

Chapter 9

Project Ideas

General Instructions:

Since there is only about 1 week to complete your project, it is important to select a reasonably doable topic. In general, the basic guidelines are that you should avoid rehashing a "canned presentation" from another course, and that you should be learning something new. That said, you are encouraged to be creative and to propose a topic other than what is listed here.

Your project could include the review and explanation of a paper in the literature connected to topics we have explored. It could be a study of some model using numerics or analysis.

The output should be a 15 min talk that summarizes what you did and what you have learned from this exploration. Feel free to extend those ideas and take them to new directions. Work in teams of 1-3 people. Above all, have fun with it.

9.1 Limit cycles in predator-prey systems

Select one of these, or work with others that share these steps.

- Investigate the Rozenzweig-MacArthur model for predator-prey cycles:

$$\frac{du}{dt} = au \left(1 - \frac{u}{K}\right) - \frac{buv}{1 + mu} \quad (9.1)$$

$$\frac{dv}{dt} = c \left(\frac{u}{1 + mu} - \frac{B}{1 + mB} \right) \quad (9.2)$$

Here $u(t)$ are prey and $v(t)$ are the predators. Your investigation should include some XPP exploration of the phase-plane behaviour and the bifurcation structure of this model. You may wish to look up the history of this model and to check whether there is data that supports it. It is likely that you may find a set of parameters that have been determined experimentally for some particular predator and prey.

- See Bard’s suggestion about coupling two predator-prey systems, for example by predators that occasionally sample each other’s prey. Find out what happens when such oscillating systems are coupled.

9.2 Hibernating (quiescent) species

Recall that in lectures by Karl Haderler, we have examined the result of “quiescence”, i.e. a form of each species that is removed from the interactions and growth due to a hibernation phase. In particular, the following system was mentioned:

$$\frac{du}{dt} = au \left(1 - \frac{u}{K}\right) - \frac{buv}{1 + mu} - p_1u + q_1w \quad (9.3)$$

$$\frac{dv}{dt} = c \left(\frac{u}{1 + mu} - \frac{B}{1 + mB}\right) - p_2v + q_2z \quad (9.4)$$

$$\frac{dw}{dt} = p_1u - q_1w \quad (9.5)$$

$$\frac{dz}{dt} = p_2v - q_2z \quad (9.6)$$

Use the analysis done in class together with XPP or Matlab exploration to find out how the system behaves with and without this hibernation phase.

9.3 Myxobacteria

Consider applications of the correlated random walk models described by Prof Karl Haderler (i.e. motion at constant speed with random turning) to the motion of the single-cell organisms called myxobacteria. Find suitable parameter values and analyze the behaviour of the system. XPP or Matlab can be used to study these numerically, to complement the analysis described in class.

9.4 Patterns and Reaction-Diffusion

Use XPP or Matlab to explore the kinetics of the Grey-Scott Model:

$$\frac{du}{dt} = -uv^2 + f(1 - u) + D_u \frac{\partial^2 u}{\partial x^2} \quad (9.7)$$

$$\frac{dv}{dt} = uv^2 - (f + k)v + D_v \frac{\partial^2 v}{\partial x^2} \quad (9.8)$$

(In 1D, you can modify the file rd2.ode to simulate this or any other reaction-diffusion system). You will find that this model has more interesting pattern-forming properties in 2D. See any of Michael Ward’s students or look online to find out more.

9.5 Microtubule growth and shrinking

Pick one or another of these approaches.

- Write down the equations (PDE's) satisfied by the plus ends of microtubules that grow and shrink in a 1D cell. Assume that the minus ends are all stabilized at $x = 0$ (the centrosome) and do not move. Use the information in the paper by Komarova to determine parameter values. If you can, simulate the system in XPP or Matlab. (Komarova Yu.A., Vorobjev I.A. and Borisy, G.G. 2002. Life cycle of MTs: persistent growth in the cell interior, asymmetric transition frequencies and effects of the cell boundary. *J. Cell Sci.* 115: 3527-3539)
- Write an XPP Gillespie simulation for several microtubules growing in a depletable pool of tubulin subunits. Compare your approach to that of Gregoratti (2006) *J Cell Sci*, or Janulevicius (2006) *Biophys J*.

9.6 Switches

Review the classical paper by Gardner et al (Gardner TS, Cantor CR, Collins JJ. (2000), Construction of a genetic toggle switch in *Escherichia coli*, *Nature*. 403(6767):339-42.) It would be easy to explore the system in the phase plane using XPP.

9.7 Bistability

There have been a number of accessible papers on bistability in the context of biochemical systems. One example is

Ferrell JE Jr. (2002) Self-perpetuating states in signal transduction: positive feedback, double-negative feedback and bistability. *Curr Opin Cell Biol.* 14(2):140-8.

However, not all is as simple as it looks. It has been shown by Marty Feinberg's group that figuring out which biochemical systems are consistent with bistability is challenging. Consider reviewing the paper:

Craciun G, Tang Y, Feinberg M. (2006) Understanding bistability in complex enzyme-driven reaction networks. *Proc Natl Acad Sci U S A.* 103(23):8697-702.

These two papers and others like them could make for paired or a team project.

9.8 Multivalent ligand binding kinetics

You are asked to model and understand the kinetics of a multivalent ligand "tetramer" that is used experimentally to label T-cells (immune cells). Part of the project could be to look up where this technique has been used and to

report on how it aids the identification of rare cells. Related to but not quite the same as the other compartmental models we discuss.

Figure 9.1 illustrates the binding of a 4-legged ligand ("tetramer") to receptors on the surface of a T cell (TCR's). Only 3 up to the 4 legs of the tetramer can be bound at any one time, and each leg bind to a single TCR. Assume that the total number of surface receptors per T-cell, R_{tot} is a known constant and let $R(t)$ be the number of receptors that are still available to bind.

Assume that each leg of the ligand would (on its own) bind to the first TCR at rate k_{on} , that additional legs can (each) bind at rate k_x and that each leg unbinds at rate k_{off} .

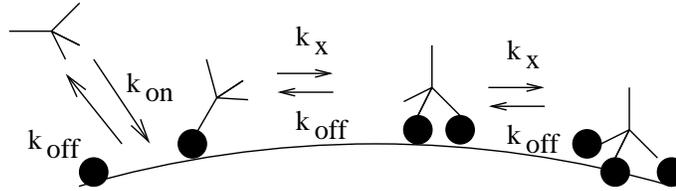


Figure 9.1: A tetramer binding to cell-surface receptors

Write down a set of differential equations for the number of ligand molecules bound with 1, 2, and /or 3 legs, (C_1, C_2, C_3) per T-cell. It may be helpful to define $\beta = /, \bar{r} = R/$

Characterize the steady state distribution of ligand in each of these three classes.

Let

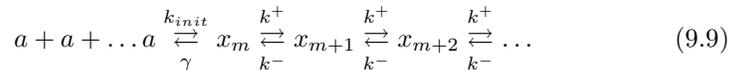
$$C_b = C_1 + C_2 + C_3$$

be the amount of bound ligand. An experiment is run as follows: first, ligand is allowed to bind to the T cells and equilibrium is attained. Then the free ligand is removed, and the experimenter follows the gradual release of the bound ligand.

Determine the half-life of the bound tetramers.

9.9 Polymer size distribution: the effect of nucleation

Suppose that the pool of available monomers is (artificially) kept constant, i.e. $a =$ monomer concentration $=$ constant. Consider the nucleation of a polymer in which m monomers have to assemble into the first stable aggregate, as shown below:



The first step is different from all other steps. Once an m -mer is formed, it can grow by addition of a single monomer, or it can collapse to m monomers. From then on, each polymer can gain or lose a single monomer.

Consider the following questions:

- Write down a set of ODE's for x_j the number of polymers of length $j = m, m + 1, \dots$ per unit volume. What are the units of the parameters?
- Show that there is a value of λ such that the steady state polymer length distribution satisfies

$$x_j = B\lambda^j$$

- From the above information, find the values of the constants B and λ .
- Analyze this system or simulate it to explore its behaviour. Is there more than one possible outcome?
- Devise experiments that would allow you to estimate the values of the parameters $m, k^+, k^-, k_{init}, \gamma$ from steady state or dynamic behaviour of the system.
- In a mixture of pure actin monomers it is thought that filaments start from either dimers or trimers. How would these be distinguishable?
- If time permits, you may want to look up Craft, Wein and Selkoe's model of amyloid polymers to compare with your results, or search for "micellization" online.

9.10 Polymers and aggregates in disease

Pick one of the below, or work with others that are interested in similar ideas.

- **Application to fibrin:** Read and present the paper by Weisel and Nagaswami (1992) BJ 63: 111-128 on the application of modeling polymerization and self-assembly to fibrin clot formation. Here the process involves not just linear growth, but also aggregation of protofibrils. Project could include simulations, and/or more recent followup literature survey.
- **Prions and Mad cows: (a Canada-US issue)** Read and report on the paper by Collins et al (2004) PLoS Biol 2 (10) e 321. This paper explore the growth of prions where breakage of the fibers is important. Understand the model and compare it with those we discussed. Simulations and/or other literature review on amyloid or prion growth could round out this project.

9.11 Cell motility models

Select one of the below:

- (1) Read the following paper and present the methods and findings of the authors about one type of cell motility. D. Bottino, A. Mogilner, T. Roberts, M. Stewart, and G. Oster. How nematode sperm crawl. *J. Cell Sci.*, 115(Pt 2):367384, January 2002.
- (2) Read and present the following paper: B. Rubinstein, K. Jacobson, and A. Mogilner. Multiscale two-dimensional modeling of a motile simple-shaped cell. *SIAM Multiscale Model. Simul.*, 3(2):413439, 2005.