Biomaterials for controlled delivery of cells and drugs: the helpful hydrogel

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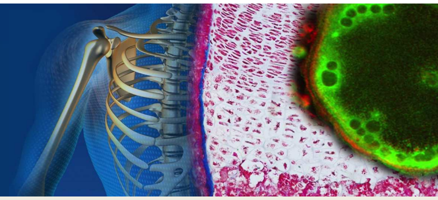

Abstract

Modifying the physical properties of materials for specific applications in tissue engineering is fundamental for biomaterials science. Using gelatin hydrogels as a model system, this educational module will demonstrate how material properties can be tuned to control cell behavior and drug delivery in different tissue environments. The stiffnesses of tissues in the body will be compared (fat, muscle, and bone), and the importance of matching biomaterial and host tissue stiffness will be discussed. Hydrogels of varying stiffnesses will be produced by altering the weight percent of gelatin (Jell-O®) in the hydrogels, and students will discuss which hydrogel is best suited for each tissue environment. The exciting concept of stem cells, their applications in healing tissue, and the role biomaterials play in controlling stem cell behavior to enhance tissue healing will be discussed. In addition to investigating stem cell behavior, students will learn how alterations in hydrogel composition can be used to control the rate of drug release within the body. Students will examine the diffusion of food coloring through hydrogels by varying the weight percent gelatin and understand the relationship between the rate of drug diffusion and hydrogel properties such as mesh size. Finally, students will brainstorm potential applications for the varying drug release profiles observed.

How Stiff am I? Modifying Hydrogel Properties for Tissue Engineering & Stem Cell Delivery

The ability to modify material properties to match specifications is a fundamental concept in biomaterials engineering, tissue engineering, and regenerative medicine. In this section of the educational module, students will compare the stiffnesses of a variety of tissue types by qualitative inspection of chicken bone, muscle, and fat. They will then learn about the importance of matching the properties of the biomaterial to that of the host tissue.

Figure 1: Students from a local elementary school investigate hydrogel material properties in a similar module target at younger audiences.

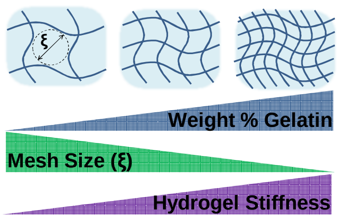

Figure 2: Students will investigate how hydrogel composition can be altered to control resulting material properties such as mesh size and stiffness.

Students will then be introduced to hydrogels, their formation, and network structure. By investigating hydrogels made with varying weight percentages of gelatin (Jell-O®), students will learn how hydrogel mesh sizes and stiffnesses can be tuned for a variety of tissue engineering applications. Students will draw comparisons between the hydrogel and chicken tissue stiffnesses, and determine which gel is best suited for use in each tissue environment.

Required Material	Required Amount	Suggested Source	Cost ($)
Jell-O®, or alternate colored gelatin	3 boxes, in different colors	Grocery store	**2.25**
Measuring cups	1 set	Grocery store	5
Mixing bowls	3	Grocery store	3
Ice cube trays	3	Grocery store	7
Re-sealable containers	3	Grocery store	3
Chicken	1 whole chicken, cut into pieces	Grocery store	**5**
Gloves	1 box	Grocery store	**4**
Background Material	1	Download online	0
Script	1	Download online	0

Table 1: Required materials, sources, and cost estimates for Jell-O® based demo. All amounts and costs are based on a class of 25 students. Classrooms are assumed to have free access to: water, a microwave, refrigerator, printing/copying equipment, standard cutlery, and paper towels. Recurring costs are indicated in bold.

Next, students will learn about stem cells. Self-renewal, differentiation, and potential sources of adult stem cells will be discussed, as will therapeutic applications of these exciting cells. The use of biomaterials such as hydrogels for therapeutic stem cell delivery will be outlined, with a focus on how material stiffness affects stem cell differentiation into different cell types. Students will draw comparisons between the gelatin hydrogels of varying stiffnesses, and hypothesize which gel will cause cells to differentiate down neuro- myo- and osteo- genic lineages.

Students will expand their scientific vocabulary through the discussion of stem cell behavior, and apply their new knowledge as they identify therapeutic applications for each of the gelatin hydrogel investigated.

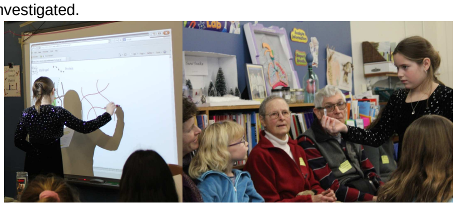

Figure 3: A student teaches parents and classmates about hydrogels after participation in a similar UR-SFB biomaterials education outreach program.

Learning objectives:

- Tissues have varying material properties (stiffnesses) based on their functions
- Matching biomaterial and host tissue properties is a critical design consideration in tissue engineering
- Hydrogels are highly crosslinked, hydrophilic networks
- Hydrogel mesh sizes and stiffnesses can be controlled by varying gel composition
- Stem cells are an exciting, versatile cell type that can be used for a variety of therapeutic applications
- Stem cell behavior (differentiation) can be controlled by altering biomaterial properties
- Biomaterials such as hydrogels can be used to deliver stem cells for therapeutic applications

How Quick am I? Modifying Hydrogel Properties for Controlled Drug Delivery

The ability to modify material properties for controlled drug release is important for medical applications. In this section of the educational module, students will investigate how varying material mesh size can be used to control the diffusion of a model drug (food coloring).

By modifying the weight percentage of gelatin within the hydrogels, mesh size will be varied. Students will then add a model drug to the center of the hydrogel, and investigate the differences in drug diffusion as a result of differences in mesh size. Students will draw connections between the gel properties and rate of drug release, and will apply their knowledge as they identify therapeutic applications for each hydrogel network.

Required Material	Required Amount	Suggested Source	Cost ($)
Clear gelatin, such as Knox®	1	Grocery store	**0.75***
Petri dish or clear flat bottom dish	4	Online	**10**
Food coloring	1	Grocery store	**0.25***
Stopwatch/wristwatch	4	Online	40**
Digital Camera	1, Optional	Online	25
Background Material	1	Download online	0
Script	1	Download online	0
Assessment worksheet	25	Download online	0

Table 2: Required materials, sources, and cost estimates. Classrooms are assumed to have all materials from the "How Stiff am I?" portion of the module. Recurring costs are indicated in bold. *Purchasable volumes contain enough material for multiple module iterations; costs given as per 25 students. **Classroom clock can be used as a cost-saving alternative.

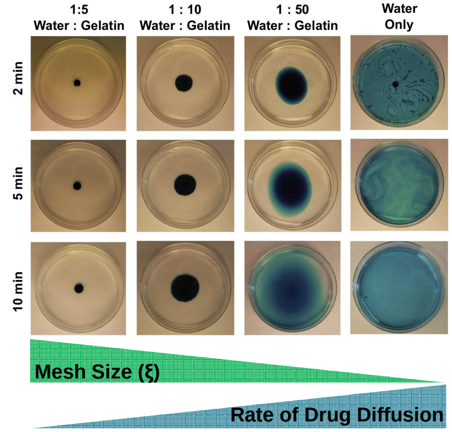

Figure 4: Students will investigate how hydrogel composition (weight percent gelatin) can be altered to control the mesh size of the hydrogel networks, controlling the rate of drug diffusion (blue food coloring) within the biomaterials.

Advanced modification:

Students will take digital images of the drug diffusion at each time point, and use a free analysis program (ImageJ) made available by the National Institute of Health to calculate the food coloring diffusion area for each hydrogel. Students will then plot time versus diffusion area for each of the gelatin molds. By calculating the slope of the best-fit lines, students will determine the diffusivity (in cm^2/s) of food coloring in each hydrogel. The differences in diffusivity can then be compared to the hydrogel composition. This modification also requires students have access to computers equipped with ImageJ and Microsoft Excel (or similar). A cost-saving alternative method includes measuring the diameter and manually calculating and plotting the dye-covered area and best-fit lines using graph paper.

Learning objectives:

- Biomaterials such as hydrogels can be used to deliver drugs
- Diffusion is the process where molecules move from areas of high to low concentration
- Hydrogel mesh size can be used to control the rate of drug diffusion within hydrogels
- Material properties such as mesh size can be altered to control drug release for therapeutic applications
- Collection and graphical representation of data can provide useful insight to the biomaterial system being investigated

Required and Provided Resources

Costs per 25-Student Classroom:

- Setup cost: $20-80
- Recurring cost: $20

Teaching Resources Provided:

- Summary of scientific background
- References to relevant literature for additional background knowledge
- Required materials, suggested sources, and cost estimates
- Cost-saving alternative methods
- Detailed instructions for module preparation and setup
- Detailed script for classroom activities
- Clearly defined learning objectives
- List of relevant scientific vocabulary
- Suggestions for advanced modifications to further enhance student comprehension and involvement
- Post-module assessment worksheet and key

Educational Objectives Achieved

Scientific Vocabulary Learned:

- Biomaterials
- Crosslinking
- Differentiation
- Diffusion
- Drug Delivery
- Hydrogels
- Hydrophilic
- Hydrophobic
- Mesh Size
- Modulus of Elasticity
- Myogenic
- Neural
- Neurogenic
- Osteogenic
- Polymer
- Self-renewal
- Stem Cell
- Tissue Engineering
- Weight Percent

Fundamental Biomaterials Questions Answered:

- What is a biomaterial?
- What is a hydrogel?
- How are hydrogels formed?
- What is diffusion?
- What is a stem cell?
- Why is it important to control the properties of a biomaterial?
- How can biomaterial properties (like stiffness) be controlled?
- How can biomaterials be used with stem cells?
- How can biomaterials be used to control drug delivery?
- How can biomaterial properties be altered to control drug release?
- What is tissue engineering?
- What is regenerative medicine?
- What is drug delivery?

National Science Education Standards for 5-8th Grade Addressed[1]:

- Physical Science: Properties and changes of properties in matter
- Life Science: Structure and function in living systems
- Science and Technology: Abilities of technological design
- Science in Personal and Social Perspectives: Science and technology in society

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References: [1] National Research Council. *National Science Education Standards.* Washington, DC: The National Academies Press, 1996.

Society For Biomaterials