Problem Set 5 for CaSB 186
Due March17, 2017 in Lab section
(Late problem sets will lose 10 points per day)

1. Consider a system of stem cells that have a per-capita death rate, δ, and divide with a per-capita rate, β. When the stem cells divide the original stem cell remains and the daughter cell is either a new stem cell or a non-stem cell with probability, α. The non-stem cells die at a per-capita rate, γ, and divide with a per-capita rate ρ. Consider a single time step, dt, that is short enough that only one cell death and cell division takes place in a time step. The total number of cells—stem cells plus non-stem cells—does not change in time, similar to a crypt in the colon.
   a. Write down equations for the transition probabilities for $P_{i+1\to i}=P_{dec}$ and $P_{i-1\to i}=P_{inc}$ where i here would be the abundance or population size for the stem cells.
   b. Express the equations in terms of $\eta_i=i/N$ and calculate the mean/velocity term and variance/diffusion term. What is the associated Kolmogorov/Diffusion/Fokker-Planck equation for this?
   c. Take the ratio of the mean and variance term and integrate over η. Recall from class that the equilibrium solution for these types of equations is proportional to $\mathrm{Exp}[-2\int^{\eta}(M_{\eta'}/V_{\eta'})d\eta']$. What is the form of this term for this problem?
   d. When the death and division rates of stem cells are slow compared with the death and division rates of non-stem cells, can you make any approximations to simplify the term in part c that is proportional to the equilibrium solution?

2. a. Use dimensional analysis to determine an equation for the velocity of a wave of blood through a single vessel. Use intuition to determine which parameters this velocity should depend on such as elasticity, *E*, density, ρ, wall thickness, *d*, vessel length, *l*, and vessel diameter, *d*, from the middle of the vessel to the outside wall. If possible, derive an equation with the correct power-law dependence on this combination of parameters. If the combination of some parameters cannot be uniquely determined from dimensional analysis, explain why. If part is left arbitrary, what is a simple choice you can make for the form of the equation?
   b. Find approximate values for the parameters in your equation that you need to calculate the speed of blood leaving a human aorta. This should be doable using the internet. How does this compare to the velocity of blood leaving the heart of a mouse or a whale, assuming only the diameter of the heart is changing?

3. a. When simulating a vascular network and each blood vessel must be tracked separately and we record the vessel location with a (j,k) scheme and record the radius, length, and linear velocity in double-point precision (8 bytes), then how many vessels can be tracked if we have 12GB of RAM

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available? Estimate how many levels in the vascular system this corresponds to for an n=2 and for an n=3 bifurcating network?
b. Given the following data for a canine vascular system.

Level	Number of units	Vessel radius (μm)	Vessel length (mm)
0	1	1639±83	18.11±1.81
1	5	929±97	2.64±1.94
2	11±1	602±57	1.74±1.35
3	23±1	417±40	1.33±0.69
4	56±2	266±30	1.24±0.60
5	183±18	152±25	0.72±0.42
6	555±38	88.1±11	0.40±0.23
7	1351±71	61.5±4.6	0.27±0.13
8	3794±319	44.4±4.9	0.20±0.09
9	7993±852	31.7±4.9	0.15±0.07
10	52,001±4378	13.3±2.8	005±0.03

What is the average branching ratio, n, and what are the scaling ratios for the radii, $\beta = r_{k+1}/r_k$, and length, $\gamma = l_{k+1}/l_k$, expressed in terms of the branching ratio?

4. Consider a vascular network that is grid-like, such that nearest neighbors are all connected and each branching junction has three vessels connected to it (like bifurcating branching (n=2) for a hierarchical tree). Starting from the heart (i.e., some central location), the blood can go through a vessel either to the "right" or "left". When the blood reaches the next branching junction (i.e., node), it cannot travel back through the vessel from which it entered, and it must go the opposite direction (right versus left or vice versa) than it did at the previous node due to a series of inter-connected valves. As the blood continues to traverse the network, it must alternate directions through vessels forever after that. Prove that if this pattern continues (including in the venous system if bloods enter there) that the blood must eventually return to the heart. This is equivalent to proving that the flow cannot get stuck traveling forever through a loop of vessels of which the heart is not a part. (Hint: Consider the "dual" network constructed by replacing each vessel with a node at its mid-point and connecting these new nodes only if the original vessels were connected at an original node. Map the flow through the original network onto what flow means through the new "dual" network and consider what this means about loops. In the figure below, the first diagram is a path through the original network, and the second diagram is a path through the dual network.)

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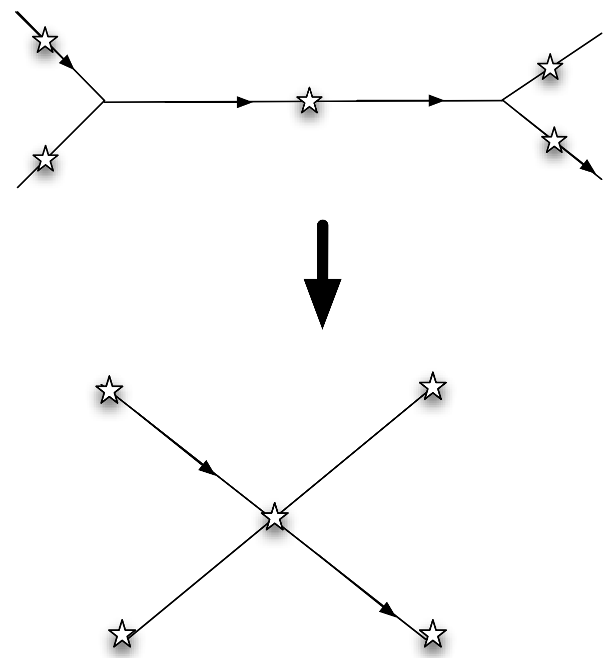

5. Analyze the robustness of the steady state level of X with respect to cell-cell variation in the production rate, β, for the auto-repression case and equations studied in class, with Hill function $1/(1+(X/K)^n)$ and degradation rate, α. Calculate the parameter sensitivity coefficient of the steady state concentration, X^{st}, with respect to β in the limit X>>K. The parameter sensitivity coefficient of property A with respect to parameter B, denoted S(A,B), is defined as the relative change in A for a given small relative change in B, that is,

$$S(A,B)=(\Delta A/A)/(\Delta B/B)=(B/A)(dA/dB).$$

How does this change as n increases?

EXTRA CREDIT (10 points):

6. Rewriting series in terms of integrals and vice versa is often central to approximations for our modeling approach. Show that we can express the ratio of the following two series as a Gaussian-type integral

$$\frac{x+\frac{x^3}{3\bullet 1}+\frac{x^5}{5\bullet 3\bullet 1}+\frac{x^7}{7\bullet 5\bullet 3\bullet 1}+\dots}{1+\frac{x^2}{2\bullet 1}+\frac{x^4}{4\bullet 2\bullet 1}+\frac{x^6}{6\bullet 4\bullet 2\bullet 1}+\dots}=\int_0^x e^{-\frac{t^2}{2}}dt$$