Qualifying Exam **Biomathematics I** **25 Aug 2019**

Instructions:

- This exam consists of 5 problems and is 2 hours in duration.
- Please write neatly and legibly.
- Show ALL work for full credit. Give EXACT answers when possible.

Problem 1 A model for a sexually transmitted disease includes the following classes: female and male infectives (I_F and I_M, respectively) and female and male susceptibles (S_F and S_M, respectively). It assumes that there is no acquired resistance, that is, once infectives recover, they rejoin the susceptibles.

$$\begin{aligned}
\frac{dS_F}{dt} &= -\beta_f S_F I_M + \alpha_f I_F, \\
\frac{dI_F}{dt} &= \beta_f S_F I_M - \alpha_f I_F, \\
\frac{dS_M}{dt} &= -\beta_m S_M I_F + \alpha_m I_M, \\
\frac{dI_M}{dt} &= \beta_m S_M I_F - \alpha_m I_M,
\end{aligned}$$

where β_i and α_i, $i = f, m$, are positive parameters.

(a) Briefly give a description of the model in biological terms and show that:

$$I_* + S_* = N_*, \qquad * = F, M,$$

where N_* are constants.

(b) Find the disease free equilibrium (DFE) of the above system and derive conditions for its stability.

(c) The above system also admits a single diseased or endemic equilibrium state. Under the condition that the DFE is unstable, show that the endemic equilibrium is stable. (Hint: You do *not* need to compute the endemic equilibrium explicitly. It will help to eliminate S_F and S_M from the model using the conservation laws from (a). This will result in 2 coupled ordinary differential equations for I_F and I_M. Compute the Jacobian matrix of this system and use the trace-determinant condition to establish stability.)

Problem 2 A single population model with very fast predation is given by:

$$\frac{dN}{dt} = \lambda N \left(1 - \frac{N}{K}\right) - \mu \left(1 - \exp\left(-\frac{N^2}{\epsilon A^2}\right)\right), \qquad 0 < \epsilon \ll 1,$$

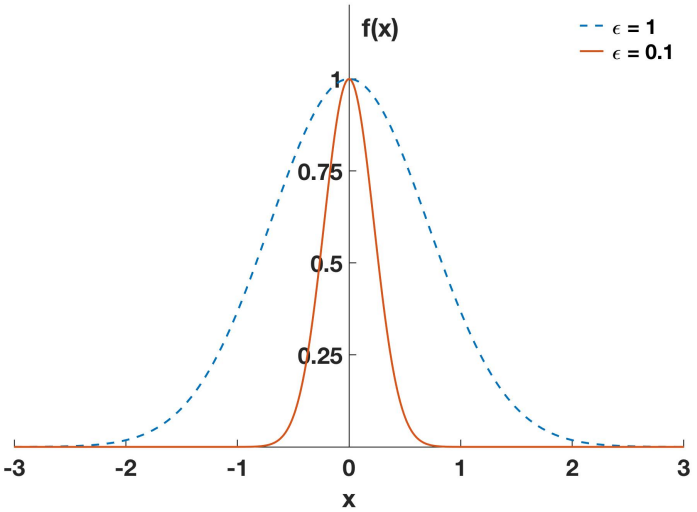
where N(t) is the prey population at time t, and λ, K, μ and A are positive parameters.

(a) By an appropriate non-dimensional rescaling of N and t, show that the above equation transforms to:

$$\frac{dn}{d\tau} = \alpha n \left(1 - \frac{n}{\beta}\right) - \left(1 - \exp\left(-\frac{n^2}{\epsilon}\right)\right),$$

where α and β are positive non-dimensional parameters.

(b) On the same set of axes, sketch the graphs of the functions $g(n) = \alpha n \left(1 - \frac{n}{\beta}\right)$ and $h(n) = 1 - \exp\left(-\frac{n^2}{\epsilon}\right)$ for positive n remembering that ϵ is small, that is, $0 < \epsilon \ll 1$. You may wish to draw 2-3 possible graphs for $g(n)$ in particular, given that this depends on model parameters. To assist you, a graph of the function $f(x) = \exp(-x^2/\epsilon)$ is provided for a couple of different values of ϵ.



(c) Under what conditions on the parameters α and β can the model admit 3 non-zero and positive steady states? You may assume that since $\epsilon \ll 1$, $h(n)$ rapidly approaches 1. (Hint: The graph of $g(n)$ is an upside down parabola. For what value of n does it reach its maxima?)

(d) Could this model exhibit hysteresis?

Problem 3 The following model for competition between Neanderthal man (N) and Early Modern man (E) has been proposed:

$$\begin{aligned} \frac{dN}{dt} &= N\,(\alpha - \delta\,(N+E) - \beta)\,, \\ \frac{dE}{dt} &= E\,(\alpha - \delta\,(N+E) - s\beta)\,, \end{aligned}$$

where, α, β and δ are positive parameters ($\alpha > \beta$) and $s < 1$ is a measure of the difference in mortality of the two species.

(a) What do the various terms (in either equation) represent? Provide units for α, β and δ. You may assume that N and E represent population densities.

(b) Non-dimensionalize the system by choosing the following scaling:

$$u = \frac{\delta N}{\alpha - \beta}, \qquad v = \frac{\delta E}{\alpha - s\beta}, \qquad \tau = t(A - B).$$

(c) Find all steady-states of the non-dimensional system and examine their stability.

(d) From (c), you should have concluded that Early Modern man will drive Neanderthal man to extinction. That is, as $t \to \infty$, $N \to 0$ and E approaches a non-zero steady state. Express this steady state in dimensional terms. Hence conclude, that for large t, N decays according to the law:

$$N(t) = C\,e^{-\beta(1-s)t},$$

for some constant C. (Hint: Consider the equation governing dN/dt. Make the following assumptions: (i) $N \ll 1$ so that N^2 terms may be neglected; and (ii) $E \approx$ its steady state.)

Problem 4 In 1979, a rabies pest, arrived in France from its eastern border. Foxes were the main carriers of the disease. These foxes are divided into two classes, susceptible ($S(t)$) and infective ($I(t)$). The proposed model is:

$$\begin{aligned} \frac{dS}{dt} &= r\,(S+I)\left(1-\frac{S}{K}\right) - \beta\,S\,I, \\ \frac{dI}{dt} &= \beta\,S\,I - \gamma\,I, \end{aligned}$$

where, r, K, β and γ are positive parameters.

(a) Examine the stability of the disease free equilibrium (DFE): $(K, 0)$.

Assume for the rest of this problem that the DFE is unstable, so that the disease is endemic.

(b) One method to eradicate the rabies pest consists of killing the foxes, for instance by hunting or laying traps. Assuming that fox kill is proportional to their densities, the model equations then transform to:

$$\begin{aligned} \frac{dS}{dt} &= r\,(S+I)\left(1-\frac{S}{K}\right) - \beta\,S\,I - \delta\,S, \\ \frac{dI}{dt} &= \beta\,S\,I - \gamma\,I - \delta\,I. \end{aligned}$$

Under what conditions on the rate of hunting δ is the stability of the DFE guaranteed?

(c) An alternative strategy may be vaccination, administered via vaccine-impregnated baits, that confers partial immunity from contracting the disease. That is:

$$\begin{aligned} \frac{dS}{dt} &= r\,(S+I)\left(1-\frac{S}{K}\right) - \beta\,(1-\nu)\,S\,I, \\ \frac{dI}{dt} &= \beta\,(1-\nu)\,S\,I - \gamma\,I, \end{aligned}$$

where $0 \leq \nu \leq 1$ is the vaccination efficacy. What value of ν guarantees the stability of the DFE?

Problem 5 Consider the classical enzyme-substrate reaction in biochemistry, in which an enzyme E binds reversibly to a substrate S to form a complex C, which, in turn, irreversibly yields a product P and the enzyme is recovered:

$$E + S \underset{k_r}{\overset{k_f}{\rightleftharpoons}} C \overset{k_p}{\rightarrow} P + E$$

Here, k_i denote rate constants for the reaction.

(a) Assuming mass action kinetics, write down a system of differential equations governing the rates of change of the concentrations of the various species involved in this reaction. Use conservation of enzyme to eliminate the variable E from these equations. You may assume as. initial conditions:

$$E(0) = E_0, \qquad S(0) = S_0, \qquad C(0) = 0, \qquad P(0) = 0.$$

(b) In the standard quasi steady state assumption (QSSA), we set the rate of complex formation to 0, and obtain the following simplified system (you do *not* have to derive these):

$$\begin{aligned} \frac{dS}{dt} &= -k_p \frac{E_0\, S}{K_m + S}, \\ \frac{dP}{dt} &= k_p \frac{E_0\, S}{K_m + S}, \qquad \text{where} \qquad K_m = \frac{k_p + k_r}{k_f}. \end{aligned}$$

A limitation of this approach is that the standard QSSA is only valid when $\dfrac{E_0}{S_0 + K_m} \ll 1$.

An alternative approach is the *total QSSA* (tQSSA), which is valid for a much broader range of parameter values. In this part, you will derive the tQSSA model. First, replace the variable S from the reduced system you found in (a) with the total substrate concentration $\overline{S}$ defined as:

$$\overline{S} = S + C.$$

Write down the new system of equations for the variables $\overline{S}$, C and P, with appropriate initial conditions. Next, set $dC/dt = 0$ as in standard QSSA. This should yield a quadratic equation for C involving E_0, $\overline{S}$ and K_m. Make one further assumption, and ignore the C^2 term. Then, solve the resultant linear equation in C to obtain a simple expression for C in terms of E_0, $\overline{S}$ and K_m. Finally, substitute this expression for C in the equation for $\overline{S}$ to obtain the tQSSA model.