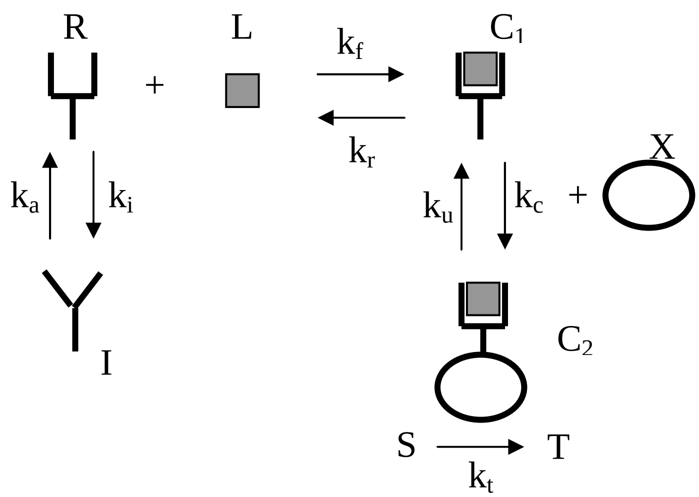
Question 1:

Consider the following model for agonist-induced generation a transcription factor T.

- Receptor for agonist exhibits both inactive (I) and active (R) binding forms.
- Agonist L reversibly binds to its monovalent <u>active</u> receptor to form the complex C_1.
- Complex C_1 associates reversibly with the adaptor protein X to form the complex C_2.
- Complex C_2 catalyses conversion of the substrate S into the transcription factor T.



R = number of free active receptors
I = number of free inactive receptors
L = free ligand concentration
C_1 = number of complexes 1
X = number of free adaptor X
C_2 = number of complexes 2
S = substrate concentration
T = transcription factor concentration

R_T = total number of receptors/cell
X_T = total number of adaptor X/cell
S_T = total concentration of substrate

(i) Derive time-dependent governing equations for R, C_1, C_2, and T as a function of R_T, X_T, S_T, L and rate constants. Assume no ligand depletion.

(ii) Assuming that and $k_a >> k_i$, derive an expression for the rate of accumulation of the total number of occupied receptors.

(iii) Using your answer for (ii), derive an expression for C_2 at <u>steady state</u> knowing that $C_2 = 2C_1$. Plot C_2 vs. L indicating important values/parameters.

Question 2:

Blood flow in the human cardiovascular system is pulsatile and has a characteristic waveform shape.

A. Graph the flow waveforms as a function of time in the ascending aorta, the abdominal aorta, and in the renal artery. Be sure to identify the zero flow point on your graph.

B. Explain the differences in waveform phasic nature in these three arteries in terms of 1-D fluid mechanics or a lumped parameter system.

C. Predict the flow waveform shapes in the brachial artery and common carotid arteries based on your model described in Part B.

D. Describe how these hemodynamic conditions may contribute to the development of atherosclerosis in the human.

Question 3:

You are asked to evaluate the cortical bone phenotype in a mutant mouse model in which the gene for a specific protein known to be present in bone is knocked out. You are given femurs from mutant mice as well as wild-type controls from the same background strain.

A. Describe what kind of mechanical test you would perform on the bones and why? Sketch the corresponding stress distribution on a cross-section of the femoral diaphysis.

B. What assumptions would you make about the material properties of the cortical bone? Show mathematically the form of an appropriate constitutive model.

C. What parameters would you measure from your mechanical test?

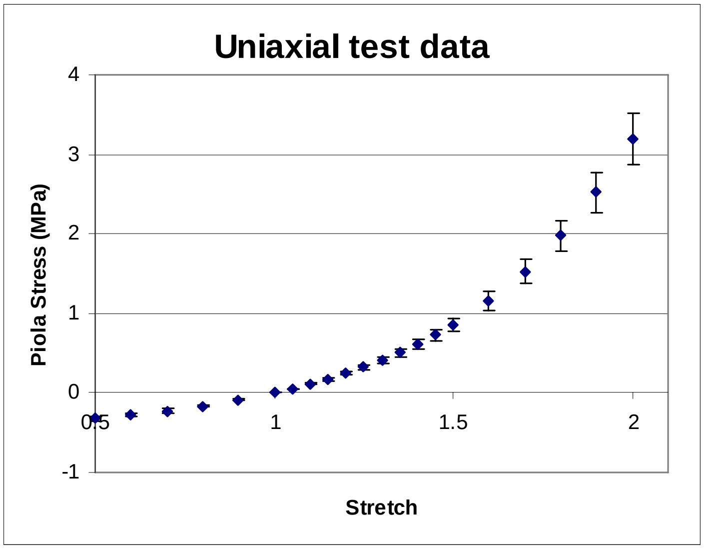
D. Explain how you would determine material properties of the cortical bone.

E. Assuming you find differences in both the structural and material properties, what additional measurements would you make to help explain your results?

F. If you find no differences in either the structural or material properties, what are the possible explanations for this finding?

Problem 4

Consider the experimental data from uniaxial, constant strain rate tests on samples of calf skin. The Piola stress (P) is plotted versus the stretch (λ).



Three strain energy functions have been proposed to describe the 1-D behavior of this tissue:

1. $\rho_o W = A(\lambda - 1)^2$
2. $\rho_o W = B(\lambda - 1)^3$
3. $\rho_o W = C(\lambda - 1)^2 + D(\lambda - 1)^4$

Based on fits only to the data for $1 \le \lambda \le 1.5$, the following best fit parameters were determined

A	B	C	D
0.8 MPa	1.25 MPa	0.6 MPa	0.6 MPa

a) Derive expressions for the Piola stress for each of these strain energy functions.

b) Tabulate values of the Piola stress and the Kirchoff stress for λ=-0.8, λ=1.2, and λ=1.6

c) Discuss the advantages/disadvantages of <u>each of the three</u> proposed strain energy functions for describing a tissue such as skin.