Mathematical Biology - Lecture 1 - general formulation

course description

Learning Outcomes

This course is aimed to be accessible both to masters students of biology who have a good understanding of the introductory course to mathematical modeling and to masters students in applied mathematics looking to broaden their application areas. The course extends the range of usage of mathematical models in biology, ecology and evolution. Biologically, the course looks at models in evolution, population genetics and biological invasions. Mathematically the course involves the application of multivariable calculus, ordinary differential equations, stochastic models and partial differential equations. In order to pass the course (grade 3) the student should be able to

•formulate and solve mathematical models of evolution in terms of optimization and game theory problems;
•use techniques from stochastic processes to describe population genetics;
•use techniques from partial differential equations to describe spread of genes, disease and other biological material;
•explain how these techniques are applied in scientific studies and applied in ecology and epidemiology.

course description

Content

•The use of mathematical models in biology, ecology and evolution. Several Variable Calculus, Ordinary Differential Equations, Stochastic Modelling, Partial Differential Equations.

The course will consist of some of the following sections:Evolutionary Invasion Analysis: introduction to game theory; concept of evolutionary stability; general technique for invasion analysis.Population genetics: Stochastic models of genetics; Genetic structure and selection in subdivided populations; Kin selection and limited dispersal.Diffusion in biology: Constructing diffusion models; diffusion as approximation of stochastic systems; biological waves; pattern formation and Turing bifurcations; Chemotaxis.Networks in biology: Spread of disease in contact networks; random graphs; moment closure techniques in complex graphs.

course description

- **Lecture 1**

course description - why mathematical biology? - some useful definitions - general formulation

- **Lecture 2**

diseases and epidemics

- **Lecture 3**

population growth, competition between species

- **Lecture 4**

regulatory and communication processes at the cellular and macroscopic level - separation of time scales

- **Lecture 5**

diffusion and propagation phenomena in biology

- **Lecture 6**

Evolutionary biology

- **Lab 1**

practice with matlab - symbolic and graphical tools - homework 1

- **Lab 2**

working on homework 1 - homework 2

- **Lab 3**

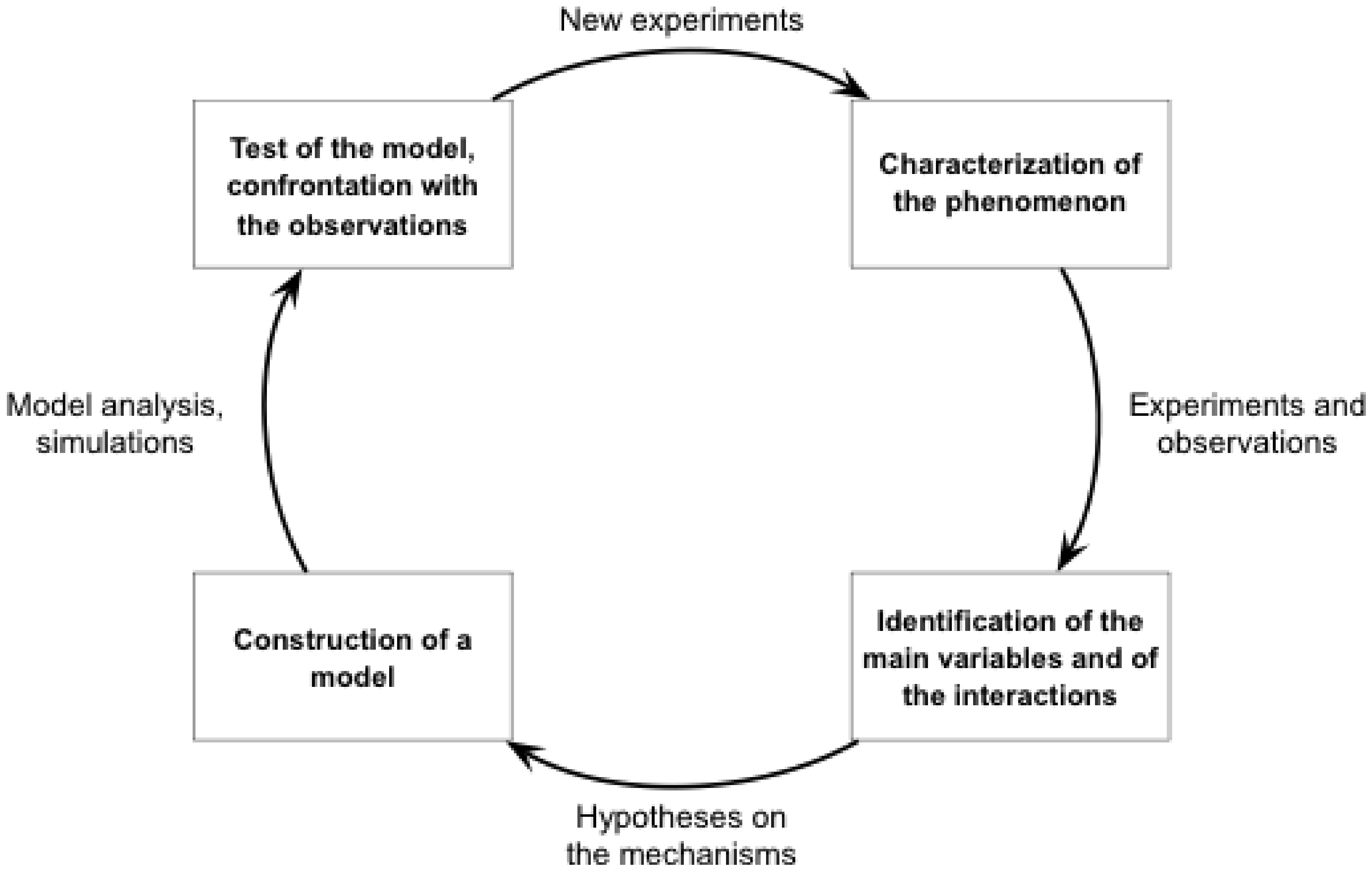
reading lab and practice lab about SIR models - handling homework 1

- **Lab 4**

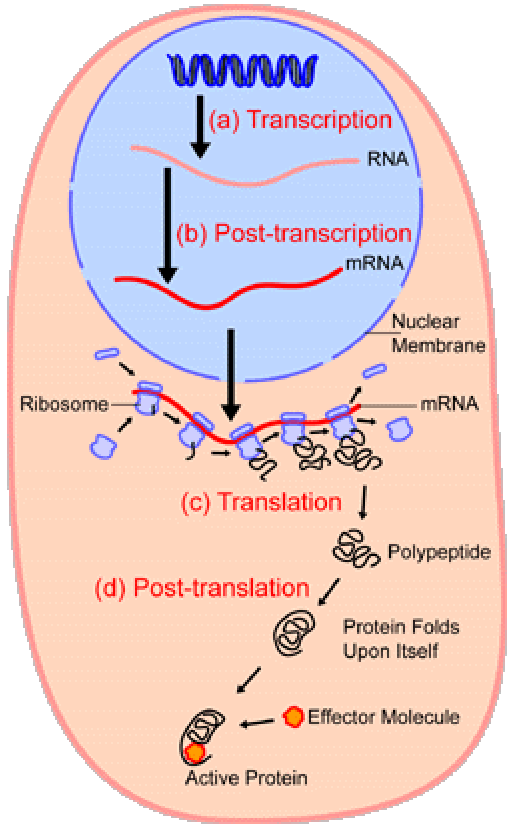
working on homework 2 - homework 3

why mathematical biology ?

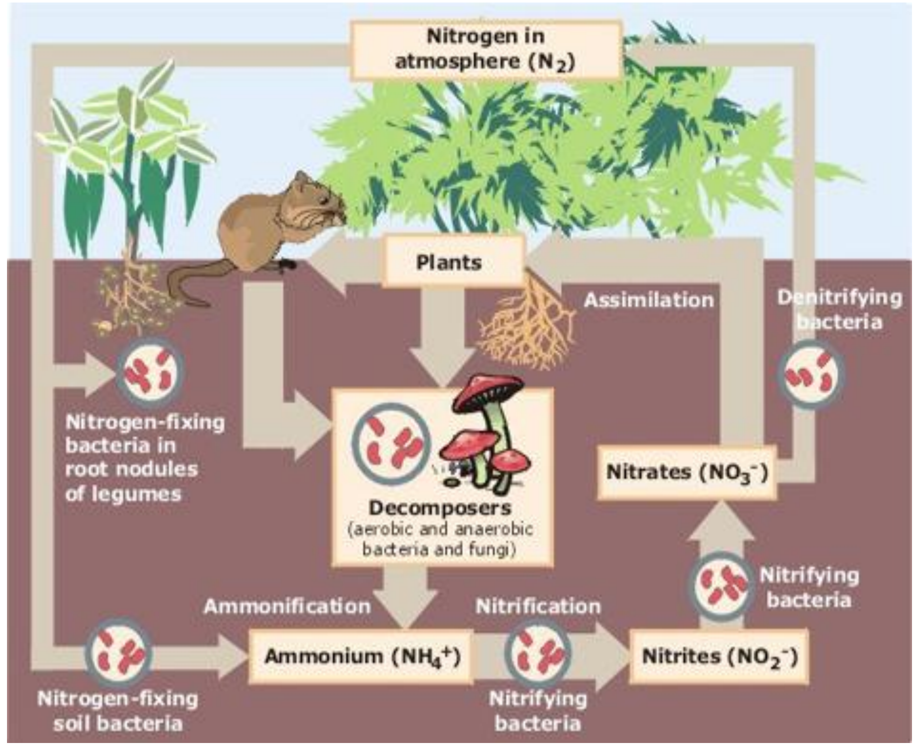
- formalize an understanding of the system
- make predictions about the system
- give ideas for new experiments
- make comparisons and analogies between different systems
- to understand “correctly”?



systems – micro and macro



what is the system?
a cell? an organ? a collection of organs?
the individual members of a species?
the entire species?
an ecosystem?
...



we will study systems and the system is the object of our interest
the tools we use depends on the nature and type of the system

a system is dynamical if it changes properties with time

dynamical systems, nonlinearity, self-organization, ...

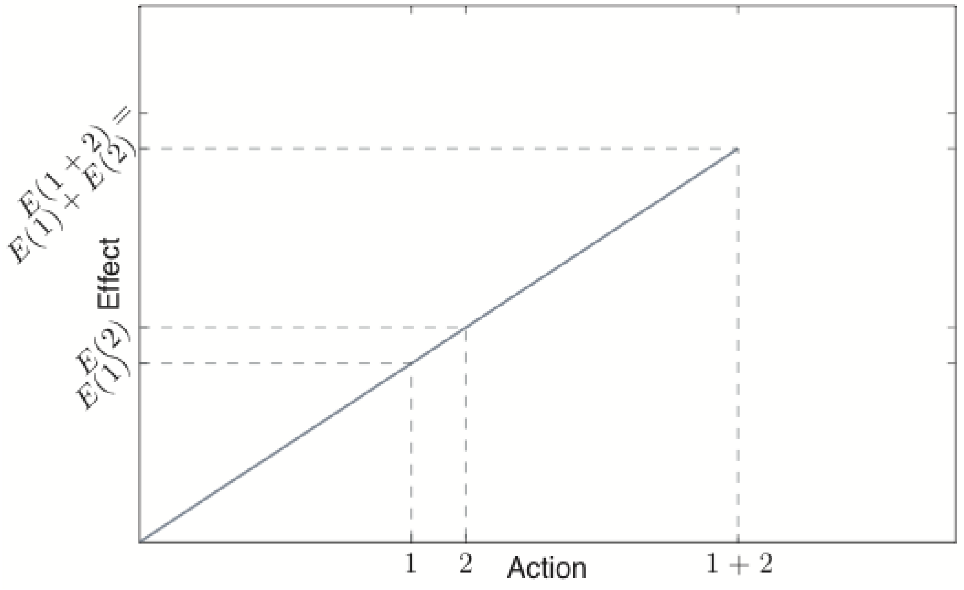
Dynamical system :

Properties of the solutions generated by a set of evolution equations.

linear perspective

➡system subjected to well-defined external conditions will follow a unique course

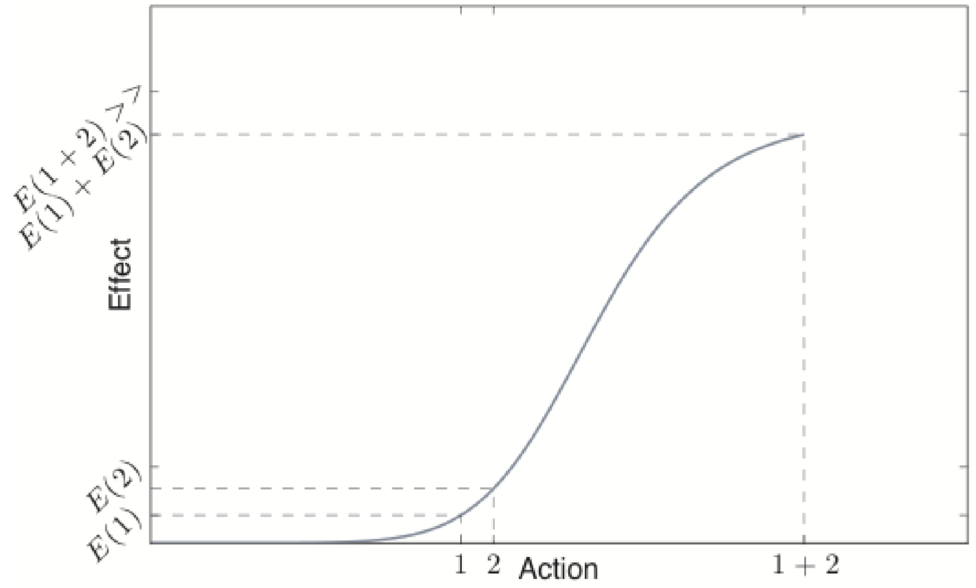
➡small change in conditions → slight change in the system's response.



nonlinear perspective

➡small causes may induce large effects.

➡new effects, unexpected structures and events



dynamical systems, nonlinearity, self-organization, ...

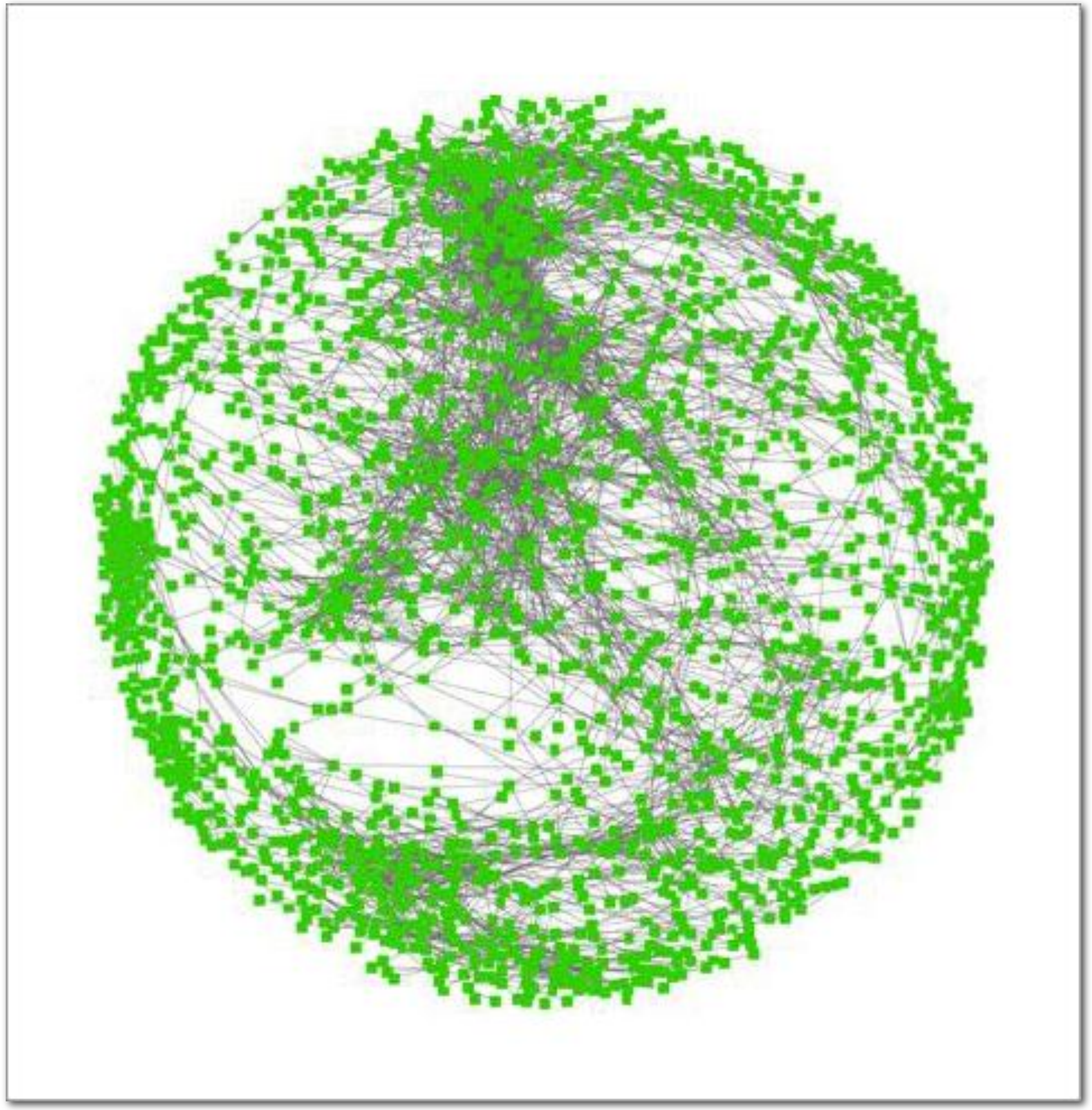
Self-organization
spontaneous emergence of spatial, temporal or functional order in systems subjected to constraints.

➡ this new paradigm emerged in the 50's and 60's.

opposition between the Newtonian deterministic and static point of view (**being**) and self-organising evolutionary (**becoming**) point of view. the idea that the dynamics of a system can tend, by itself, to make it more orderly, is very old. The first statement of it was by **René Descartes**, in the fifth part of his **Discours de la méthode**, where he presents it hypothetically, as something God could have arranged to happen, if He hadn't wanted to create everything Himself. Descartes elaborated on the idea at great length in a book called **Le Monde**, which he never published during his life.

some examples

Metabolic genes interactions



genetic network structure of central metabolic genes

- green nodes : genes
- links: genetic interaction. Short links = similar genetic information

some examples

Genetic information

DNA double helix

- identification of codes responsible of e.g., diseases

some examples

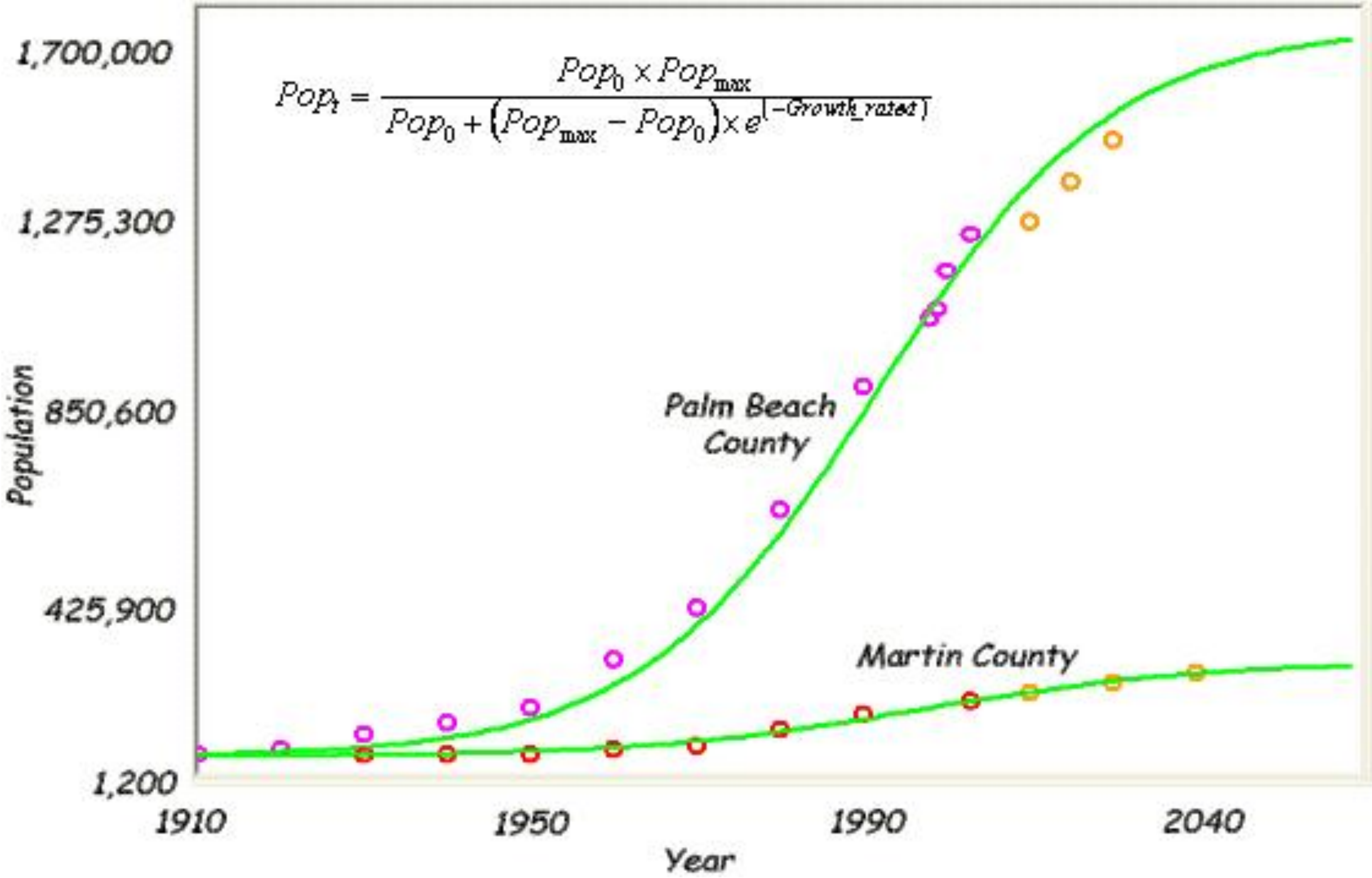
self-assembly, collective motion in fish schools

some examples

exploration patterns in ants, slime moulds building rail networks

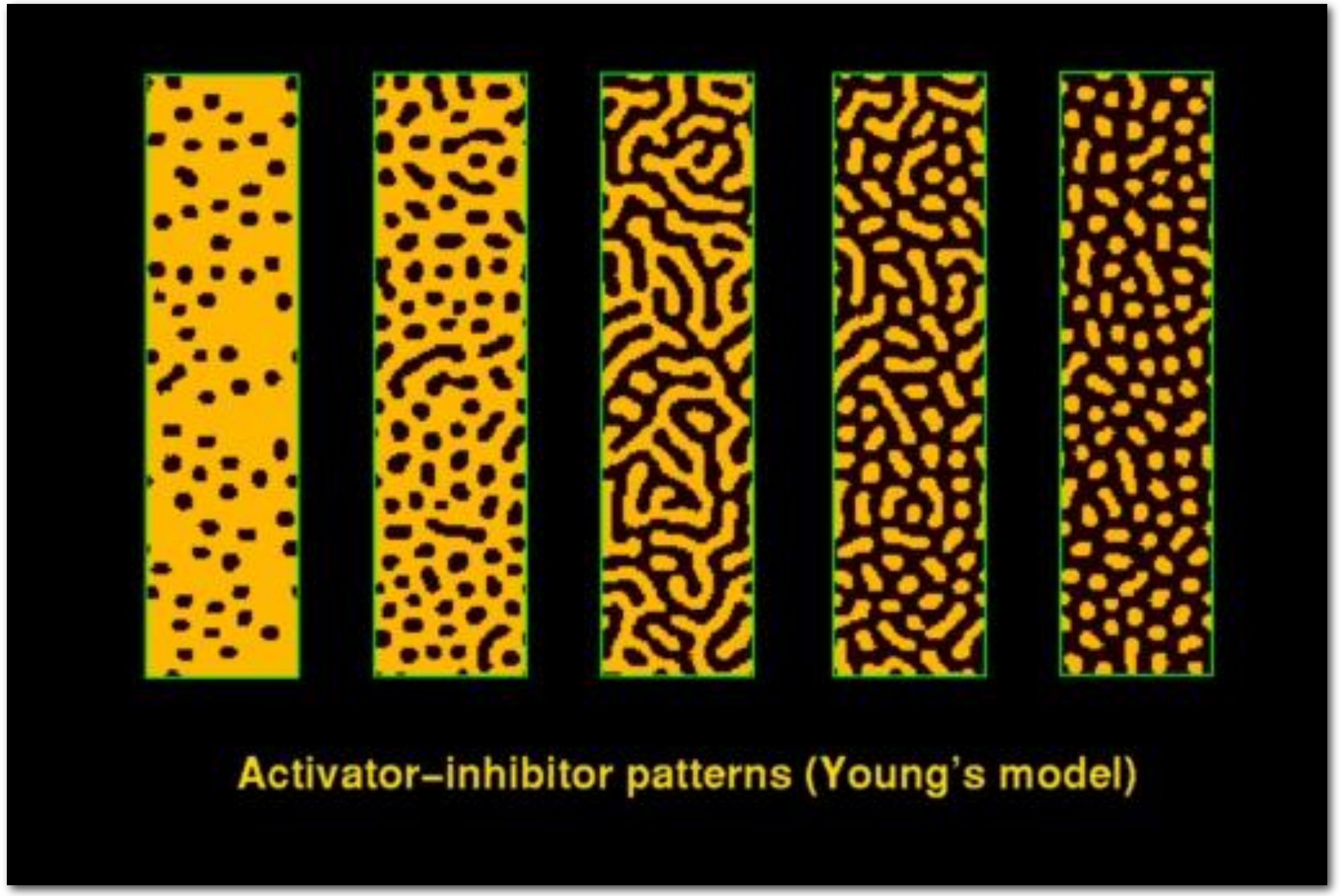
some examples

population growth



some examples

how the leopard got his (or her) spots



on time

dynamical systems change in time but how does time itself change?

all systems are continuous time but changes are not measurable at small intervals

discrete-time systems:

useful when describing events that are interesting only at periodic intervals, say generations

difference equations used: $x_{i,n+1} = x_{i,n} + f(x_{1,n}, \dots, x_{N,n})$

continuous-time systems:

differential equations used: $\frac{dX_i}{dt} = F_i(X_1, \dots X_n, \lambda)$

general formulation

useful notions

Balance equation

Equations describing the evolution laws of variables of interest. How these variables change in time ?

Steady-state

state of the system describing its final state, e.g., the variables reach a value that do not change on time anymore

Stability

response of a system to a perturbation removing it from its steady state

Asymptotic stability

the perturbation tends to zero as time goes to infinity

Phase space

abstract n-dimensional space spanned by all the variables describing the system

Invariant set

object embedded in the phase space that is mapped onto itself during the evolution generated by the evolution equations

Bifurcation diagram

diagram representing all the steady states of the system as a function of a single parameter

general formulation

Typical implementation

Evolution in the form of **Ordinary Differential Equations**

$$\frac{dX_i}{dt} = F_i\left(X_1, \ldots X_n, \lambda\right)$$

λ: parameters (e.g. birth rates)

In physics, there are many examples – in mechanics, the Hamiltonian equations describe the time evolution of a system of particles

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathbf{p}(t) = -\frac{\partial}{\partial \mathbf{q}}\mathcal{H}(\mathbf{q}(t), \mathbf{p}(t), t)$$

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathbf{q}(t) = +\frac{\partial}{\partial \mathbf{p}}\mathcal{H}(\mathbf{q}(t), \mathbf{p}(t), t)$$

Once H is specified as a function of p and q, we can set up the equations as ODEs. But even then this is an extremely difficult problem to solve.

Similar systems are studied in chemistry – rates of reactions depend on chemical concentrations and the balance (or master equation) is written down as a set of ODEs.

$$E + S \underset{k_r}{\overset{k_f}{\rightleftharpoons}} ES \xrightarrow{k_{\text{cat}}} E + P$$

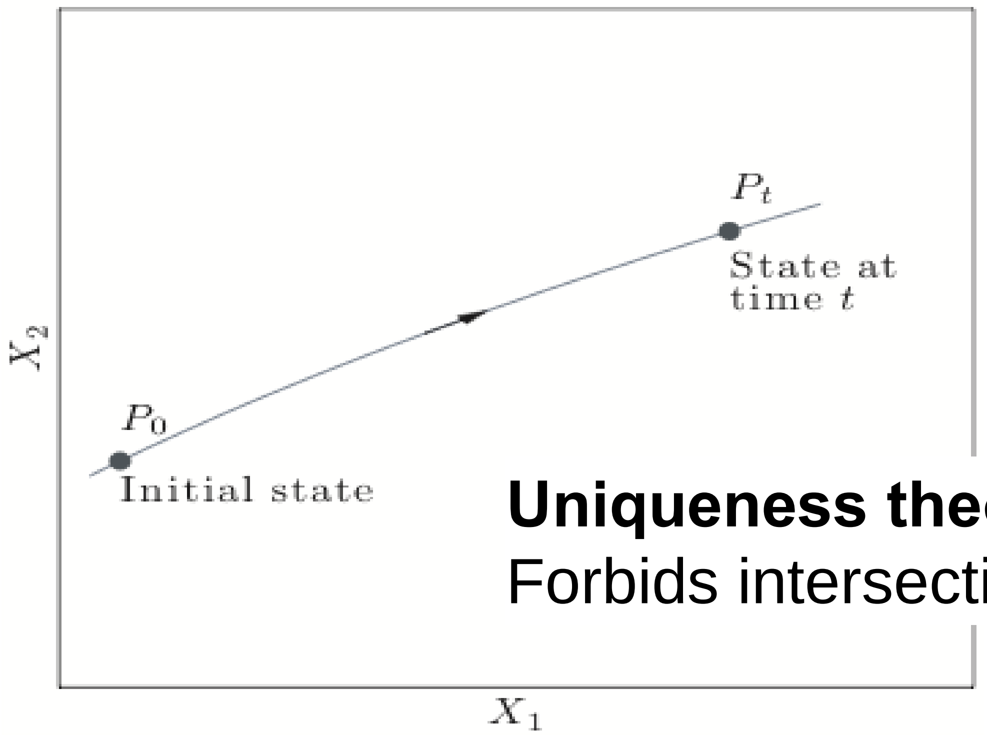
$$\begin{aligned}
d[S]/dt &= -\ k_f[E][S] + k_r[ES] \\
d[E]/dt &= -\ k_f[E][S] + k_r[ES] + k_{\text{cat}}[ES] \\
d[ES]/dt &= +\ k_f[E][S] - k_r[ES] - k_{\text{cat}}[ES] \\
d[P]/dt &= \qquad\qquad\qquad\qquad\quad + k_{\text{cat}}[ES]
\end{aligned}$$

general formulation

Phase space

Most natural systems do not have analytic solutions.

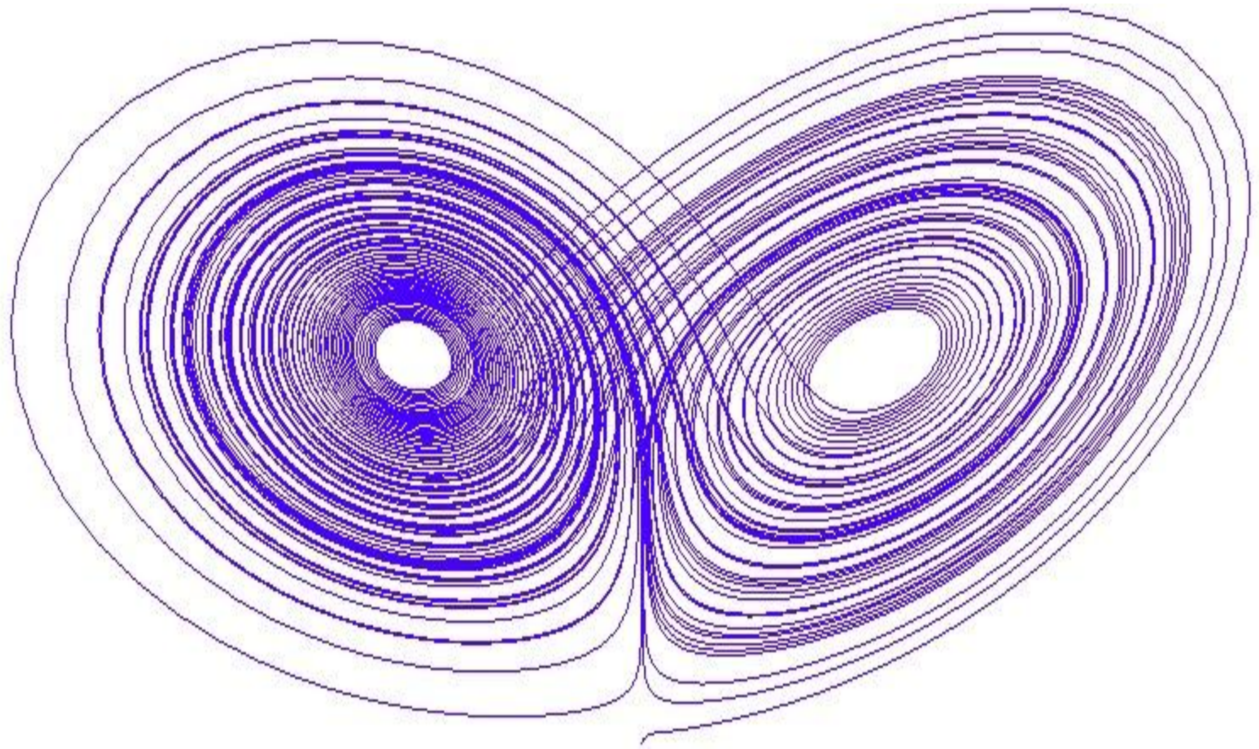
To understand the characteristics of the system we then take a geometric view to get a feel for how the system evolves.



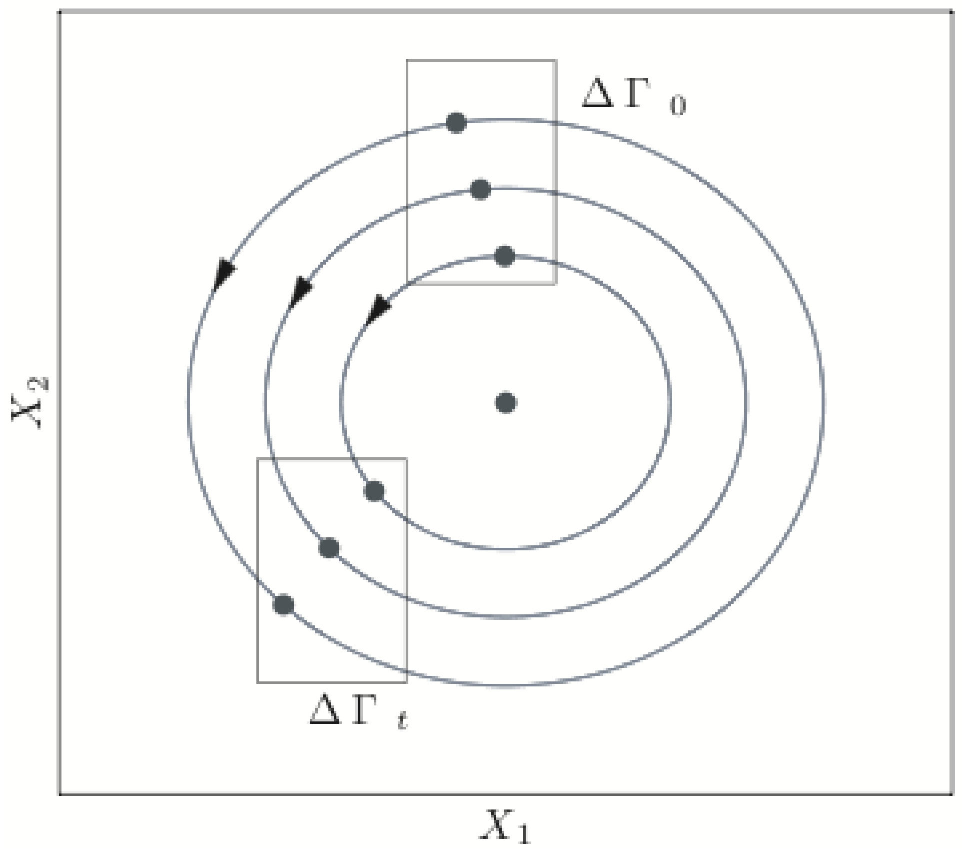
Uniqueness theorem.
Forbids intersection of trajectories

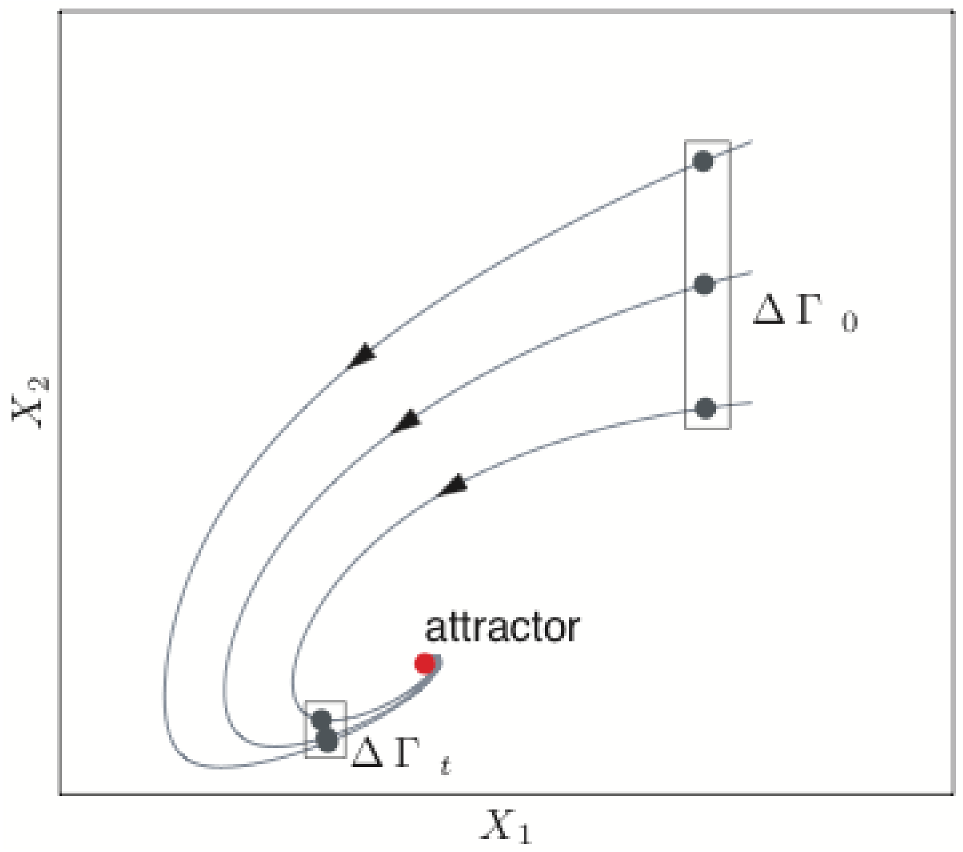
Invariant sets

- **0-d** : fixed points solution of F_i representing physically the steady-states of the system
- **1-d** : closed curves, representing a periodic behaviour
- **higher dimension** : Tori (quasi-periodic behaviour), Fractals (chaotic behaviour)



Conservative and dissipative systems, attractors





Conservative system : $|\Delta\Gamma_0| = |\Delta\Gamma_t|$.

Dissipative system : $|\Delta\Gamma_t| < |\Delta\Gamma_0|$ (for sufficiently long times)

general formulation

Stability

Response to a perturbation removing the system from an initial "reference" set s

$$X_i\left(t\right) = X_{i,s} + \delta x_i\left(t\right)$$

- Stability : system remains in a neighborhood of $X_{i,s}$
- Assymptotic stability: $\delta x_i\left(t\right) \to 0$ as $t \to \infty$

Self-organization viewed as a problem of loss of stability of the "trivial" states (e.g., the fixed points) and evolution towards more intricate attractors.

general formulation

Stability

$$\frac{dX_i}{dt} = F_i\left(\{X_j\}, \lambda\right) \qquad j = 1, ...n$$

- Search for reference state, usually among the steady states

$$F_i\left(\{X_{j,s}\}, \lambda\right) = 0$$

- Linearize around $\{X_{j,s}\}$

$$X_j = X_{j,s} + \delta x_j \qquad \frac{d\delta x_i}{dt} = \sum_j \left(\frac{\partial F_i}{\partial X_j}\right)_s \delta x_j$$

$$\text{Solution in the form}$$
$$\delta x_i = u_i \mathrm{e}^{\omega_\alpha t}$$

- Determine the eigenvalues ω_α $(\alpha = 1, ...n)$ of the operator (Jacobian matrix)

$$\underset{\approx}{J} = \left(\frac{\partial F_i}{\partial X_j}\right)_s$$

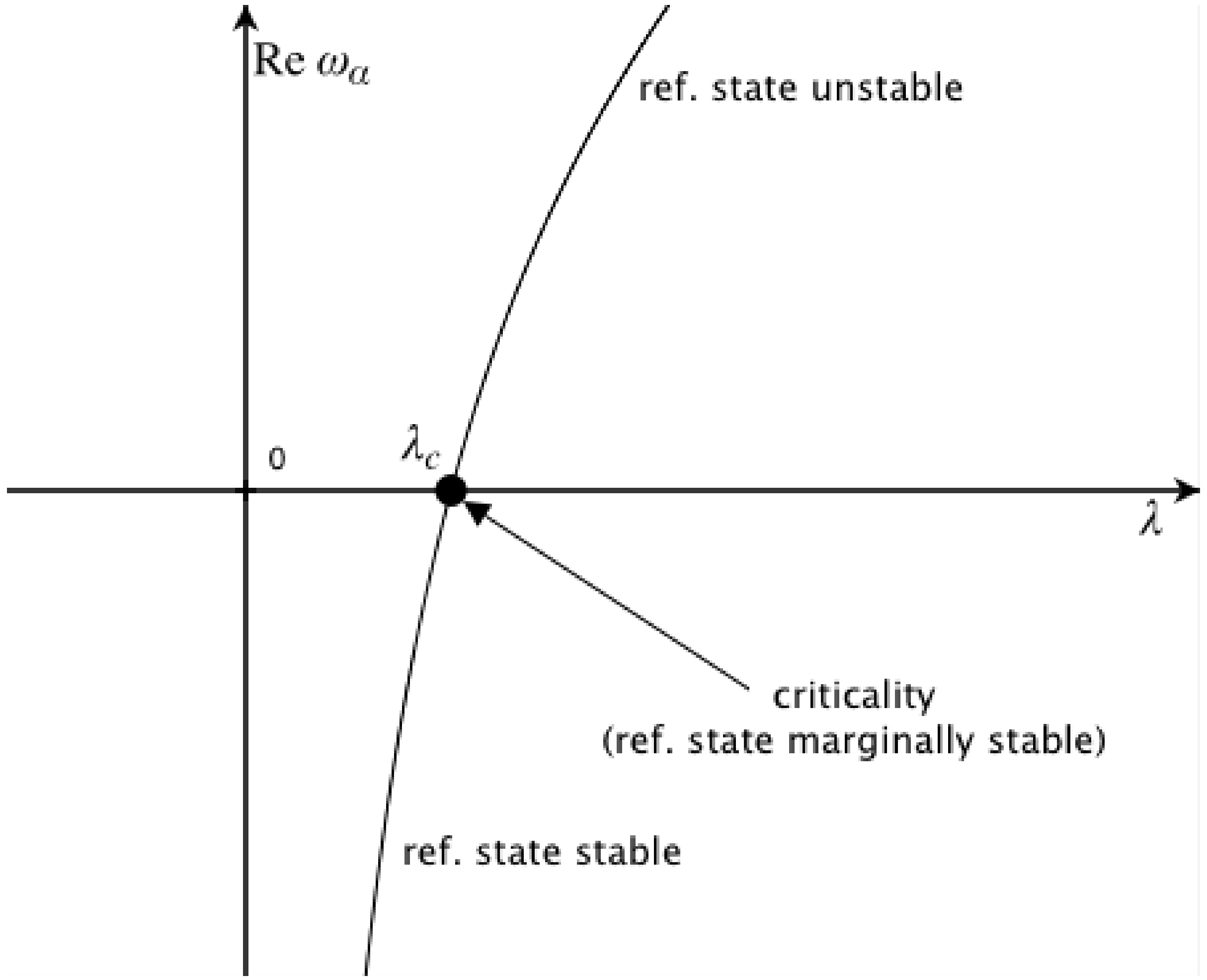
as roots of the characteristic equation det $\left|\left(\frac{\partial F_i}{\partial X_j}\right)_s - \omega \delta_{ij}^{\mathrm{kr}}\right| = 0$

general formulation

Stability

Parameter values λ_c at which the real part of one of the ω_α's changes sign:

$$\mathrm{Re}\ \omega_\alpha\left(\lambda_c\right) = 0$$



Bifurcation

Parameter λ_c beyond which the steady state X_{is} becomes unstable :

new solutions can emerge

general formulation

Exercise :

Find the steady-states, compute the stability analysis and sketch the bifurcation diagram of this equation

$$\frac{dX}{dt} = \alpha X - \beta X^3$$