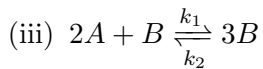
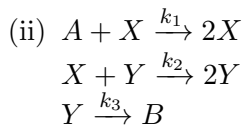
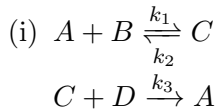


4G7 examples sheet 1

1 Mass action models from reaction schemes

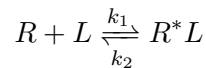
Write down ordinary differential equations (ODEs) corresponding to the following reaction schemes:



How many steady state solutions exist for reaction (iii)?

2 Activation-repression model

(i) Suppose a ligand, L , activates a receptor through binding:



where the states, R and R^* indicate the inactive and active form of the receptor, respectively. Show that if the reactions above occur rapidly, the level of receptor activity as a function of ligand concentration can be modelled as:

$$[R^*] = \frac{[L]}{K + [L]}$$

then show that if L **inhibits** the receptor we have:

$$[R^*] = \frac{K}{K + [L]}$$

.

(ii) Use the models in (i) to account for transcription factor activity in a model of mRNA production:

$$\dot{m} = \alpha - \beta m$$

For what range of values of the concentration of the transcription factor can mRNA production be considered constant?

3 Negative feedback regulation

Suppose a protein, p , is produced from mRNA, m , and that p inhibits its own transcription:

$$\begin{aligned}\dot{m} &= \frac{k_1}{k_2 + p} - \gamma_1 m \\ \dot{p} &= k_3 m - \gamma_2 p\end{aligned}$$

Show that this has a stable positive fixed point. What assumptions have been made about the interaction of the protein with transcriptional apparatus? How might you modify this model so that transcription depends on an external signal that is encoded in the concentration of another species, s , while retaining negative feedback regulation?

4 Sensitivity of negative autoregulation

The sensitivity of system/quantity A with respect to parameter/variable B is defined as:

$$S(A, B) := \frac{\partial A/A}{\partial B/B}.$$

Compute the sensitivity of the steady state level of an autoregulated species X whose rate of production is governed by:

$$\dot{X} = \frac{\alpha K^n}{K^n + X^n} - \beta X$$

with respect to the production rate coefficient, α .

5 Lotka model

In the 1920s Lotka proposed the reaction scheme in question 1(ii) as a candidate for a chemical oscillator. Sketch the flow field for this system assuming the concentration of A is fixed (hint: it may be useful to work in non-dimensional units).

At the time, Lotka's proposal was criticised for being unphysical because it appears to violate thermodynamics. What is the basis of this criticism? Can it be reconciled?

6 Toggle switch

Sketch the phase plane for the following reaction system:

$$\begin{aligned}\dot{x} &= \frac{k}{k + y^n} - \beta x \\ \dot{y} &= \frac{k}{k + x^n} - \beta y\end{aligned}$$

for values of $n = \{1, 2, 3\}$. Provide a qualitative description of how the number of equilibria vary as parameters k and β are varied. Explain why this system is a candidate for a molecular switch.

7 Linearisation, qualitative analysis of ODEs

The following model describes the rate of growth of the density of bacterial cells N in an environment with a concentration of nutrient, C :

$$\begin{aligned}\dot{N} &= \alpha \frac{C}{1+C} N - N \\ \dot{C} &= -\frac{C}{1+C} N - C + \eta\end{aligned}$$

- (i) Comment on the terms in this model and provide an interpretation of their meaning.
- (ii) Compute and classify the equilibria of the system by calculating the linearisation around each fixed point. Sketch the phase plane.

8 No limit cycles in linear systems

A *limit cycle* is a "stable" periodic solution, $\mathbf{x}(t)$, to an ODE system $\dot{\mathbf{x}} = \mathbf{f}(\mathbf{x})$ with the property that nearby solutions converge to the set $\{\mathbf{x}(\mathbf{t}) | \dot{\mathbf{x}}(\mathbf{t}) = \mathbf{f}(\mathbf{x})\}$ following small perturbations. In particular, the amplitude of a limit cycle oscillation is independent of initial conditions.

By making an appropriate sketch, show that a two dimensional linear dynamical system cannot contain limit cycles.

9 Solutions of the diffusion equation

The diffusion equation in one dimension is:

$$\frac{\partial p}{\partial t} = D \frac{\partial^2 p}{\partial x^2}.$$

- (i) Assume the solution is of the form $p(x, t) = T(t)X(x)$ and show that:

$$\frac{1}{DT(t)} \frac{\partial T}{\partial t} = \frac{1}{X(x)} \frac{\partial^2 X}{\partial x^2} \quad (1)$$

- (ii) Notice that the left and right hand sides of (1) depend only on time and location, respectively. For this equality to hold generally, both sides must therefore equal a constant. Call this constant λ^2 and find the general form of the solution, considering cases where λ^2 is positive as well as negative.

- (iii) How might the general form of solution in (ii) be used to solve the diffusion equation starting from a specified initial distribution for p , i.e. the boundary condition $p(x, 0) = p_{init}(x)$? (Hint: the answer involves Fourier series!)

10 Discrete random walk model of diffusion

Let the 1D location of a particle be x_t , where location is discretised into bins of width l and time is discretised as $t = 0, 1, 2, \dots$. Assume the particle starts at the origin at time $t = 0$ and that at each timestep it moves $x_{t+1} = x_t \pm l$ with equal probability. Calculate the expected value and variance of the location of the particle at an arbitrary time $t > 0$.