Linear Conjugacy of Chemical Reaction Networks

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Objectives

We are interested in determining the dynamics of chemical reaction networks under the assumption of mass-action kinetics.

It is often the case that dynamical properties of a system which is too complicated to analyse directly can be found by comparing the system to a related one with known dynamics.

Linear Conjugacy

Consider two mass-action systems $\mathcal{N}$ and $\mathcal{N}'$ and let $\Phi(\mathbf{x}_0, t)$ denote the flow associated with $\mathcal{N}$ and $\Psi(\mathbf{y}_0, t)$ denote the flow associated with $\mathcal{N}'$. We will say $\mathcal{N}$ and $\mathcal{N}'$ are **linearly conjugate** if there exists a linear mapping $\mathbf{h} : \mathbb{R}^m_{>0} \mapsto \mathbb{R}^m_{>0}$ such that $\mathbf{h}(\Phi(\mathbf{x}_0, t)) = \Psi(\mathbf{h}(\mathbf{x}_0), t)$ for all $\mathbf{x}_0 \in \mathbb{R}^m_{>0}$.

We have been researching conditions under which **two different reaction networks** can possess the **same qualitative dynamics**. Importantly, linearly conjugate systems share many qualitative properties. The conditions of the following theorem are based on the **reaction graph** of the network.

Let $\mathcal{C}_{react}$ denote the set of reactant complexes in either the complex set $\mathcal{C}$ or the complex set $\mathcal{C}'$.

Theorem

Suppose that for the rate constants $k_i > 0$, $i = 1, \ldots, r$, there exist constants $b_i > 0$, $i = 1, \ldots, \tilde{r}$, and $c_j > 0$, $j = 1, \ldots, m$, such that, for every $\mathcal{C}^0 \in \mathcal{C}_{react}$,

$$\sum_{\substack{i=1 \\ \mathcal{C}_i = \mathcal{C}^0}}^{r} k_i(\mathbf{z}'_i - \mathbf{z}_i) = T \sum_{\substack{i=1 \\ \tilde{\mathcal{C}}_i = \mathcal{C}^0}}^{\tilde{r}} b_i(\tilde{\mathbf{z}}'_i - \tilde{\mathbf{z}}_i)$$

where $T = \text{diag}\{c_j\}_{j=1}^m$. Then $\mathcal{N}$ is linearly conjugate to $\mathcal{N}'$ with rate constants

$$\tilde{k}_i = b_i \Pi_{j=1}^m c_j^{\tilde{z}_{ij}}, \qquad i = 1, \ldots, \tilde{r}.$$

Chemical Reaction Networks

We will let $\mathcal{A}_j$ denote the **species** of the network and define $|\mathcal{S}| = m$ where $\mathcal{S}$ is the set of distinct species of the network.

Consider the **elementary reaction set**

$$\mathcal{R}_i : \quad \Sigma_{j=1}^m z_{ij}\mathcal{A}_j \longrightarrow \Sigma_{j=1}^m z'_{ij}\mathcal{A}_j, \quad i = 1, \ldots, r$$

where $z_{ij}, z'_{ij} \in \mathbb{Z}_{\geq 0}$ are the **stoichiometric coefficients** of the i^{th} reaction. The set of all reactions in the network will be denoted $\mathcal{R}$ so that $|\mathcal{R}| = r$.

The set of stoichiometric distinct **complexes** (the combined terms to the left or right of the reaction arrow) will be given by $\mathcal{C}_i$, $i = 1, \ldots, n$. The **chemical reaction network** $\mathcal{N}$ can then be given by the triplet $\mathcal{N} = (\mathcal{S}, \mathcal{C}, \mathcal{R})$.

Mass-Action Kinetics

A common assumption in chemical kinetics is that **the rate of a reaction is proportional to the product of the reactant concentrations**. For example, if the complex $\mathcal{A}_1 + \mathcal{A}_2$ catalyzes a reaction, the rate of the reaction would be proportional to $[\mathcal{A}_1][\mathcal{A}_2]$. This mass-action kinetics assumption is valid for large-scale, continuously stirred reaction systems.

Mass-action kinetics gives rise to the governing system of differential equations

$$\frac{d\mathbf{x}}{dt} = \mathbf{f}(\mathbf{x}) = \Sigma_{i=1}^r k_i \left(\mathbf{z}'_i - \mathbf{z}_i\right) \mathbf{x}^{\mathbf{z}_i}$$

where $\mathbf{x}^{\mathbf{z}_i} = \Pi_{j=1}^m x_j^{z_{ij}}$ and $k_i > 0$ is the rate constant for the i^{th} reaction.

Examples

$$\mathcal{N}: \left\{\begin{array}{c} \mathcal{A}_1 + 2\mathcal{A}_2 \xrightarrow{k_1} \mathcal{A}_1 + 3\mathcal{A}_2 \\ \mathcal{A}_1 + 3\mathcal{A}_2 \xrightarrow{k_2} \mathcal{A}_1 + \mathcal{A}_2 \\ \mathcal{A}_1 + \mathcal{A}_2 \xrightarrow{k_3} 3\mathcal{A}_1 \\ 2\mathcal{A}_1 \xrightarrow{k_4} \mathcal{A}_2. \end{array}\right. \implies \mathcal{N}': \left\{\begin{array}{c} \mathcal{A}_1 + 2\mathcal{A}_2 \underset{\tilde{k}_2}{\overset{\tilde{k}_1}{\rightleftarrows}} \mathcal{A}_1 + 3\mathcal{A}_2 \\ \mathcal{A}_1 + \mathcal{A}_2 \underset{\tilde{k}_4}{\overset{\tilde{k}_3}{\rightleftarrows}} 2\mathcal{A}_1. \end{array}\right.$$

The networks are linearly conjugate with $\mathbf{h}(\mathbf{x}) = [2x_1, x_2]$ and $\tilde{k}_1 = 2k_1$, $\tilde{k}_2 = 4k_2$, $\tilde{k}_3 = 2k_3$ and $\tilde{k}_4 = 4k_4$.

$$\mathcal{N}: \left\{\begin{array}{c} \mathcal{A}_1 + 2\mathcal{A}_2 \xrightarrow{\epsilon} \mathcal{A}_1 \\ 2\mathcal{A}_1 + \mathcal{A}_2 \xrightarrow{1} 3\mathcal{A}_2 \\ \mathcal{A}_1 + 3\mathcal{A}_2 \xrightarrow{1} \mathcal{A}_1 + \mathcal{A}_2 \\ \mathcal{A}_1 + \mathcal{A}_2 \xrightarrow{1} 3\mathcal{A}_1 + \mathcal{A}_2 \end{array}\right. \implies \mathcal{N}': \left\{\begin{array}{ccc} \mathcal{A}_1 + 2\mathcal{A}_2 & \xrightarrow{\tilde{k}_1} & \mathcal{A}_1 + \mathcal{A}_2 \\ \tilde{k}_4 \uparrow & \nearrow_{\tilde{k}_5} & \downarrow \tilde{k}_2 \\ \mathcal{A}_1 + 3\mathcal{A}_2 & \xleftarrow[\tilde{k}_3]{} & 2\mathcal{A}_1 + \mathcal{A}_2 \end{array}\right.$$

The networks are linearly conjugate with $\mathbf{h}(\mathbf{x}) = [2x_1, x_2]$ and $\tilde{k}_1 = 4\epsilon$, $\tilde{k}_2 = 2$, $\tilde{k}_3 = 4$, $\tilde{k}_4 = 4(1-t)$ and $\tilde{k}_5 = 2t$ for $0 \leq t < 1$.

$$\mathcal{N}: \left\{\begin{array}{c} \mathcal{A}_1 \xrightarrow{k_1} 2\mathcal{A}_1 + 2\mathcal{A}_2 \\ 2\mathcal{A}_1 + 2\mathcal{A}_2 \xrightarrow{k_2} \mathcal{A}_2 \\ \mathcal{A}_2 \xrightarrow{k_3} \mathcal{A}_1 + \mathcal{A}_2. \end{array}\right. \implies \mathcal{N}': \left\{\begin{array}{ccc} \mathcal{A}_1 + \mathcal{A}_2 & \underset{\tilde{k}_6}{\overset{\tilde{k}_3}{\leftrightarrows}} & \mathcal{A}_2 \\ \tilde{k}_4 \downarrow & \searrow^{\tilde{k}_5} & \uparrow \tilde{k}_2 \\ \mathcal{A}_1 & \xrightarrow[\tilde{k}_1]{} & 2\mathcal{A}_1 + 2\mathcal{A}_2. \end{array}\right.$$

The networks are linearly conjugate with $\mathbf{h}(\mathbf{x}) = [x_1, x_2]$ and $\tilde{k}_1 = k_1$, $\tilde{k}_2 = k_2$, $\tilde{k}_3 = k_3$, and $\tilde{k}_4 = \tilde{k}_5 = \tilde{k}_6 = t$ for any $t > 0$.

Locally Stable Dynamics

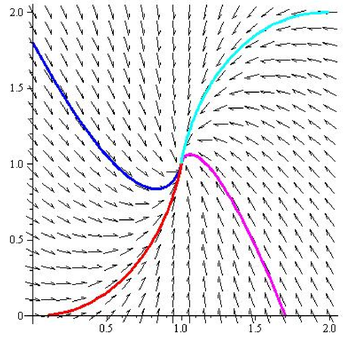
A mass-action system is said to possess **locally stable dynamics** if there is a single positive equilibrium concentration within each invariant space of the system and that equilibrium concentration is asymptotically stable.

Weakly Reversible Networks

A chemical reaction network $\mathcal{N}$ is said to be weakly reversible if a path in the reaction graph from one complex to another implies a path back. For example, cyclic networks like

$$\mathcal{N}: \quad \begin{array}{ccc} \mathcal{O} & \xrightarrow{k_1} & \mathcal{A}_1 \\ {\scriptstyle k_3}\nwarrow & & \swarrow{\scriptstyle k_2} \\ & \mathcal{A}_2. & \end{array}$$

There are well-known and easily-derived conditions on the reaction graph of a weakly reversible network which guarantee locally stable dynamics. The above system has dynamics given by:



References

[1] G. Craciun and C. Pantea, *Identifiability of chemical reaction networks,* J. Math. Chem. 44 (2008), no. 1, pp. 244–259.

[2] M.D. Johnston and D. Siegel, *Linear Conjugacy of Chemical Reaction Networks,* submitted.