Maintaining the Body's Chemistry: Dialysis in the Kidneys

Membranes and Proteins: Dialysis, Detergents and Proton Gradients Experiment

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Key Concepts

- Kidney Structure and Function
  - Filtration, Reabsorption, and Secretion
  - Nephron
- Membranes and Channels
  - Size and Shape
  - Polarity Considerations
- Diffusion and Concentration Gradients
  - Dynamic Equilibrium
  - Membranes and Concentration Gradients in the Kidneys
- Artificial Membranes and Dialysis

Related Tutorials

- *Iron Use and Storage in the Body: Ferritin and Molecular Representations*
- *Blood, Sweat, and Buffers: pH Regulation During Exercise*

Structure and Function of the Kidneys: Overview

Blood performs two essential functions: bringing nutrients and oxygen to the cells of the body and carrying waste materials away from cells. In order to serve these purposes, the chemical composition of the blood must be carefully controlled. Blood contains particles of many different sizes and types, including cells, proteins, dissolved ions, and organic waste products. The largest responsibility for maintaining the chemistry of the blood falls on the kidneys, a pair of organs located just behind the lining of the abdominal cavity. The kidneys remove harmful particles from the blood, regulate the blood's ionic concentrations, and retain essential particles in the blood (Figure 1). They act like dialysis units for blood, making use of the different sizes of the particles and specially maintained concentration gradients. Blood passes through the membrane-lined tubules of the kidney, which are analogous to the semi-permeable dialysis bag used in Experiment 2.

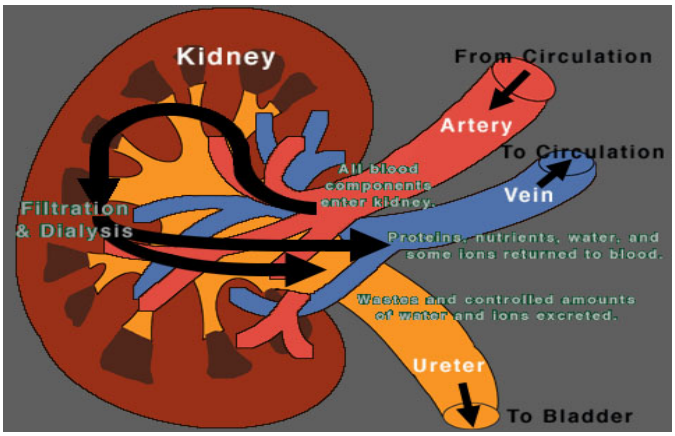


Figure 1: Kidney Anatomy

Blood enters the kidney through the renal artery. In the kidney, the blood undergoes filtration and dialysis to separate the particles that will be removed from the body (through the ureter to the bladder) from those that will be returned to the circulating blood (through the renal vein).

The kidneys have three basic mechanisms for separating the various components of the blood: filtration, reabsorption, and secretion. These three processes occur in the **nephron** (Figure 2), which is the most basic functional unit of the kidney. Each kidney contains approximately one million of these functional units. The nephron contains a cluster of blood vessels known as the **glomerulus**, surrounded by the hollow **Bowman's capsule**. The glomerulus and Bowman's capsule together are known as the **renal corpuscle**. Each Bowman's capsule leads into a membrane-enclosed, U-shaped tubule that empties into a collecting duct. The collecting ducts from the various nephrons merge together and ultimately empty into the bladder.

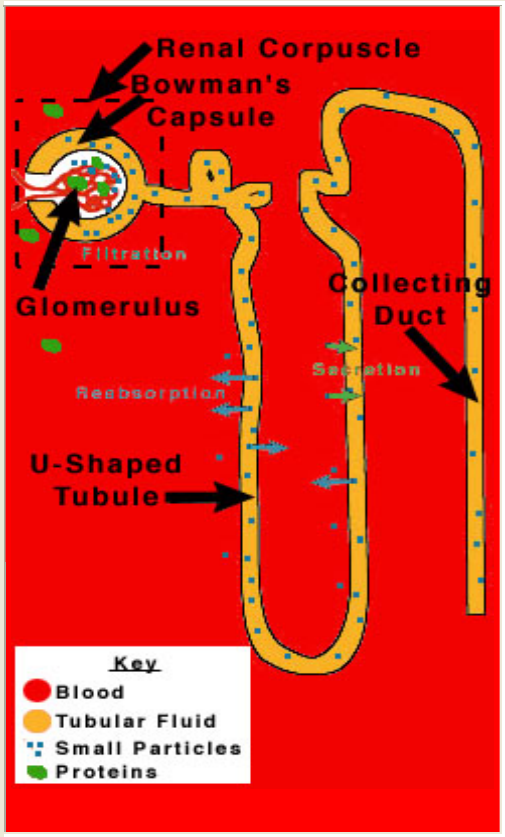


Figure 2: The Nephron

Nephron Segment	Function
Renal Corpuscle: • Glomerulus • Bowman's Capsule	**Filtration:** Glomerulus filters proteins and cells from the blood. All other blood components pass into Bowman's capsule, then into the tubule.
U-Shaped Tubule	**Reabsorption and Secretion:** Semipermeable membranes surrounding the tubule allow selective passage of particles back into the blood (reabsorption), or from the blood into the tubule (secretion).
Collecting Duct	**Collection:** Collects all material that has not returned to the blood through the tubular membranes. This material exits the kidney as urine.

Table 1: Kidney segment function

Renal Corpuscle

Filtration occurs in the renal corpuscle. Blood first enters the kidney through the renal artery. The renal artery (see Fig 1) branches into a network of tiny blood vessels called arterioles, which carry the blood into the tiny vessels of the glomerulus. *Proteins and cells remain in the arterioles because they are too large to pass through the membrane channels of the glomerulus; hence, they remain circulating in the blood throughout the body.* Small particles (*e.g.*, ions, sugars, and ammonia) are able to pass through the membranes into Bowman's capsule. These smaller components then enter the membrane-enclosed tubule in essentially the same concentrations as in the blood.

Tubule

The tubule functions as a **dialysis unit**, in which the fluid inside the tubule is the internal solution and the blood (in capillaries surrounding the tubule) acts as the external solution. Particles may pass through the membrane and return to the blood stream in the process known as **reabsorption**, which is analogous to the movement of particles from the internal solution to external solution in the dialysis experiment performed in lab. Alternatively, particles may pass through the membrane from the blood into the tubule during **secretion**, which is analogous to the movement of particles from the external solution to internal solution in the dialysis experiment. The most important particles that are secreted from the blood back into the tubules are H^+ and K^+ ions, as well as organic ions from foreign chemicals or from the natural by-products of the body's metabolism.

Collecting Duct

The blood components that remain in the nephron when the fluid reaches the collecting duct are excreted from the body. The collecting ducts from different nephrons combine and feed into the ureter. The ureters (one from each kidney) enter the bladder, which leads to the urethra, where the liquid waste is excreted from the body.

Membrane Channels

From the overview of kidney function above, it is clear that blood components (*e.g.*, water, ions, sugars) must be able to pass between the nephron tubules and the blood-filled capillaries surrounding them. However, phospholipid-bilayer membranes are not permeable to polar molecules since the interior lipid region of the membrane is nonpolar. Polar components of blood cannot cross the membranes surrounding the tubules (Figure 3A) *unless* these membranes contain specialized channels.

The channels required for passage of polar blood components are formed by proteins embedded in the phospholipid-bilayer membrane (Figure 3B). These proteins typically have membrane-spanning cylindrical shapes, which are composed of hydrophobic surface amino acid residues and hydrophilic internal core residues. The hydrophobic surface interacts with the non-polar tails of the phospholipids in the bilayer. The hydrophilic interior forms a "tunnel" that allows ions and polar molecule to pass through. The size of the hydrophilic tunnel determines the size of the particles that will be able to pass through the channel. These channels may be left open continuously, or they may be opened and closed by elaborate cellular gating mechanisms. Ultimately, passage of particles through the membrane is dictated by the size, shape, and polarity of the channel.

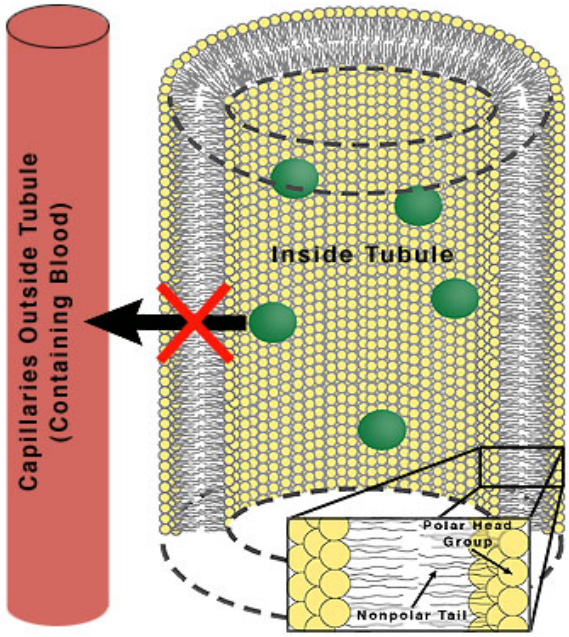


Figure 3A: Simplified nephron tubule

This is a schematic diagram of a segment of a nephron (with no protein channels) shown as a lengthwise slice. Polar molecules (green) cannot travel out of the tubule because they are insoluble in the hydrophobic (nonpolar) lipid interior of the membrane. *Passage of ions requires specialized channels.*
Note: For simplicity, the tubule is depicted here as being enclosed by a single membrane. In fact, the tube and capillaries are lined with cells that are surrounded by membranes. A particle must travel across several membranes in order to move between the interior of the tubule and the blood containing capillaries.

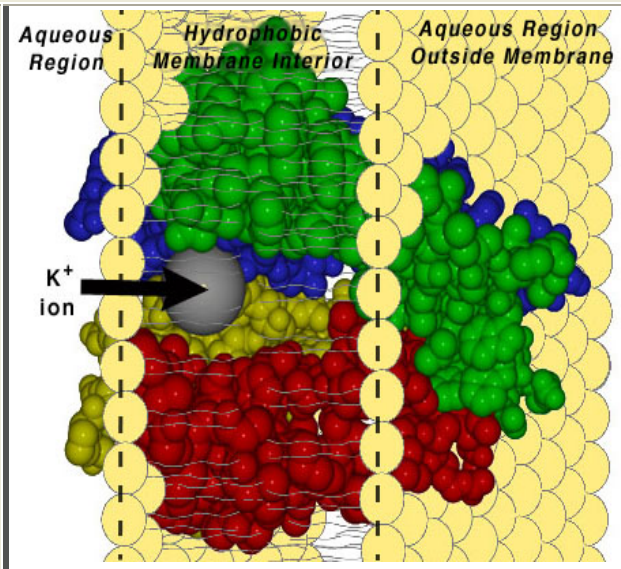


Figure 3B: Potassium channel

This is a CPK representation of the cross section of a potassium channel embedded in a schematic phospholipid bilayer. Structurally, the protein is composed of four polypeptide chains (shown in different colors) that span the width of the membrane, with a hollow space through which potassium ions may pass. Click on the *link* to see a different view.

Note: The coordinates for this protein were determined by x-ray crystallography, and the protein component of this image was rendered using SwissPDB Viewer and POV-Ray (see References).

Diffusion and Concentration Gradients

Diffusion describes the mixing of two different substances that are placed in contact. The substances may be gases, liquids, or solids. Diffusion occurs due to random migration of particles. Although particles move in every direction, there is a **net flow** of the particles from a more concentrated solution to a less concentrated solution (this is commonly referred to as going "down the concentration gradient"). As the number of particles in the more concentrated solution diminishes and in the less concentrated solution increases, the difference in concentration between the two solutions (**concentration gradient**) becomes smaller (see Movie below). This process continues until the concentrations of the two solutions are equal. When this occurs, particles continue to move between the two solutions, but there is no net flow in any one direction, *i.e.*, the concentrations do not change.

This state is called **dynamic equilibrium**. All else being equal, the rate of the net flow is greater when the concentration gradient is greater.

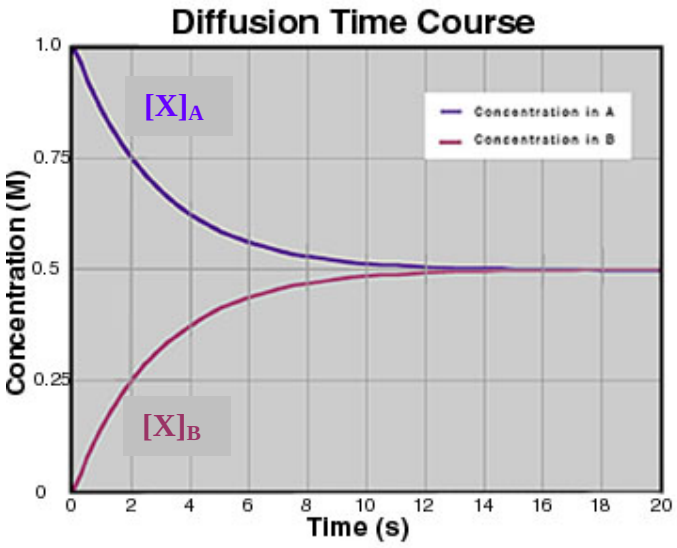


Figure 4: Diffusion kinetics

The graph plots the time course of the changes in concentration that occur after solution A with a 1.0 M concentration of some particle (X) is placed in contact (via a semipermeable membrane) with solution B with a 0.0 M concentration of X. Over time, the system reaches **dynamic equilibrium**.

To view a QuickTime movie showing the movement of the particles associated with this graph, please click on the buttons to the right.

View the Movie

Download QuickTime 4

Membranes and Concentration Gradients in the Kidneys

How do the kidneys actually filter the blood to remove the necessary particles in the proper amounts? The specialized semi-permeable membranes of the nephron, protein channels, and protein pumps act in conjunction with concentration gradients to perform the dialysis functions of the kidney.

Lipid-soluble substances can easily pass through the phospholipid membrane, and so these substances tend to be readily reabsorbed into the blood. This can be a problem because many drugs and toxins, such as the pesticide DDT, are lipid-soluble. Hence, removal of these toxins is very difficult.

Most of the components of the blood, however, are polar or charged and require protein channels to cross the membrane. The channels in the nephrons are specialized to allow only the passage of particular types of particles, based on size, shape, and charge interactions with the amino acids lining the channel interior. The kidneys control the concentration of different species in two ways: by regulating the number of channels in the membrane and the number of channels that are open. In the end, most waste products undergo only partial reabsorption, so large amounts of the substance remain in the tubule and are thus removed from the body in the urine. In contrast, useful plasma components, such as water, nutrients, and inorganic ions, are completely reabsorbed.

To demonstrate how the specialized membranes of the kidneys work to maintain the blood's chemistry properly, we shall consider three different blood-plasma components (Na^+, H_2O, and urea) and how the flow of each component between the nephron tubule and the surrounding blood-containing capillaries is controlled.

Urea Reabsorption (Using Channels; Movement of Particles Down (With) a Concentration Gradient)

Urea is a waste product formed in the liver during the metabolic breakdown of proteins. Due to its small size, urea easily enters the tubule during the filtration step in the glomerulus. Even though it might seem that all of the urea will be excreted, only half of this urea actually reaches the urine. The tubular membranes are permeable to urea. Therefore, as urea flows down the tube, it flows from high concentration (inside the tubule) to low concentration (in the blood containing capillaries) until dynamic equilibrium is reached. The urea in the tubules is eventually excreted via the collecting duct, but it is only half the amount of the glomerular filtrate.

Sodium Reabsorption (Using Pumps; Movement of Particles Against a Concentration Gradient)

Certain segments of the nephron tubule contain proteins that *use energy* to pump sodium ions out of the tubule and into the blood (Figure 5). Sodium is therefore *actively* reabsorbed into the blood. In this case, the proteins in the membranes act like pumps, using energy to move particles "against the concentration gradient" (i.e., so the more concentrated solution becomes even more concentrated). The amount of sodium ions that are reabsorbed can be controlled by the hormone aldosterone. High levels of aldosterone promote sodium pump activity, which increases sodium reabsorption into the blood. When aldosterone levels are low, the pumps are less active, more sodium remains in the tubules, and more sodium is excreted.

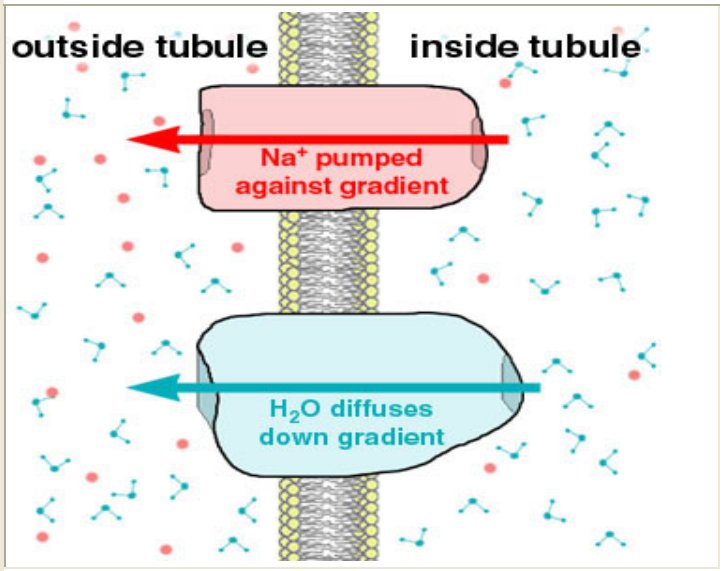


Figure 5: Transport strategies

This schematic diagram shows the reabsorption of Na^+ ions (pink) and water (blue). Na^+ is pumped against the concentration gradient from the inside to the outside of the tubule. H_2O crosses the tubular membrane into the blood outside the tubule by diffusion through a channel, down the concentration gradient.

Water Reabsorption (Using Channels; Movement of Particles Down a Concentration Gradient)

The active pumping of sodium ions out of the tubule causes the water concentration inside the tubule to increase. Conversely, the water concentration in the blood decreases. The result is a water concentration gradient between the tubule fluid and the blood. Some portions of the tubular membrane are impermeable to water, but other portions contain hydrophilic channels through which water can flow. In these areas, water exits the tubule and enters the blood through these hydrophilic channels by passive diffusion (Figure 5). In the collecting duct, the permeability of the membrane can be altered by the hormone vasopressin, also known as antidiuretic hormone (ADH). When the body needs to retain water, as in dehydration situations, the pituitary secretes ADH. Higher ADH levels cause the water-permeability of these membranes to increase. Therefore, large amounts of water are reabsorbed

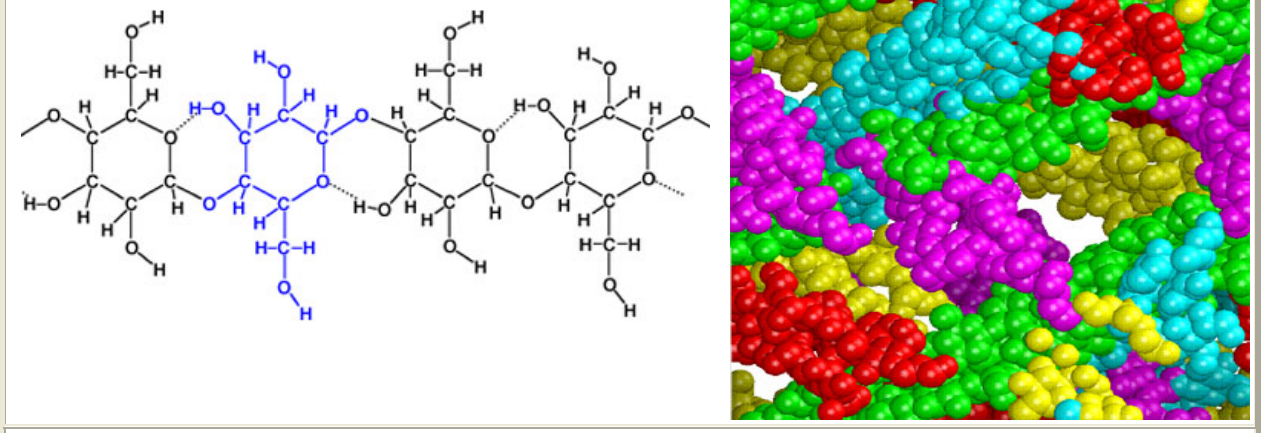
into the blood, and only a little water will be excreted in the urine. When the body has plenty of water, the level of ADH remains low, causing this portion of the membrane to become relatively impermeable to water. In this case, a larger amount of water remains in the collecting duct and is excreted.

Artificial Kidney Dialysis

When the kidneys do not function properly, dialysis must be performed artificially to prevent toxic waste build up in the blood and tissues. Failing kidneys are responsible for **uremia**, which means "urine in the blood." Eventually, waste build-up causes cell death.

Artificial Membranes

To separate the components of blood, artificial kidneys use cellulose membranes in place of the phospholipid-bilayer membranes used by real kidneys. This cellulose membrane is the same type of membrane that you used in this experiment. Cellulose is a polymer of glucose molecules that form long, straight chains. Parallel chains form linkages with one another by hydrogen bonding to make strong fibers. These fibers in turn interact to form the strong, sheet-like structure of the membrane. The arrangement of the cellulose fibers may contain gaps (Figure 6) which form the pores through which particles may pass from one side of the membrane to the other. Like the membrane proteins in the real kidney, the size of the gaps determines the size of the particles that will be able to pass through the membrane.



View this Molecule Interactively

Figure 6 – Artificial membranes

On the left is a two-dimensional representation of a cellulose polymer. One glucose unit is shown in blue. On the right is a CPK representation of cellulose membrane with fibers (each differently colored) that interact to form a sheet-like structure. Note the gaps between the fibers: these are the pores in the membrane.

Note: The coordinates for this model were determined using molecular-mechanics calculations, and the image was rendered using the Insight II molecular-modeling system from Molecular Simulations, Inc. (see *References*)

Types of Artificial Kidney Dialysis

Two types of artificial kidney dialysis are used clinically. **Hemodialysis** uses a cellulose-membrane tube that is immersed in a large volume of fluid. The blood is pumped through this tubing and then back into the patient's vein. The membrane has a molecular-weight cut-off that retains proteins and cells in the blood but allows most solutes to pass out of the tubing. The external solution in which the tubing is immersed is a salt solution with ionic concentrations near or slightly lower than the desired concentrations in the blood. If a particular species is high in concentration in the blood-derived internal solution, then it flows into the external fluid. In this manner, excess substances in the blood are removed from the body. To maintain the blood's concentration of a species, the external solution is made to have the same concentration of that species as the blood. In such a case, the two solutions are in dynamic equilibrium, and so the blood's concentration does not change.

Peritoneal dialysis uses the lining of the patient's abdominal cavity, known as the peritoneum, as a dialysis membrane. Fluid is injected into the abdominal cavity, and solutions diffuse from the blood into this fluid. After several hours, the fluid is removed with a needle and replaced with new fluid. The patient is free to perform normal activities between fluid changings.

Summary

By filtration, reabsorption, and secretion mechanisms, the kidneys separate and regulate the components of the blood. Some of these components (e.g., proteins) are filtered from the fluid entering the tubule at the glomerulus and remain in the blood. Other particles (e.g., water, ions, and sugar) are reabsorbed by the blood or secreted from the blood to maintain the proper concentrations; these processes occur while the fluid is flowing through the tubule. Any blood components that remain in the nephron when the fluid reaches the collecting duct (e.g., waste products such as urea) are excreted from the body.

The reabsorption and secretion of the blood components depend on the ability of these components to cross the nonpolar interior of the membrane surrounding the nephron tubule. The polar blood components can only pass through the membrane via special protein channels. The size of the channel can determine which polar or charged particles will be able to cross the membrane through the channel.

The concentrations of the blood components are maintained by diffusion (going down the gradient) through the membrane (via the protein channels if the component is polar) or by pumping (going against the gradient). Hence, the ability of the kidneys to remove harmful particles from the blood, and to regulate the concentration of other particles in the blood, depends on the chemical concepts of polarity and diffusion. The use of “pumps” made of proteins and the permeability of tubule membranes can be altered by hormones such as aldosterone and vasopressin.

When the kidneys do not function properly, the components of blood can be separated by artificial semipermeable membranes such as cellulose membranes, a polymer of glucose molecules. The peritoneum, which is the lining of the abdominal cavity, can also function as a dialysis membrane. Thus, the artificial kidney dialysis uses the same chemical principles that are used naturally in the kidneys to maintain the chemical composition of the blood. Diffusion across semipermeable

membranes, polarity, and concentration gradients are central to the dialysis process for both natural and artificial kidneys.

Additional Links:

- The National Kidney Foundation is an advocacy organization for kidney health and helping those with kidney disease. This site contains press releases and fact sheets about kidney disease.
- Renalnet Kidney Information Clearinghouse provides a wealth of information about the kidneys, particularly about artificial dialysis and other treatment options for kidney disease.
- The Renalworld website includes a large number of resources pertaining to the kidneys.

References:

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Insight II graphical program; Molecular Simulations, Inc. URL: *http://www.msi.com.*

Persistence of Vision Ray Tracer (POV-Ray). URL: *http://www.povray.org*.

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Acknowledgements:

The authors thank Dewey Holten, Michelle Gilbertson, Jody Proctor and Carolyn Herman for many helpful suggestions in the writing of this tutorial.

The development of this tutorial was supported by a grant from the Howard Hughes Medical Institute, through the Undergraduate Biological Sciences Education program, Grant HHMI# 71199-502008 to Washington University.

Revised June 2007.

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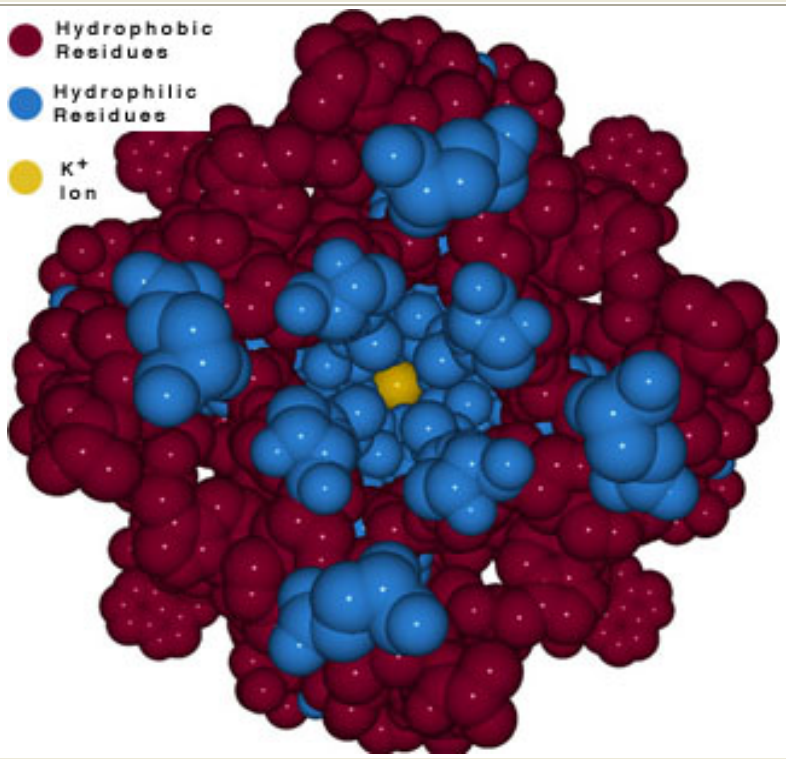
Another View of the Potassium Channel



This is a view through the opening of the same potassium channel shown in Figure 3B. Notice that the inner core is lined with hydrophilic amino-acid residues (blue) that interact favorably with the charge on the ion (yellow). The outer areas of the channel contain hydrophobic amino-acid residues (plum), which interact favorably with the hydrophobic lipids in the membrane.

Note: The coordinates for this protein were determined by x-ray crystallography, and the image was rendered using SwissPDB Viewer and POV-Ray (see References).

View this Molecule Interactively

Note: To view the molecule interactively, please use Chime, and click on the button to the left.