

Solutions to Review Problems for Exam 2

1. A patient is given the drug theophylline intravenously at a constant rate of 43.2 mg/hour to relieve acute asthma. You can imagine the drug as entering a compartment of volume 35,000 ml. (This is an estimate of the volume of the part of the body through which the drug circulates.) The rate at which the drug leaves the patient is proportional to the quantity there, with proportionality constant 0.082.

- (a) Write a differential equation for the quantity, $Q = Q(t)$, in milligrams, of the drug in the body at time t hours.

Solution: Use the conservation principle for a one-compartment model to get

$$\begin{aligned}\frac{dQ}{dt} &= \text{Rate of } Q \text{ in} - \text{Rate of } Q \text{ out} \\ &= 43.2 - 0.082Q.\end{aligned}$$

Thus,

$$\frac{dQ}{dt} = -k(Q - \bar{Q}),$$

where $k = 0.082$ and $\bar{Q} = \frac{43.2}{0.082} \doteq 526.83$. □

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

Answer: $\bar{Q} = \frac{43.2}{0.082} \doteq 526.83$. □

- (c) Assuming that the patient's body contains none of the drug initially, give $Q(t)$ for all t , and sketch an approximate graph of Q as a function of t .

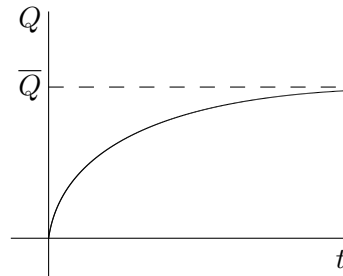


Figure 1: Sketch of graph of $Q(t)$

Solution: Use separation of variables to get

$$Q(t) = \bar{Q} + ce^{-kt},$$

for some constant c . Since $Q(0) = 0$, we get that

$$Q(t) = \bar{Q}(1 - e^{-kt}).$$

□

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

Solution:

$$\lim_{t \rightarrow \infty} Q(t) = \lim_{t \rightarrow \infty} \bar{Q}(1 - e^{-kt}) = \bar{Q}.$$

□

2. [Harvesting] The following differential equation models the growth of a population of size $N = N(t)$ that is being harvested at a rate proportional to the population density

$$\frac{dN}{dt} = rN \left(1 - \frac{N}{K} \right) - EN, \quad (1)$$

where r , K and E are parameters and non-negative parameters with $r > 0$ and $K > 0$.

(a) Give an interpretation for this model. In particular, give interpretation for the term EN . The parameter E is usually called the harvesting *effort*.

Answer: This equation models a population that grows logistically and that is also being harvested at a rate proportional to the population density. □

(b) Calculate the equilibrium points for the equation (1), and give conditions on the parameters that yield a biologically meaningful equilibrium point. Determine the nature of the stability of that equilibrium point. Sketch possible solutions to the equation in this situation.

Solution: Write

$$\begin{aligned} g(N) &= rN \left(1 - \frac{N}{K} \right) - EN \\ &= rN \left(1 - \frac{N}{K} - \frac{E}{r} \right) \\ &= -\frac{r}{K}N \left[N - K \left(1 - \frac{E}{r} \right) \right]. \end{aligned}$$

We then see that equilibrium points of equation (1) are

$$N_1^* = 0 \quad \text{and} \quad N_2^* = K \left(1 - \frac{E}{r} \right).$$

The second equilibrium point is biologically meaningful if $N_2^* > 0$, and for this to happen we require that $E < r$; that is, the harvesting effort is less than the intrinsic growth rate.

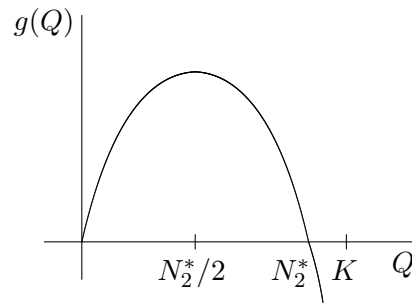
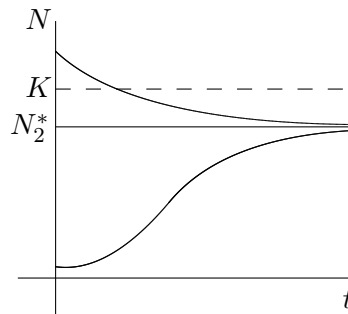
Figure 2: Graph of $g(N)$ 

Figure 3: Possible Solutions

To determine the nature of the stability of N_2^* for the case $E < r$, consider the graph of g in Figure 2. Observe from the graph that $g'(N_2^*) < 0$. It then follows from the principle of linearized stability that N_2^* is asymptotically stable.

The solid curves in Figure 3 show some possible solutions of the equation \square

- (c) What does the model predict if $E \geq r$?

Solution: If $E = r$, then

$$\frac{dN}{dt} = -\frac{r}{K}N^2 < 0$$

for $N > 0$. It then follows that $N(t)$ will always be strictly decreasing and so the population will go extinct. In fact, using separation of variables, we obtain that the solution for $N(0) = N_o$ is given by

$$N(t) = \frac{N_o K}{K + N_o r t},$$

which tends to 0 as $t \rightarrow \infty$.

On the other hand, if $E > r$, then

$$\begin{aligned}\frac{dN}{dt} &= -\frac{r}{K}N \left[N - K \left(1 - \frac{E}{r} \right) \right] \\ &= -\frac{r}{K}N^2 + KN(r - E) \\ &< -\frac{r}{K}N^2 < 0,\end{aligned}$$

and so again we conclude the $N(t)$ will be always decreasing to 0. \square

3. [Harvesting, continued] Suppose that $0 < E < r$ in equation (1), and let \bar{N} denote the positive equilibrium point. The quantity $Y = E\bar{N}$ is called the *harvesting yield*.

(a) Find the value of E for which the harvesting yield is the largest possible; this value of the yield is called the *maximum sustainable yield*.

Solution: \bar{N} is N_2^* in the previous problem. Consequently, the yield is given by

$$Y(E) = EN_2^* = EK \left(1 - \frac{E}{r} \right) = EK - \frac{K}{r}E^2.$$

Taking derivatives with respect to E , we obtain that

$$Y'(E) = K - \frac{2K}{r}E \quad \text{and} \quad Y''(E) = -\frac{2K}{r} < 0.$$

Thus, by the second derivative test, $Y(E)$ has a maximum when $E = \frac{r}{2}$.

\square

(b) What is the value of the equilibrium point for which there is the maximum sustainable yield?

Solution: The maximum value of Y is

$$Y(r/2) = \frac{r}{2}K \left(1 - \frac{r/2}{r} \right) = \frac{rK}{4}.$$

\square

4. We have seen that the (continuous) logistic model

$$\frac{dN}{dt} = rN \left(1 - \frac{N}{K} \right),$$

where r and K are positive parameters, has an equilibrium point at $\bar{N} = K$.

- (a) Let $g(N) = rN \left(1 - \frac{N}{K}\right)$ and give the linear approximation to $g(N)$ for N close to K :

$$g(K) + g'(K)(N - K).$$

Observe that $g(K) = 0$ since K is an equilibrium point.

Solution: Compute the derivative $g'(N)$ to get

$$g'(N) = r - \frac{2r}{K}N.$$

Then,

$$g'(K) = r - \frac{2r}{K}K = -r$$

and therefore the linear approximation to $g(N)$ for N near K is

$$-r(N - K).$$

□

- (b) Let $u = N - K$ and consider the linear differential equation

$$\frac{du}{dt} = g'(K)u.$$

This is called the *linearization* of the equation

$$\frac{dN}{dt} = g(N)$$

around the equilibrium point $\bar{N} = K$. Use separation of variables to solve the linearized equation. What happens to $|u(t)|$ as $t \rightarrow \infty$, where u is any solution to the linearized equation?

Solution: Solve the equation

$$\frac{du}{dt} = -ru$$

to obtain that

$$u(t) = ce^{-rt}$$

for some constant c . Then,

$$|u(t)| = |c|e^{-rt}$$

and therefore

$$\lim_{t \rightarrow \infty} |u(t)| = 0.$$

□

- (c) Use your result in the previous part to give an explanation as to why any solution to the logistic equation that begins very close to K can be approximated by

$$K + u(t),$$

where u is a solution to the linearized equation.

Solution: Let $N(t)$ denote a solution to the logistic equation with $N(0) = N_o$ and N_o very close to K . Then $|u(0)| = |N_o - K|$ is very small and consequently,

$$|u(t)| = |N_o - K|e^{-rt} < |N_o - K| \quad \text{for all } t > 0.$$

Thus, $|u(t)|$ is very small for all $t > 0$ and therefore the function $g(N(t))$ is very close to its linear approximation

$$-r(N - K) = -ru.$$

Consequently, a solution of $\frac{dN}{dt} = g(N)$ can be approximated by a solution of

$$\frac{dN}{dt} = -r(N - K),$$

or

$$\frac{du}{dt} = -ru.$$

Thus, $N(t) - K$ can be approximated by $u(t)$ for all $t > 0$, and therefore

$$N(t) \approx K + u(t).$$

□

- (d) Suppose that $N = N(t)$ is a solution to the logistic equation that starts at N_o , where N_o is very close to K . Find an estimate of the time it takes for the distance $|N(t) - K|$ to decrease by a factor of e . This time is called the *recovery time*.

Solution: Since

$$N(t) \approx K + u(t),$$

$$N(t) \approx K + (N_o - K)e^{-rt}.$$

for all $t > 0$. So,

$$|N(t) - K| \approx |N_o - K|e^{-rt}$$

for all $t > 0$.

We want to know the time t for which

$$|N(t) - K| = \frac{|N_o - K|}{e}.$$

This is approximated by the time t for which

$$|N_o - K|e^{-rt} = \frac{|N_o - K|}{e}$$

or

$$e^{-rt} = e^{-1}$$

This yields that $rt = 1$, or $t = 1/r$. □

5. 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*).

Solution: If the number of division cycles is n , then the total bacterial population is $N = 2^n$ at the end of the n division cycles. During that period of time, there have been

$$1 + 2 + 2^2 + \dots + 2^{n-1}$$

divisions since each bacterium in previous generations has divided. If we denote the number of divisions by D , then we see that

$$2D = 2 + 2^2 + \dots + 2^{n-1} + 2^n = D + 2^n - 1.$$

It then follows that $D = 2^n - 1$, and so the number of divisions is $2^n - 1$ or $N - 1$. □

- (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?

Solution: The probability that there are no mutants at the end of the n^{th} division cycle, is the probability that there have been no mutations in the $N - 1$ divisions that have occurred. The probability of no mutation in one division is $1 - a$. It then follows that

$$p_o = (1 - a)^{N-1}.$$

Writing a as $\frac{\mu}{N}$ we then have that

$$p_o = \left(1 - \frac{\mu}{N}\right)^{-1} \left(1 - \frac{\mu}{N}\right)^N.$$

Thus, for N very large,

$$p_o \approx \lim_{N \rightarrow \infty} \left\{ \left(1 - \frac{\mu}{N}\right)^{-1} \left(1 - \frac{\mu}{N}\right)^N \right\} = e^{-\mu}.$$

□

- (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 $a \cdot 2^{n-1}$.

Solution: Since a is the probability of a mutation in a bacterium per division, then the fraction of bacteria that can mutate in the $(n - 1)^{\text{st}}$ division cycle is

$$\frac{a \cdot (\text{number of bacteria})(\text{number of divisions})}{\text{number of bacteria}} = a \cdot 2^{n-1},$$

since each bacterium divides. □

- 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?

Solution: There will be exactly one mutant if there is exactly one mutation in the D divisions and that mutation occurred in the $(n - 1)^{\text{st}}$ division cycle.

$$p_1 = P[\text{only one mutation occurred}] \cdot P[\text{mutation occurred at } (n-1)^{\text{st}} \text{ cycle}]$$

By part (a), $P[\text{one mutation at } (n - 1)^{\text{st}} \text{ cycle}] = a \cdot 2^{n-1}$.

If D denotes the number of divisions in n cycles, then $D = N - 1$, where $N = 2^n$. Thus the probability that exactly one mutation occurred is the probability that no mutation occurs in $N - 2$ of those divisions. Thus,

$$P[\text{only one mutation occurred}] = (1 - a)^{N-2}.$$

It then follows that

$$p_1 = (1 - a)^{N-2} \cdot a \cdot 2^{n-1} = \frac{aN}{2}(1 - a)^{N-2}.$$

Writing μ for aN we then have $p_1 = \frac{\mu}{2} \left(1 - \frac{\mu}{N}\right)^{N-2}$. Therefore, letting $N \rightarrow \infty$, we get that

$$p_1 \approx \frac{\mu}{2} e^{-\mu}.$$

□

- (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.

Solution: p_2 is the sum of the probability that two mutations occurred in the $(n-1)$ -cycle, and the probability that only one mutation occurred in the $(n-2)$ -cycle.

Let $D = N - 1$ denote the total number of divisions.

The probability that only one mutation occurred in the $(n-2)$ -cycle is probability that no mutation occurred in all but three of the divisions (the ones that will stem from the single bacterium that mutates in that cycle), times the probability that a mutation will occur in that cycle. The former is $(1 - a)^{N-4}$ and the latter is $2^{n-2}a$, or $\frac{N}{4}a$. It then follows that

$$P[\text{only one mutation occurred in } (n-2)\text{-cycle}] = (1 - a)^{N-4} \cdot \frac{aN}{4}.$$

The probability that only two mutations occurred in the $(n-1)$ -cycle is the probability that no mutations occur in all but two of the divisions, times the probability that two mutations occur during that cycle. The former is $(1 - a)^{N-3}$ and the latter is $a2^{n-1} \cdot a(2^{n-1} - 1)$, or $a^2 \cdot \frac{N}{2} \left(\frac{N}{2} - 1\right)$. Thus,

$$P[\text{two mutations occurred in } (n-1)\text{-cycle}] = (1 - a)^{N-3} a^2 \cdot \frac{N}{2} \left(\frac{N}{2} - 1\right).$$

We then have that

$$\begin{aligned} p_2 &= (1 - a)^{N-4} \cdot \frac{aN}{4} + (1 - a)^{N-3} a^2 \cdot \frac{N}{2} \left(\frac{N}{2} - 1\right) \\ &= (1 - a)^{N-4} \cdot \frac{aN}{4} + (1 - a)^{N-3} \frac{(aN)^2}{4} \left(1 - \frac{2}{N}\right) \end{aligned}$$

Substituting μ for aN we then get that

$$p_2 = \left(1 - \frac{\mu}{N}\right)^{N-4} \cdot \frac{\mu}{4} + \left(1 - \frac{\mu}{N}\right)^{N-3} \frac{\mu^2}{4} \left(1 - \frac{2}{N}\right).$$

Letting $N \rightarrow \infty$, we then get that

$$p_2 \approx \frac{\mu}{4}e^{-\mu} + \frac{\mu^2}{4}e^{-\mu} = \frac{1}{4}\mu(1 + \mu)e^{-\mu}.$$

□

- (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.

Solution: $P[r \geq 3] = 1 - (P[r = 0] + P[r = 1] + P[r = 2])$. Thus, by parts (2)–(4),

$$P[r \geq 3] = 1 - p_0 - p_1 - p_2 \approx 1 - e^{-\mu} - \frac{\mu}{2}e^{-\mu} - \frac{1}{4}\mu(1 + \mu)e^{-\mu}.$$

This can be rewritten as

$$P[r \geq 3] \approx 1 - e^{-\mu} \left(1 + \frac{3}{4}\mu + \frac{1}{4}\mu^2\right).$$

□

6. Suppose we are interested in tracking the proportions of the genotypes GG , Gg and gg in a very large population, and that, initially, those proportions are p_o , q_o and r_o , respectively.

- (a) Let a denote the proportion of allele G in the entire population and b be that of allele g . Find a and b in terms of p_o , q_o and r_o .

Solution: An individual in a population will have the allele G if its genotype is GG or Gg ; in the first case there are two instances of the allele, while in the second there is only one. It then follows that

$$a = \frac{2 \times [\text{proportion of genotype } GG] + 1 \times [\text{proportion of genotype } Gg]}{2},$$

where we have divided by 2 since each individual has 2 alleles. Thus,

$$a = p_o + \frac{1}{2}q_o.$$

Similarly,

$$b = \frac{1}{2}q_o + r_o.$$

□

- (b) Assuming random mating between individuals of the various genotypes, compute the proportions p_1 , q_1 and r_1 of the genotypes GG , Gg and gg , respectively, in the first generation.

Solution: We need to consider all the possible nine crossings:

$$\begin{array}{lll} GG \times GG & GG \times Gg & GG \times gg \\ Gg \times GG & Gg \times Gg & Gg \times gg \\ gg \times GG & gg \times Gg & gg \times gg \end{array}$$

Assume that these crossings are all equally likely. Out of the nine crossings, only

$$GG \times GG, Gg \times Gg, GG \times Gg, \text{ and } Gg \times GG$$

produce the genotype GG : the first one with probability 1, the second with probability $1/4$, and the last two with probability $1/2$. It then follows that

$$\begin{aligned} p_1 &= 1 \times [\text{probability of } GG \times GG] \\ &\quad + \frac{1}{4} \times [\text{probability of } Gg \times Gg] \\ &\quad + \frac{1}{2} \times [\text{probability of } GG \times Gg] + \frac{1}{2} \times [\text{probability of } Gg \times GG] \\ &= p_o^2 + \frac{1}{4}q_o^2 + p_oq_o. \end{aligned}$$

Similarly, since the crossings

$$GG \times Gg, GG \times gg, Gg \times GG, Gg \times Gg, Gg \times gg, gg \times GG, gg \times Gg$$

produce the phenotype Gg with probabilities $1/2$, 1 , $1/2$, $1/2$, $1/2$, 1 and $1/2$, respectively, we have that

$$\begin{aligned} q_1 &= \frac{1}{2}p_oq_o + p_or_o + \frac{1}{2}q_op_o + \frac{1}{2}q_o^2 + \frac{1}{2}q_or_o + r_op_o + \frac{1}{2}r_oq_o \\ &= p_oq_o + q_or_o + 2p_or_o + \frac{1}{2}q_o^2. \end{aligned}$$

By the same token, since the crossings

$$Gg \times Gg, Gg \times gg, gg \times Gg, gg \times gg$$

produce the phenotype gg with probabilities $1/4$, $1/2$, $1/2$ and 1 , respectively,

$$r_1 = \frac{1}{4}q_o^2 + \frac{1}{2}q_or_o + \frac{1}{2}r_oq_o + r_o^2 = \frac{1}{4}q_o^2 + q_or_o + r_o^2.$$

□

- (c) Verify that p_1 , q_1 and r_1 are given by a^2 , $2ab$ and b^2 , respectively, where a and b are as in part (a).

Solution: Compute

$$a^2 = \left(p_o + \frac{1}{2}q_o\right)^2 = p_o^2 + p_oq_o + \frac{1}{4}q_o^2 = p_1,$$

$$\begin{aligned} 2ab &= 2\left(p_o + \frac{1}{2}q_o\right)\left(\frac{1}{2}q_o + r_o\right) \\ &= 2\left(\frac{1}{2}p_oq_o + p_or_o + \frac{1}{4}q_o^2 + \frac{1}{2}q_or_o\right) \\ &= p_oq_o + 2p_or_o + \frac{1}{2}q_o^2 + q_or_o \\ &= q_1, \end{aligned}$$

and

$$b^2 = \left(\frac{1}{2}q_o + r_o\right)^2 = \frac{1}{4}q_o^2 + q_or_o + r_o^2 = r_1.$$

□