Deterministic reaction networks – part I: Existence/uniqueness of positive equilibria

Stefan Müller

Faculty of Mathematics, University of Vienna

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Outline

1. Reaction networks:
   stoichiometry and kinetics
   dynamical system

2. Equilibria:
   existence/uniqueness
   results depending on network properties or not

3. Abstract framework:
   parametrized systems of generalized polynomial equations
   "positive algebraic geometry"

1. Reaction networks

Modeling framework

- chemistry
- biology (ecology, epidemiology)
- economics, engineering

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Every power-law dynamical system
(and hence every polynomial dynamical system)
arises from a
reaction network with (generalized) mass-action kinetics.

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Example:
species $= \{\mathsf{A}, \mathsf{B}, \mathsf{C}, \mathsf{D}\}$
complexes $= \{\mathsf{A}+\mathsf{B}, \mathsf{C}, 2\mathsf{A}, \mathsf{A}, \mathsf{D}\}$ formal sums of scecies
reacts $= \{\mathsf{A}+\mathsf{B} \to \mathsf{C}, \mathsf{C} \to \mathsf{A}+\mathsf{B}, \mathsf{C} \to 2\mathsf{A}, 2\mathsf{A} \to \mathsf{A}+\mathsf{B}, \mathsf{A} \to \mathsf{D}, \mathsf{D} \to \mathsf{A}\}$

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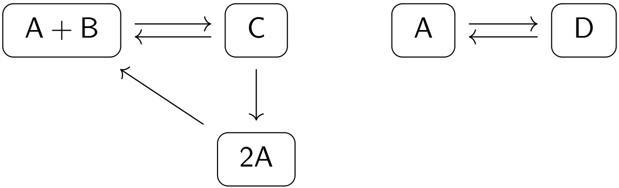
reacts = $\{A + B \to C, C \to A + B, C \to 2A, 2A \to A + B, A \to D, D \to A\}$

Definition induces *complex-reaction* graph:



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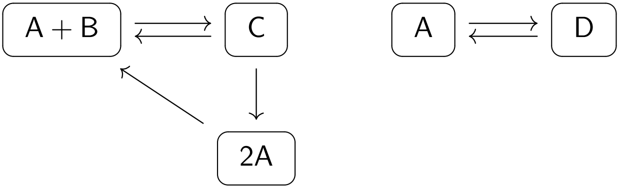

linkage classes: components of graph
graph *weakly reversible*: components strongly connected

Definitions

Modern definition:
reaction network = (graph, map)
map: vertices → complexes

M & Regensburger (2014). *Generalized Mass-Action Systems and Positive Solutions of Polynomial Equations with Real and Symbolic Exponents*, Proceedings of the 16th International Workshop *Computer Algebra in Scientific Computing* (CASC)

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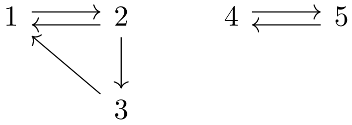

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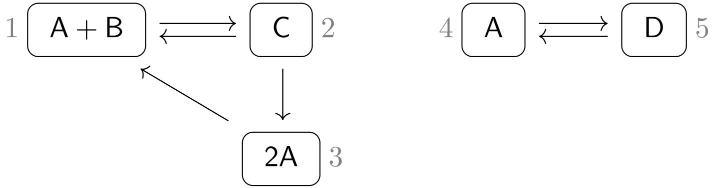

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Classical vs. modern

Example:

$$0 \rightleftarrows \mathsf{A} \rightleftarrows 2\mathsf{A} \rightleftarrows \mathsf{A} + \mathsf{B} \rightleftarrows 2\mathsf{B}$$

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Subnetworks:

$$0 \rightleftarrows A \rightleftarrows 2A \qquad 2A \rightleftarrows A + B \rightleftarrows 2B$$

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Not a network in the sense of the classical definition,
but in the sense of the modern definition.

Stoichiometry - what happens in a reaction

Examples of elementary (chemical) reactions:

$$\mathsf{A} \to \mathsf{B}, \quad \mathsf{A} + \mathsf{B} \to \mathsf{C}, \quad \mathsf{A} + \mathsf{B} \to \mathsf{C} + \mathsf{D}, \quad 2 \cdot \mathsf{A} \to \mathsf{B}, \quad \ldots$$

complexes of at most two molecular species

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General (or composite) reaction:

$$\mathsf{a} \cdot \mathsf{A} + \mathsf{b} \cdot \mathsf{B} + \mathsf{c} \cdot \mathsf{C} + \ldots \quad \to \quad \mathsf{a}' \cdot \mathsf{A} + \mathsf{b}' \cdot \mathsf{B} + \mathsf{c}' \cdot \mathsf{C} + \ldots$$

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General (or composite) reaction:

$$a \cdot A + b \cdot B + c \cdot C + \ldots \quad \to \quad a' \cdot A + b' \cdot B + c' \cdot C + \ldots$$

Autocatalysis:

chemistry	*epidemiology*	*ecology*
$A + B \to 2 \cdot A$	$I + S \to 2 \cdot I$	$F + R \to 2 \cdot F$
not in one step	I ... infected	F ... fox
	S ... susceptible	R ... rabbit

M, Flamm, Stadler (2022), *What makes a reaction network "chemical"?*, J of Cheminformatics

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Proper part of a reaction network must be conservative!

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Example:

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in/outflow "reactions": $0 \rightleftarrows \mathsf{A}$

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Futile cycles must not contain irreversible reactions!

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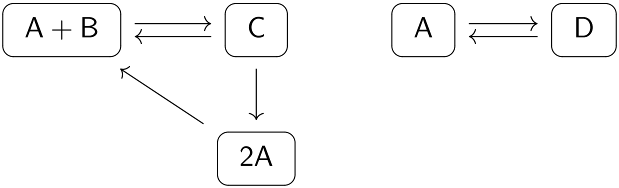

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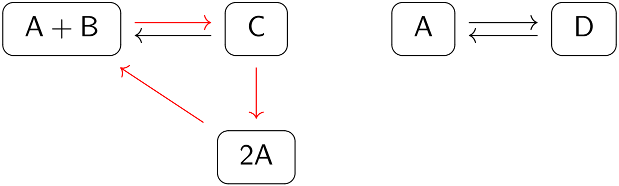

perpetuum mobile

Stoichiometry - more abstractly

With n species A, B, C, ..., we write

$$\mathsf{a} \cdot \mathsf{A} + \mathsf{b} \cdot \mathsf{B} + \mathsf{c} \cdot \mathsf{C} + \ldots \quad \rightarrow \quad \mathsf{a}' \cdot \mathsf{A} + \mathsf{b}' \cdot \mathsf{B} + \mathsf{c}' \cdot \mathsf{C} + \ldots$$

as

$$y \rightarrow y' \quad \text{with} \quad y, y' \in \mathbb{R}^n_{\geq}.$$

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For example, we write

$$1\,\mathsf{A}+1\,\mathsf{B}\rightarrow 1\,\mathsf{C}$$

as

$$y\rightarrow y' \quad \text{with} \quad y=\begin{matrix}\mathsf{A}\\ \mathsf{B}\\ \mathsf{C}\\ \vdots\end{matrix}\begin{pmatrix}1\\1\\0\\0\end{pmatrix},\ y'=\begin{pmatrix}0\\0\\1\\0\end{pmatrix},$$

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$$y \to y' \quad \text{with} \quad y = \begin{matrix}\mathsf{A}\\\mathsf{B}\\\mathsf{C}\\\vdots\end{matrix}\begin{pmatrix}1\\1\\0\\0\end{pmatrix},\ y' = \begin{pmatrix}0\\0\\1\\0\end{pmatrix}, \quad y' - y = \begin{pmatrix}-1\\-1\\1\\0\end{pmatrix}.$$

Kinetics - how fast a reaction happens

Rate of reaction $y \to y'$:

$$r_{y\to y'}(x) \geq 0$$

with concentrations/fractions of species $x \in \mathbb{R}^n_{\geq}$

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Results for

- "general" kinetics
- monotone, power-law, Michaelis-Menten, ...
- mass-action kinetics (MAK):

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monomial $x^y = \prod_{i=1}^n (x_i)^{y_i}$

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for example, for

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we have

$$r_{\mathsf{A}+\mathsf{B} \to \mathsf{C}}(x) = k_{\mathsf{A}+\mathsf{B} \to \mathsf{C}} \, x_{\mathsf{A}}^{1} \, x_{\mathsf{B}}^{1}.$$

Formal definitions

Reaction network (G, y):

graph $G = (V, E)$, $V = \{1, \ldots, m\}$, $E \subseteq V \times V$, ℓ connected components
map $y \colon V \to \mathbb{R}^n_{\geq}$ complexes

Edge $(i \to i') \in E$ (via map y) represents reaction $y(i) \to y(i')$.

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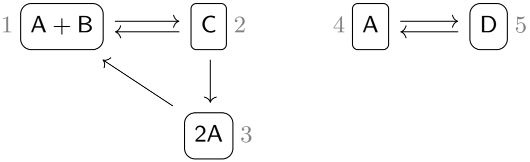
$$\frac{\mathrm{d}x}{\mathrm{d}t} = \sum_{i \to i' \in E} \big(y(i') - y(i)\big)\, k_{i \to i'}\, x^{y(i)}$$

Example with MAK



$$\frac{\mathrm{d}}{\mathrm{d}t}\begin{pmatrix} x_{\mathsf{A}} \\ x_{\mathsf{B}} \\ x_{\mathsf{C}} \\ x_{\mathsf{D}} \end{pmatrix} = N r_k(x) = \begin{array}{c} \\ \mathsf{A} \\ \mathsf{B} \\ \mathsf{C} \\ \mathsf{D} \end{array} \begin{array}{c} \begin{array}{cccccc} 12 & 21 & 23 & 31 & 45 & 54 \end{array} \\ \begin{pmatrix} -1 & 1 & 2 & -1 & -1 & 1 \\ -1 & 1 & 0 & 1 & 0 & 0 \\ 1 & -1 & -1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 & -1 \end{pmatrix} \end{array} \begin{pmatrix} k_{12}\, x_{\mathsf{A}} x_{\mathsf{B}} \\ k_{21}\, x_{\mathsf{C}} \\ k_{23}\, x_{\mathsf{C}} \\ k_{31}\, (x_{\mathsf{A}})^2 \\ k_{45}\, x_{\mathsf{A}} \\ k_{54}\, x_{\mathsf{D}} \end{pmatrix}$$

stoichiometric matrix N, rate vector $r_k(x)$

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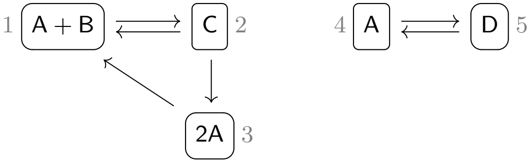

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complex matrix Y, Laplacian matrix A_k, monomial vector x^Y

Important objects

$$\frac{\mathsf{d}x}{\mathsf{d}t} = \sum_{i \to i' \in E} \big(y(i') - y(i)\big)\, r_{i \to i'}(x) = \underbrace{Y I_E}_{N}\, r(x)$$

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MAK:

$$\frac{\mathsf{d}x}{\mathsf{d}t} = Y \underbrace{I_E \operatorname{diag}(k) I_{E,s}^{\mathsf{T}}}_{A_k} x^Y = \begin{cases} N \left(k \circ x^V\right) \\ Y A_k\, x^Y \end{cases} \qquad V = Y I_{E,s}$$

Power-law kinetics

$$1\,\mathsf{A} + 1\,\mathsf{B} \rightarrow \mathsf{C}$$

$$r_{\mathsf{A+B\rightarrow C}}(x) = k_{\mathsf{A+B\rightarrow C}}\, x_{\mathsf{A}}^{1.1}\, x_{\mathsf{B}}^{0.8}$$

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- generalized mass-action kinetics (GMAK):
  keep stoichiometry and add kinetics,

$$\boxed{\begin{matrix}\mathsf{A}+\mathsf{B}\\ (\,1.1\ \mathsf{A} + 0.8\ \mathsf{B}\,)\end{matrix}} \to \boxed{\begin{matrix}\mathsf{C}\\ (\,\dots\,)\end{matrix}}$$

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$$\boxed{\begin{matrix}\mathsf{A+B} \\ (\,1.1\,\mathsf{A} + 0.8\,\mathsf{B}\,)\end{matrix}} \to \boxed{\begin{matrix}\mathsf{C} \\ (\,\ldots\,)\end{matrix}}$$

in general, for reaction $y \to y'$ with rate $r_{y\to y'}(x) = k_{y\to y'}\, x^{\tilde{y}}$,

$$\boxed{\begin{matrix}y \\ (\,\tilde{y}\,)\end{matrix}} \to \boxed{\begin{matrix}y' \\ (\,\ldots\,)\end{matrix}}$$

Formal definitions - continued

Generalized mass-action system $(G, y, \tilde{y}, k)$:

graph $G = (V, E)$, $V = \{1, \ldots, m\}$, $E \subseteq V \times V$, ℓ connected components
map $y \colon V \to \mathbb{R}^n_{\geq}$ (stoichiometric) complexes
map $\tilde{y} \colon V_s \to \mathbb{R}^n_{\geq}$ kinetic-order complexes
map $k \colon E \to \mathbb{R}_{>}$ rate constants

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Edge reaction $y(i) \to y(i')$ with rate $r_{i \to i'}(x) = k_{i \to i'} \, x^{\tilde{y}(i)}$

$i \to i'$

$$\begin{pmatrix} y(i) \\ (\, \tilde{y}(i) \,) \end{pmatrix} \to \begin{pmatrix} y(i') \\ (\, \ldots \,) \end{pmatrix}$$

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Important objects - continued

Decomposition (stoichiometry, graph, kinetic orders):

$$\frac{\mathrm{d}x}{\mathrm{d}t} = \begin{cases} N\left(k \circ x^{V}\right) \\ Y A_k \, x^{\tilde{Y}} \end{cases} \qquad V = \tilde{Y} I_{E,s}$$

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MAK = GMAK with $\tilde{Y} = Y$ and hence $\tilde{S} = S$ and $\tilde{\delta} = \delta$

Modeling: MAK via GMAK

SIR (susceptible, infected, removed) model:

$$0 \xrightarrow{b} \mathsf{S}, \quad \mathsf{S} \xrightarrow{d} 0, \quad \mathsf{S} + \mathsf{I} \xrightarrow{i} 2\,\mathsf{I}, \quad \mathsf{I} \xrightarrow{r} \mathsf{R}, \quad \mathsf{I} \xrightarrow{d} 0, \quad \mathsf{R} \xrightarrow{d} 0$$

constant population size, $b = d$:

$$\mathsf{S} \underset{b}{\overset{d}{\rightleftarrows}} 0 \xleftarrow{r+d} \mathsf{I}, \quad \mathsf{S} + \mathsf{I} \xrightarrow{i} 2\,\mathsf{I}$$

assume MAK: $1\,\mathsf{S} + 1\,\mathsf{I} \xrightarrow{i} 2\,\mathsf{I}, \quad r_i = k_i\, x_{\mathsf{S}}^1\, x_{\mathsf{I}}^1$

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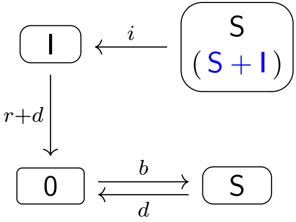
SIR model (with MAK via GMAK):



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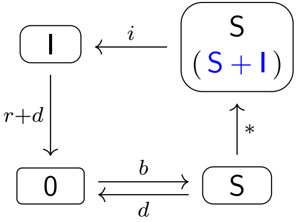

2. Equilibria

Positive equilibria for GMAK:

$$Z_k = \{x \in \mathbb{R}^n_> \mid Y A_k \, x^{\tilde{Y}} = 0\}$$

Positive complex-balanced equilibria (CBE):

$$C_k = \{x \in \mathbb{R}^n_> \mid A_k \, x^{\tilde{Y}} = 0\}$$

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Basic facts:

- If $C_k \neq \emptyset$ (for some k), then G is weakly reversible,
  that is, the components of the graph are strongly connected.
- If $C_k \neq \emptyset$, then $C_k = x_k^* \circ \mathrm{e}^{\tilde{S}^\perp}$ has a *monomial* parametrization,
  that is, it is given by *binomial* equations.
- If $\delta = 0$, then $Z_k = C_k$.
  recall: $\delta = \dim(\ker Y \cap \operatorname{im} I_E)$ and $\operatorname{im} A_k \subseteq \operatorname{im} I_E$.

Deficiency zero for MAK

$\delta = 0$ theorem (Horn & Jackson 1972, Horn 1972, Feinberg 1972)

For MAK,
there exists a unique positive equilibrium,
which is complex-balanced and asymptotically stable,
in every stoichiometric class $x' + S$ and for all rate constants k,
if and only if $\delta = 0$ and G is weakly reversible.

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unique and stable solution for all (unknown) model parameters

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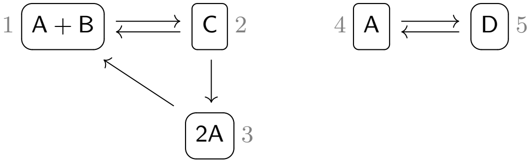
Result:
unique and stable solution for all (unknown) model parameters
vs.
multiple or unstable solutions for some (realistic) parameters

Example



$$\frac{\mathsf{d}}{\mathsf{d}t}\begin{pmatrix} x_\mathsf{A} \\ x_\mathsf{B} \\ x_\mathsf{C} \\ x_\mathsf{D} \end{pmatrix} = N\left(k \circ x^V\right) = \begin{array}{c} \\ \mathsf{A} \\ \mathsf{B} \\ \mathsf{C} \\ \mathsf{D} \end{array} \begin{array}{c} \begin{array}{cccccc} 12 & 21 & 23 & 31 & 45 & 54 \end{array} \\ \begin{pmatrix} -1 & 1 & 2 & -1 & -1 & 1 \\ -1 & 1 & 0 & 1 & 0 & 0 \\ 1 & -1 & -1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 & -1 \end{pmatrix} \end{array} \begin{pmatrix} k_{12}\, x_\mathsf{A} x_\mathsf{B} \\ k_{21}\, x_\mathsf{C} \\ k_{23}\, x_\mathsf{C} \\ k_{31}\, (x_\mathsf{A})^2 \\ k_{45}\, x_\mathsf{A} \\ k_{54}\, x_\mathsf{D} \end{pmatrix}$$

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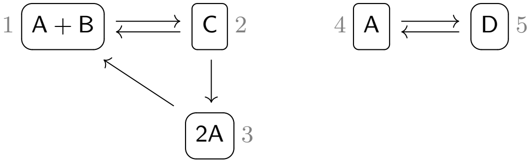

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$$m = 5, \quad \ell = 2, \quad \dim S = 3$$

$$\delta = m - \ell - \dim S = 0$$

G is weakly reversible.

Extensions

Kinetics:

- MAK
- power-law, GMAK
- monotonic

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Conditions:

- necessary
- sufficient
- equivalent

Injectivity $\implies$ uniqueness

Craciun & Feinberg (2005). *Multiple equilibria in complex chemical reaction networks: I. The injectivity property*, SIAM J of Applied Mathematics

Positive equilibria for MAK:
(with in/outflows for all species)

$$0 = \frac{\mathrm{d}x}{\mathrm{d}t} = \sum_{i \to i' \in E} \big(y(i') - y(i)\big)\, k_{i \to i'}\, x^{y(i)} =: f_k(x),$$

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Theorems (Craciun, Feinberg 2005)

The following statements are equivalent:

- f_k is injective for all $k \in \mathbb{R}^E_>$.
- $\det(\frac{\partial f_k}{\partial x}) \neq 0$ for all $x \in \mathbb{R}^n_>$ and $k \in \mathbb{R}^E_>$.
- All nonzero coefficients in $\det(\frac{\partial f_k}{\partial x})$ have the same sign.

Injectivity $\implies$ uniqueness

Craciun, Garcia-Puente, Sottile (2010). *Some Geometrical Aspects of Control Points for Toric Patches*, Mathematical Methods for Curves and Surfaces

Positive equilibria for power-law kinetics:
($N, V \in \mathbb{R}^{n\times r}$ and $k \in \mathbb{R}^r_>$)

$$0 = \frac{\mathrm{d}x}{\mathrm{d}t} = \sum_{j=1}^{r} n^j \cdot k_j \, x^{v^j} = N\left(k \circ x^V\right) := f_k(x),$$

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- $\det(N_I) \det(V_I) \geq 0$ for all $I \subseteq [r]$ of cardinality n (or '≤ 0' for all I) and $\det(N_I) \det(V_I) \neq 0$ for some I.

Injectivity $\implies$ uniqueness: compatibility classes

Feliu & Wiuf (2012). *Preclusion of switch behavior in reaction networks with mass-action kinetics*, J of Applied Mathematics and Computing

Gnacadja (2012). *A Jacobian criterion for the simultaneous injectivity on positive variables of linearly parameterized polynomials maps*, Linear Algebra and its Applications

Linear dependencies:

$$L\,x(t) = c \quad \text{with} \quad L \in \mathbb{R}^{l\times n} \text{ s.t. } LN = 0$$

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Theorems (Feliu & Wiuf 2012, Gnacadja 2012)

The following statements are equivalent:

- f_k is injective on compatibility classes for all $k \in \mathbb{R}^r_>$.
- $\tilde{f}_k$ is injective for all $k \in \mathbb{R}^r_>$.
- $\ker \frac{\partial f_k}{\partial x} \cap \operatorname{im} N = \{0\}$ for all $x \in \mathbb{R}^n_>$ and $k \in \mathbb{R}^r_>$.
- $\det(\frac{\partial \tilde{f}_k}{\partial x}) \neq 0$ for all $x \in \mathbb{R}^n_>$ and $k \in \mathbb{R}^r_>$.

Injectivity $\iff$ uniqueness

M & Regensburger (2012). *Generalized mass action systems: complex balancing equilibria and sign vectors of the stoichiometric and kinetic-order subspaces*, SIAM J on Applied Mathematics

CBE for GMAK:

$(S = \ker W$, $\tilde{S} = \ker \tilde{W}$ with $W \in \mathbb{R}^{d \times n}$, $\tilde{W} \in \mathbb{R}^{\tilde{d} \times n}$ and $x^* \in \mathbb{R}^n_>)$

$$F_{x^*}(\xi) := \sum_{j=1}^{n} w^j \cdot x_j^* \, \xi^{\tilde{W}^j} = W \left(x^* \circ \xi^{\tilde{W}} \right),$$

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Injectivity (M & Regensburger 2012)

The following statements are equivalent:

- F_{x^*} is injective for all x^*.
- $\frac{\partial F_{x^*}}{\partial \xi}$ is injective for all ξ and x^*.
- $\operatorname{sign}(S) \cap \operatorname{sign}(\tilde{S}^\perp) = \{0\}$.

Concordance $\iff$ injectivity $\implies$ uniqueness

Shinar & Feinberg (2012). *Concordant chemical reaction networks*, Mathematical Biosciences

Concordance $\iff$ injectivity $\implies$ uniqueness

Shinar & Feinberg (2012). *Concordant chemical reaction networks*, Mathematical Biosciences

Reaction network (G, y) with *weakly monotonic* kinetics r:

For every $x, x' \in \mathbb{R}^n_>$ and $(i \to i') \in E$,

1. $r_{i\to i'}(x') > r_{i\to i'}(x) \implies$ there is $j \in \mathrm{supp}(y(i))$ s.t. $x'_j > x_j$, and
2. $r_{i\to i'}(x') = r_{i\to i'}(x) \implies x'_j = x_j$ for all $j \in \mathrm{supp}(y(i))$ or there are $j, j' \in \mathrm{supp}(y(i))$ s.t. $x'_j > x_j$ and $x'_{j'} < x_{j'}$.

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Shinar & Feinberg (2012). *Concordant chemical reaction networks*, Mathematical Biosciences

Reaction network (G, y) with *weakly monotonic* kinetics r:

For every $x, x' \in \mathbb{R}^n_>$ and $(i \to i') \in E$,

- (i) $r_{i\to i'}(x') > r_{i\to i'}(x) \implies$ there is $j \in \operatorname{supp}(y(i))$ s.t. $x'_j > x_j$, and
- (ii) $r_{i\to i'}(x') = r_{i\to i'}(x) \implies x'_j = x_j$ for all $j \in \operatorname{supp}(y(i))$ or there are $j, j' \in \operatorname{supp}(y(i))$ s.t. $x'_j > x_j$ and $x'_{j'} < x_{j'}$.

A network is *not concordant*, if there are $\alpha \in \ker N$ and $0 \neq \beta \in \operatorname{im} N$ such that, for all $(i \to i') \in E$,

- (i) $\alpha_{i\to i'} \neq 0 \implies \operatorname{sign}(\alpha_{i\to i'}) = \operatorname{sign}(\beta_j)$ for some $j \in \operatorname{supp}(y(i))$, and
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Concordance $\iff$ injectivity $\implies$ uniqueness

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Theorem (Shinar & Feinberg 2012)

The map $Nr(x)$ is injective on compatibility classes
for all weakly monotonic kinetics $r(x)$
if and only if the reaction network is concordant.

More results

Wiuf & Feliu (2013). *Power-law kinetics and determinant criteria for the preclusion of multistationarity in networks of interacting species*, SIAM J on Applied Dynamical Systems

Feliu (2014). *Injectivity, multiple zeros, and multistationarity in reaction networks*, Proceedings of the Royal Society A

M, Feliu, Regensburger, Conradi, Shiu, Dickenstein (2016). *Sign Conditions for Injectivity of Generalized Polynomial Maps with Applications to Chemical Reaction Networks and Real Algebraic Geometry*. Foundations of Computational Mathematics

Reviews

Banaji & Pantea (2016). *Some Results on Injectivity and Multistationarity in Chemical Reaction Networks*, SIAM J on Applied Dynamical systems 63 pages

Feliu, M, Regensburger (2019), *Characterizing injectivity of classes of maps via classes of matrices*, Linear Algebra and its Applications 26 pages

Unique existence: Deficiency zero for GMAK

$\tilde{\delta} = 0$ theorem (M & Regensburger 2014)

$C_k \neq \emptyset$ for all k iff $\tilde{\delta} = 0$ and G is weakly reversible.

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$\delta = \tilde{\delta} = 0$ theorem ?

For GMAK, there exists a unique positive CBE
in every stoichiometric class $x' + S$ and for all rate constants k
iff $\delta = \tilde{\delta} = 0$, G is weakly reversible, and conditions$(S, \tilde{S})$.

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conditions$(S, \tilde{S})$?

$S = \ker W$, $\tilde{S} = \ker \tilde{W}$ with $W \in \mathbb{R}^{d \times n}$, $\tilde{W} \in \mathbb{R}^{\tilde{d} \times n}$:

existence/uniqueness of CBE in every $x' + S$ for all k	$\Longleftrightarrow$	surjectivity/injectivity of $F_c(x) = W(c \circ \mathrm{e}^{\tilde{W}^\mathsf{T} x})$ for all c

□

Unique existence: Deficiency zero for GMAK

Theorem (M, Hofbauer, Regensburger et al 2019)

F_c is bijective for all c iff

(i) $\operatorname{sign}(S) \cap \operatorname{sign}(\tilde{S}^\perp) = \{0\}$,

(ii) for every nonzero $\tilde{\tau} \in \operatorname{sign}(\tilde{S}^\perp)_\oplus$, there is a nonzero $\tau \in \operatorname{sign}(S^\perp)_\oplus$ such that $\tau \leq \tilde{\tau}$, and

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Proof.

Hadamard's global inversion theorem,
polyhedral geometry, oriented matroids □

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Aichmayr et al (2024). *A SageMath Package for Elementary and Sign Vectors with Applications to Chemical Reaction Networks*, submitted

Sign vectors

Vector $x \in \mathbb{R}^n$, sign vector $\operatorname{sign}(x) \in \{-, 0, +\}^n$:

$$\operatorname{sign}\begin{pmatrix}-1\\0\\2\end{pmatrix} = \begin{pmatrix}-\\0\\+\end{pmatrix}$$

Set $S \subseteq \mathbb{R}^n$:

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Partial order on signs $\implies$ partial order on sign vectors:

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Sign vector set $\Sigma \subseteq \{-, 0, +\}^n$:

$$\overline{\Sigma} = \{\tau' \in \{-, 0, +\}^n \mid \tau' \leq \tau \text{ for some } \tau \in \Sigma\}$$

Robustness

Small perturbations of the kinetic orders $\tilde{Y}$ (or the exponents $\tilde{W}$), that is, of the subspace $\tilde{S}$ in the Grassmannian

Theorem (M et al 2019)

F_c is bijective for all c and *for all small perturbations* $\tilde{S}_\epsilon$
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Robust $\delta = \tilde{\delta} = 0$ theorem (M et al 2019)

For GMAK, there exists a unique positive CBE
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Robust $\delta = 0$ theorem (M et al 2019)

For MAK, if $\delta = 0$ and G is weakly reversible,
then there exists a unique positive equilibrium in every stoichiometric class,
for all rate constants, and *for all small perturbations of the kinetic orders*.

Stability of CBE for GMAK

Sign (vector) conditions sufficient for linear stability:
negative of (scaled or reduced) Jacobian is P-matrix (and sign-symmetric)

- cycle decomposition of the graph
- new decomposition of the graph Laplacian,
  monomial evaluation orders ("strata" of $\mathbb{R}^n_>$)

  extend asymptotic stability of CBE for MAK (differential *equations*)
  to "binomial differential *inclusions*"

M & Regensburger (2024). *Sufficient conditions for linear stability of complex-balanced equilibria in generalized mass-action systems*, SIAM Journal on Applied Dynamical Systems

M (2023). *On a new decomposition of the graph Laplacian and the binomial structure of mass-action systems*, Journal of Nonlinear Science

3. Polynomial systems

Positive equilibria of generalized mass-action systems:

$$0 = \frac{\mathsf{d}x}{\mathsf{d}t} = \begin{cases} Y\, A_k\, x^{\tilde{Y}} \\ N\left(k \circ x^V\right) \end{cases}$$

3. Polynomial systems

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Parametrized systems of generalized polynomial equations:

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Parametrized systems of generalized polynomial equations:

$$A \left(c \circ x^B \right) = 0$$

variables $x \in \mathbb{R}^n_>$, exponents $B \in \mathbb{R}^{n \times m}$, monomials $x^B \in \mathbb{R}^m_>$
parameters $c \in \mathbb{R}^m_>$, monomial terms $c \circ x^B \in \mathbb{R}^m_>$
coefficients $A \in \mathbb{R}^{k \times m}$

Hierarchy of polynomial systems

$$\left(c \circ x^{B}\right) \in C$$

(in-)finitely many, (non-)strict inequalities,

given by a cone C in the positive orthant

$$\downarrow$$

$$A\left(c \circ x^{B}\right) \geq 0$$

finitely many, non-strict inequalities,

involving the polyhedral cone $\{y \geq 0 \mid A\, y \geq 0\}$

$$\downarrow$$

$$A\left(c \circ x^{B}\right) = 0$$

finitely many equations,

involving the subspace cone $\{y \geq 0 \mid A\, y = 0\}$

$$\swarrow \qquad \searrow$$

$$A\, x^{B} = 0$$

fewnomial systems
(not involving parameters)

$$\frac{\mathrm{d}x}{\mathrm{d}t} = N\left(k \circ x^{V}\right) = 0$$

(generalized)
mass-action systems

Relevant objects are geometric

Example: two (non-overlapping) trinomials in three variables

$$\begin{aligned} c_1\, x^{b^1} + c_2\, x^{b^2} - c_3\, x^{b^3} \qquad\qquad\qquad\qquad\qquad\qquad &= 0, \\ c_4\, x^{b^4} + c_5\, x^{b^5} - c_6\, x^{b^6} &= 0 \end{aligned}$$

with $x \in \mathbb{R}^3_>$ and $b^i \in \mathbb{R}^3$, $i = 1, \ldots, 6$

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"normalize":

$$\begin{aligned} c_1\, x_1 + c_2\, x_2 - 1 \qquad\qquad &= 0, \\ c_4\, x_3 + c_5\, x_1^{b_1} x_2^{b_2} x_3^{b_3} - 1 &= 0 \end{aligned}$$

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$A\left(c \circ x^{B}\right) = 0$ with

$$A = \begin{pmatrix} 1 & 1 & -1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 1 & -1 \end{pmatrix}, \quad B = \begin{pmatrix} 1 & 0 & 0 & 0 & b_1 & 0 \\ 0 & 1 & 0 & 0 & b_2 & 0 \\ 0 & 0 & 0 & 1 & b_3 & 0 \end{pmatrix}, \quad c = \begin{pmatrix} c_1 \\ c_2 \\ 1 \\ c_4 \\ c_5 \\ 1 \end{pmatrix}$$

$m = 6$ monomials in $n = 3$ variables

and $\ell = 2$ classes

Geometric objects - from coefficients

(non-empty) *coefficient cone*:

$$C = \ker A \cap \mathbb{R}^m_>$$

ℓ *classes* if

$$C = C_1 \times \cdots \times C_\ell$$

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in the example,

$$C = C_1 \times C_2 \quad \text{with} \quad C_i = C_\star := \ker \begin{pmatrix} 1 & 1 & -1 \end{pmatrix} \cap \mathbb{R}^3_>$$

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coefficient set (polytope):

$$P = C \cap \Delta$$

with direct product $\Delta = \Delta_1 \times \cdots \times \Delta_\ell$ of (standard) simplices

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$$\Delta = \Delta_1 \times \Delta_2 \quad \text{with} \quad \Delta_i = \Delta_\star := \{x \in \mathbb{R}^3_\geq \mid \textstyle\sum_k x_k = 2\}$$

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Geometric objects - from coefficients

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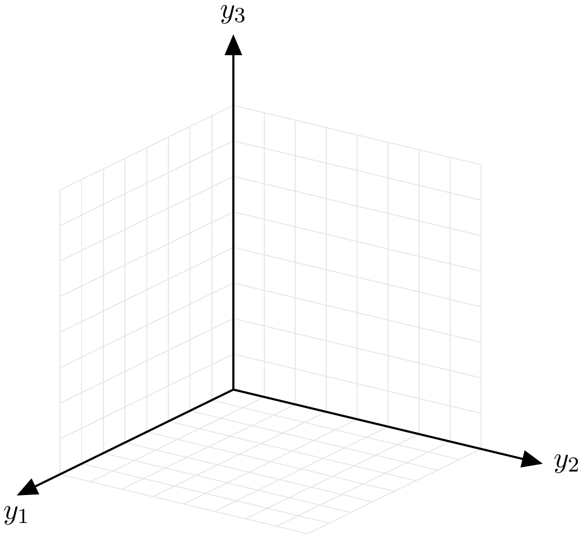

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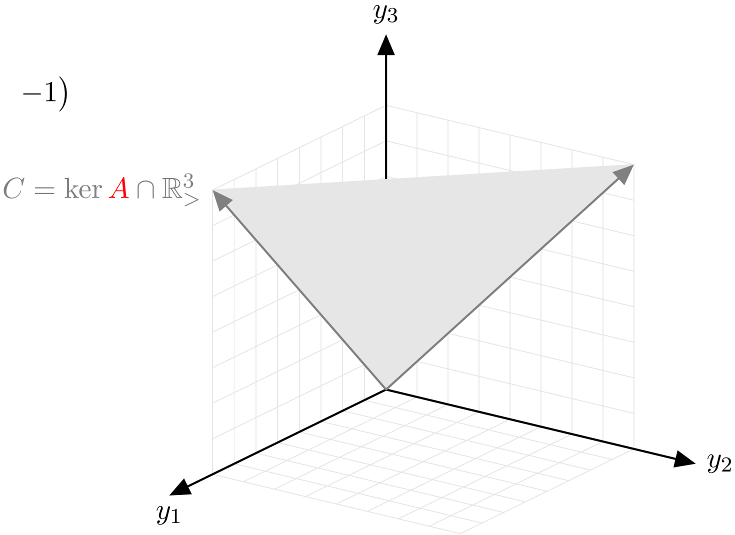

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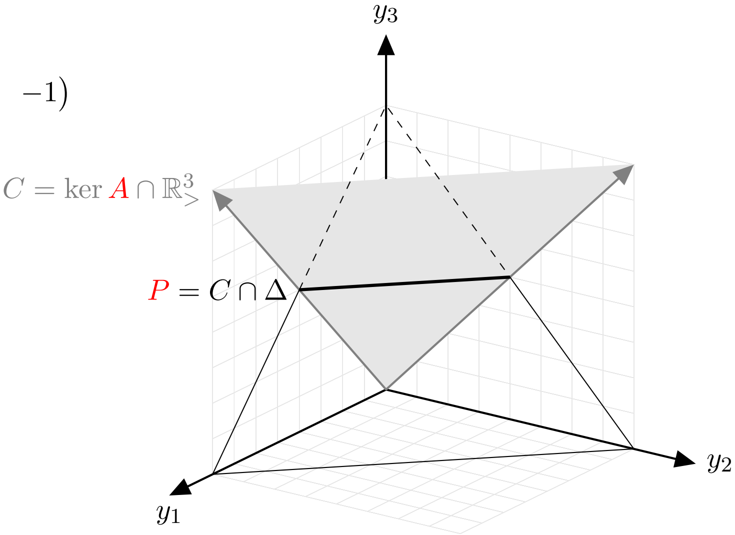

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affine dependencies between exponents within classes

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affine dependencies between exponents within classes

monomial dependency:

$$d = \dim D$$

Main result (simplified)

Theorem: polynomial $\sim$ binomial

The solution set

$$Z_c = \{x \in \mathbb{R}^n_> \mid A\,(c \circ x^B) = 0\},$$

is in one-to-one correspondence with the *solution set on the coefficient polytope*,

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With $H \in \mathbb{R}^{m \times d}$ such that $D = \operatorname{im} H$:

$$y^H = c^H$$

d binomial equations for $y \in P$

Comments

- *general* result
- *classification* of polynomial systems via dependency d (and $\dim P$)

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- result is based on *linear algebra* and *convex/polyhedral geometry*,
  but not on real algebraic geometry
- solution set Y_c can be studied with methods from *analysis*.

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  sign-characteristic functions,
  Brouwer degree, Hadamard's theorem,
  Descartes' rule of signs for functions, Wronskians, ...
- Main result (full):
  solution set Z_c can be obtained from Y_c via exponention

Example - binomial equation

$$y = \begin{pmatrix} y^1 \\ y^2 \end{pmatrix} \in P = P_1 \times P_2 : \quad y^i = \lambda_i \begin{pmatrix} 1 \\ 0 \\ 1 \end{pmatrix} + (1 - \lambda_i) \begin{pmatrix} 0 \\ 1 \\ 1 \end{pmatrix} = \begin{pmatrix} \lambda_i \\ 1 - \lambda_i \\ 1 \end{pmatrix}, \quad \lambda_1, \lambda_2 \in (0,1)$$

$$\mathcal{B} = \begin{pmatrix} B \\ J \end{pmatrix} = \begin{pmatrix} 1 & 0 & 0 & 0 & b_1 & 0 \\ 0 & 1 & 0 & 0 & b_2 & 0 \\ 0 & 0 & 0 & 1 & b_3 & 0 \\ 1 & 1 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 1 & 1 \end{pmatrix}, \quad D = \ker \mathcal{B} = \operatorname{im} z \quad \text{with} \quad z = \begin{pmatrix} b_1 \\ b_2 \\ -(b_1 + b_2) \\ b_3 \\ -1 \\ 1 - b_3 \end{pmatrix}$$

Example - binomial equation

$$y = \begin{pmatrix} y^1 \\ y^2 \end{pmatrix} \in P = P_1 \times P_2 : \quad y^i = \lambda_i \begin{pmatrix} 1 \\ 0 \\ 1 \end{pmatrix} + (1-\lambda_i) \begin{pmatrix} 0 \\ 1 \\ 1 \end{pmatrix} = \begin{pmatrix} \lambda_i \\ 1-\lambda_i \\ 1 \end{pmatrix}, \quad \lambda_1, \lambda_2 \in (0,1)$$

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$d = \dim D = 1$:

$$y^z = c^z, \quad \text{i.e.,} \quad \lambda_1^{b_1} (1-\lambda_1)^{b_2} \lambda_2^{b_3} (1-\lambda_2)^{-1} = c_1^{b_1} c_2^{b_2} c_3^{b_3} c_4^{-1} =: c^*$$

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sign-characteristic functions:

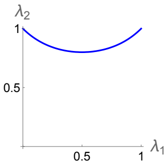
$$s_{\alpha,\beta} \colon (0,1) \to \mathbb{R}_>, \quad \lambda \mapsto \lambda^\alpha (1-\lambda)^\beta$$

separation of variables:

$$s_{b_1,b_2}(\lambda_1) = c^* s_{-b_3,1}(\lambda_2)$$

Example - solutions in λ_1, λ_2

$b_1 = 1, b_2 = 2$ and $b_3 = 2$:



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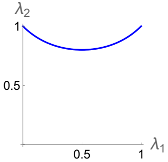

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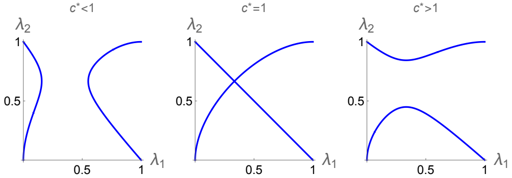

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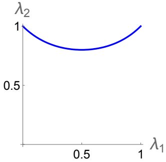

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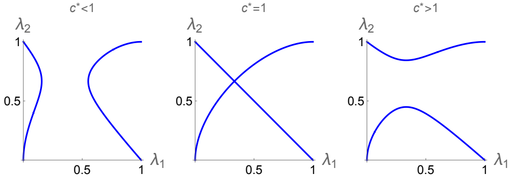
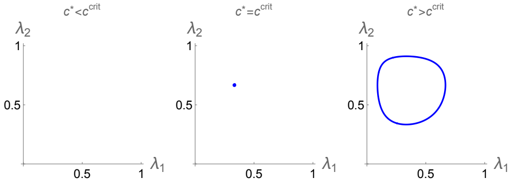


$b_1 = -1, b_2 = -2$ and $b_3 = -2$:
$c^{\text{crit}} = (\frac{27}{4})^2$



More examples

M & Regensburger (2023a). Parametrized systems of polynomial inequalitites with real exponents via linear algebra and convex geometry, arXiv:2306.13916 [math.AG]

- $d = 0$: two overlapping trinomials in four variables $(m = 4, n = 4, \ell = 1)$
  $\mathsf{X} \to \mathsf{X}_p,\ \mathsf{X}_p + \mathsf{Y} \rightleftarrows \mathsf{X} + \mathsf{Y}_p,\ \mathsf{Y}_p \to \mathsf{Y}$
- $d = 1$: one trinomial in one variable $(m = 3, n = 1, \ell = 1)$
- $d = 2$: one trinomial *equation* and one tetranomial *inequality* $(m = 7, n = 5, \ell = 2)$
  $\mathsf{X}_1 \rightleftarrows \mathsf{X}_2,\ 2\mathsf{X}_1 + \mathsf{X}_2 \to 3\mathsf{X}_1$

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M & Regensburger (2023b). Parametrized systems of polynomial equations with real exponents: applications to fewnomials, arXiv:2304.05273 [math.AG]

- $d = 1$: two non-overlapping trinomials in three variables $(m = 6, n = 3, \ell = 2)$
- $d = 1$: two overlapping trinomials in two variables $(m = 4, n = 2, \ell = 1)$
  cf. Bihan & Dickenstein & ... (2021, 2017, 2015, 2007)
- $d \geq 2$: one trinomial and one t-nomial in two variables $(m = 3 + t, n = 2, \ell = 2)$
  for $t = 3$ (two trinomials), cf. Haas (2002)

Geometric objects - from exponents (continued)

monomial difference matrix:

$$M = B\,I = \begin{pmatrix} B_1 I_{m_1} & \dots & B_\ell I_{m_\ell} \end{pmatrix} \in \mathbb{R}^{n\times(m-\ell)}$$

with "incidence" matrix

$$I = \begin{pmatrix} I_{m_1} & & 0 \\ & \ddots & \\ 0 & & I_{m_\ell} \end{pmatrix} \in \mathbb{R}^{m\times(m-\ell)}, \quad \text{where}$$

$$I_m = \begin{pmatrix} \mathrm{Id}_{m-1} \\ -1_{m-1}^{\mathsf{T}} \end{pmatrix} \in \mathbb{R}^{m\times(m-1)}, \quad \text{i.e.,} \quad I_2 = \begin{pmatrix} 1 \\ -1 \end{pmatrix},\ I_3 = \begin{pmatrix} 1 & 0 \\ 0 & 1 \\ -1 & -1 \end{pmatrix}, \dots$$

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Fact

$d = m - \ell - \dim L$

Main result (full)

Theorem

The solution set $Z_c = \{x \in \mathbb{R}^n_> \mid A\,(c \circ x^B) = 0\}$ *can be written as*

$$Z_c = \{(y \circ c^{-1})^E \mid y \in Y_c\} \circ \mathrm{e}^{L^\perp}$$

with

$$Y_c = \{y \in P \mid y^z = c^z \text{ for all } z \in D\}.$$

P ... coefficient set
D ... monomial dependency subspace
L ... monomial difference subspace

$E = I\,M^*$ ... exponentiation matrix
I ... (incidence) matrix
M^* ... generalized inverse of $M = B\,I$

Open problems and applications

$A\,(c \circ x^{B}) = 0$:

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Reaction networks:

- When do (positive) equilibria have a monomial parametrization? (depending rationally on the rate constants)
- How can results such as the deficiency one theorem be extended? (from $\delta = 1$ to $d = 1$, and from MAK to GMAK)

Thanks for your attention!