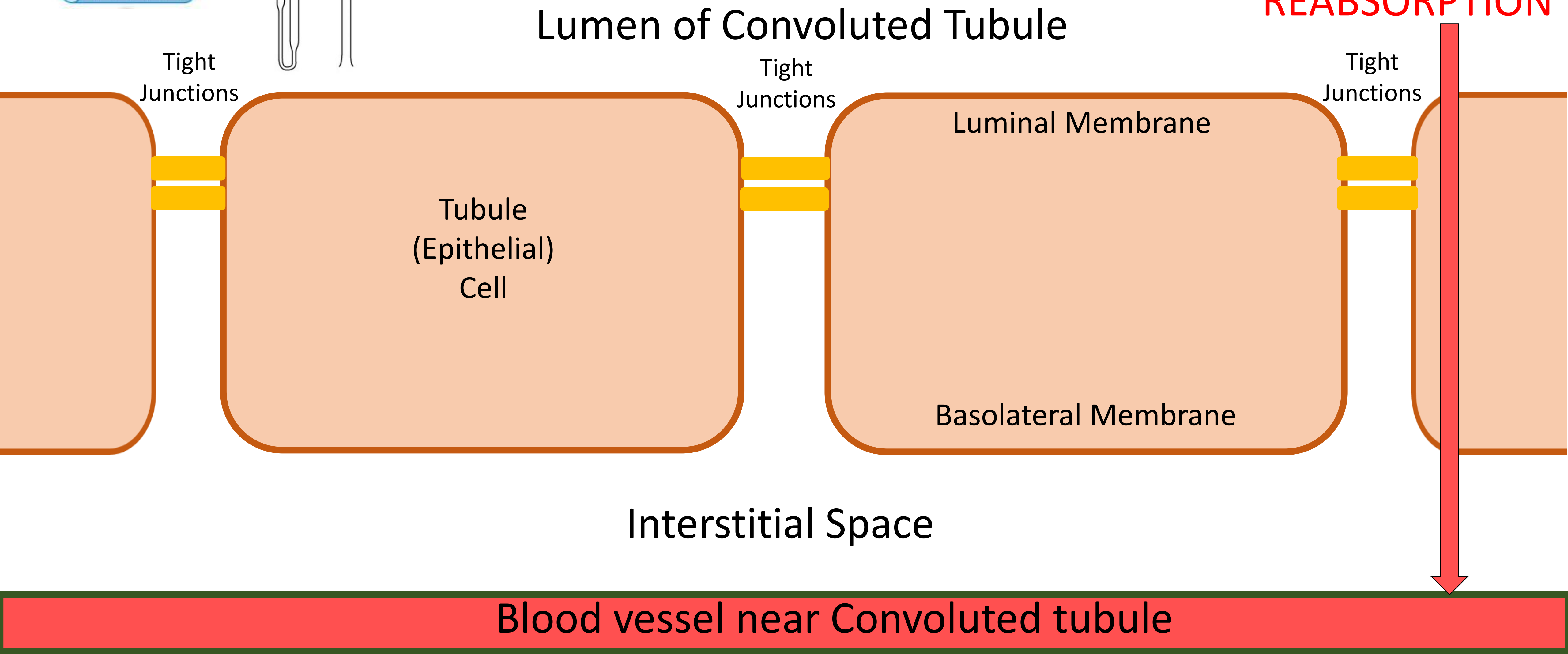
Western





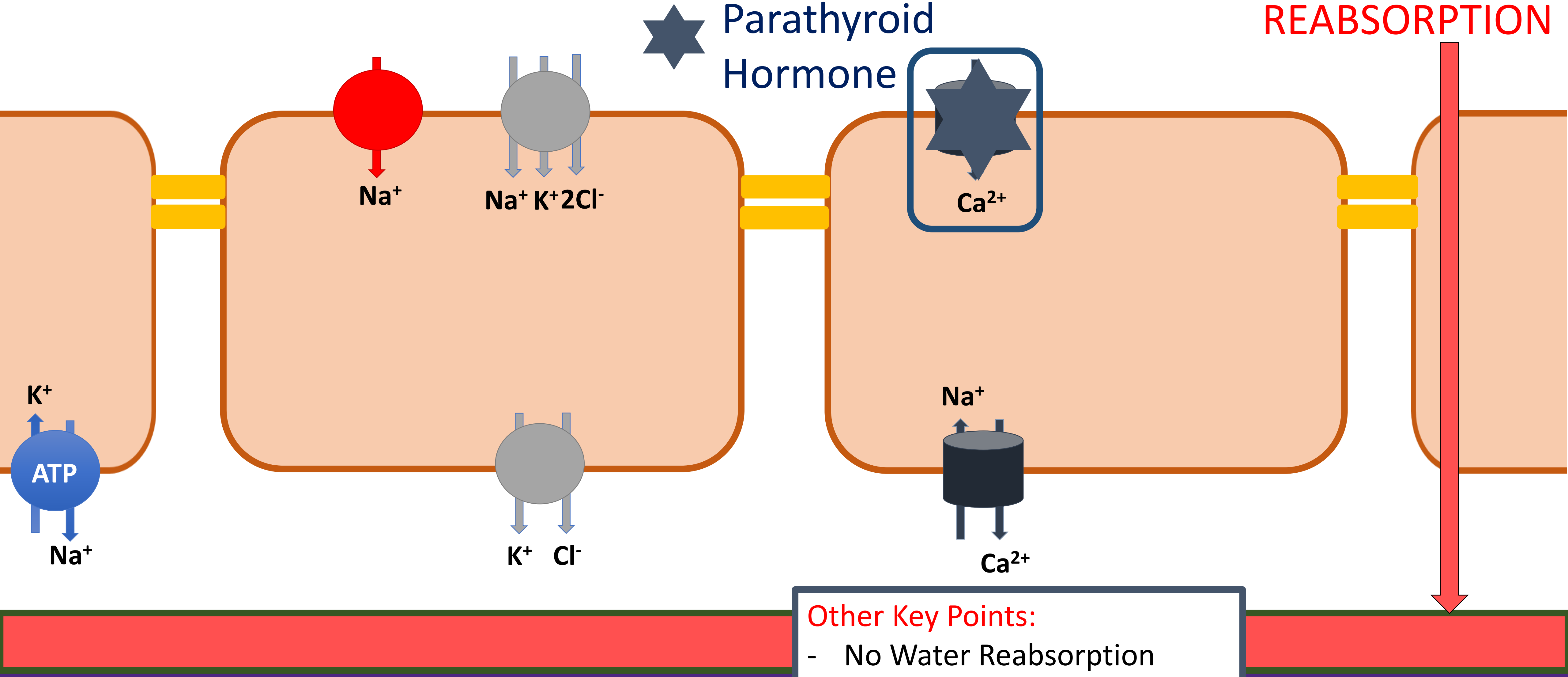
Distal Convoluted Tubule

Overall Goal:
REABSORPTION



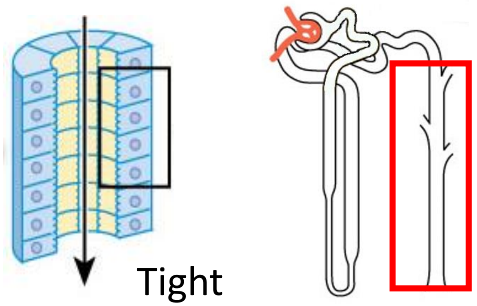
Distal Convoluted Tubule

Overall Goal:
REABSORPTION

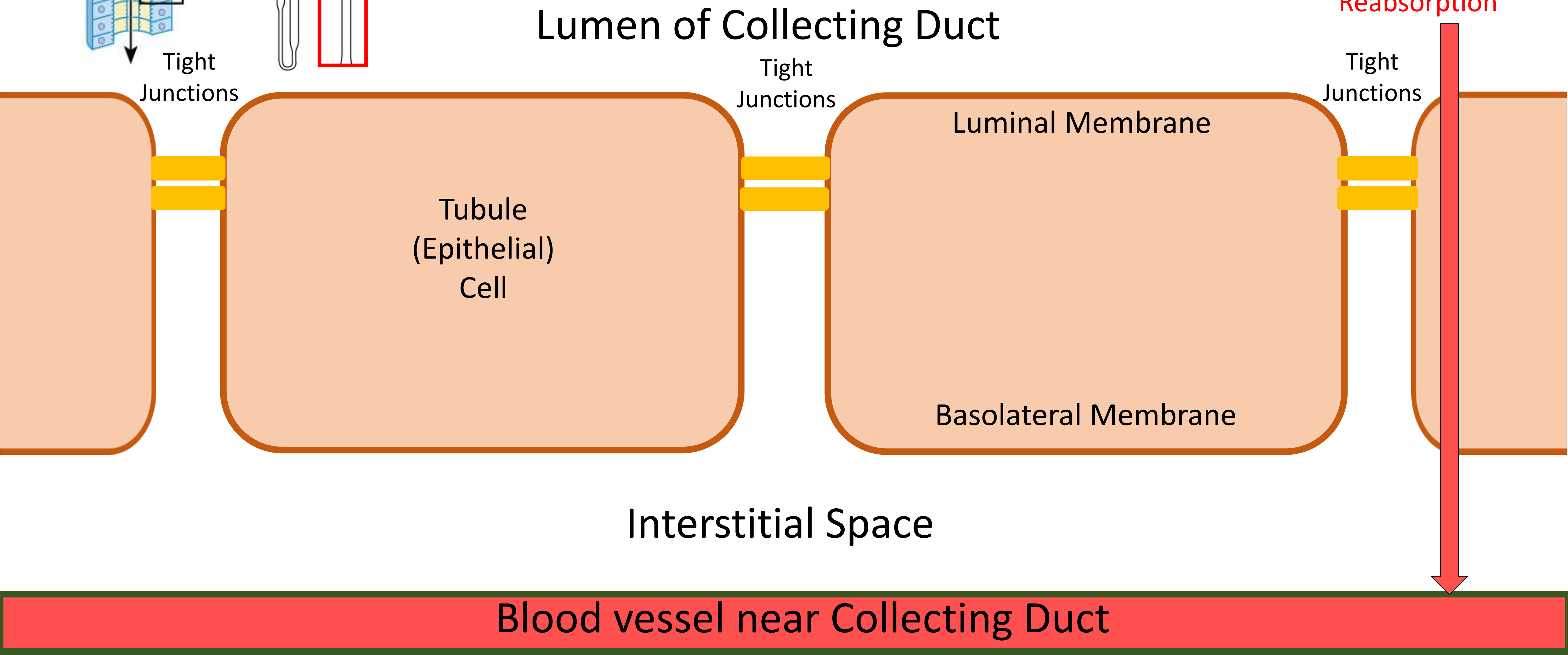


Other Key Points:
- No Water Reabsorption
- No Paracellular Transport

Collecting Duct

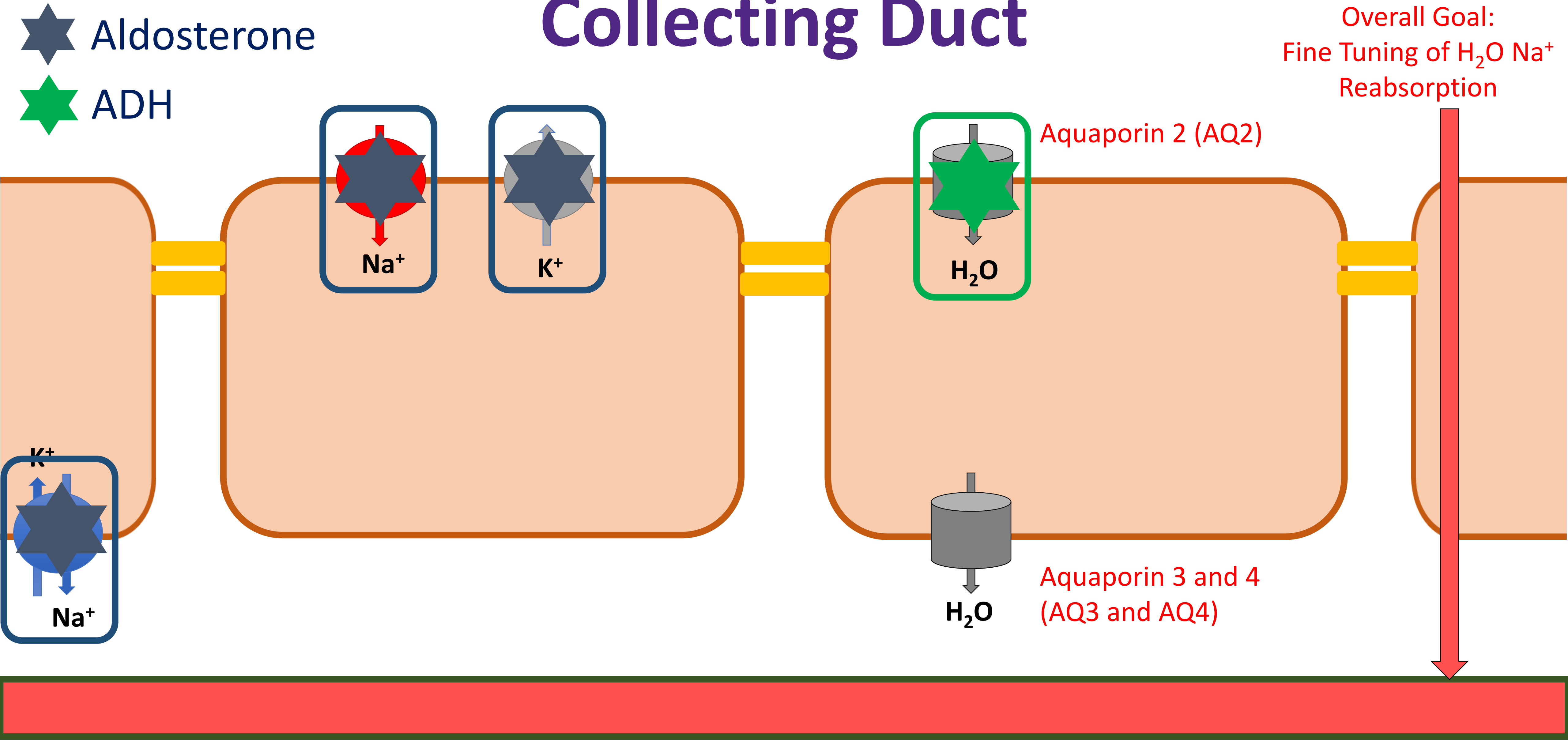


Overall Goal:
Fine Tuning of H_2O Na^+ Reabsorption



Western

Collecting Duct



Summary of Transport

	Proximal Tubule	Descending Limb	Ascending Limb	Distal Tubule	Collecting Duct
Goal	Reabsorption of everything	Water reabsorption	Ion reabsorption	Ion reabsorption	Fine tuning (water and Na)
Water	Yes	Yes	No	No	Yes
Ions	Yes (Na^+, Cl^-, K^+)	Minimal (Na^+)	Yes (Na^+, Cl^-, K^+)	Yes (Na^+, Cl^-, K^+, Ca^{2+})	Yes (Na^+)
Paracellular Transport	Yes	No	Yes	No	No
Hormone Regulation	Angiotensin II	-	-	PTH	Aldosterone ADH

Next Tutorial (Jan 28th)

- More Renal physiology!

What Questions Do You Have?

You can ask in the **Owl forums** as well!

Also anonymously ask questions in the **online dropbox**!!

Western