

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.

Possibly 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 12):

2 (out of 17):

3 (out of 12):

4 (out of 6):

5 (out of 6):

6 (out of 23):

7 (out of 12):

8 (out of 12):

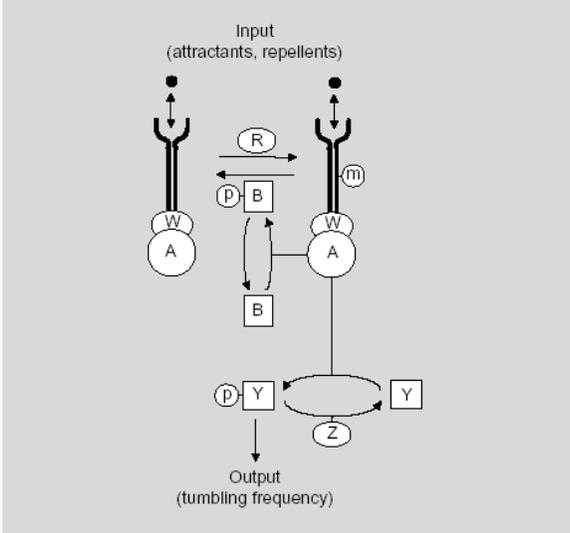
Total (out of 100):

1) Life at low Reynold's Number (12 points total)

a. Consider a small sphere sinking in water. Find an expression for the expected speed v_{terminal} with which the sphere sinks. Your expression may (or may not) contain the acceleration of gravity g , the density of water ρ_w , the density of the sphere ρ_b , the radius of the sphere a , the viscosity of water η , the thermal energy kT . If you do not recall the precise formula for the drag coefficient of a sphere then make your best (dimensionally-correct!) guess. The units of viscosity in SI is $\text{kg}/(\text{sec} * \text{meters})$ (6 pt)

b. After a time t , the sphere will have fallen approximately a distance $\langle z \rangle = v_{\text{terminal}} t$. However, life for small objects is random. What is the expected deviation $\langle (\Delta z)^2 \rangle^{0.5}$ from this mean distance? Once again, your answer may include any of the terms from above. (6 pt)

2) Robustness in Bacterial Chemotaxis (17 points total)



© Taylor & Francis Group. Figure 7.6: The Chemotaxis Signal Transduction Network. Alon, U. Chapter 7 in *An Introduction to Systems Biology: Design Principles of Biological Circuits*. Chapman and Hall / CRC, 2006. ISBN: 9781584886426. All rights reserved. This content is excluded from our Creative Commons license. For more information, see <http://ocw.mit.edu/help/faq-fair-use/>.

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

- b. What are typical tumbling frequencies for *E. coli*? (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 adaptation? (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, does the steady-state tumbling frequency vary? Yes / No (2 pts)

- g. If we over-express CheR, does the adaptation time vary? Yes / No (2 pts)

h. If we over-express CheR, does the adaptation precision vary (tumbling frequency after adaptation divided by tumbling frequency before stimulus)? Yes / No (2 pts)

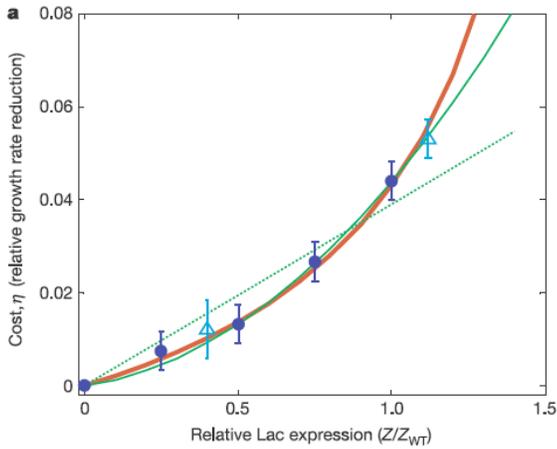
3) Patterning in a simple embryo (12 points total)

Consider a one dimensional embryo of length L . At $x = 0$ a morphogen M is produced at rate r . The morphogen then diffuses across the embryo with diffusion coefficient D , and at $x = L$ it is degraded (concentration of morphogen is zero at $x = L$). Assume that there is no degradation elsewhere in the embryo. Also note that since this is a one-dimensional embryo that a concentration has units of length^{-1} .

a. What is the equilibrium profile as a function of position? **Please draw.** (7 points)

b. Assume that in these conditions the embryo can use a threshold concentration of the morphogen M to split the embryo in half at $x^* = L/2$. If the rate of morphogen creation increases by 10%, by how much will the location x^* shift? (5 points)

4) Optimality and gene expression (6 points total)

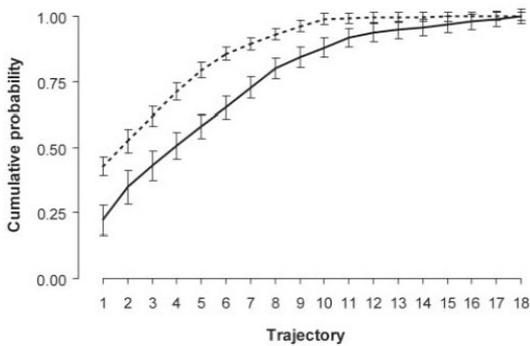


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a. What was the main point of this figure? (3 pts)

b. How was this experiment done? (3 pts)

5) Mutational paths in beta-lactamase (6 points total)



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a. What was the main point of this figure? (3 pt)

b. What is the difference between the two lines? (3 pt)**6) Clonal interference (23 points)**

Consider a population that can be modeled by the Moran process with population size N , mutation rate μ (probability per individual per generation). Assume all mutations are beneficial with fixed selection coefficient $s \ll 1$ and that $Ns \gg 1$

a. What is the mean time T_{mut} between the initial appearance of successive mutations? (3 pts)

b. How is the time between the appearance of successive mutations distributed? Write the equation for this probability density. (3 pt)

c. What is the probability that a beneficial mutant with selection coefficient $s \ll 1$ will survive stochastic extinction (in the absence of clonal interference these mutants will fix). Partial credit given for just giving the answer, but full credit requires derivation (4 pt).

d. What is the mean time T_{est} between the “establishment” of successive mutants? (2 pts)

e. How large must this mutant sub-population be before it is “established” and has only a $1/e$ chance of going extinct? (5 pt) Once again, full credit requires calculating the result.

f. What is the time T_{fix} for this more fit mutant to take over the population after becoming established (condition found in part d above)? (3 pts)

g. What is the condition relating N , μ , and s such that clonal interference is negligible? (3 pts)

7) Distribution of beneficial mutations and the rate of evolution (12 points total)

Consider a population of size N which is subject to a beneficial mutation rate μ (per individual per generation). When a mutation occurs, the individual gains fitness s drawn from an exponential distribution:

$$p(s) = \frac{1}{s_0} \exp\left[-\frac{s}{s_0}\right]$$

a. Assuming that the mutation rate is small, what is the (normalized) distribution of mutants that fix in the population $p_{\text{fix}}(s)$? Draw the distribution $p(s)$ as well as $p_{\text{fix}}(s)$. Assume very large N . (6 pt)

b. What is the expected rate of increase in fitness in this population? You can express your answer in the form of an integral. (6 pt)

8) Nash Equilibria in Mixed Strategy Games (12 points total)

In the hawk-dove game each individual is assumed to follow the aggressive "hawkish" strategy with frequency p . ($b > 0$, $c > 0$)

$$\begin{array}{c} H \\ D \end{array} \begin{array}{cc} H & D \\ \left(\begin{array}{cc} (b-c)/2 & b \\ 0 & b/2 \end{array} \right) \end{array}$$

a. If you follow strategy p_1 and your opponent follows strategy p_2 , what is your expected payout $E(p_1, p_2)$? Simplify your expressions. (3 pt)

b. What is the condition on b and c such that neither pure strategy is a Nash Equilibrium? (2 pt)

c. Assume that the condition in part (b) is satisfied, A friend tells you that the Nash Equilibrium of this game corresponds to $p^* = b/c$. Calculate $E(p, p^*)$. Is your result consistent with p^* being a Nash Equilibrium? Explain. (4 pt)

d. What is the condition for a strategy p' to be an unbeatable strategy? (express in terms of $E(\dots, \dots)$ functions). How is this different from a Nash Equilibrium? (3 pt)

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