

## Student Handout 3

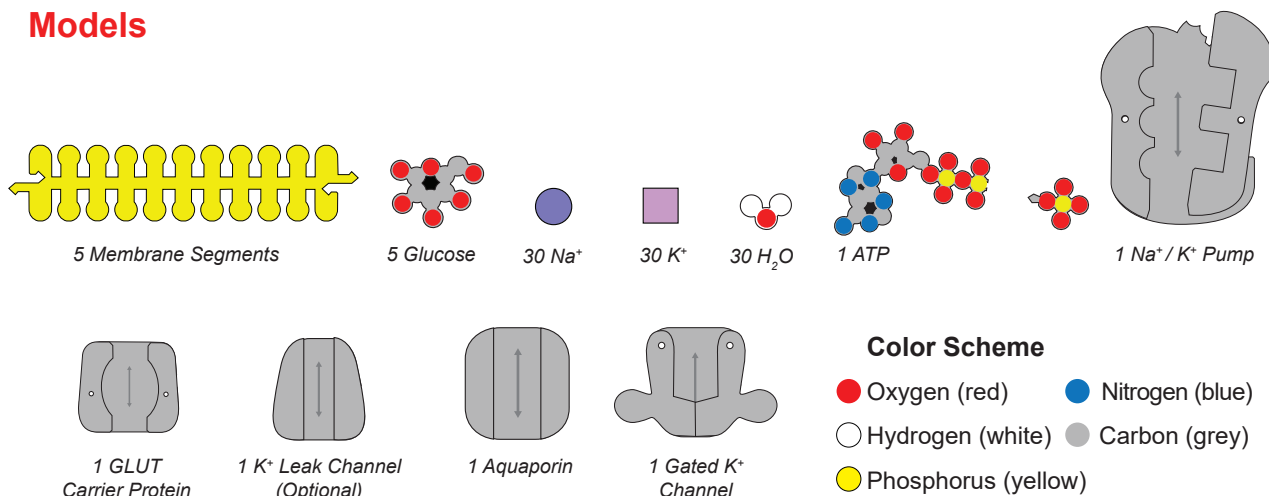
### Big Idea

Movement of ions and molecules through a membrane is facilitated by membrane-bound proteins.

### Exploring Membrane Permeability

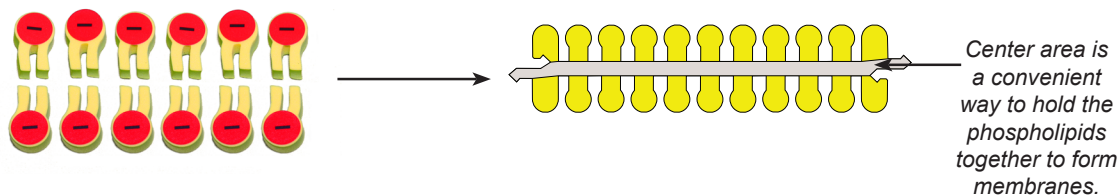
The phospholipid bilayer is only one aspect of the gatekeeper system responsible for the plasma membrane's **selective permeability**. Membrane-bound proteins play a key role in regulating the transport of ions and molecules through the plasma membrane.

### Models



You will use a simplified representation of the phospholipid bilayer in this activity.

1. Label the **hydrophilic head** and **hydrophobic tail** in the photos below.



2. Nonpolar molecules, such as hydrocarbons, CO<sub>2</sub> and O<sub>2</sub>, are hydrophobic. Explain why these molecules can easily cross the plasma membrane without the aid of proteins.

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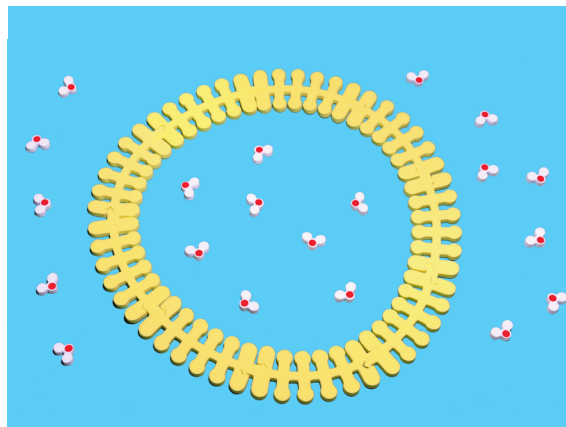
## Phospholipid Activity 3 Continued



### Misconception

There is a common misconception that a hydrophilic water molecules can easily cross the hydrophobic phospholipid bilayer. In the following activity you will model why this isn't necessarily true.

Construct a model of the passage of water through a plasma membrane, using 5 phospholipid bilayer sections to form the cell. Place 8 water molecules inside the cell (intracellular area) and 12 outside the cell (extracellular area).



3. Can you move the water molecule models through the bilayer?

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4. Identify a limitation with this model.

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A variety of polar molecules can't move through the plasma membrane on their own. Contact with hydrophobic lipid bilayer is avoided by these hydrophilic substances when they cross the plasma membrane with the help of **transport proteins**.

### Channel Proteins

Some transport proteins, known as **channel proteins**, function by having a hydrophilic channel that molecules or ions use to cross the plasma membrane. **Aquaporin** is a channel protein embedded in a cell membrane that allows water to cross the cell membrane. Aquaporin facilitates passage of up to 3 billion ( $3 \times 10^9$ ) water molecules per second!

5. Explain why water would have a difficult time diffusing across the cell membrane. Keep in mind the structure of water in your answer.

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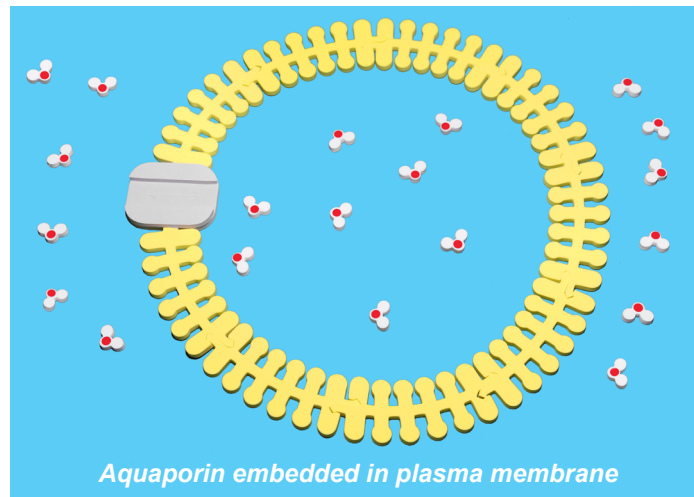
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## Phospholipid Activity 3 Continued



A solute (dissolved substance) will diffuse from where it is more concentrated to where it is less concentrated. In other words, the solute will diffuse down its concentration gradient. Insert the aquaporin protein model in the cell membrane. Aquaporin is a channel protein that permits the rapid diffusion of water across a selectively permeable membrane. Water will move to equalize the solute concentrations on each side of the membrane.



6. Model a system where the concentration of solutes (use the blue sodium ions and the purple potassium ions) inside the cell is higher than the concentration of solutes outside the cell. If the membrane is permeable to water and not the solutes, in which direction will the net flow of water occur?

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7. Construct a system where intracellular solute concentration is lower than extracellular solute concentration. Sketch your model in the space below and indicate the net flow of water in the system

## Phospholipid Activity 3 Continued

8. Predict what will happen to the cell due to the movement of the water.

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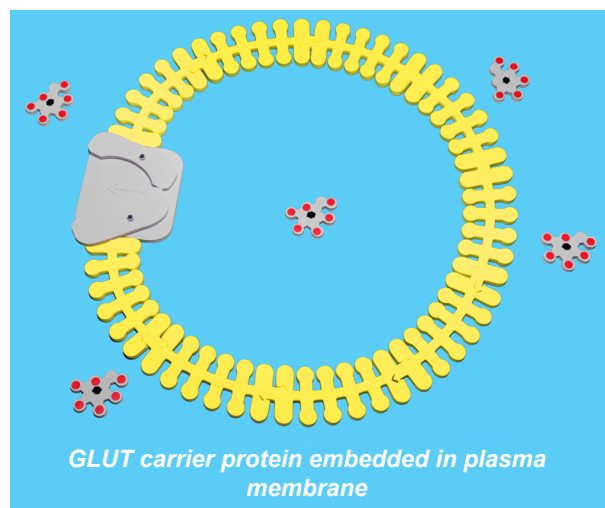
Because the water was moving with its concentration gradient, the cell did not have to expend cellular energy to move water across the plasma membrane in the above cases. Movement of a substance across a membrane without the expenditure of energy is referred to as **passive transport**. When the cell must expend energy (usually in the form of ATP) to move a substance against its concentration gradient, the process is referred to as **active transport**.

Transmembrane proteins, proteins that span the cell membrane, can assist in the passive movement of substances across the membrane. **Channel proteins**, like aquaporin, provide canals through which small molecules or ions can pass. **Facilitated diffusion** occurs when transmembrane proteins assist molecules and ions in moving across the membrane with their concentration gradient.

### Carrier Proteins

A second kind of **facilitated diffusion** occurs when a transmembrane protein binds a solute molecule on one side of the membrane, and changes shape (makes a conformational change) to deposit the solute molecule on the other side of the membrane. These transmembrane proteins are called **carrier proteins**. GLUT is an example of a protein channel frequently found in the plasma membrane of red blood cells that facilitates the movement of glucose across the cell's plasma membrane.

Remove the water molecules and aquaporin models from the cell model you have constructed. Insert the GLUT carrier protein model into the plasma membrane model. Distribute the glucose molecules so that there are more extracellular glucose molecules than intracellular glucose molecules (*right photo*).



### Phospholipid Activity 3 Continued



9. Use the model to demonstrate the movement of glucose across the cell membrane. Sketch your model in the space below.

10. Is this an example of passive or active transport? Explain your choice.

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11. Explain how GLUT is an example of facilitated diffusion.

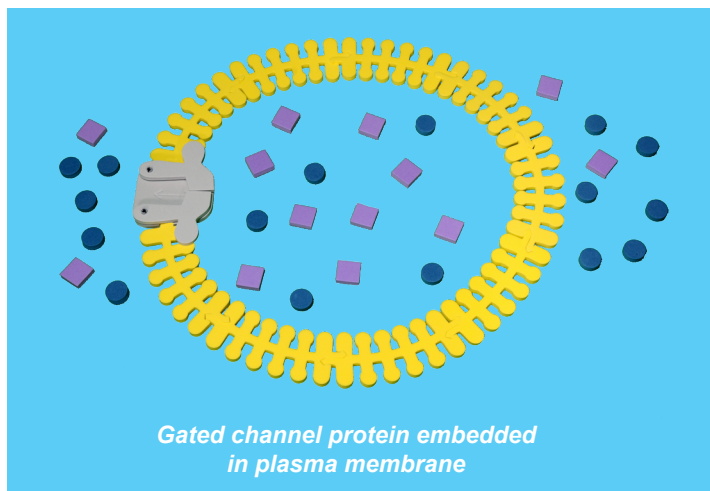
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#### Gated Channels

Remove the glucose molecules and carrier protein from the cell membrane. Insert the gated channel protein model into the plasma membrane model (*right photo*). Place 5 sodium ions (round) and 10 potassium ions (square) inside of the cell to simulate intracellular ion concentrations. Place 10 sodium ions and 5 potassium ions outside of the cell to simulate extracellular ion concentrations.



### **Phospholipid Activity 3 Continued**



Gated channels are channel proteins that open or close in response to a stimulus. For example, in nerve cells, a stimulus opens gated sodium channels and gated potassium channels to allow the specific ions to enter the cell. Other gated channels open or close when a substance, different from the one to be transported, binds to the channel. Channels that open when a substance binds to them are called ligand gated channels.

Begin the simulation with the gated  $K^+$  channel closed. After a stimulus the gates swing open.

12. If this gated channel is specific for potassium ions and based on what you know about concentration gradients, what direction will the potassium ions move through the channel?

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13. Does this gated channel demonstrate passive or active transport? Explain your answer.

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14. Speculate what other stimuli may affect the operation of channel proteins.

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15. Devise a question you might have about the operation of this channel protein.

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## Phospholipid Activity 3 Continued

Could other molecules or ions pass through aquaporin or the gated potassium channel? While the simple models of the aquaporin and gated potassium channels included in this kit don't show detail, other molecules or ions rarely pass through them. Most proteins have specific structures that restrict other molecules or ions from passing in or out of the cell.

### Selectivity Filters

In cell membrane proteins, **selectivity filters** allow the correct molecules or ions to pass through the proteins and, for the most part, prevent other molecules or ions from passing through the channel. The selectivity filters can be:

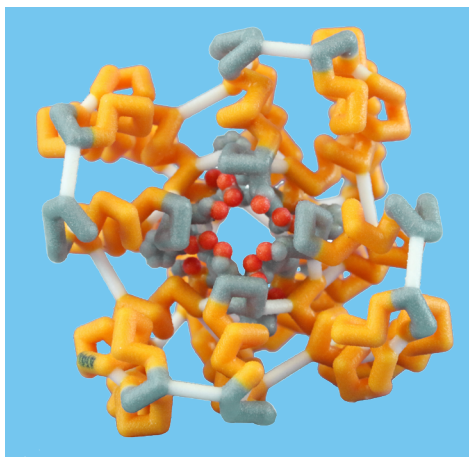
- Determined by the structural size and shape of the channel
- Specific bonds between molecules or ions and atoms within the channel
- Charged, such as admitting positively charged ions and blocking negatively charged ions
- A combination of these factors



Aquaporin Channel

### Aquaporin

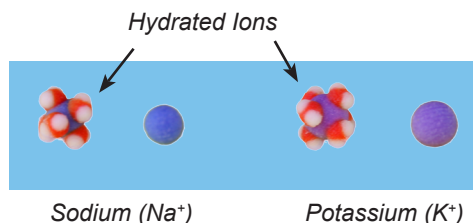
Water molecules pass through the primarily hydrophobic portions of the aquaporin channel until they reach the narrowest part of the hour-glass shaped protein (*left photo*). Then the water molecules bond first with one nitrogen and then a second before passing through the rest of the protein to enter or exit the cell. (Nitrogen are blue in the photo.)



Sodium Channel

### Sodium Channel

Sodium ions ( $\text{Na}^+$ ) flow through the protein until they reach the narrow section of the channel, which is just large enough for a sodium ion hydrated with water molecules to pass into or out of the cell. Even though potassium ( $\text{K}^+$ ) ions also have a positive charge, they are larger than sodium ions when hydrated and they can't pass through the narrow section of the channel.



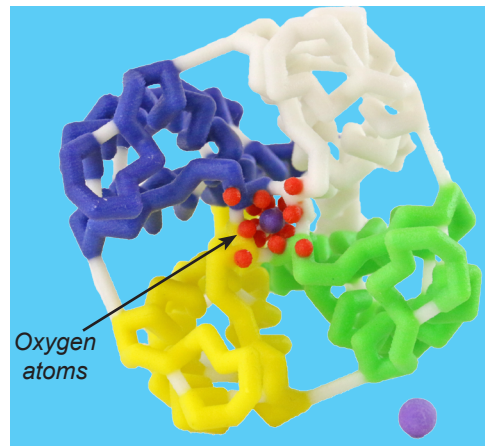
## Phospholipid Activity 3 Continued

### Potassium Channel

Even though a potassium ion is larger than a sodium ion, the opening of the potassium channel is smaller than the opening of the sodium channel.

The potassium channel has a very specific arrangement of oxygen atoms that align closely with the water molecules surrounding the potassium ion in its hydrated state (*photo right*).

About two thirds of the way through the cone-shaped potassium channel, the channel narrows enough so that the water molecules are stripped from the potassium ions, allowing them to pass through the rest of the channel. The specific arrangement of the oxygen atoms within the channel bond with and remove the water molecules and free the dehydrated potassium to easily pass through the channel. These oxygen **do not align** with or remove the water molecules hydrating the sodium. As a result, sodium ions are not able to cross the selectivity filter of the potassium channel to enter or exit the cell.



16. How then do potassium ions pass through the channel?

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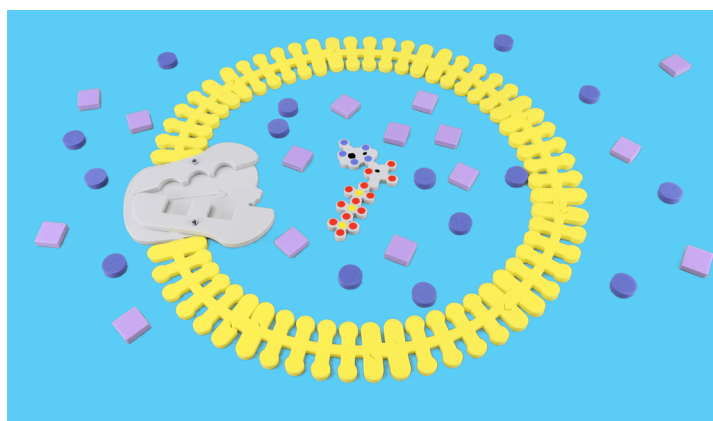
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### Active Transport - The Sodium-Potassium Pump

Remove the gated channel from the model cell you have constructed. Insert the sodium-potassium pump protein into the membrane of the model (*right photo*). Place 7 sodium ions (round) and 8 potassium ions (square) inside of the cell to simulate the intracellular environment ion concentrations. Place 8 sodium ions and 7 potassium ions outside of the cell to simulate the extracellular ion concentrations. Place the ATP molecule on the inside of the model cell.



Transport proteins that move solutes against their concentration gradients are all carrier proteins. The sodium-potassium pump is a special carrier protein that moves sodium ions against their gradient **out** of the cell and potassium ions against their gradient **into** the cell.

## Phospholipid Activity 3 Continued

Since these ions are moving against their concentration gradients, the cell must expend energy to do the work, resulting in **active transport** of these ions.

A typical animal cell has a much higher concentration of potassium ions ( $K^+$ ) and a much lower concentration of sodium ions ( $Na^+$ ) on the inside of the cell than the outside. The sodium-potassium pump uses energy in the form of ATP to move these ions against their concentration gradients to establish the *normal* intracellular ion concentrations. The action of the sodium-potassium pump can be demonstrated using the models in the following simulation:

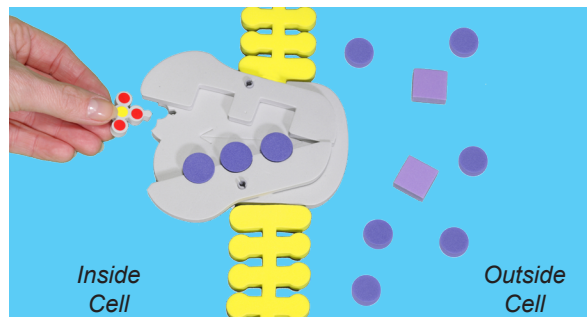
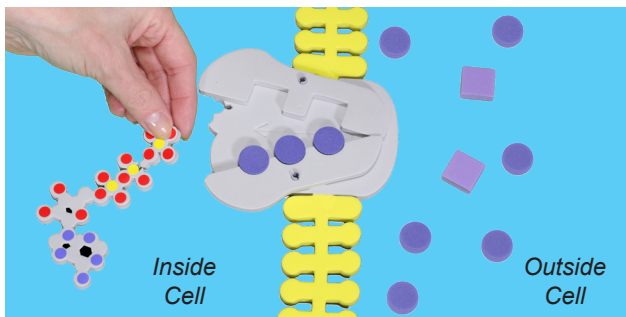
Set the sodium-potassium pump so that it is open to the inside of the cell as shown in the photo on page 8.

17. Record the initial ion concentrations in the table provided below:

| Ion Types            | Initial Amount | Amount After First Cycle | Amount After Second Cycle |
|----------------------|----------------|--------------------------|---------------------------|
| Intracellular $Na^+$ |                |                          |                           |
| Intracellular $K^+$  |                |                          |                           |
| Extracellular $Na^+$ |                |                          |                           |
| Extracellular $K^+$  |                |                          |                           |

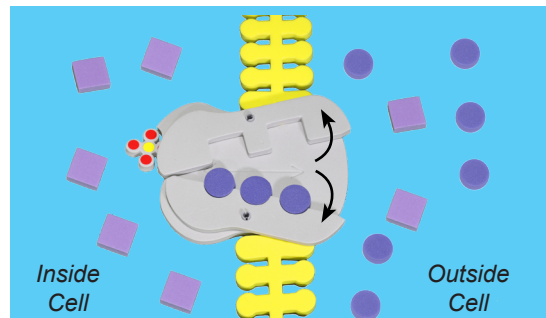
Bind three intracellular sodium ions from **inside the cell** to the appropriate spots in the protein (*right photo*).

Sodium ion binding stimulates phosphorylation of the pump protein by ATP. In other words, a phosphate group is added to the sodium-potassium pump from the ATP molecule. Detach the phosphate group from ATP molecule located **inside the cell** and bind it to the protein (*photos below*).

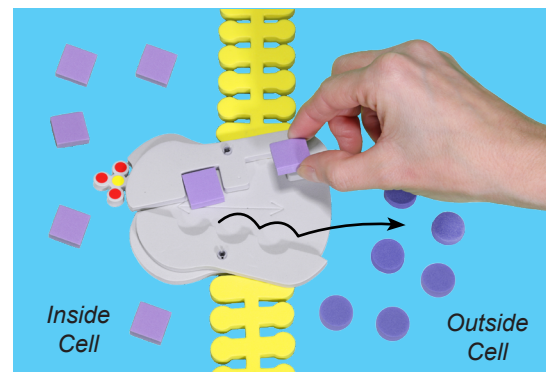


## Phospholipid Activity 3 Continued

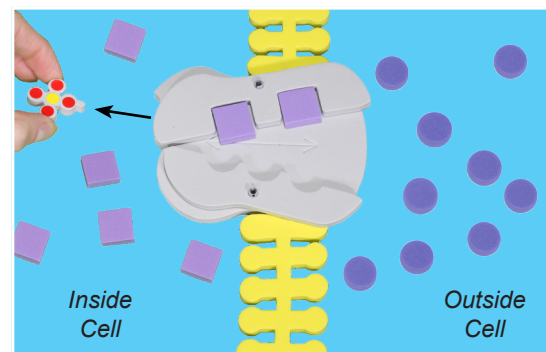
Phosphorylation causes a change in the shape of the protein. You can demonstrate this by swinging the sides of the protein so that it opens to the **outside of the cell**.



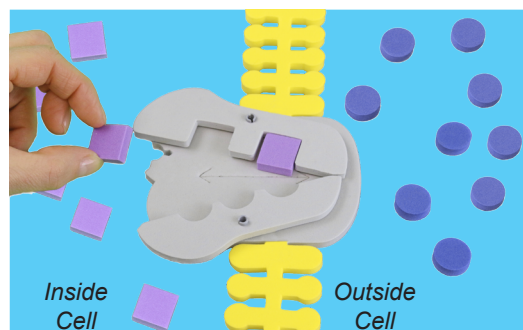
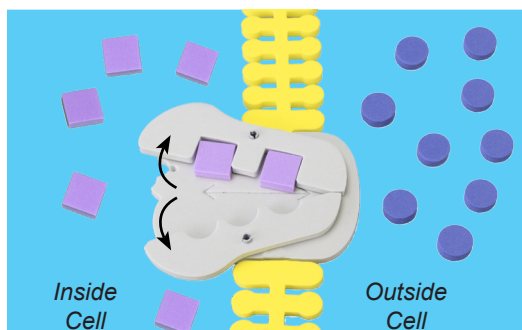
The shape change reduces the protein's binding affinity for sodium ions and increases the binding affinity for potassium ions. Remove the sodium ions from the protein and deposit them outside the cell and bind two potassium ions to the appropriate spots in the protein.



Potassium ion binding triggers the release of the phosphate group from the protein. Detach the phosphate group from the sodium- phosphate pump (*photo left*).



Loss of the phosphate group results in the restoration of the protein's original shape which then releases the potassium ions. Swing the sides of the protein back so that they open to the inside of the cell and deposit the potassium ions (see *photos below*).



**Phospholipid Activity 3 Continued**

Repeat this process once more.

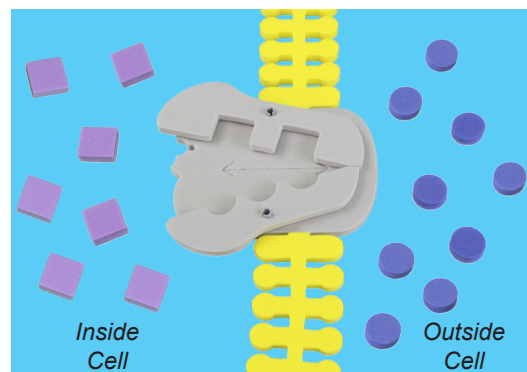
18. Record the ion concentrations after completing the first cycle of the action of the sodium-potassium pump in the table on page 9.

19. What is the initial overall positive charge inside the cell compared to the outside the cell?

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20. Compare the total intracellular positive charge to the total extracellular positive charge after one cycle of the sodium-potassium pump.

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21. Record the ion concentrations after completing the second cycle of the action of the sodium-potassium pump in the table on page 9. Compare the total intracellular positive charge to the total extracellular positive charge after the second cycle of the action of the sodium-potassium pump.

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22. Where is the sodium ion concentration highest at the beginning of the sodium-potassium pump cycle?

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23. Where is the potassium ion concentration highest at the beginning of the sodium-potassium pump cycle?

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24. What is the initial overall charge of the inside of the cell compared to the outside?

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**Phospholipid Activity 3 Continued**



25. Why is ATP required in this process?

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26. After one cycle of the sodium-potassium pump, compare the overall charge of the inside of the cell to the outside? Explain how the distribution of ions changed.

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27. Is the sodium-potassium pump a channel protein or a carrier protein? Explain your answer.

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28. Devise a question you might have about the function of the sodium-potassium pump.

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**Fun Fact**

In nerve cells, the sodium-potassium pump helps to re-establish the resting ionic concentrations after the nerve cell has fired.

**References**

Berg JM, Tymoczko JL, Stryer L. Biochemistry. 5th edition. New York: W H Freeman; 2002. Section 13.5, Specific Channels Can Rapidly Transport Ions Across Membranes. Available from: <http://www.ncbi.nlm.nih.gov/books/NBK22509/>

Cooper, Geoffrey M. The Cell: A Molecular Approach. 2nd edition. Boston University Sunderland (MA): Sinauer Associates; 2000. ISBN-10: 0-87893-106-6.