This PSET should <u>not</u> be turned in.

1 (100 pts.) Continuous and Discrete Time

A scientists grows bacteria that replicate at a positive net rate r and harvests the bacteria at a positive constant rate k. She conjectures that the population size $y(t)$ satisfies the equation

$$\dot{y}(t) = ry(t) - k. \tag{1}$$

1.A. If there are $y(t_0)$ bacteria now, how many bacteria will there be in one day, $y(t_0 + 1)$?

1.B. In part **1.A.**, you converted a continuous-time differential equation of the form $\dot{y}(t) = f(y(t))$ into an analogous discrete-time difference equation that has the form $y(t+1) = g(y(t))$. Calculate $g(g(y(t_0)))$, simplifying fully, and explain why this must be equal to $y(t_0 + 2)$.

1.C. If there are $y(t_0)$ bacteria now, how many bacteria will there be in the long run, $y(\infty)$?

2 (100 pts.) Quasispecies Dynamics

Continuing from Question 1, the scientist stops harvesting, and so the bacteria can grow exponentially with fitness $f_0 = r$. Suppose there are two sites in the bacterial genome that can each independently mutate upon division with probability u. Bacteria with a mutation at just one site have a fitness $f_1 = r + s$. Bacteria with a mutation at both of these sites have a fitness $f_2 = r + 2s$. Back-mutation is also possible: each mutant site can return to wild type upon replication with probability v. We will refer to the wild-type, single-mutant, and double-mutant bacteria as strains 0, 1, and 2, respectively.

2.A. Write down the 3×3 stochastic matrix Q of mutation prbabilities q_{ij} from strain i to strain j. Then write down the 3×3 mutation-selection matrix W of rates $w_{ij} = f_i q_{ij}$.

2.B. Let $\vec{y}$ be the row vector of strain population sizes y_i, with sum y. Let $\vec{x}$ be the row vector of frequencies $x_i = y_i/y$. Explain why

$$\dot{\vec{y}} = \vec{y}W. \tag{2}$$

2.C. Show

$$\dot{y} = \phi y \tag{3}$$

where $\phi = \vec{f}\vec{x}$ denotes average fitness. Then derive the quasispecies equation

$$\dot{\vec{x}} = \vec{x}W - \phi\vec{x}. \tag{4}$$

Now assume that there is no back-mutation (i.e. $v = 0$) and that time is re-scaled such that $r = 1$.

2.D. If the mutation confers a positive fitness advantage $s > 0$, calculate the expected strain frequencies $\vec{x}$ and average fitness ϕ at equilibrium, where $\dot{\vec{x}} = 0$, in terms of s and u.

2.E. Repeat part **2.D.** for the case of a deleterious mutation with $s < 0$. For what range of s values is only one strain viable at equilibrium? What about two strains? All three?