Solutions to Exam 2

1. Suppose that the rate at which a drug leaves the bloodstream and passes into the urine at a given time is proportional to the quantity of the drug in the blood at that time.

   (a) Write down and solve a differential equation for the quantity, $Q = Q(t)$, of the drug in the blood at time, t, in hours. State all the assumptions you make and define all the parameters that you introduce.

   Solution: By the conservation principle for a on–compartment model,
$$\frac{\mathrm{d}Q}{\mathrm{d}t} = \text{Rate of } Q \text{ in} - \text{Rate of } Q \text{ out},$$
where
$$\text{Rate of } Q \text{ in} = 0$$
and
$$\text{Rate of } Q \text{ out} = kQ,$$
for some constant of proportionality k. Thus, Q satisfies the differential equation
$$\frac{\mathrm{d}Q}{\mathrm{d}t} = -kQ,$$
which has solution
$$Q(t) = ce^{-kt} \quad \text{for all } t \geqslant 0.$$
for some constant c. □

   (b) Suppose that an initial dose of Q_o is injected directly into the blood, and that 20% of that initial amount is is left in the blood after 3 hours. Based on the solution you found in the previous part, write down $Q(t)$ for this situation and sketch its graph.

   Solution: If $Q(0) = Q_o$, then $c = Q_o$. Thus,
$$Q(t) = Q_oe^{-kt} \quad \text{for all } t \geqslant 0.$$
If $Q(3) = 0.2Q_o$, then
$$0.2Q_o = Q_oe^{-3k},$$

from which we obtain that

$$k = -\frac{1}{3}\ln(0.2) \approx 0.54.$$

It then follows that

$$Q(t) = Q_o e^{\frac{t}{3}\ln(0.2)} \approx Q_o e^{-0.54t}.$$

□

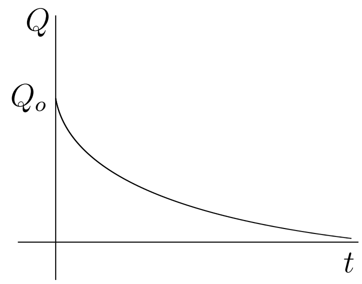

Figure 1: Sketch of graph of $Q(t)$

(c) How much of the drug is left in the patient's body after 6 hours if the patient is given 100 mg initially?

Solution: Compute

$$\begin{aligned} Q(6) &= 100e^{\frac{6}{3}\ln(0.2)} \\ &= 100e^{2\ln(0.2)} \\ &= 100\left(e^{\ln(0.2)}\right)^2 \\ &= 100(0.2)^2 \\ &= \frac{100}{25} \\ &= 4. \end{aligned}$$

Thus, there will be 4 mg of the drug left in the patient after 6 hours. □

2. The following equation models the evolution of a population that is being harvested at a constant rate:

$$\frac{dN}{dt} = 2N\left(1 - \frac{N}{200}\right) - 75$$

(a) Give an interpretation for the model.

Solution: The equation models a population that grows logistically, with intrinsic growth rate $r = 2$ and carrying capacity $K = 200$, which is also being harvested at a constant rate of 75 units or population per unit of time. □

(b) Find equilibrium points, determine the nature of their stability, and sketch a few possible solution curves.

Solution: Write

$$\begin{aligned} g(N) &= 2N\left(1 - \frac{N}{200}\right) - 75 \\ &= -\frac{1}{100}\left(N^2 - 200N + 7500\right) \\ &= -\frac{1}{100}(N - 50)(N - 150). \end{aligned}$$

We then see that equilibrium points of the equation are

$$N_1^* = 50 \quad \text{and} \quad N_2^* = 150.$$

To determine the nature of the stability of the equilibrium points, consider the graph of g in Figure 2.

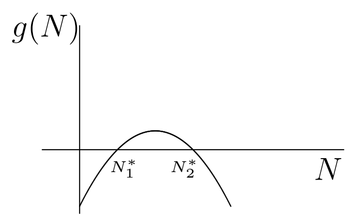

Figure 2: Graph of $g(N)$

Observe from the graph that $g'(N_1^*) > 0$. It then follows from the principle of linearized stability that N_1^* is unstable. Similarly, since $g'(N_2^*) < 0$, N_2^* is asymptotically stable.
Figure 3 shows a few possible solutions of the equation

□

(c) According to model, what will happen if at time $t = 0$ the initial population density is 47? What do you conclude?

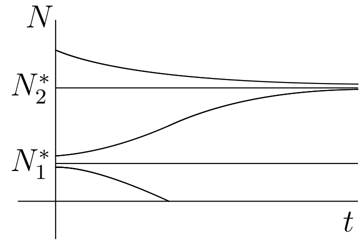

Figure 3: Possible Solutions

Solution: According to Figure 3, since $47 < N_1^*$, the population will go extinct in finite time. This is due to over–harvesting. □

3. Luria and Delbrück[1] 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.

   Solution: The mutation rate, a, is the probability that a mutation will occur during a single cell division. In n division cycles there will be $N = 2^n$ bacteria and $2^n - 1$, or $N - 1$, divisions. The probability that there is no mutation in any of the cell divisions is then

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

   If we write $\mu = a(N - 1) \approx aN$, the average number of mutations,

[1] (1943) *Mutations of bacteria from virus sensitivity to virus resistance. Genetics*, **28**, 491–511

then

$$p_o \approx \left(1 - \frac{\mu}{N}\right)^{N-1} \approx e^{-\mu}$$

when N is very large.

Alternatively, if we model the number of mutations, $M(n)$, by a Poisson random variable with parameter $\mu = \mu(n)$, where n is the number of division cycles, then the probability of no mutations is

$$p_o = P[M(n) = 0] = e^{-\mu(n)} = e^{-\mu}. \qquad \square$$

$\square$

(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, 52 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;

***Solution**:* In this case $p_o \approx 0.52$; so that, from $p_o = e^{-\mu}$, we obtain that

$$\mu \approx -\ln(p_o) = -\ln(0.52) \doteq 0.65. \qquad \square.$$

$\square$

ii. The mutation rate, a; that is, the proportion of mutations per cell division in bacteria.

There are two possible answers to this question:

Answer 1: $a \approx \dfrac{\mu}{N} \approx \dfrac{0.65}{2.8 \times 10^8} \doteq 2.3 \times 10^{-9}$.

Answer 2: Integrating $\mu'(t) = aN(t)$ with respect to t, we obtain that

$$\mu(t) = \frac{a}{k}(N(t) - 1),$$

where k is the *per capita* growth rate of the bacteria. If t is measured in numbers of division cycles, then $N(t) = 2^t$ and therefore $k = \ln 2$. When $t = n$ and n is very large,

$$\mu(n) \approx \frac{a}{\ln 2} 2^n = \frac{aN}{\ln 2}.$$

Therefore, $a \approx \ln 2 \dfrac{\mu}{N} \approx (0.6931) \dfrac{0.65}{2.8 \times 10^8} \doteq 1.6 \times 10^{-9}$.