Problem Set 4 for CaSB 186
Due March 6, 2017 in Lab section
(Late problem sets will lose 10 points per day)

1. Consider a system with a single substrate that can bind with two different types of enzymes to produce two different types of products.
   a. Write down all of the Michaelis-Menten type equations for this system.
   b. What are all of the conserved quantities or constraints for this system? Show these quantities are conserved in time by showing the correct corresponding Michaelis-Menten type equations sum to zero.
   c. Use the Quasi-Steady State Approximation (QSSA) to solve for the rate of production of each of the two types of products.
   d. Is your solution similar to or the same as the solution from class? Are your two equations for production rate in part c. coupled together in any way? If not, what assumption or part of the model would you change to create a coupling?

2. a. Consider a random walker who is walking on a lattice of spatial sites with a spacing of 1 between each site, and at each new time step the walker takes a step either to the left or the right with an equal probability of ½ for each. Also let time go forward one step at a time so that after *n* time steps, there are *n* steps in space that have been taken, so the maximum spatial distance of the walker from the origin is *n*. The spatial location must lie within the set of spatial sites (-*n*,-(*n*-1),...,-1,0,1,...,(*n*-1),*n*). Explicitly write out the non-zero probabilities for being at all possible sites for the first 6 time steps, again assuming only one spatial step can be taken per one time step.
   b. Check that the sum of all probabilities at each time step is equal to 1 and show that the probability of being at spatial site *i* at time *n* for part a is
   $$P(i,n)=\frac{1}{2^n}\frac{n!}{\left(\frac{n+i}{2}\right)!\left(\frac{n-i}{2}\right)!}$$
   Can you explain why this formula is correct? Moreover, show this formula satisfies the recursion relation.
   $$P(i,n)=\frac{1}{2}P(i-1,n-1)+\frac{1}{2}P(i+1,n-1)$$

3. What is the expectation value for the time in the past at which 3 distinct loci would coalesce into a single loci for the most recent common ancestor? Assume the population size is 2N>>*t*>>1 where *t* is time and assume only genetic drift and the Wright-Fisher model.

4. a. The fundamental signature of diffusion is that mean spatial distance from the origin increases like the square root of time, $x \propto \sqrt{t}$. One might guess a solution to the diffusion equation would depend on a single parameter that encapsulates this relationship, namely the ratio of $\psi = x/\sqrt{t}$. Alternatively, instead of a ratio, one might guess it depends on the difference of these

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factors, such as $x - c\sqrt{t}$, which can also be expressed as $\sqrt{t}\left(\frac{x}{\sqrt{t}} - c\right) = \sqrt{t}g(\psi)$. Consequently, as a general guess for a solution one might try $f(x,t) = t^p g(\psi)$, where p is an arbitrary but constant exponent to be determined. Substitute $f(x,t) = t^p g(\psi)$ into the diffusion equation,

$$\frac{\partial f(x,t)}{\partial t} = D\frac{\partial^2 f(x,t)}{\partial x^2}$$

which is a partial differential equation, and use the chain rule to show you can write this as an ordinary differential equation in the variable ψ.

b. Show when p=-1/2, this differential equation can be expressed as

$$\frac{d}{d\psi}\left[\frac{\psi}{2}g(\psi) - D\frac{dg(\psi)}{d\psi}\right] = 0$$

It turns out this is the only choice of p that makes the equation easily solvable.

c. Solve this equation and find the solution for the case that you have the boundary condition

$$\left.\frac{dg(\psi)}{d\psi}\right|_{\psi=0} = 0$$

meaning that at the origin (x=0) the solution is at a maximum (because the derivative is zero), and this makes sense because the origin is the most probable position for the random walker to be as time moves forward. That is, the distribution of possible locations is symmetric about the origin (because there is nothing to break this symmetry), so the origin is the expectation value or the mean value for the location of the random walker and also the most likely or maximally likely location because on average the walker keeps going back and forth from one side to the other.

d. Partial differential equations are solved using a variety of methods, including the one above, but also one known as separation of variables in which you would guess or look for a solution of the form $f(x,t) = h(x)u(t)$ where h and u are unspecified, separable functions of only x and t respectively. Can your solution to part c. be found using this method? Or do you think a different solution could be found using this method? You do not need to actually find the solution.