Ruling out Hopf bifurcations in biochemical reaction networks

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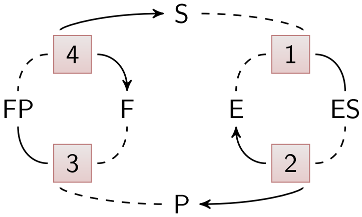
The futile cycle can not give rise to Hopf bifurcations

$$E + S \rightleftharpoons ES \rightarrow E + P$$

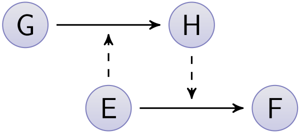
$$F + S \leftarrow FP \leftrightharpoons F + P$$



Ingredients

1. DSR graph
2. P_0-matrices
3. Second additive compound matrices

DSR graphs

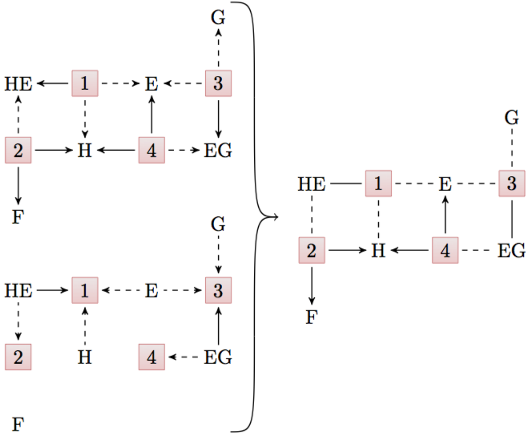


$$H + E \rightleftharpoons HE \to H + F$$

$$E + G \rightleftharpoons EG \to E + H$$

$$\Gamma = \begin{array}{cc} \begin{bmatrix} -1 & 1 & 0 & 1 \\ -1 & 0 & -1 & 1 \\ 1 & -1 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & -1 & 0 \\ 0 & 0 & 1 & -1 \end{bmatrix} & \begin{array}{l} \mathrm{H} \\ \mathrm{E} \\ \mathrm{HE} \\ \mathrm{F} \\ \mathrm{G} \\ \mathrm{EG} \end{array} \end{array}$$

$$V = \begin{array}{cc} \begin{bmatrix} - & 0 & 0 & 0 \\ - & 0 & - & 0 \\ + & - & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & - & 0 \\ 0 & 0 & + & - \end{bmatrix} & \begin{array}{l} \mathrm{H} \\ \mathrm{E} \\ \mathrm{HE} \\ \mathrm{F} \\ \mathrm{G} \\ \mathrm{EG} \end{array} \end{array}$$



DSR graphs and P_0 matrices

Theorem [Banaji, Craciun 2009] If the DSR graph associated to Γ and V satisfies condition $(*)$

$(*)$ *all e-cycles are s-cycles and*
no two e-cycles have odd intersection

then ΓV is a P_0-matrix.

• In particular, for an open kinetic system whose Jacobian is $J = -\Gamma V$, multiple equilibria are ruled out.
• The success of the theorem depends on some sign compatibility between Γ and V (satisfied for systems with reasonable kinetics).

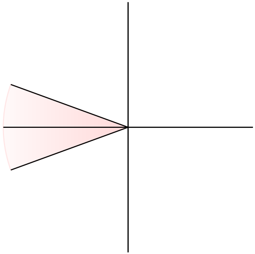
P_0-matrices

- square matrices all of whose principal minors are nonnegative.

Theorem (Kellog)

If $\lambda = re^{i\theta}$ is an eigenvalue of an $n \times n$ P_0-matrix then

$$|\theta - \pi| \geq \pi/n\,.$$



Second additive compounds $J^{[2]}$ of Jacobian matrices

$J \in \mathbb{R}^{n\times n}$ with $\mathrm{Spec}\ J = \{\lambda_1 \ldots, \lambda_n\}$.

$J^{[2]}$ is an $\binom{n}{2} \times \binom{n}{2}$ matrix and

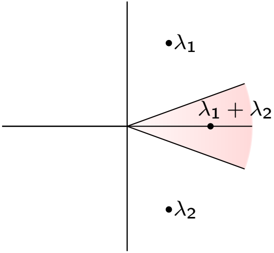
$$\mathrm{Spec}\ J^{[2]} = \{\lambda_i + \lambda_j | 1 \leq i < j \leq n\}.$$

Moreover, if $J = \Gamma V$ where $\Gamma, V^t \in \mathbb{R}^{n\times m}$ we can write

$$J^{[2]} = \overline{\mathbf{L}}^{\Gamma} \underline{\mathbf{L}}^{V}.$$

$\overline{\mathbf{L}}^{\Gamma}, (\underline{\mathbf{L}}^{V})^t \in \mathbb{R}^{\binom{n}{2}\times nm}$

What if $-J^{[2]}$ is a P_0 matrix?



$$\text{Spec } J \backslash \mathbb{R} \subset \overline{\mathbb{C}_-}$$

No Hopf bifurcation!

Line of thought

Cycle structure of the DSR graph assoc. with $\overline{\mathbf{L}}^{\Gamma}$ and $\underline{\mathbf{L}}^{V}$

$\Downarrow$

$-J^{[2]}$ is a P_0 matrix

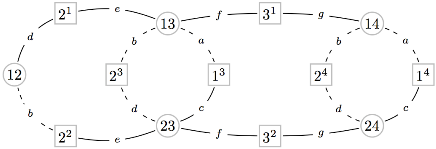
$\Downarrow$

no Hopf bifurcations

The DSR$^{[2]}$ graph

- defined to be the DSR graph of $\overline{\mathbf{L}}^{\Gamma}$ and $\underline{\mathbf{L}}^{V}$.

$$\Gamma = \begin{pmatrix} a & b & 0 \\ -c & d & 0 \\ 0 & e & f \\ 0 & 0 & g \end{pmatrix} ; \; V \in \mathrm{Q}(-\Gamma^{t})$$

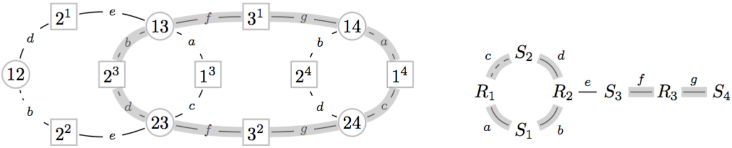


Above DSR$^{[2]}$ satisfies condition $(*)$, therefore $-J^{[2]}$ is a P_0-matrix;

no Hopf bifurcations.

Relationships between DSR and DSR$^{[2]}$ structures

- cycles in DSR$^{[2]}$ "project" to closed walks in DSR:



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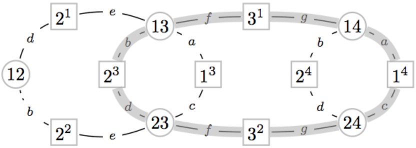

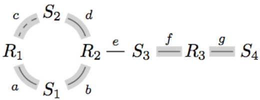

- in various cases, condition ($*$) for DSR$^{[2]}$ translates into nice conditions on DSR:

Theorem (Angeli, Banaji, Pantea, *Comm. Math. Sci.* 2014)

Suppose a reaction network has all stoichiometric coefficients equal to 1 and each species participates in at most two reactions. Then Hopf bifurcations are ruled out for any choice of general kinetics.

Thank you!

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