State transition models of biomolecular dynamics

A few research questions

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Overview

State transition dynamics: basic concepts

- **state transition (ST) dynamics**: (S, q)
  - S : (discrete) **state space**
  - $q : S \to \mathcal{P}(S)$: [total] transition **dynamics**
  - $\mathbf{x} \to \mathbf{y} \stackrel{def}{=} \mathbf{y} \in \mathbf{q}(\mathbf{x})$: (binary) transition relation
  - $q(X) \stackrel{def}{=} \bigcup_{s \in X} q(s)$: extension to **quasistates** $X \subseteq S$
- **orbit** : $(X_i | i \in \mathbb{N})$ t.c. $\forall i.\ X_{i+1} = q(X_i)$
- **eventually periodic** orbit of origin X :
  $\exists k \geq 0\ \exists n > 0.\ q^{k+n}(X) = q^k(X)$ (**periodic** orbit if $k = 0$)
- orbit **(eventually) included** in another one: $(\exists i \geq 0.) \forall j (\geq i) X_j \subseteq X'_j$
- **basin** B : $\emptyset \neq B \subseteq S$ s.t. $q(B) \subseteq B$
- s**-trajectory** : $\xi : \mathbb{N} \to S$ s.t. $\xi(0) = s$ and $\forall i \geq 0.\ \xi(i) \to \xi(i+1)$
- s**-flight** $\stackrel{def}{=}$ **injective** s**-trajectory**

Deterministic ST dynamics: recurrence, attractors

Classical dynamics concepts:
attracting set, recurrence, attractor

- take **two distinct modal flavours** in the general, nondeterministic case, see [(Manca *et al.*, 2005), (Scollo *et al.*, 2006)]
- no modal difference in the **deterministic case** (where the concepts of orbit and trajectory practically coincide):

- state x is **recurrent** if $x \in q^n(x)$ for some $n > 0$
- an **attracting set** A of a basin B is a nonempty subset of B s.t.
  $\forall x \in B\ \exists k \in \mathbb{N} :\ \forall n \geq k\ \ q^n(x) \subseteq A$
- the **attractor** of a basin B is a minimal attracting set of B (under inclusion)
- the attractor of a basin B exists iff B has no flights
- when the attractor of B exists, it is the set of recurrent states in B

ST dynamics: a contrived example

a simple model of epidemic propagation

as well as of unstable catalythic reaction:

$CG \longrightarrow GG$

$C \longrightarrow C$

$G \longrightarrow \lambda$

$G \longrightarrow K$

$G \longrightarrow G$

- **instability** of agent G: it either dies or recovers (becoming immune: K)
- **states** : $(|C|+|K|, |G|)$
- **transitions** can be determined by equipping rules with a measure of **relative strength**

P systems: basic concepts

P systems: a computational model based on

- **multiset rewriting rules**
- workspace **compartmentalization**

- *biological counterparts*:
  - **biochemical reactions**
  - **membranes**
- evolution strategies in (variants of) P systems:
  - **maximal parallelism**, usually
  - or some other **fixed** strategy
- this is **inadequate** to model most biological phenomena: evolution depends on the state, so strategy may **change**

Metabolic P systems

a possible way out: **metabolic** P systems [(Bianco *et al.*, 2006a), (Bianco *et al.*, 2006b), (Manca, 2006)]:

- **metabolic rules**: multiset rewriting rules equipped with **reaction maps**:

  real-valued functions of the system state, that tell the **competitive strength** of each metabolic rule
- each metabolic rule:
  - **consumes** finite amounts of those biochemical resources whose **types** occur in the **pattern** (the lhs)
  - **produces** corresponding amounts of biochemical resources according to its rhs

P metabolic algorithm

generalizing Avogadro's molar units:

- only finite amounts of biochemical resources are available: their allocation to rules obeys a **mass partition principle**, where each rule gets an amount of each needed resource that is an integer multiple of the rule's **reaction unit**
- the latter depends on the reaction map and on the number of occurrences of resource types in the pattern
- **PMA** [(Manca, 2006)] is the simple algorithm that, at each state, computes the resource allocation to metabolic rules according to their reaction maps and reaction units

Research questions: state transition dynamics

Moving from structureless to topological state spaces:

- definability of **weaker** notions of **recurrence**

  that is: replace **exact** occurrence of a state in its own trajectory with **approximate** occurrence

- definability of **weaker** notions of **attraction**

  that is: replace **exact** inclusion of orbits in the attracting set with **approximate** inclusion

- **generalization** of the characterization results obtained in [(Scollo *et al.*, 2006)], linking recurrence and attractors, under the aforementioned weakings

  at least for the **deterministic case**

Research questions: metabolic P system models

two levels in metabolic P system modeling of biochemical dynamics:

- **stoichiometry:** the metabolic rules
- **regulation:** the reaction maps

- basic question (roughly): **how to get those models. . .**

  . . . for a given biochemical behaviour?
  This is the general **simulation problem**

- easier (?) question: assume the rules are given, how to get their **reaction maps?**

  This may be called the **regulation problem**

- even easier (??) question: assumes the rules are given and the **form** of reaction maps is nown (polynomial, say), how to get the values of their **unknown parameters** (the coefficients, say)?

  This may be called the **tuning problem**

- an instructive case study:
  Goldbeter' s model of mitotic oscillation in early amphibian embryos

State transition dynamics


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Metabolic P systems


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