

Name:

7.32/7.81J/8.591J: Systems Biology

Exam #2

Instructions

- 1) Please do not open the exam until instructed to do so.
- 2) This exam is closed-book and closed-notes.
- 3) Please do all problems.
- 4) Use the back of sheets if you need more space.

Helpful equation: In the Moran Process, a mutant with relative fitness r present as i individuals in a population of size N has a probability of fixing given by:

$$x_i = \frac{1 - \frac{1}{r^i}}{1 - \frac{1}{r^N}}$$

Scores

1 (out of 8):

2 (out of 15):

3 (out of 15):

4 (out of 20):

5 (out of 10):

6 (out of 5):

7 (out of 10):

8 (out of 12):

9 (out of 5):

Total (out of 100):

1) Master Equation (8 pts total)

You are the owner of a restaurant and you know that customers enter the restaurant randomly at a rate $f = 5 \text{ hr}^{-1}$, and each individual leaves at a rate $g = 0.5 \text{ hr}^{-1}$.

a. Write the master equation to describe the time evolution $p_n(t)$ of the probability that there will be n customers at time t in the restaurant. (2 pts)

b. At a particular time ($t = 0$), you count 20 people in the restaurant. What is the expected number of customers as a function of time? (3 pts)

c. If you wait for a long time, what is the probability distribution for the number of customers? Please write the equation of the distribution and specify the numerical value of any parameters. (3 pts)

2) Life at low Reynold's Number (15 pts)

a. Roughly how fast does *E. coli* swim? (2 pts)

1. 3 nm/sec
2. 30 nm/sec
3. 300 nm/sec
4. 3 μ m/sec
5. 30 μ m/sec
6. 300 μ m/sec
7. 3 mm/sec
8. 30 mm/sec

b. After stopping swimming, roughly how far does the cell drift before stopping? (3 pts)

1. ≤ 1 nm
2. 10 nm
3. 100 nm
4. 1 μ m
5. 10 μ m
6. 100 μ m
7. ≥ 1 mm

c. Consider a small pore with radius through which salt is diffusing from a chamber on the right, in which the concentration of salt is c_0 , to a chamber on the left, in which the concentration is zero.

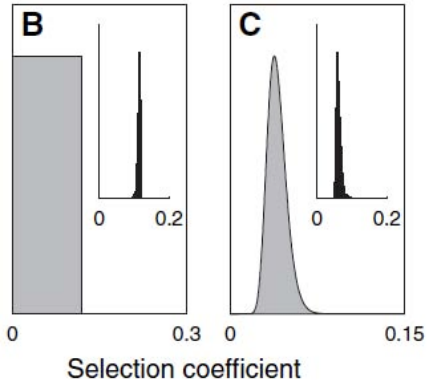
i) How does the total flow of salt through the pore scale with the concentration on the right? (2 pt)

ii) How does the total flow of salt through the pore scale with the diffusion constant of salt? (2 pt)

iii) How does the total flow of salt through the pore scale with the radius of the pore? (3 pt)

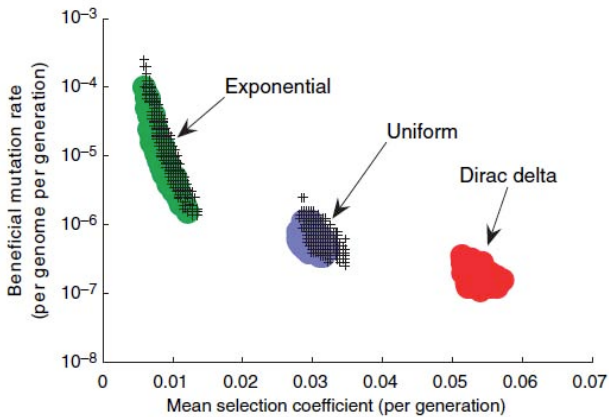
d. How does the typical time for angular "reorientation" of a sphere scale with the radius of the sphere? (3 pts)

3) Distribution of beneficial mutations (15 points)



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a. What are the authors trying to show in this figure? What is the difference between the main figures and the inset? (3 pts)



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b. What is the primary point of this figure? (3 pts)

c. Draw the distribution of beneficial mutations that corresponds to each of the allowed regions of parameter space for each of the **three** underlying distributions in the previous figure. Please label the x-axis. (3 pts)

d. Why is the mean selection coefficient different for the three distributions? (e.g. Why is the mean selection coefficient larger for the delta function than for the exponential?). (3 pts)

e. Why is the rate of beneficial mutations different for the three distributions? (e.g. Why is the beneficial mutation rate larger for the exponential than for the delta function?). (3 pts)

4) Robustness in Bacterial Chemotaxis (20 points)

a. How does binding of an attractant alter the activity of the complex CheW/A? (2 pts)

b. What are typical tumbling frequencies? (2 pts)

c. How far does an E. coli swim during a typical run? How does this help the cell to “measure” the concentration gradient? (2 pts)

d. What does the equation below describe? What are the two key assumptions embodied in this equation that yield perfect adaption? (5 pts)

$$\frac{d(X_m + X_m^*)}{dt} = V_R R - \frac{V_B B X_m^*}{K + X_m^*}$$

f. If we over-express CheR then how does the steady-state tumbling frequency vary? (3 pts)

g. If we over-express CheR then how does the adaptation time vary? (3 pts)

h. If we over-express CheR then how the adaptation precision vary (tumbling frequency after adaptation divided by tumbling frequency before stimulus)? (3 pts)

5) Dorsal region patterning in the *Drosophila* embryo (10 points)

In the example of robust embryo patterning given in Uri's book, the spatio-temporal dynamics of the inhibitor I , morphogen M , and protease P can be described by the following set of equations:

$$\frac{\partial I}{\partial t} = D_I \frac{\partial^2 I}{\partial x^2} - kIM$$

$$\frac{\partial C}{\partial t} = D_C \frac{\partial^2 C}{\partial x^2} + kIM - \alpha_c PC$$

$$\frac{\partial M}{\partial t} = \alpha_c PC - kIM$$

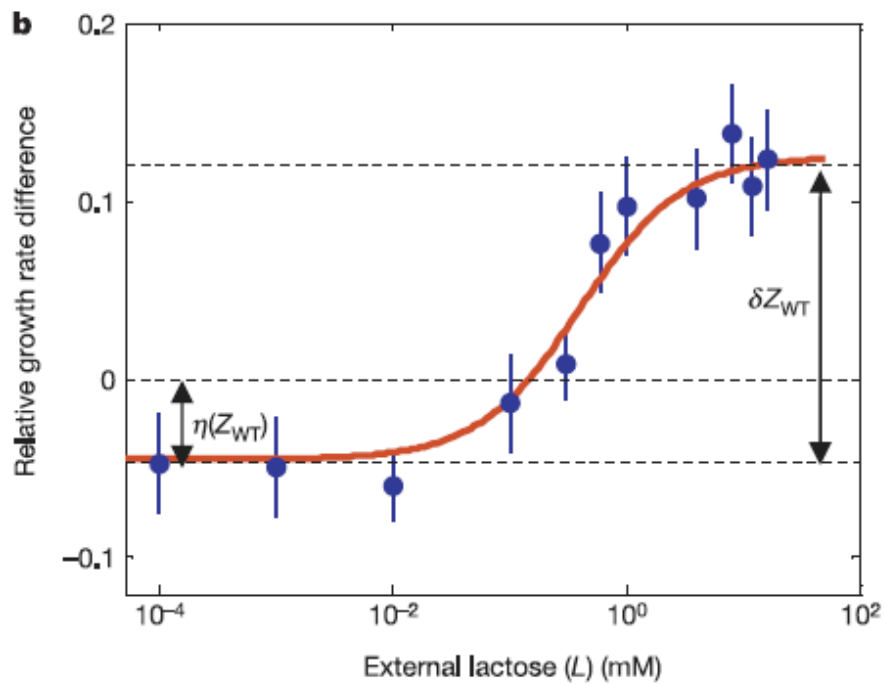
a. What is species C ? (2 pts)

b. How does the diffusion of the morphogen change after binding to the inhibitor? Is this the change that you would expect when a molecule gets bigger? (3 pts)

c. What does the protease degrade? (3 pts)

d. What does the protease act on? (2 pts)

6) Optimality and gene expression (5pts)



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a. In this figure from the Dekel and Alon paper, what does $\eta(Z_{WT})$ and δZ_{WT} and represent? What is Z_{WT} ? (3pts)

b. How was this experiment done? (2pts)

7) Evolution in finite populations (10 pts)

In parts (a) and (b), specify the probability that the mutant A with relative fitness r will reach fixation. Assume a Moran process.

a. Population of sizes $N = 100$, where strain A has a growth advantage of 0.1% and starts out at a frequency of 20%. (3 pts)

b. Population of sizes $N = 1000$, where strain A has a growth deficit of 2% and starts out at a frequency of 70%. (3 pts)

c. Assume that the distribution of beneficial mutations is described by $p(s) = \exp(-s/s_0)/s_0$, with $s_0 \ll 1$. Please draw the distribution of mutations that reach fixation in the limit of large population size and small mutation rate. (4 pts)

9) Evolution and sequence spaces (5 pts)

Consider a large population where the the fitness of genotypes is described by:

00: 1

01: 1.1

10: 1.3

11: 2

If the population starts in state 00, then in the limit of small mutation rate what is the probability that the population will take the 00 -> 01 -> 11 path to the fitness peak?

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