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Teacher's Guide

Understanding Movement of Molecules across the Cell Membrane

Grade Level: High school & undergraduate

Subject area: Biology

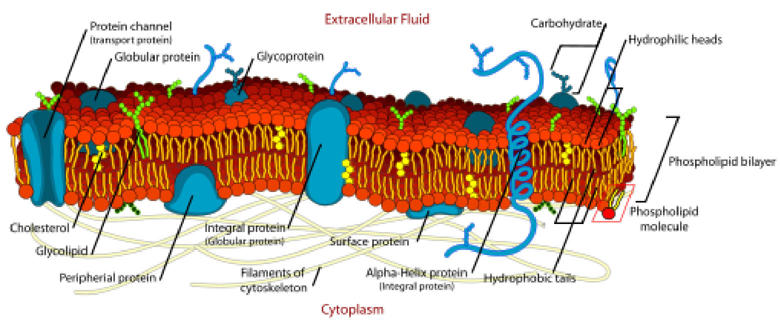
Time required: 70 minutes

Learning Objectives: 1. Understand permeability of cell membrane; 2. Understand materials moving across cell membranes are nanoscale in size.

Summary: This lesson uses a macro-model to demonstrate the diffusion of molecules across the cell membrane. A deshelled egg serves as the cell model to observe movement in and out of the "cell". Students will learn that the cell membrane is composed of a complex nano-structured membrane that regulates diffusion and mobility of membrane biomolecules. The purpose is to examine permeability properties of plasma membranes and give students a better understanding of how substances, nano in size move into and out of a cell.

Lesson Background: The human body is a very complex and intricate structure mainly composed of trillions of tiny cells all nano in size organized into many levels of structural organization. Nano means one billionth (10^{-9}) and one meter is equal to a billion nanometers. Most cells in your body are about 5,000 nm across or less, which is about 1/20th the width of a strand of hair. Cell membranes are only 10 nm thick!! The simplest level of structural hierarchy in the human body is the chemical level. Chemicals are even smaller in size than cells, as chemicals enter and exit the cell. At the chemical level, atoms, tiny building blocks of matter, combine to form molecules such as water and proteins. Molecules, in turn associate in specific ways to form organelles, basic components of the microscopic cells. Groups of cells, with similar structure and function form tissues that in turn makes up organs. Organs are arranged into organ systems that work together collectively to allow the body to function as a whole.

It is important to note that membranes are held together by hydrophobic and hydrophilic interactions between lipid molecules. This concept forms the basis for the Fluid Mosaic Model developed by Singer and Nicolson in 1972. With continuing research, we now know that membrane interactions are very complex and consist of a mix of interactions that are not fully understood. These interactions result in a membrane nanostructure that regulates diffusion and mobility of membrane biomolecules. These effects are now recognized as



Fluid Mosaic Model from Wikipedia: https://commons.wikimedia.org/wiki/File:Cell_membrane_detailed_diagram_en.svg

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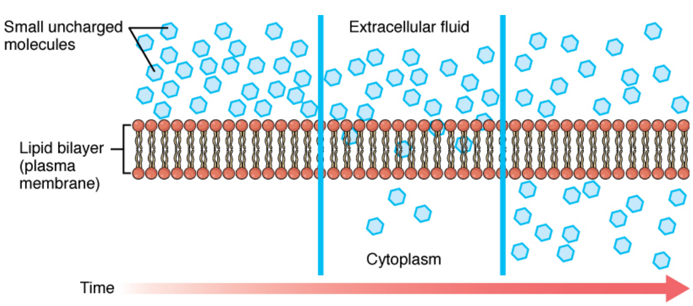
important regulators in cell signaling. What is cell signaling and why is it important? Cell signaling is part of any communication process that governs basic activities of cells and coordinates multiple-cell actions. The ability of cells to perceive and correctly respond to their microenvironment is the basis of development, tissue repair, and immunity, as well as normal tissue homeostasis. Errors in signaling interactions and cellular information processing may cause diseases such as cancer, autoimmunity, and diabetes. By understanding cell signaling, clinicians may treat diseases more effectively and, theoretically, researchers may develop artificial tissues. (From Wikipedia Cell Signaling). The recognition that cell membranes exhibit nanoscale structure has had a profound impact on the study of cell signaling and membrane physiology.

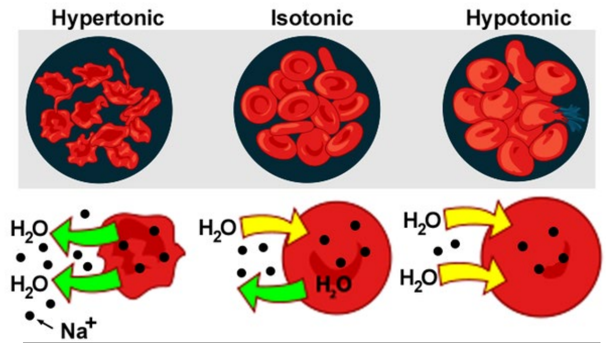
Though not very often recognized, it is the work of the cell and its tiny nanostructures (organelles) within it that play key roles in maintaining life. The ultimate goal of our body is to maintain a constant state of balance known as *homeostasis*. The state of “balance” we refer to spans across the entire functioning surface of your body. The body works to maintain blood pressure, pulse, respiration rates, glucose levels, calcium levels, and many other variable factors. Whenever one of these variable factors goes outside of the “normal” range, the body goes out of its state of balance and disease can occur. The science of nano-biotechnology allows doctors to implant nano-devices and nanoparticles into the body to attempt to keep the body in a state of balance along with decreasing the risk of disease. Nano-biotechnology is best described as helping modern medicine progress from treating symptoms to generating cures and regenerating biological tissues.

In our bodies, the task of maintaining homeostasis is carried out by cell transport, moving molecules into and out of a cell. This phenomenon occurs across the outer covering of a cell, the plasma membrane. The membrane is *selectively permeable* meaning that it only allows select nano-sized molecules to move across it. Transport through the plasma membrane occurs in two basic ways: passive and active transport. *Active transport* is carried out with the help of ATP, an intracellular source of energy. *Passive transport* is carried out when the concentration or pressure differences influence movement. A concentration gradient exists when there is a difference in concentration between the inside and outside of the cell. The numbers of molecules present influence the cells concentration on either side. The greater the numbers of molecules, the higher the concentration on that side.



Simple diffusion across cell membrane. Wikipedia: https://commons.wikimedia.org/w/index.php?curid=30131172

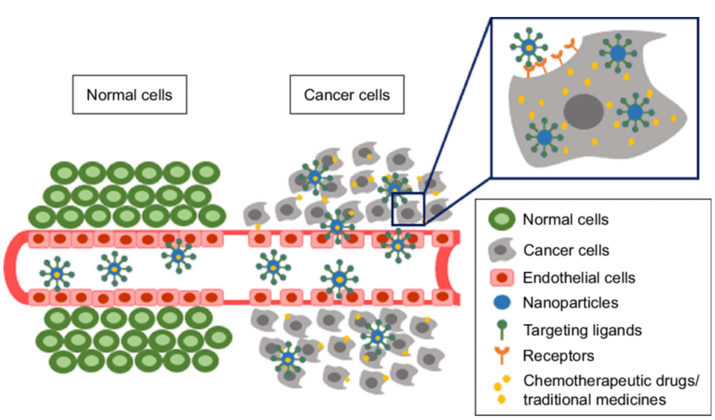
Diffusion, a passive process, is the movement of molecules from an area of higher concentration to an area of lower concentration. *Osmosis*, a special form of diffusion, is the movement of solvent; usually water, down its concentration gradient. When cells move molecules from one side to the other, it can possibly cause the cell to change shape and or/weight. A solution surrounding the cell that contains the same solute/water concentration as the inside of the cell is considered *isotonic*. There is no water movement because equilibrium already exists. A solution surrounding the cell that contains a higher concentration of solutes than are present inside the cells is considered *hypertonic*. The cell will loose weight or crenate and shrink in an effort to establish equilibrium. A solution surrounding the cell that contains a lower concentration of solutes than are present in cells is considered *hypotonic*. The cell will gain weight and possibly lyse or burst in an effort to establish equilibrium.



Hypertonic, isotonic & hypotonic solutions & impact on red blood cells. Wikipedia: https://commons.wikimedia.org/wiki/File:Osmotic_pressure_on_blood_cells_diagram.svg

Both diffusion and osmosis occur naturally in many places within the human body. The kidneys, which filter blood, carry out both of these processes on a regular basis. Sometimes, matter limits our body such as in kidney failure. When matter limits the body, it can no longer conduct those functions necessary to maintain life. Imbalance of variable factors such as blood pressure, pulse, respiration rates, and glucose levels, can eventually lead to organ failure if not addressed. If organs fail, the body is no longer be able to maintain life.

Nanotechnology is the study of manipulating matter on an atomic and molecular scale. It is used to make incredibly small things the size of organelles or even smaller. With the usage of nanotechnology, we are now able to aid in cell transport to help sustain life. The interactions of nanoparticles with cellular membranes and transport processes have major implications for the biology, toxicology, and pharmacology of nanoscale materials Nanoparticles and nanodevices are able to enter the body and help maintain functioning of tissues and organs that are no longer able to perform on their own. Many different types of nanoparticles are being explored for drug delivery. Several types are already in FDA approved use. Nanoparticles can be functionalized to attach to only certain types of cells giving targeted drug delivery. They can also be functionalized to be soluble in body fluid obviating drug insolubility problems. It is important to understand and predict the behaviors of nanoparticles in a physiological setting as we increase their use. This also includes the importance of regulating these nanoparticles. Researchers are working to determine the physical interaction of nanoparticles with cell membranes, including their transport across them. This is a major thrust for both pharmacological and toxicological studies. This experiment will



Passive targeting and active targeting mechanisms of nanoparticles. Creative Commons BY-NC. Full citation in Resources.

demonstrate, via a macro-model, the movement of molecules into and out of a cell in a manner such as will be used by nanoparticles and nanodevices.

Sources:

1. Elaine N. Marieb, Susan J. Mitchell, Human Anatomy & Physiology Laboratory Tenth Edition Manual 2011
2. Nanooze. Issue 8, 2010. Accessed at: https://www.nnci.net/nanooze.

Resources:

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- Cell Signaling: https://en.wikipedia.org/wiki/Cell_signaling
- Introduction to Cell Signaling: https://www.khanacademy.org/science/biology/cell-signaling/mechanisms-of-cell-signaling/a/introduction-to-cell-signaling
- Mahamad, N, Plengsuriyakarn, T. and Na-bangchang, K. 2018. ,Application of active targeting nanoparticle delivery system for chemotherapeutic drugs and traditional/herbal medicines in cancer therapy: A systematic review. Accessed at: https://www.researchgate.net/publication/326182871_Application_of_active_targeting_nanoparticle_delivery_system_for_chemotherapeutic_drugs_and_traditionalherbal_medicines_in_cancer_therapy_A_systematic_review.
- Nanodevices in medicine – an overview: https://www.sciencedirect.com/topics/materials-science/nanodevices. A summarizing of different journal articles and cook chapters.
- Nanodevices in Diagnostics: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2962874/
- Singer SJ, Nicolson GL. The Fluid Mosaic Model of the Structure of Cell Membranes. Science. 1972;175:720–731. [PubMed] [Google Scholar]
- Tissue Engineering: https://en.wikipedia.org/wiki/Tissue_engineering
- Tissue Engineering and Regenerative Medicine: https://www.nibib.nih.gov/science-education/science-topics/tissue-engineering-and-regenerative-medicine

Pre-requisite Knowledge: Students should know cell structure and the basics of movement of materials in and out of a cell.

Safety Information: Caution students to be careful when handling eggs as they are very delicate after sitting in solution and may break easily.

Materials: (12 groups of 2 each)

- 48-52 deshelled eggs (procedure below)
- Large container to hold eggs for deshelling
- (12) 400-ml beakers
- (12) weight boats
- (6) wax markers,
- (6) laboratory balances
- 2L distilled water

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- 2L 30% sucrose solution
- paper towels
- timer/stop watch

You may want to have students define these before proceeding with the activity. The definitions could be assigned as homework or classwork. Class discussion of the terms is recommended to ensure students have no misconceptions.

Vocabulary and Definitions:

1. *Selectively permeable:* a property of cell membranes that only allows certain molecules to enter or exit the cell i.e., only allows select nano-sized molecules to move across it.
2. *Active transport:* is the movement of molecules or ions against a concentration gradient (from an area of lower to higher concentration). This does not ordinarily occur so such transport requires energy often carried out with the help of ATP, (an intracellular source of energy) and enzymes.
3. *Passive transport:* is carried out when the concentration or pressure differences influence movement. A concentration gradient exists when there is a difference in concentration between the inside and outside of the cell.
4. *Diffusion*: a passive process, is the movement of molecules from an area of higher concentration to an area of lower concentration.
5. *Osmosis*: a special form of diffusion, is the movement of solvent; usually water, down its concentration gradient.
6. *Homeostasis*: in biological systems, it is the tendency to maintain stability while adjusting to conditions that are optimal for survival.
7. *Hypertonic*: a solution where the concentration of solutes is greater outside the cell than inside it.
8. *Hypotonic*: a solution where the concentration of solutes is greater inside the cell than outside of it.
9. *Isotonic*: where the concentration of solutes outside the cell is equal to the concentration of solutes inside the cell.
10. *Nanoscale*: measured in nanometers; typically referring to materials between 1 and 100 nm but others use up to several hundred nanometers.
11. *Nanometer*: $1x10^{-9}$ or one billionth of a meter.
12. *Nanotechnology*: Nanotechnology is science, engineering, and technology conducted at the nanoscale, which is about 1 to 100 nanometers. It is the study and application of extremely small things and can be used across all the other science fields, such as chemistry, biology, physics, materials science, and engineering.

Advance Preparation:

Deshell eggs 48 to 72 hours before the day of the lab. To deshell eggs: immerse eggs in vinegar. After 24 hours, gently rub eggs under running water to remove shell. If there is any shell remaining, immerse in fresh vinegar. Repeat rubbing under water and immersion in fresh vinegar until all shell has been removed. Give each group 2 deshelled eggs, two 400-ml beakers, 200 ml distilled water, 200 ml 30% sucrose solution (instructions below), wax markers, paper towels, weight boat, and laboratory balance.

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30% sucrose solution: To make 100 mL, dissolve 30 g sucrose in about 70 mL 0.1M Phospahet buffered saline (PBS) or water; once dissolved, make up volume to 100 mL total by adding 0.1M PBS or water.

Directions for the Activity:

1. Obtain two deshelled eggs and two 400-mL beakers. **Note**: the relative concentration of solutes in deshelled eggs is about 14%. Number the beakers 1 and 2 with the wax marking pencil. Half fill beaker 1 with distilled water and beaker 2 with 30% sucrose solution.
2. Carefully blot each egg by rolling it **gently** on a paper towel. Place a weight boat on a laboratory balance and tare balance (that is, make sure the scale reads 0.0 with the weigh boat on the scale). Weigh egg 1 in the weigh boat, record the initial weight in the data chart and gently place it into beaker 1. Repeat for egg 2, placing it in beaker 2.
3. After 20 minutes, remove egg 1 and gently blot it and weigh it. Record the weight, and return it into beaker 1. Repeat for egg 2, returning it into beaker 2. Repeat this procedure at 40 minutes and 60 minutes.
4. Calculate the change in weight of each egg at each time period, and enter that number in the data chart below. Also, calculate the percent change in weight for each time period and enter that number in the data table.

Cleanup: Discard eggs in the trash. Wash chemicals down the sink unless instructor indicates other method of disposal.

Next Generation Science Standards:

- HS-LS1-3. Plan and conduct an investigation to provide evidence that feedback mechanisms maintain homeostasis.
  - LS1.A. Structure and function
- Crosscutting: stability and change
- Science and Engineering Practices: Developing and using models.

Optional: Experimental design challenge described in the student guide

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Student Worksheet

(with answers)

Understanding Movement of Molecules across the Cell Membrane

Introduction:

Despite differences in structure and function, all living cells in multicellular organisms have a surrounding cell membrane. This cell membrane is known as the plasma membrane. Just as the the outer layer of your skin separates your body from the environment, the cell membrane separates the inner contents of a cell from its outer or exterior environment. This cell membrane provides a protective barrier around the cell and regulates which materials can pass in or out. With continuing research, we now know that membrane interactions are very complex and consist of a mix of interactions that are not fully understood. These interactions result in a membrane *nanostructure* that regulates diffusion and mobility of membrane biomolecules.

The human body is a very complex and intricate structure mainly composed of trillions of tiny cells all nano in size organized into many levels of structural organization. Nano means one billionth (10^{-9}) and one meter is equal to a billion nanometers. Most cells in your body are about 5,000 nm across or less, which is about 1/20th the width of a strand of hair. Cell membranes are only 10 nm thick!!

The ultimate goal of our body is to maintain a constant state of balance more formerly known as *homeostasis*. Whenever the body goes out of this state of balance, disease can occur.

The task of maintaining homeostasis is carried out by cell transport, moving molecules into and out of a cell. This phenomenon occurs across the outer covering of a cell, the plasma membrane. The membrane is selectively permeable meaning that it only allows select nano-sized molecules to move across. Transport through the plasma membrane occurs in two basic ways: passive and active transport. *Active transport* is carried out with the help of ATP, an intracellular source of energy. *Passive transport* is carried out when the concentration or pressure differences influence movement. A concentration gradient exists when there is a difference in concentration between the inside and outside of the cell. The numbers of molecules present influence the cells concentration on either side. The greater the numbers of molecules, the higher the concentration on that side.

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Your teacher may ask you to define these before proceeding to the activity.

Vocabulary and Definitions:

1. *Selectively permeable*
2. *Active transport*
3. *Passive transport*
4. *Diffusion*
5. *Osmosis*
6. *Homeostasis*
7. *Hypertonic*
8. *Hypotonic*
9. *Isotonic*
10. *Nanoscale*
11. *Nanometer*
12. *Nanotechnology*

Make a prediction: What will occur to a deshelled egg (14% concentration) if placed in a 30% sucrose solution? What is the same egg is placed in distilled water?

If an egg of 14% concentration is placed in a 30% sucrose solution, it is predicted that water will move out of the egg and the egg will shrink. If an egg of 14% concentration is placed in a distilled water solution, it is predicted that water will move into the egg and the egg will gain weight.

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Materials:

- 2 deshelled eggs (procedure below)
- 400-ml beaker
- weight boat
- wax markers
- laboratory balance
- 2L distilled water
- 2L 30% sucrose solution
- paper towels
- timer/stop watch

Directions for the Activity:

1. Obtain two deshelled eggs and two 400-mL beakers. **Note**: the relative concentration of solutes in deshelled eggs is about 14%. Number the beakers 1 and 2 with the wax marking pencil. Half fill beaker 1 with distilled water and beaker 2 with 30% sucrose solution.
2. Carefully blot each egg by rolling it **gently** on a paper towel. Place a weight boat on a laboratory balance and tare balance (that is, make sure the scale reads 0.0 with the weigh boat on the scale). Weigh egg 1 in the weigh boat, record the initial weight in the data chart and gently place it into beaker 1. Repeat for egg 2, placing it in beaker 2.
3. After 20 minutes, remove egg 1 and gently blot it and weigh it. Record the weight, and return it into beaker 1. Repeat for egg 2, returning it into beaker 2. Repeat this procedure at 40 minutes and 60 minutes.
4. Calculate the change in weight of each egg at each time period, and enter that number in the data chart below. Also, calculate the percent change in weight for each time period and enter that number in the data table.

Record Your Observations: (may put in lab notebook)

Data from Experiment						
Time	**Egg 1 (in distilled H2O)**	**Weight change**	**%Change**	**Egg 2 (in 30% sucrose)**	**Weight change**	**% Change**
Initial weight (g)		-	-		-	-
20 min.						
40 min.						
60 min.						

Analyze the Results:

1. Did you observe what you predicted? If not, how did your observation differ from your prediction? Answers will vary.

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2. Do your observations leave you with anymore questions? Do they enable you to make predictions? If so, what are they? Answers will vary.

Draw Conclusions:
3. Based on your results, do you feel that egg 1 and/or egg 2 displayed properties of hypertonicity, hypotonicity or iostonicity? Explain your answer.

Design Challenge:
Design an experiment to test other molecules that you would like to examine their movement across the cell membrane. What other variables would you test? Would you want to use the same eggs or ones that have not been tested? What type of molecules would you examine? Large versus small? Vitamins, minerals, salts? Design your experiment and have the instructor approve your design before testing. Follow the experimental procedures of above. Write up your results and then share as a short presentation to the class.

Cleanup: Discard eggs in the trash. Wash chemicals down the sink unless instructor indicates other method of disposal.

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