Teacher Preparation Notes for “Cell Membrane Structure and Function”

This minds-on activity includes two hands-on experiments and numerous analysis and discussion questions to help students understand how the molecular composition and organization of a cell membrane result in its selective permeability. Students learn how the phospholipid bilayer and membrane proteins play key roles in the cell membrane function of regulating what gets into and out of the cell. Specific topics covered include ions, polar and nonpolar molecules; simple diffusion through the phospholipid bilayer; facilitated diffusion through ion channels or carrier proteins; active transport; exocytosis and endocytosis.

You may want to precede this activity with "Introduction to Osmosis" (available at http://serendipstudio.org/sci_edu/waldron/#osmosis).

These Teacher Preparation Notes include:
- Learning Goals (pages 1-2)
- Equipment and Supplies, including preparation before class (pages 2-3)
- Instructional Suggestions and Background Information
  - General (page 3)
  - Experiment 1 – Diffusion across a Synthetic Selectively Permeable Membrane (page 4)
  - Experiment 2 – Polar vs. Nonpolar Molecules (pages 4-5)
  - How Phospholipids and Proteins Combine to Form the Selectively Permeable Cell Membrane (pages 5-8)
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- Possible Follow-Up Activities and Sources for Figures in Student Handout (pages 11-12)

Learning Goals

In accord with the Next Generation Science Standards:
- Students learn the Disciplinary Core Idea (LS1.A) "Multicellular organisms have a hierarchical structural organization, in which anyone system is made up of numerous parts and is itself a component of the next level."
- Students engage in recommended Scientific Practices, including:
  - “Using Models: Develop and/or use multiple types of models to provide mechanistic accounts and/or predict phenomena…”
  - “Interpreting Data: Evaluate the impact of new data on a working explanation and/or model of a proposed process or system.”
  - “Constructing Explanations: Apply scientific ideas, principles, and/or evidence to provide an explanation of phenomena…”

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1 By Drs. Ingrid Waldron and Jennifer Doherty, Department of Biology, University of Pennsylvania, 2018. These Teacher Preparation Notes and the related Student Handout are available at http://serendipstudio.org/exchange/waldron/diffusion

2 In the osmosis activity, students learn about selectively permeable cell membranes by experimenting with chicken eggs and answering analysis and discussion questions. This activity helps students to prepare for Performance Expectation MS-LS1-2, "Develop and use a model to describe the function of a cell as a whole and ways parts of cells contribute to the function."

This activity helps students understand these Crosscutting Concepts:

- "Structure and Function: The functions and properties of natural and designed objects and systems can be inferred from their overall structure, the way their components are shaped and used, and the molecular substructures of its various materials."

- “Systems and System Models: Models can be used to predict the behavior of a system, but these predictions have limited precision and reliability due to the assumptions and approximations inherent in models.”

This activity helps students to prepare for the Performance Expectation, HS-LS1-2: “Develop and use a model to illustrate the hierarchical organization of interacting systems that provide specific functions within multicellular organisms.”

Specific Learning Goals include:

- In biological organisms, each cell is surrounded by a selectively permeable cell membrane which regulates what gets into and out of the cell.\(^4\)
- A selectively permeable membrane allows some types of molecules and ions to pass through, but not others.
- Small nonpolar molecules can diffuse across the phospholipid bilayer of the cell membrane.
- Membrane channel proteins and carrier proteins allow ions and polar molecules to cross the cell membrane.
- In passive transport, diffusion results in the net movement of substances from a region of higher concentration to a region of lower concentration.
- In active transport, membrane carrier proteins use energy to pump ions or molecules from a region of lower concentration to a region of higher concentration.
- Large molecules such as proteins do not cross the cell membrane, but proteins can be secreted from the cell by exocytosis.
- Endocytosis, exocytosis and digestive enzymes work together to rid the body of harmful bacteria.

**Equipment and Supplies** (per group of 2-4 students)

**For Experiment 1**

- 250 ml beaker or other container with some way to measure 200 mL of water
- 4 ml of 1% starch solution, corn or potato (To prepare ~1 liter of 1% starch solution, mix 10 g of corn starch or potato starch in 50 mL of room temperature distilled water. Bring 1000 mL of distilled water to a full boil. Add the slurry of starch to the boiling water and stir for at least 2 minutes while the mixture continues to boil. Starch is insoluble in cold water and the mixture needs to be boiled for the starch to stay in solution. Allow several hours for the starch solution to cool.)
- 0.8 mL of iodine-potassium iodide solution (IKI)
- 2 1-mL transfer pipettes (You can use fewer pipettes if your students are reliable about not cross-contaminating solutions. Also, if your iodine is in dropper bottles, you may want to provide your students with an estimate of the number of drops in 0.8 mL; typically there are 20 drops per milliliter, but drops can vary in size.)

\(^4\) A selectively permeable membrane is also called a semipermeable membrane. The cell membrane is also called a plasma membrane to distinguish it from the multiple membranes inside cells, especially eukaryotic cells. The term plasma membrane is introduced on page 9 of the Student Handout. Obviously, if you prefer, you can replace cell membrane with plasma membrane throughout the Student Handout.
- 15 cm of 1” dialysis tubing (Before the lab, cut the dialysis tubing into 15 cm lengths and soak these pieces in distilled water for 15 + minutes.)
- 2 12 cm pieces of string or 2 dialysis clamps
- Distilled water
- Paper Towels

For Experiment 2
- 2 10-ounce clear plastic cups (These taller cups have the advantage of preventing food dye drops from splattering outside the cup, but you can use smaller clear plastic cups.)
- Water
- 30-40 mL of cooking oil (we have had good luck with canola oil, but we assume that other types would work equally well)
- Beaker that students can use to pour the oil gently down the side of the plastic cup
- 1-mL transfer pipette
- Food dye (We have had the best success with McCormick green food color; McCormick red food color seems to be a little bit denser and therefore tends to fall through the layer of oil; you will want to have the food coloring in a container where students can use their transfer pipette.)

Instructional Suggestions and Background Information
We estimate that it will require 2-3 45-50 minute periods to complete this activity. If you want to complete the hands-on part of the activity in a 45-50 minute period, you may want to complete pages 1-2 in the Student Handout on the day before the hands-on part of the activity.

In the Student Handout, numbers in bold indicate questions for the students to answer and ➢ indicates a step in the experimental procedure for the students to do.

For the analysis and discussion questions, you can maximize student participation and learning, by having your students work individually, in pairs, or in small groups to complete groups of related questions and then having a class discussion after each group of related questions. In each discussion, you can probe student thinking and help them develop a sound understanding of the concepts and information covered before moving on to the next group of related questions.

A key is available upon request to Ingrid Waldron (iwaldron@upenn.edu). The following paragraphs provide additional instructional suggestions and background information – some for inclusion in your class discussions and some to provide you with relevant background that may be useful for your understanding and/or for responding to student questions.

Question 1 helps students recognize that different figures in the Student Handout are drawn at very different scales. For question 1b, the estimate of 1-10 billion protein molecules can be found in https://www.ncbi.nlm.nih.gov/pubmed/24114984. Students should be able to realize that a billion three-dimensional protein molecules of the linear dimensions shown in the Student Handout would not fit into either a tennis ball or a basketball. To arrive at the estimate that a cell at the same scale as the protein molecule would be roughly the size of a large cathedral or mosque, I compared the diameter of proteins (~5-12 nm) and animal cells (~10-100 µm) and used online data about the dimensions of large cathedrals and mosques. To review the relative sizes of various molecules and cells with your students, you may want to use either or both of these resources:
**Experiment 1 – Diffusion across a Synthetic Selectively Permeable Membrane**

This experiment uses a highly simplified model of a cell, with a synthetic selectively permeable membrane between an internal aqueous solution with large molecules and an external aqueous solution with ions. Subsequent sections of this activity develop a more complex and realistic model of the cell membrane.

After filling and tying their dialysis tube bags students need to rinse the bags thoroughly in fresh water to remove any spilled starch solution from the outside. If you do not have a sink, a series of large containers of water will work.

Iodine (I₂) is relatively insoluble in water, so potassium iodide (KI) is included to make iodine-potassium iodide solution; this results in the formation of iodine ions (I⁻) which are soluble in water. When iodine ions and starch are in the same solution the iodine ions get bound up in the beta amylose coils of the starch. This is what causes the color change of starch from clear or milky white to blue-black or purple. With enough time, the tan iodine solution will get lighter as the iodine ions continually diffuse through the dialysis tubing and become bound up.

**While your students are waiting** for the effects of diffusion to become observable, they should complete page 4 of the Student Handout. If necessary for your students, you may want to review diffusion. (For this purpose, you may want to use an animation of diffusion which is available at [https://authoring.concord.org/activities/12/pages/77/9bfc37ad-69e1-4ab3-9e7c-85e630d78838](https://authoring.concord.org/activities/12/pages/77/9bfc37ad-69e1-4ab3-9e7c-85e630d78838).) You may want to explain that diffusion is relatively rapid over very short distances, but diffusion is very slow over long distances due to collisions which repeatedly change the direction of molecular motion. This explains why the students need to wait 20-30 minutes to see the results of their experiment. It also explains why cells need to be tiny (or at least very thin).

In answering question 10, students should be aware that it is impossible to prove a hypothesis like “small ions can cross this synthetic selectively permeable membrane, but large molecules cannot”. The results of Experiment 1 will provide initial support for this hypothesis. Tests with multiple additional small ions and large molecules would be needed to provide strong support for this hypothesis. However, proof is impossible, since it is not possible to test for permeability to all small ions and all large molecules. In contrast, a single counterexample could disprove this hypothesis as an absolute truth, although the hypothesis might still be a useful generalization.

**Experiment 2 – Polar vs. Nonpolar Molecules**

In this experiment, students learn how a lipid layer with nonpolar molecules can serve as a barrier to the diffusion of ions. It may seem that a fluid layer of oil is nothing like a cell membrane. However, the consistency of a cell membrane is closer to a layer of oil than to the synthetic membrane used in Experiment 1. The phospholipid bilayer in the cell membrane is fluid, allowing lateral motion of both phospholipid molecules and many of the embedded protein molecules. (This motion is limited by protein interactions with the cytoskeleton.) This explains why the current model of cell membrane structure is called the fluid mosaic model ([http://anatomyandphysiologyi.com/the-plasma-membrane-structure/](http://anatomyandphysiologyi.com/the-plasma-membrane-structure/)).
For question 13, a useful discussion of why “like dissolves like” is available at https://socratic.org/questions/how-is-molecular-polarity-related-to-solubility.

If a student pours the oil too quickly or from too high up, the oil may initially mix with the water; then, the student will have to wait a little while for the oil to separate from the water. To understand why the oil separates from the water students should refer back to question 13. The greater density of the water explains why the oil floats on top of water. The Student Handout instructs students to make tiny drops of dye, since larger drops of dye tend to fall through the oil layer due to their greater momentum, combined with the greater density of the food coloring.

How Phospholipids and Proteins Combine to Form the Selectively Permeable Cell Membrane

The diagram of the phospholipid molecule in question 18a of the Student Handout is helpful, both to explain the phospholipid name and also to indicate why the phospholipid layer is permeable to small nonpolar molecules, but not to ions. This diagram, unlike almost all textbook diagrams of the phospholipid bilayer, shows that the lipid component of phospholipid molecules is larger than the ionic component.

Experiments with synthetic lipid bilayers have shown the following results:
- greatest permeability for nonpolar molecules such as O₂, CO₂ and steroid hormones
- limited permeability for the very small uncharged polar molecule, H₂O (Rapid transport of water across the cell membrane requires aquaporin, a channel protein.)
- very low permeability for large uncharged polar molecules like glucose and sucrose
- virtually no permeability for ions like H⁺, Na⁺, K⁺, Cl⁻.

After question 20, we suggest that you discuss the following points. The impermeability of the phospholipid bilayer to ions is predicted by the model developed in Experiment 2. This contrasts with the permeability to I⁻ of the synthetic membrane in Experiment 1. This example illustrates the limitations of dialysis tubing as a model of the selectively permeable cell membrane. This provides the opportunity to discuss the Crosscutting Concept, “Systems and System Models: Models can be used to predict the behavior of a system, but these predictions have limited precision and reliability due to the assumptions and approximations inherent in models.” Models are simplified representations of complex natural structures, phenomena or systems, so all models fail to completely accurately represent the complex reality they describe.
When you discuss the proteins embedded in the cell membrane, you may want to ask your students to predict which parts of the outer surface of these membrane proteins would be expected to be hydrophilic vs. hydrophobic.

Passive transport depends on diffusion, which moves substances from a region of higher concentration to a region of lower concentration. Passive transport includes:

- simple diffusion of small nonpolar molecules through the phospholipid bilayer
- facilitated diffusion of ions through specific channel or pore proteins
- facilitated diffusion of polar molecules like glucose, other sugars, and amino acids which are carried across the membrane by conformational changes of transport proteins.

In our bodies, transport of small nonpolar molecules also depends on solubility in water (e.g. in the blood). O₂ has limited solubility in water (which is why it is useful for blood to have oxygen transport proteins like hemoglobin). CO₂ has much greater solubility in water because of the following chemical reactions:

\[
CO₂ + H₂O \leftrightarrow H₂CO₃ \leftrightarrow H^+ + HCO₃^-
\]

For ions, the direction of passive diffusion depends on the electrochemical gradient, which includes both differences in concentration and differences in charge inside vs. outside the cell membrane.

Your students may be interested to know that cystic fibrosis is caused by mutations in the gene for a Cl⁻ channel (https://www.webmd.com/children/what-is-cystic-fibrosis#1; https://www.cff.org/Research/Research-Into-the-Disease/Basics-of-the-CFTR-Protein/).
Active transport proteins use energy to pump ions or molecules from a region of higher concentration to a region of lower concentration. As shown in the figure below, ATP often provides the energy for active transport, e.g. for pumping Na+ out of cells.\(^7\)

As shown in the figure to the right, the concentration gradient for one substance can be used to move another substance against its concentration gradient. For example, the concentration gradient of Na\(^+\) provides the energy to move glucose into cells in the lining of the small intestine and in kidney tubules.

(Figure source = https://qph.fs-quoracdn.net/main-qimg-5e26204deade37be96474dad6557f23-c)

\(^7\) An animation that shows how this pump works is available at http://highered.mheducation.com/sites/0072495855/student_view0/chapter2animation__how_the_sodium_potassium_pump_works.html.
Questions 18-22 provide multiple opportunities to discuss the **Structure and Function Crosscutting Concept**: "The functions and properties of natural and designed objects and systems can be inferred from their overall structure, the way their components are shaped and used, and the molecular substructures of its various materials." You may want to bring up this Crosscutting Concept as you discuss the phospholipid bilayer, channel proteins and transport proteins or you may want to have a discussion after question 22 where you ask students to identify multiple aspects of this Structure and Function Crosscutting Concept.

Questions 25 and 26 can be used for formative assessment. To facilitate your class discussion of the unique and shared features of simple diffusion, facilitated diffusion and active transport, you may want to have each group of students prepare the Venn diagram in question 25 on a whiteboard.\(^8\)

The Student Handout includes only quite simple diagrams of the structure of a cell membrane. The figure below shows a more complete diagram. The Student Handout also omits discussion of additional cell membrane functions, e.g. cell-cell recognition and protein receptors for chemical signals such as some types of hormone.

\[^8\text{For this purpose you would want one whiteboard per student group in your largest class. To obtain whiteboards, you can go to Home Depot and ask them to cut a 8' x 4' whiteboard (e.g. EUCATILE Hardboard Thrifty White Tile Board) into six pieces with the dimension 32" x 24". They should have a power saw rig that allows their employees to cut the pieces very easily. They should not charge to cut them and the product cost is reasonable.}\]

Some important tips for using whiteboards:
- Coat the white boards with Endust (or similar product) before using. Every once in a while wipe them clean and reapply Endust.
- Do not use markers that are old or almost empty. The ink from these are more difficult to erase.
- Black markers erase easiest.
- Best if boards are erased immediately after use.
- Teacher and/or students can take a picture of the information on the board if they want to save it.
Exocytosis and Endocytosis
To help students understand and remember the terms exocytosis and endocytosis, you may want to explain that “endo” means within or into and “exo” means outside or out of; “cyte” refers to cell; and “osis” means process. As a mnemonic for your students, you may want to link exocytosis to exit and endocytosis to enter.

Question 27 introduces phagocytosis as one type of endocytosis. The lysosome that provides the digestive enzymes also contains nitric oxide and reactive oxygen intermediates that help to kill the bacteria. The membrane around each lysosome plays a crucial role in protecting the cytoplasm from the harmful effects of the digestive enzymes contained in the lysosome. Lysosomal enzymes work best in an acidic environment; when the lysosome is active, the lysosome membrane pumps in protons. If a lysosome breaks open or leaks, the lysosomal enzymes are not very active because the cytoplasm has a neutral pH. In addition to their role in phagocytosis, lysosomes play a role in breaking down old or damaged organelles so their constituent molecules can be reused. This is one example of the dynamic nature of cells.

The Student Handout figure for question 28 illustrates several important general points:
• There are many internal membranes in eukaryotic cells. These allow localization of specific functions within the cell. To distinguish the cell membrane surrounding the cell from these internal membranes, the cell membrane is often called the plasma membrane.
• Multiple parts of the cell cooperate to accomplish specific cell functions.
• Cells are dynamic, not static. To further illustrate the dynamism of cells, you may want to use an animation of vesicle transport (available at https://www.youtube.com/watch?v=y-uuk4Pr2i8).

The figure in question 28 in the Student Handout shows protein secretion by exocytosis, as well as formation of lysosomes that contain protein digestive enzymes. The figure below shows that a and similar mechanism inserts membrane proteins in the plasma membrane.

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9 Prokaryotic cells have fewer internal membranes and organelles than eukaryotic cells, but the difference is not as absolute as biologists have traditionally thought. Recent research has shown that many photosynthetic prokaryotes have extensive internal membranes where photosynthesis takes place and several bacterial species have internal membrane-bound organelles.
An astute student may notice that the protein is synthesized by a ribosome on the outside of the endoplasmic reticulum and, as the protein is synthesized, it crosses the membrane of the endoplasmic reticulum. As shown in the figure below, the protein crosses the endoplasmic reticulum membrane through a water-filled protein pore. (This type of protein translocator is also observed in the membranes of mitochondria, chloroplasts and bacteria.)
The examples discussed in questions 27 and 28 can help students understand that cells are made up of organelles which are made up of molecules. 10 This provides the opportunity to discuss the Disciplinary Core Idea: “Multicellular organisms have a hierarchical structural organization, in which any one system is made up of numerous parts and is itself a component of the next level.”

Possible Follow-Up Activities
As a follow-up to this activity, you may want to:

- use the supplementary question about cooperation between the cell membrane and various organelles provided on the last page of these Teacher Preparation Notes
- have your students use microscopes, Elodea and various chemicals to study osmosis and rates of diffusion across the plasma membrane for molecules of different size and hydrophobicity as directed in "Diffusion across Biological Membranes" (available at http://faculty.buffalostate.edu/wadswogj/courses/BIO211%20Page/lectures/lab%20pdf's/Diffusion%20lab%2006a.pdf).
- discuss with your students the contributions of selectively permeable membranes and osmosis to dialysis treatment of patients with kidney failure. (A useful introduction is available at http://en.wikipedia.org/wiki/Dialysis)

Sources for Figures in Student Handout (All other figures were created by the authors.)

- Polar water molecule on page 4 – modified from http://www.citruscollege.edu/lc/archive/biology/PublishingImages/c02_08.jpg
- Phospholipid bilayer figure on pages 6 and 8 – modified from https://unsig11cellmembrane.wikispaces.com/file/view/PhospholipidDiagram1.jpg/164811335/PhospholipidDiagram1.jpg
- Passive transport across cell membrane on page 7 – modified from https://www.smore.com/8jen8-human-cells
- Endocytosis and exocytosis on page 9 – https://slideplayer.com/slide/2328076/8/images/36/Figure+5.8+Endocytosis+and+Exocytosis.jpg
- Protein secretion on page 9 – modified from https://images.slideplayer.com/16/5205959/slides/slide_25.jpg

10 These points and the dynamism of cells are reinforced in the analysis and discussion activity, “Structure and Function of Molecules and Cells” (http://serendipstudio.org/exchange/bioactivities/SMolecCell).
Possible Supplementary Question
to Foster Student Understanding of How Different Cell Parts Cooperate

The different parts of a cell need to cooperate to accomplish cell functions. For example:

- The cell membrane maintains the internal conditions that the other parts of the cell need in order to function properly.
- Cell membrane structure and function depend on inputs from several other parts of the cell.

29. This simplified diagram of a eukaryotic cell identifies several organelles that contribute to normal cell membrane structure and function. In the table below, explain how these organelles contribute to normal cell membrane structure and function.

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<th>Cell Organelle</th>
<th>How This Organelle Contributes to Normal Cell Membrane Structure and Function</th>
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This supplementary question illustrates several features of the cooperation between the cell membrane and various organelles. The cell membrane maintains the chemical makeup of the cytosol that is needed for the cell to function properly; thus, the cell membrane contributes to homeostasis for the cell. At the same time, the mitochondria produce ATP which is needed for primary active transport and the nucleus, ribosomes, rough endoplasmic reticulum and Golgi apparatus work together to produce membrane proteins. A more complete version of the figure is available at [https://www.timvandevall.com/wp-content/uploads/animal-cell-diagram-1.png](https://www.timvandevall.com/wp-content/uploads/animal-cell-diagram-1.png)