Freie Universität Berlin

Fachbereich Mathematik und Informatik

Origins of Parasitism

(Likelihood, parsimony and other algorithms for ancectral state reconstruction)

Version 1

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Inhaltsverzeichnis

1 Introduction

Lecture 1. (21.4.17)

Related to computational systems biology
Molecular biology

- Biological macromolecules
- Macromolecular interactions
- Pathways, networks, systems

(Subfields: pathway informatics, systems informatics)

Definition 1. Systems biology: Understand how components of a biological system interact to perform complex biological function.

Challenges:

- Different levels of complexity
    - Many components, huge amount of data, non-trivial interactions
- Intuitive reasoning not sufficient
- Need for mathematical and computational models and tools

$\rightarrow$ Predictive biology
Research cycle TODO: Research cycle...

Network topology

- Graph-based modeling
- Stoichiometric / constaint-based modeling

Network dynamics

- Continuous modeling
- Discrete modeling
- Stochastic modeling
- Hybrid modeling

Important issues

- Abstraction vs. precision
- Quantitative vs. qualitative
- Determinisitc vy. Non-deterministic

Outline

i) Continuous models

ii) Discrete models

iii) Constraint-based models

iv) Stochastic and hybrid models

2 Chemical kinetics

Lecture 2. (21.4.17)

2.1 Modeling simple reactions

$X, Y, \ldots$ chemical species
$x(t), y(t), \ldots$ concentrations
$\dot{x} = \dot{x}(t) = \frac{\mathrm{d}x}{\mathrm{d}t}(t)$
Modeling assumption: Reaction rate is propotional to the product of the reaction concentrations.
Decay: $X - k- > ;\dot{x} = -kx$ (1)
Transformation: $X - k- > Y, \dot{x} = -kx, \dot{y} = kx$ (2)
Dissociation: $Z - k- > X + Y, \dot{z} = -kz, \dot{x} = kz, \dot{y} = kz$
Biomolecular reaction: $X + Y - k- > Z, \dot{z} = kxy, \dot{x} = -kxy = \dot{y}$ (z is a biolinear function, because it is linear in x and y)
Reversible reaction: $X + Y < -k^-, k^+- > Z, \dot{z} = k^+xy - k^-z, \dot{x} = k^-z - k^+xy = \dot{y}$
Dimerization: $X + X < - \ldots - > Y[2X < - > Y]$
$\dot{x} = -2k^+x^2 + 2k^-y$
$\dot{y} = -k^+x^2 - k^-y$
*k stands for kinetic parameter

2.2 Chemical reaction networks

Lecture 3. (24.4.17)

Example 1. $n_S = 3$ species: $S_1 = H, S_2 = 0, S_3 = H_2O$

$n_r = 2$ reactions: $R_1 : \underbrace{2H}_{\alpha_1 1} + \underbrace{O}_{\alpha_2 1} \longrightarrow \underbrace{H_2O}_{\beta_3 1}$ $R_2 : \underbrace{H_2O}_{\alpha_3 2} \underbrace{2H}_{\beta_1 2} + \underbrace{O}_{\beta_2 2}$ $\Gamma = \begin{array}{c c} & \begin{array}{cc} R_1 & R_2 \end{array} \\ \begin{array}{c} H \\ O \\ H_2O \end{array} & \begin{pmatrix} -2 & +2 \\ -1 & +1 \\ +1 & -1 \end{pmatrix} \end{array} = \begin{pmatrix} k_1[H]^2[O] \\ k_2[H_2O] \end{pmatrix}$

$S(t) = \begin{pmatrix} S_1(t) \\ S_2(t) \\ S_3(t) \end{pmatrix} = \begin{pmatrix} [H] \\ [O] \\ [H_2O] \end{pmatrix}$
$R_1(S) = k_1[H] * [H] * [O] = [H]^2[O]$
$R_2(S) = k_2[H_2O]$
...
$\frac{\mathrm{d}S}{\mathrm{d}t} = \Gamma * R(S)$ $\frac{\mathrm{d}[H]}{\mathrm{d}t} = -2k_1[H]^2[O] + 2k_2[H_2O]$
$\frac{\mathrm{d}[O]}{\mathrm{d}t} = -k_1[H]^2[O] + k_2[H_2O]$
$\frac{\mathrm{d}[H_2O]}{\mathrm{d}t} = k_1[H]^2[O] - k_2[H_2O]$

bis Folie 2008...

Example 2. $\dot{x} = -kx, x(0) = 1(\dot{x}(t) = -kx(t))$
$n = 1$:
Assume $k = -2$ TODO: picture
$n = 2$:
$\dot{x}_1 = x_1 + x_2$ $\dot{x}_2 = x_1 - x_2$ $x(0) = (11)$

Example 3. TODO: example via computation... see programm

Lecture 4. (24.4.17)

2.2.1 Phase space

Autonomous equation $\dot{x} = f(x)$, with $x \in D \subseteq \mathbb{R}^n$.
D is called **phase space**.
$x(t) = (x1(t), \ldots, xn(t))$ is called **phase point**.
When t varies, x(t) will move through phase space **trajectory** / **orbit**
$f(x)$ can be interpreted as velocity vector.
If the existence and uniqueness theorem applies, trajectories in phase space never intersect.

2.2.2 Steady states

Nullcline: $N_i = x \in D | \dot{x}_i = f_i(x) = 0$, for $i = 1, \ldots, n$.
A point $a \in D$ with $f(a) = 0$ (i.e., $f_i(a) = \dot{x}_i = 0, \forall i = 1, \ldots, n$) is called a **critical/singular/equilibrium point** or a **steady state**.
It corresponds to the **equilibrium** or **stationary solution** $x(t) = a, \forall t$.
It follows from the existence and uniqueness theorem that a steady state can never be reached from outside in finite time (otherwise two solutions would intersect).

2.2.3 Attractors and periodic solutions

A critical point $x = a$ of the equation $\dot{x} = f(x)$ is called a **positive attractor** if there exists a neighborhood $\omega a \subseteq \mathbb{R}^n$ of a such that $x(0) \in \Omega a implies lim_{t \to \infty} x(t) = a$.
If this property holds for $t \to -\infty$, then $x = a$ is called a **negative attractor**.
A solution $x(t)$ of $\dot{x} = f(x)$ is called **periodic** if there exists $T > 0$ such that $x(t + T) = x(t), \forall t \in \mathbb{R}$.

Lemma 1. Periodic solutions correspond to closed trajectories in phase space and vice versa.

A **limit cycle** is an isolated closed trajectory. **Isolated** means that neighboring trajectories are not closed; they spiral either toward or away from the limit cycle.
TODO: picture 8