Cell membrane potentials and transport through membranes

- Electrical potentials exist across the membranes of virtually all cells of the body
- This potential varies from one cell type to another and is determined by the transport proteins in the cell membrane such as ion channels and ion pumps
- Certain cells create waves of changing membrane potential that act as impulses such as **action potentials** in nerve impulses
- Other cells can use a change in membrane potential to activate certain cells functions such as secretion
- Cells also use this membrane potential for transport purposes as is the case for secondary active transport using an electrochemical gradient
- During the resting period of a cell, when it is not activated by certain stimulation its membrane potential is called **resting membrane potential**
- Some cells have a continuously changing membrane potential for example cardiac pacemaker cells

Resting Membrane Potential in Different Cell Types

Cell Type	Resting Potential (mV)
Neurons	−60 to −70
Skeletal muscle	−85 to −95
Smooth muscle	−50 to −60
Cardiac muscle	−80 to −90
Hair cell (cochlea)	−15 to −40
Astrocyte	−80 to −90
Erythrocyte	−8 to −12
Photoreceptor	−40 (dark) to −70 (light)

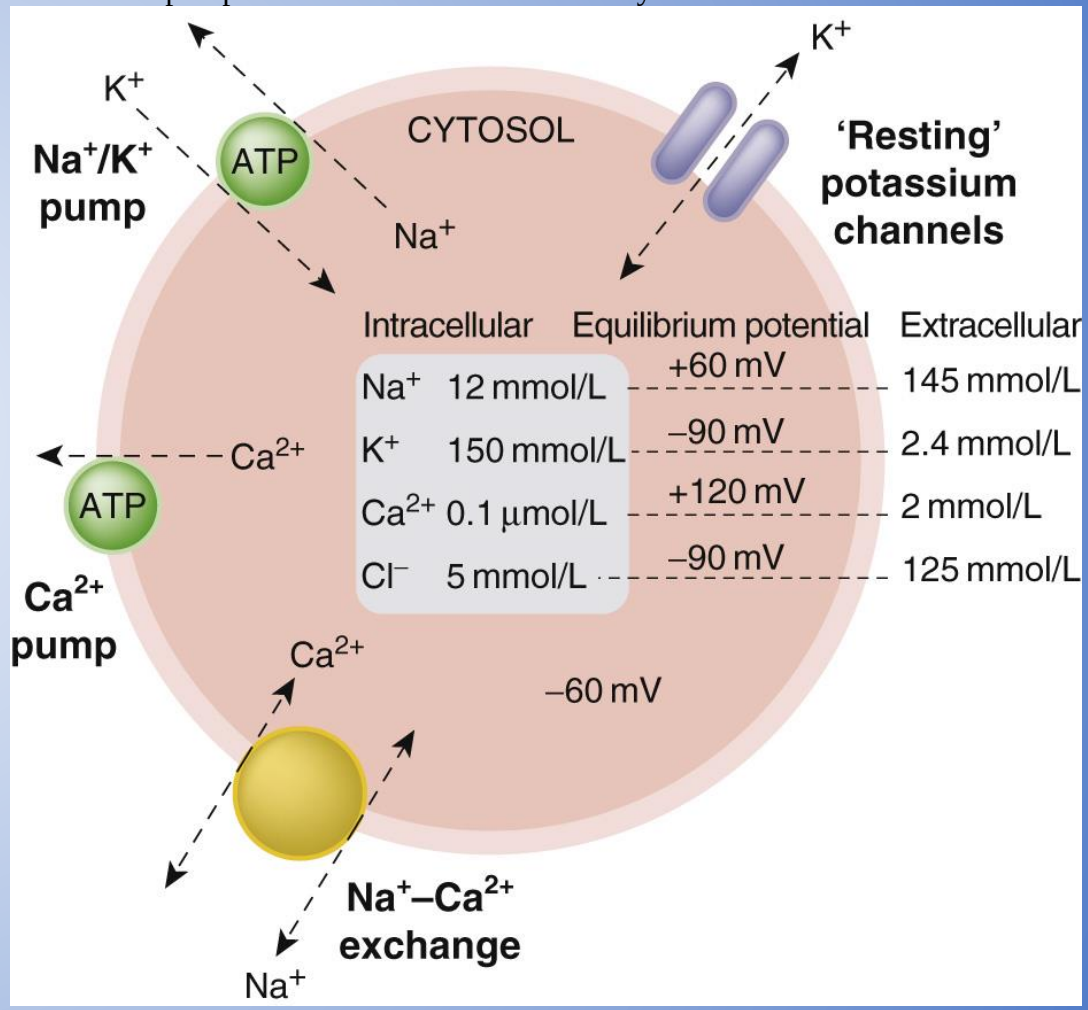
From:
Guyton and Hall Textbook of Medical Physiology, Fourteenth Edition, 2021, Hall, John E., PhD, chapter "Membrane Potentials and Action Potentials"

Literature:
Nolte's The Human Brain Eighth Edition, 2021, Vanderah, Todd W., PhD, chapter «Electrical Signaling by Neurons»
Guyton and Hall Textbook of Medical Physiology, Fourteenth Edition, 2021, Hall, John E., PhD, chapter "Membrane Potentials and Action Potentials"

Establishment of cell membrane Potentials

- Resting membrane potential is actually continuously maintained by cells various membrane ion pumps and ion channels
- This requires ATP energy and for this reason several cells are very sensitive and continuously require supply of nutrients and O_2 to generate this ATP in mitochondria
- Dielectric constant of water is ~40-fold greater than that of the hydrocarbon interior of the cell membrane and this reduces the electrostatic force between ions in water
- This low dielectric constant of the hydrocarbon interior of the cell membrane blocks any transit of ions trough this area unless there are special membrane proteins (ion channels) that allow it
- While the ATP-dependent ion pumps are called electrogenic transporters and distribute ions asymetrically their actual contribution to the membrane potential is small
- When the Na^+ - K^+ pump in the giant squid axon membrane is specifically inhibited with a cardiac glycoside, the immediate positive shift in membrane potential is only 1.4 mV while the resting potential in those cells ir -60mV

Membrane pumps and channels that establish asymetrical distribution of ions



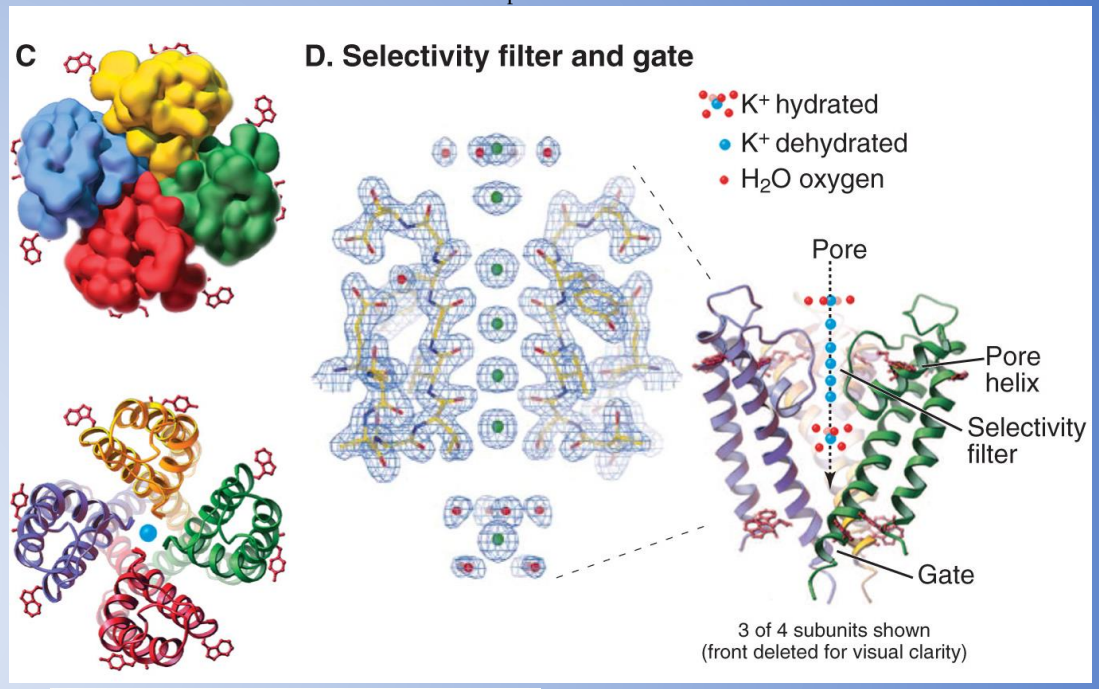
From:
Rang & Dale's Pharmacology, Ninth Edition, 2020, Ritter, James M., chapter "How drugs act : Cellular aspects – excitation, contraction and secretion"

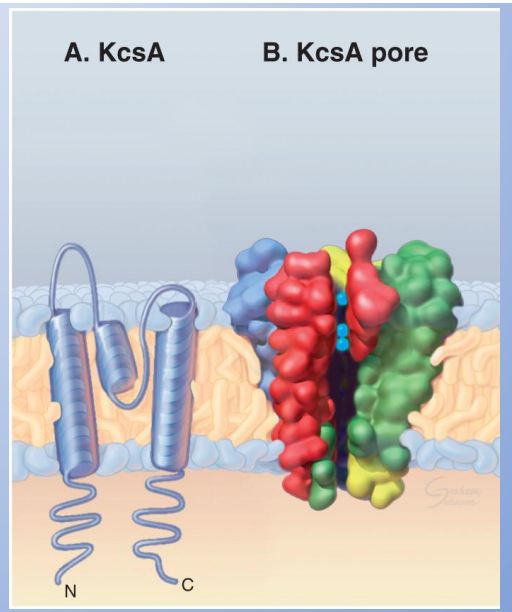
Literature:
Nolte's The Human Brain Eighth Edition, 2021, Vanderah, Todd W., PhD, chapter «Electrical Signaling by Neurons»
Guyton and Hall Textbook of Medical Physiology, Fourteenth Edition, 2021, Hall, John E., PhD, chapter "Membrane Potentials and Action Potentials«
Rang & Dale's Pharmacology, Ninth Edition, 2020, Ritter, James M., chapter "How drugs act : Cellular aspects – excitation, contraction and secretion"

Protein channels with selective permeability

From:
Cell Biology, Third Edition, Pollard, Thomas D., MD, 2007
chapter "Membrane channels"

- Usually only one or few types of molecules can pass trough a protein formed membrane channels
- The interior of those channels determines what type of ion or molecule can pass such a channel
- This is determined by the diameter, shape, nature of the electrical charges and polarity along the interior of channel
- For example K^+ channels permit passage of potassium ions across the cell membrane about 1000 times more readily than they permit passage of Na^+ ions
- This kappens because K^+ channels contain selectivity filter part
- Lining the selectivity filter are carbonyl oxygens that can bind K^+ ion like water molecules do in a solution
- When hydrated (water surrounded) K^+ ions enter the selectivity filter, they interact with the carbonyl oxygens and shed most of their bound water molecules, permitting the dehydrated potassium ions to pass through the channel and this is less likely to happen for a smaller Na^+ ion
- Fatty acids facing part of the channel is hydrophobic allowing the channel to remain in cells membrane



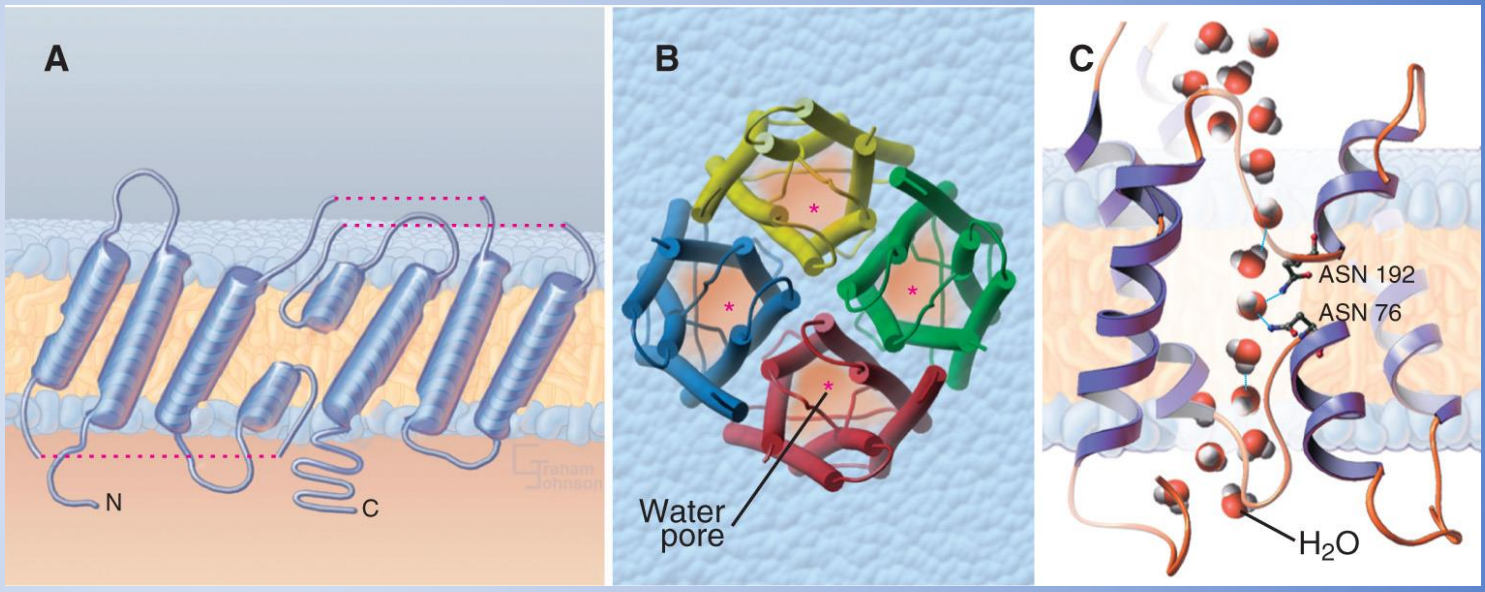


A, Transmembrane topology. The short helix and loop between the two transmembrane helices are called a P loop because they form the pore. **B,** Space-filling model with each subunit shaded a different color and with a cutaway view to expose the central pore, which contains three K^+ ions *(blue).* **C,** Views from outside the cell. Aromatic side chains (shown as stick figures) at both ends of the transmembrane helices of each subunit project radially into the lipid. **D,** Selectivity filter and gate. The blue mesh shows the electron density of the region of two subunits flanking the selectivity filter. The stick figure is the molecular model with five *(red)* carbonyl oxygens lining the pore and coordinating with four bound K^+ ions *(green)* . *Red* waters surround K^+ ions on both sides of the pore. The ribbon model has the front subunit removed to reveal the central pore. Starting on the extracellular side, the 4.5-nm–long pore consists of a negatively charged vestibule; the 1.2-nm–long selectivity filter with binding sites for four dehydrated K^+ ion; a central cavity with space for a single hydrated K^+; a gate (closed here); and a negatively charged cytoplasmic vestibule.

Literature:
Cell Biology, Third Edition, Pollard, Thomas D., MD, 2007 chapter "Membrane channels«
Guyton and Hall Textbook of Medical Physiology, Fourteenth Edition, 2021, Hall, John E., PhD, chapter "Membrane Potentials and Action Potentials«

Water channels - aquaporins

- Because of the hydrophobic interior of cell membrane polar water molecules can’t easily pass through cells membrane
- Still most cells are water permeable at least in some area of the cells membrane
- This is accomplished by special water channels called aquaporins
- There are many genes (at least 13) for those channels so different cells can express different aquaporin genes
- Hydrogen bonding of water molecules with a pair of asparagine residues at a narrow point in the pore allows the channel to be selective for water
- Movement in our out of the cell is passive and determined by the osmotic pressure
- Peter C. Agre, an American Society of Nephrology member, received 2003 Nobel Prize in Chemistry for his discovery of the aquaporin water channels that for a long time eluded scientists



WATER CHANNELS.
A, Membrane topology of aquaporin-1 deduced from the primary structure. The two halves of the polypeptide have similar sequences but are inverted relative to each other. B, Structure determined by electron crystallography, showing four identical units, each with a pore (red asterisk). Helices are depicted as cylinders. C, Detail of the water pore, with a chain of water molecules crossing the membrane. Two asparagines in the middle of the pore hydrogen bond one water.
(Courtesy P. Agre, Johns Hopkins Medical School, Baltimore, MD. For reference, see PDB file 1FQY and Murata K, Mitsuoka K, Hirai T, et al. Structural determinants of water permeation through aquaporin-1. Nature . 2000;407:599–605.)

From:
Cell Biology, Third Edition, Pollard, Thomas D., MD, 2007
chapter "Membrane channels"

Literature:
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Guyton and Hall Textbook of Medical Physiology, Fourteenth Edition, 2021, Hall, John E., PhD, chapter "Membrane Potentials and Action Potentials«
Peter Agre, 2003 Nobel Prize winner in chemistry, Mark A Knepper, 2004

Water channels - aquaporins

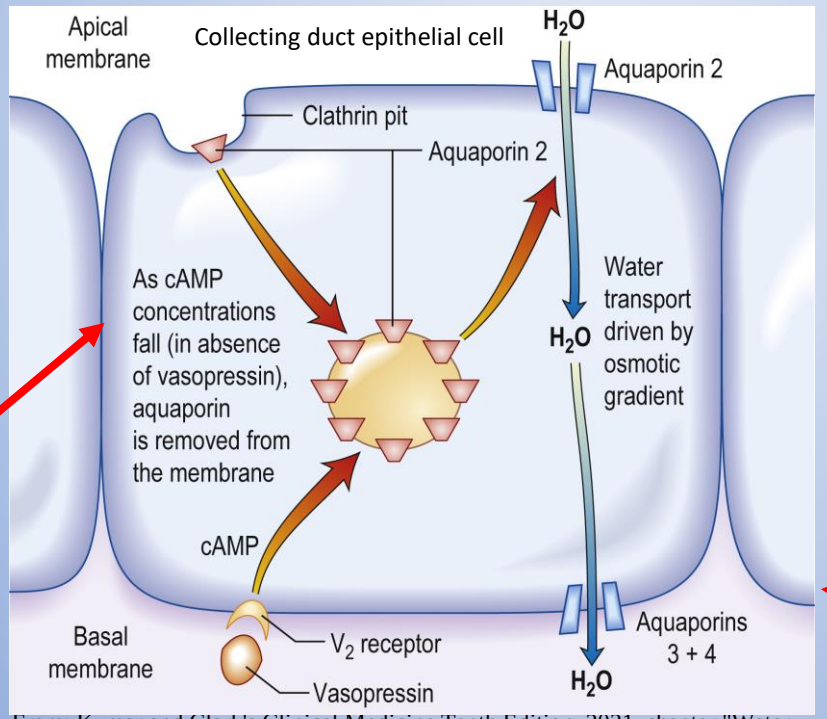
- Our kidneys posses tube like structures created by epithelial cells called tubules and ducts that contain plasma ultrafiltrate precursor of urine
- Those tubules and ducts allow kidneys to control how much water and solutes we lose in urine or retain
- After leaving collecting ducts the fluid in ducts becomes urine and exits from the kidney
- If our body needs to retain water collecting duct cells apical membranes become permeable to water and water will be resorbed from these ducts into the surrounding area and returned to our body
- This will allow the kidney to excrete urine that is highly concentrated (darker, with less water)
- This is regulated by a hormone called vasopressin or antidiuretic hormone (ADH), this hormone binds to its receptors and collecting duct cells and allows membrane vesicles containing AQP2 channels to fuse with the apical membrane

High osmolarity area around collecting duct

Water inside the duct would move to the higher osmolarity area surrounding the duct

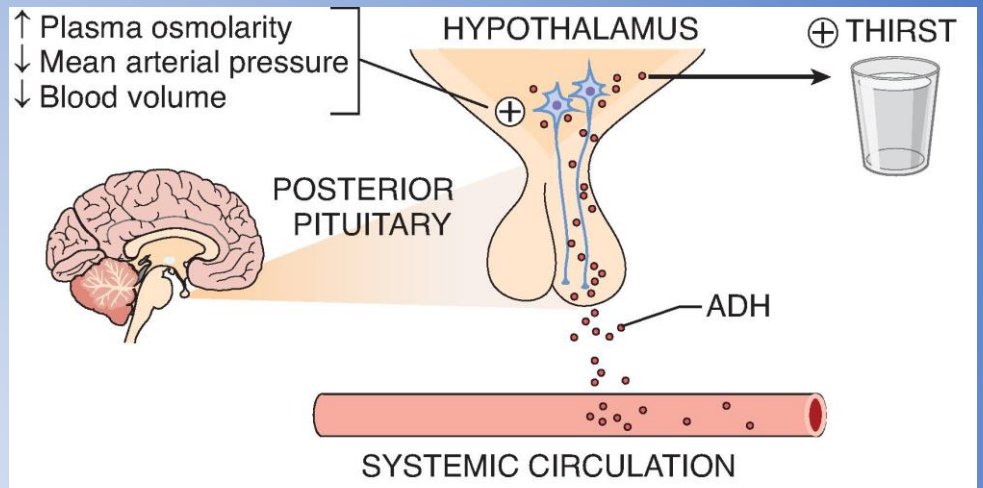
Water molecules can only pass this duct if the apical membranes contain aqp2 aquaporins that permit this passage

Cross section of a kidney collecting duct from Wheater's Functional Histology Sixth Edition, 2014

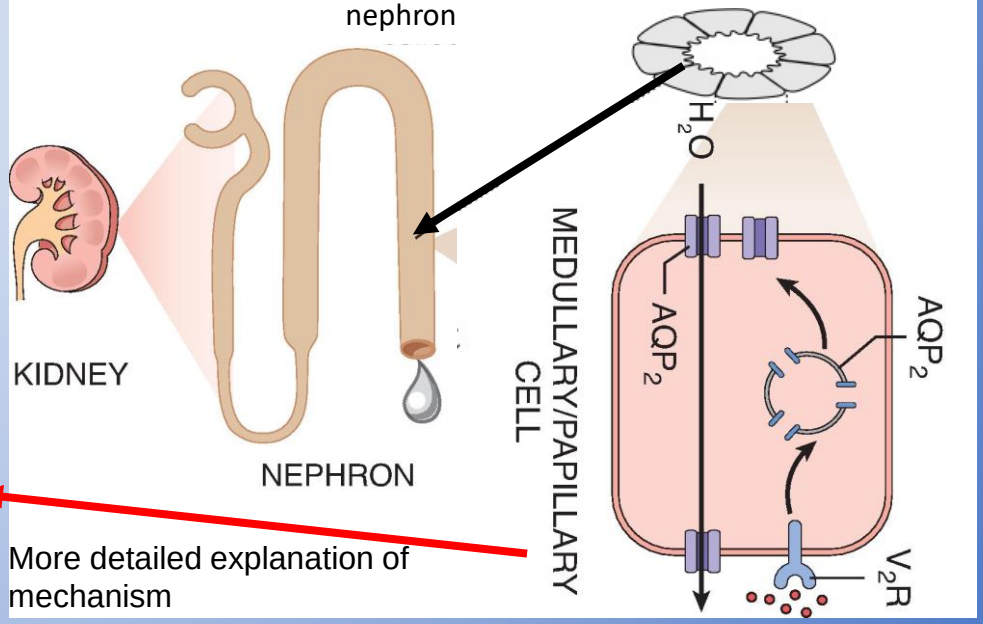


Intercellular juctions prevent AQP2 to move from apical to basal part of cells membrane

From: Kumar and Clark's Clinical Medicine Tenth Edition, 2021, chapter "Water balance, fluids and electrolytes"



Collecting duct of a nephron



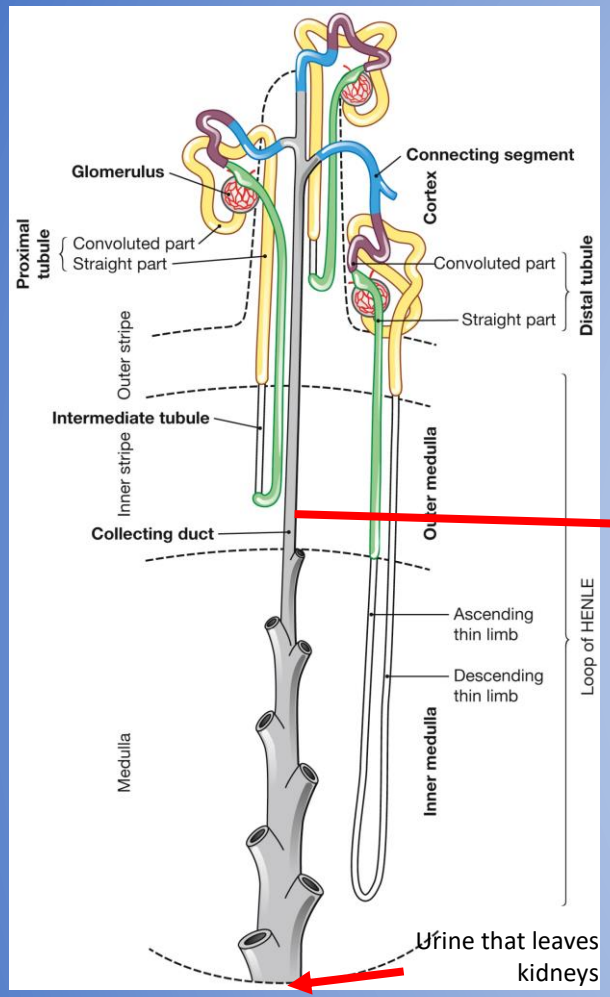
More detailed explanation of mechanism

From: National Kidney Foundation Primer on Kidney Diseases Eighth Edition, 2023, chapter "Hypernatremia and Hyperosmolar Disorders«

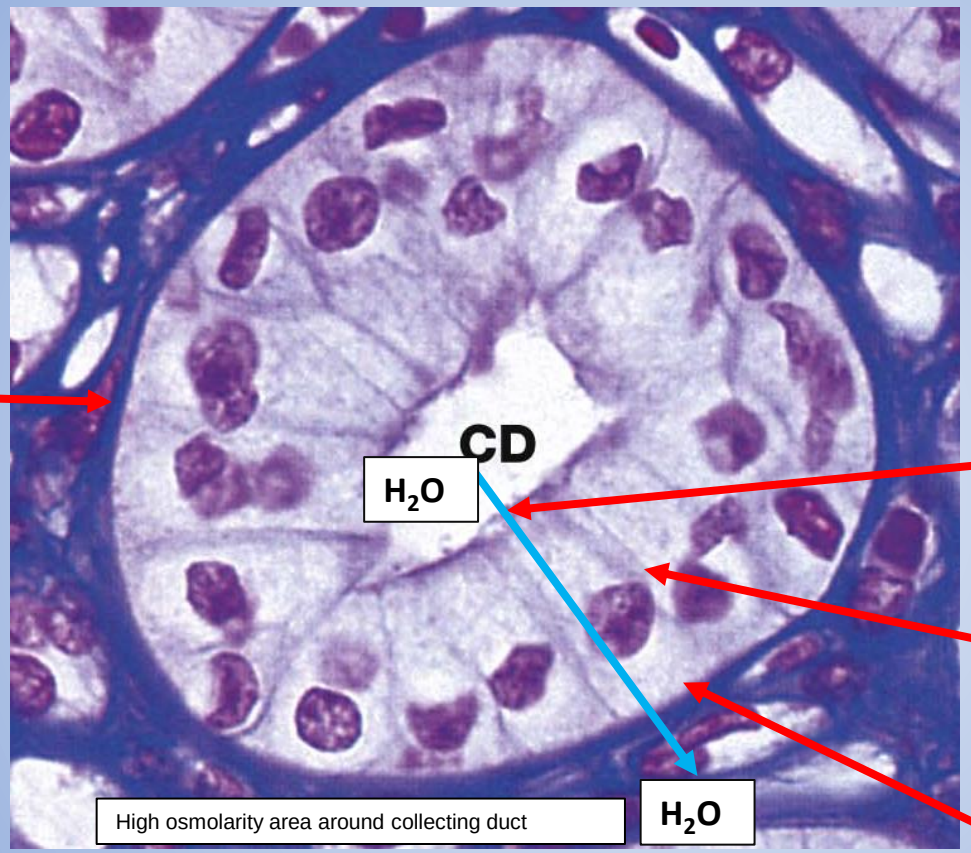
Literature:

National Kidney Foundation Primer on Kidney Diseases Eighth Edition, 2023, chapter "Hypernatremia and Hyperosmolar Disorders«
Kumar and Clark's Clinical Medicine Tenth Edition, 2021, chapter "Water balance, fluids and electrolytes"

Water channels - aquaporins



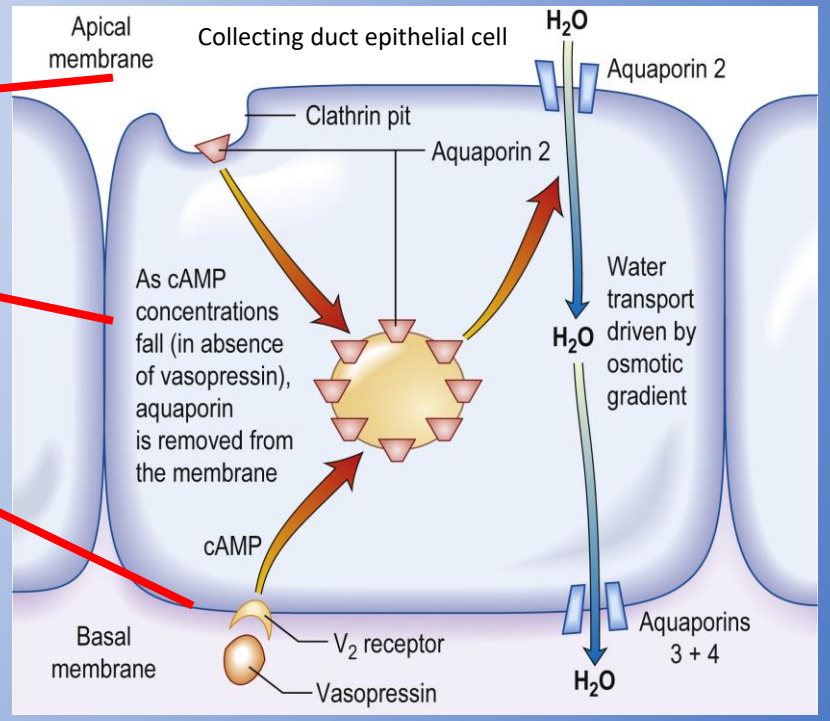
Kidneys nephron tube system from Sobotta Clinical Atlas of Human Anatomy, Hombach-Klonisch, Sabine



Cross section of a kidney's collecting duct (tube made from epithelial cells) from Wheater's Functional Histology Sixth Edition, 2014

Water molecules can only pass this epithelial duct if the apical cell membrane contains AQP2 channels

If cAMP levels in cell drop (no vasopressin stimulation) AQP2 is removed with clathrin pits and no water is resorbed from ducts (apical membrane is no permeable to water) and we produce dilute urine to remove excess water from our body

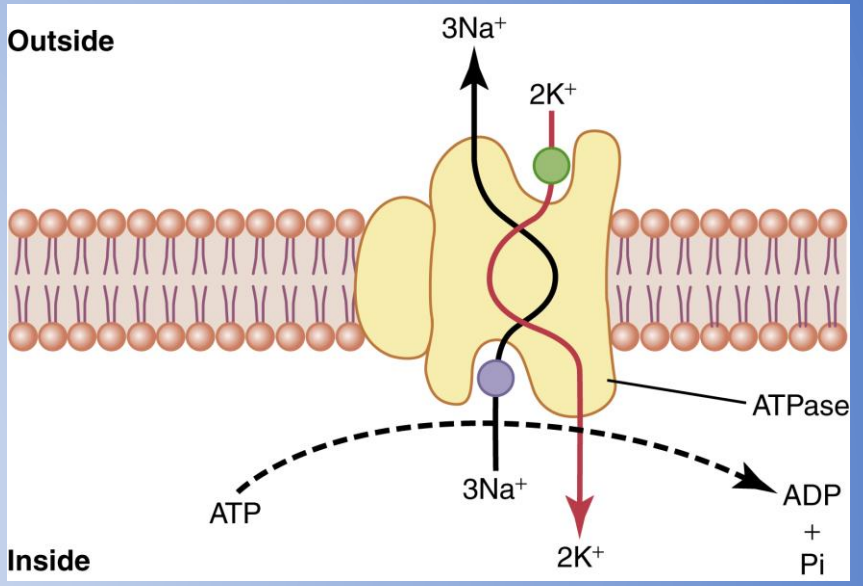


From: Kumar and Clark's Clinical Medicine Tenth Edition, 2021, chapter "Water balance, fluids and electrolytes"

Literature:
National Kidney Foundation Primer on Kidney Diseases Eighth Edition, 2023, chapter "Hypernatremia and Hyperosmolar Disorders«
Kumar and Clark's Clinical Medicine Tenth Edition, 2021, chapter "Water balance, fluids and electrolytes"

Ion pumps and active transport

- Among the substances that are transported by primary active transport are sodium and potassium (Na^+ - K^+ pump), hydrogen (proton pumps in stomach), calcium, chloride, and a few other ions
- This is called primary actve transport because it uses ATF energy while secondary active transport uses established concentration and electrical charge differences (electrochemical gradient)
- When two K^+ ions bind on the outside of the carrier protein and three Na^+ ions bind on the inside, the ATPase function of the protein becomes activated
- Activation of the ATPase function leads to cleavage of one molecule of ATP, splitting it to adenosine diphosphate (ADP) and liberating a high-energy phosphate bond of energy
- This liberated energy is believed to cause a chemical and conformational change in the protein carrier molecule, extruding three Na^+ ions to the outside and two K^+ ions to the inside
- Pumps are powered by ATP hydrolysis and hence are called ATPases and are enzymes that can also work in reverse
- If the electrochemical gradients for Na^+ and K^+ are **experimentally** increased to the degree that the energy stored in their gradients is greater than the chemical energy of ATP hydrolysis, these ions will actually move down their concentration gradients, and the Na^+ - K^+ pump will synthesize ATP from ADP and phosphate untill an equlibrium is reached
- Under physiological conditions this is impossible and ATP hydrolysis releases a lot of free energy and cells do not even reach equilubrium



Postulated mechanism of the sodium-potassium pump. ADP, Adenosine diphosphate; ATP, adenosine triphosphate; Pi, phosphate ion.

From:
Guyton and Hall Textbook of Medical Physiology, Fourteenth Edition, 2021, Hall, John E., PhD, chapter «ransport of Substances Through Cell Membranes «

Literature:
Cell Biology, Third Edition, Pollard, Thomas D., MD, 2007 chapter «Membrane channels«
Guyton and Hall Textbook of Medical Physiology, Fourteenth Edition, 2021, Hall, John E., PhD, chapter «Membrane Potentials and Action Potentials«
Medical Physiology, Third Edition, Boron, Walter F., MD, PhD, 2017, chapter "Transport of Solutes and Water"

Ion pumps and active transport

- For some cells like neurons 60% to 70% of the cell's energy requirement may be devoted to pumping Na^+ and K^+ ions
- One of the most important functions of the Na^+ - K^+ pump is to control the cell volume
- Inside the cell are large numbers of proteins and other organic molecules that cannot escape from the cell
- Most of these proteins and other organic molecules are negatively charged and, therefore, attract large numbers of potassium, sodium, and other positive ions
- All these molecules and ions lead to increased intracellular osmotic pressure and cause osmosis of water to the interior of the cell
- Without pumps this would lead to swelling of the cell untill it bursts
- In 1957 Jens Christian Skou discovered an enzyme, Na+/K+-ATPase, and shared the 1997 Nobel Prize in Chemistry for this discovery

Literature:
Cell Biology, Third Edition, Pollard, Thomas D., MD, 2007 chapter «Membrane channels«
Guyton and Hall Textbook of Medical Physiology, Fourteenth Edition, 2021, Hall, John E., PhD, chapter «Membrane Potentials and Action Potentials»
Medical Physiology, Third Edition, Boron, Walter F., MD, PhD, 2017, chapter "Transport of Solutes and Water"
https://www.nobelprize.org/prizes/chemistry/1997/skou/facts/

Establishment of cell membrane potentials

- Cell membrane potentials actualy depens on ionic concentration gradients established by ion pumps
- To see how this works we fist have to look at K^+ equlibrium potential
- K^+ concentration is great inside a cell but very low outside the membrane because of K^+ is pumped in and Na^+ outside
- The K^+ ions will move out of the cell because of the concentration gradient
- This will creat an inbalance of charge that will prevent further movement of K^+ ions
- The initial net outward movement of K^+ ions required to establish this membrane potential is actually extremely small, just enough to charge up the membrane capacitance—and no significant change in intracellular or extracellular K^+ concentration results
- The net outward movement of only about 175 million K^+ ions is enough to establish the predicted membrane potential of −94 mV across the membrane of a spherical cell 100 μm in diameter
- Although this sounds like a lot of ions, a cell this size with an intracellular K^+ concentration of 130 mM contains about 4×10^{13} K^+ ions, so the net loss of K^+ ions required to establish this membrane potential is less than 0.001% of the starting number

Literature:
Nolte's The Human Brain Eighth Edition, 2021, Vanderah, Todd W., PhD, chapter «Electrical Signaling by Neurons»
Guyton and Hall Textbook of Medical Physiology, Fourteenth Edition, 2021, Hall, John E., PhD, chapter "Membrane Potentials and Action Potentials«

Establishment of cell membrane potentials

- The diffusion potential across a membrane that exactly opposes the net diffusion of a particular ion through the membrane is called the Nernst potential and at equilubrium it can also be called the equilibrium potential of that particular dffising ion
- Potential can be determined using Nernst equation and potential is determined by the ratio of the concentrations of that specific ion on the two sides of the membrane
- The following equation, called the Nernst equation, can be used to calculate the Nernst potential for any univalent ion at the normal body temperature of (37°C)
- The value 61 is calculated from temberature and various constants such and gas constant R and value 61 can change with temperature
- Z is the charge of ion 2 for calcium and 1 for potassium
- EMF is the electromotive force in milivolts

$$\text{EMF (millivolts)} = \pm \frac{61}{z} \times \log \frac{\text{Concentration inside}}{\text{Concentration outside}}$$

From:
Guyton and Hall Textbook of Medical Physiology, Fourteenth Edition, 2021, Hall, John E., PhD, chapter "Membrane Potentials and Action Potentials«

Literature:
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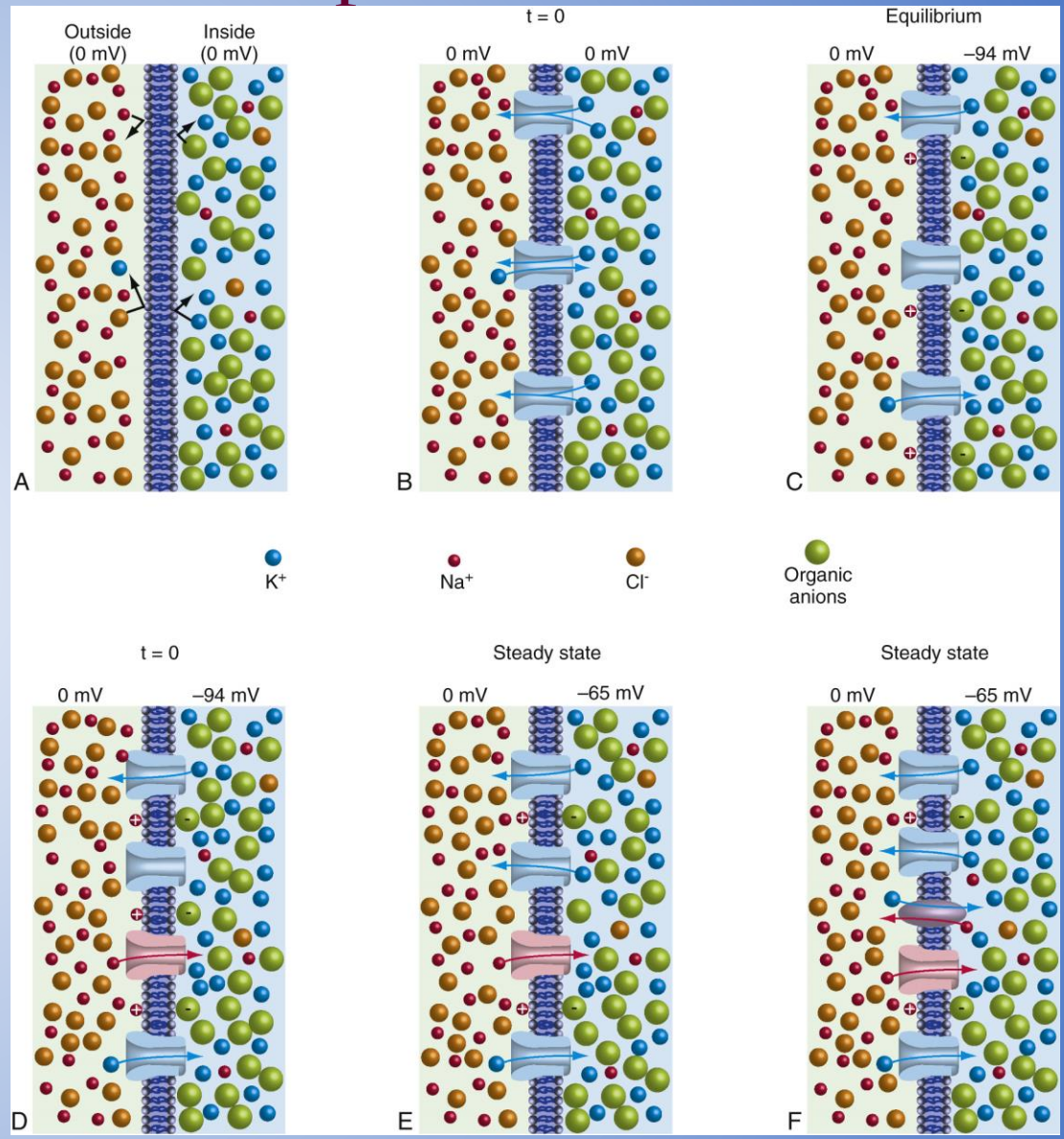
Establishment of cell membrane potentials

Development and maintenance of a resting membrane potential:

- **A** - lipid bilayer by itself is impermeable, allowing no charge separation to develop
- **B** - adding K^+ channels initially results in net movement of K^+ ions out of the cell (K^+ ions are free to move in either direction, but because there are more inside the cell, more move from inside to outside than in the opposite direction)
- **C** At equilibrium, a vanishingly small number of excess extracellular K + ions results in cations (mostly Na^+ ions) lining up on the outside of the membrane, counterbalanced by anions on the inner surface of the membrane. This accounts for the resting membrane potential, which develops abruptly across the membrane. K^+ ions still flow through their channels, but now equal numbers move out (down the concentration gradient) and in (down the voltage gradient).
- **D** Addition of a small number of Na^+ channels causes a small inward movement of Na^+ ions, driven not just by the Na^+ concentration gradient but also by the intracellular negativity.
- **E** A steady state is reached in which equal numbers of cations move inward and outward across the membrane. However, there is a net inward movement of Na + and outward movement of K^+
- **F** The Na + /K + ATPase is an exchange pump that compensates for the net Na + and K + fluxes in **E**



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Literature:
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Establishment of cell membrane potentials

- The Goldman Equation Is used to calculate the diffusion potential when the membrane is permeable to several different ions
- When a membrane is permeable to several different ions, the diffusion potential that develops depends on three factors:
  - The polarity of the electrical charge of each ion
  - The permeability of the membrane (P in formula) to each ion
  - The concentration (C in formula) of the respective ions on the inside (i) and outside (o) of the membrane.
- Thus, the following formula, called the Goldman equation or the Goldman-Hodgkin-Katz equation, gives the calculated membrane potential on the inside of the membrane when two univalent positive ions, sodium (Na^+) and potassium (K^+), and one univalent negative ion, chloride (Cl^-), are involved
- This formula explains how changes in cells permeablity to certain ion as is the case when additional Na^+ channels open can reverse the cells potential from negative to positive
- Cells is the phenomenon for signaling and functional change based on changed membrane potential

$$\text{EMF (millivolts)} = -61 \times \log \frac{C_{Na_i^+} P_{Na^+} + C_{K_i^+} P_{K^+} + C_{Cl_o^-} P_{Cl^-}}{C_{Na_o^+} P_{Na^+} + C_{K_o^+} P_{K^+} + C_{Cl_i^-} P_{Cl^-}}$$

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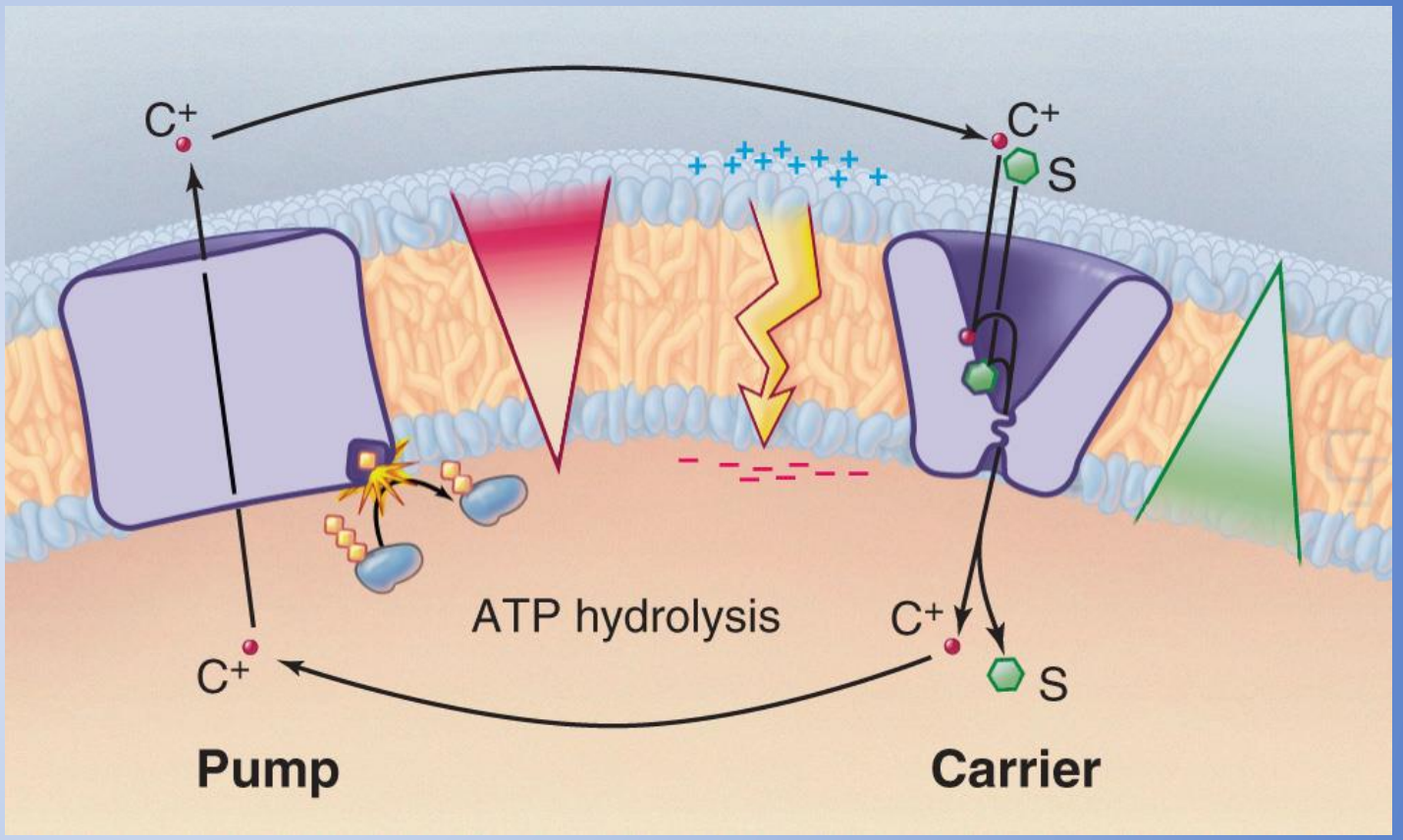
Established ion gradients can be used for transport

- Electrochemical gradients of a cell can be used to transport other substances
- A substance that cell wats to import moes against its concentration gradient while an ion moves in the direction where the particular concentration of the ion is smaller and charge is opposite
- Example is Na^+ that moves inside a cell where the concentration of Na^+ is smaller and charge of cells interior is opposite (negative)
- This process is called secondary actve transport
- Electrochemical potential (membrane potential) across a membrane represents a reservoir of stored energy that was released by ATP hydrolysis when this potential was generated
- This is similar to roll a rock up a mountain and then allow it to roll down releasing this stored potential energy
- Carriers and other membrane proteins use the potential energy of ion gradients to drive other processes



MODEL CHEMIOSMOTIC CYCLE IN A MEMBRANE SURROUNDING A CLOSED SPACE.
An adenosine triphosphate (ATP)-driven pump transports a cation C^+ out of the compartment. The energy derived from ATP is stored as a concentration gradient of C^+ *(red triangle)* and a membrane potential *(yellow arrow)* across the membrane. The carrier uses the electrochemical gradient of C^+ to drive the transport of both C^+ and a solute up a concentration gradient *(green triangle)* across the membrane.

From:
Cell Biology, Third Edition, Pollard, Thomas D., MD, 2007 chapter «Membrane Physiology«

Literature:
Cell Biology, Third Edition, Pollard, Thomas D., MD, 2007 chapter «Membrane Physiology«

Example of epithelial transprt mechanism

- Molecules can pass through cells (transcellular pathway) or between epithelial cells in a paracellular pathway that is dependent on how sealed the intercellular species are
- Tight junctions can completely seal off this pathway which is important in certain absorptive processes
- Transcellular movement of molecules usually requires specific membrane transport proteins on the apical and basolateral membrane
- Only small nonpolar molecules can move without the aid of such transport proteins

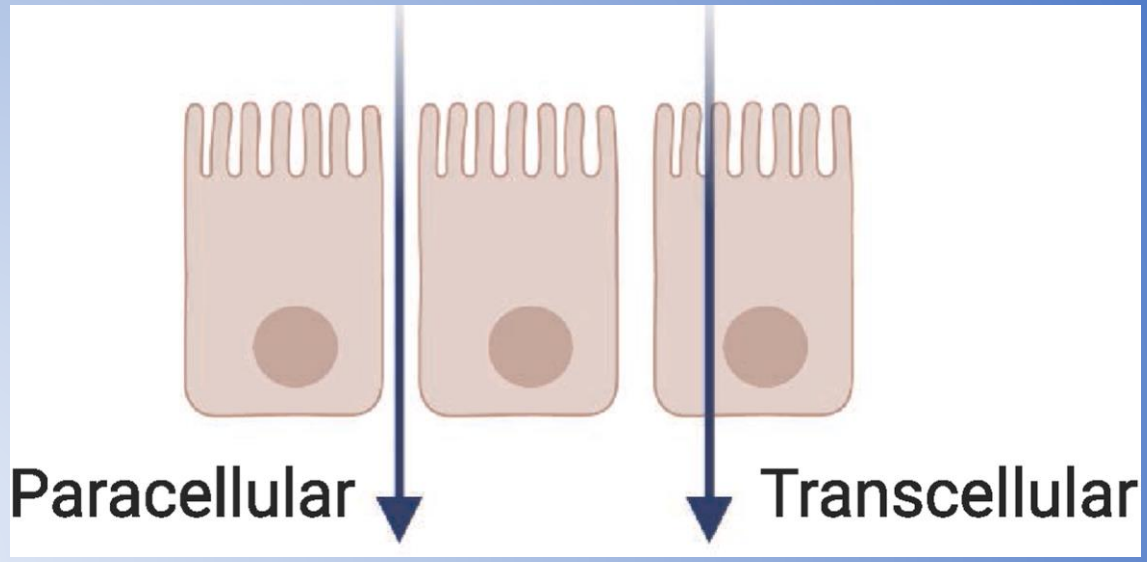
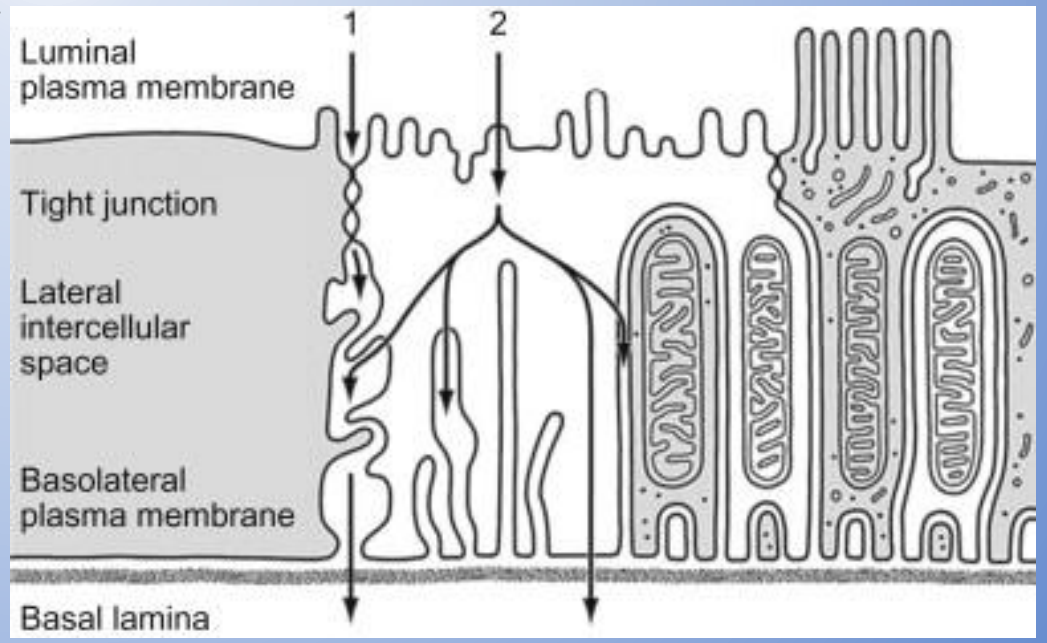


Image from article Intestinal permeability in type 1 diabetes: An updated comprehensive overview, Mia Øgaard Mønsted et al, Journal of Autoimmunity Volume 122, 2021

Schematic drawing, demonstrating the essential structural features of renal transporting epithelia.

(1) Paracellular route through the tight junction and the lateral intercellular spaces; (2) Transcellular route, across the apical plasma membrane, which may be augmented by short microvilli, microfolds (not shown) or long microvilli of uniform length, called " brush border," across the cytoplasm, and across the basolateral plasma membrane; the latter may be augmented by infoldings of the basal plasma membrane or by basolateral processes of the cells, which narrowly interdigitate with each other. The lateral interdigitating processes contain large mitochondria.

(2) From Seldin and Giebisch's The Kidney Fifth Edition, Alpern, Robert J, 2013, chapter "Structural Organization of the Mammalian Kidney"



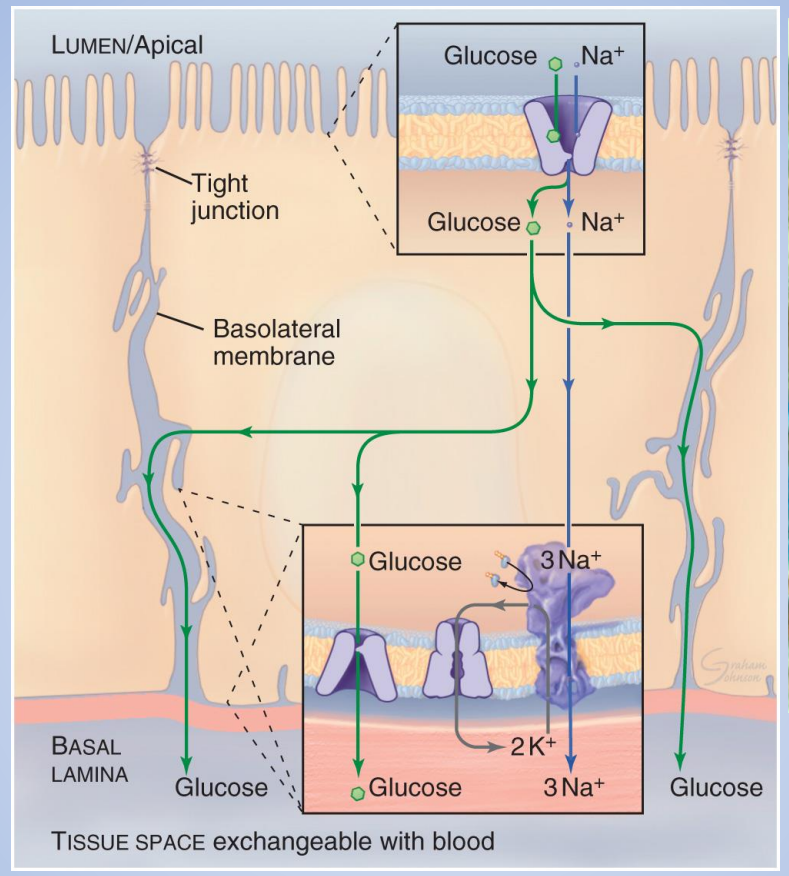
Literature:
Cell Biology, Third Edition, Pollard, Thomas D., MD, 2007 chapter «Membrane Physiology«

Example of epithelial transprt mechanism

- Many cells employ similar or almost identical transport mechanisms such as absorptive cells in the kidney or gun (small intestine)
- Net transport across such epithelium depends on cell-to-cell contacts (such as tight junctions) and separate apical and basolateral parts (compartments) of the cells membrane, preventing membrane proteins from the apical compartment from moving into the basolateral compartment
- The lateral and basal sides of the cell are not fully separated by junctions and are called together as a single unit – basolateral membrane
- Tight junctions also restrict diffusion of solutes between the apical and basolateral compartments of the extracellular space preventing paracellular transport completely or partially (with some leak) depending on how tight the seal is

Here glucose is used as an example

- Na + - K+ pump is located in the basolateral plasma membrane, this membrane often forms processes and folds to increase its surface for these pumps that generate an electrochemical gradient
- SGLT (sodium glucose cotransporters such as SGLT1 1 or 2) are Na + /glucose symporter, restricted to the apical plasma membrane, electrochemical gradent pulls Na + inwards but it can only enter the cell together with the glucose that is pulled inside the cell against its concentration gradient, this allows full absorption of glucose from lumen of gut or kidney tubule
- GLUT (glucose transporter such as GLUT5) are glucose uniporter, restricted to the basolateral cell membrane, as glucose accumulates inside the cell it tends to leave through basolateral membrane (facilitated diffusion)
- In this area capillaries uptake and transport away this glucose for use in our body

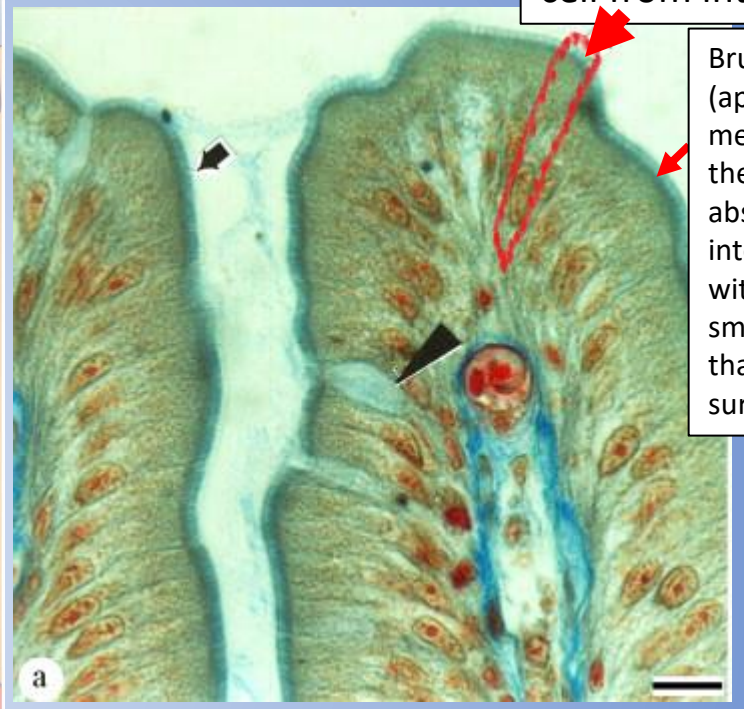


GLUCOSE TRANSPORT BY THE INTESTINAL EPITHELIUM.
Tight junctions seal the epithelium of polarized epithelial cells. Na + K + -adenosine triphosphatase (ATPase) pumps (space-filling model) in the basolateral plasma membrane drive Na + /glucose symporters in the apical plasma membrane (upper inset) and glucose uniporters in the basolateral plasma membrane (left icon in lower inset) to move glucose from the lumen of the intestine to the blood. Basolateral K + channels (middle icon) recycle K + pumped into the cell.

From:
Cell Biology, Third Edition, Pollard, Thomas D., MD, 2007 chapter «Membrane Physiology«

Columnar epithelial cell from intestine

Brush border (apical membrane) of the columnar absorptive intestinal cell with many small microvilli that increase surface area



Platyfish intestine fixed in ethanol–formaldehyde and stained with Heidenhain's Azan (trichrome) stain

From: Histochemical study on the intestine goblet cells in cichlid and poecilid species (Teleostei), I.L. Leknes, 2009, Tissue and Cell Volume 42, Issue 1

Microvilli in transmission electron microscopy

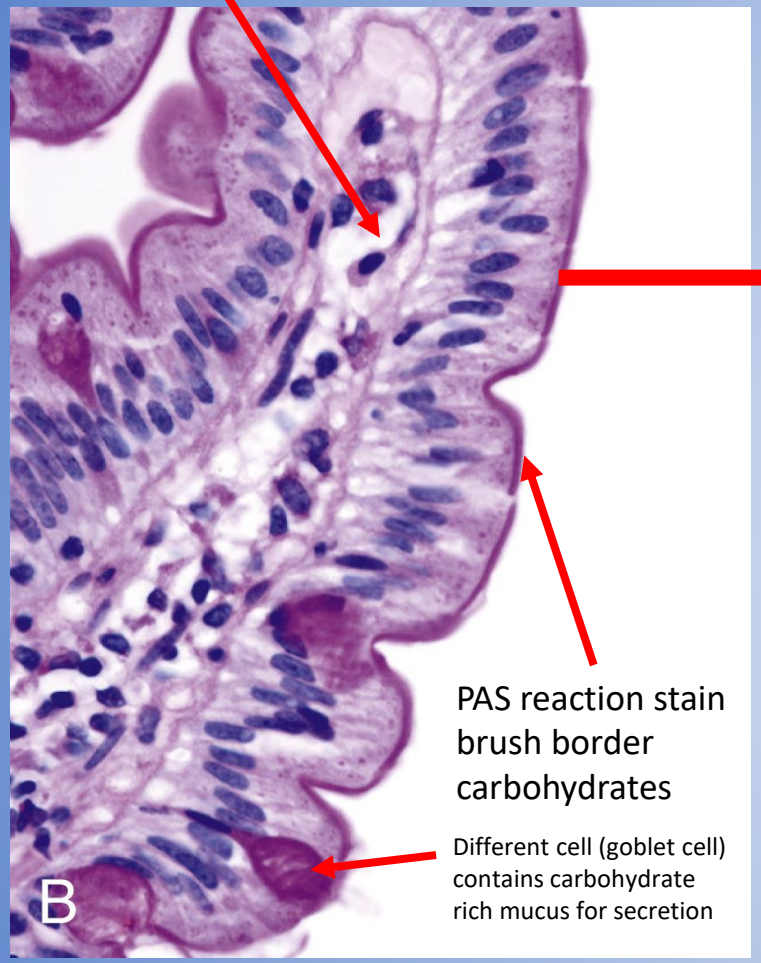
Tight cell junctions in transmission electron microscopy

Small intestine epithelial cell microvilli and TJ regions of a mouse

From:
From: Bifidobacteria Stabilize Claudins at Tight Junctions and Prevent Intestinal Barrier Dysfunction in Mouse Necrotizing Enterocolitis, Kelly R. Bergmann et al, 2013, American Journal of Pathology, The Volume 182, Issue 5

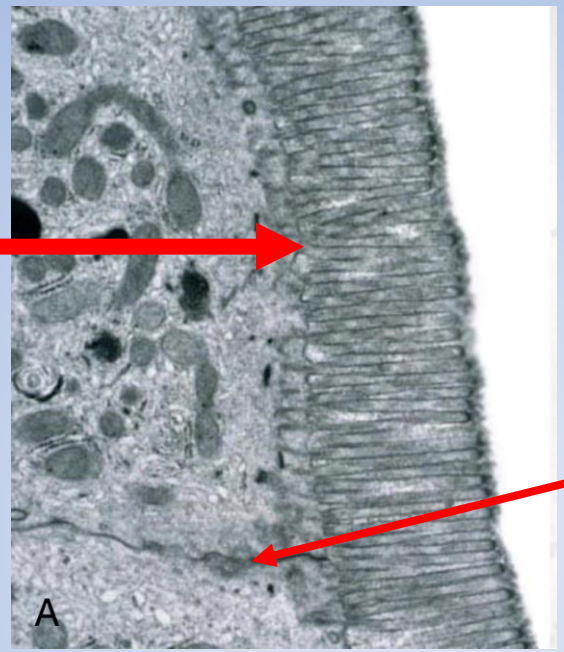
Literature:
Cell Biology, Third Edition, Pollard, Thomas D., MD, 2007 chapter «Membrane Physiology«

Structure of absorptive epithelial cells



The brush border of the normal intestine is well outlined by PAS stain because the glycocalyx sugars are densly packed and give intense staining

From: Surgical Pathology of the GI Tract, Liver, Biliary Tract and Pancreas Fourth Edition, 2023 chapter "Enteropathies Associated with Chronic Diarrhea and Malabsorption in Childhood"



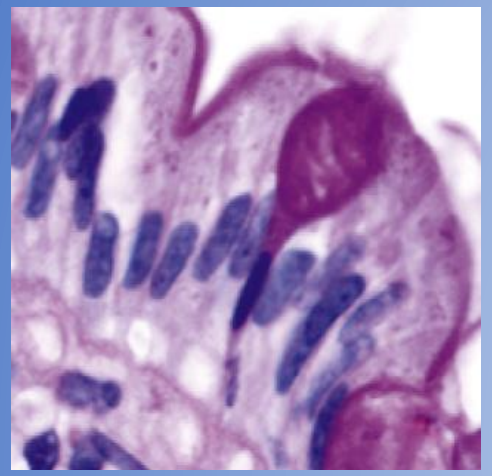
Finer details of the brush border microvilli can only be distinguished in electron microscopy only upper part of the cell is visible

From: Surgical Pathology of the GI Tract, Liver, Biliary Tract and Pancreas Fourth Edition, 2023 chapter "Enteropathies Associated with Chronic Diarrhea and Malabsorption in Childhood"

- Absorptive epithelial cells surface (brush border) has ~3000 microvilli, each ~1 μm long, whose tips are covered with a thick glycocalyx layer
- Glycocalyx coat (from Greek glykys = sweet, kalyx = husk) is found on all human cells
- The glycocalyx consists of sugars and the proteins and lipids to which these sugars are attached and such coat exists (sugars stain with PAS)
- Glycocalyx coat and protects the microvilli from autodigestion by enzymes in the small intestine
- It also contains enzymes attached to cell membrane (such as lactase) that function in terminal digestion of dipeptides and disaccharides into their monomers that can then be absorbed by the cell

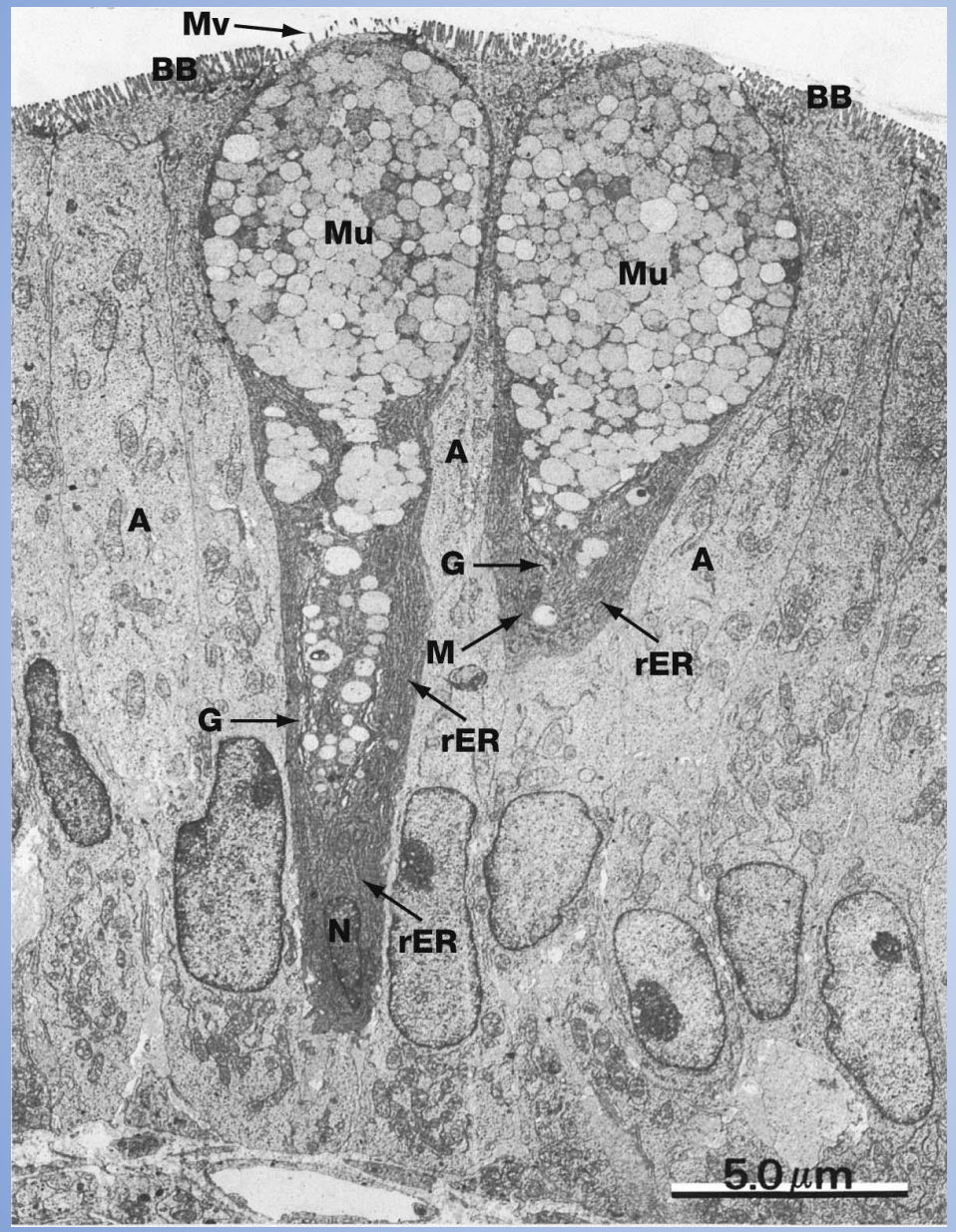
Literature:
The Emerging Role of the Mammalian Glycocalyx in Functional Membrane Organization and Immune System Regulation, Leonhard Möckl, 2020, Frontiers in Cell and Developmental Biology
Textbook of Histology, Fifth Edition, Gartner, Leslie P., PhD, 2021, chapter "Digestive System : Alimentary Canal«
Gastrointestinal Physiology, Ninth Edition, Johnson, Leonard R., PhD, 2019 chapter «Digestion and Absorption of Nutrients»

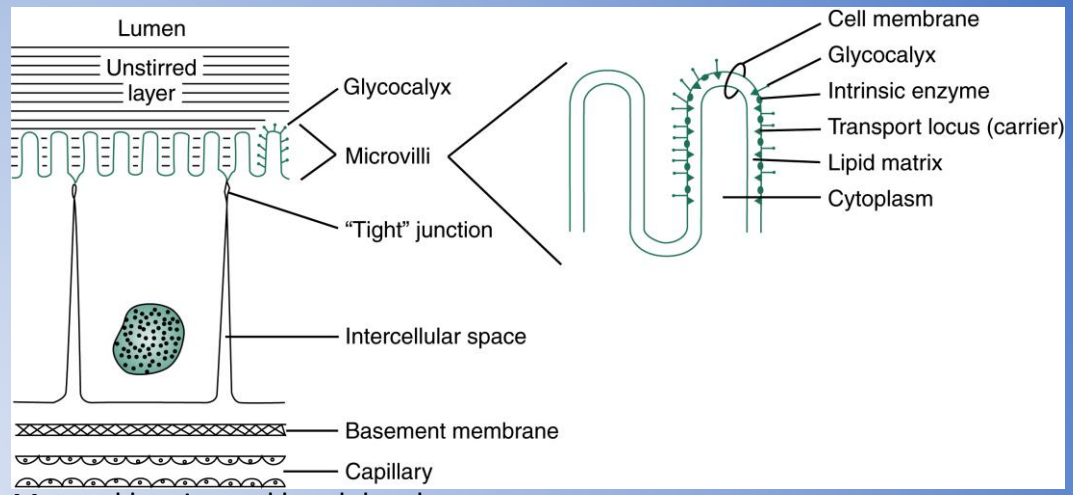
Structure of absorptive epithelial cells



The brush border of the normal cells and a goblet cell filled with PAS+ mucus

From: Surgical Pathology of the GI Tract, Liver, Biliary Tract and Pancreas Fourth Edition, 2023 chapter "Enteropathies Associated with Chronic Diarrhea and Malabsorption in Childhood"





Mucosal barrier and brush border structure. From: Gastrointestinal Physiology, Ninth Edition, Johnson, Leonard R., PhD, 2019 chapter «Digestion and Absorption of Nutrients»

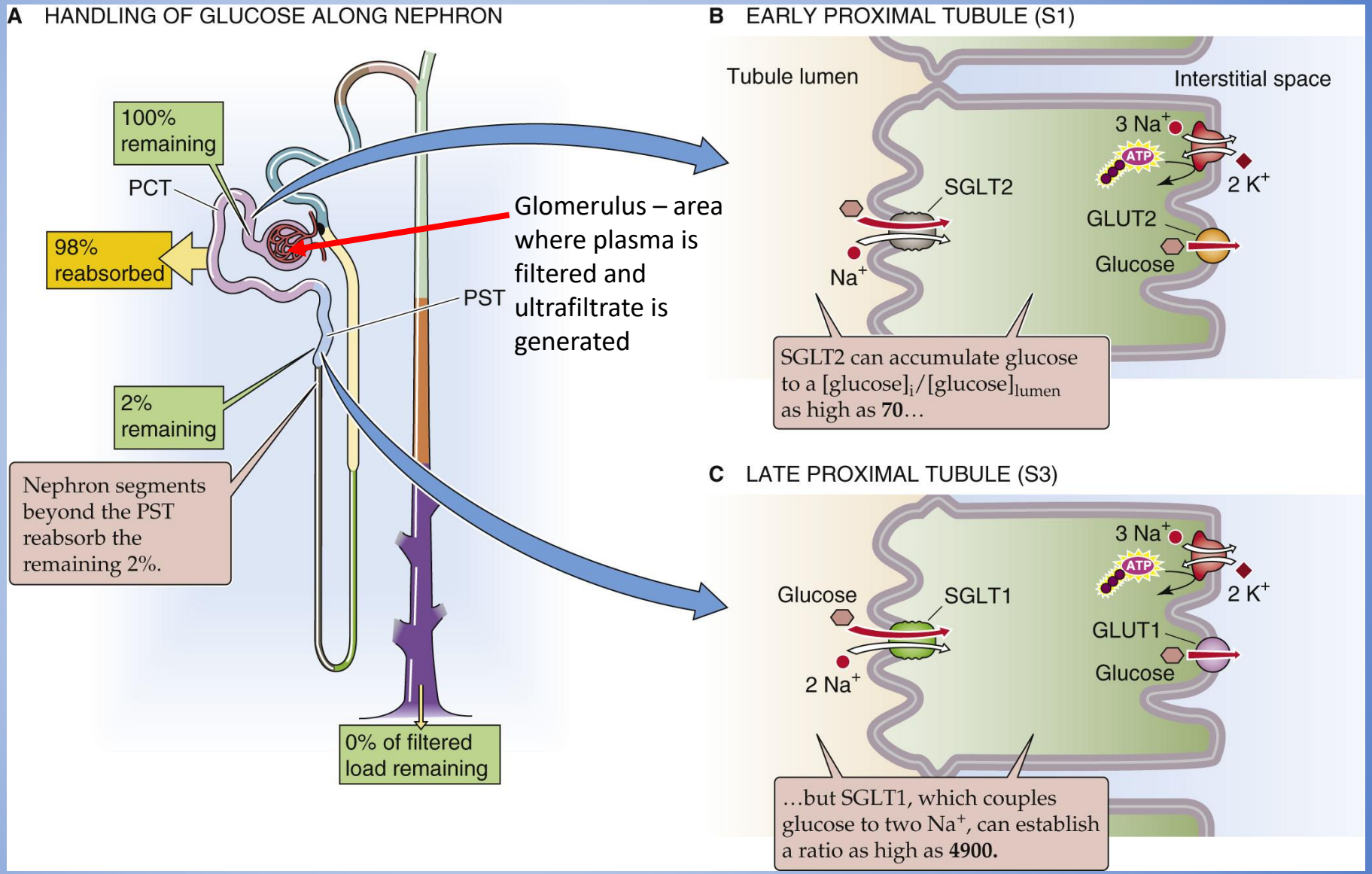
This micrograph shows two goblet cells among columnar **absorptive cells A** (or enterocytes) of the small intestine. **Nucleus N**; **rough endoplasmic reticulum rER** and **mitochondria M**; **Golgi apparatus G**. The protein component of mucigen is synthesised by the rough endoplasmic reticulum and passed to the Golgi apparatus where it is combined with carbohydrate and packaged into membrane-bound secretory granules **containing mucigen Mu** . Goblet cells secrete at a steady basal rate and may be stimulated by local irritation to release their entire mucigen contents. **Sparse microvilli Mv** are seen at the surface of the goblet cell. Note the microvilli forming the **brush border BB** of the absorptive cells.

Mucus has a variety of functions. In the upper gastrointestinal tract, it protects the intestinal lining cells from autodigestion, whilst in the lower tract, it lubricates the passage of faeces. In the respiratory tract it protects the lining from drying, contributes to the humidification of inspired air and acts as a sticky surface trap for fine dust particles and microorganisms. Goblet cells also secrete various anti-microbial factors.

From Wheater's Functional Histology Sixth Edition, 2014

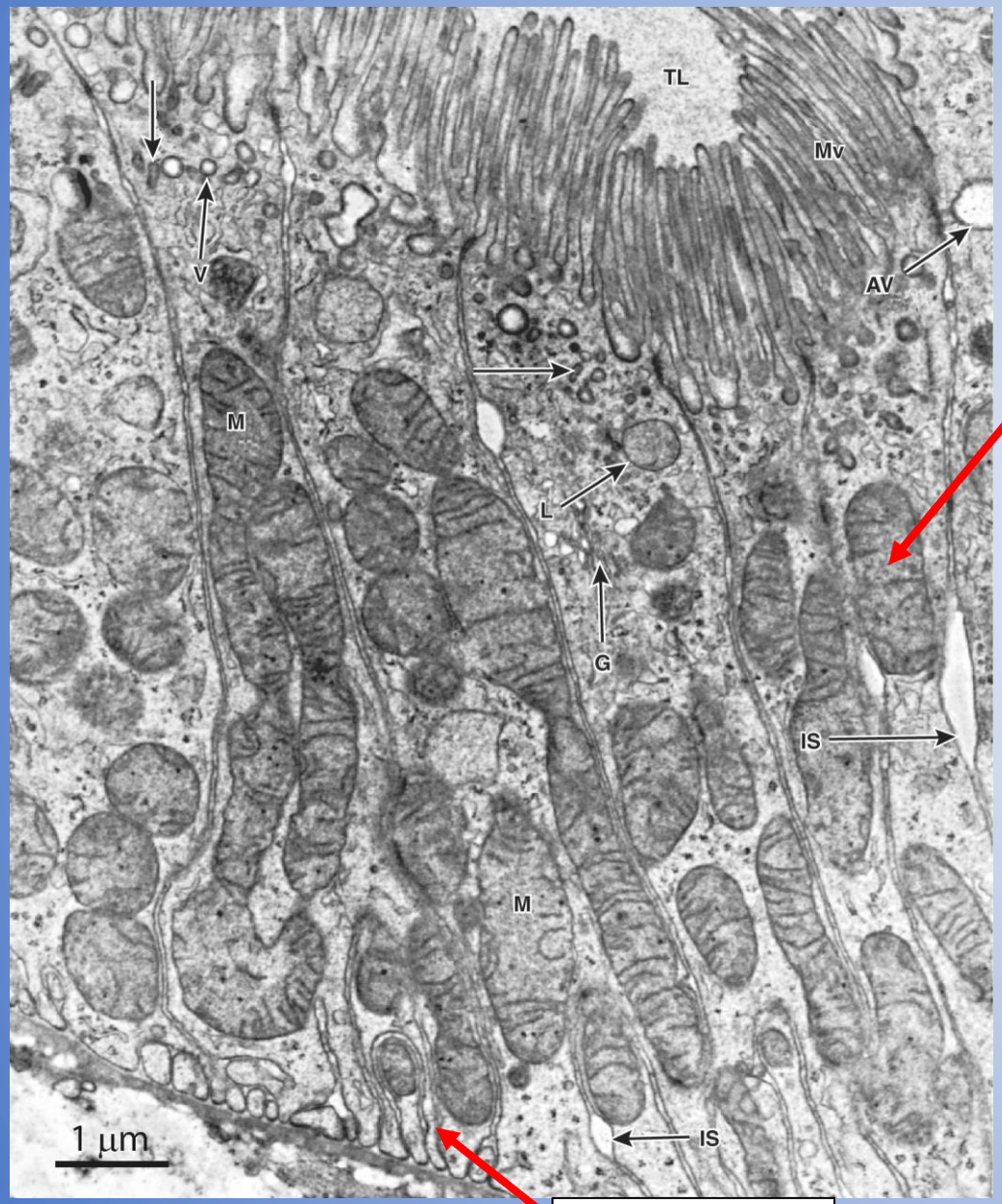
Structure of absorptive epithelial cells

- Glucose is reabsorbed from plasma ultrafiltrate in the kidney's proximal convoluted tubule (PCT)
- The yellow box indicates the fraction of the filtered load that the proximal tubule reabsorbs
- The green boxes indicate the fraction of the filtered load that remains in the lumen at various sites
- The values in the boxes are approximations.
- PST - proximal straight tubule

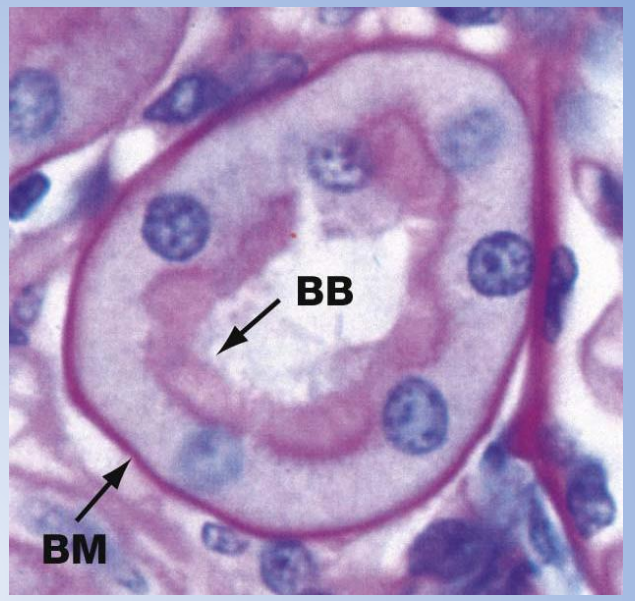


Literature:
Medical Physiology, Third Edition, Boron, Walter F., MD, PhD, 2017, chapter "Transport of Urea, Glucose, Phosphate, Calcium, Magnesium, and Organic Solutes"

Structure of absorptive epithelial cells



Mitochondria Provide ATP for Na +/- K+ pumps



Cross section of a kidney's proximal convoluted tubule (tube made from epithelial cells) staned with PAS from Wheater's Functional Histology Sixth Edition, 2014

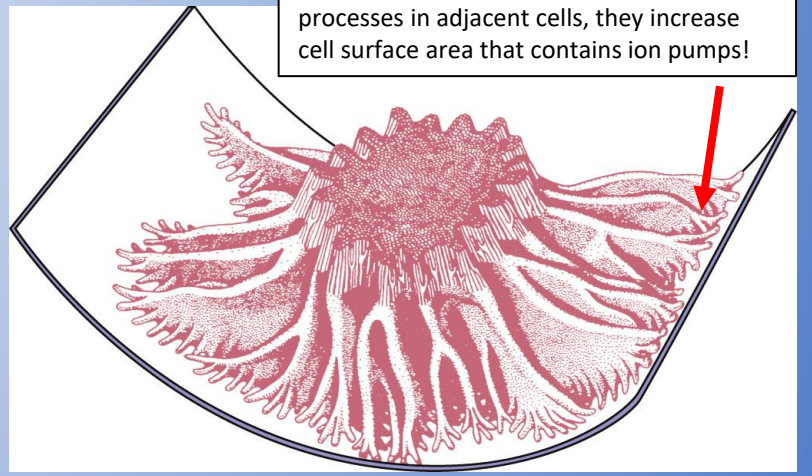
BB – brush border
BM – basal membrane

Transmission electron micrograph of the proximal convoluted tubule cells (absorptive) from a normal human kidney.

The mitochondria (M) are elongated and tortuous, occasionally doubling back on themselves.

The endocytic apparatus, composed of apical vacuoles (AV) , apical vesicles (V) , and apical dense tubules (arrows) , is well developed. G , Golgi apparatus; IS , intercellular space; L , lysosome; Mv , microvilli forming the brush border; TL , tubule lumen.From Brenner and Rector's The Kidney, Eleventh Edition, Yu, Alan S.L., MB, BChir, 2020, chapter "Anatomy of the Kidney"

Large lateral processes, often containing mitochondria, extend outward from the primary ridges and interdigitate with similar processes in adjacent cells, they increase cell surface area that contains ion pumps!



Schematic drawing illustrating the three-dimensional configuration of the proximal convoluted tubule cell.

(From Welling LW, Welling DJ. Shape of epithelial cells and intercellular channels in the rabbit proximal nephron. Kidney Int. 1976;9:385–394.).) Brenner and Rector's The Kidney, Eleventh Edition, Yu, Alan S.L., MB, BChir, 2020, chapter "Anatomy of the Kidney«)

Literature:
Brenner and Rector's The Kidney, Eleventh Edition, Yu, Alan S.L., MB, BChir, 2020, chapter "Anatomy of the Kidney"