

How to Make People Pill Better

Target Grade: Elementary School

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Site: Thousand Oaks A

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Brief Overview

In this lesson, mentees will be exploring the conditions that influence and affect the design and development of medicine. In the first module, we will introduce the digestive system and the blood-brain barrier, the two primary components involved with the drug ingestion and absorption process. Within this first module, we will then develop that discussion by exploring the challenges presented by the blood-brain barrier in drug absorption as a highly selective semipermeable membrane. Following this, we will then tackle the challenges presented by the digestive system on the chemical level in the second module by considering the consequences of exposure to the acid within the stomach. We will then conclude the lesson in the third module by having our mentees develop their own medicine pills that successfully deliver their contents. After the lesson, the mentees should understand not only the general method by which drugs are transported and processed biologically, but also the biological and chemical factors that influence drug design in order to effectively and efficiently deliver medication.

Teaching Goals

- **Biomedical Engineering:** The intersection of biology, medicine, and engineering.
- **Digestive System:** the system by which ingested food is acted upon by physical and chemical means to provide the body with absorbable nutrients and to excrete waste products.
- **Solubility:** chemical property of how well a solute dissolves in a solvent
- **Engineering Design Process:** An iterative process of trial and error.

Careers and Applications

From pills for colds and flus, to antibiotics in livestock feed, to recreational and therapeutic plants/chemicals, drugs are an inherent and integral component of our everyday lives. The design process by which drugs are developed and produced is a constantly evolving and progressing field as a result of research results that help us better understand how drugs are interpreted and processed by the body.

As we better understand the biology and chemistry behind our bodies as a consequence of improving technology and exploration, we achieve a better understanding of the limitations that affect how drugs are absorbed within our bodies. This encourages new research and developments in drug design as to how we can best address and match these limitations to better improve the efficiency and effectiveness of these drugs, as well as introduce new drugs to take advantage of new methods of drug delivery. The success of drugs thus far, and the developing successes of drugs today are due in large part to a multifaceted effort from a broad range of fields and experts, including biologists, chemists, engineers, and more!

Agenda

- Introduction
- Module 1: We're going on a trip in our favorite blood vessel (20 min)
- Module 2: Protect the Pill! (10 min)
- Module 3: Does Size Matter? (30 min)
- Conclusion

Introduction

To open the lesson, mentors can ask the mentees what is the first thing that comes to mind when you say "medicine" (maybe avoid opening with the word "drug"). Mentees might mention various characteristics regarding being sick or it tasting bad, but ideally someone will mention the word "pill". If not, you can further lead the discussion by asking what different ways they might have taken medicine or have seen medicine take form in. This can be developed by asking some students why they might think drugs come in pill form* rather than another format or method, and what kind of purpose or benefits a pill structure might serve in administering medicine.

The introduction can then transition into the introduction of the first module by exploring the overall biological method by which drugs are both transported and absorbed via first-pass metabolism in the digestive system and the blood-brain barrier in the brain.

*(<https://www.consumerlab.com/answers/are-liquid-vitamins-better-than-pills/liquid-vitamins/>, <https://medicare-europe.co.uk/science-clinical-data/liquids-vs-pills.html>)

Module 1: We're going on a trip in our favorite blood vessel

Introduction

In this module, the mentees will learn about how the medicine they take travel through their body. They will follow the journey of the drug molecules, learn about where they can and cannot go, and how they might be transformed by our digestive system.

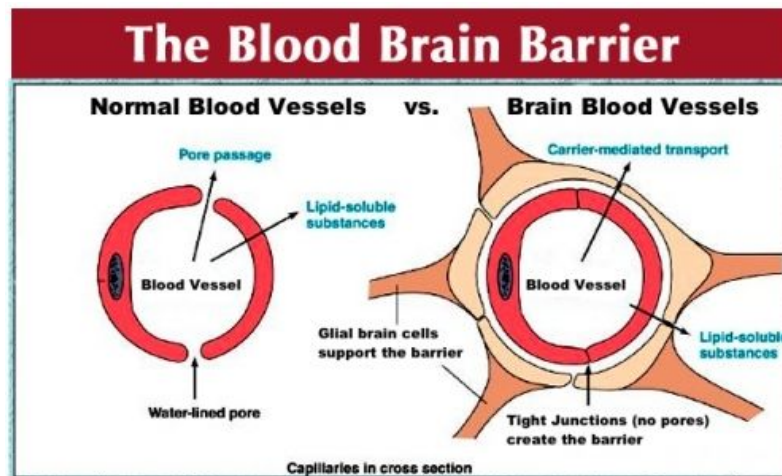
Teaching Goals

1. **First-pass metabolism:** the concentration of the drug is greatly reduced by the digestive system and liver before it circulates the rest of the body
2. **Blood-brain barrier (BBB):** The tight bounding of blood vessel wall cells in the brain acts as a barrier between the bloodstream and extracellular space, allowing only

certain substances to pass through.

Background for Mentors

Drugs taken via the oral-digestive route must go through the gastro-intestinal tract and the liver before being delivered to the rest of the body. Some drugs are partially metabolized in the guts, but most are heavily reduced in concentration by liver metabolism. The liver acts as a filter, where drugs go through potential **biotransformation** and are metabolized by enzymes. As a result, sometimes only a small proportion of the drug reaches the systemic circulation and its target tissue, but this differs in different drugs. The fraction of the drug absorbed into the systemic circulation is its **bioavailability**. The reduction of drug concentration after passing by the gastrointestinal tract and the liver is known as the **first-pass metabolism**.



Regular blood vessels throughout the body have pores that allow substances (such as drug molecules) to pass through to get to the target body part. Cells (endothelial) of the blood vessel wall in the brain are quite different, as they are very tightly bound and have no pores. It acts as a barrier between the bloodstream and the extracellular space in the brain, allowing only certain substances like water and oxygen to pass through, and prevents toxins and pathogens, etc. from crossing from the circulatory system into the brain. This is called the **blood-brain barrier** (BBB). Substances can cross the BBB via transport or diffusion. Smaller, hydrophobic/lipophilic molecules (remember the phospholipid bilayer!) can cross BBB through diffusion, whereas glucose, amino acids, and a few other proteins can be transported via membrane transport proteins. When designing medicines for headache, for example, biomedical engineers need to keep this in mind! For example, ibuprofen, a headache medicine, is lipophilic and can cross the BBB. Additional research paper looking at ibuprofen's ability to cross the BBB: <https://www.ncbi.nlm.nih.gov/m/pubmed/16715377>

Materials

- Coffee grounds (~100g)
- Coffee filter (1 piece)
- A plastic beaker/container ~400mL

Procedure

1. Set up coffee filter on container.

2. Pour coffee with coffee grounds through coffee filter into the container.
3. Emphasize that only the coffee goes through, but the coffee grounds do not.

Additional Notes for Mentors

Tell the mentees that water molecules are small enough to pass through the tiny holes in the coffee filter, but the coffee grounds are too chunky to pass through. This is analogous to the semipermeable membrane, where only certain things can pass through.



Module 2: Protect the Pill!

Introduction

In this demo, we will illustrate the process of pill covering design by designing a pill covering that will protect from the acidic environment of the stomach.

Teaching Goals

1. **Solubility:** chemical property of how well something (a solute) dissolves in something else (solvent).
 - a. **Solute:** substance that dissolves.
 - b. **Solvent:** substance that dissolves solute.
2. The **stomach is acidic/has a low pH** so we need to design pill coverings that can withstand this acidic pH.

Background for Mentors

Once we have medication designed, how do we administer it to the body? Turns out, it's more complicated than we thought! **Biomedical engineers** have to take environmental factors, such as the nature of our different organs, into account when they design pill coverings for medication. Most times, the medicine we receive should be designed to reach the intestines because the intestines have an absorptive surface. However, in order to reach the intestines, the pills must first be able to safely go through the stomach (we'll learn more about the digestive pathway in the following lesson about sugars - another possible connection!).

The active components of a pill are enclosed and protected by the pill capsule. The lining, usually made from gelatin, prevents the pill's dosage from being released before it's supposed to. To achieve this via an orally ingested pill would require some protection that can safely pass through the hydrochloric acid (pH ~3) in our stomachs, but which will dissolve in the basic (pH ~7-9) environment of the small intestine. The stomach has an acidic pH - **acids** can be thought of as just a surplus of positively charged Hydrogen ions (H^+) floating around in water, which subsequently bond to and dismantle some susceptible complex organic structures.

Solubility is the chemical property of how well something (a **solute**) dissolves in something else (a **solvent**). In the stomach the **solvent** is the hydrochloric acid because it is dissolving the **solute**, which is anything that passes through the stomach having a high **solubility**. In our example, the solute is the pill.

In this module, we will be showing the importance of designing a strong pill covering through a demo! We will use skittles to represent the pill, vinegar to represent the acidic nature of the stomach, and make pill coverings out of different materials. We will design different pill coverings, and see how those coverings protect the Skittles from disintegrating into the vinegar solvent. We have five different pill coverings:

1. Paper
2. Scotch Tape
3. Masking Tape
4. Plastic Wrap
5. Cornstarch paste

Materials (per site)

- 1 cup of cornstarch
- 1 pack of skittles
- 6 clear dixie cups
- 1 small piece of paper
- 1 small piece of plastic wrap
- 1 roll of tape
- 1 small bottle of vinegar

Procedure

1. This is a demo led in the front of the room by one mentor. First, introduce the concept that the pH of the stomach is acidic and in order to deliver medicine to our body, our medicine needs to be protected such that it won't degrade in the stomach. Explain that we will be modeling this using skittles (pills) and vinegar (acidic stomach).
 - a. This is a great opportunity to connect this lesson to Week 8's chemistry lesson when we learned about acids and bases?
2. Pour vinegar (half cup full) into 5 cups.
3. Prepare the different pill coverings by wrapping them around the skittle:
 - a. Paper
 - b. Scotch Tape

- c. Masking Tape
 - d. Plastic Wrap
 - e. Cornstarch paste
 - i. Prepare this by mixing two tablespoons of cornstarch with a half cup of water in the last dixie cup.
4. Place the five pills into each of their respective cups and make observations about what's happening: is the color of the skittle coming off and into the vinegar? Is there no observed change? Will some pills lose their "covering" earlier than others?
5. You should expect to see:
- a. Paper - paper will quickly fall off the pill and color will come off of the pill.
 - b. Scotch Tape - most effective solution, pill is protected well and we will see little color loss.
 - c. Masking Tape - pretty effective but not as effective as scotch tape. After 10 minutes, color will fall off.
 - d. Plastic Wrap - Not super effective, color falls off eventually.
 - e. Cornstarch paste - The worst one, cornstarch paste will "pull" the color of the skittle and disintegrate in the vinegar.

Some pictures of what we saw are included below!

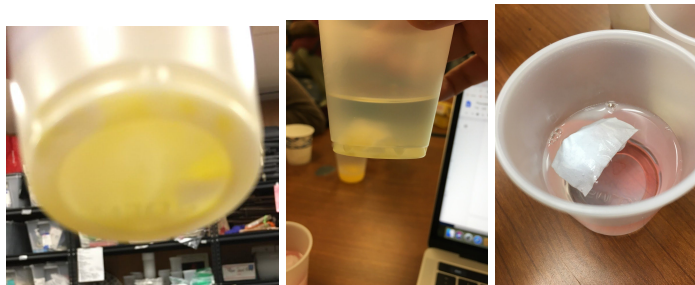


Figure: Picture A: Cornstarch Pill, Picture B: Plastic Wrap Pill, Picture C: Paper Pill

Module 3: Does Size matter?

Introduction

The goal is to introduce students to the field of nanotechnology, especially applications of delivering medicine into your body. Research is being done to put medicine in dna and rna containers to make them small enough so that none of the strong medicine can get out or into the wrong path. The student will try and create a durable box that will not spill its contents while it through a zipline to stimulate durability in small objects

Teaching Goals

1. **Nanotechnology** is a field of technology that deals with very small objects and the size of the object is what helps its purpose
2. **Smaller can be better for several reasons**
 - a. It is more cost effective and sustainable because it uses less materials
 - b. Depending on the material being used it can be sturdier to use smaller pieces.
3. **Engineering Design Process:** An iterative process of trial and error.

Background for Mentors

DNA or deoxyribonucleic acid is a long molecule that contains our unique genetic code. Like a recipe book it holds the instructions for making all the proteins in our bodies. It carries genetic instructions for the development, functioning, growth and reproduction of all known organisms and many viruses. DNA is structured as a double helix, like a twisted ladder. The sides of the ladder are composed of sugar phosphate backbones, while the rungs of the ladder are composed of base pairs. Each base pair is composed of two of four different nucleobases: adenine, thymine, guanine, and cytosine, connected by a hydrogen bond. Adenine is always bonded with thymine, and guanine is always bonded with cytosine, which can be remembered by ATGC.

Nanotechnology broadly refers to the manipulation of matter on the molecular level in scales smaller than 1 micrometre, normally 1 to 100 nanometers, and the fabrication of devices within that size range. It is a highly multidisciplinary field, drawing from fields such as applied physics, materials science, colloidal science, device physics, supramolecular chemistry, and even mechanical and electrical engineering. In the scope of medicine, nanotechnology is being applied to development for diagnostic techniques, antibacterial treatments, wound treatment, cell treatment, and more. In this module, we explore the specifics of nanotechnology applied to drug delivery to specific types of cells (such as cancer cells). These parties are engineered so that they are attracted to diseased cells, which allows direct treatment of those cells. This technique reduces damage to healthy cells in the body and allows for earlier detection of disease.

The **Engineering Design Process** is an iterative process of trial and error. Pretty self-explanatory at this point.

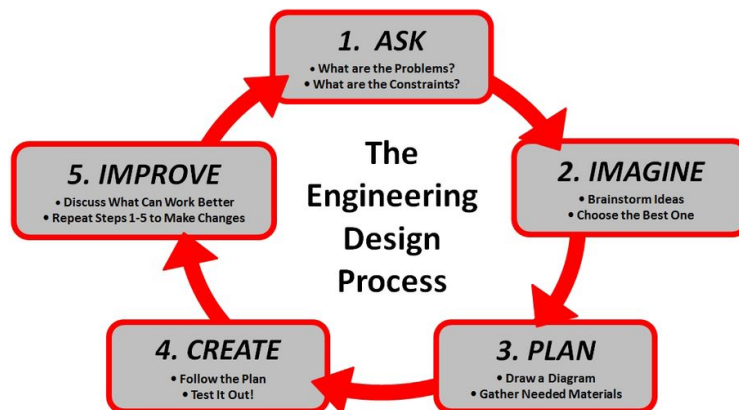


Figure: Engineering Design Process, Mr. Fleming Science.

Materials

- Tape (2 rolls per site)
- Popsicle sticks (50 per site)
- Pipe cleaners (20 per site)
- Rubberbands (20 per site)
- String (zipline) (2 rolls per site)
- Candy (leftover from previous module)

Procedure

1. Have students get into groups of 3-4 per group. Distribute 6 popsicle sticks, 8 straws, 6 pipe cleaners, 6 inches of string, tape.
2. Design a container with any kind of design using popsicle sticks or straws (or some sort of combination) that can go down a zipline without any of the contents spilling or falling out of it. Make sure its a closed container!
 - a. Emphasize that the smaller the box the better
 - b. Also emphasize the engineering design process
3. To make the zipline, attach a string to a wall and the ground such that the angle formed is steep (sample zipline shown in picture below).
4. Make a loop with string, straws, or pipe cleaners on container for zipline to go through.
5. Test each container with 3 pieces of candy and seeing how many pieces fall out. Put loop into zipline and let the container go. There will be one zipline going from wall to wall for groups to test out containers.
6. Tell the kids they can eat the candy if it all makes it to the other end.

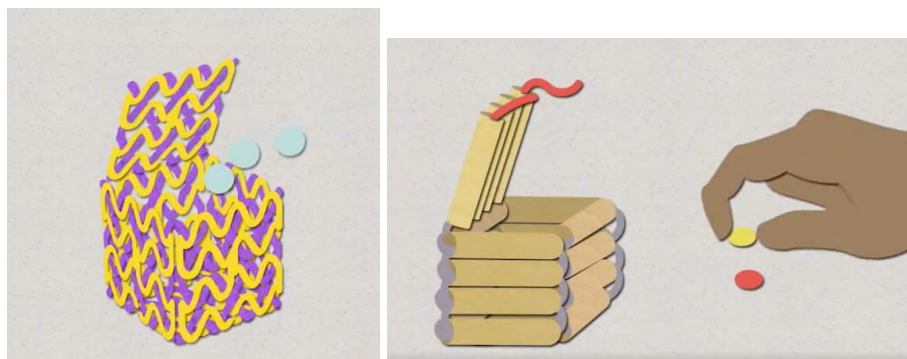


Figure: Sample Box Designs

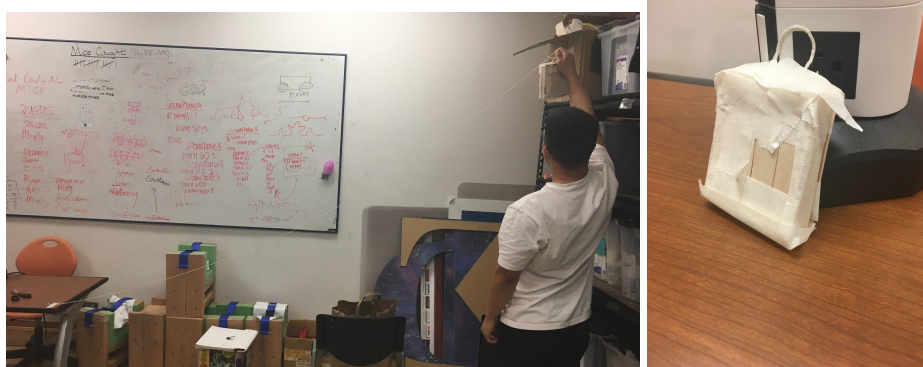


Figure: Sample Zipline (left) and Sample Container (right).

Additional Notes for Mentors

Show some pictures of possible containers to students if they struggle with this activity.

Conclusion

To conclude the lesson, ask students questions about the general structure by which drugs are absorbed by the body. Then extend that into a review of what challenges each component of that structure presents to being able to safely and effectively deliver drugs. Conclude with a final discussion of what we can do to address these issues.

References

- Blood Brain Barrier
 - <https://www.christopherreeve.org/blog/research-news/blood-brain-barrier-the-spinal-cord>
 - <https://home.apu.edu/~skinnest/k12life8-12/dialysis.htm>
 - <https://www.youtube.com/watch?v=e9sN9gOEdG4>
 - <https://www.ncbi.nlm.nih.gov/pubmed/6362950>
- Protect the Pill
 - http://www.crsceience.org/lessonplans/5_Protect_That_Pill_BioE_14-15.pdf
- Build a DNA Inspired Container <https://www.curiositymachine.org/challenges/100/>

Summary Materials Table

Material	Amount per Group	Expected \$\$	Vendor (or online link)
Coffee Filter	1 per class	0	Stephanie has this
Coffee Grounds	1 cup per class	0	Stephanie has this
Large Plastic Cup	1 per class	0	Bechtel
Cornstarch	1 cup per class	0	Bechtel
Skittles	1 pack per class	\$1.50	Walgreens
Dixie Clear Cups	6 per class	0	Bechtel
Paper	1 half piece per class	0	Bechtel
Plastic Wrap	1 small piece per class	0	Bechtel
Tape	3 rolls per site	0	Bechtel
Vinegar	1 small bottle per site	0	Bechtel
Popsicle sticks	50 per site	0	Bechtel
Pipe Cleaners	20 per site	0	Bechtel
Rubberbands	20 per site	0	Bechtel

String	2 rolls per site	0	Bechtel
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