Question 1:

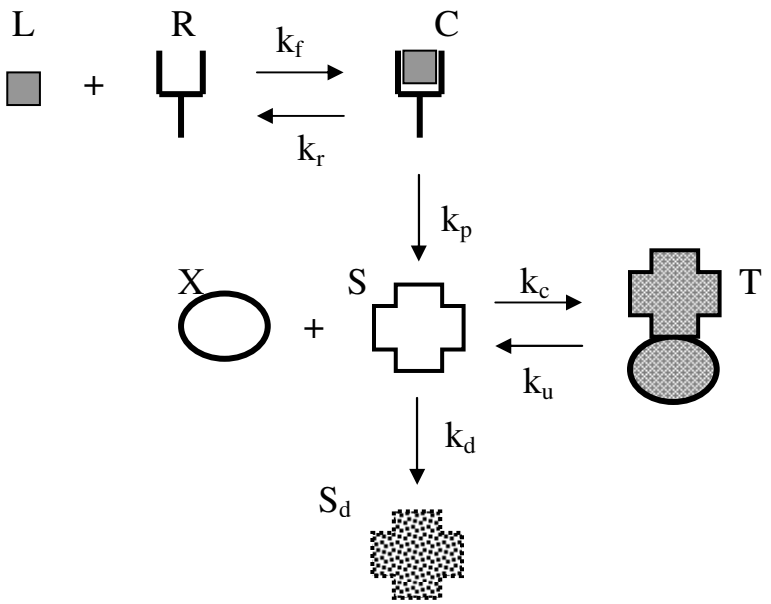
a. Vascular endothelial cells are exposed to laminar flow and the associated shear stress. In responding to this flow environment, the vascular endothelial cells exhibit altered gene expression and secretory characteristics. If one was to develop a mathematical model of this response to flow, how would one go about developing such a model? What would one need to include? What type of experimental data would be needed?

b. In the ascending aorta of a human, what is the shape of the flow waveform? What is the phase relationship between the pressure waveform and the flow waveform? Can there be turbulence in the aorta? If so, under what conditions?

Question 2:

Consider a simple model for LIF-induced stem cell differentiation.

- LIF (L) reversibly binds to its monovalent receptor to form the complex C.
- Formation of C leads to creation of a secondary messenger S at a rate proportional to the concentration of C. No C is consumed in the formation of S.
- S interacts with the inactive transcription factor X to form the active transcription complex T. T translocates to the cell nucleus and activates phenotype-specific gene expression in a fashion linearly proportional to its concentration.
- S degrades to S_d following first order kinetics.



R = number of free receptors
C = number of complexes
L = free LIF ligand concentration
X = number of inactive transcription factor
S = number of second messenger
T = number of active transcription complexes
S_d = concentration of degraded S

R_T = total number of receptors/cell
X_T = total number of effector X/cell

(i) Derive time-dependent governing equations for C, S, and T as a function of R_T, L, X_T, and rate constants. Assume no ligand depletion.

(ii) Obtain expressions for steady state values of C and T as a function of R_T, L, X_T, and rate constants.

Question 3:

In a recent study, Elliot *et al.* (Ann Biomed Eng., 31:599-605, 2003) investigated the effects of various structural modifications on the viscoelastic properties of mouse tail tendon fascicles from normal mice (CTL), decorin knockout mice (DKO), and mice with inhibited transcription (so reduced content) of collagen I (C1M). All samples were examined at 8 weeks of age (CTL8, DKO8, C1M8) and controls were also examined at 3 weeks of age (CTL3). Fascicles were tested in tension with 5 sequential stress relaxation steps (rapid ramp followed by 10 min. relaxation), and data for each sample were fit with Fung's QLV (quasilinear viscoelastic) model.

Note that in the following, stress is defined as the measured force divided by the initial area, while strain is defined as the change in length divided by the original length. Questions on the next page.

Fung's QLV model:

$$\sigma(\varepsilon,t) = G(t)\cdot\sigma^{e}(\varepsilon)$$

$$G(t) = \frac{[1 + C\{E_1(t/\tau_2) + E_1(t/\tau_1)\}]}{[1 + C\ln(\tau_2/\tau_1)]}, \qquad (1)$$

where $E_1(t)$ is

$$E_1(y) = \int_0^{\infty} \frac{e^{-t}}{t} dt. \qquad (2)$$

The elastic stress was defined as

$$\sigma^{e}(\varepsilon) = A(e^{B\varepsilon} - 1). \qquad (3)$$

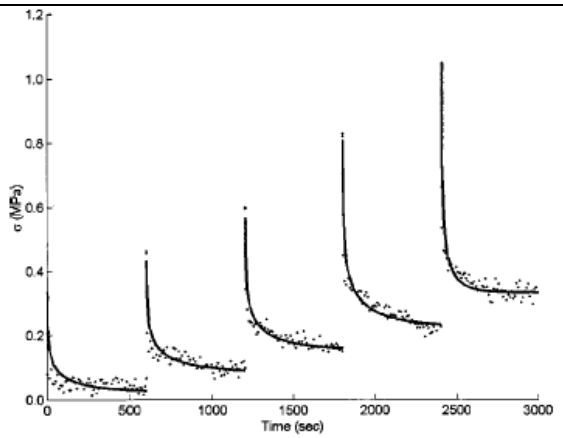


FIGURE 2. Representative stress–relaxation response and QLV curve fit results for five incremental steps of ε=0.005. For this fascicle, average R^2= 0.92.

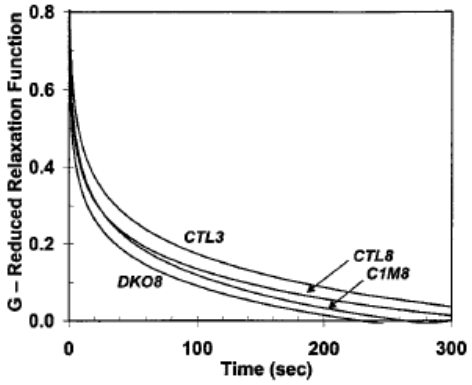


FIGURE 3. Reduced relaxation function [*G*, Eq. (1)] using average QLV parameters for each group.

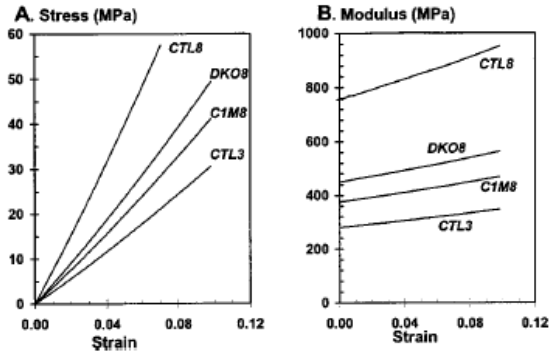


FIGURE 4. Instantaneous elastic response using average QLV parameters for each group.

Question 3 (continued):

a. What is the fundamental assumption underlying the QLV model? How does it differ from linear viscoelastic models and true nonlinear viscoelastic models?

b. What specifically does the term σ^e represent? What do the constants A and B represent (how does each affect the predicted behavior)?

c. What specifically does the reduced relaxation function *G(t)* represent? What do the constants C, τ_1, τ_2 represent (how does each affect the predicted behavior)?

d. The results of the model fits are presented below and in the graphs on the previous page. Using these results, discuss the differences in behavior between the following groups. Discuss both the "elastic" response and the time-dependent response.
   i. CTL3 vs. CTL8 (effect of age in control mice)
   ii. CTL8 vs. C1M8

e. For an instantaneously applied strain, which group would you expect to have the greatest initial stiffness? Which group has the highest equiplibrium (or residual) stiffness?

TABLE 2. QLV parameters for each group: mean±std. dev.

Group	Area (mm^2)	A (MPa)	B	AB (MPa)	C	τ_1 (s)	τ_2 (s)
DKO8 (n=11)	0.0106±0.0024	199±110	2.26±0.58	457±290	2.25±1.11	0.041±0.065	263±98
C1M8 (n=11)	0.0054±0.0024	176±74	2.11±0.66	347±143	2.14±1.63	0.153±0.131	310±47
CTL3 (n=10)	0.0042±0.0018	128±82	2.18±0.84	248±181	1.37±0.53	0.240±0.140	345±108
CTL8 (n=16)	0.0079±0.0020	281±196	3.13±2.57	650±386	1.26±0.53	0.082±0.064	323±71
p value		0.005	0.3	0.006	0.04	<0.0005	0.1
Post hoc comparisons (p<0.05)		CTL8 > C1M8 and CTL3		CTL8 > C1M8 and CTL3	DKO8 > CTL8 and CTL3 C1M8 > CTL8	CTL3 > all others C1M8 > DKO8	CTL3> DKO8 (p=0.1)

Problem 4:

Consider the in-plane (XY) deformation of a thin sheet of skin under loads that you impose in the lab. You mark three points on the surface (A,B,C).

Before deformation, you measure the positions (in mm) of the 3 points as:

A	(10,10)
B	(10,20)
C	(25,20)

After deformation, you measure the new positions as:

A'	(9.9,9.9)
B'	(10.4,20.9)
C'	(26.4,19.7)

a) Find an expression for the local deformation gradient, assuming that out-of-plane deformations are negligible (we will revisit this).

b) Compute the components of the infinitesimal strain tensor and the Green strain tensor.

c) Is a small strain approximation valid here? Why or why not?

d) For an isotropic material, do you expect the XX or YY component of the Kirchoff stress to be greater? Would your answer change for a transversely isotropic material?