Large deviations theory for chemical reaction networks

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Chemical reaction networks

A chemical reaction network $(\mathcal{S}, \mathcal{C}, \mathcal{R})$ is defined by the sets

- $\mathcal{S} = \{s_1, s_2, \ldots, s_d\}$ of chemical species,
- $\mathcal{R} = \{r_1, r_2, \ldots, r_m\}$ of chemical reactions,
- $\mathcal{C} = \bigcup_{r \in \mathcal{R}} \{c^r_{\mathrm{in}}, c^r_{\mathrm{out}}\}$ of chemical complexes.

Example (Musterbeispiel):

$$\emptyset \xrightarrow{r_1} A + B \xrightarrow{r_2} 2B \xrightarrow{r_3} A$$

- $\mathcal{S} = \{A, B\}$
- $\mathcal{R} = \{r_1, r_2, r_3\}$
- $\mathcal{C} = \{\emptyset, \{A + B\}, \{2B\}, \{A\}\} = \{(0,0), (1,1), (0,2), (1,0)\}$

The model: deterministic dynamics

Deterministic dynamics given by solution $x(t)$ solving

$$\frac{\mathrm{d}x}{\mathrm{d}t} = \sum_{r \in \mathcal{R}} \lambda_r(x) c^r \qquad \text{with} \qquad x(0) = x_0 \ ,$$

With possible *transitions* (jumps) and *reaction rates*

$$c^r := c^r_{\mathrm{out}} - c^r_{\mathrm{in}} \qquad \text{and} \qquad \lambda_r(x) := k_r \prod_{i=1}^{d} x_i^{(c^r_{\mathrm{in}})_i}$$

For example, for $\emptyset \rightharpoonup^{\mathrm{r}_1} A + B \rightharpoonup^{\mathrm{r}_2} 2B \rightharpoonup^{\mathrm{r}_3} A$ we have

$$c^{r_2} = \begin{pmatrix} 0 \\ 2 \end{pmatrix} - \begin{pmatrix} 1 \\ 1 \end{pmatrix} = \begin{pmatrix} -1 \\ 1 \end{pmatrix} \qquad \text{and} \qquad \lambda_{r_2}(x) = k_2 x_A x_B \ .$$

The model: stochastic dynamics

$$\emptyset \xrightarrow{r_1} A + B \xrightarrow{r_2} 2B \xrightarrow{r_3} A$$

We study the evolution of

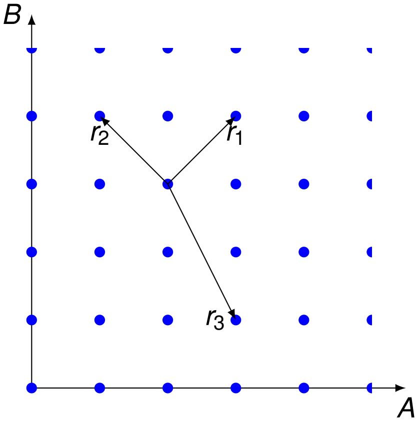
$$N_t \in (\mathbb{N}_0)^d \ ,$$

with reaction rates

$$\Lambda_r(N) = k_r \prod_{i=1}^{d} \binom{N_i}{(c^r_{\mathrm{in}})_i} (c^r_{\mathrm{in}})_i! \ ,$$

where $k_r > 0$ (mass action), *e.g.* ,

$$\Lambda_{r_2}(N) = k_2 N_A N_B$$



The model: scaling

$$\emptyset \xrightarrow{r_1} A + B \xrightarrow{r_2} 2B \xrightarrow{r_3} A$$

For a fixed volume v we define

$$X_t^v = v^{-1} N_t \in (v^{-1}\mathbb{N}_0)^d \ ,$$

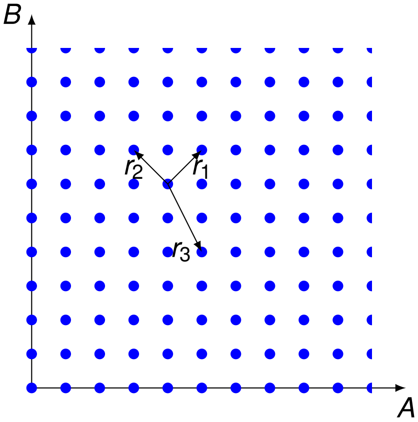
and rescale

$$c^r \to v^{-1} c^r \text{ and } \Lambda_r(N) \to v\Lambda_r^v(x) \ ,$$

where

$$\Lambda_r^v(x) = \frac{k_r}{v^{\|c\|_1}} \prod_{i=1}^{d} \binom{v x_i}{(c_{\mathrm{in}}^r)_i} (c_{\mathrm{in}}^r)_i!$$

$$\approx k_r \prod_{i=1}^{d} x_i^{(c_{\mathrm{in}}^r)_i} = \lambda_r(x) \ ,$$



Law of Large Numbers scaling

The generator of the scaled process is

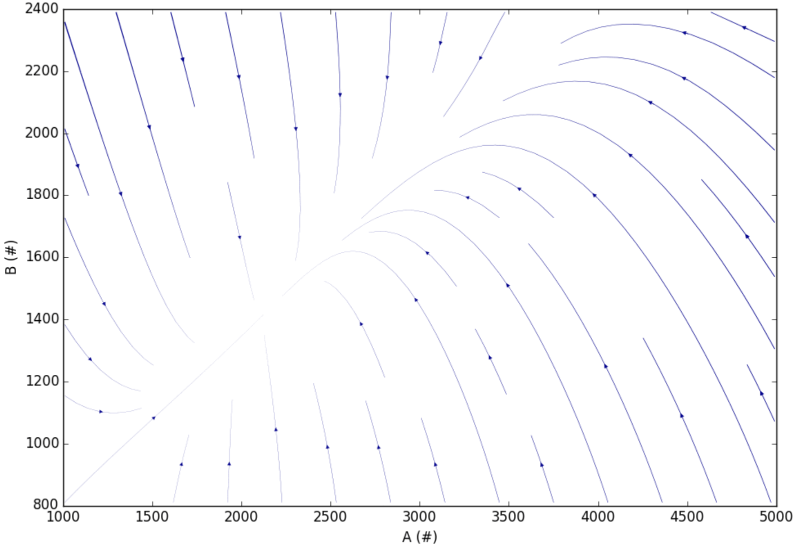
$$\mathcal{L}_v f(x) := v \sum_{r \in \mathcal{R}} \Lambda_r^v(x) \left(f(x - v^{-1} c^r) - f(x) \right) .$$

The paths of X_t^v converge, for $v \to \infty$ and $X_0^v \to x_0$, to $x(t)$ solving

$$\frac{\mathrm{d}x}{\mathrm{d}t} = \sum_{r \in \mathcal{R}} \lambda_r(x) c^r \qquad \text{with} \qquad x(0) = x_0 \ ,$$

The set of deterministic trajectories is also called *fluid limit* [**?**].

Fluid limit



2400
2200
2000
1800
1600
1400
1200
1000
800
B (#)
1000
1500
2000
2500
3000
3500
4000
4500
5000
A (#)

Nonequilibrium quasi-potentials

For a path $z \in AC_{0,T}(\mathbb{R}^d_+)$ define the Lagrangian and the cost function

$$L(z, z') := \sup_{\theta \in \mathbb{R}^d} \left[\theta \cdot z' - \sum_{r \in \mathcal{R}} \lambda_r(z) \left(e^{\theta \cdot c^r} - 1 \right) \right] ,$$

$$I_{0,T}(z) := \int_0^T L\left(z(s), z'(s)\right) \mathrm{d}s .$$

Then, the *quasi-potential* in a set $D \subset \mathbb{R}^d_+$ between $x, y \in D$ is

$$\mathcal{V}_D(x, y) := \inf_{t \geq 0} \inf_{\substack{z(0)=x, z(t)=y, \\ z(s) \in D \text{ for } 0<s<t}} I_{0,t}(z) .$$

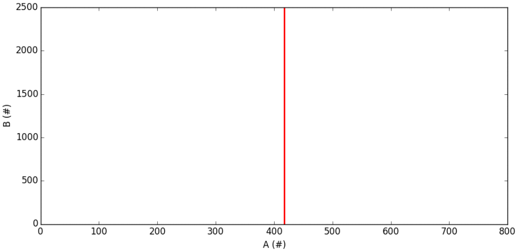
This defines a notion of distance in the set of attractors.

Exit times I

Theorem ([**?**])

Let Π *be the unique, globally attractive* ω*-limit set of the compact* $D \subset \mathbb{R}_+^d$ *and* τ_D *the first exit time from D. For* $x \in F \subsetneq D$ *we have*

$$\lim_{v \to \infty} \frac{1}{v} \log \mathbb{E}_x \left[\tau_D\right] = \min_{x \in \Pi,\ y \in \partial D} \mathcal{V}_D(x, y) \, .$$



The main issues

Obstacles for the application of large deviation principle:

1. Process is degenerate at the boundary ($\lambda_r(x) = 0$ there):

   The network $A \rightharpoonup 2A \rightharpoonup \emptyset$ is "trapped" in $A = 0$, since

   $$\lambda_{r_1}(0) = 0 \qquad \text{and} \qquad \lambda_{r_2}(0) = 0 \, .$$

2. Rates $\lambda_r(x)$ are not globally Lipschitz continuous:

   The network $2A \rightharpoonup 3A$ explodes in finite time, since

   $$\dot{x}_A = x_A^2 \text{ with } x(0) = 1 \text{ diverges at } t = 1/3 \, .$$

Asiphonic CRN

A non-empty subset $\mathcal{P} \subset \mathcal{S}$ is called a *siphon* [**?**] if every reaction $r \in \mathcal{R}$ with at least one output from $\mathcal{P}$ also has some input from $\mathcal{P}$.

Examples:

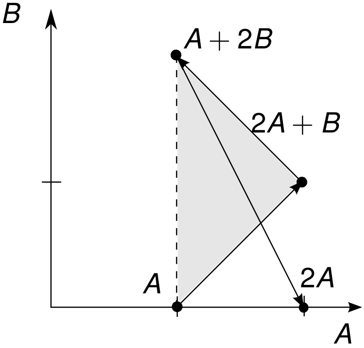
- $\mathcal{P} = \{A\}$ is a siphon of

$$A \rightharpoonup 2A \rightharpoonup \emptyset\,,$$

- $\mathcal{P} = \{A, B\}, \{A\}$ are a siphons of

$$A \rightharpoonup 2A{+}B \rightharpoonup A{+}2B \rightharpoonup 2A\,,$$

  whereas $\{B\}$ is not.



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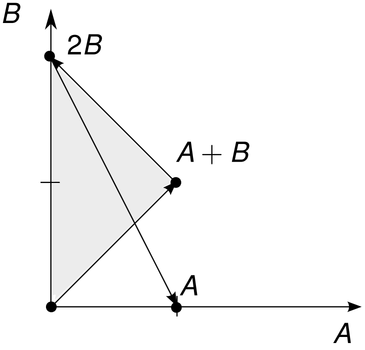
- The "Musterbeispiel"

$$\emptyset \rightharpoonup A + B \rightharpoonup 2B \rightharpoonup A \,,$$

  has no siphon:
  it is *asiphonic*.



Strongly endotactic CRN

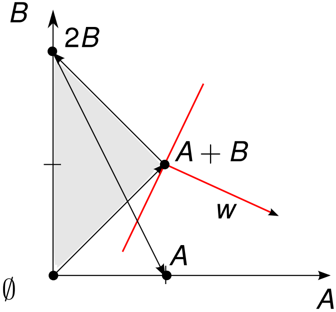
The network $(\mathcal{S}, \mathcal{C}, \mathcal{R})$ is called *strongly endotactic* [**?**] if, for all $w \in S^{d-1}$, the set $\mathcal{R}_w = \arg\max_{r \in \mathcal{R}}\{w \cdot c^r_{\mathrm{in}}\}$ contains at least one reaction satisfying $w \cdot c^r < 0$, and no reaction with $w \cdot c^r > 0$.

Examples:

- All closed cycles,
- The network

$$\emptyset \xrightarrow{r_1} A + B \xrightarrow{r_2} 2B \xrightarrow{r_3} A$$

can be represented in $\mathbb{N}_0^2$.



The “Strongly endotactic” property can be checked algorithmically.

Conditions for LDT

Theorem (A., Dembo, Eckmann)

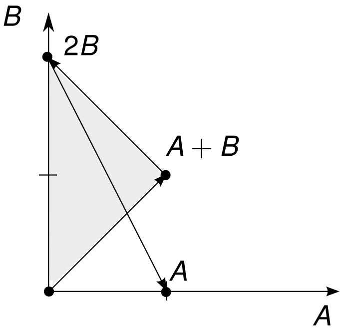
If the network $(\mathcal{S}, \mathcal{C}, \mathcal{R})$

(a) *is Strongly endotactic,*

(b) $\mathrm{Co}\{c^r\}_{r\in\mathcal{R}} = \mathbb{R}^d$,

(c) *has no siphon* $\mathcal{P} \subset \mathcal{S}$.

then Wentzell-Freidlin estimates apply to the exit times τ_D *of the sample paths of* X_t^v .



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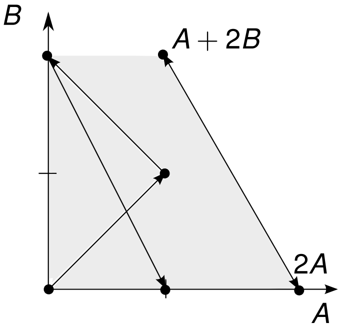

Conjecture

The condition (a) can be relaxed to "there exists an absorbing set for the dynamics of the mass action ODEs modeling $(\mathcal{S}, \mathcal{C}, \mathcal{R})$.

References