

Some Basic Concepts in Analysis of Nonlinear Dynamical Systems

INRIA Grenoble - Rhône-Alpes and IBIS



- IBIS: systems biology group at INRIA/Université Joseph Fourier/CNRS
 - Analysis of bacterial regulatory networks by means of models and experiments
 - Biologists, computer scientists, mathematicians, physicists, ...

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Introduction

- Module on regulatory networks requires knowledge of basic concepts on nonlinear dynamical systems
- Aim of this course is to review these concepts by means of two-dimensional examples:
 - Steady states and stability
 - Limit cycles
 - Bifurcations

Strogatz, *Nonlinear Dynamics and Chaos*, Addison-Wesley, 1994

Steady states and stability

- Phase portrait

Phase space, vector field, trajectory, steady state, closed orbit, existence and uniqueness, ...

- Stability of steady states

Stability, asymptotic stability, ...

- Determination of stability

Jacobian matrix, linear system, characteristic equation, eigenvalues, classification of steady states, ...

- Phase portrait

Stable and unstable manifold, nullcline, basin of attraction, separatrix, ...

Lotke-Volterra model of competition

- Classical model used to describe competition between two species in population dynamics

Example: two species (e.g., rabbits and sheep) that are competing for the same food supply (e.g., grass)

- Lotke-Volterra model of competition

$$\dot{x} = r_1 x \left(1 - \frac{x}{k_1} - b_1 \frac{y}{k_1} \right)$$

$$\dot{y} = r_2 y \left(1 - \frac{y}{k_2} - b_2 \frac{x}{k_2} \right)$$

- $x, y \geq 0$: population sizes
- $r_1, r_2 \geq 0$: maximum growth rates
- $k_1, k_2 \geq 0$: carrying capacities
- $b_1, b_2 \geq 0$: competition parameters

Edelstein-Keshet, *Mathematical Models in Biology*, SIAM, 2005

Limit cycles and bifurcations

- Limit cycles
 - Stable and unstable limit cycles, ...
- Finding limit cycles
 - Poincare-Bendixson theorem, trapping region, ...

Glycolytic oscillations

- Glycolysis is fundamental biochemical process concerned with breakdown of carbon sources to yield energy and precursors of macromolecules
- In some species, under specific conditions, oscillations have been shown to occur

Goldbeter, *Biochemical Oscillations and Cellular Rhythms*, Cambridge University Press, 1997

- Minimal model of glycolytic oscillations

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

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

- $x, y \geq 0$: concentrations of adenosine diphosphate (ADP) and fructose-6-phosphate (F6P)
- $a, b \geq 0$: kinetic parameters

Sel'kov, *Eur. J. Biochem.*, 4:79-86, 1968

Bifurcations

- Bifurcations

Bifurcation, different types of bifurcation, ...

Auto-activation in gene regulation

- Proteins may activate expression of their own gene
Ubiquitous motif in gene regulatory networks, see later courses
- Classical model of auto-activation in gene expression

$$\dot{x} = -ax + y$$

$$\dot{y} = \frac{x^2}{1 + x^2} - by$$

- $x, y \geq 0$: concentrations of protein and mRNA
- $a, b \geq 0$: degradation parameters

Griffith, *Mathematical Neurobiology*, Academic Press, 1971

Merci

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