

Assignment 8: Cell and Tissue Mechanics

EN 585.729 Cell and Tissue Engineering

Problems

1. The Hagen-Poiseuille equation describes flow through a cylindrical tube. We discussed this in the context of blood flow but it is also applicable to respiration where air flows through cylindrical alveoli. Please use this equation to explain why breathing is so difficult for someone suffering from just mild asthma.

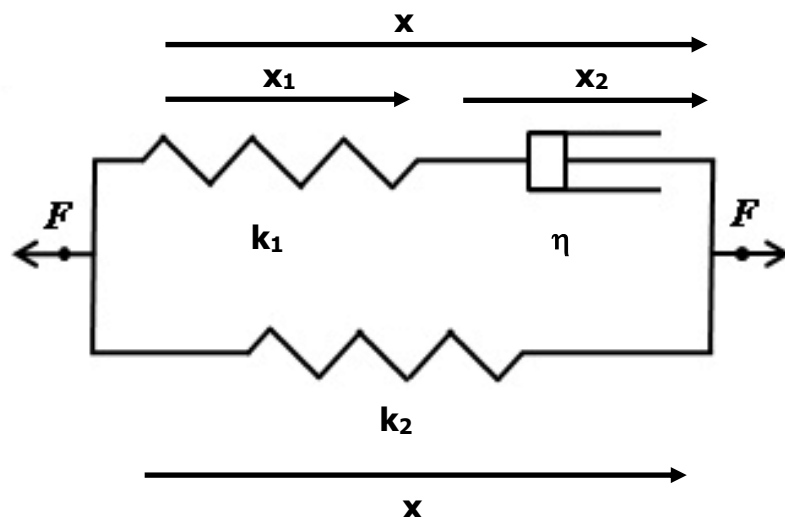
In a person with asthma, the airways (trachea, bronchi, bronchioles) are inflamed with a secretion of excessive thick mucus which lines up these airways. This leads to a decrease of the diameter of these airways available for air flow. In the airways, the flow of air could be considered laminar and incompressible (Reynolds number is 2,084 in the trachea to drop to 0.01 in bronchioles and alveoli [1]). Even if assumptions of the Hagen-Poiseuille equation are not strictly verified for the respiratory tract; it shows that resistance to the air is inversely proportional to fourth power of the radius:

$$R = (8 \times \eta \times L) / (\pi \times R^4)$$

η : viscosity, L: length of the cylinder, R: radius

Therefore a small decrease in the radius of the airways causes a large increase in the airway resistance, decreasing significantly the amount of oxygen a person with asthma can inspire which explains the difficulty of these people to breath during an asthma period.

2. Derive the ordinary differential equation for the Kelvin viscoelastic solid (pictured below). Show **all of your work** (each step!) for full credit.



We have:

$$F_1 = k_1 X_1 = \eta \, dX_2/dt$$

$$F_2 = k_2 X$$

$$F_{\text{tot}} = F_1 + F_2$$

Taking the derivative on both sides

$$dF_{\text{tot}}/dt = dF_1/dt + dF_2/dt$$

$$= k_1 \, dX_1/dt + k_2 \, dx/dt$$

$X = X_1 + X_2$, thus $X_1 = X - X_2$ and $dX_1/dt = dx/dt - dX_2/dt$, substituting in the last equation gives:

$$dF_{\text{tot}}/dt = k_1 (dx/dt - dX_2/dt) + k_2 \, dx/dt$$

$$= (k_1 + k_2) \, dx/dt - k_1 \, dX_2/dt$$

$$\text{From } F_1 = \eta \, dX_2/dt \text{ and } F_{\text{tot}} = F_1 + F_2$$

$$dF_{\text{tot}}/dt = (k_1 + k_2) \, dx/dt - k_1 (F_1/\eta)$$

$$= (k_1 + k_2) \, dx/dt - k_1/\eta (F_{\text{tot}} - F_2)$$

Rearranging the terms:

$$dF_{\text{tot}}/dt + k_1/\eta \, F_{\text{tot}} = (k_1 + k_2) \, dx/dt + k_1/\eta \, F_2$$

$$dF_{\text{tot}}/dt + k_1/\eta \, F_{\text{tot}} = (k_1 + k_2) \, dx/dt + k_1 \, k_2/\eta \, x$$

The final ODE is:

$$\mathbf{F_{\text{tot}} + (\eta/k_1) \, dF_{\text{tot}}/dt = \eta \, (k_1 + k_2)/k_1 \, dx/dt + k_2 \, x}$$

Finally, $2 \, F = F_{\text{tot}}$ and replacing in the previous equation:

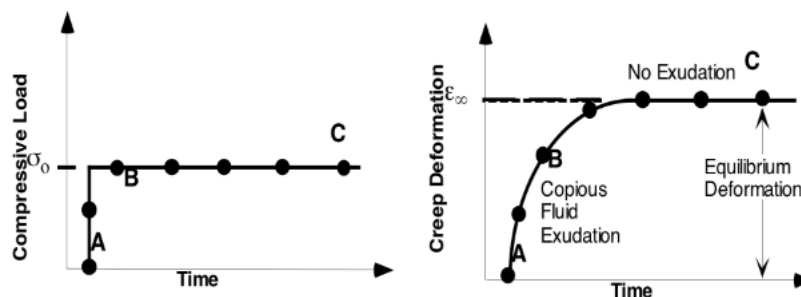
$$\mathbf{F + (\eta/k_1) \, dF/dt = \eta \, (k_1 + k_2)/(2 \, k_1) \, dx/dt + k_2/2 \, x}$$

3. In lecture we discussed the biomechanics of articular cartilage and how important it is for tissue engineers to understand these mechanics in order to design successful tissue substitutes.

- a. Based on the shape of the confined compressive load test on cartilage what type of model would you use to describe it mechanically and why?

The confined compressive load test applies a constant compressed load σ_0 , it's a one-time action which could be represented by the step function shown on the graph on the left. This step function is similar to the load vs. time of the Spring model. Once released, the compressive load applied goes back immediately to 0.

- b. What components (dashpots and springs...) describe the behavior shown below on the right? What phase(s) of cartilage are represented by the component(s)?



The behavior shown on the right is the creep vs. time of the Voigt model. Initially the creep deformation is relatively rapid, and corresponds to a large fluid exudation. This part of the graph characterizes the fluid phase of the cartilage. As the creep deformation slows down and approaches a constant value, the fluid flow slows similarly. At equilibrium, the creep deformation is constant and the fluid flow has stopped; characteristic of the solid phase of the cartilage.

4. Over the last two weeks you've read on the use of microscale topographies (Nikkhah et al. Engineering microtopographies to control the cell-substrate interface). In 300 words or less please explain how microtopographies can be employed in the development of engineered tissues. What tissue properties can they influence? What cell behaviors can they control?

Mechanobiology, through the mechanical cues provided by cell-substratum and cell-cell contacts expressed in the form of shear stress, hydrostatic pressure, stiffness, or

intercellular tugging, affects cellular proliferation, migration, and stem cell differentiation.

Microtopographies have been used to study, understand and recreate these cues:

- Studies have demonstrated that geometries of the microstructures on the substrate like pillars [2], wells [3], pits [4], pyramidal shapes [5], curved surfaces [6]; including height and width can influence cell alignment, their morphologies and polarities [7].
- Cell migration direction and velocity can be regulated by microscale topographies. Average migration speed is higher on microgrooved substrates than on flat surfaces [8,9,10,11]. In vitro, stiffness of the substrate can also guide cell migration (durotaxis) [12].
- Substrates with different patterns have provided physical stimulation for systematic differentiation of stem cells. In a study, neural stem cell (NSCs) cultured on chitosan films differentiated into astrocytes [13].

For neural tissue engineering, combination of uniquely designed micro grooves or pillars with molecules such as laminin [14] or nerve growth factors secreting astrocytes [15], or Schwann cells [16], have induced neurite alignment, extension, growth and differentiation. This research is particularly important for spinal cord injuries (SCIs) therapies to promote nerve regeneration. Multichannel conduits with seeded Schwann cells have mediated greater nerve regeneration and shortened the time for recovery in rats with transected spinal cord or sciatic nerves [17,18].

Engineered cardiac tissue have been able to recreate the anisotropy and mechanical properties of the myocardium; with an increase on cardiomyocytes systolic intracellular Ca^{2+} and slower diastolic rise in calcium [19].

In bone and cartilage tissue engineering, significant progresses have been made. Kirmizidis et al. [20], were able to align osteoblasts by varying the width of the grooves. Critical for cartilage repair, Moutos et al. [21], induced uniform spreading of chondrocytes with rounded morphologies.

Sources:

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