Realizations through Weakly Reversible Networks and the Globally Attracting Locus

Abhishek Deshpande
International Institute of Information Technology Hyderabad

Joint work with Samay Kothari and Jiaxin Jin

- A **biochemical reaction** can happen in the transformation of one molecule to a different molecule inside a cell. Biochemical reactions are mediated by enzymes, which are biological catalysts that can alter the rate and specificity of chemical reactions inside cells.

- A **biochemical reaction** can happen in the transformation of one molecule to a different molecule inside a cell. Biochemical reactions are mediated by enzymes, which are biological catalysts that can alter the rate and specificity of chemical reactions inside cells.

- The key processes in biological and chemical systems are described by **biochemical reaction networks**.

- A **biochemical reaction** can happen in the transformation of one molecule to a different molecule inside a cell. Biochemical reactions are mediated by enzymes, which are biological catalysts that can alter the rate and specificity of chemical reactions inside cells.

- The key processes in biological and chemical systems are described by **biochemical reaction networks**.

- A biochemical reaction network comprises a set of **complexes** (**reactants** and **products**), and a set of **reactions**.

$$\text{Complexes:} \quad \{H_2, O_2, H_2O\}$$

$$\text{A reaction:} \quad \underbrace{2H_2 + O_2}_{reactant} \rightarrow \underbrace{2H_2O}_{product}$$

Mass-action kinetics and Euclidean embedded graph

- **Standard deterministic mass-action kinetics** says that the rate at which a reaction occurs is proportional to the concentrations of the reactant species.

$$\text{Reaction: } \underbrace{X_1 + X_2}_{reactant} \xrightarrow{k} \underbrace{X_3 + X_4}_{product}$$

x_i : the concentration of species X_i,

k : the reaction rate constant,

Reaction rate: kx_1x_2.

Mass-action kinetics and Euclidean embedded graph

- **Standard deterministic mass-action kinetics** says that the rate at which a reaction occurs is proportional to the concentrations of the reactant species.

$$\text{Reaction: } \underbrace{X_1 + X_2}_{reactant} \xrightarrow{k} \underbrace{X_3 + X_4}_{product}$$

x_i : the concentration of species X_i,

k : the reaction rate constant,

Reaction rate: kx_1x_2.

- A reaction network can be regarded as a **Euclidean embedded graph** $G = (V, E)$, where $V \subset \mathbb{R}^n_{\geq 0}$ is the set of vertices of the graph, and $E \subset V \times V$ is the set of oriented edges of G.

Example: The Lotka-Volterra systems can be considered as a reaction network in XY-plane with 6 complexes and 3 reactions.

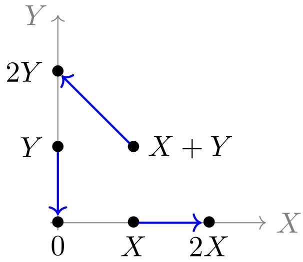
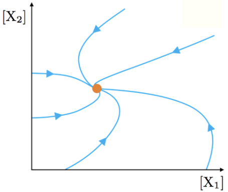
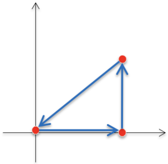


Figure: A reaction network of the Lotka-Volterra system.

$$\begin{aligned} \text{Species:} \quad & \mathcal{S} = \{X, Y\}, \\ \text{Complexes:} \quad & \mathcal{C} = \{X, X+Y, Y, 2X, 2Y, 0\}, \\ \text{Reactions:} \quad & \mathcal{R} = \{X \to 2X, X+Y \to 2Y, Y \to 0\}. \end{aligned}$$

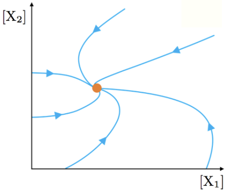


$$\varnothing \xrightarrow{0.7} X_1 \xrightarrow{1} X_1 + X_2 \xrightarrow{1} \varnothing$$

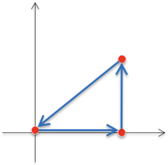


(a)

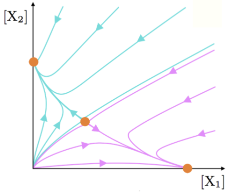
Figure: Reaction networks and Euclidean embedded graphs.



$$\varnothing \xrightarrow{0.7} X_1 \xrightarrow{1} X_1 + X_2 \xrightarrow{1} \varnothing$$

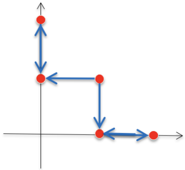


(a)



$$X_1 + X_2 \xrightarrow{1} X_1 \underset{1}{\overset{3}{\rightleftharpoons}} 2X_1$$

$$X_1 + X_2 \xrightarrow{2} X_2 \underset{1}{\overset{2}{\rightleftharpoons}} 2X_2$$



(b)

Figure: Reaction networks and Euclidean embedded graphs.

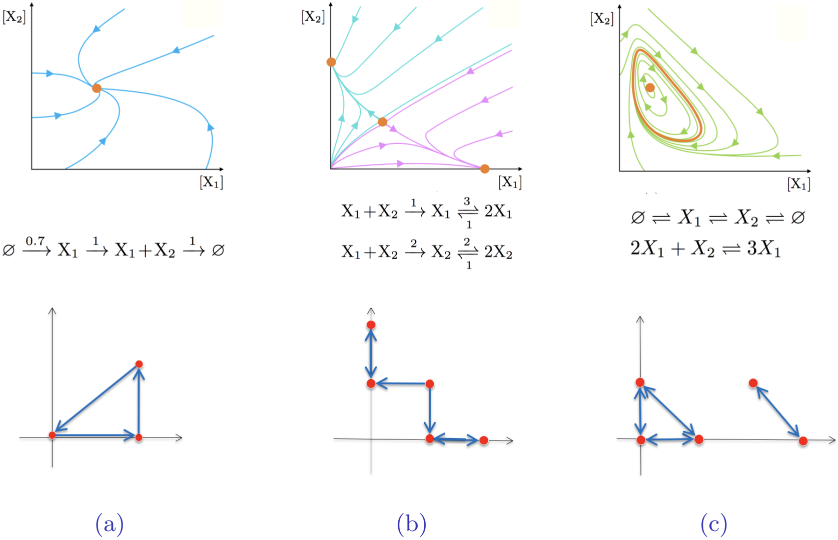


Figure: Reaction networks and Euclidean embedded graphs.

Weakly reversible

Let $G = (V, E)$ be a Euclidean embedded graph.

- The set of vertices is partitioned by its **connected components** called linkage classes, and we identify them by the subset of vertices that belong to that connected component.

Let $G = (V, E)$ be a Euclidean embedded graph.

- The set of vertices is partitioned by its **connected components** called linkage classes, and we identify them by the subset of vertices that belong to that connected component.

- A graph $G = (V, E)$ is **weakly reversible**, if every edge in any linkage class is part of an oriented cycle.
- $G \subseteq_{wr} G'$ will denote that G is a weakly reversible subgraph of G'.

Mass-action system

Let $G = (V, E)$ be a Euclidean embedded graph.

- Let $\boldsymbol{k} = (k_{\boldsymbol{y}\to\boldsymbol{y}'})_{\boldsymbol{y}\to\boldsymbol{y}'\in G} \in \mathbb{R}^{E}_{>0}$ be a vector of *rate constants*. We call $(G, \boldsymbol{k})$ a ***mass-action system***, and its ***associated dynamical system*** is given by

$$\frac{d\boldsymbol{x}}{dt} = \sum_{\boldsymbol{y}\to\boldsymbol{y}'\in E} \underbrace{k_{\boldsymbol{y}\to\boldsymbol{y}'}\boldsymbol{x}^{\boldsymbol{y}}}_{\text{reaction rate}} \times \underbrace{(\boldsymbol{y}' - \boldsymbol{y})}_{\text{change of species}},$$

where $\boldsymbol{x}^{\boldsymbol{y}} = x_1^{y_1} x_2^{y_2} \cdots x_n^{y_n}$ with $\boldsymbol{x} \in \mathbb{R}^n_{>0}$ is the vector of *concentrations* of the chemical species in the system.

Invariant polyhedron

Given the mass-action system

$$\frac{d\boldsymbol{x}}{dt} = \sum_{\boldsymbol{y}\to\boldsymbol{y}'\in E} k_{\boldsymbol{y}\to\boldsymbol{y}'} \boldsymbol{x}^{\boldsymbol{y}} (\boldsymbol{y}' - \boldsymbol{y}).$$

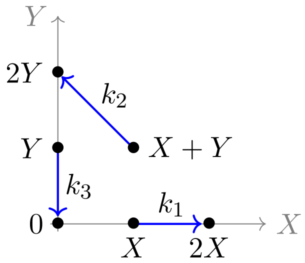
- ***The stoichiometric subspace*** is the vector space spanned by the reaction vectors with $\mathcal{S} = \text{span}\{\boldsymbol{y}' - \boldsymbol{y} : \boldsymbol{y} \to \boldsymbol{y}' \in E\}$.
- For any positive vector $\boldsymbol{x}_0 \in \mathbb{R}^n_{>0}$, the set $\mathcal{S}_{\boldsymbol{x}_0} := (\boldsymbol{x}_0 + S) \cap \mathbb{R}^n_{>0}$ is known as the ***(affine) invariant polyhedron*** of $\boldsymbol{x}_0$.

Example: Recall a reaction network of the Lotka-Volterra system in XY-plane. Given a rate constants vector $\boldsymbol{k} = (k_{\boldsymbol{y}\to\boldsymbol{y}'})_{\boldsymbol{y}\to\boldsymbol{y}'\in G} \in \mathbb{R}^E_{>0}$, the mass-action system $(G, \boldsymbol{k})$ is given by

$$X \xrightarrow{k_1} 2X, \quad X+Y \xrightarrow{k_2} 2Y, \quad Y \xrightarrow{k_3} 0.$$

Then the associated dynamical system is

$$\frac{d\boldsymbol{x}}{dt} = k_1 x_1 \begin{pmatrix} 1 \\ 0 \end{pmatrix} + k_2 x_1 x_2 \begin{pmatrix} -1 \\ 1 \end{pmatrix} + k_3 x_2 \begin{pmatrix} 0 \\ -1 \end{pmatrix} = \begin{pmatrix} k_1 x_1 \quad - k_2 x_1 x_2 \\ k_2 x_1 x_2 - k_3 x_2 \end{pmatrix}.$$

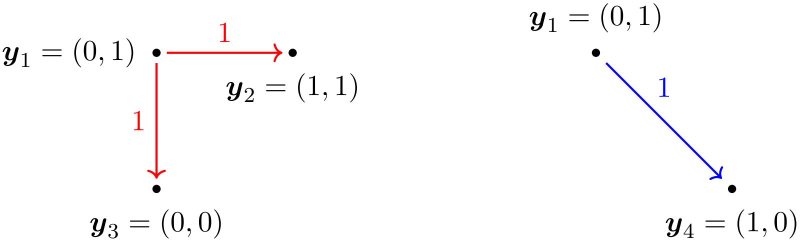


Two mass-action systems $(G, \boldsymbol{k})$ and $(G', \boldsymbol{k}')$ are said to be **dynamically equivalent**, if for every vertex $\boldsymbol{y}_0 \in V \cup V'$,

$$\sum_{\boldsymbol{y}_0 \to \boldsymbol{y} \in E} k_{\boldsymbol{y}_0 \to \boldsymbol{y}} (\boldsymbol{y} - \boldsymbol{y}_0) = \sum_{\boldsymbol{y}_0 \to \boldsymbol{y}' \in E'} k'_{\boldsymbol{y}_0 \to \boldsymbol{y}'} (\boldsymbol{y}' - \boldsymbol{y}_0). \tag{1}$$

We let $(G, \boldsymbol{k}) \sim (G', \boldsymbol{k}')$ denote that two systems $(G, \boldsymbol{k})$ and $(G', \boldsymbol{k}')$ are dynamically equivalent.

Example: Figure 3 gives an example of two dynamically equivalent mass-action systems.



(a) $G = (V, E)$ (b) $G' = (V', E')$

Figure: The mass-action systems in (a) and (b) are dynamically equivalent.

Dynamical Inclusion

Let G and G' be two E-graphs. Then the dynamics of G is said to be **included** within the dynamics of G', denoted by $G \sqsubseteq G'$, if for any $\boldsymbol{k} \in \mathbb{R}_{>0}^{|E|}$, there exists $\boldsymbol{k}' \in \mathbb{R}_{>0}^{|E'|}$ such that $(G, \boldsymbol{k}) \sim (G', \boldsymbol{k}')$.

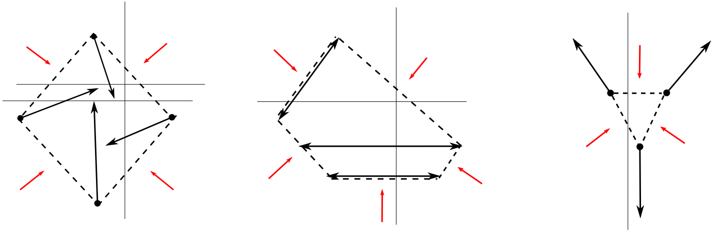
We are now ready to pose the central question of this talk

Question: Given an E-graph $G = (V, E)$, what are the necessary and sufficient conditions on G such that there exists an E-graph $G' \subseteq_{wr} G_c$ and $G \sqsubseteq G'$ (Here G_c refers to the complete graph on the source vertices of G)? [1]

[1]: J. Jin, G. Craciun, and P. Yu. "An efficient characterization of complex-balanced, detailed-balanced, and weakly reversible systems". In: *SIAM J. Appl. Math.* 80.1 (2020), pp. 183–205

Endotactic Networks

- Intuition: Endo -"Inward pointing networks"
- Can be verified using the "parallel sweep test".



(a) (b) (c)

(a) and (b) are endotactic, but (c) is not endotactic.

G. Craciun, F. Nazarov, and C. Pantea, Persistence and permanence of mass-action and power-law dynamical systems, SIAM J. Appl. Math., 73(1), 305–329.

Necessary Conditions for the dynamics an E-Graph G to be included in the dynamics of a Weakly Reversible E-graph G_1

[2]:S. Kothari, J. Jin, and **Deshpande, A.** "Realizations through Weakly Reversible Networks and the Globally Attracting Locus". In: *arXiv preprint arXiv:2409.04802* (2024)

Necessary Conditions for the dynamics an E-Graph G to be included in the dynamics of a Weakly Reversible E-graph G_1

G is endotactic. [2]

[2]:S. Kothari, J. Jin, and **Deshpande, A.** "Realizations through Weakly Reversible Networks and the Globally Attracting Locus". In: *arXiv preprint arXiv:2409.04802* (2024)

Net reaction vector and graph

Let $(G, \boldsymbol{k})$ be a mass-action system. For every vertex $\boldsymbol{y} \in V$, the **net reaction vector** associated with $\boldsymbol{y}$ is defined as follows:

$$\boldsymbol{w}_{\boldsymbol{y}} = \sum_{\boldsymbol{y} \to \boldsymbol{y}' \in E} k_{\boldsymbol{y} \to \boldsymbol{y}'} (\boldsymbol{y}' - \boldsymbol{y}).$$

Let $(G, \boldsymbol{k})$ be a mass-action system. The **E-graph corresponding to the net reaction vectors of** $(G, \boldsymbol{k})$, denoted by $G_{\boldsymbol{W}(\boldsymbol{k})}$, is defined as follows:

- All source vertices of $G_{\boldsymbol{W}(\boldsymbol{k})}$ correspond to the source vertices of G.
- For every source vertex $\boldsymbol{y}$ of $G_{\boldsymbol{W}(\boldsymbol{k})}$, there exists a corresponding target vertex $\hat{\boldsymbol{y}}$ and an edge $\boldsymbol{y} \to \hat{\boldsymbol{y}} \in G_{\boldsymbol{W}(\boldsymbol{k})}$ such that

$$\hat{\boldsymbol{y}} - \boldsymbol{y} = \boldsymbol{w}_{\boldsymbol{y}},$$

where $\boldsymbol{w}_{\boldsymbol{y}}$ is the net reaction vector associated with $\boldsymbol{y}$ of G.

Idea: Let $(G, \boldsymbol{k})$ and $(G', \boldsymbol{k}')$ be two mass-action systems. Suppose $G_{\boldsymbol{W}(\boldsymbol{k})}$ is the E-graph corresponding to the net reaction vectors of $(G, \boldsymbol{k})$. If G' is weakly reversible and $(G, \boldsymbol{k}) \sim (G', \boldsymbol{k}')$, then $G_{\boldsymbol{W}(\boldsymbol{k})}$ is endotactic.

Theorem 1

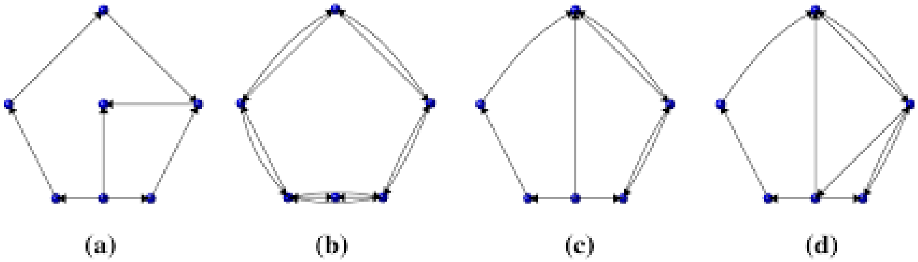
Let $G = (V, E)$ and $G' = (V', E')$ be two E-graphs. If G' is weakly reversible and $G \sqsubseteq G'$, then G is endotactic. Therefore, G being endotactic is a necessary condition for its dynamics to be included in the dynamics of a weakly reversible E-graph.

Sufficient Conditions for the Dynamics of E-Graph G to be Included in the Dynamics of a Weakly Reversible E-graph G_1

We start with the two-dimensional case:

Let $G = (V, E)$ be a strongly endotactic 2D E-graph with a two-dimensional stoichiometric subspace. Then there exists a weakly reversible single linkage class E-graph $G' \neq G$ such that $G \sqsubseteq G'$ if and only if at least one of the following holds:

- all source vertices of G lie on boundary of $\mathbf{New}(G)$.
- there exists a source vertex $\boldsymbol{y}_0$ on the boundary of $\mathbf{New}(G)$, such that the net reaction vector corresponding to $\boldsymbol{y}_0$ points strictly in the interior of $\mathbf{New}(G)$.

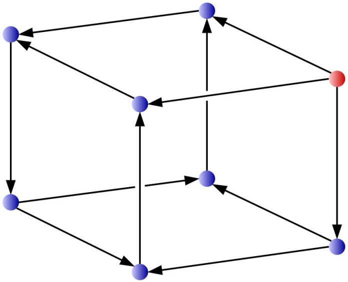


D. F. Anderson, J. D. Brunner, G. Craciun, M. D. Johnston, On classes of reaction networks and their associated polynomial dynamical systems, J. Math. Chem., 58 (2020): 1895-1925.

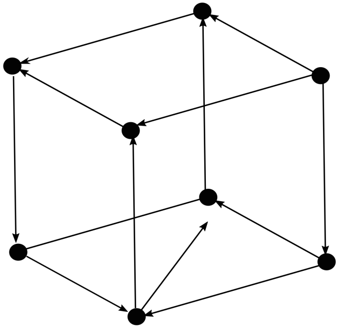
Sufficient Conditions for an E-Graph G Dynamics to be Included in the Dynamics of a Weakly Reversible E-graph G_1

Higher dimensions !

This limitation is illustrated in following figure which presents a counterexample where there is no weakly reversible E-graph whose dynamics can include the dynamics generated by this network.



Let $G = (V, E)$ be an E-graph that has ℓ linkage classes, denoted by $L_1, \ldots, L_\ell$, and p terminal strongly connected components, denoted by $T_1, \ldots, T_p$. For every $\boldsymbol{k} \in \mathbb{R}_{>0}^{|E|}$, every terminal strongly connected component T_i contains a vertex whose net reaction vector points strictly in the interior of $\mathbf{New}(L_j)$ with $T_i \subset L_j$. Then there exists a weakly reversible E-graph G' such that $G \sqsubseteq G'$.



Toric Locus, Disguised Toric Locus and Globally Attracting Locus

Complex-balanced system

- Let $(G, \boldsymbol{k})$ be a mass-action system, a state $\boldsymbol{x}_0 \in \mathbb{R}^n_{>0}$ is a ***positive steady state*** if

$$\sum_{\boldsymbol{y} \to \boldsymbol{y}' \in G} k_{\boldsymbol{y} \to \boldsymbol{y}'} \boldsymbol{x}_0^{\boldsymbol{y}} (\boldsymbol{y}' - \boldsymbol{y}) = \boldsymbol{0}.$$

Complex-balanced system

- Let $(G, \boldsymbol{k})$ be a mass-action system, a state $\boldsymbol{x}_0 \in \mathbb{R}^n_{>0}$ is a ***positive steady state*** if

$$\sum_{\boldsymbol{y} \to \boldsymbol{y}' \in G} k_{\boldsymbol{y} \to \boldsymbol{y}'} \boldsymbol{x}_0^{\boldsymbol{y}} (\boldsymbol{y}' - \boldsymbol{y}) = \mathbf{0}.$$

- A positive steady state $\boldsymbol{x}_0 \in \mathbb{R}^n_{>0}$ is ***complex-balanced*** if for every vertex $\boldsymbol{y}_0 \in V_G$, we have

$$\underbrace{\sum_{\boldsymbol{y}_0 \to \boldsymbol{y}' \in G} k_{\boldsymbol{y}_0 \to \boldsymbol{y}'} \boldsymbol{x}_0^{\boldsymbol{y}_0}}_{\text{outgoing flux on } \boldsymbol{y}_0} = \underbrace{\sum_{\boldsymbol{y} \to \boldsymbol{y}_0 \in G} k_{\boldsymbol{y} \to \boldsymbol{y}_0} \boldsymbol{x}_0^{\boldsymbol{y}}}_{\text{incoming flux on } \boldsymbol{y}_0}.$$

Complex-balanced system

- Let $(G, \boldsymbol{k})$ be a mass-action system, a state $\boldsymbol{x}_0 \in \mathbb{R}^n_{>0}$ is a ***positive steady state*** if

$$\sum_{\boldsymbol{y} \to \boldsymbol{y}' \in G} k_{\boldsymbol{y} \to \boldsymbol{y}'} \boldsymbol{x}_0^{\boldsymbol{y}} (\boldsymbol{y}' - \boldsymbol{y}) = \boldsymbol{0}.$$

- A positive steady state $\boldsymbol{x}_0 \in \mathbb{R}^n_{>0}$ is ***complex-balanced*** if for every vertex $\boldsymbol{y}_0 \in V_G$, we have

$$\underbrace{\sum_{\boldsymbol{y}_0 \to \boldsymbol{y}' \in G} k_{\boldsymbol{y}_0 \to \boldsymbol{y}'} \boldsymbol{x}_0^{\boldsymbol{y}_0}}_{\text{outgoing flux on } \boldsymbol{y}_0} = \underbrace{\sum_{\boldsymbol{y} \to \boldsymbol{y}_0 \in G} k_{\boldsymbol{y} \to \boldsymbol{y}_0} \boldsymbol{x}_0^{\boldsymbol{y}}}_{\text{incoming flux on } \boldsymbol{y}_0}.$$

- If $(G, \boldsymbol{k})$ has a complex-balanced steady state, then it is called **a complex-balanced system** or **toric dynamical system**.

Example: This system is complex-balanced. For example, at the vertex $(0, 1)$, there is one reaction going into it with flux value 3, and there are two reactions leaving this vertex, with sum of fluxes being $2 + 1 = 3$.

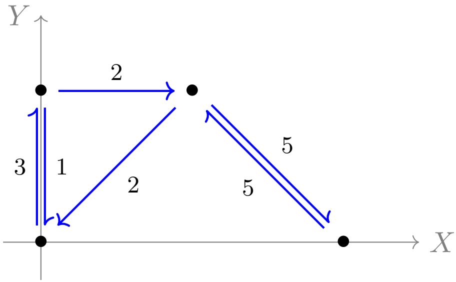


Figure: An example of a complex-balanced system. The positive numbers on any edge is the flux of that reaction $\boldsymbol{y} \to \boldsymbol{y}'$.

Example: This system is complex-balanced. For example, at the vertex $(0,1)$, there is one reaction going into it with flux value 3, and there are two reactions leaving this vertex, with sum of fluxes being $2+1=3$.

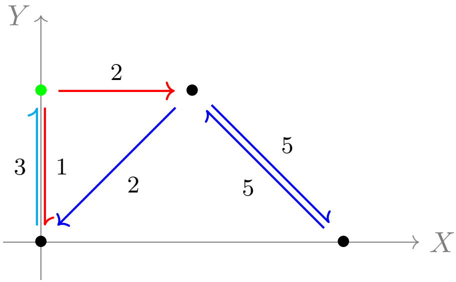


Figure: An example of a complex-balanced system. The positive numbers on any edge is the flux of that reaction $\boldsymbol{y} \to \boldsymbol{y}'$.

Toric locus

- Consider a E-graph $G = (V, E)$, let $\mathcal{V}(G) \subseteq \mathbb{R}^E_{>0}$ denote the set of parameters $\boldsymbol{k} \in \mathbb{R}^E_{>0}$, for which the dynamical system generated by $(G, \boldsymbol{k})$ is toric (i.e., complex-balanced).

[3]: F. Horn. "Necessary and sufficient conditions for complex balancing in chemical kinetics". In: *Arch. Ration. Mech. Anal.* 49.3 (1972), pp. 172–186

Toric locus

- Consider a E-graph $G = (V, E)$, let $\mathcal{V}(G) \subseteq \mathbb{R}^E_{>0}$ denote the set of parameters $\boldsymbol{k} \in \mathbb{R}^E_{>0}$, for which the dynamical system generated by $(G, \boldsymbol{k})$ is toric (i.e., complex-balanced).

- $\mathcal{V}(G)$ is called the **toric locus** of toric dynamical systems given by the Euclidean embedded graph G.

[3]: F. Horn. "Necessary and sufficient conditions for complex balancing in chemical kinetics". In: *Arch. Ration. Mech. Anal.* 49.3 (1972), pp. 172–186

Toric locus

- Consider a E-graph $G = (V, E)$, let $\mathcal{V}(G) \subseteq \mathbb{R}^{E}_{>0}$ denote the set of parameters $\boldsymbol{k} \in \mathbb{R}^{E}_{>0}$, for which the dynamical system generated by $(G, \boldsymbol{k})$ is toric (i.e., complex-balanced).
- $\mathcal{V}(G)$ is called the **toric locus** of toric dynamical systems given by the Euclidean embedded graph G.
- In [3], it shows that given an E-graph $G = (V, E)$,
  1. If $G = (V, E)$ is weakly reversible, then $\mathcal{V}(G) \neq \emptyset$.
  2. If $G = (V, E)$ is not weakly reversible, then $\mathcal{V}(G) = \emptyset$.

[3]: F. Horn. "Necessary and sufficient conditions for complex balancing in chemical kinetics". In: *Arch. Ration. Mech. Anal.* 49.3 (1972), pp. 172–186

Deficiency and Deficiency Zero Theorem

Let $G = (V, E)$ be a reaction network with ℓ connected components and the stoichiometric subspace $\mathcal{S}$. Suppose that $s = \dim S$, then the **deficiency** of the network G is given by

$$\delta = |V| - \ell - s \geq 0.$$

Deficiency Zero Theorem

A mass-action system is complex-balanced for every set of positive rate constants if and only if it is weakly reversible and deficiency zero.

Example:t This system is weakly reversible and deficiency zero.

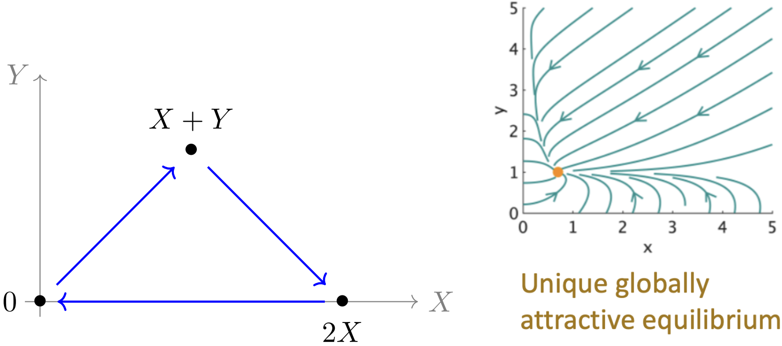


Figure: An example of a weakly reversible and deficiency zero system. It is complex-balanced for any positive rate constants

The dimension of the toric locus $\mathcal{V}(G)$

Consider an E-graph $G = (V, E)$ with ℓ connected components. Let s be the dimension of the stoichiometric subspace $\mathcal{S}$, then

$$\dim(\mathcal{V}(G)) = |E| - (|V| - l - s).$$

[4]: G. Craciun, A. Dickenstein, A. Shiu, and B. Sturmfels. "Toric dynamical systems". In: *J. Symbolic Comput.* 44.11 (2009), pp. 1551–1565

The dimension of the toric locus $\mathcal{V}(G)$

Consider an E-graph $G = (V, E)$ with ℓ connected components. Let s be the dimension of the stoichiometric subspace $\mathcal{S}$, then

$$\dim(\mathcal{V}(G)) = |E| - (|V| - l - s).$$

Let $G = (V, E)$ be a weakly reversible E-graph. Then the codimension of the toric locus $\mathcal{V}(G) \subseteq \mathbb{R}^E_{>0}$ is δ [4].

[4]: G. Craciun, A. Dickenstein, A. Shiu, and B. Sturmfels. "Toric dynamical systems". In: *J. Symbolic Comput.* 44.11 (2009), pp. 1551–1565

Disguised Toric Systems

- Recall that the **toric locus** on an E-graph G is

$$\mathcal{K}(G) := \{\boldsymbol{k} \in \mathbb{R}^{E}_{>0} \; \big| \text{the mass-action system generated by } (G, \boldsymbol{k}) \text{ is toric}\}.$$

- A dynamical system of the form

$$\frac{\mathrm{d}\boldsymbol{x}}{\mathrm{d}t} = \boldsymbol{f}(\boldsymbol{x}),$$

is called **disguised toric** on G, if it is realizable on G for some $\boldsymbol{k} \in \mathcal{K}(G) \subseteq \mathbb{R}^{E}_{>0}$, i.e., it has a **complex-balanced realization** on $G = (V, E)$.

[5]: **J. Jin**, G. Craciun, and **Deshpande, A.** "A Lower Bound on the Dimension of the Disguised Toric Locus". In: *In revision by SIAM Journal on Applied Algebra and Geometry* (2023)

Disguised Toric Locus

Let $G = (V, E)$ and $G' = (V', E')$ be two E-graphs.

(a) Define the set $\mathcal{K}_{disg}(G, G')$ as

$$\mathcal{K}_{disg}(G, G') := \{\boldsymbol{k} \in \mathbb{R}^E \mid \text{the dynamical system } (G, \boldsymbol{k}) \text{ is disguised toric on } G'\}.$$

Let $G = (V, E)$ and $G' = (V', E')$ be two E-graphs.

(a) Define the set $\mathcal{K}_{disg}(G, G')$ as

$$\mathcal{K}_{disg}(G, G') := \{\boldsymbol{k} \in \mathbb{R}^E \;\big|\; \text{the dynamical system } (G, \boldsymbol{k}) \text{ is disguised toric on } G'\}.$$

(b) We define the **disguised toric locus** of G as

$$\mathcal{K}_{disg}(G) = \bigcup_{G' \sqsubseteq G_c} \mathcal{K}_{disg}(G, G'),$$

where G_c represents the complete graph of G.

The Globally attracting locus of G

Consider an E-graph $G = (V, E)$. The **globally attracting locus** of G is defined as follows:

$$\mathcal{K}_{global}(G) := \big\{ \boldsymbol{k} \in \mathbb{R}^{|E|}_{>0} \;\big|\; (G, \boldsymbol{k}) \text{ has a globally attracting steady state} \\ \text{within each stoichiometric compatibility class} \big\}$$

Flux vector

Let $G = (V, E)$ be an E-graph.

- Let $\boldsymbol{J} = (J_{\boldsymbol{y_i} \to \boldsymbol{y_j}})_{\boldsymbol{y_i} \to \boldsymbol{y_j} \in E} \in \mathbb{R}^E_{>0}$ denote a **flux vector**, whose component $J_{\boldsymbol{y_i} \to \boldsymbol{y_j}} = k_{\boldsymbol{y_i} \to \boldsymbol{y_j}} x^{\boldsymbol{y_i}} > 0$ is called the **flux** of the reaction $\boldsymbol{y_i} \to \boldsymbol{y_j}$.

Flux vector

Let $G = (V, E)$ be an E-graph.

- Let $\boldsymbol{J} = (J_{\boldsymbol{y_i} \to \boldsymbol{y_j}})_{\boldsymbol{y_i} \to \boldsymbol{y_j} \in E} \in \mathbb{R}^E_{>0}$ denote a **flux vector**, whose component $J_{\boldsymbol{y_i} \to \boldsymbol{y_j}} = k_{\boldsymbol{y_i} \to \boldsymbol{y_j}} x^{\boldsymbol{y_i}} > 0$ is called the **flux** of the reaction $\boldsymbol{y_i} \to \boldsymbol{y_j}$.

- A flux vector $\boldsymbol{J}$ is called a **complex-balanced flux vector** , if at each vertex $\boldsymbol{y}_0 \in V$,

$$\sum_{\boldsymbol{y} \to \boldsymbol{y}_0 \in E} J_{\boldsymbol{y} \to \boldsymbol{y}_0} = \sum_{\boldsymbol{y}_0 \to \boldsymbol{y}' \in E} J_{\boldsymbol{y}_0 \to \boldsymbol{y}'}$$

Flux vector

Let $G = (V, E)$ be an E-graph.

- Let $\boldsymbol{J} = (J_{\boldsymbol{y_i} \to \boldsymbol{y_j}})_{\boldsymbol{y_i} \to \boldsymbol{y_j} \in E} \in \mathbb{R}^{E}_{>0}$ denote a **flux vector**, whose component $J_{\boldsymbol{y_i} \to \boldsymbol{y_j}} = k_{\boldsymbol{y_i} \to \boldsymbol{y_j}} x^{\boldsymbol{y_i}} > 0$ is called the **flux** of the reaction $\boldsymbol{y_i} \to \boldsymbol{y_j}$.

- A flux vector $\boldsymbol{J}$ is called a **complex-balanced flux vector** , if at each vertex $\boldsymbol{y}_0 \in V$,

$$\sum_{\boldsymbol{y} \to \boldsymbol{y}_0 \in E} J_{\boldsymbol{y} \to \boldsymbol{y}_0} = \sum_{\boldsymbol{y}_0 \to \boldsymbol{y}' \in E} J_{\boldsymbol{y}_0 \to \boldsymbol{y}'}$$

- Recall that $\boldsymbol{x}_0 \in \mathbb{R}^{n}_{>0}$ is a ***complex-balanced steady state*** , if for every vertex $\boldsymbol{y}_0 \in V_G$,

$$\sum_{\boldsymbol{y}_0 \to \boldsymbol{y}' \in G} k_{\boldsymbol{y}_0 \to \boldsymbol{y}'} \boldsymbol{x}_0^{\boldsymbol{y}_0} = \sum_{\boldsymbol{y} \to \boldsymbol{y}_0 \in G} k_{\boldsymbol{y} \to \boldsymbol{y}_0} \boldsymbol{x}_0^{\boldsymbol{y}}$$

Sufficient condition for $\mathcal{K}_{global}(G) \neq \emptyset$

We now present the linear program designed to determine whether $\mathcal{K}_{disg}(G) \neq \emptyset$.

Linear program (P2): Given an E-graph G, consider its complete graph $G_c = (V, E_c)$. Find $\boldsymbol{J} = (J_{\boldsymbol{y}\to\boldsymbol{y}'})_{\boldsymbol{y}\to\boldsymbol{y}'\in E} \in \mathbb{R}^{|E|}_{>0}$ and $\boldsymbol{J}' = (J'_{\boldsymbol{y}\to\boldsymbol{y}'})_{\boldsymbol{y}\to\boldsymbol{y}'\in E_c} \in \mathbb{R}^{|E_c|}_{\geq 0}$ satisfying for every $\boldsymbol{y}_0 \in V$,

$$\sum_{\boldsymbol{y}_0\to\boldsymbol{y}_i\in E} J_{\boldsymbol{y}_0\to\boldsymbol{y}_i}(\boldsymbol{y}_i - \boldsymbol{y}_0) = \sum_{\boldsymbol{y}_0\to\boldsymbol{y}_j\in E_c} J'_{\boldsymbol{y}_0\to\boldsymbol{y}_j}(\boldsymbol{y}_j - \boldsymbol{y}_0), \tag{2}$$

$$\sum_{\boldsymbol{y}_0\to\boldsymbol{y}\in E_c} J'_{\boldsymbol{y}_0\to\boldsymbol{y}} = \sum_{\boldsymbol{y}'\to\boldsymbol{y}_0\in E_c} J'_{\boldsymbol{y}'\to\boldsymbol{y}_0}. \tag{3}$$

Theorem

Let $G = (V, E)$ be an endotactic E-graph with a two-dimensional stoichiometric subspace. Assume that the linear program $(P2)$ has a solution, then $\mathcal{K}_{global}(G) \neq \emptyset$[5, 6].

[5, 6]: **J. Jin**, G. Craciun, and **Deshpande, A.** "A Lower Bound on the Dimension of the Disguised Toric Locus". In: *In revision by SIAM Journal on Applied Algebra and Geometry* (2023), J. Jin, G. Craciun, and **Deshpande A.** "On the connectivity of the Disguised Toric Locus". In: *Accepted by Journal of Mathematical Chemistry* (2023)

Thomas type models

Consider the network G shown in Figure below. This is commonly used to model the oxidation of uric acid by oxygen in the presence of the enzyme uricase. In this context, the species X and Y represent uric acid and oxygen, respectively.

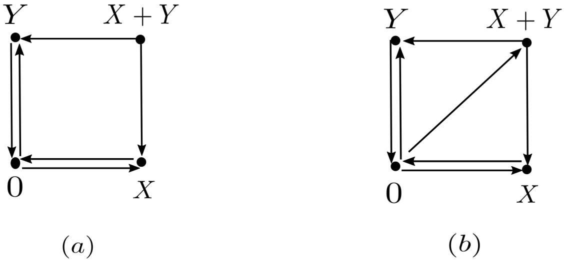


Figure: (a) An E-graph G represents the Thomas type model. (b) The weakly reversible E-graph G' includes the dynamics of the network G in (a).

We now consider the linear program (P2), which has a solution as follows:

$$
\begin{aligned}
&J'_{0\to X} = J'_{0\to Y} = J'_{X+Y\to X} = J'_{X+Y\to Y} = 1,\\
&J'_{X\to 0} = J'_{Y\to 0} = J'_{0\to X+Y} = 2,\\
&J_{0\to X} = J_{0\to Y} = 3,\ J_{X+Y\to X} = J_{X+Y\to Y} = 1,\ J_{X\to 0} = J_{Y\to 0} = 2.
\end{aligned}
$$

We now consider the linear program (P2), which has a solution as follows:

$$
\begin{aligned}
&J'_{0\to X} = J'_{0\to Y} = J'_{X+Y\to X} = J'_{X+Y\to Y} = 1,\\
&J'_{X\to 0} = J'_{Y\to 0} = J'_{0\to X+Y} = 2,\\
&J_{0\to X} = J_{0\to Y} = 3,\ J_{X+Y\to X} = J_{X+Y\to Y} = 1,\ J_{X\to 0} = J_{Y\to 0} = 2.
\end{aligned}
$$

We obtain that $\mathcal{K}_{disg}(G, G') \neq \emptyset$. Further, we have $\mathcal{K}_{disg}(G) \subseteq \mathcal{K}_{global}(G)$, therefore we conclude $\mathcal{K}_{global}(G) \neq \emptyset$.

Modified Selkov models

Consider the network G shown in Figure below. This network is an example of a modified *Selkov model*, commonly used to model glycolysis, a multi-step anaerobic process in which glucose is broken down into pyruvate.

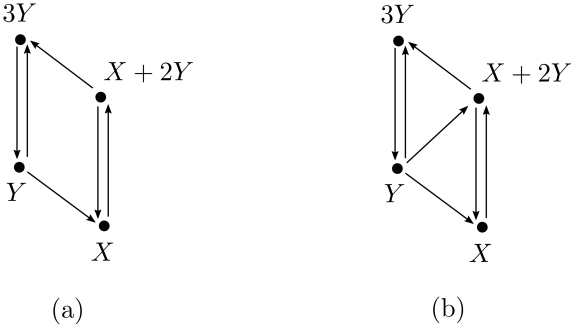


Figure: (a) An E-graph G represents the modified Selkov network. (b) The weakly reversible E-graph G' includes the dynamics of the network G in (a).

We now consider the linear program (P2), which has a solution as follows:

$$\begin{gathered}J'_{Y\to 3Y} = J'_{Y\to X+2Y} = J'_{Y\to X} = J'_{X+2Y\to X} = 1,\\ J'_{X+2Y\to 3Y} = J'_{X\to X+2Y} = 2, J'_{3Y\to Y} = 3, J_{X+2Y\to X} = 1,\\ J_{Y\to 3Y} = J_{Y\to X} = J_{X+2Y\to 3Y} = J_{X\to X+2Y} = 2,\ J_{3Y\to Y} = 3.\end{gathered}$$

We now consider the linear program (P2), which has a solution as follows:

$$
\begin{gathered}
J'_{Y\to 3Y} = J'_{Y\to X+2Y} = J'_{Y\to X} = J'_{X+2Y\to X} = 1, \\
J'_{X+2Y\to 3Y} = J'_{X\to X+2Y} = 2, J'_{3Y\to Y} = 3, J_{X+2Y\to X} = 1, \\
J_{Y\to 3Y} = J_{Y\to X} = J_{X+2Y\to 3Y} = J_{X\to X+2Y} = 2,\ J_{3Y\to Y} = 3.
\end{gathered}
$$

we obtain that $\mathcal{K}_{disg}(G, G') \neq \emptyset$. Further we get that $\mathcal{K}_{disg}(G) \subseteq \mathcal{K}_{global}(G)$, therefore we conclude $\mathcal{K}_{global}(G) \neq \emptyset$.

Summary

Summary

- Necessary conditions for the dynamics of an E-graph to be included in the dynamics of a weakly reversible E-graph.

Summary

- Necessary conditions for the dynamics of an E-graph to be included in the dynamics of a weakly reversible E-graph.
- Sufficient conditions for the dynamics of an E-graph to be included in the dynamics of a weakly reversible E-graph.
  - Two dimensional networks.
  - Higher dimensional networks.

Summary

- Necessary conditions for the dynamics of an E-graph to be included in the dynamics of a weakly reversible E-graph.
- Sufficient conditions for the dynamics of an E-graph to be included in the dynamics of a weakly reversible E-graph.
  - Two dimensional networks.
  - Higher dimensional networks.
- Toric Locus, Disguised Toric Locus, Globally Attracting locus.

References

[1] J. Jin, G. Craciun, and P. Yu. "An efficient characterization of complex-balanced, detailed-balanced, and weakly reversible systems". In: *SIAM J. Appl. Math.* 80.1 (2020), pp. 183–205 (cit. on p. 18).

[2] S. Kothari, J. Jin, and **Deshpande, A.** "Realizations through Weakly Reversible Networks and the Globally Attracting Locus". In: *arXiv preprint arXiv:2409.04802* (2024) (cit. on pp. 20, 21).

[3] F. Horn. "Necessary and sufficient conditions for complex balancing in chemical kinetics". In: *Arch. Ration. Mech. Anal.* 49.3 (1972), pp. 172–186 (cit. on pp. 34–36).

[4] G. Craciun, A. Dickenstein, A. Shiu, and B. Sturmfels. "Toric dynamical systems". In: *J. Symbolic Comput.* 44.11 (2009), pp. 1551–1565 (cit. on pp. 39, 40).

[5] **J. Jin**, G. Craciun, and **Deshpande, A.** "A Lower Bound on the Dimension of the Disguised Toric Locus". In: *In revision by SIAM Journal on Applied Algebra and Geometry* (2023) (cit. on pp. 41, 49).

[6] J. Jin, G. Craciun, and **Deshpande A.** "On the connectivity of the Disguised Toric Locus". In: *Accepted by Journal of Mathematical Chemistry* (2023) (cit. on p. 49).

Thank you !