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**9th Grade Biology**

*Jello as a Model of Liver Elasticity*

**Introduction**. *Mechanobiology* is an interdisciplinary field of science that aims to unveil the mechanisms by which cells engage with and depend on their mechanical environment[1]. In live tissue, the *extracellular matrix* (ECM) creates a physical scaffold for tissues and organs while also providing the mechanical cues required by cells to grow, differentiate, and maintain healthy tissue[2]. The ECM of all cells consists of water, polysaccharides, and proteins, though each tissue has unique properties. Across diverse tissues, however, common changes in ECM occur with disease, exacerbating the progression and negative effects of diseases such as aging, chronic inflammation, fibrosis, and cancer.

*Collagen* is the most abundant protein in the ECM, providing elasticity and stiffness, and is conserved among all animals[3]. Healthy tissue function depends on proper collagen content, which mediates a tradeoff between stiffness and flexibility. In response to injury, fibroblasts recruited to the site of injury play a central role in inflammatory response, producing new ECM required for the growth and differentiation of the cells that form new replacement tissues[4]. In the case of chronic injury, chronic inflammation frequently leads to excess fibroblast activity, excessive ECM deposition, and increased tissue stiffness (with loss of flexibility).

*Liver fibrosis* occurs with excessive accumulation of ECM including collagen[5]. Advanced liver fibrosis results in cirrhosis, liver failure, and portal hypertension. The main causes of liver fibrosis in industrialized countries are chronic Hepatitis C infection, alcohol abuse, and nonalcoholic steatohepatitis (non-alcoholic fatty liver). The accumulation of ECM proteins changes the mechanical properties of liver tissue, leading to cellular malfunction and increased resistance to blood flow through the liver.

**Purpose**. Our purpose is to use jello as a model of elasticity and stiffness for both healthy and fibrotic liver. Mechanical properties of liver and jello both depend largely on the presence of collagen. As a result, both are elastic materials whose stiffness depends on collagen content. With this in mind, we aim to:

- *Measure stiffness of EACH of our three liver models*
- *Calculate both stress (related to force) and strain (related to displacement)*
- *Prepare a graph of stress versus strain for EACH liver model*
- *Relate the stress/strain curve of each liver model to liver function and HEALTH*

**Procedure.** You have been given three liver samples (jellos – red, green, and orange). To the best of your ability, determine the following without harming the samples (<u>we will need them for testing!!!</u>)

**1.** Define what it means for a material to be elastic. Then, for each sample, describe elasticity as high or low.

**2.** Rank the samples from most to least stiff.

**Measuring Stiffness.**

**3.** Choose 1 jello sample to begin with. Use your ruler to measure the height of the sample in centimeters and record in **Table 1**, below. Then, place 2 washers on the sample. Under the weight of the washers, the sample will depress slightly. Observe and record the height at the surface of the washer where it meets the sample.

Proceed until all data has been recorded for the jello sample.

At higher weights, the sample may FAIL. Should this occur, simply record the weight at which this happens and proceed to the next jello sample for testing.

**4.** Repeat the procedure above (#3) for each of the other two jello samples, recording data in **Table 1**, below. For AT LEAST ONE of the samples, prior to FAILURE, remove all weight and observe the elasticity of the material as it returns to original height – confirm this by re-performing the ZERO-WASHER height measurement.

**Table 1.** Measurements of Stiffness for 3 jello (liver) samples.

| *Measurements* | | Force (# of washers) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | 0 | 2 | 4 | 6 | 8 | 10 | 12 | 14 | 16 |
| Displacement (cm) | Jello#1 | | | | | | | | | |
| | Jello#2 | | | | | | | | | |
| | Jello#3 | | | | | | | | | |

**Calculating Stress and Strain.** *Stress* is a measure of force applied per unit surface area to a material. *Strain* is a measure of displacement by the material in response to the stress.

**5.** Find the digital class data sheet. Make a personal copy of the sheet named "Jello-based Liver Modeling". Then, enter your data from **Table 1**, above. Values for Tables 2 and 3 will autocalculate, and the graph will autogenerate as well. Save a copy of all three tables and graph in your online folder.

**Plotting Stress versus Strain.** Unique materials have unique stress/strain relationship. The ratio of stress to strain is commonly called *Young's Modulus* and you should think of Young's Modulus as a measure of stiffness for an elastic material.

**6.** Observe the stress versus strain curve for each of the three jello (liver) samples. Consider why one is higher and one is flatter. Also consider the shape of each curve. Do your best to relate each curve to the data you measured and the properties you observed for each sample.

**7.** On the axes below, produce a duplicate of the stress/strain curve found in the datasheet.

**Analysis.**

**8.** Describe the relationship between stress and strain.

**9.** Consider the stiffer sample and the more flexible sample:

a. How does the stress/strain relationship differ between them?

b. How does Young's Modulus differ between them?

**10.** Working with your graph of stress and strain, identify the sample that is most flexible. Then, identify the point at which liver displacement is approximately 25%. Circle this point, and identify strain that produced the 25% displacement for the most flexible sample. **Record here**:______________

**11.** Now, working with the graph, identify the sample that is most stiff. Then, identify the same displacement value, and the corresponding strain required to produce 25% displacement. **Record here:**______________

**12.** Compare the strain required to produce 25% displacement in flexible versus stiff liver samples.

**Conclusion and Extension.** Relating Jello testing to Young's Modulus and Young's Modulus to liver health and disease.

**13.** To the best of your ability, and in your own words, describe/explain the following:

a. Elastic material

b. Stress

c. Strain

d. Young's modulus

**14.** To the best of your ability, and in your own words, do the following:

a. Based on your data, predict which jello (liver) sample had the most collagen. Justify the prediction.

b. Based on your data, identify which sample (color) best matches each jello mix:

| Sample Color | Sample Recipe |
|---|---|
| | 1X collagen |
| | 2X collagen |
| | 4X collagen |

**15.** Review the introduction to create a simple diagram (below) for the chain of events between injury and fibrosis in liver and other flexible tissues.

**16.** Consider the three major causes of liver disease in industrialized nations. Choose one condition and offer a hypothesis for how the cause could lead to a fibrotic outcome.

 

**17.** Brainstorm other body organs or tissues that, similarly to liver, require a tradeoff between stiffness and flexibility. Once you have identified an organ or tissue, research fibrosis in the tissue and read about CAUSES, NEGATIVE HEALTH EFFECTS, AND PREVALENCE of the condition. Record your findings below.

**Citations.**

**References and Further Reading.**


**1.** *What is mechanobiology?*. Center for Engineering MechanoBiology. (2022, September 2). https://cemb.upenn.edu/what-is-mechanobiology/

**2.** Frantz C, Stewart KM, Weaver VM. The extracellular matrix at a glance. J Cell Sci. 2010 Dec 15;123(Pt 24):4195-200. doi: 10.1242/jcs.023820. PMID: 21123617; PMCID: PMC2995612.

**3.** *PDB101: Molecule of the month: Collagen*. RCSB. (n.d.). https://pdb101.rcsb.org/motm/4

**4.** Tracy LE, Minasian RA, Caterson EJ. Extracellular Matrix and Dermal Fibroblast Function in the Healing Wound. Adv Wound Care (New Rochelle). 2016 Mar 1;5(3):119-136. doi: 10.1089/wound.2014.0561. PMID: 26989578; PMCID: PMC4779293.

**5.** Bataller R, Brenner DA. Liver fibrosis. J Clin Invest. 2005 Feb;115(2):209-18. doi: 10.1172/JCI24282. Erratum in: J Clin Invest. 2005 Apr;115(4):1100. PMID: 15690074; PMCID: PMC546435.

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