Curriculum Units by Fellows of the Yale-New Haven Teachers Institute
2006 Volume V: Engineering in Modern Medicine

Launch Biotechnology into Your Classroom: Drug Delivery and Diffusion

Curriculum Unit 06.05.01
by Karen A. Beitler

Introduction

Biotechnology and biomedical technology offer limitless potential in outstanding job opportunities for students with a pioneering spirirt and a gift for inovation. We have hardly noticed the influx of biotechnological inventions into our lives. Primetime television shows such as CSI, Forensic Files, Grey's Anatomy, ER, and House have brought the latest biotechnological advances in medical research right into our own living rooms. These shows often portray biomedical techniques, and biotechnical devices such as new imaging methods, prostethesis, and various types of drug delivery systems. Crimes are solved and lives are saved using imaging techniques, DNA fingerprinting, implants, transplant and prostheic limbs. New instrumentation and techniques are being developed everyday. This enormous exposure has brought biomedical techniques and biotechnology to the forefront of education.

Biomedical devices have demanding requirements; they can not be toxic or provoke immune response. They must be reliablle, small in size, light in weight and quiet. People are living longer and individuals are enjoying a better quality of life due to biomedical inventions that allow self-administration and freedom. Medicine and technology have worked together to improve drug administration, diagnotisic devices, and quality of life. This unit will explore a few of the new types of drug delivery and introduce students to new options of study in the fields of both medicine and science.

Designed to specifically enhance student understanding of how drugs are delivered to patients in a variety of situations, the focus will be on new biomedical technologies such as transdermal patches, drug delivering disks and non invasive procedures that seek to maximize efficacy of the drug at the target cellular level and minimize side effects to other parts of the organsim. In addition students will research biomedical engineering and technology from the standpoint of careers.

The unit assumes prior knowledge of basic systems of the body, specifically the integuementary system and the processes of osmosis and diffusion across membranes. The narrative reviews the anatomy, physiology and the important processes of diffusion and osmosis as related to our skin. The lesson plans introduce this knowledge to the students and include activities centered around drug delivery to specific diseased areas thereby introducing students to how biomedical technologists develop methods of drug delivery to control or

cure disease states. The plans also include a Webquest in biotechnology and a research project on biomedical careers.

Objectives

Describe how a living thing is organized; prior knowledge of body systems
Explain how equilibrium is established as a result of diffusion; homeostasis
Distinguish between diffusion and osmosis, review.
Explain how substances cross the cell membrane through facilitated diffusion.
Acquire knowledge of the historical development of biomedical engineering
Explore the bridge between medicine and technology
Apply knowledge to solve how to deliver medicine using biomedical techniques
Explain the physical basis of drug delivery
Name four ways that a drug can be administered,
Discuss the advantages and disadvantages of each method.
Describe some potential consequences of drug interactions.
Discover application of biomedical devices.
Explore fields of research in biomedical engineering.
Learn techniques of internet research.
Research a career path.
Prepare a presentation to introduce the class to the particular career.

Academic setting

This unit is written primarily for teachers of AP Biology but can be modified for other levels of High School Biology. Post exam time for advanced placement students is a time to enhance and apply the knowledge they have gained through rigorous study throughout the year. In a series of lectures, activities and labs, this unit will review important aspects of human organism as a whole and enhance student knowledge of the field of biomedical technology and introduce students to new career paths. The goal is to heighten awareness of the vast array of new technologies in patient treatment that target the treatment of diseases by employing hands-on application of these techniques in a simulated situation. Students will then be exposed to potential careers in the biomedical field.

Narrative

Rooted in biology, physics, mathematics and chemistry, bioengineering is a new and emerging field of study. The National Institute of Health defines bioengineering as a process which " integrates physical, chemical, or mathematical sciences and engineering principles for the study of biology, medicine, behavior, or health. It advances fundamental concepts, creates knowledge for the molecular to the organ systems levels, and develops innovative biologics, materials, processes, implants, devices, and informatics approaches for the prevention, diagnosis, and treatment of disease, for patient rehabilitation, and for improving health" (1) . Biotechnology involves new methods to enhance the quality of life through tissue and integrating cellular engineering; biomaterials and biological signal processing, imaging, instrumentation; biomechanics, integrative biology; transport phenomena, systems analysis and electrophysiology. These technologies provide new and exciting avenue for those with an interest in the medical field and technology.

This paper will explore technology that is still in its infancy but has enormous potential for future generations. The field of transdermal delivery has opened the door to pain free delivery of medication that provides constant continuous release, bypasses the digestive system and minimizes adverse side effects of medications. Transdermal delivery (TDS) is currently FDA approved for approximately twelve different drugs (2) . TDS has advantages over oral dosage however molecular size plays key role in whether or not a drug can be administered this way. Tiny spheres and discs smaller than a dime made of polymer micelles that dissolve over time have been inserted into patients with tumors carrying chemotherapy drugs. The field is relatively new and expanding every day. In order to understand transdermal delivery of medication the student will need a thorough understanding of the processes involved for such a system to work. The processes of diffusion and equilibrium in the context of human physiology and drug delivery will be explored.

Diffusion

Diffusion is the process by which molecules move from an area of high concentration to an area of low concentration until they are equal. Diffusion occurs whenever the concentrations of substances are not evenly distributed in an area. The unequal distribution of particles in an area is called a concentration gradient. Molecules will move without an energy input, therefore diffusion is a passive process. This spontaneous movement caused by the excited intermingling of two or more types of molecules or in the case of gases the

'mean free path of collisions" with other atoms or molecules [3] . The distance the molecules travel can be measured, therefore the diffusion can be predicted. For solids, diffusion can be thought of as a mass moving through a path in another mass; the size of the pathway can be measured, again the diffusion can be predicted with some degree of accuracy.

Diffusion in liquids, however, causes a problem. There is not an adequate model for liquids because of convection. Convection is the molecular movement caused by fluid motion. Convection can be caused by heat, which introduces differences in fluid density or gravity Earth's gravity acts on a liquid keeping it in motion, this motion gets confused in the calculation of movement of particles. Particles are in constant random movement that results in the absorption of heat from the surrounding area. The more that is absorbed the faster the particle moves. All that thermal heat makes it difficult to know if the exchange of the particles is only from diffusion or if it is enhanced by thermal motion. Think of a teabag placed in a cup of hot water, is the tea diffusing through the liquid by itself passively or does the temperature of the water add to the rate of diffusion? We all know that diffusion in heated substances happens more quickly. We can mix the powdered cocoa into warm water a lot faster than into cold water. Even in the absence of increased temperature; gravity causes enough friction between molecules to make the measurement of liquid diffusion difficult. The random motion of the particles drives diffusion, molecules tend to move away from their highest concentration and molecules of different types tend to intermix. Liquid diffusion can best be measured under no gravity situations.

Diffusion is the process of movement of particles; osmosis is diffusion of water molecules. Water or any other molecule will move across a membrane, passively, until they reach a state of equilibrium. Diffusion depends on the diffusion area, the concentration gradient of the substance moving, and a constant known as the diffusion coefficient (also known as permeability [4] . No energy is required or released.

Equilibrium

The cell is a highly organized structure that maintains a dynamic equilibrium. Dynamic equilibrium is defined as a condition in which "the parts of a system are in continuous motion, but they move in opposing directions at equal rates so that the system as a whole does not change" [5] .

The driving force for passive transport across a membrane is the energy of a difference in concentration of molecules; the difference between the numbers of particles inside as compared to the number outside. This energy is defined as the electrochemical gradient and is the sum of chemical and electrical energy. Both cations and anions will continue to equilibrate themselves from the intracellular fluid across a membrane until their overall chemical and electrical gradients are in balance. There will be a small net charge across the membrane, inside negative, that resists the tendency of any ions to move back down their concentration gradient. This is called the Donnan equilibrium and is naturally occurring in all cells because their membranes are semi-permeable [6]. Because molecules carry different charges and are of differing molecular size; cells can reach a resting potential where inter and extra cellular components are approximately equal. Scientists can take advantage of this when designing drug delivery systems; the flow of molecules is from the higher concentration to the target area.

Membrane Structure and Function

Lipids and proteins make up most cell membranes, although carbohydrates can be present too. Phospholipids are the type of lipids often found in cellular membranes; they contain hydrophilic (water-loving) and

hydrophobic (water-fearing) ends, as do most membrane proteins. The current model that represents a cell membrane is called the fluid mosaic model. [7] .

This model shows a fluid structure made of various proteins in bilayer of phospholipids. The proteins are thought to drift rapidly and laterally within the double layer of phospholipids. It is thought that the cytoskeleton of the cell regulates the speed and direction of movement of the proteins in the phospholipids bilayer. A membrane remains fluid until temperature decreases and the phospholipids solidify according to the amount of saturated hydrocarbons in their hydrophobic tails. Just as bacon grease solidifies into lard; the fluidity of the membrane decreases as temperature decreases [8] .

The structure of the membrane of the cell results in selective permeability; many molecules in a high level of organization determine what will enter into and exit from a cell. Many small molecules and ions move across the plasma membrane of a cell. Oxygen, sugars, amino acids and other nutrients enter the cell and metabolic wastes leave all at differing rates. Hydrophobic molecules can dissolve in and across the lipid bilayer. Polar and hydrophilic ions are impeded by the hydrophobic core. Other molecules, sugars and water pass slowly, some use transport proteins to pass through the membrane. The permeability of a cell's membrane is determined by the selective double layer of phospholipids, channel proteins that facilitate molecule crossing and temperature. The direction of traffic across a membrane is determined by other factors.

Diffusion of molecules across a cell membrane is a spontaneous process regulated by thermal motion (heat energy) and concentration of particles [9] . When no other forces exist molecules will diffuse down their concentration gradient, unaffected by other molecules until they reach equilibrium, this is called passive transport. Rates of diffusion will vary dependent on molecular size.

The diffusion of water molecules across a semi-permeable membrane creates a phenomenon called osmosis. The Life Science Dictionary from Northwestern University defines osmosis as "bulk flow of water through a semipermeable membrane into another aqueous compartment containing solute at a higher concentration" [10] .

The ability of the cell to gain or lose water is known as its tonicity [11] . Tonicity is crucial to living organisms and is determined by osmosis. Animal cells have special adaptations of osmoregulation to control water balance and keep a cell from becoming hypertonic or hypotonic. Hypertonic solutions contain a higher concentration of solute than intercellular content. This causes and outflow of water and shrinkage of the cell.

Hypotonic cells can become overfilled with water, they can swell and burst because osmosis of water is to the inside of the cell due to a low solute concentration in the water. Water balance and electrolyte (salts, minerals, nutrients) balance in cells are closely linked. An organism's body will work to keep the total amount of water and the levels of electrolytes in the bloodstream in equilibrium. When the level of a salt becomes too high, thirst develops, leading to an increased intake of liquid. In response to thirst, a hormone is secreted by the brain that causes the kidneys to excrete less urine. An increased amount of water in the bloodstream is the result; the salt is diluted and the equilibrium is restored. When salt levels become too low, the kidneys will excrete more urine, decreasing the amount of water in the bloodstream.

Diffusion and drug delivery in Human Physiology

The form and function of an animal are described as its physiology. Animal cell, tissues, organs and systems are organized in a hierarchy of complexity. Cells that are alike perform a specific function as do tissues that

are similar. The organization is specific to the function. For example, the skin is responsible for regulation of body temperature, protection, sensation, excretion, and immunity. Its cells are specifically permeable to allow exchange of molecules, thus the skin is said to breathe. The skin is also a blood reservoir and synthesizes Vitamin D [12]. This system is made up of cells that are similar and perform together to carry out these specific functions. Controlled delivery of a drug can occur when scientists mimic a natural system so the cell thinks it is taking in one of its own parts.

The integumentary system includes the body's largest organ, called the skin. It is made up of many components and two basic layers; the epidermis and the dermis. The outer layer and thinnest component of the skin is the epidermis. [13]. the second layer is called the dermis. The epidermis has no primary blood supply; capillary loops extend up from the dermis to supply it with blood and oxygen.

The thin epidermis has three basic layers; the stratum corneum, a granular layer and a basal layer. This layer varies in thickness from 0.04 mm on the eyelids to 1.6 mm on the palms, of the hand [14]. The stratum corneum and is made of two types of cells. Keratinocytes die and flatten into tightly packed layers, 15 layers thick. [15]. and melanocytes produce the skin's pigmentation and provide ultraviolet protection. The layers are held together by lipid cells called the lamellae. Within the keratinocytes are lamellar granules, small organs that grow in number as the cells mature. The entire surface is covered by a layer of protein and then a layer of lipids. All this is less than 20 um wide. The stratum corneum is constantly shedding, it contains protein called keratin. Keratin is formed from dead keratinocytes and protects the skin. Keratin gives the skin a leather-like feel and waterproof quality.

The next layer called the granular layer contains the most numerous cells. These layers of squalors cells, known as living keratinocytes, form the protective layer of skin. As they grow older, these cells are called corneocytes and form the stratum corneum. This layer can also contain cells called Langerhans cells that regulate T cells in an immunological response and Merkel cells that response to outside stimuli are also found here [16]. Merkel cells connect to nerve endings in the epidermis to the dermis, thereby communication is established. Beneath the keratinocytes lies the basal layer, it is the inner most layer of the epidermis. The cells of the basal layer of the epidermis continually divide and reproduce to replenish the outer layers.

The dermis is the middle layer of skin. This is where the hair follicles, oil glands, fat cells and lymph and blood vessels are found. The dermis is held together by a protein called collagen and is made of fibrocytes. The dermis gives strength and resilience to this large organ. The dermis is composed of living cells, tiny muscle fiber attached to hair follicles, sensory neurons, blood vessels and glands. Oil is produced here to soften the skin and sweat to cool it. Below the dermis is a network of collagen and fat cells, known as the subcutaneous layer. These cells are the energy reserves, the shock-absorbers and the insulators for the body.

The epidermis is replaced approximately every 39 days, with 13 days in proliferation, 13 days for the maturation of the keratinocytes, and 13 days for stratum corneum transit [17]. The balance maintained between the making keratinocytes and production corneocytes is tightly regulated. As the cells mature they are replaced to develop an effective skin barrier. The skin's integrity is maintained by the constant regeneration and repair activities of the dermal layer.

Diffusion and Drug Delivery

In the past drug delivery has been mostly oral. Herbal or plant remedies were made by the local 'expert' to accompany ceremony and ancient acupuncture. The ancient Greeks considered illness to be a part of life and

treated it with "diet, baths, fomentations and gruel" [18] . Jewish and later Arabic medical school passed on the knowledge of what worked and what did not; surgeries and herbs were joined by" casts, cauterization, venesection "treatment of wound and began using chemicals and distillation to enhance oral medication.

In the ninth through thirteenth centuries medicine flourished at the school of Salerno is Italy; graduated students called themselves doctor, the learned one [19] . Many avenues were explored in the Renaissance and anatomy of the human body was mapped. Anatomy lead to questions about physiology and blood was found to move in a circle. Medical training became more prevalent and continues today. As researchers have learned more about the human body, they have sought ways to combat the maladies that besiege it.

Early physicians used a variety of ways to give their patients medications. Types of drug delivery are ever-expanding as we grow in knowledge about the human body. There are five basic types of drug delivery system available today. They are outlined in Table 1.

This paper will brief explain the advantages and disadvantages of each, with a focus on transdermal delivery systems.

Table 1 - Types of Drug Delivery

(table available in print form)

For over 4,000 years physicians have treated disease and injury with pills, topical remedies and various other applications [20] . After a description of the circulatory system was explained and accepted, physicians began to inject medicine into the skin. In 1884 the modern hypodermic syringe was developed and intravenous injection was developed. [21] . Intravenous delivery was quick and efficient because drugs did not get filtered through the digestive system. Dose regulation was difficult to determine, however, and it was an uncomfortable procedure that needed a specialist to deliver. The risk of infection was high when the skin was punctured. Intravenous drugs needed to be monitored, this causes inconvenience and discomfort for the patient, physicians sought to control drug delivery in other ways. Topical medication was developed, but it only is effective with certain drugs and specific conditions, Buccal or sublingual medications were found to be very effective, but also limited to certain drugs and specific conditions. Scientist sought systems that controlled drug dosage, were convenient for patient and physician and caused minimal discomfort.

With the development of polymers other system of drug delivery were developed, Polymers are long sequences of molecules of one or more species of atoms or groups of atoms linked to each other to each other by primary, usually covalent bonds [22] . Transdermal drug delivery systems (TDS) were developed that came into direct contact with the stratum corneum and utilize diffusion to get past this layer and dispense their product into the system. There have been several designs of transdermal systems that generally consist of a membrane or reservoir to contain the drug and a means of attachment to the skin. TDS have advantages over oral dosages of medication. The patient doesn't need to remember to take a dose at a certain time, the amount of medication can be regulated and delivery is constant.

There are two types of transdermal systems; matrix and reservoir and two types of matrix systems; monolithic and adhesive [23] . Reservoir systems deliver medication at a more constant rate. They are made of three layers; a non-permeable backing, a drug reservoir and a membrane surface that controls the rate of drug delivery (see Figure A). The matrix systems differ in that the drug in a monolithic system is contained in a rate-controlling matrix as opposed to being in the adhesive layer, both have an impermeable backing (Figures

B & C) [24] . The molecular structure of the drug and the polymer used to house the drug are important. Systems are designed with a particular molecular structure in mind, this helps control the distribution of the drug as it diffuses through the system. Matrix systems have the drug uniformly distributed throughout the layer. This system also must take into account the molecular structure of the drug to insure proper diffusion into the body.

Changes in the environment can affect the polymer. A change in pH causes a swelling in the polymer and release of the drug. A change in ionic strength or the type of chemical present; can be used to change the content in the matrix and allow release of the drug at different rates. [25] Testing for different structure of polymer includes a series of amendments to be sure the system will perform under differing conditions. The design of the transdermal system is fairly simple. However the confidence and efficiency of the system is more complex when considering the intricacies of designing systems that are non-toxic, small, reliable, and do not provoke an immune response.

Transdermal Drug Delivery Systems

Figure A

(image available in print form)

Figure B

(image available in print form)

Figure C

(image available in print form)

Some natural systems release enzymes -- in this case drugs can be released when the enzyme is present it will work on the polymer, causing it to release the drug. Magnetic or electrical fields can be applied to cause swelling in polymer that drugs are encased in and release of medication over time. A change in temperature can have an effect on polymers as seen in ultrasound irradiation where temperature increase causes release of the medicine from the polymer [26] . Not all the research has been done and there are exciting fields opening up in the discovery of how a body will react to certain types of molecules. As we explore these fields we learn more about how our body systems work and we are discovering new ways to target and deliver specific medication to shrink tumors, cure disease, and enhance peoples lives as they age.

The major disadvantage of TDS systems is that is only suitable for drugs of a specific molecular size. As new biomaterials are developed and the ability of materials to biodegrade or change their ability to be absorbed by the body improves, drug delivery systems will change again. Biomaterials have two major advantages over non-biodegradable material; they do not elicit immune response from the organism and some can regenerate healthy tissue [27] . The field of reconstruction of injured, diseased, or aged tissues is a promising field of study.

Scientists have found that drugs encapsulated in microscopic pouches made of layers of phospholipids can 'fool' the body. These are called pouches are called liposomes and are made up of many layers [28] . Liposomes help shield healthy cells from drug toxicity because their phospholipids are identical to those that make up cell membranes. One side of the liposomes is hydrophilic and the outside is hydrophobic. In this way liposome mimic cell membranes and can fuse into the bilayers there by delivering drugs (or genes in the case of gene

therapy) to the inside of the cell or delivery drugs by phagocytosis. Polymer matrices allow bioactive agents to diffuse through the pores of the polymer system and into the target cell area.

The future may show us controlled drug delivery systems that are implanted in the body to deliver drugs at a constant rate to a specific site and may be controlled by the bodies own natural release of enzymes. An increase or decrease in temperature or pH, magnetic, electrical and ultrasound are also being explored to help release medication to a targeted site [29]. Polymers are being developed to work within a persons system to deliver the agents they need. New biomaterials are being tested to possibly line organs, mimic biological systems, and serve as chemical reactors or as medium for cell growth [30]. Aerosol drug delivery is currently being tested; microspheres and other polymers are in clinical trials. Tissues engineering is yet another field that has grown out of a need to deliver remedies to precise locations. The discovery and use of transdermal systems have set biomedical engineers on a path that holds great promise for the future in medicine.

Biomedical engineering and biotechnology are emerging fields. There is much to learn about the human body and the $6 million dollars worth of chemicals it has in various interdependent reactions each second of the day [31]. New careers fields are ever-expanding and discoveries are being made daily. Research in to the biotechnological or biomedical fields will reveal a surprising number of enterprises students can explore. The medical field has branched out past the traditional doctor and nurse, students can explore specializations of the traditional fields that deal with patient care or they can look to the growing field of research and laboratories. Imaging a future where you are scanned, diagnosed, medicated and cured in a matter of minutes. Doctor's roles are changing as the field of biomedical technology is growing. Student research into this subject for possible career selection is important to their futures and ours.

Lesson Plans and Methods

This unit will transverse human systems, diffusion of drugs through a system, treatment of disease, new techniques in drug delivery and career paths. The lessons are designed to enhance prior knowledge of human systems, disease and treatment of disease and careers in biomedical technology. Depending on the level of student, this unit will take approximately five weeks to complete. Some activities are intentially left with brief guidelines so as to encourage student inquiry and research. The culminating paper is a short research paper that explores the career of someone in the biomedical engineering field. The project is designed in a student research and exploratory format.

LP 1: Definitions & Review of Human Systems ppt - 2 weeks

> The first week is spent in review of the human body systems and general discussion of disease and how it could affect a human body system. A power point is presented to the class and each system is discussed with the students. Students will review body systems on their own through a webquest and create their own 7-slide power point. After all students review each other's slide. Week 2 - students will view a Teacher demonstration of gel electrophoresis and complete a lab activity showing how fast molecules can move through "holes" in a membrane.

Lab Activity 1 : How particles move (see Appendix A)

LP 2: Review of diffusion; Present definitions and types of Diffusion - 1 week

Teacher lecture and discussion : Introduction; Drug delivery systems
Student Research: How medication is given, how molecules travel
Demonstrations; air freshener; potassium permaganate in 3 temp of water; grow a sponge animal

Lab Activity 2: Diffusion and Transdermal Patches

LP 3: Review of osmosis; Comparison of drug delivery systems- 1 week

Teacher lecture & discussion: Hydophobic vs. hydrophylic; Membranes and Molecules
Student research: Angioplasty

Lab Activity 3 - Drug Delivery inside the heart (see Appendix A)

LP 4: Biomedical Technology; What is it and what does it do? -- 1 week

Lecture & discussion; Biomedical techniques and Drug delivery systems

Student Activity: Web research, citations and presentations

Lab Activity 4 - Webquest in Biotechnology

Diffusion:

Biotechnology: http://www.biotechnologyonline.gov.au/

Biotech regulation :http://www.morst.govt.nz/wayfinder/

LP 5: Careers and Biomedical in Biotechnology engineering -- 1 week

Lecture & discussion; Career choices in Biomedical in Biotechnology engineering

Lab Activity 5 - Careers and Research in Biotechnology and Biomedical Engineering (see Appendix A)

Appendix A- Lab Activities

(Note to Teachers: these activities were formatted for this paper; please copy and reformat with spaces for use with your students; for answers to questions or PPT email karen.beitler new-haven.k12.ct.us and I will send them to you.)

Lab Activity 1 - How particles move

Sand & Sieves and Electrophoresis

Objectives

1. Explain how molecules move through a semi-permeable membrane

2. Define diffusion and osmosis

3. Observe electrophoresis of molecules of different sizes.

Background

Molecules are not all the same size. It is often difficult to envision diffusion and understand electrophoresis because the different size molecules are not visible. This activity will involve a teacher demonstration and a student lab to demonstrate the process of diffusion of molecules.

Electrophoresis is a process that uses electricity to separate different size molecules for identification. A group of proteins in blood plasma are often identified this way in order to diagnose or monitor a variety of serious illnesses. Electrophoresis takes advance of the movement of electrically charged particles under the influence of an electric field. The force on molecules in an electrical field is called the , this force moves at right angles to an electrical field. The process is also used in amplifying and sequencing genes, detecting mutations, detecting infection and drug development.

Initial Observations; (What do I know?)

Prelab Questions (Homework);

Vocabulary: Define electricity, protein, buffer, sieve

Research question: What is electrophoresis and how is it used?

Procedure I: Teacher demonstration

1. Materials; electrophoresis chamber, electrophoresis power supply, pre-made agar gel, buffer solution,

commercial food colors, pipette and tips

2. Make a written record of which sample you will load in each well of the gel. You may find it helpful to load samples in every other well.

3. Place the gel form on a black or dark surface to help you see the wells in the agar. Be

careful not to puncture the bottoms of the wells as you load the samples.

4. Place the gel in the electrophoresis chamber.

5. Make sure that the wells are closest to the negative (black) electrode.

6. Prepare the buffer solution and add it to the chamber.

7. Place the lid on the chamber and connect the electrode leads to the power supply.

8. Connect the black lead to the negative terminal and the red lead to the positive terminal.

9. Turn on the power supply and adjust the voltage to 50-100 volts.

10. Run the gel for 5-10 minutes. Observe the samples separating into different colors.

11. Turn off the power supply, disconnect the electrode leads, and remove the chamber lid.

12. Remove the gel from the electrophoresis chamber and analyze your results.

13. Record and evaluate the results of the electrophoresis.

14. Analyze and write a summative conclusion

Make Some Predictions

1. What will happen when the sand is poured through the sieve?

2. How does pouring sand through a sieve demonstrate how molecules move through a gel?

Procedure II: Student activity

1. Materials; 3 sieves of different size screen, sand, scale and 2 weighing trays.

2. Weigh out 10 grams of sand.

3. Pour the sand through the screen with the largest holes onto a new weighing tray;

weigh and record weight of the sand that went through the screen.

4. Pour the weighed sand through the second screen; collect onto a weighing tray and

weigh the sand that went through and record.

5. Pour the weighed sand through the last screen; onto a clean weighing tray. Weigh and

record.

6. Analyze data and make a summative conclusion; relate your activity to the teacher demonstration.

Questions:

1. What does each of the following represent in this experiment?

a. the sand represents _____ because _____.

b. the screen represents _____because _____

2. What happens to the sand as it passed through the screens?

3. How is this procedure similar to electrophoresis? How is it different?

Date Table 1_____

(table available in print form)

Post Lab Analysis

1. Based on your observations of the teacher demonstration, what happened to the dyes?

placed in the wells at the positive (red) end of the chamber?

2. What forces helped the dyes to move?

3. Why did some colors move farther towards the positive pole than others??

4. Describe how gel electrophoresis could be useful in police work.

Lab Activity 2 Diffusion and Transdermal Patches

Diffusion of Medication

Objectives

1. Explain facilitated diffusion of a substance across a semi permeable membrane

(potato)

2. Use indicators to determine the presence of a substance

3. Observe equilibrium

4. Show how medication travels through cell

Initial Observations ;(What do I know?)

Prelab Questions (homework);

1. Define facilitated diffusion, equilibrium and indicator.

2. What happens when iodine comes in contact with starch?

Procedure

1. Materials; evaporating dish, Petri dish or small beaker, forceps, slice of potato, paper towel, Lydol's iodine solution, eyedropper, 50% Vitamin C solution, adhesive bandage, small knife, stop watch or clock, clear ruler

2. Read all lab procedures.

3. Use forceps to put the potato slice into the evaporating dish, pat dry with a paper towel if it has been soaking in water

4. Use the knife to make small cut in the potato.

5. Using an eyedropper to place one drop of iodine in the center of the cut, measure the size of the drop immediately, note any color change, and start a timer.

6. While you are waiting, answer the lab questions

7. Make observations at 5, 10, and 15 minutes; measure the size of the drop and examine all sides of the potato each time using the forceps to turn it.

8. Record observations in the data table

9. After fifteen minutes, use the forceps to add 3 drops of Vitamin C solution to the adhesive bandage. Place the bandage over the cut.

8. Make observations as before at 5, 10, and 15 minutes: record size of color change circle

9. Set the potato in a safe place for 24 hours.

10. Make a final observation and record

Make Some Predictions

1. Are the potato cells permeable to iodine? How do you know?

2. What do potato cells contain? How does the iodine help you show this?

3. What do you think will happen with the size of the drop of iodine as time goes by?

4. What will happen to the iodine when the Vitamin C is added?

5. If the iodine was a germ that attacked starch cells; predict what the Vitamin C would do.

Questions:

1. Define diffusion:

2. Define equilibrium

3. Molecules tend to move from areas of _____ concentration to areas of _____

concentration. What is the main difference between osmosis and diffusion?

4. Why is iodine called an indicator? What color is iodine? What does it indicate?

5. When the iodine is dropped on the potato what color is it? Does it change color? Why?

6. What does each of the following represent in this experiment?

a. the potato represents _____ because
_____.

b. the iodine represents _____because

_____.

c. the Vitamin C represents _____because

_____.

7. What happens to the iodine when the Vitamin C solution is placed on it?

Data Table_____

(table available in print form)

Observation after 24 hours:

Post Lab Analysis

1. Based on your observations, which substance moved, the iodine or the starch?
2. How did you determine this?
3. The potato slice was permeable to which substance?
4. What happened when the Vitamin C solution was placed on the iodine/starch complex?
5. Sketch potato, bandage with Vitamin C solution tablet below in the space below. Use arrows to illustrate how diffusion occurred in this lab.
6. Describe a scenario where germs enter the skin through a break in it. What happens when the medicine is delivered to the site?

Lab Activity 3 - Drug Delivery inside the heart

Delivering drugs with a stent

Objectives

1. Define percutaneous coronary intervention

2. Describe the mechanism of a heart attack

3. Demonstrate insertion of a catheter, stent and angioplasty balloon

4. Observe expansion of a stent

5. Explain how drug-eluting stents can be used deliver medication

Background observations

Advances in the field of biomedical technology have led to better treatment for patients with blocked arteries. In the last activity you saw how medication can be delivered by applying it to the skin it travels into the body. In the event of a heart attack, where a blockage is the cause, the goal is to restore blood flow to the heart muscle in as little time as possible. In the past few years there have been dramatic advances in the techniques and devices used open an artery. This simple lab simulation will help demonstrate the overall procedure in "balloon" surgery.

What is a heart attack? The medical term for heart attack is myocardial infarction; a heart attack is when the blood supply to the muscle in the heart is restricted or stopped. This happens when an artery leading to the heart (coronary artery) is blocked. The blockage is often caused by a build up of a fat-like substance called plaque. The process of plaque build up is called atherosclerosis and is caused by layers of fat, cholesterol, calcium, and other substances found in the blood lining the arteries. As it grows, the buildup of plaque narrows the inside of the artery and, in time, may restrict blood flow. Plaque deposits can burst, rupture, or block an artery- this leads to a heart attack. If the supply of blood to the heart is cut off for more than a few minutes, heart muscle will have permanent damage; this can disable or even kill someone.

When a surgeon makes a recommendation for a patient to have a percutaneous coronary intervention he is basically saying that a catheter (a thin, soft, flexible tube that can expand and will allow things to go through without damage to the insertion point) will be inserted into an artery of the body, usually near the heart. Depending on the severity of the blockage the catheter may deliver a wire mesh sleeve, called a stent, which would be left in place to hold the artery open, and the stent may also be coated with plaque dissolving drugs. What the catheter does deliver is a balloon which can be slowly inflated to unblock the artery and restore blood flow. A polymer infused with medication is 'painted' onto the stent. The medication is slowly released into the artery delivering plaque-dissolving medication as the polymer itself is broken down by the body's natural processes.

Initial observations; (What do I know?)

Pre-lab Questions (homework)

1. What is a heart attack?

2. What causes arthrosclerosis?

3. How does plaque cause a blockage?

4. What is a catheter?

5. How does a stent help in an angioplasty

6. What are ways of dissolving plaque inside an artery?

Procedure:

1. Materials; 8x11 sheet of paper, tape, snack bag with ends cut off, straw, small balloon, soft measuring tape, tissue paper or scraps

2. Cut a strip of paper 14 cm x 28cm.

3. Fold the paper 1 cm along the 14 cm end, crease. Turn the paper over and fold it back 1 cm.

4. Continue to fold in this manner until you have folded and creased the whole length.

5. Tape one end of the folder "fan" to the other along the entire length so that you have a folded cylinder. Measure the circumference of the folded cylinder; record.

6. Set this aside and stretch your balloon, blow air into it a few times to be sure it will expand.

7. Cut the ends off the sides of a small snack baggie and 'clog' the 'artery' with two or three 5 cm squares of tissue or scrap paper. Measure the circumference of your artery.

8. Insert a straw half way into a balloon, seal with a small piece of tape. Measure the circumference of the straw; record.

9. Make a prediction about what you think will happen when your balloon and stent are inserted into your 'artery'...

10. Carefully insert the straw, balloon side first, into the paper cylinder about one half the ways. Measure the circumference of the paper cylinder with the balloon inserted.

11. Slowly slide the paper cylinder with a balloon and straw inside the plastic bag.

12. Holding the bag in your hand, slowly blow into the straw to inflate the balloon.

13. Observe how the paper cylinder expands. Measure the circumference of the plastic bag with the paper cylinder inflated; record.

14. Remove the straw/balloon; Measure the circumference of the plastic bag; record.

15. Describe the procedure you have just demonstrated in a 200-400 word essays, using the new medical terms you have learned. Include answers to the questions below.

Questions:

1. What is a percutaneous coronary intervention?

2. What is a heart attack?

3. How do doctors try to prevent heart damage in the event of a blocked artery?

4. Describe the balloon angioplasty procedure

5. What does each of the following represent in this experiment?

a. the folded paper cylinder represents _____ because

_____ .

b. the balloon represents _____because

_____.

c. the straw represents _____because

_____.

d. the plastic bag represents _____because

_____.

6. How does this simple activity demonstrate the angioplasty procedure performed when an artery is blocked?

Lab Activity 5 - Career Path Research

Career path research- library & web research; presentation

Careers in Biotechnology-- student questions

1. What is biotechnology?

2. What are some possible careers in biotechnology? - Choose one for research

3. What is a (your choice)?

4. What are some of the specialty things this person does?

5. Where do these people work?

6. What does the future demand look like for this type of career?

7. How should I prepare for a career in (your choice)?

8. How do I select a biomedical engineering academic program?

9. What is the difference between the various degrees offered in this field?

10. What are some little known facts about your choice of field?

11. Helpful resources (minimum 3)

1. *Careers in Biomedical Engineering* found at http://www.bmes.org/careers.asp
2. http://www.competitionmaster.com/pages/career/careers_in_biotechnology.html
3. http://www.biotechnologyonline.gov.au/
4. http://www.morst.govt.nz/wayfinder/

Appendix B

National Science Standards 9-12

UCP 1: Systems, order, and organization

UCP 3: Change, constancy, and measurement

UCP 5: Form and function

SAI 1: Abilities necessary to do scientific inquiry

SAI 2: Understandings about scientific inquiry

ST 1: Abilities of technological design

ST 2: Understandings about science and technology

SPSP 6: Science and technology in local, national, and global challenges

HNS 1: Science as a human endeavor

HNS 2: Nature of scientific knowledge

HNS 3: Historical perspectives

LS 4a: The atoms and molecules on Earth cycle among the living and nonliving components of the biosphere

LS 5f: Matter and energy flow through different levels of organization of living systems and between living systems.

PS 2: Structure and properties of matter

PS 3: Chemical reactions

PS 6: Interactions of energy and matter

ST 2: Understandings about science and technology

Appendix C

Resources for Students

1. Campbell, N.A. & Reese.J. (2004). *Biology* . New York. Pearson-Benjamin Cummings 7th ed. P. 835-839
2. Alcamo. E. I. et al...(2002). *Modern Biology* .Texas Holt, Rhinehart & Winston. p. 922
3. Starr, C. & Taggart, R. (1994). Biology;The Unity and diversity of Life. New York. Wadsworth. 7th ed. p. 549, 634
4. Biomedical Engineering Society (1999) *Careers in Biomedical Engineering* retrieved June 15 from http://www.bmes.org/careers.asp
5. Valentinuzzi ME. (2004). pg. 396
6. Marconi,(2000). Power through our Human Systems http://cte.jhu.edu/techacademy/web/2000/marconi/hottopic.html
7. The American Heritage® Dictionary of the English Language, Fourth Edition. 2000 The Houghton Mifflin Company. http://www.bartleby.com/61/58/P0355800.html

Appendix D

Resources for Teachers

1. Alcamo. Edward I. et al...(2002). *Modern Biology* Austin,Texas Holt, Rhinehart & Winston

2. Campbell, Neil A. & Reese. (2004) *Biology* , Pearson-Benjamin Cummings 7th edition 835-39

3. Fore-Plifger, J. (2004) Epidermal Skin Barrier: Implications for the Wound Care Practitioner, Part I. *The* . Retrieved June 19, 2006

from http://www.findarticles.com/p/articles/mi_qa3977/is_200410/ai_n9461227.

4. Marconi, G.M.(2002). Power through our Human Systems . Retrieved May 28,2006 from http://cte.jhu.edu/techacademy/web/2000/marconi/hottopic.html.

5. Wood, L.C. Jackson, S. M. Elias, P. M. Grunfeld, C. & Feingold, K. R. (1992). Cutaneous barrier perturbation stimulates cytokine production in the epidermis of mice. . *Journal of Clinical Invest* ing *90* (2): 482-487.

Notes

---

1. Watson 1997

2. Sommers-Nielson 2004

3. Violas 1995

4. Alamo 2002

5. McCandless 1997

6. Ophardt 2003

7. Campbell 2004

8. Campbell 2004

9. Campbell 2004

10. Lefers 2004

11. Campbell 2004

12. Campbell 2004

13. Alcamo 2002

14. Campbell 2004

15. Maged 1998

16. Maged 1998

17. Maged 1998

18. Carr 2003

19. Carr 2003

20. Saltzman 2006

21. Saltzman 2006

22. Young 2002

23. Sommers-Nielson 2004

24. Sommers-Nielson 2004

25. Sommers-Nielson 2004

26. Brannon-Pappas1997

27. Chu, 2003

28. Brannon-Pappas1997

29. Brannon-Pappas1997

30. Brannon-Pappas1997

31. Saltzman 2006

Bibliography

1. Alcamo. E. I. et al...(2002). *Modern Biology* .Texas Holt, Rhinehart & Winston.

2. Biomedical Engineering Society. (1999) *Careers in Biomedical Engineering.* Retrieved June 15, 2006 from http://www.bmes.org/careers.asp.

3. Brannon-Pappas, L. (1997). Biomaterials, *Medical Plastics and Biomaterials Magazine.* Retrieved June 27, 2006 from http://www.devicelink.com/mpb/archive/97/11/003.html.

4. Campbell, N.A. & Reese.J. (2004). *Biology* . New York. Pearson-Benjamin Cummings 7th ed.

5. Carr, Dr. I. (2002). The Far Beginnings- a brief history of medicine. *Hippocrates on the Web.* retrieved June 26, 2006 at http://umanitoba.ca/faculties/medicine/history/histories/briefhis.html

6. Chu, C. (2004). Biodegradable polymeric Biomaterials: An Updated Over view. In Park, J. & Bronzino. (Eds.), *Biomaterials; Principals and Application.* Washington D.C., CRC Press.

7. Cullen T.V. Advances in drug delivery systems. *Modern Drug Discovery.* Retrieved June 27, 2006 from http://pubs.acs.org/subscribe/journals/mdd/v04/i04/html/MDD04FeatureVogelson.html.

8. Elias, P.M., Menon, G.K. (1991). Structural and lipid biochemical correlates of the epidermal permeability barrier. Advances in Lipid Research. 24:1-26, 1991.

9. . . ., . & . (1997).Aspects on the physiology of human skin: studies using particle probe analysis. *38* (4):373-86. Retrieved June 26, 2006 at http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9297687&dopt.

10. Henry,C.M. (2002). Drug Delivery *Chemical & Engineering News 80* (34). 39-47. Retrieved June 27, 2006 from http://pubs.acs.org/cen/coverstory/8034/8034drugdelivery.html.

11. Higdon, J. PhD. (2003). Iodine. *The Linus Pauling Institute.* Retrieved May 15, 2006 from http://lpi.oregonstate.edu/infocenter/minerals/iodine/.

12. . (1994).Understanding transdermal medication. *Professional Nurse 10* (2), 121-5.

13. Kennish, L. & Reidenberg, B. (2005). .A review of the effect of occlusive dressings on lamellar bodies in the stratum corneum and relevance to transdermal absorption. *Dermatology Online Journal* 11 (3) 7. Retrieved May2006 from http://dermatology.cdlib.org/113/reviews/lamellar/reidenberg.html.

14. Hachem, J.P. Crumrine, D. Fluhr, J. Brown, B.E. Feingold, K.R. Elias, P.M.(2003). pH directly regulates epidermal permeability barrier homeostasis, and stratum corneum integrity/cohesion. *J Invest Dermatol 121* 345-53. Retrieved May 26 from http://www.3m.com/us/healthcare/manufacturers/dds/jhtml/patch_anatomy.jhtml

15. Lefers,M. (2004). *Life Science Dictionary.* retrieved July 15, 2006 from www.biochem.northwestern.edu/holmgren/Glossary/Definitions/Def-O/osmosis.html

16. Loth H. (1989). Skin permeability, Methods & Findings in Experimental & Clinical Pharmacology. 11(3):155-64.

17. Maged N. K. M.D. (1998),. Cutaneous Sensory System. *The Electronic Textbook of Dermatology* . Retrieved June 13, 2006 from http://www.telemedicine.org/anatomy.htm#physiology.

18. McCandless, John R, Jr. *(1997)* Diffusion, Osmosis and Cell membranes retrieved May 20, 2006 from http://biology.arizona.edu/sciconn/lessons/mccandless/default.html.

19. National Research Council. (1986). National Science Standards. Washington D.C. National Academy Press.

20. Watson, Dr J. (1997). NIH Working definition of Bioengineering. *National Institutes of Health Bioengineering Consortium.* Retrieved June 20, 2006 from www.becon2.nih.gov/bioengineering_definition.htm.

21. Ophardt, C. E. (2003), . *Virtual Chembook* . Retrieved May 2006 from http://www.elmhurst.edu/~chm/vchembook/548starchiodine.html.

22. Saltzman, W. M. & Tran, V. (2006). BiomolecularEngineering and Biotechnology, *Biomedical Engineering: Bridging medicine and technology*.

23. Schultz, S.G. (1998), .A century of (epithelial) transport physiology: from vitalism to molecular cloning. *American Journal of Physiology and Cell Physiology 274* , (1), C13-C23. Retrieved June 21, 2006 from http://ajpcell.physiology.org/cgi/content/full/274/1/C13?maxtoshow=&HITS=10&hits=10&RESULTFORMAT=1&andorexacttitle=and&andorexacttitleabs=and&fulltext=solutes+and+human+skin&andorexactfulltext=and&searchid=1&FIRSTINDEX=50&sortspec=relevance&resourcetype=HWCIT.

24. Sommers-Nielson. (2004). The Sticking Points of Transdermal Systems . *The DUR Discovery* . Retrieved June 30, 2006 from http://idahodur.isu.edu/newsletter/Winter2006.pdf.

25. Starr, C. & Taggart, R. (1994). Biology;The Unity and diversity of Life. New York. Wadsworth. 7th ed.

26. Tomassen, Dr. S.F.B. (2005).Uptake, secretion of water by the plasma membrane of animal and human cells. . Retrieved June 20, 2006, from http://www.medicalnewstoday.com/medicalnews.php?newsid=30690.

27. Tortora, G.J. & Grabowski, S.R. (1993). Principles of Anatomy and Physiology (7th Edition). *HarperCollins College Publisher.* New York. [ISBN0-06-046702-9] Retrieved June 26 2006 at http://www.wildcrafted.com.au/Articles/Anatomy_and_Physiology/The_Skin.html.

28. University of Maryland Medical Center. Anatomy of the Skin. *Dermatology* , Retrieved June 12, 2006 from http://www.umm.edu/dermatology-info/anatomy.htm.

29. Valentinuzzi M.E. (2004). Understanding the Human Machine, a Primer for Bioengineering. Singapore. *World Scientific* . 396.

30. Velosa, A. (1995). Diffusion processes in Molten semiconductors. *NASA* . Retrieved at http://microgravity.grc.nasa.gov/expr3/dpims.htm, June 7, 2006

31. Young, R.J. & Lovell, P.A. *Introduction to Polymers* Second Edition. London. Nelson Thornes, Ltd.