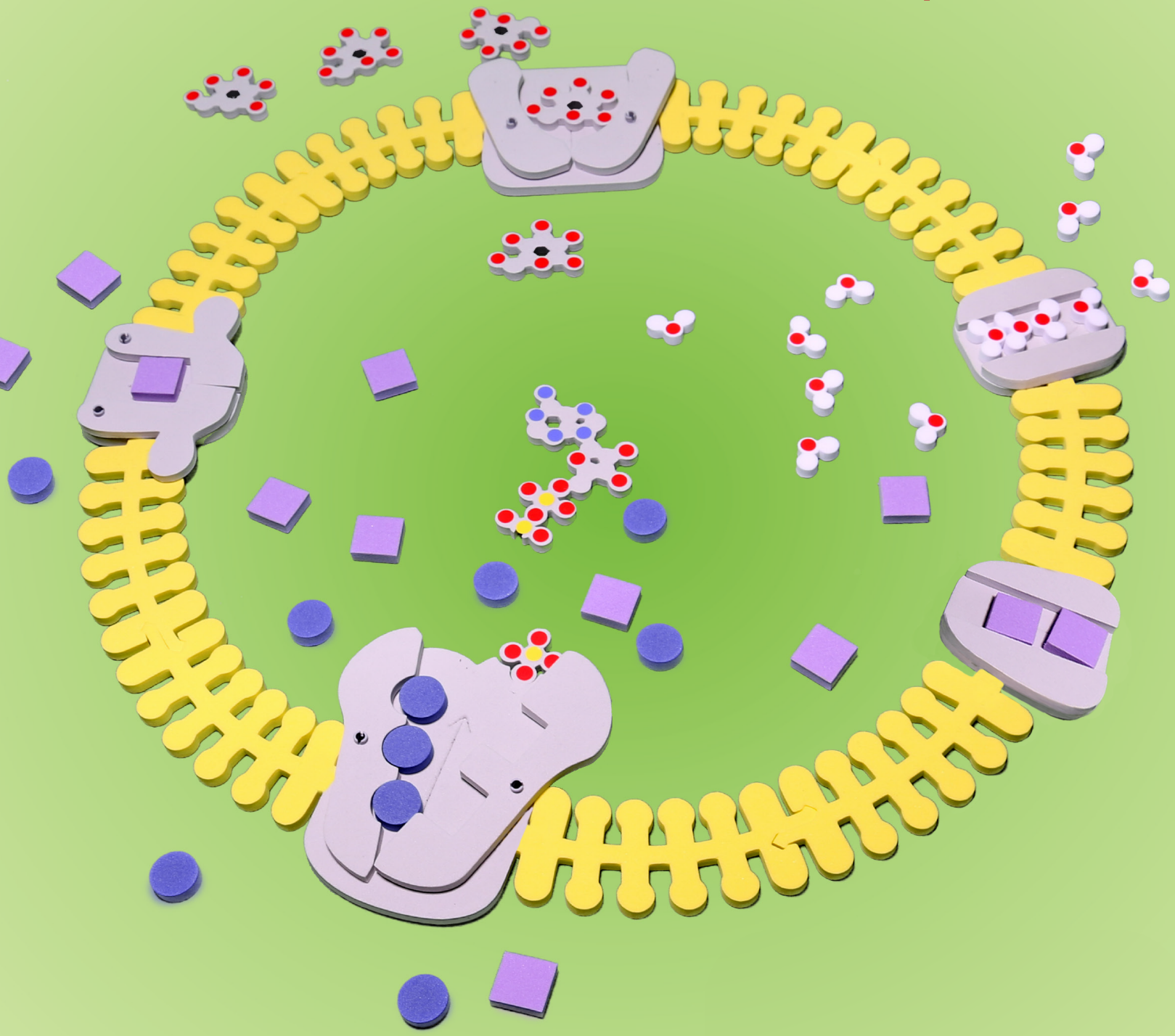
PHOSPHOLIPID & MEMBRANE TRANSPORT KIT©

1-Group Set



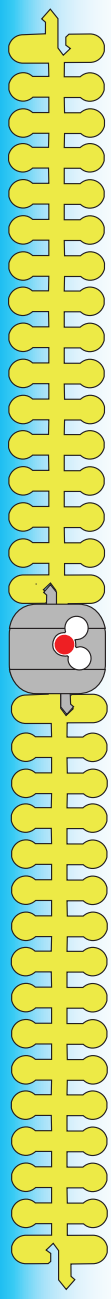
3-D Molecular Designs

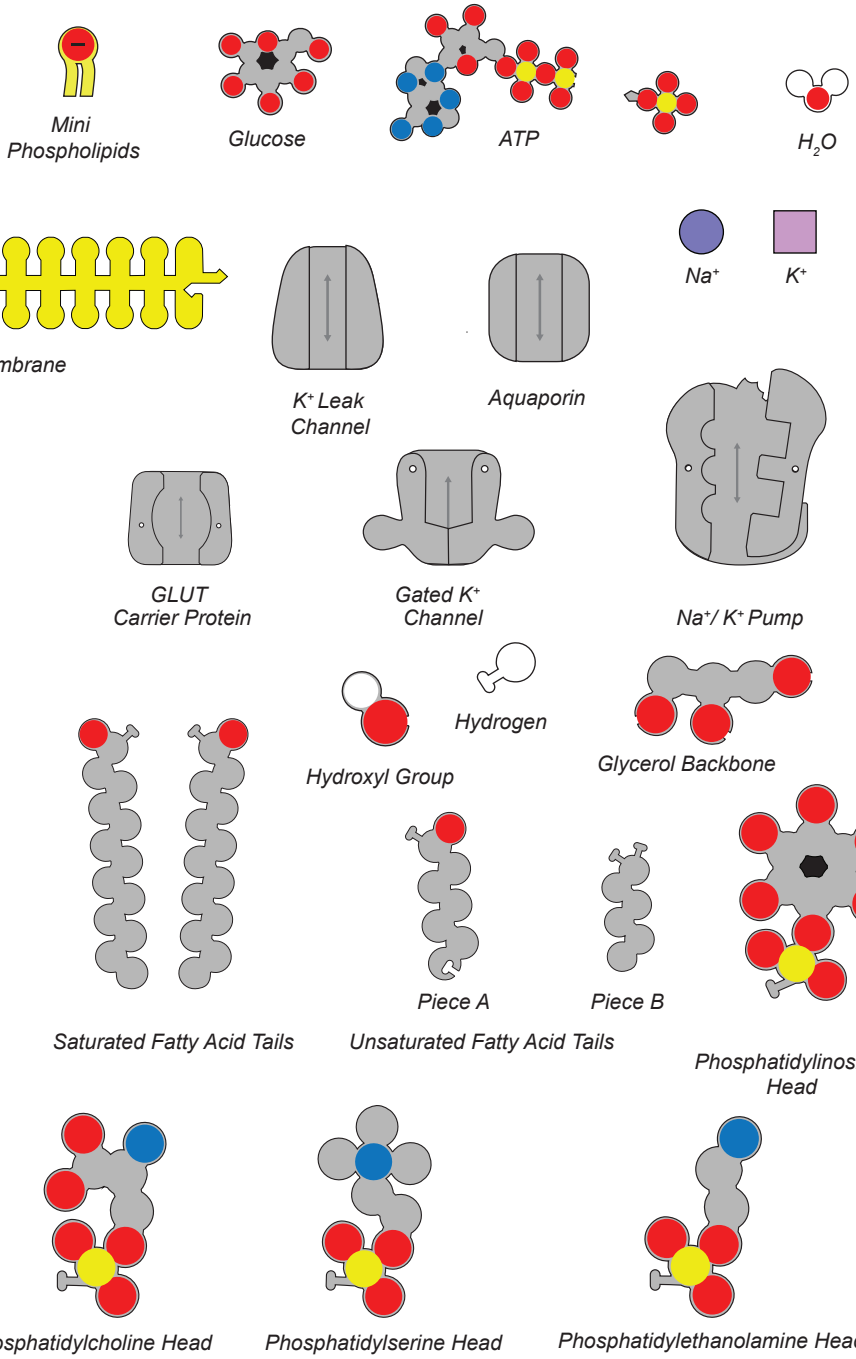
...where molecules become real™

3dmoleculardesigns.com

1-Group Contents List

50 Mini Phospholipids
1 Sticker Sheet
5 Membranes
5 Glucose
1 ATP
30 H_2O
28 Na^+
28 K^+
1 Aquaporin (D)
1 K^+ Leak Channel (E)
1 GLUT Carier Protein (A)
1 Na^+/K^+ Pump (C)
1 Gated K^+ Channel (B)
6 Plastic Pegs





Large Phospholipids

3 Saturated Fatty Acid Tails
2 Piece A Unsaturated Fatty Acid Tails
2 Piece B Unsaturated Fatty Acid Tails
9 Hydroxyl Groups
9 Hydrogens
1 Glycerol Backbone
1 Phosphatidylinositol Head
1 Phosphatidylcholine Head
1 Phosphatidylserine Head
1 Phosphatidylethanolamine Head

Teacher Notes, Student Handouts and supporting materials at
3dmoleculardesigns.com/Teacher-Resources/Phospholipid-Membrane-Transport-Kit.htm

⚠WARNING:
CHOKING HAZARD -- This product contains small parts and should be kept out of the reach of children under the age of 3, because the parts or their pieces may present a choking hazard to small children.

CAUTION:
This is a science education product, not a toy. It is not intended for children under 8 years old.

Assembly Instructions

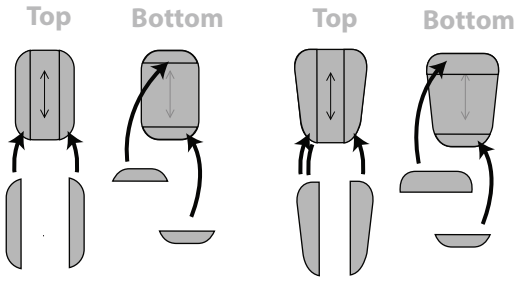
Please allot approximately 45 minutes to assemble protein channels and affix stickers to pieces before use (per kit). Follow these step-by-step instructions to ensure proper assembly. (Multiply the number of proteins and pieces by 3 if you have the 3-Group Kit.)

Channel Assembly

Punch out each gray, foam channel protein while using the letters (A,B,C,D,E) as guides to match up the corresponding gray, sticky-back foam pieces and gray, foam paddles.

1 Aquaporin (D) and 1 K^+ Leak Channel (E)

Affix 2 top and 2 underside gray, sticky-back foam pieces to each of these channels, as shown in the illustrations to the right. The longer top pieces should be affixed to the side with the deepest imprinted arrow, **parallel** with the arrow. The shorter underside pieces should be affixed to the back, **perpendicular** to the arrow. Please note: all gray, sticky-back pieces should line up with the edges of the channels when you attach them.

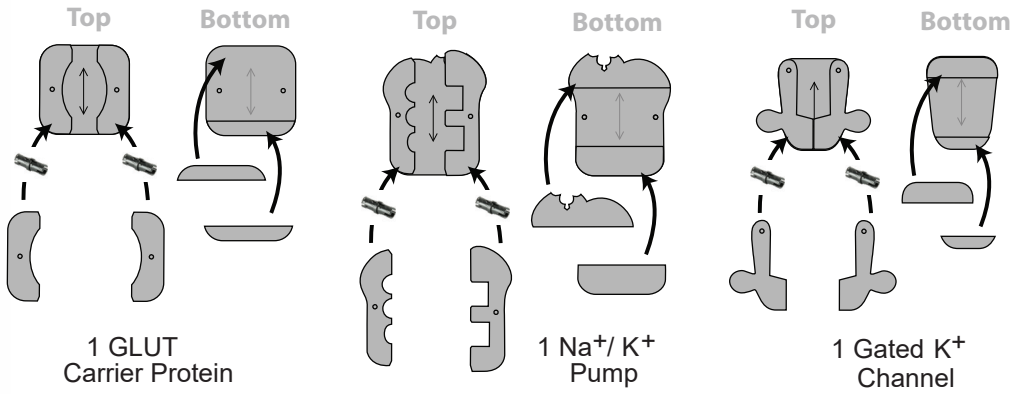


1 Aquaporin

1 K^+ Leak Channel

1 GLUT Carrier Protein (A), 1 Na^+/K^+ Pump (C) and 1 Gated K^+ Channel (B)

The gray, sticky-back foam pieces that correspond with each of these channels go on the underside only (where the imprinted arrow is fainter), **perpendicular** to the arrow. Again, all gray, sticky-back pieces should line up with the edges of the channels. Once the underside pieces are affixed, flip the channels over and proceed with paddle assembly, following the illustrations and directions below.



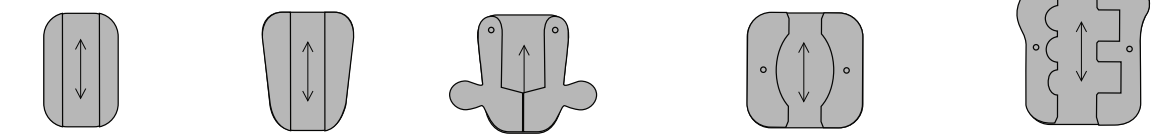
1 GLUT Carrier Protein

1 Na^+/K^+ Pump

1 Gated K^+ Channel

Insert plastic pegs in the top pieces, as shown in the illustrations to the left. Then, attach those pieces to the bottom pieces (with the deepest-imprinted arrows up and sticky-back foam down.)

Assembled Channels



1 Aquaporin

1 K^+ Leak Channel

1 Gated K^+ Channel

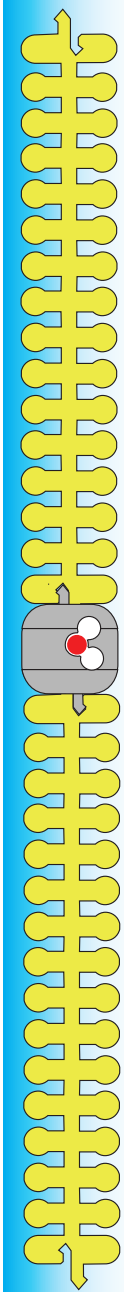
1 GLUT Carrier Protein

1 Na^+ / K^+ Pump

We have provided optional sticker labels for the channel proteins. You may elect to use either the name labels or the letter labels, or both. They may be placed on the tops or undersides of the pieces.

Assembly Instructions

Please allot approximately 45 minutes to assemble protein channels and affix stickers to pieces before use (per kit). Follow these step-by-step instructions to ensure proper assembly. (Multiply the number of proteins and pieces by 3 if you have the 3-Group Kit.)



50 Mini Phospholipids

Negative Charge

Affix medium red stickers with black negative charge symbols to the yellow, foam mini phospholipids pieces, as shown in the illustration.

30 H_2O

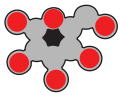
Affix small red stickers to the 30 white, foam H2O pieces, as shown in the illustration.

CPK Color Scheme

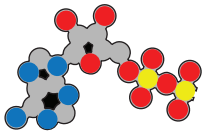
- Oxygen
- Nitrogren
- Phosphorus
- Hydrogen
- Carbon

5 Glucose and 1 ATP

Affix stickers to the 5 gray, foam glucose pieces and 1 gray, foam ATP piece, as shown in the illustration.



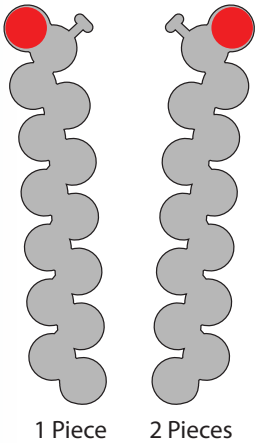
5 Glucose



1 ATP

Large Phospholipids

Affix large red, blue and yellow stickers and medium white stickers to the gray, foam phospholipid pieces, as shown in the illustrations below.

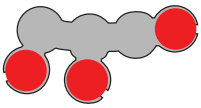


1 Piece 2 Pieces

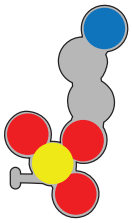
Saturated Fatty Acids Tails

9 Hydroxyl Groups

9 Hydrogen (no stickers required)



1 Glycerol Backbone

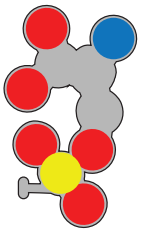


1 Phosphatidylethanolamine Head

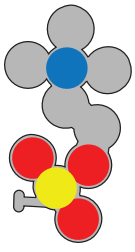
2 A Pieces

Unsaturated Fatty Acids Tails

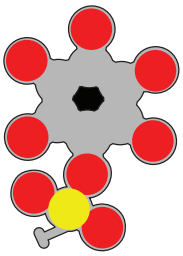
2 B Pieces (no stickers required)



1 Phosphatidylserine Head



1 Phosphatidylcholine Head



1 Phosphatidylinositol Head

Teacher Notes

Activity Guide

This activity guide for the **Phospholipid & Membrane Transport Kit©** will help you consider different ways you may use these materials. We encourage you to modify these lessons and activities to meet the learning objectives and needs of your specific students.

Objectives

Use the model pieces in the kit to:

- **Compare** and **contrast** the structure of a saturated fatty acid with an unsaturated fatty acid.
- **Model** a dehydration synthesis reaction in the formation of a triglyceride or phospholipid.
- **Examine** the general amphipathic structure of a phospholipid.
- **Compare** and **contrast** various models of phospholipids.
- **Explore** the interaction between phospholipids and water.
- **Construct** a phospholipid monolayer, micelle and bilayer and relate it to plasma membrane structure.
- **Identify** and **simulate** the function of the various types of channel proteins involved in membrane transport.

- **Student Handout 1** introduces students to the composition and structure of triglycerides and phospholipids. Students use foam representations of glycerol and three fatty acids to model a dehydration synthesis of a triglyceride. Additionally, students may model phospholipid synthesis using foam representations of glycerol, two fatty acids and various hydrophilic heads.

- **Student Handout 2** guides students through a series of activities using simplified representations of phospholipids to model a phospholipid monolayer, micelle and liposome.

- **Student Handout 3** familiarizes students with various forms of membrane transport. Students learn about passive transport by using foam representations of aquaporin to move water molecules across the cell membrane, a carrier protein to move glucose molecules, and a gated K^+ channel to move ions out of the cell. Finally, a foam representation of the sodium-potassium pump is used to learn about active transport. Students also become acquainted with the channel protein selectivity filters of a few select channel proteins.

Teacher Notes Continued

Teacher Notes for Student Handout 1

Page 2

A supplemental video on fatty acids produced by the Szostak Lab at Massachusetts General Hospital may be accessed at *exploringorigins.org/fattyacids.html.*

Page 4

The concept of trans fat may be introduced here.

Page 5

In 1901, German chemist Wilhelm Normann showed that liquid oils could be hydrogenated and patented the process. Procter & Gamble acquired the U.S. rights to the Normann patent and began marketing the first hydrogenated shortening, Crisco, in 1911.

Page 8

Only give students one head if you do not wish to teach all the kinds of phospholipids.

Plasma membranes are often described as **fluid mosaic models** - fluid because lipids and proteins float around freely - and mosaic because of the many different proteins that are embedded in the phospholipid bilayer.

Page 9

A PDF of the large, textbook phospholipid can be found at *3dmoleculardesigns.com/Teacher-Resources/Phospholipid-Membrane-Transport-Kit/Student-Handout-1-and-Key.htm*.

Teacher Notes for Student Handout 2

Page 1

Eric Kessler is Director of the Bioscience Program at the Blue Valley School District's Center for Advanced Professional Studies (CAPS) in Overland Park, Kansas, where he facilitates molecular, microbial, organismal, and ecological research with his students. He holds three undergraduate degrees and a master's degree in biology. Eric was named a Milken Educator in 2007 and received the Ron Mardigian Memorial Biotechnology Explorer Award in 2013. He introduced the MSOE Center for BioMolecular Modeling (CBM) to this activity in 2003.

The water beaker PDF for the Kessler Activity can be found at *3dmoleculardesigns.com/Teacher-Resources/Phospholipid-Membrane-Transport-Kit/Student-Handout-2-and-Key.htm*. You'll also find a beaker of **oil**. After the activity, you may wish to have your students demonstrate how the phospholipids woould orient themselves in oil.

Page 4

Flippases, Floppases and Scrambleases

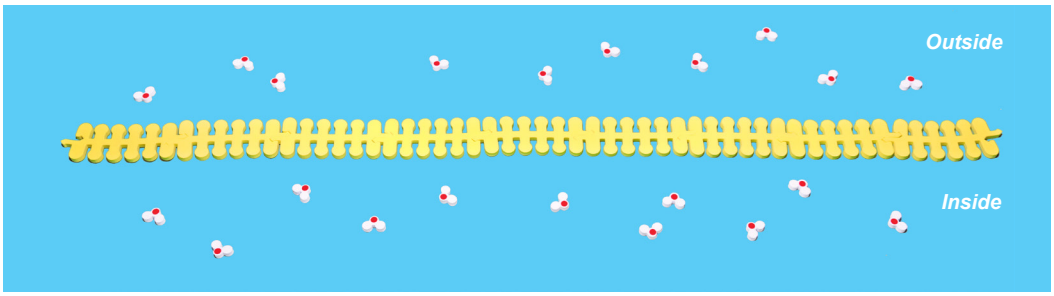
There are enzymes that assist in moving phospholipids from one layer to the other. Flippases move phospholipids in the outer leaflet to the inner leaflet. Floppases move phospholipids in the inner leaflet to the outer leaflet. Scrambleases may move the phospholipids in either direction.

Teacher Notes Continued

Teacher Notes for Student Handout 3

Page 2

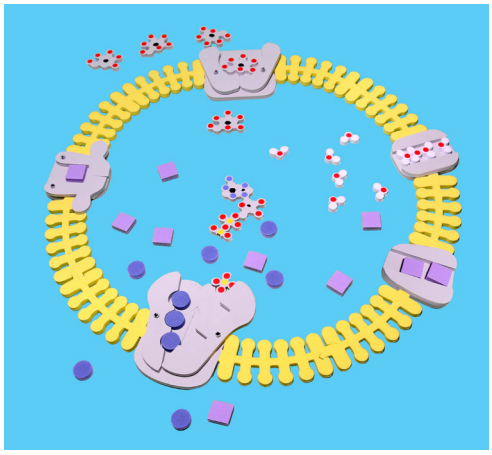
You may opt to set up the membrane in a linear fashion (shown below) if more conducive to your teaching environment.



Page 4

Consider using the kit to introduce the terms **hypertonic**, **hypotonic** and **isotonic**.

You may choose to illustrate the complexity of the plasma membrane by having students model a membrane with multiple channels embedded in it *(shown right)*.



Page 5

Consider introducing the terms **uniporter**, **symporter** and **antiporter** when students explore facilitated diffusion.

You may opt to use the gated K^+ channel to represent a voltage gated Na^+ channel.

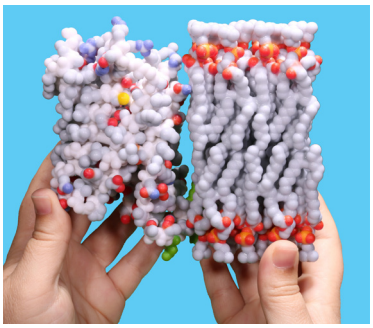
An excellent supplemental video by the **Theoretical and Computational Biophysics Group** of the **National Institutes of Health** (NIH) Center for Macromolecular Modeling and Bioinformatics at the Beckman Institute, University of Illinois at Urbana-Champaign, may be viewed at *ks.uiuc.edu/Gallery/Movies/aquaporin-movie-explanation.html*.

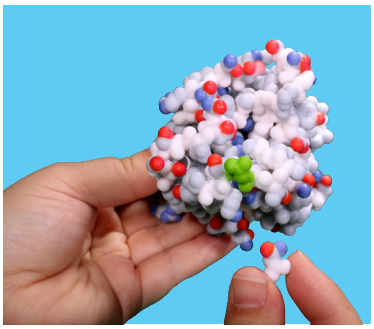
Teacher Notes Continued

Other Available Physical Models

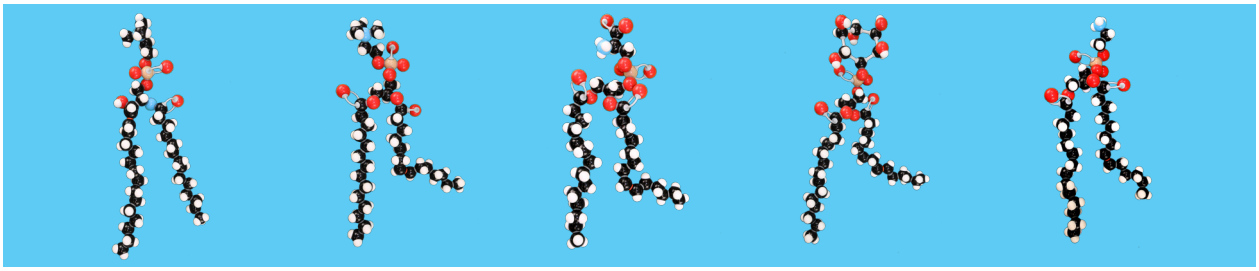
Additional 3D Molecular Designs' products that may help your students understand phospholipids:

- Molecules of Life Collection© Cell Membrane with Phospholipid and Aquaporin with Asparagine





- Phospholipid Modeling Set



Sphingomyelin | Phosphatidylcholine | Phosphatidylserine | Phosphatidylinositol | Phosphatidylethanolamine

They are available for purchase at *3dmoleculardesigns.com*. Molecules of Life Collection© Models are also available through the MSOE Lending Library at *cbm.msoe.edu/MSOELendingLibrary/*.

National Standards

Connections to: A Framework for K-12 Science Education

*Practices, Crosscutting Concepts, and Core Ideas**

Dimension 1. Scientific and Engineering Practices

1. Asking Questions (for science) and Defining Problems (for engineering)
2. Developing and Using Models
6. Constructing Explanations (for science) and Designing Solutions (for engineering)
7. Engaging in argument from evidence
8. Obtaining, evaluating, and communicating information

Dimension 2. Crosscutting Concepts

1. Patterns
2. Cause and Effect: Mechanism and Explanation
3. Scale, proportion, and quantity
6. Structure and function
7. Stability and change

Dimension 3. Disciplinary Core Ideas

Physical Science

PS1: Matter and its Interactions

PS1: Matter and Its Interactions
PS1.A: Structure and Properties of Matter
PS1.B: Chemical Reactions
PS1.C: Nuclear Processes

Life Science

LS 1: From Molecules to Organisms: Structures and Processes

LS1.A: Structure and Function
LS1.B: Growth and Development of Organisms
LS1.C: Organization for Matter and Energy Flow in Organisms
LS1.D: Information Processing

Engineering, Technology and Applications of Science

ETS1: Engineering Design

ETS1.A: Defining and Delimiting an Engineering Problem
ETS1.B: Developing Possible Solutions
ETS1.C: Optimizing the Design Solution

Student Handout 1

Big Idea

In the biological sciences, a dehydration synthesis (condensation reaction) is typically defined as a chemical reaction that involves the loss of water from the reacting molecules. This reaction is used in the formation of carbohydrates, proteins, triglycerides and phospholipids.

Introduction to Lipids

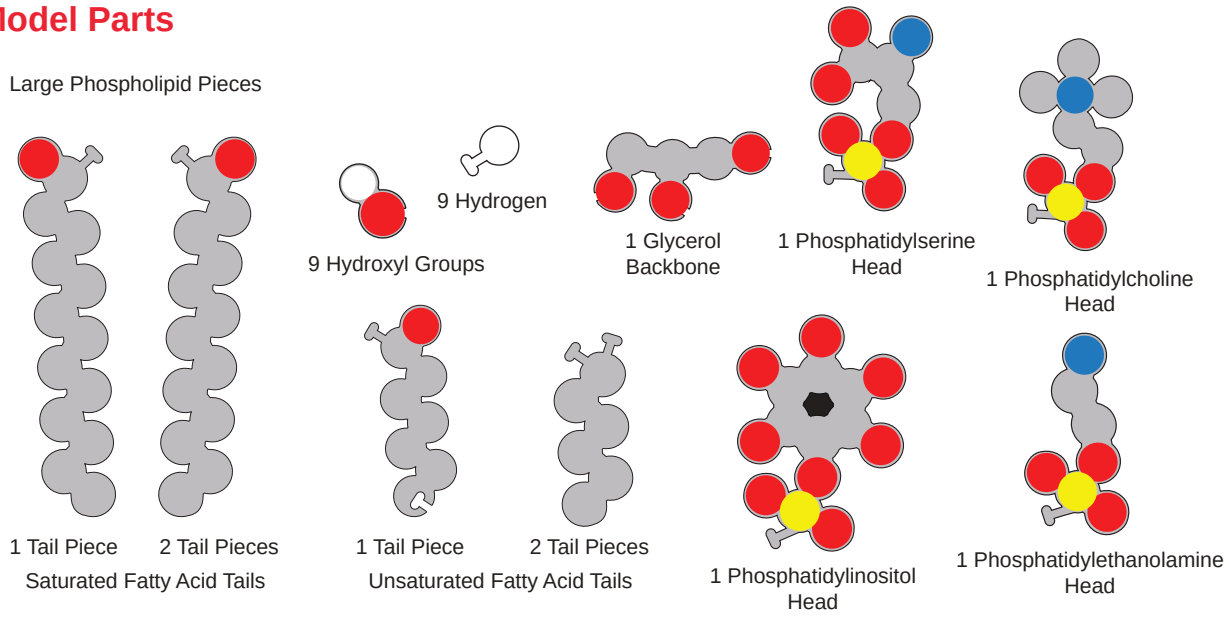
Biomolecules are molecules unique to living systems and include **carbohydrates**, **proteins**, **nucleic acids** and **lipids**. Lipids are a diverse group of organic compounds primarily composed of carbon, hydrogen and oxygen. Fatty acids, triglycerides, phospholipids, fat-soluble vitamins and steroids are a few examples of molecules classified as **lipids**.

The main biological functions of the many varied types of lipids include:

- energy storage
- protection
- insulation
- regulation of physiological processes

Some lipids serve as the structural components of cell membranes.

Model Parts



Color Scheme

Oxygen (red)	Nitrogen (blue)	Phosphorus (yellow)	Hydrogen (white)	Carbon (grey)

Note: This kit follows CPK coloring except for phosphorous, which we show in yellow.

Phospholipid Activity 1 Continued

Hydrophobic and Hydrophilic Properties

Understanding the concepts of **hydrophobic** and **hydrophilic** are key to understanding membrane structure. You can divide the words into their two parts to find clues to their meaning. "Hydro" means water and "phobic" means fear of. Hydrophobic regions of molecules don't interact with water molecules.

1. Separate the word hydrophilic into two parts and record what each of these parts means.
   Hydro means _____and *philic* means_____.

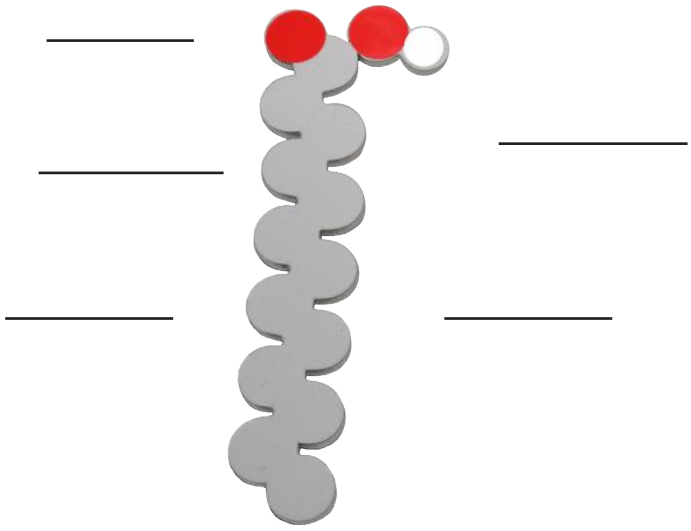
2. What characteristics would a hydrophilic molecule exhibit?
   _____

You may also see hydrophobic molecules called non-polar and hydrophilic molecules called polar.

What's a Lipid?

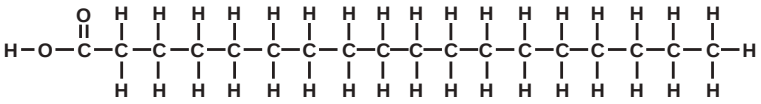
Fatty acids are **linear chains of carbon and hydrogen atoms** with an **organic acid group** (-COOH) at one end. Examine the model of a fatty acid pictured in the box below.

1. Review the image of the phospholipid tail, one of the foam model pieces in the kit.
   a. Label the carbon, oxygen and hydrogen atoms, and note the hydrophobic and hydrophilic regions of the molecule.
   b. Draw the molecular formula for this fatty acid.

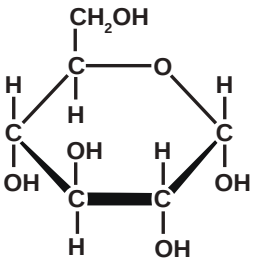


Phospholipid Activity 1 Continued

2. Look at the chemical structures of the common fatty acid stearic acid and the common carbohydrate glucose. Compare the proportion of carbon atoms to oxygen atoms in the table below.



Stearic Acid



Glucose

Substance	Formula	# of C atoms	# of O atoms	Ratio of C:O	Ratio of C:H
Stearic acid					
Glucose					

3a. What do you notice about the amount of oxygen in a fatty acid compared to oxygen in a carbohydrate?

_____

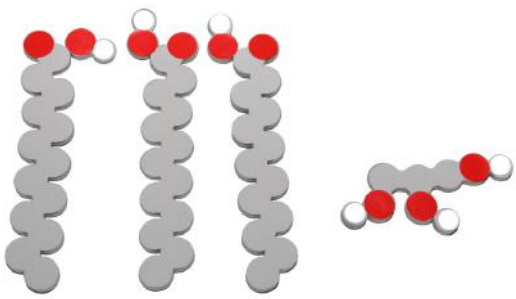
_____

3b. What do you observe about the ratio of carbon to hydrogen in a fatty acid compared to a carbohydrate?

_____

Triglycerides are neutral fats. Some triglycerides are considered **fats** and others **oils**. When a triglyceride is a **solid** at room temperature it is a **fat**. When a triglyceride is a **liquid** at room temperature it is an **oil**. The two building blocks that compose triglycerides are fatty acids and glycerol.

4. Label the glycerol and fatty acids in the diagram below.



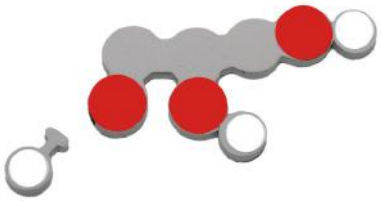
Phospholipid Activity 1 Continued

Forming Triglycerides

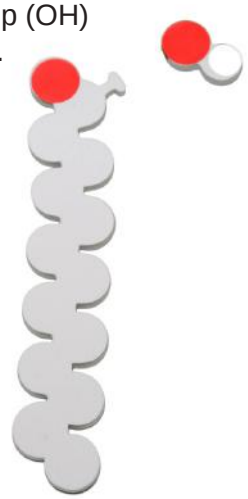
In this activity you will model a dehydration synthesis reaction in the formation of a triglyceride and determine the resulting products.

1. Begin with glycerol and three of the straight-chain fatty acids as the reactants in this simulation. A fatty acid is said to be saturated if the carbons comprising the tail are all singly bonded to each other.

2. Remove one of the hydrogen (H) atoms from the glycerol.

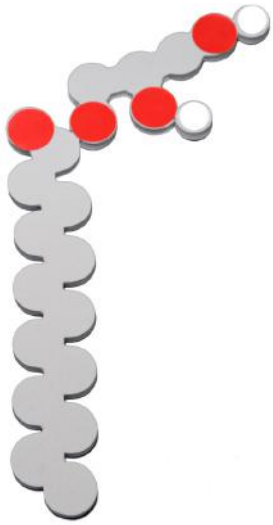


3. Remove the hydroxyl group (OH) from one of the fatty acids.

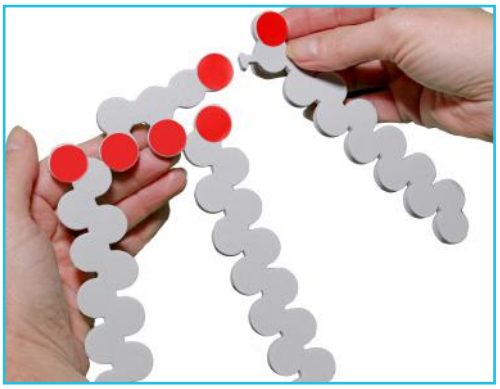


4. Combine the H and the OH.

5. Join the fatty acid to the glycerol.



6. Repeat this process with the two remaining fatty acids.



Phospholipid Activity 1 Continued

a. How many water molecules were formed in this reaction? _____

b. What are the final products of this dehydration synthesis?

_____

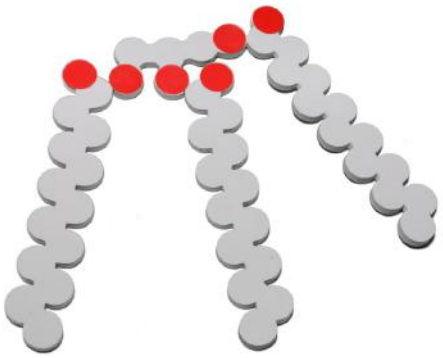
_____

c. Predict whether you think this resulting triglyceride would most likely be a fat or an oil? Explain your reasoning.

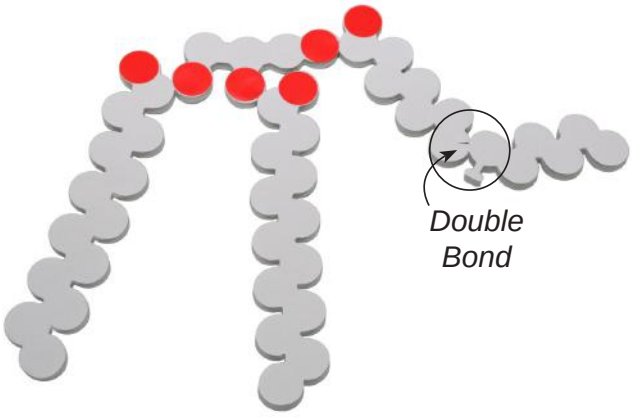
_____

_____

_____



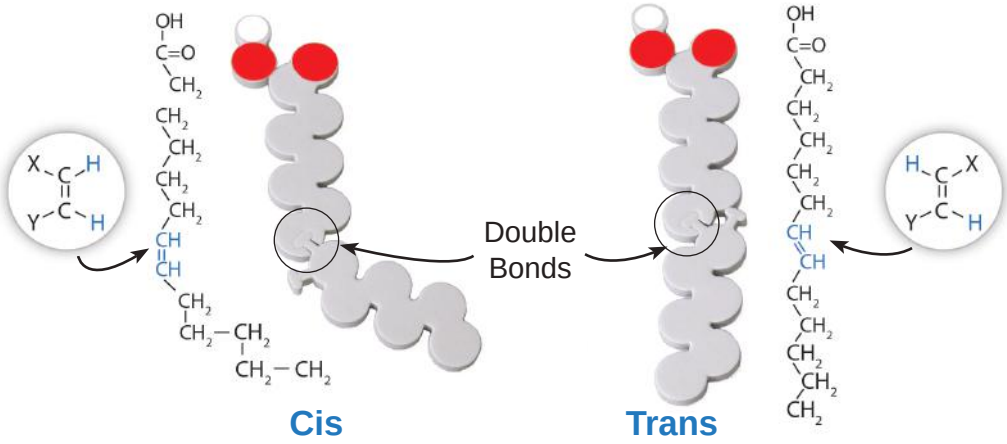
7. Substitute the third fatty acid tail with the two-part fatty acid tail. The post and hole connection in the two-part tail symbolizes a **double bond** between the carbons. When one or more double bonds are present between the carbons in the tail of the fatty acid, the molecule is **unsaturated**.



Phospholipid Activity 1 Continued

The double bond in an unsaturated fatty acid may form one of two possible configurations: *trans* or *cis*. You may model the trans configuration by attaching the second piece of the tail to the first to produce a straighter chain. The *cis* configuration may be modeled by producing a kinked configuration. Most naturally-occurring unsaturated fats are in the cis configuration.

If the hydrogens associated with the double bonded carbons are on the same side, the fatty acid is called *cis*. If the hydrogens associated with the double bonded carbons are on opposite sides, the fatty acid is called *trans*. (See illustrations below.)



d. Which configuration produces the bigger **kink** in the structure of the hydrocarbon chain of the triglyceride?

_____

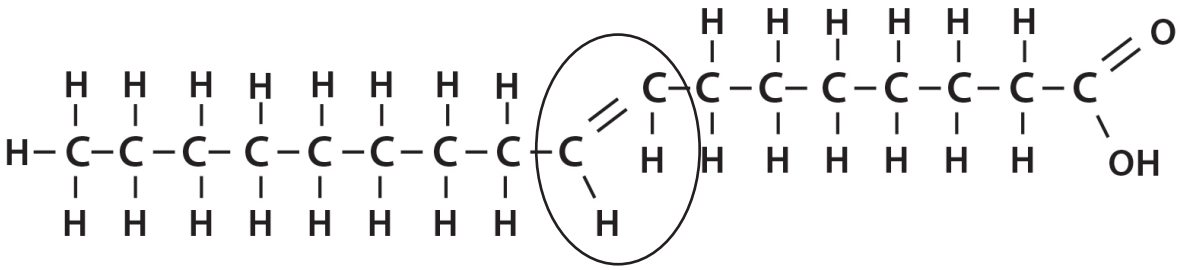
_____

e. Explain how the cis or trans configurations might contribute to the triglyceride being an oil or a fat?

_____

_____

Phospholipid Activity 1 Continued



f. Is the fatty acid in the diagram above in the cis or trans configuration? Explain.

_____

_____

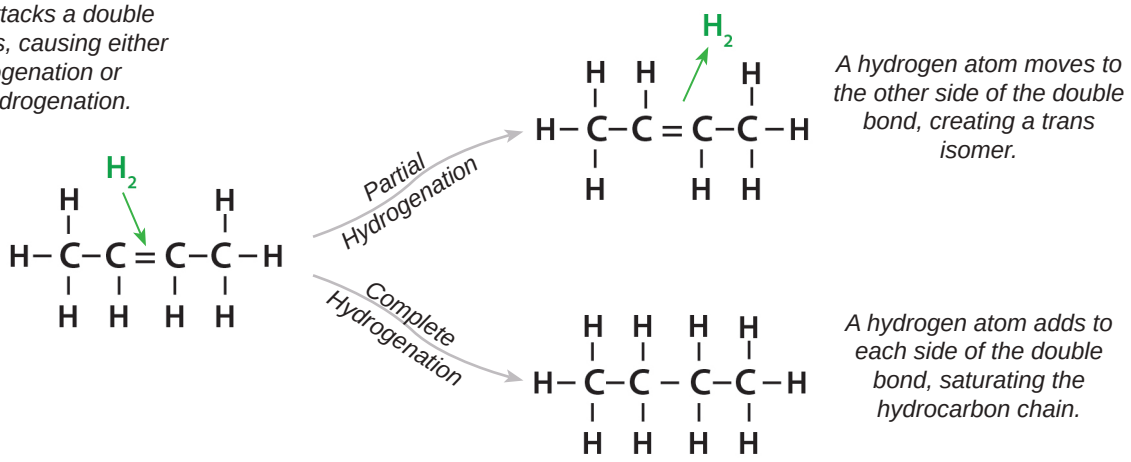
_____

Hydrogenation occurs when hydrogen atoms are added to an unsaturated fatty acid tail, causing double bonds between atoms to become single bonds.

Full hydrogenation occurs when all double bonds convert to single bonds resulting in a saturated fatty acid.

Partial hydrogenation occurs when some of the double bonds are replaced with single ones. Trans fat may be created in partial hydrogenation.

Hydrogen attacks a double bond of a cis, causing either partial hydrogenation or complete hydrogenation.



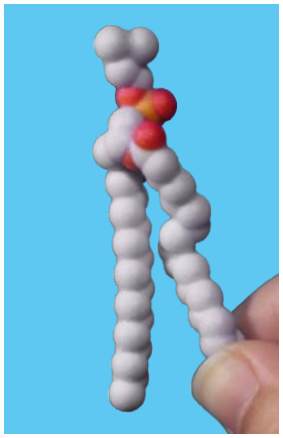
A hydrogen atom moves to the other side of the double bond, creating a trans isomer.

A hydrogen atom adds to each side of the double bond, saturating the hydrocarbon chain.

Phospholipid Activity 1 Continued

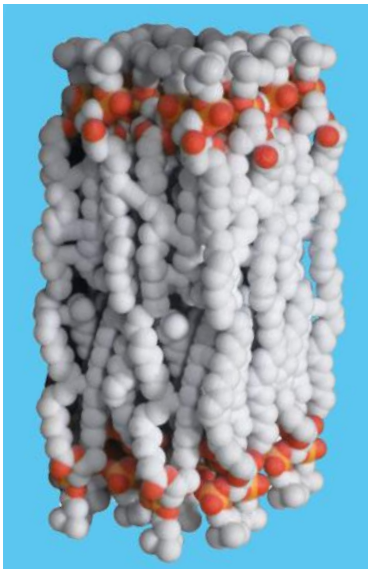
Introduction to Plasma Membranes

The **plasma membrane** is the structural boundary that separates the cell from its surroundings and controls what substances move into and out of the cell. As only some substances are allowed to cross the membrane, the plasma membrane demonstrates the property of **selective permeability**. The plasma membrane is also called a cell membrane.



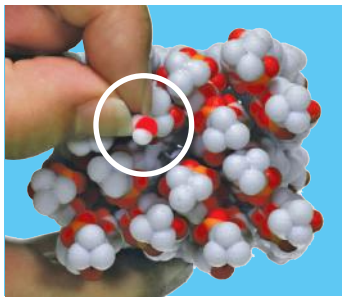
Plasma membranes primarily consist of phospholipids. Note the hydrophobic and hydrophilic regions of the lipid.

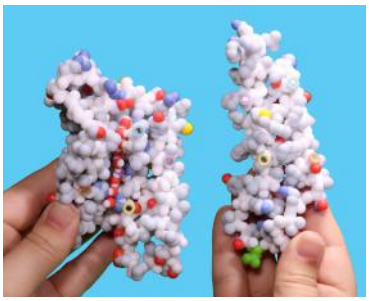
In particular, the plasma membrane of mammalian red blood cells (erythrocytes) has been the focus of cell membrane study because these cells do not contain nuclei or internal membranes. They represent a source from which a pure plasma membrane may be easily isolated for analysis. In 1925, Dutch scientist Evert Gorter and his research assistant F. Grendel extracted lipids from the membranes of a known number of red blood cells which corresponded to a known surface area of plasma membrane. The surface area occupied by a monolayer of the extracted lipid and the air/water interface was then determined. The results of their experiment showed that the surface area of the lipid monolayer was twice that occupied by the erythrocyte plasma membrane, leading to the conclusion that the plasma membrane consists of two layers called the **lipid bilayers**.



In the plasma membrane the hydrophobic tails come together while the hydrophilic heads of each layer orient themselves toward the watery environments inside and outside of the cell.

The most abundant lipids in most membranes are **phospholipids**. The ability of phospholipids to spontaneously form membranes is inherent to their **amphipathic** (containing both hydrophilic and hydrophobic regions) nature. The “head” of a phospholipid is composed of the negatively- charged phosphate group and may contain other polar groups. The tail of a phospholipid usually consists of long fatty acid hydrocarbon chains.





Water molecules (shown in the circle in the photo left) can pass in and out of a cell through a plasma membrane, but not easily. ***Aquaporin****, a protein embedded in the membrane (shown in the photo right), facilitates passage of water molecules in and out of the cell.*

These models are from 3D Molecular Designs' Molecules of Life Collection©. They can be borrowed from the MSOE Lending Library **cbm.msoe.edu/teachRes/library/ml.html** *or purchased from 3D Molecular Designs* **3dmoleculardesigns.com/Education-Products/Molecules-of-Life-Collection.htm**.

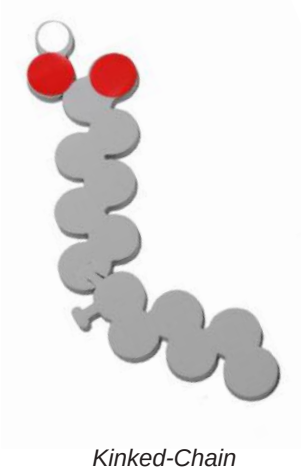
Phospholipid Activity 1 Continued

Focus on Phospholipids

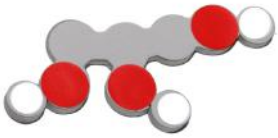
The building blocks of a phospholipid include two fatty acid tails, the glycerol backbone and a phosphate head. In this next activity you will model a dehydration synthesis reaction in the formation of a phospholipid.

1. Begin with one of the straight-chain fatty acids (saturated), the kinked-chain fatty acid (unsaturated), glycerol and one of the phospholipid heads as the reactants in this simulation.

Straight-Chain Saturated Fatty Acid (Trans Configuration)



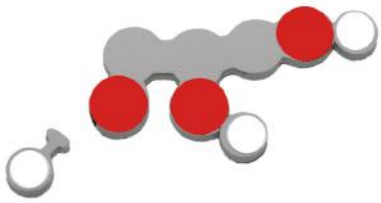
Kinked-Chain Unsaturated Fatty Acid (Cis Configuration)



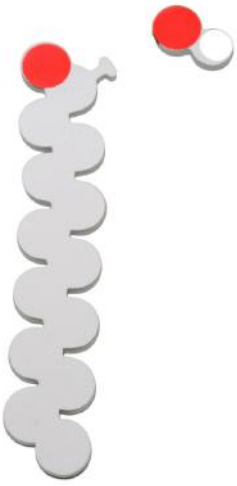
Glycerol

Phosphate Head (Phosphotidlycholine)

2. Remove one of the hydrogen (H) atoms from the glycerol.



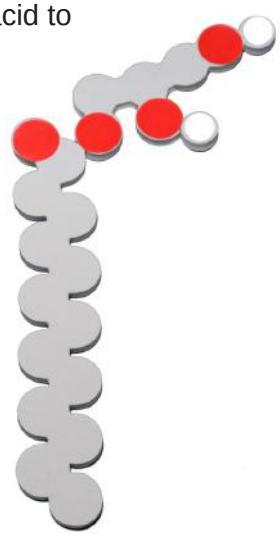
3. Remove the hydroxyl group (OH) from one of the straight fatty acids.



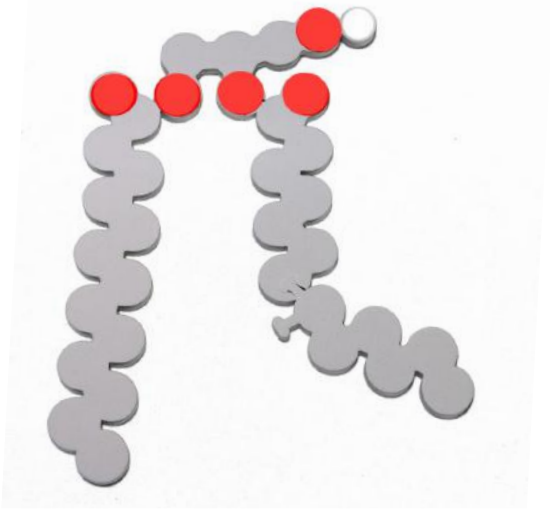
4. Combine the H and the OH.

Phospholipid Activity 1 Continued

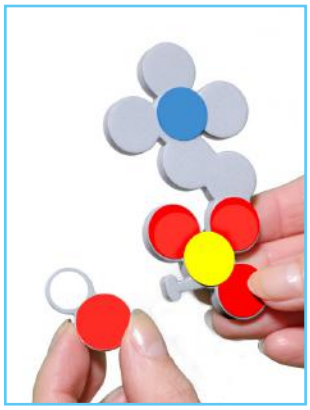
5. Join the fatty acid to the glycerol.

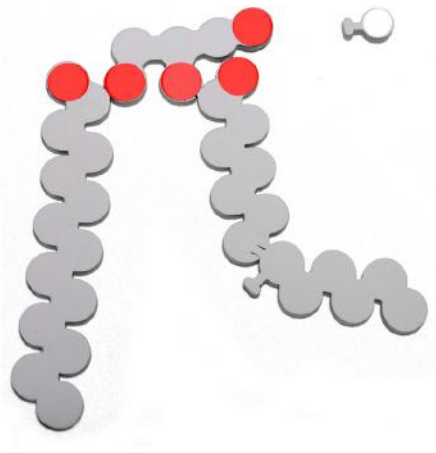


6. Repeat this process with the unsaturated fatty acid.



7. Remove the hydroxyl group from the phospholipid head and the final hydrogen (H) atom from the glycerol.

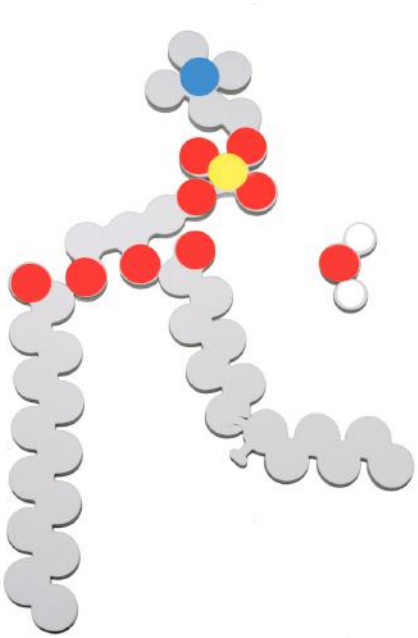




8. Combine each H with each OH.

Phospholipid Activity 1 Continued

9. Bind the phospholipid head to the glycerol backbone.



a. What type of reaction was used in the formation of your phospholipid?

_____

_____

_____

b. Remembering definitions of the terms **hydrophobic** and **hydrophilic,** deconstruct the word ***dehydration.***

_____

_____

_____

c. Define ***dehydration synthesis***.

_____

_____

_____

d. In the dehydration synthesis reactions you modeled, what parts did you combine to form a triglyceride and phosopholipid?

_____

_____

e. How many water molecules did you synthesize? _____

f. Compare and contrast dehydration synthesis of a triglyceride to a phospholipid.

_____

_____

_____

Phospholipid Activity 1 Continued

g. Sketch the specific structural formula of the phospholipid model you synthesized in the space provided below. Label the hydrophilic and hydrophobic regions of your structure.

Phospholipid Activity 1 Continued

h. Explain why you labeled the phospholipid parts as you did in your sketch on page 12.

i. Compare your structure to that of the other groups in the room. Record any similarities you observe in these phospholipid structures.

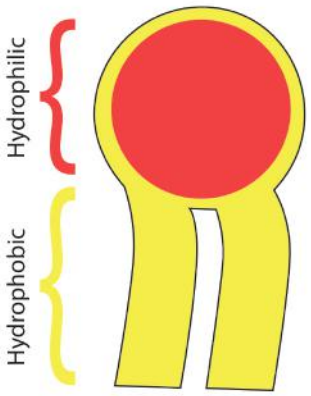
j. Based on these similarities a simplified representation may also be used to indicate phospholipid structure. Sketch a simple model in the space below. Label the hydrophobic and hydrophilic portions of this simplified model.

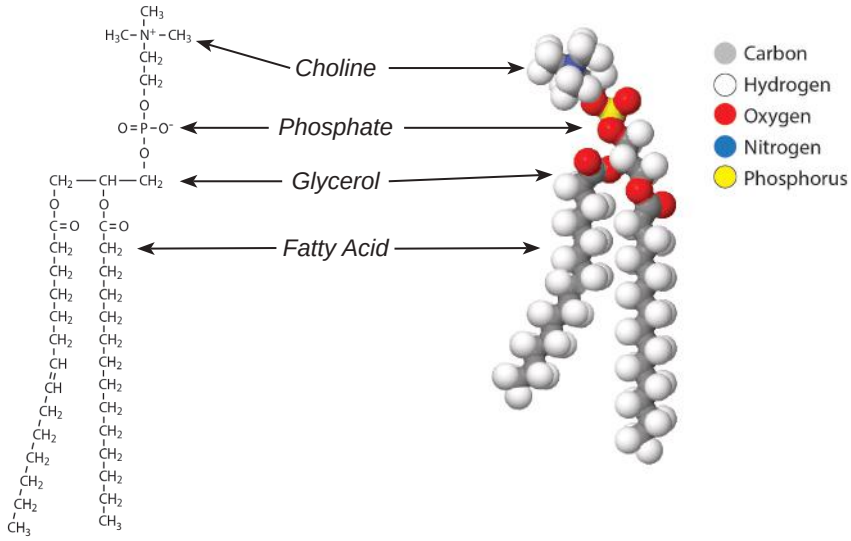
k. Record any differences in the specific structures you have observed between these phospholipids.

Phospholipid Activity 1 Continued

There are four major phospholipids that comprise the plasma membrane. Phosphatidylcholine and sphingomyelin make up the outer leaflet layer of the membrane while phosphatidylethanolamine and phosphatidylserine make up the inner leaflet of the layer membrane. A fifth phospholipid, phosphatidylinositol, is also found in the inner leaflet layer of the plasma membrane. Although phosphatidylinositol is a minor membrane component, it plays a major role in cell signaling.

The general structure of a phospholipid is most often represented by the phosphatidylcholine structure:





Student Handout 2

Big Idea

Cell membranes are composed of a phospholipid bilayer.

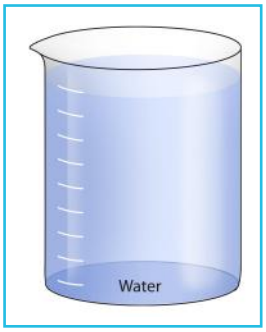
The Kessler Membrane Activity

The Spontaneous Assembly of Membranes

Models

50 Mini Phospholipids with Negative Charge

20 H_2O



Water Beaker Sheet

Monolayer

1. Use 8 of the phospholipid models. Using the laminated sheet of the beaker of water, arrange the 8 phospholipids to show how the phospholipids will orient themselves in water.

   Sketch your result below. Label the hydrophobic and hydrophilic parts of the phospholipids.

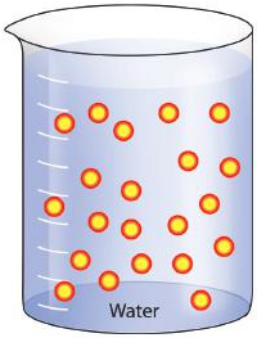
The Kessler Membrane Activity Continued

Micelle Structure

2. Using the same 8 phospholipids, rearrange them in the beaker so that they are submerged in the water while still maintaining the correct hydrophobic and hydrophilic interactions.

   Sketch your result below.

This structure is called a **micelle**. Micelles form when phospholipids are mixed with water. Micelles can act as **emulsifiers** to form emulsions. An emulsion is a combination of two liquids that normally won't mix together, such as oil and water or soap and water, which mix together so that one liquid is suspended within the other.



Liposome Structure

3. Construct a structure that is both submerged in the water and contains water on the inside. You may use as many of the phospholipids in your kit as you wish.

   Sketch the resulting structure below.

The Kessler Membrane Activity Continued

4. Based on the structure of a phospholipid, explain the reasoning for your arrangement.

_____

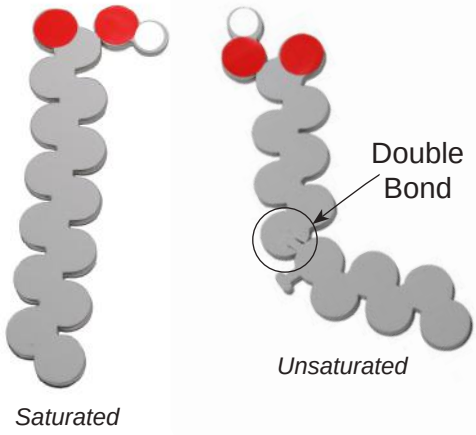
_____

_____

The resulting structure is referred to as a **liposome**. As your model shows, the liposome vesicle is composed of the phospholipid bilayer, with water or other liquid in the middle to faciliate delivery of the nutrients or pharmaceutical drugs.

Upon closer examination of the hydrophobic tails of the models (right), you may notice that in one of the tails all of the carbons are connected with single bonds. These hydrocarbon tails are **saturated**.

In the second tail, a double bond connects two adjacent carbons. The presence of a double bond creates a **kink** in the structure of this hydrocarbon chain. The hydrocarbon tails containing a double bond or bonds between adjacent carbons are **unsaturated**.



5. Develop an explanation for the necessity of having **kinks** in the hydrophobic tail of the phospholipids that make up cell membranes.

_____

_____

_____

6. How might the cis or trans configuration (as described in *Student Handout 1*) contribute to the fluidity of the plasma membrane?

_____

_____

7. Develop an explanation for why fluidity in the cell is important.

_____

_____

The Kessler Membrane Activity Continued

8. Compare the number of phospholipids in the inside leaflet to the number in the outside leaflet.

9. What happens to the structure if inside phospholipids flop to the outside layer?

10. How do you think phospholipids move from outer to inner leaflets in a bilayer?

Student Handout 3

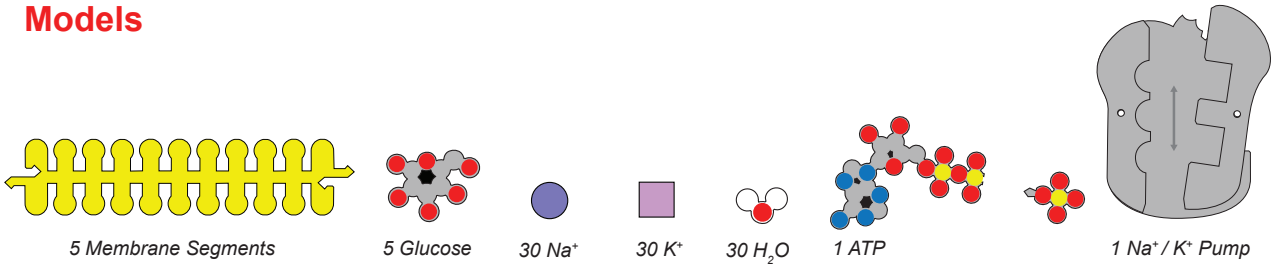
Big Idea

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

Exploring Membrane Permeability

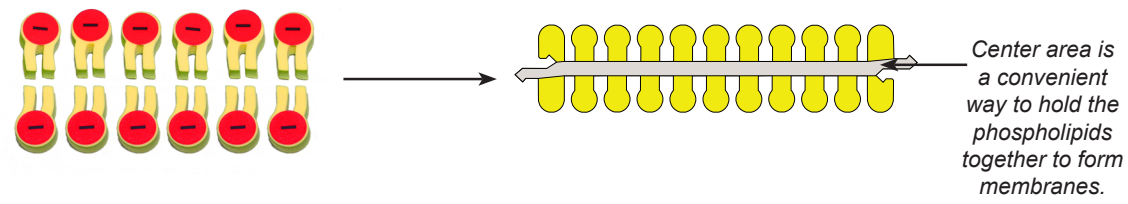
The phospholipid bilayer is only one aspect of the gatekeeper system responsible for the plasma membrane's **selective permeability**. Membrane-bound proteins play a key role in regulating the transport of ions and molecules through the plasma membrane.

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.

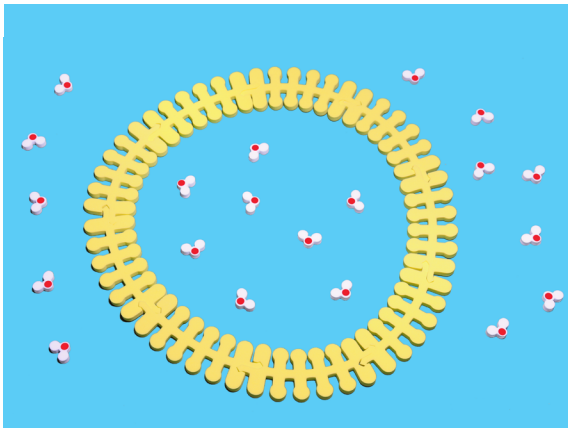


2. Nonpolar molecules, such as hydrocarbons, CO_2 and O_2, are hydrophobic. Explain why these molecules can easily cross the plasma membrane without the aid of proteins.

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?

_____

4. Identify a limitation with this model.

_____

_____

_____

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 (3×10^9) 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.

_____

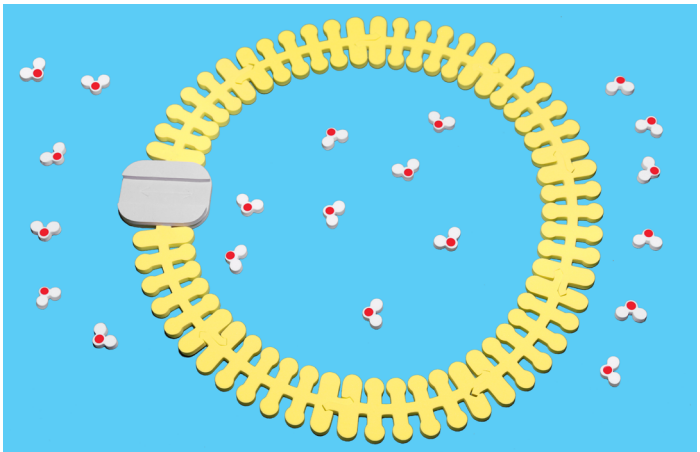
_____

_____

_____

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.



Aquaporin embedded in plasma 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 next flow of water occur?

_____

_____

_____

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.

_____

_____

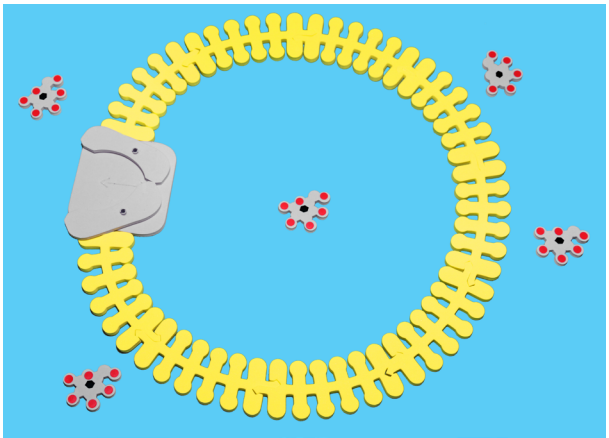
Because the water was moving with its concentration gradient, the cell did not have to expend cellular energy to move water across the plasma membrane in the above cases. Movement of a substance across a membrane without the expenditure of energy is referred to as **passive transport**. When the cell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



GLUT carrier protein embedded in plasma membrane

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.

_____

_____

_____

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

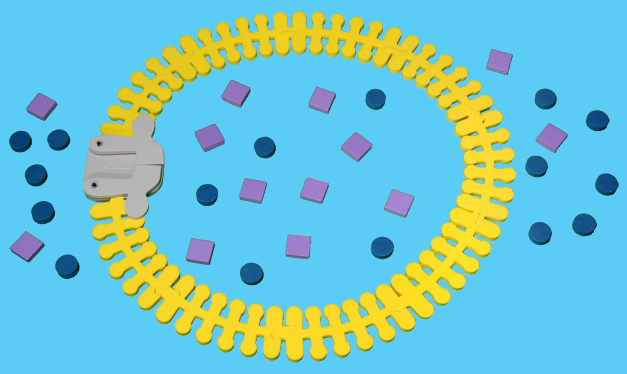
_____

_____

_____

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.



Gated channel protein embedded in plasma membrane

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?

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

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

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

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

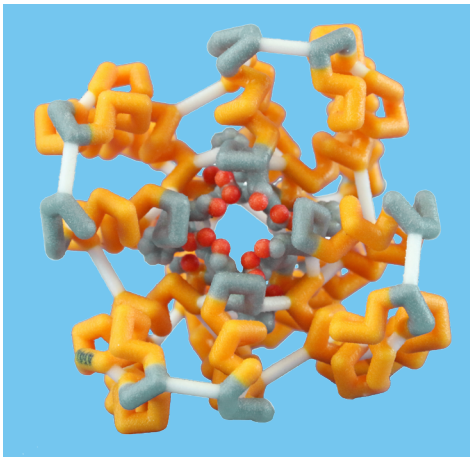
In cell membrane proteins, **selectivity filters** allow the correct molecules or ions to pass through the proteins and, for the most part, prevent other molecules or ions from passing through the channel. The selectivity filters can be:

- 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

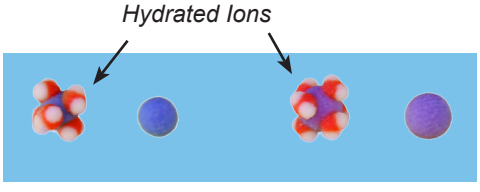
Water molecules pass through the primarily hydrophobic portions of the aquaporin channel until they reach the narrowest part of the hour-glass shaped protein (*left photo*). Then the water molecules bond first with one nitrogen and then a second before passing through the rest of the protein to enter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



Sodium Channel

Sodium Channel

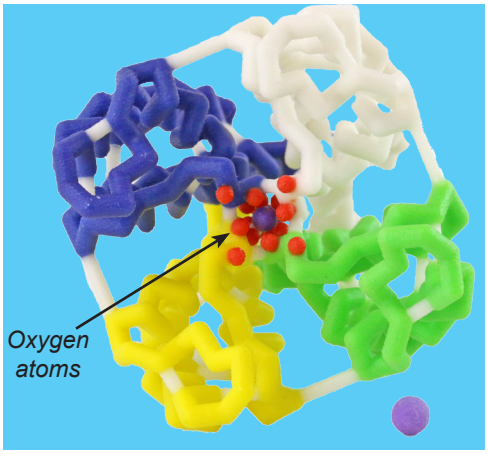
Sodium ions (Na^+) flow through the protein until they reach the narrow section of the channel, which is just large enough for a sodium ion hydrated with water molecules to pass into or out of the cell. Even though potassium (K^+) ions also have a positive charge, they are larger than sodium ions when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



Sodium (Na^+) *Potassium (K^+)*

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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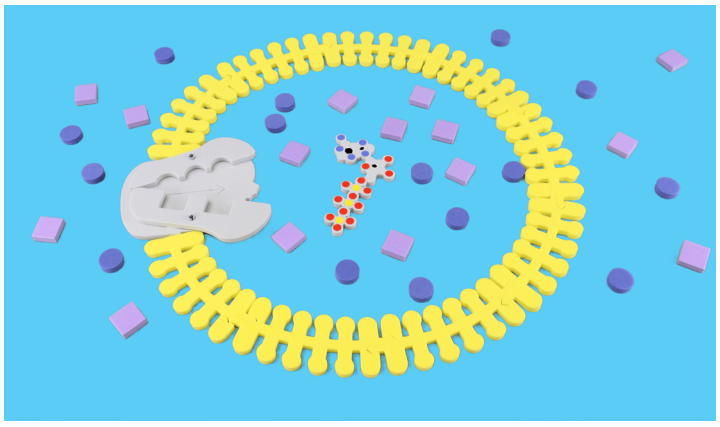
Active Transport - The Sodium-Potassium Pump



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:

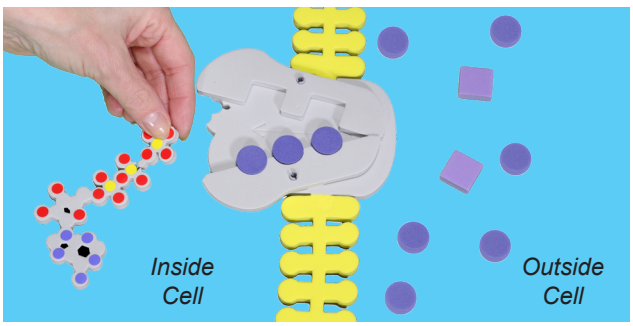
Set the sodium-potassium pump so that it is open to the inside of the cell as shown in the photo on page 8.

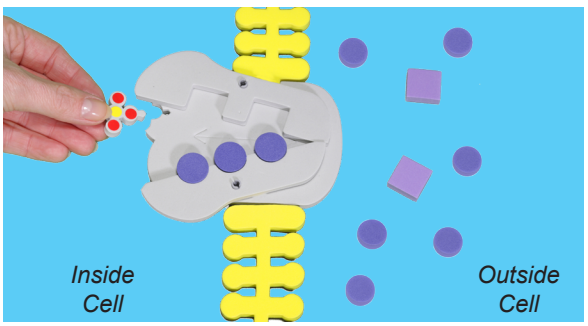
17. Record the initial ion concentrations in the table provided below:

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*).

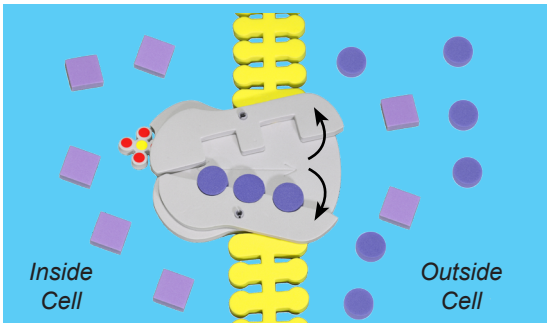
Sodium ion binding stimulates phosphorylation of the pump protein by ATP. In other words, a phosphate group is added to the sodium-potassium pump from the ATP molecule. Detach the phosphate group from ATP molecule located **inside the cell** and bind it to the protein (*photos below*).



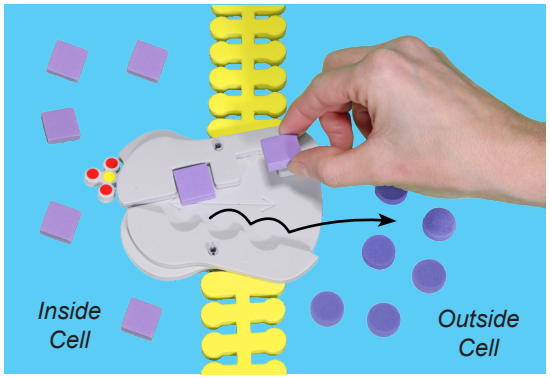


Phospholipid Activity 3 Continued

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**.

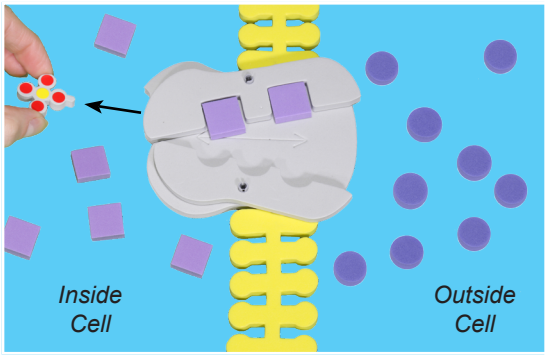


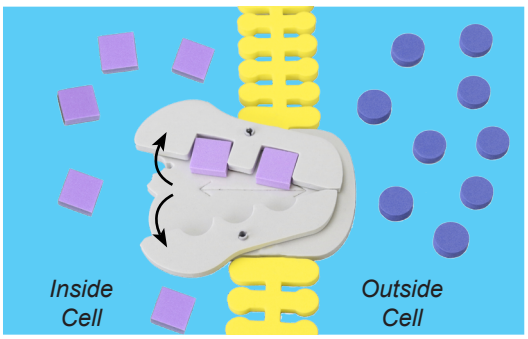
The shape change reduces the protein's binding affinity for sodium ions and increases the binding affinity for potassium ions. Remove the sodium ions from the protein and deposit them outside the cell and bind two potassium ions to the appropriate spots in the protein.

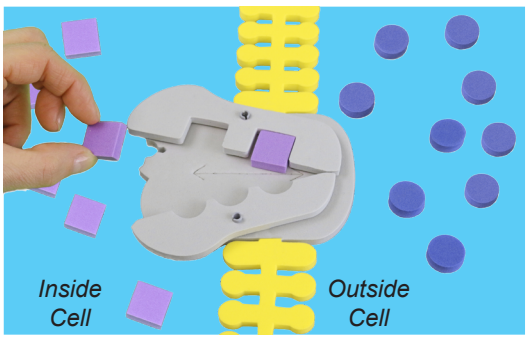


Potassium ion binding triggers the release of the phosphate group from the protein. Detach the phosphate group from the sodium- phosphate pump (*photo left*).

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)*.





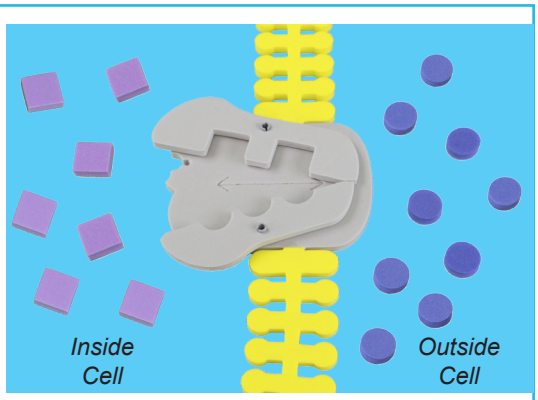


Phospholipid Activity 3 Continued

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?



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

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.

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

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

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

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.