Math Tutorial
National Short Course in Systems Biology

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Topics

With a focus on **statistical methods**, **data mining**, and **machine learning**

Thursday: (covered by me)

- matlab tutorial
- intro to probability and statistics
- data analysis: clustering (k-means, hierarchical, EM) and PCA

Friday: (covered by Prof Alex Ihler)

- intro to machine learning
- regression methods
- classification methods: k-nearest neighbor, naive Bayes, decision tree, perceptron
- graphical models: hidden Markov models, Gaussian graphical models, Bayesian network

MATLAB tutorial

Exercise 1: logistic map

The logistic map is a polynomial mapping used to model population size in discrete time. It is mathematically written as

$$x_{n+1} = rx_n(1 - x_n)$$

where

- $x_n \in [0, 1]$ represents the population at year n (x_0 represents the initial population, at year 0)
- $r > 0$ represents a combined rate of reproduction and starvation

Exercise:

- Write a MATLAB function $f(r, x_0, n)$ to return the population values of the first n years with an initial value of x_0 and a fixed parameter r
- Plot and observe the dynamics of the population size for different choices of r:
  - $r = 0.5$
  - $r = 1.5$
  - $r = 2.5$
  - $r = 3.2$
  - $r = 4$

Exercise 2: recursion

Write a MATLAB function to implement:

$$f(x,k) = \sqrt{\sqrt{\cdots\sqrt{x}}}$$

where k is the number nested square roots.

Multistability

Consider the lysis-lysogeny switch model in phage lambda

$$\frac{dx}{dt} = \frac{\alpha x^2}{1 + (1 + \sigma_1)x^2 + \sigma_2 x^4} - \gamma x + 1$$

Exercise: choose $\alpha = 50, \gamma = 20, \sigma_1 = 1, \sigma_2 = 5$

- Write a matlab code to display the trajectory of x
- Try different initial conditions and observe the steady states of the system

Biological oscillators

Consider the following two coupled differential equations:

$$\dot{x} = -x + ay + x^2 Y$$
$$\dot{y} = b - ay - x^2 y$$

Exercise:

- Write down the fixed point of the system
- Determine the stability condition of the fixed point
- Implement a MATLAB code to display the trajectory of the states. Compare the behaviors of the system for different choices of a and b. In particular, can you find a stable limit cycle solution?

Biological oscillators (analysis)

Consider the following two coupled differential equations:

$$\dot{x} = -x + ay + x^2 Y$$
$$\dot{y} = b - ay - x^2 y$$

The nullclines are

$$y = \frac{x}{a + x^2} \quad y = \frac{b}{a + x^2}$$

There is only one fixed point $(x^*, y^*) = (b, \frac{b}{a+b^2})$. The condition for the fixed point to be stable is:

$$\Delta = a + b^2 > 0$$
$$\tau = -\frac{b^4 + (2a - 1)b^2 + (a + a^2)}{a + b^2} > 0$$

When these conditions are not satisfied, the system exhibits stable oscillations.

Reaction-diffusion equations

Consider the following reaction-diffusion system, often called the 'Turing-Gierer-Meinhardt theory',

$$\begin{aligned}\frac{\partial a}{\partial t} &= r_a + k_a \frac{a^2}{i} - \gamma_a a + D_a \frac{\partial^2 a}{\partial x^2} \\ \frac{\partial i}{\partial t} &= k_i a^2 - \gamma_i i + D_i \frac{\partial^2 i}{\partial x^2}\end{aligned}$$

where

- a and i are the concentrations of an activator and an inhibitor
- the activator is produced at a constant rate r_a
- the activator operates as a dimer while the inhibitor operates as a monomer
- γ_a and γ_i are first-oder decay parameters; D_a and D_i are diffusion constants

Reaction-diffusion equations: simplified

Choosing dimensionless variables yields

$$\begin{aligned}\frac{\partial A}{\partial \tau} &= 1 + R\frac{A^2}{I} - A + \frac{\partial^2 A}{\partial s^2}\\ \frac{\partial I}{\partial \tau} &= Q(A^2 - I) + P\frac{\partial^2 I}{\partial s^2}\end{aligned}$$

Exercise:

- Write down the spatially homogenous solution of the system
- Determine the stability condition of the spatially homogenous solution
- Implement a MATLAB code to display the trajectory of the states. Compare the behaviors of the system for different choices of R, P, Q.

Reaction-diffusion equations: analysis

Spatially homogeneous solutions:

$$\bar{A} = R + 1 \qquad \bar{I} = (R+1)^2$$

The stability matrix evaluated at the homogeneous solution is

$$\begin{bmatrix} \frac{2R\bar{A}}{\bar{I}} - 1 & -\frac{R\bar{A}^2}{\bar{I}^2} \\ 2\bar{A}Q & -Q \end{bmatrix} = \begin{bmatrix} \frac{R-1}{R+1} & -\frac{R}{(R+1)^2} \\ 2(R+1)Q & -Q \end{bmatrix}.$$

Thus the fixed point solution is stable only if

$$\frac{R-1}{R+1} < Q \qquad Q > 0$$

Reaction-diffusion equations: analysis (cont'd)

Spatially inhomogeneous solutions: Explore the stability of the system around the homogenous solutions. Let $A(s,\tau) = \bar{A} + A'(s,\tau)$, $I(s,\tau) = \bar{I} + I'(s,\tau)$. We have

$$\frac{\partial A'}{\partial \tau} = \frac{R-1}{R+1}A' - \frac{R}{(R+1)^2}I' + \frac{\partial^2 A'}{\partial s^2}$$
$$\frac{\partial I'}{\partial \tau} = 2Q(1+R)A' - QI' + P\frac{\partial^2 I}{\partial s^2}$$

Try the solution in the form of $A'(s,\tau) = \hat{A}(\tau)\cos(s/l)$, $I'(s,\tau) = \hat{I}(\tau)\cos(s/l)$. We have

$$\frac{d\hat{A}}{\partial \tau} = \left(\frac{R-1}{R+1} - \frac{1}{l^2}\right)\hat{A} - \frac{R}{(R+1)^2}\hat{I}$$
$$\frac{d\hat{I}}{\partial \tau} = 2Q(1+R)\hat{A} - (Q + \frac{P}{l^2})I'$$

This yields the stability condition:

$$\frac{Q}{P}l^4 + \left(\frac{Q}{P} - \frac{R-1}{R+1}\right)l^2 + 1 > 0$$

which is satisfied if $\frac{Q}{P} > \frac{R-1}{R+1}$.