Introduction to Mathematical Biology
Exercises 4.1-4.4

4.1 *Enzymes with two substrates.* Many enzymes catalyse reactions between two substrates as they create a chemical bond between two different molecules (e.g. link glucose and fructose to make sucrose, which is the common table sugar). These enzymes must bind both substrates before the reaction can take place. Assume that the two substrates S_1 and S_2 are bound (and possibly released) in a fixed order: S_2 can bind to the enzyme only if the enzyme has S_1 already bound. The chemical reactions are then as follows:

$$E + S_1 \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} X_1, \quad X_1 + S_2 \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} X_2, \quad X_2 \xrightarrow{k_3} E + P$$

(a) Extend the Michaelis-Menten model (discussed in the lecture) to the above system. Identify the fast and the slow processes.
(b) Find the quasi-equilibrium of the fast processes. (You may assume that this equilibrium is stable.)
(c) Obtain a differential equation for the concentration of the product (P). Compare this equation to the analogous equation in the Michaelis-Menten model. Investigate the limits when (i) the concentration of S_1 goes to infinity; (ii) the concentration of S_2 goes to infinity. Show that in both cases, we recover the simple Michaelis-Menten kinetics discussed in the lecture, but with different parameters.

4.2 *Prebiotic replicators.* It is thought that before the emergence of life proper, RNA-like molecules were replicating themselves in an autocatalytic reaction, where the replication of one RNA molecule is helped by another (identical) RNA molecule acting as an "RNA-enzyme" called ribozyme. In this autocatalytic reaction, the replication rate ("birth rate") of a given copy of the RNA molecule, bx, is proportional to the concentration of RNA, x, because to replicate one copy, another is needed as a ribozyme (this is quite similar to sexual reproduction, where one individual, the female, needs another individual, the male, to be able to reproduce). In addition to the autocatalytic reproduction, RNA molecules replicate also spontaneously without catalysis by another RNA molecule (as if a female gave birth without a male), at some (low) rate a. The speed of replication is also proportional to the concentration of free monomers from which RNA is synthesized (i.e., "food"), c. The RNA molecules decay at a constant rate μ. The concentration of RNA therefore changes according to

$$\frac{dx}{dt} = [ac(t) + bx(t)c(t) - \mu]\, x(t)$$

The total number of monomers, including free monomers and monomers incorporated into an RNA molecule, is constant. One RNA molecule contains k monomers. We therefore have that $c(t)+kx(t) = c_0$ is constant, and we can use this conservation law to rewrite the model into an autonomous ODE,

$$\frac{dx}{dt} = [(a + bx(t))(c_0 - kx(t)) - \mu]\, x(t)$$

Perform a bifurcation analysis of this model with respect to the decay rate μ.

4.3 *Selection in the logistic model for bacterial growth.* Recall the model we used to derive logistic growth for bacteria limited by some nutrient,

$$\frac{dN}{dt} = \Big(b[c_0 - kN] - \mu\Big)N$$

where $k > 0$ is the amount of nutrient necessary to make one bacterium, $c_0 > 0$ is the total amount of nutrient of which kN is incorporated into N bacteria, and reproduction is proportional to the amount of free nutrient $[c_0 - kN]$; death occurs at a constant rate $\mu > 0$. Here the nutrient is e.g. an essential amino acid or iron, which does not reproduce like a prey species and is not replenished from the outside but is freed when a bacterium dies. Suppose that n bacterial strains grow together using the same resource. Each strain has its own characteristic parameters b_i, k_i and μ_i, so that we have the system of ODEs

$$\frac{dN_i}{dt} = \Big(b_i\big[c_0 - \sum_{j=1}^{n} k_j N_j\big] - \mu_i\Big)N_i$$

for $i = 1, ..., n$. Show that in this model, natural selection maximizes the value of b/μ at equilibrium. (Note that k_i is also a property of a strain but it is irrelevant in natural selection.)

4.4 *Population dynamics and selection with environmental pollution.* Consider n different strains of bacteria that grow together and produce the same toxic substance that pollutes their environment. The joint population dynamics is given by

$$\begin{aligned} \frac{dN_i}{dt} &= b_i N_i - (\mu_i + \rho T)N_i \\ \frac{dT}{dt} &= \sum_{i=1}^{n} \alpha_i N_i - \delta T \end{aligned}$$

for $i = 1, ..., n$. $T(t)$ is the concentration of the toxin, which is produced at rate $\alpha_i > 0$

by strain i and decays exponentially at rate $\delta > 0$. $b_i > 0$ and $\mu_i \geq 0$ are the (constant) birth rate and background death rate of strain i, respectively, and the toxin kills at a rate proportional to its concentration, $\rho T(t)$ (same for each strain). Assume that the toxin is produced and decays much faster than the bacteria (b_i and μ_i for all i and ρ are much smaller than α_i and δ), so that the toxin concentration achieves a quasi-equilibrium $\hat{T}$.

(a) Show that the population size of a single strain ($n = 1$) grows according to the logistic model.
(b) Show that when several strains grow together, density dependence is nonselective such that the strain(s) with the highest intrinsic growth rate $b_i - \mu_i$ spreads and all other strains go extinct.