Asymptotic stability of delayed complex balanced reaction networks with non-mass action kinetics

Mihály András Vághy, Gábor Szederkényi

Pázmány Péter Catholic University
Faculty of Information Technology and Bionics

5th of November, 2024

Outline

- introduction, motivation
- non-mass action CRNs
- quasi-thermostatic and quasi-thermodynamic CRNs
- complex balanced CRNs
- delayed CRNs
- examples

Background

- a wide class of (nonnegative) dynamical systems can be modeled in the kinetic (CRN) framework

- in many applications, the incorporation of time delay is essential to describe the observed phenomena

- model class introduced and explained in: (Roussel, M. R. (1996). The use of delay differential equations in chemical kinetics. *The Journal of Physical Chemistry*, 100(20), 8323-8330)

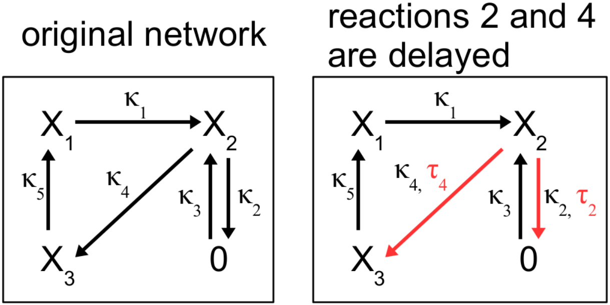
- there are important relations between reaction graph structure and qualitative dynamics (naturally, fewer results on delayed networks)

- related contributions to be mentioned by M. Mincheva, M.R. Roussel, G. Craciun, C. Pantea, P.Y. Yu, H. Komatsu, H. Nakajima, G. Lipták, K.M. Hangos, G. Szederkényi

Delayed chemical reaction networks: idea

- **Basic idea**: assign time delays to certain reactions
- consumption of reactants is immediate, while formation of products is delayed (discrete or distributed)
- delayed reactions may substitute cascades (subsystems) or describe transport delays, infection delays etc.

Simple compartmental (linear) example (e.g., a mass convection network):



Introduction

The dynamics of mass action kinetic systems can be given as

$$\dot{x}(t) = \sum_{k=1}^{M} \kappa_k x^{y_k}(t)\big(y_{k'} - y_k\big) = YK\Gamma\big(x(t)\big), \tag{1}$$

where

- $x(t) \in \overline{\mathbb{R}}_+^N$ is the state vector (concentration of species),
- there are M reactions, with stoichiometric vectors $y_k,\ y_{k'} \in \mathbb{N}^N$,
- $\kappa_k > 0$ is the reaction rate constant,
- vector exponential: $x^y = \prod_{i=1}^N x_i^{y_i}$,
- the Y complex matrix contains y_k vectors as columns,
- K is the weighted negative Laplacian of the reaction graph,
- the elements of the $\Gamma(x)$ column vector are x^{y_k},
- the set of stoichiometric vectors is $\mathcal{K}$.

Motivation

We wish to generalize certain stability results of (1) to include non-mass-action (e.g., Michaelis-Menten or Hill-type) kinetics. We consider systems of the form

$$\dot{x}(t) = \sum_{k=1}^{M} \kappa_k \gamma^{y_k}\big(x(t)\big)\big(y_{k'} - y_k\big) = YK\Gamma\big(x(t)\big), \tag{2}$$

where $\gamma(x) = \big[\gamma_1(x_1)\ \gamma_2(x_2)\ \cdots\ \gamma_N(x_N)\big]^\top$.

The γ_i functions

- are increasing and continuously differentiable,
- satisfy $\gamma_i(0) = 0$,
- satisfy further technical regularity assumptions.

Some examples:

- mass action kinetics: $\gamma_i(s) = s$,
- Michaelis-Menten-type kinetics: $\gamma_i(s) = \frac{s}{k+s}$ for some $k > 0$.
- Hill-type kinetics: $\gamma_i(s) = \frac{s^n}{k+s^n}$ for some $k > 0$ and $n > 0$.

Positive stoichiometric compatibility classes

The reaction vector of reaction k is $y_{k'} - y_k$. The linear span of the reaction vectors is the stoichiometric subspace $\mathcal{S}$, defined as

$$\mathcal{S} = \operatorname{span}\left\{ y_{k'} - y_k \middle| k = 1, 2, \ldots, M \right\}.$$

For $p \in \mathbb{R}_+^N$ the positive stoichiometric compatibility class $\mathcal{S}_p$ is given as

$$\mathcal{S}_p = \left\{ x \in \mathbb{R}_+^N \middle| x - p \in \mathcal{S} \right\}.$$

Integrating (2) yields

$$x(t) = x(0) + \left(\sum_{k=1}^{M} \kappa_k \int_0^t \gamma^{y_k}\big(x(t)\big)\,\mathrm{d}t \right) \big(y_{k'} - y_k \big)$$

showing that $x(t) \in \mathcal{S}_{x(0)}$ for $t \geq 0$; that is, the positive stoichiometric compatibility classes are positively invariant under (2).

Quasi-thermostatic CRNs

A positive vector $\overline{x} \in \mathbb{R}_{+}^{N}$ is called a positive equilibrium of (2) if $x(t) \equiv \overline{x}$ is a solution.

We define $\rho(x) = \log\big(\gamma(x)\big)$ and say that a kinetic system is *quasi-thermostatic* w.r.t. the positive vector $\overline{x}$ if the set of positive equilibria is identical to

$$\mathcal{E} = \left\{\tilde{x} \in \mathbb{R}_{+}^{N} \middle| \rho(\tilde{x}) - \rho(\overline{x}) \in \mathcal{S}^{\perp}\right\},$$

where the logarithm is taken element-wise. Such a system is quasi-thermostatic w.r.t. to any element of $\mathcal{E}$, thus we usually omit $\overline{x}$ from the definition.

Theorem

Assume that (2) *is quasi-thermostatic. Then every positive stoichiometric compatibility class contains exactly one positive equilibrium.*

Quasi-thermodynamic CRNs

We say that a kinetic system is *quasi-thermodynamic* w.r.t. the positive vector $\overline{x}$ it the system is quasi-thermostatic w.r.t. $\overline{x}$ and

$$\big(\rho(x) - \rho(\overline{x})\big) \cdot f(x) \leq 0 \tag{3}$$

holds for $x \in \mathbb{R}^N_+$, with equality holding of $f(x) = 0$ or, equivalently, if $\rho(x) - \rho(\overline{x}) \in \mathcal{S}^\perp$. Again, such a system is quasi-thermodynamic w.r.t. any element of $\mathcal{E}$.

Theorem

Assume that (2) *is quasi-thermodynamic. Then, each positive stoichiometric compatibility class contains precisely one positive equilibrium and that equilibrium is locally asymptotically stable, and there is no nontrivial periodic trajectory along which all species concentrations are positive.*

Quasi-thermodynamic CRNs

The proof relies on the entropy-like logarithmic Lyapunov function

$$V(x,\overline{x}) = \sum_{i=1}^{N} \int_{\overline{x}_i}^{x_i} \big(\log \gamma_i(s) - \log \gamma_i(\overline{x}_i)\big)\,\mathrm{d}s\,,$$

since (3) is equivalent to $\nabla V(x,\overline{x}) \cdot f(x) \leq 0$.

We say that the Lyapunov function is *entropy-like*, since for mass action kinetic systems it has the form

$$V(x,\overline{x}) = \sum_{i=1}^{N} \big(x_i(\log x_i - \log \overline{x}_i - 1) + \overline{x}_i\big) = \sum_{i=1}^{N} \left(x_i \log \frac{x_i}{\overline{x}_i} + \overline{x}_i - x_i\right).$$

Complex balanced CRNs

An equilibrium $\overline{x}$ is called *complex balanced* if $K\Gamma(\overline{x}) = 0$ or, equivalently, if for every complex $\eta \in \mathcal{K}$ we have that

$$\sum_{k:\eta=y_k} \kappa_k \gamma^{y_k}(\overline{x}) = \sum_{k:\eta=y_{k'}} \kappa_k \gamma^{y_k}(\overline{x}).$$

Theorem

If a kinetic system admits a positive complex balanced equilibrium, then every positive equilibrium is complex balanced.

Theorem

A complex balanced kinetic system is quasi-thermodynamic.

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Delayed CRNs

We consider delayed kinetic systems of the form

$$\dot{x}(t) = \sum_{k=1}^{M} \kappa_k \Big(\gamma^{y_k}\big(x(t-\tau_k)\big) y_{k'} - \gamma^{y_k}\big(x(t)\big) y_k \Big), \tag{4}$$

where $\tau_k \geq 0$. The initial data is a continuous function that maps $[-\tau, 0]$ into $\overline{\mathbb{R}}_+^N$; that is, it is an element of $\overline{\mathcal{C}}_{+,\tau} = C([-\tau, 0], \overline{\mathbb{R}}_+^N)$, where $\tau = \max_k \tau_k$. The set of positive initial data is denoted by $\mathcal{C}_{+,\tau}$.

The solution corresponding to an initial function $\psi \in \overline{\mathcal{C}}_{+,\tau}$ at time $t \geq 0$ is denoted by $x^{\psi}(t) \in \overline{\mathbb{R}}_+^N$. When we want to refer to the solution as a function, we denote it by $x_t^{\psi} \in \overline{\mathcal{C}}_{+,\tau}$.

A positive vector $\overline{x} \in \mathbb{R}^N$ is called a positive equilibrium of (4) if $x(t) \equiv \overline{x}$ is a solution. Thus, the equilibria of the delayed system (4) and the nondelayed system (2) coincide.

Compatibility classes of delayed CRNs

The delayed positive stoichiometric compatibility classes are defined as

$$\mathcal{D}_\theta = \left\{\psi \in \mathcal{C}_{+,\tau} \middle| c_v(\psi) = c_v(\theta) \text{ for all } v \in \mathcal{S}^\perp \right\},$$

where the functional c_v is given by

$$c_v(\psi) = v \cdot \left[\psi(0) + \sum_{k=1}^{M} \left(\kappa_k \int_{-\tau_k}^{0} \gamma^{y_k}\big(\psi(s)\big)\,\mathrm{d}s\right) y_k\right], \qquad \psi \in \mathcal{C}_{+,\tau}.$$

Clearly, $\psi \in \mathcal{D}_\theta$ if and only if $\psi \in \mathcal{C}_{+,\tau}$ and

$$\psi(0) - \theta(0) + \sum_{k=1}^{M} \left(\kappa_k \int_{-\tau_k}^{0} \Big(\gamma^{y_k}\big(\psi(r)\big) - \gamma^{y_k}\big(\theta(s)\big)\Big)\,\mathrm{d}s\right) y_k \in \mathcal{S}.$$

Compatibility classes of delayed CRNs

Theorem

For every $\theta \in \mathcal{C}_{+,\tau}$ the positive stoichiometric compatibility class $\mathcal{D}_\theta$ is a closed subset of $\mathcal{C}_{+,\tau}$. Moreover, $\mathcal{D}_\theta$ is positively invariant under (4)*; that is, if $\psi \in \mathcal{D}_\theta$, then $x_t^\psi \in \mathcal{D}_\theta$ for all $t \geq 0$.*

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Quasi-thermostatic delayed CRNs

Since the equilibria of (4) and (2) coincide, we do not have to modify our definition of quasi-thermostaticity.

Theorem

Assume that the kinetic system (4) *is quasi-thermostatic. Then, for every* $\theta \in \mathcal{C}_{+,\tau}$ *the corresponding delayed positive stoichiometric compatibility class* $\mathcal{D}_\theta$ *of the system* (4) *contains exactly one positive equilibrium.*

Quasi-thermodynamic delayed CRNs

We define the Lyapunov-Krasovskii functional

$$V(\psi,\overline{x}) = \sum_{i=1}^{N} \int_{\overline{x}_i}^{\psi_i(0)} \left(\log \gamma_i(s) - \log \gamma_i(\overline{x}_i)\right) \mathrm{d}s$$

$$+ \sum_{k=1}^{M} \kappa_k \int_{-\tau_k}^{0} \left(\gamma^{y_k}(\psi(s))\left(\log \gamma^{y_k}(\psi(s)) - \log \gamma^{y_k}(\overline{x}) - 1\right) + \gamma^{y_k}(\overline{x})\right) \mathrm{d}s\,.$$

We say that a delayed kinetic system is quasi-thermodynamic w.r.t. $\overline{x}$ if it is quasi-thermostatic w.r.t. $\overline{x}$ (we can omit $\overline{x}$ as before) and

$$\dot{V}(x_t,\overline{x}) \leq 0.$$

Theorem

Assume that the kinetic system (4) *is quasi-thermodynamic. Then, every positive equilibrium of the system is Lyapunov stable relative to its positive stoichiometric compatibility class.*

Complex balanced delayed CRNs

Theorem

Assume that the delayed kinetic system (4) *is complex balanced. Then it is quasi-thermodynamic. Moreover, each positive equilibrium is locally asymptotically stable relative to its positive stoichiometric compatibility class and there is no nontrivial periodic trajectory along which all species concentrations are positive.*

Interpretation of delayed entropy

$$V(\psi,\overline{x}) = \sum_{i=1}^{N} \int_{\overline{x}_i}^{\psi_i(0)} \big(\log\gamma_i(s) - \log\gamma_i(\overline{x}_i)\big)\,\mathrm{d}s$$

$$+ \sum_{k=1}^{M} \kappa_k \int_{-\tau_k}^{0} \Big(\gamma^{y_k}(\psi(s))\Big(\log\gamma^{y_k}(\psi(s)) - \log\gamma^{y_k}(\overline{x}) - 1\Big) + \gamma^{y_k}(\overline{x})\Big)\,\mathrm{d}s.$$

- first sum describes the entropy (or free energy) of the current concentration configuration
- the second sum describes the 'residual' entropy of the history
- Why does the second term resemble the mass action entropy?

$$\sum_{i=1}^{N} \big(x_i(\log x_i - \log\overline{x}_i - 1) + \overline{x}_i\big)$$

Chain method

Let us assume that there is only one delayed reaction.

$$\begin{aligned}\dot{x}(t) = \sum_{k=1}^{M-1} \kappa_k \gamma^{y_k}\left(x(t)\right)\left(y_{k'} - y_k\right) \\ + \kappa_M\left(\gamma^{y_M}\left(x(t-\tau_M)\right)y_{M'} - \gamma^{y_M}\left(x(t)\right)y_M\right).\end{aligned} \tag{5}$$

Idea is to approximate the delayed reaction $y_M \cdot X \xrightarrow{\kappa_M, \tau_M} y_{M'} \cdot X$ with a cascade of nondelayed mass action reactions:

$$y_M \cdot Z \xrightarrow{\kappa_M} V_1 \xrightarrow{L/\tau_M} V_2 \xrightarrow{L/\tau_M} \cdots \xrightarrow{L/\tau_M} V_L \xrightarrow{L/\tau_M} y_{M'} \cdot Z.$$

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Chain method

The approximating dynamics is given by

$$\begin{aligned}
\dot{z}(t) &= \sum_{k=1}^{M-1} \kappa_k \gamma^{y_k}\big(z(t)\big)\big(y_{k'} - y_k\big) + \frac{L}{\tau_M} v_L(t) y_{M'} - \kappa_M \gamma^{y_M}\big(z(t)\big), \\
\dot{v}_1(t) &= \kappa_M \gamma^{y_M}\big(z(t)\big) - \frac{L}{\tau_M} v_1(t), \\
\dot{v}_i(t) &= \frac{L}{\tau_M} v_{i-1}(t) - \frac{L}{\tau_M} v_i(t), \quad 2 \le i \le L.
\end{aligned} \tag{6}$$

If (5) is complex balanced, then (6) is complex balanced as well.
If the initial data of (5) is $\theta(t)$, then if the initial data of (6) is set to

$$z(0) = \theta(0), \qquad v_i(0) = \kappa_M \int_{-i\frac{\tau_M}{L}}^{-(i-1)\frac{\tau_M}{L}} \gamma^{y_M}\big(\theta(s)\big)\,\mathrm{d}s,$$

then the equilibrium of (6) is

$$\overline{z} = \overline{x}, \qquad \overline{v_i} = \kappa_M \frac{\tau_M}{L} \gamma^{y_M}(\overline{x}).$$

Chain method

The Lyapunov function can be given as

$$
\begin{aligned}
&V^L\big(z(t), v(t), \overline{z}, \overline{v}\big)\\
&= \sum_{i=1}^{N} \int_{\overline{z}_i}^{z_i} \big(\log \gamma_i(s) - \log \gamma_i(\overline{z}_i)\big)\,\mathrm{d}s + \sum_{i=1}^{L} \left(v_i \log \frac{v_i}{\overline{v}_i} + \overline{v}_i - v_i \right)\\
&= \sum_{i=1}^{N} \int_{\overline{x}_i}^{z_i} \big(\log \gamma_i(s) - \log \gamma_i(\overline{x}_i)\big)\,\mathrm{d}s\\
&+ \sum_{i=1}^{L} \left(v_i \log \frac{v_i}{\kappa_M \frac{\tau_M}{L} \gamma^{y_M}(\overline{x})} + \kappa_M \frac{\tau_M}{L} \gamma^{y_M}(\overline{x}) \right).
\end{aligned}
$$

Chain method

We introduce the approximations

$$z(t) \approx x(t),$$

$$v_i(t) \approx \kappa_M \int_{t-i\frac{\tau_M}{L}}^{t-(i-1)\frac{\tau_M}{L}} \gamma^{y_M}\left(x(s)\right) \mathrm{d}s \approx \kappa_M \frac{\tau_M}{L} \gamma^{y_M}\left(x\left(t - i\frac{\tau_M}{L}\right)\right)$$

to get

$$V^L\left(z(t), v(t), \overline{z}, \overline{v}\right) \approx \sum_{i=1}^{N} \int_{\overline{x}_i}^{x_i} \left(\log \gamma_i(s) - \log \gamma_i(\overline{x}_i)\right) \mathrm{d}s$$

$$+ \sum_{i=1}^{L} \kappa_M \frac{\tau_M}{L} \left[\gamma^{y_M}\left(x\left(t - i\frac{\tau_M}{L}\right)\right) \log \frac{\gamma^{y_M}\left(x\left(t - i\frac{\tau_M}{L}\right)\right)}{\gamma^{y_M}\left(\overline{x}\right)}\right.$$

$$\left. + \gamma^{y_M}\left(\overline{x}\right) - \gamma^{y_M}\left(x\left(t - i\frac{\tau_M}{L}\right)\right)\right].$$

Taking the limit $L \to \infty$ yields our Lyapunov-Krasovskii functional.

Example 1

$$2X_1 \underset{\kappa_2=2,\tau_2=0.5}{\overset{\kappa_1=1}{\rightleftharpoons}} X_2.$$

If we assume mass action kinetics, then the system takes the form

$$\dot{x}(t) = \kappa_1\left(x_1^2(t)\begin{bmatrix}0\\1\end{bmatrix} - x_1^2(t)\begin{bmatrix}2\\0\end{bmatrix}\right) + \kappa_2\left(x_2(t-\tau_2)\begin{bmatrix}2\\0\end{bmatrix} - x_2(t)\begin{bmatrix}0\\1\end{bmatrix}\right).$$

The stoichiometric subspace and its orthogonal complement is

$$\mathcal{S} = \operatorname{span}\left\{\begin{bmatrix}-2\\1\end{bmatrix}\right\} \qquad \mathcal{S}^\perp = \operatorname{span}\left\{\begin{bmatrix}1\\2\end{bmatrix}\right\}.$$

It is easy to verify that $[2\ 2]^\top$ is a positive complex balanced equilibrium, and thus the positive equilibria are given by

$$\mathcal{E} = \left\{x \in \mathbb{R}_+^2 \,\middle|\, \begin{bmatrix}\log x_1 - \log 2\\ \log x_2 - \log 2\end{bmatrix} \in \mathcal{S}^\perp\right\}.$$

Example 1

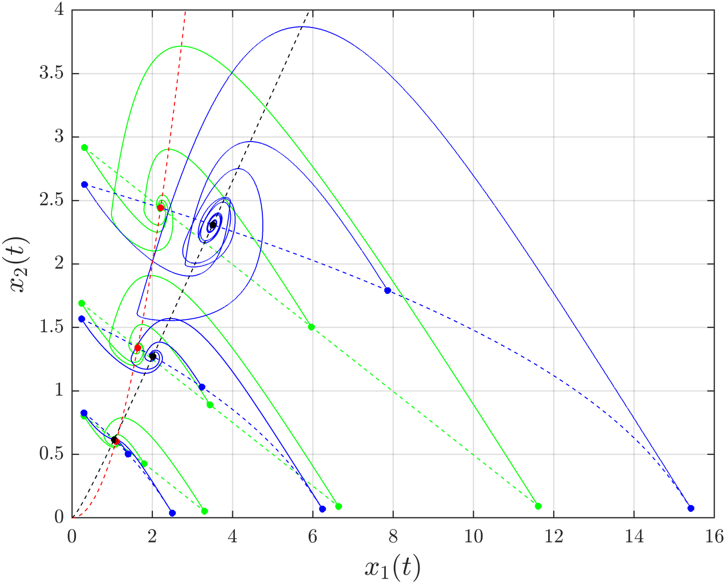
With $\gamma_1(s) = \frac{s^2}{1+s}$ and $\gamma_2(s) = \frac{s^3}{1+s}$ the transformed system takes the form

$$\dot{x}(t) = \kappa_1 \left(\frac{x_1^4(t)}{\big(1 + x_1(t)\big)^2} \begin{bmatrix} 0 \\ 1 \end{bmatrix} - \frac{x_1^4(t)}{\big(1 + x_1(t)\big)^2} \begin{bmatrix} 2 \\ 0 \end{bmatrix} \right) + \kappa_2 \left(\frac{x_2^3(t-\tau_2)}{1 + x_2(t-\tau_2)} \begin{bmatrix} 2 \\ 0 \end{bmatrix} - \frac{x_2^3(t)}{1 + x_2(t)} \begin{bmatrix} 0 \\ 1 \end{bmatrix} \right).$$

Is it easy to verify that $\begin{bmatrix} \frac{\sqrt{5}}{2} + \frac{1}{2} & 1 \end{bmatrix}^\top$ is a positive complex balanced equilibrium, and thus the positive equilibria are given by

$$\mathcal{E} = \left\{ x \in \mathbb{R}_+^2 \,\middle|\, \begin{bmatrix} \log \frac{x_1^2}{1+x_1} - \log 1 \\ \log \frac{x_2^3}{1+x_2} - \log \frac{1}{2} \end{bmatrix} \in \mathcal{S}^\perp \right\}.$$

Example 1



Example 2

Let us consider the set of reversible reactions

$$3X_1 \underset{\kappa_2=\frac{2.8}{3}}{\overset{\kappa_1=\frac{1.4}{3}}{\rightleftharpoons}} 3X_2$$

$$3X_1 \underset{\kappa_4=0.126,\tau_4=0.4}{\overset{\kappa_3=0.1}{\rightleftharpoons}} 2X_1 + X_2$$

$$3X_2 \underset{\kappa_6=0.063,\tau_6=0.6}{\overset{\kappa_5=0.1}{\rightleftharpoons}} 2X_1 + X_2$$

with the transformations $\gamma_1(s) = s$ and $\gamma_2(s) = \frac{s^2}{1+s}$. The stoichiometric subspace and its orthogonal complement are

$$\mathcal{S} = \operatorname{span}\left\{ \begin{bmatrix} -3 \\ 3 \end{bmatrix} \right\} \qquad \mathcal{S}^{\perp} = \operatorname{span}\left\{ \begin{bmatrix} 3 \\ 3 \end{bmatrix} \right\}.$$

Example 2

The system takes the form

$$
\begin{aligned}
\dot{x}(t) = {}& \kappa_1 \left(x_1^3(t) \begin{bmatrix} 0 \\ 3 \end{bmatrix} - x_1^3(t) \begin{bmatrix} 3 \\ 0 \end{bmatrix} \right) + \kappa_2 \left(\frac{x_2^6(t)}{\big(1 + x_2(t)\big)^2} \begin{bmatrix} 3 \\ 0 \end{bmatrix} - \frac{x_2^6(t)}{\big(1 + x_2(t)\big)^2} \begin{bmatrix} 0 \\ 3 \end{bmatrix} \right) \\
& + \kappa_3 \left(x_1^3(t) \begin{bmatrix} 2 \\ 1 \end{bmatrix} - x_1^3(t) \begin{bmatrix} 3 \\ 0 \end{bmatrix} \right) \\
& + \kappa_4 \left(x_1^2(t - \tau_4) \frac{x_2^2(t - \tau_4)}{1 + x_2(t - \tau_4)} \begin{bmatrix} 3 \\ 0 \end{bmatrix} - x_1^2(t) \frac{x_2^2(t)}{1 + x_2(t)} \begin{bmatrix} 2 \\ 1 \end{bmatrix} \right) \\
& + \kappa_5 \left(\frac{x_2^6(t)}{\big(1 + x_2(t)\big)^2} \begin{bmatrix} 2 \\ 1 \end{bmatrix} - \frac{x_2^6(t)}{\big(1 + x_2(t)\big)^2} \begin{bmatrix} 0 \\ 3 \end{bmatrix} \right) \\
& + \kappa_6 \left(x_1^2(t - \tau_6) \frac{x_2^2(t - \tau_6)}{1 + x_2(t - \tau_6)} \begin{bmatrix} 0 \\ 3 \end{bmatrix} - x_1^2(t) \frac{x_2^2(t)}{1 + x_2(t)} \begin{bmatrix} 2 \\ 1 \end{bmatrix} \right).
\end{aligned}
$$

Example 2

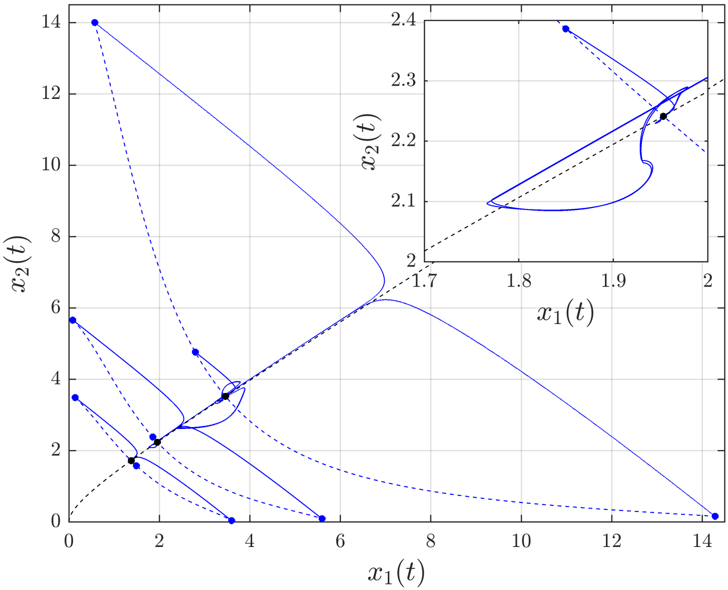
It is easy to verify via the Cardano formula that

$$\overline{x} = \begin{bmatrix} \sqrt[3]{2} \\ \sqrt[3]{\frac{1}{2} + \sqrt{\frac{23}{108}}} + \sqrt[3]{\frac{1}{2} - \sqrt{\frac{23}{108}}} \end{bmatrix}$$

is a positive complex balanced equilibrium, and thus the positive equilibria are given by

$$\mathcal{E} = \left\{ x \in \mathbb{R}^2_+ \middle| \begin{bmatrix} \log x_1 - \log \overline{x}_1 \\ \log \frac{x_2^2}{1+x_2} - \log \frac{\overline{x}_2^2}{1+\overline{x}_2} \end{bmatrix} \in \mathcal{S}^\perp \right\}.$$

Example 2



14
12
10
8
6
4
2
0
0
2
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6
8
10
12
14
$x_1(t)$
$x_2(t)$
2.4
2.3
2.2
2.1
2
1.7
1.8
1.9
2
$x_1(t)$
$x_2(t)$

Summary

- stability of a wide class of delayed non-mass-action CRNs was studied
- quasi-thermostatic property $\Longrightarrow$ one positive equilibrium on each positive compatibility class
- quasi-thermodynamic property $\Longrightarrow$ each positive equilibrium is Lyapunov-stable
- Lyapunov-Krasovskii functional given (actual $+$ 'residual' entropy)
- complex balance $\Longrightarrow$ quasi thermodynamic $+$ local asymptotic stability (within positive compatibility class)

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