Review Problems for Exam 2

1. Consider a pond that initially contains 10 million gallons of fresh water.[1] Water containing an undesirable chemical flows into the pond at a rate of 5 million gallons per year and the mixture in the pond flows out at the same rate. Suppose the concentration of the chemical in the incoming water is 2 grams per gallon. Let $Q(t)$ denote the amount of the chemical in grams in the pond at time t.

   (a) Write a differential equation for the quantity $Q = Q(t)$, where t is measured in years.

   (b) Give the equilibrium solution, $\overline{Q}$, to the equation in part (a).

   (c) Give $Q(t)$ for all t, and sketch an approximate graph of Q as a function of t.

   (d) What is the limiting value of $Q(t)$ as $t \to \infty$?

2. Consider a tank used in certain hydrodynamic experiments.[2] After one experiment, the tank contains 200 liters of a dye solution with a concentration of 1 gram per liter. To prepare for the next experiment, the tank is to be rinsed with fresh water flowing at the rate of 2 liter per minute. The well–stirred solution flows out at the same rate. Find the time that will elapse before the concentration in the tank reaches 1% if its initial value.

3. Luria and Delbrück[3] devised the following procedure (known as the *fluctuation test*) to estimate the *mutation rate, a*, for certain bacteria:

   Imagine that you start with a single normal bacterium (with no mutations) and allow it to grow to produce several bacteria. Place each of these bacteria in test–tubes each with media conducive to growth. Suppose the bacteria in the test–tubes are allowed to reproduce for n division cycles. After the n^{th} division cycle, the content of each test–tube is placed onto a agar plate containing a virus population which is lethal to the bacteria which have not developed resistance. Those bacteria which have mutated into resistant strains will continue to replicate, while those that are sensitive to the virus will die. After certain time, the resistant bacteria will develop visible colonies on the plates. The number of these colonies will then correspond to the number of resistant cells in each test tube at the time they were exposed to the virus.

   (a) Estimate the probability, p_o, that at the end of the n division cycles there will be no resistant bacteria. State all assumptions you make and justify your answer.

[1] Adapted from Example 3 on page 34 of *Elementary Differential Equations and Boundary Value Problems,* Seventh Edition, by Boyce and DiPrima. Wiley, New York, 2001

[2] Problem 1 on page 57 of *Elementary Differential Equations and Boundary Value Problems,* Seventh Edition, by Boyce and DiPrima. Wiley, New York, 2001

[3] (1943) *Mutations of bacteria from virus sensitivity to virus resistance. Genetics,* **28**, 491–511

(b) In one of the experiments of Luria and Delbrück in 1943, they observed that out of 100 cultures, each of about 2.8×10^8 bacteria, 57 showed no resistant bacteria. Use this information to estimate:

i. The average number of mutations, μ, that occurred before the bacteria were exposed to the virus;

ii. The mutation rate, a; that is, the probability that a given bacterium will mutate in a division cycle.

4. Imagine a culture grown from a single bacterium. Suppose that there have been n division cycles. Assume that no bacterium has died during those cycles.

(a) How large is the culture? How many divisions have there been? Assume that all divisions that occur during the same cycle happen at the same time (these are usually referred to as *synchronous divisions*).

(b) Recall that the mutation rate, a, gives the probability that a given bacterium will mutate during a division. Let N denote the total bacterial population in a culture grown out of a single bacterium in n division cycles. Show that the probability, p_o, of no mutants present after the n division cycles can be approximated by $e^{-\mu}$, where $\mu = aN$ and N is very large.

Suggestion: If D is the number of divisions that have occurred in n division cycles, what is the probability that no mutation has occurred in any of those divisions? What happens to this probability as N tends to infinity?

(c) There will be exactly one mutant in the culture after n division cycles if no mutation occurs in the first $n-2$ cycles, and exactly one mutation occurs in the $(n-1)^{\text{st}}$ cycle.

i. Explain why the probability of one mutation in the $(n-1)^{\text{st}}$ cycle is $a \cdot 2^{n-1}$.

ii. Estimate the probability, p_1, that there will be exactly one mutant in the culture after n division cycles, if the culture size, N, is very large.

Suggestion: If D is the number of divisions that have occurred in n division cycles, what is the probability that no mutation has occurred in $D-1$ of those divisions, and exactly one mutation occurs in one division? What happens to this probability as N tends to infinity?

(d) If the number of mutants, r, in the culture is equal to 2, two bacteria might have mutated during the $n-1$ division cycle, or one bacterium might have mutated during the $n-2$ cycle giving rise to 2 mutants after cell division in the $n-1$ cycle. Estimate the probability, p_2, of this event for N very large.

(e) Use your results in the previous three parts to estimate the probability that there will be 3 or more resistant bacteria in the culture after n division cycles when the population size, N, is very large.