BM2053 Mathematical Models & Systems Biology

Problem Set 1

Instructions

1. You are not supposed to submit the solutions to these questions.
2. To get the most out of these, solve all the problems on your own.

Questions

1. For each of the following 1D systems, find all fixed points as a function of the parameter r, determine their stability, classify the bifurcation that occurs at $r = 0$, and sketch the bifurcation diagram (plot x^* vs. r, using solid lines for stable and dashed lines for unstable fixed points)

   (a) $\dot{x} = (x + 1)(r + 2x - x^2)$

   (b) $\dot{x} = r \ln(x) + x - 1$

   (c) $\dot{x} = e^{-x}(rx + x - x^3)$

   (d) $\dot{x} = \dfrac{r + x^2}{1 + x^2}$

   (e) $\dot{x} = rx - \tan^{-1}(x)$

2. Consider the system $\dot{x} = r + x - \ln(1 + x)$ defined for $x > -1$.

   (a) Find the critical value r_c at which a bifurcation occurs.

   (b) Classify the type of bifurcation.

   (c) Sketch the 1D phase line trajectories for $r < r_c$, $r = r_c$, and $r > r_c$.

3. Consider the 2D system

$$\dot{x} = y - ax$$
$$\dot{y} = \mu + x^2 - y$$

   (a) Show that the fixed points lie on a parabola in the (x, y) plane.

   (b) Determine the critical parameter value μ_c (in terms of a) where a saddle-node bifurcation occurs.

   (c) Construct the Jacobian matrix and verify the stability of the branches on either side of μ_c.

4. A system with imperfection parameter h is governed by $\dot{x} = h + rx - x^3$.

   (a) For $h = 0$, identify the bifurcation type at $r = 0$.

   (b) For $h \neq 0$, find the critical curve in the (r, h) parameter plane that separates regions with 1 fixed point from regions with more than one fixed points.

5. Consider a protein/gene concentration $g(t)$ regulated by an autoregulatory feedback loop with basal expression S and linear degradation at rate k_d

$$\frac{dg}{dt} = S + \frac{V_{max} g^2}{K_m^2 + g^2} - k_d g$$

   (a) Non-dimensionalize the equation. How many free parameters are there in this system?

   (b) Analyze the behavior of this system as the parameter S is changed.

(c) Sketch the bifurcation diagram.

6. Consider a single-variable reduction of a symmetric two-gene mutual inhibition network (where promoter expression is suppressed by repressor v)

$$\frac{du}{dt} = \frac{\alpha_1}{1+v^\beta} - u$$
$$\frac{dv}{dt} = \frac{\alpha_2}{1+u^\gamma} - v$$

Assume a symmetric system where $\alpha_1 = \alpha_2 = \alpha$ and $\beta = \gamma = 2$.

(a) Find the fixed point u^* corresponding to equal expression levels ($u^* = v^*$).

(b) Calculate the critical coupling strength α_c at which this symmetric fixed point loses stability via a pitchfork bifurcation, leading to two stable memory states (bistability).

(c) What is $\beta = \gamma = 1$

7. A biochemical signaling molecule S is produced at a constant background rate S_0 and consumed via an enzymatic reaction that exhibits substrate inhibition (e.g., substrate inhibition in phosphofructokinase kinetics)

$$\frac{dS}{dt} = S_0 - \frac{V_{max}S}{K_m + S + \frac{S^2}{K_i}}$$

(a) Define dimensionless variables $u = S/K_m$ and $\tau = \left(\frac{V_{max}}{K_m}\right) t$. Reduce the ODE to

$$\frac{du}{d\tau} = s_0 - \frac{u}{1+u+\kappa u^2}$$

Identify the dimensionless parameters s_0 and κ in terms of physical constants.

(b) Show that for a fixed parameter value of κ, as the synthesis rate s_0 increases, the system undergoes two saddle-node bifurcations.

(c) Sketch the steady-state substrate concentration u^* as a function of the production parameter s_0. Identify the regions of bistability and hysteresis.

8. Consider a gene regulator x that exhibits basal expression, non-linear positive self-regulation (cooperative auto-activation with Hill coefficient $n = 2$), and a quadratic clearance mechanism

$$\frac{dx}{dt} = rx + x^3 - x^5$$

(where r represents the net growth/basal activation parameter relative to natural linear degradation).

(a) Identify all fixed points x^* as a function of r.

(b) Determine the critical value r_c where a subcritical pitchfork bifurcation occurs at $x^* = 0$.

(c) Find the parameter range $r \in (r_1, r_c)$ where the system exhibits bistability between the origin $x^* = 0$ and two non-zero steady states.

(d) Sketch the full bifurcation diagram (x^* vs. r), using solid lines for stable states and dashed lines for unstable states.

9. A bacterial population $N(t)$ feeds on a nutrient supplied at a constant rate S_0. At high population densities, metabolic toxicity limits growth, modeled as

$$\frac{dN}{dt} = \mu N\left(1 - \frac{N}{K}\right) - \frac{\gamma N^2}{1+N^2}$$

(a) Define non-dimensional variables $x = N/K$ and $\tau = \mu t$ to rewrite the population dynamics in dimensionless form

$$\frac{dx}{d\tau} = x(1-x) - \frac{Rx^2}{A^2+x^2}$$

Express R and A in terms of μ, γ, and K.

(b) Assuming $A \ll 1$, show that varying the toxicity parameter R induces a saddle-node bifurcation that causes a sudden collapse (extinction) of the bacterial population.

(c) Determine the critical threshold R_c above which survival is no longer possible.