Designing Protective Drug Coatings

Objectives:

This module has been designed to introduce students to the principles of engineering design to formulate solutions for biomedical problems. Students will be introduced with a problem and encouraged to design methodologies or devices to solve it. Specifically, students will learn about the digestive system and the challenges associated with drug delivery. Students will design a drug coating and then test their designs to understand the numerous challenges that biomedical engineers face when designing drug delivery systems.

During this activity and after completion, students should be able to:

- Be aware of the role of engineers in medicine and biology.
- Apply the steps of the Engineering Design Process for solving biomedical problems.
- Describe the engineering design considerations that go into developing drug coatings.
- List characteristics and qualities that are important for a drug coating.

Pre-Activity
(5 mins)
- "Draw an Engineer"
- Pre-test to assess current knowledge on topic

Broad Engineering
(2 mins)
- Introduce engineering and biomaterials
- "Engineers I know"

Topic Research
(5 mins)
- Provide basic understanding of biological system

Define Problem
(2 mins)
- Identify biomedical problem to solve
- Define design constraints

Brainstorm
(5 mins)
- Encourage students to collaboratively brainstorm solutions

Construct a Prototype
(15 mins)
- Build the solution

Test and Assess
(10 mins)
- Students present their designs
- Test device
- Using design constraints, assess the success of the design

Discuss
(3 mins)
- Discuss how to improve devices

Post-Activity
(3 mins)
- Reinforce key concepts
- "Draw an Engineer"

Introduction:

A drug is a specially made medicine that is used to improve your health if you are ever to become sick. Usually your doctor will prescribe you a particular type of drug, depending on the illness or disease that you may have. These drugs can be administered or delivered in many different ways, for example by mouth or injection. Oral administration, or delivery of a drug by the mouth, has its challenges. Sometimes the drugs we want to deliver orally can diffuse away too quickly; that is, the drug may break down into smaller sizes and disperse throughout the body too quickly. This is often a bad thing if you want your drug to stay in the stomach for a period of 10 days which is the typical duration of a stomach ulcer or bacterial infection. If that is

<u>BIOMEDICAL ENGINEERING</u>

The Biomedical Engineer: Pre-test

1. What is Engineering?

2. Do you know any engineers?

3. What is your perception of engineers? What does an engineer look like? Drawings are Encouraged. ☺

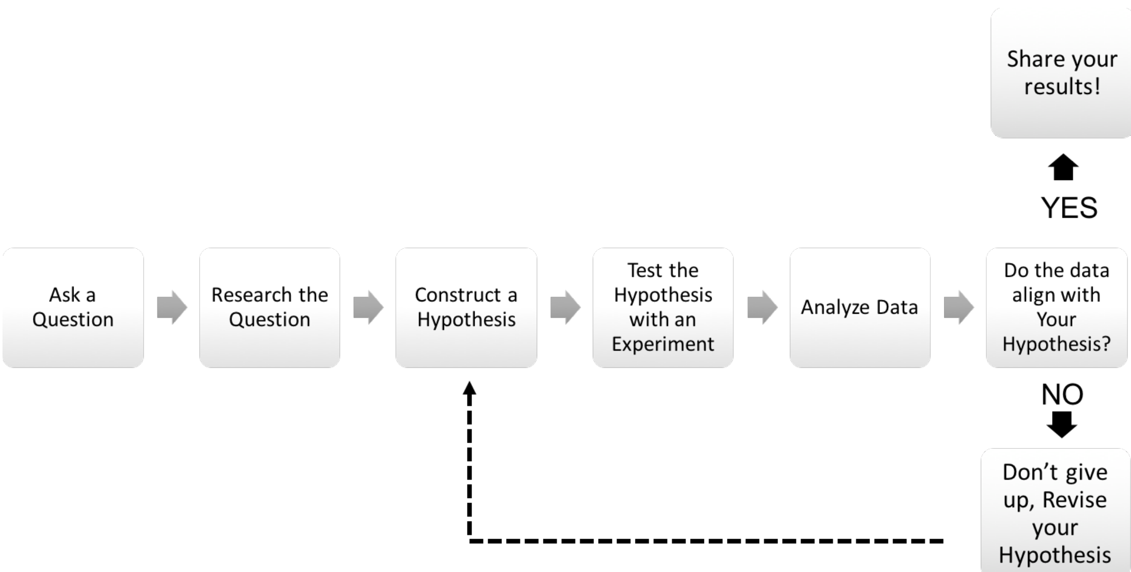
4. Do you know what the engineering method is? If yes, please explain.

Checking your Understanding Questions

5. What is Engineering?

6. What is Biomedical Engineering?

7. How does the scientific method differ from the engineering method?



The Engineering Process

Step one: What is the problem we are trying to solve?

Step Two: Research the problem you are trying to solve.

What are drug coatings and why are they important?

What can drug coatings be made of?

How does the stomach digest food and how do the intestines absorb nutrients?

Step Three: What are the important Design Criteria?

1.

2.

3.

4.

Step Four and Five: Use this space (or the back of this page, if needed) to sketch, list pros and cons, or record notes about your design ideas

Step Six: Test your prototype

Prepare a short presentation (~1 min) that explains how your drug coating and why you chose to build this coating.

Step Seven: Did your coating work? What could you have done differently?

Real Life Solution to Control Drug Release: Enteric Polymer Coatings

1. Why is it important to control the release of a drug?

2. What do hydrophobic and hydrophilic mean?

3. Why use vegetable oil? Sugar? Corn starch or flour?

4. What are enteric polymer coatings?

5. How can drug designers control the release of drugs using polymers?

the case, the drug has high solubility and therefore low efficacy because it is no longer around to do the job it was designed for. Drug delivery can be difficult for this very reason, therefore biomedical engineers who like most other engineers are challenged with developing a solution for a difficult problem. A biomedical engineer who works in the field of drug delivery typically uses various designs of a biomaterial, such as a polymer, before selecting one that can encapsulate or coat an oral drug. There are many criteria for this design process. For example, in order for his/her biomaterial to be safe to swallow, it must not be toxic or too large that it will block any pathways throughout the digestive system. An incredibly helpful tool that all engineers use, including biomedical engineers, is the Engineering Design Process. Furthermore, it is important to a biomedical engineer that they understand human anatomy and physiology, especially if they plan on delivering their prototype drug coating into the sensitive parts of the body such as the stomach or intestines.

Vocabulary

Anatomy: The branch of science concerned with the bodily structure of humans, animals, and other living things.

Biomaterial: Any material that interacts with the body to repair, augment, or replace the bodies' functions.

Biomedical engineer: An occupation that use the principles of math, physics, and chemistry to design instruments and devices to solve clinical problems.

Diffusion: The movement of molecules in a random fashion to create an evenly concentrated environment.

Drug: Therapeutic agent; any substance, other than food, used in the prevention, diagnosis, alleviation, treatment, or cure of disease.

Drug delivery: Engineering systems to help with the delivery of a pharmaceutical agent to a person or animal, to achieve a therapeutic effect. Drug delivery systems help get drugs where they're needed, at the levels needed to have the desired effect.

Efficacy: The capacity for producing a desired result. For example, how much a drug is able to inhibit; if it causes 100% inhibition, it has a high efficacy.

Encapsulation: As refers to pharmaceuticals, a shell-like method of coating drug molecules to enable release at specific times using diffusion.

Engineer: A person who applies understanding of science and math to creating things for the benefit of humanity and our world.

Engineering Design Process: A series of steps that engineers follow to come up with a solution to a problem.

Oral administration: A method of drug administration using the mouth and digestive tract to achieve adsorption into the bloodstream.

Physiology: The branch of science that deals with the normal functions of living organisms and their parts.

Polymer: A chemical compound that is composed of repeating subunits. They can be derived from nature or created in a chemical synthesis lab, and are commonly used in biomaterials engineering.

Prototype: A first attempt or early model of a new product, device or creation.

Solubility: The property of a substance to dissolve into solution.

Toxicity: The degree of harmfulness of a substance to humans.

Materials

This module builds off a previous activity. Please see corresponding worksheets for full explanation of activities. The additional items allow students to select the best materials to solve the problem.

- popsicle sticks
- paper clips
- stapler
- scissors
- straws
- cotton balls
- toothpicks
- liquid glue
- tape

New Required Materials:

- skittles
- Sprite
- corn starch
- flour
- sugar
- oil
- plastic cups
- ziplock bags
- small containers to store the liquids

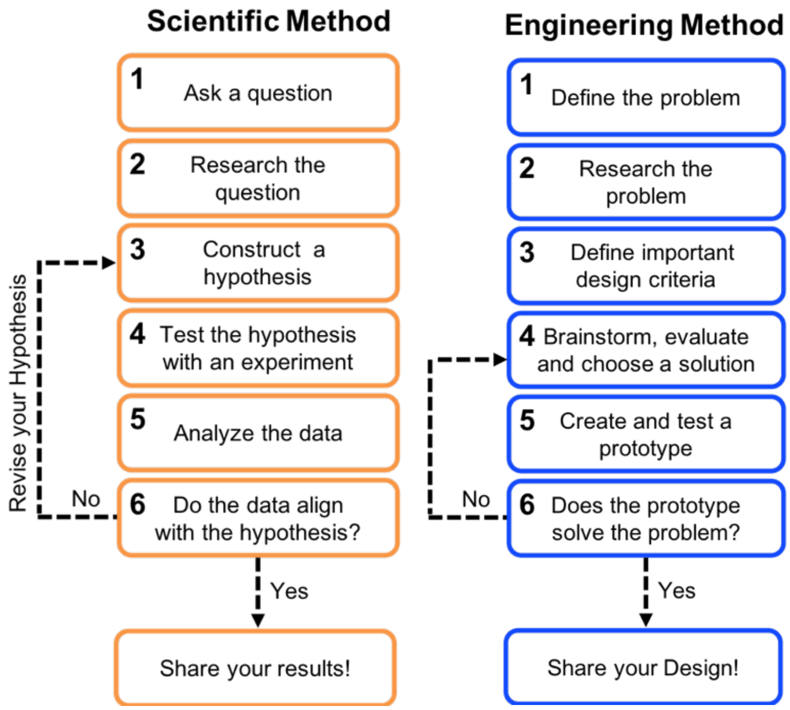
Procedures:

1. **Assess students appreciation for engineers and STEM field prior to hands-on activity**

   Ask students to complete pre-activity, “Draw an Engineer”. After they complete the activity, show students pictures of engineers (collogues, friends etc.) you know that defy stereotypes.

2. **Compare and contrast the scientific method to the engineering method**

As you progress through the module, point out the different steps in the engineering method as you encounter them.



3. **Introduction to Drug delivery and the digestive system.**

   Read the introduction to the class to introduce the topic of drug delivery through the digestive system, drug coating application and the Engineering Design Process, then lead a pre-activity discussion and brainstorming session so students gain a basic understanding of the various oral drug coating requirements and material resources to meet these needs. Be sure to ask the students if they did not understand any vocabulary and, if so, answer with the definition accordingly. Play the following 5 minute video on the digestive system. Intro to the digestive system: https://www.youtube.com/watch?v=VwrsL-ICZYo

4. **Explain the problem**

   Explain how properties of the coating can change how the drug is delivered and how it takes affect on the body. Can a coating be too thick? Will thicker coatings affect how quickly the drug is released? What happens it tastes awful? Do you think different materials will affect how the drug is released (Oil vs sugar)?
   If materials and time permit, show to students an uncoated skittle dissolving in 7up.

5. **Establish Design Constraints**

   Discuss important factors to consider when creating designs. Example design constraints are below.

Design Constraints – Designing a Drug	
Ease and speed of design	Is the coating complicated to make? Does the coating release the drug in an appropriate amount of time?
Patient Compliance	Is the coating too bulky to swallow? Are the size and shape appropriate for human consumption?
Consideration of closed systems	Are the coating or coating by-products appropriate for digestion? Will any components cause GI distress?
Usage of materials	How many supplies are used? Does the amount of supplies complicate or weaken the overall design?

6. **Ask students to design their own drug coating.**

   Explain that the students will design and create their own drug protective coating. They will test their prototypes by placing their drug (skittle candy) with their coating into diet Sprite and watching the reaction. Encourage a short brainstorming session followed by a hands on design session. If you have extra materials/time, allow the students to experiment with different coatings to find a final design. Inform students that they will need to provide a quick explanation about their design to the class.

7. **Evaluate student prototypes based on design constraints**
   Have each student group present their design to the class. If it's appropriate for your classroom, keep score (stopwatch and/or scoring 1-5 of each design criteria.)

8. **Ask students how they would change their designs knowing what they know now.**

   Reinforce that the engineering method is iterative. Start a discussion about which designs worked the best and which designs could have been improved. Remind students that engineering designs usually fail the first time and that it is important to redesign and build from previous design flaws.

9. **Show students real life examples of drug delivery systems.**

   Depending on the age of the students, you can introduce simple coatings such as sugar coatings to more complex polymer coated drugs.

10. **Assess students appreciation for engineers and STEM field after completion of module**

    Ask students to complete the Draw an Engineer Test. The expectation is that after students have been presented with this module they can have a better understanding of what an engineer is.

Conclusions:
At the end of this module, students must:

- Have an improved understanding of the digestive systems and its components
- Be knowledgeable about drug coatings, interactions with stomach, and how different coatings control release.
- Be aware of the role of engineers in medicine and biology
- Design different drug coatings with an understanding of how coatings effect release.

This module was developed for 2016 Biomedical Explorations: Bench to Bedside and adapted for the Society for Biomaterials Education Challenge by:

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Building a Catheter to Remove Plaque Buildup in Arteries

Objectives:

This module has been designed to introduce students with the principles of engineering design to formulate solutions to biomedical problems. Students will be introduced with a problem and encouraged to design methodologies or devices to solve it. Specifically, students will learn about clogged arteries (the problem) and construct catheters to restore blood flow (solution). These activities are best completed by using the corresponding worksheets. Below is an example layout of the module.

Pre-Activity

(5 mins)

- "Draw an Engineer"
- Pre-test to assess current knowledge on topic

Broad Engineering

(2 mins)

- Introduce engineering and biomaterials
- "Engineers I know"

Topic Research

(5 mins)

- Provide basic understanding of biological system

Define Problem

(2 mins)

- Identify biomedical problem to solve
- Define design constraints

Brainstorm

(5 mins)

- Encourage students to collaboratively brainstorm solutions

Construct a Prototype

(15 mins)

- Build the solution

Test and Assess

(10 mins)

- Students present their designs
- Test device
- Using design constraints, assess the success of the design

Discuss

(3 mins)

- Discuss how to improve devices

Post-Activity

(3 mins)

- Reinforce key concepts
- "Draw an Engineer"

Introduction:

The cardiovascular system is composed of the heart and the network of arteries, veins, and capillaries that transport blood throughout the body. The blood carries oxygen and essential nutrients to all of the living cells in the body, and also carries waste products from the tissues to the systems of the body through which they are eliminated.

Arteries are blood vessels that carry blood rich in oxygen throughout your body. They go to your brain as well as to the tips of your toes. Healthy arteries have smooth inner walls and blood flows through them easily. Some people, however, develop clogged arteries. Clogged arteries result from a buildup of a substance called plaque on the inner walls of the arteries. Arterial plaque can reduce blood flow or, in some instances, block it altogether.

Clogged arteries greatly increase the likelihood of heart attack, stroke, and even death. Because of these dangers, engineers have been trying to design methods and instruments to remove the plaque and restore blood flow.

Vocabulary:

Angioplasty: Procedure to restore blood flow through artery. A thin tube with a small balloon on the end is inserted into a blood vessel with an occlusion. When the tube is in place, the balloon is inflated to push the plaque outward against the wall of the artery. This widens the artery and restores blood flow.

Artery: A blood vessel that carries blood high in oxygen content away from the heart and to the tissues.

Biomedical Engineer: biomedical engineers use the principles of math, physics, and chemistry to design instruments, devices, and software to solve clinical problems

Catheter: A medical device in form of a thin tube that can be inserted into a body cavity or vessel to allow drainage or administration of fluids.

Endothelial Cells: A thin layer of cells that line the interior surface of all blood vessels. Endothelial cells play an important role in the transport of oxygen and nutrients to the tissues.

Plaque: Fatty matter, calcium, proteins, and inflammatory cells build up within the arteries to form plaques of different sizes that obstruct the flow of blood

Prototype: A first attempt or early model of a new product, device or creation

Red Blood Cells: A disk-shaped, biconcave cell in the blood that contains hemoglobin and transports oxygen and carbon dioxide to and from the tissues

Vein: A blood vessel that returns blood from the body tissues to the heart

Materials:

For this module, you will need:

- Clear 1.5'' diameter and 1' long tube
- Play dough (two different colors)
- Clown balloons
- Air pump for clown balloons
- Food dye (red)
- Shoe boxes
- Plastic 4 L containers

Disposables:

- Popsicles
- Paper clips
- Stapler
- Scissors
- Straws
- Cotton balls
- Toothpicks
- Tape

Procedures

1. **<u>BEFORE MEETING WITH STUDENTS</u> Build artery prototype:**
   Construct two prototypes, one of a healthy artery and one of a clogged artery. The clear 1.5'' diameter and 1' long tube represents the blood vessel.
   For the healthy artery prototype, cover the internal surface of the tube with a very thin layer of red play dough as shown below in Figure 1. This represents the endothelial cells lining the blood vessels.

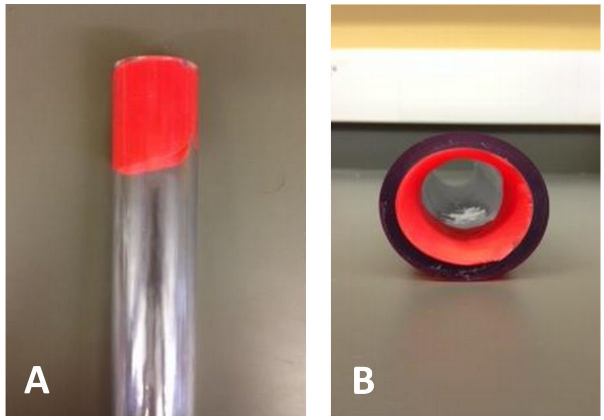


Figure 1: (A) Side and (B) cross-sectional view of a healthy artery prototype

For a clogged artery prototype, cover the endothelial cell layer described above with a thicker layer of yellow play dough (Figure 2). This second layer represents the plaque clogging the artery.

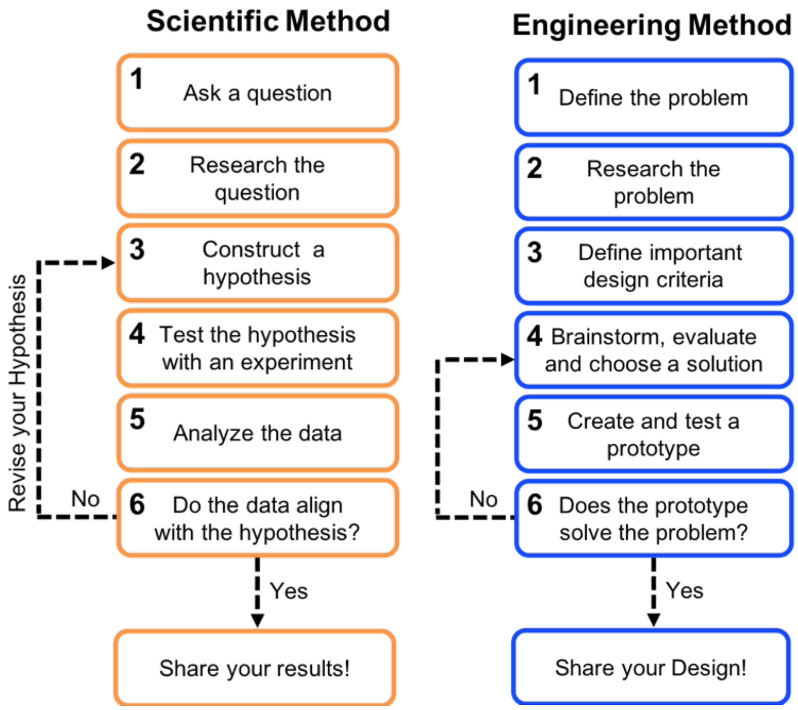
Figure 2: Cross-sectional view of a blocked artery prototype

Ensure that the second play dough layer is thicker than the previous layer so that it obstructs the flow of fluid (i.e. blood) running down the tube (i.e. artery).

2. **Assess students appreciation for engineers and STEM field prior to hands-on activity:** Ask students to complete pre-activity, “Draw an Engineer” After they complete the activity, show students pictures of engineers (collogues, friends etc.) you know that defy stereotypes.

3. **Compare and contrast the scientific method to the engineering method**

As you progress through the module, point out the different steps in the engineering method as you encounter them.



4. **Introduction to circulatory system and components:**
   Play the following 6 minute video to introduce the basic concepts of circulatory system or present students with any other materials that expands their understanding of the circulatory system and its components
   Exploring the Heart- The Circulatory System: https://www.youtube.com/watch?v=-s5iCoCaofc

   Show prototypes of a blocked and healthy artery

5. **Explain the problem:**
   Demonstrate that blocked arteries have different flow than healthy arteries. Allow red colored water to flow down both artery prototypes, healthy and blocked. The healthy artery allows more water to flow through than the blocked artery. Therefore, the nutrients and oxygen carried out by the blood will be able to reach the tissues faster in the healthy artery versus the blocked artery.
   Emphasize the fact that the red layer represents the endothelial cells and the yellow layer represents the plaque. Students need to be aware that a catheter or any other methodology should remove the plaque (yellow) without disturbing the endothelial lining (red) which could lead to further damages and hemorrhages.

6. **Establish design constraints.**
   Discuss important factors to consider when creating designs. Example design constraints are below.

Design Constraints- Clearing a Clog	
Ease and speed of design	How much time does it take to removed a plaque? Is the plaque removed or modified?
Damage to healthy tissues	Does the design minimize the damage to healthy tissue? How much plaque is left behind?
Consideration of closed systems	How would this design work if this wasn't a tube with two openings? Is this design minimally invasive?
Usage of materials	How many supplies are used? Does the amount of supplies complicate or weaken the overall design?

7. **Ask students to build a catheter prototype to remove artery occlusion:**
   Provide students with a clogged artery prototype and a shoe box full of supplies to build a catheter that can remove the plaque in the artery minimizing the damages in the endothelial cells lining the blood vessel. Allow students to work for 20 min in catheter construction. Inform students that they will need to provide a quick explanation about their design to the class.

8. **Evaluate student prototypes based on design constraints**
   Have each student group present their design to the class. If it's appropriate for your classroom, keep score (stopwatch and/or scoring 1-5 of each design criteria.)

9. **Ask students how they would change their designs knowing what they know now.**
   Reinforce that the engineering method is iterative. Start a discussion about which designs worked the best and which designs could have been improved. Remind students that engineering designs usually fail the first time and that it is important to redesign and build from previous design flaws.

10. **Introduce the balloon catheter (angioplasty) to the class and explain advantages over other designs**
    A balloon catheter is a type of "soft" catheter with an inflatable balloon at its tip. Once the catheter has been introduced in the artery, the balloon is inflated to disrupt the plaque and enlarge the narrow opening.

11. **Assess students appreciation for engineers and STEM field after completion of module**
    Ask students to complete the Draw an Engineer Test. The expectation is that after students have been presented with this module they can have a better understanding of what an engineer is

Conclusions:

At the end of this module, students must:

- Have an improved understanding of the circulatory system and its components
- Be knowledgeable about clogged arteries, how these affect blood flow, and the detrimental impact it can have in a person's life
- Be aware of the role of engineers in medicine and biology
- Design solutions to remove plaque in arteries and restore blood flow
- Comprehend function mechanism of balloon catheter or angioplasty

This module was developed for the Society for Biomaterials Education Challenge by:

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This module is supported by: NSF DMR 1455201

<u>BIOMEDICAL ENGINEERING</u>

The Biomedical Engineer: Pre-test

1. What is Engineering?

2. Do you know any engineers?

3. What is your perception of engineers? What does an engineer look like? Drawings are Encouraged. ☺

4. Do you know what the engineering method is? If yes, please explain.

Checking your Understanding Questions

5. What is Engineering?

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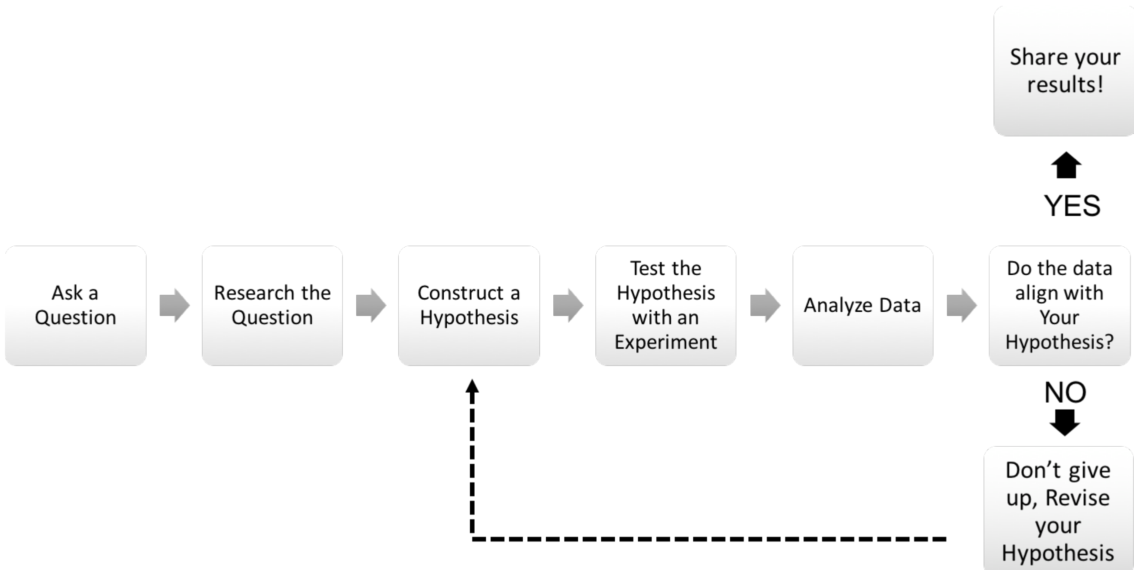
7. How does the scientific method differ from the engineering method?



The Engineering Process

Step one: What is the problem we are trying to solve?

Step Two: Research the problem you are trying to solve**.**

Why does a blocked artery pose a problem?

What are the artery blockages composed of?

Is the circulatory system open or closed?

Step Three: What are the important Design Criteria?

1.

2.

3.

4.

Step Four and Five: Use this space (or the back of this page, if needed) to sketch, list pros and cons, or record notes about your design ideas

Step Six: Test your prototype
Prepare a short presentation (~1 min) that explains how your device works and why you chose to build this design.

Step Seven: Did your device work? What could you have done differently?

Real Life Solution to Blocked Arteries: Angioplasty

1. What is an Angioplasty?

2. What is a Stent?

3. What is a Drug-Eluting Stent?

4. What are surface coatings and why are they important?

5. Why is controlled release an asset for biomedical implants?