Injectivity and surjectivity of generalized polynomial maps and sign vectors

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$$\frac{\mathsf{d}x}{\mathsf{d}t} = F_k(x) = N\,v_k(x) = N(k \circ x^V)$$

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Injectivity of generalized polynomial map F_k
on all cosets of $\mathrm{im}(N)$ and for all k:

- sufficient condition for precluding multiple steady states
  on all compatibility classes and for all rate constants
- generalized Descartes' rule of signs

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Injectivity and surjectivity of generalized polynomial map $\tilde{f}_{x^*}$:

- equivalent to existence and uniqueness of *special* steady states
- generalized Birch's Theorem

Chemical reaction networks

Stoichiometry:

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

reactants A, B and product C

Mass-action kinetics:

$$v = k\, x_{\mathsf{A}}^{1}\, x_{\mathsf{B}}^{1}$$

rate constant $k > 0$
concentrations $x_{\mathsf{A}}(t), x_{\mathsf{B}}(t) \geq 0$

Contribution to network dynamics:

$$\frac{\mathsf{d}}{\mathsf{d}t}\begin{pmatrix} x_{\mathsf{A}} \\ x_{\mathsf{B}} \\ x_{\mathsf{C}} \\ x_{\mathsf{D}} \\ \vdots \end{pmatrix} = k\, x_{\mathsf{A}} x_{\mathsf{B}} \begin{pmatrix} -1 \\ -1 \\ 1 \\ 0 \\ \vdots \end{pmatrix} + \cdots$$

Example

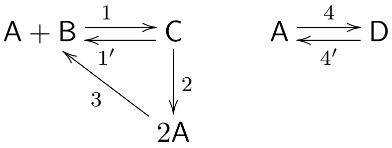
$$\begin{tikzcd} \mathsf{A} + \mathsf{B} \arrow[r, shift left, "1"] & \mathsf{C} \arrow[l, shift left, "1'"] \arrow[d, "2"] \\ & 2\mathsf{A} \arrow[ul, "3"] \end{tikzcd} \qquad \begin{tikzcd} \mathsf{A} \arrow[r, shift left, "4"] & \mathsf{D} \arrow[l, shift left, "4'"] \end{tikzcd}$$

complexes A+B, C, 2A, A, D

$$\frac{\mathrm{d}x}{\mathrm{d}t} = N\, v_k(x) = \begin{pmatrix} -1 & 1 & 2 & -1 & -1 & 1 \\ -1 & 1 & 0 & 1 & 0 & 0 \\ 1 & -1 & -1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 & -1 \end{pmatrix} \begin{pmatrix} k_1\, x_{\mathsf{A}} x_{\mathsf{B}} \\ k_{1'}\, x_{\mathsf{C}} \\ k_2\, x_{\mathsf{C}} \\ k_3\, x_{\mathsf{A}}^2 \\ k_4\, x_{\mathsf{A}} \\ k_{4'}\, x_{\mathsf{D}} \end{pmatrix}$$

stoichiometric matrix N, rate vector v_k

Example



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stoichiometric matrix N, rate vector v_k

$$= {\color{blue}Y}\, A_k\, x^{\color{blue}Y} = \begin{pmatrix} 1 & 0 & 2 & 1 & 0 \\ 1 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 \end{pmatrix} \begin{pmatrix} -k_1 & k_{1'} & k_3 & 0 & 0 \\ k_1 & -(k_{1'}+k_2) & 0 & 0 & 0 \\ 0 & k_2 & -k_3 & 0 & 0 \\ 0 & 0 & 0 & -k_4 & k_{4'} \\ 0 & 0 & 0 & k_4 & -k_{4'} \end{pmatrix} \begin{pmatrix} x_{\mathsf{A}} x_{\mathsf{B}} \\ x_{\mathsf{C}} \\ x_{\mathsf{A}}^2 \\ x_{\mathsf{A}} \\ x_{\mathsf{D}} \end{pmatrix}$$

complex matrix Y, graph Laplacian A_k

Deficiency zero theorem

$$\frac{\mathsf{d}x}{\mathsf{d}t} = N\,v_k(x) \quad \Rightarrow \quad x(t) - x(0) \in S = \mathrm{im}(N)$$

stoichiometric subspace S

Deficiency:

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

m complexes, ℓ components

Weakly reversible network: each component strongly connected

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Theorem

A reaction network has a unique, asymptotically stable, positive (special) steady state for all initial conditions and all rate constants if and only if it is weakly reversible and has deficiency zero. *(Horn-Jackson '72, Horn '72, Feinberg '72)*

Special steady states

$$Y A_k x^Y = 0$$

Complex balancing equilibria:

$$Z_k = \left\{ x > 0 \mid A_k x^Y = 0 \right\}$$

Deficiency:

$$\delta = \dim(\ker(Y) \cap \mathrm{im}(A_k))$$

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$\delta = 0 \quad \Rightarrow \quad$ all equilibria complex balancing

$$x^* \in Z_k \quad \Rightarrow \quad Z_k = \{x^* \circ \mathrm{e}^v \mid v \in S^\perp\}$$

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$S = \ker(W)$ with $W = (w^1, \ldots, w^n) \in \mathbb{R}^{d \times n}$ (with full rank d):

$$Z_k = \{x^* \circ \xi^W \mid \xi \in \mathbb{R}^d_>\}$$

monomial parametrization

Birch's theorem

Existence/uniqueness of complex balancing equilibria
for all initial conditions and all rate constants:

$$\{x^* \circ \xi^W \mid \xi \in \mathbb{R}^d_>\} \cap (x' + S)$$

contains exactly one element for all $x^* > 0$ and all $x' > 0$

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$\Leftrightarrow$ Surjectivity/injectivity of the generalized polynomial map

$$f_{x^*} \colon \mathbb{R}^d_> \to C^\circ \subseteq \mathbb{R}^d, \quad \xi \mapsto \sum_{k=1}^{n} x^*_k \, \xi^{w^k} w^k$$

for all $x^* > 0$, where $C = \mathrm{cone}(W)$

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Theorem

The map f_{x^*} is a real analytic isomorphism for all $x^* > 0$.

(Birch '63, Horn-Jackson '72, Fulton '93)

Generalized mass-action kinetics

Stoichiometry:

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

Generalized mass-action kinetics:

$$v = k\, x_{\mathsf{A}}^{a}\, x_{\mathsf{B}}^{b}$$

kinetic orders $a, b \in \mathbb{R}$

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Stoichiometry *and* kinetic orders:

$$\mathsf{A} + \mathsf{B} \to \mathsf{C} \qquad\qquad a\,\mathsf{A} + b\,\mathsf{B} \to c\,\mathsf{C}$$

$$Y = \begin{pmatrix} 1 & 0 & \\ 1 & 0 & \\ 0 & 1 & \dots \\ 0 & 0 & \\ \vdots & \vdots & \end{pmatrix} \qquad\qquad \tilde{Y} = \begin{pmatrix} a & 0 & \\ b & 0 & \\ 0 & c & \dots \\ 0 & 0 & \\ \vdots & \vdots & \end{pmatrix}$$

Network dynamics:

$$\frac{\mathrm{d}x}{\mathrm{d}t} = Y\, A_k\, x^{\tilde{Y}}$$

Special steady states

$$Y\,A_k\,x^{\tilde{Y}} = 0$$

Stoichiometric and kinetic-order subspaces:

$$S = \ker(W) \quad \text{and} \quad \tilde{S} = \ker(\tilde{W})$$

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for all initial conditions and rate constants:
Surjectivity/injectivity of

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for all $x^* > 0$.

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for all $x^* > 0$.

Mass-action kinetics: $\tilde{Y} = Y$
Deficiency zero, Birch's theorem: $\tilde{S} = S$, $\tilde{W} = W$

How much can we perturb the exponents/subspace/cone?

Sign vectors

Generalized Birch's theorem

The polynomial map $\tilde{f}_{x^*}$ is a real analytic isomorphism for all $x^* > 0$, if $\sigma(\tilde{S}) = \sigma(S)$ and $(+, \ldots, +)^T \in \sigma(S^\perp)$.

sign vectors of subspace = oriented matroid

computation of sign conditions: chirotopes (maximal minors)

Proof: Birch's theorem, face-lattice isomorphism, Brouwer degree

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Generalized deficiency zero theorem

A weakly reversible and conservative reaction network with deficiency zero has a unique positive steady state for all initial conditions, all rate constants, and all kinetic orders with $\sigma(\tilde{S}) = \sigma(S)$.

Minimal example

Stoichiometry and kinetic orders:

$$\mathsf{A} + \mathsf{B} \rightleftharpoons \mathsf{C} \qquad\qquad a\,\mathsf{A} + b\,\mathsf{B} \rightleftharpoons c\,\mathsf{C}$$

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Stoichiometric and kinetic-order subspaces:

$$S = \operatorname{im}(-1,-1,1)^T = \ker \begin{pmatrix} 1 & 0 & 1 \\ 0 & 1 & 1 \end{pmatrix}, \quad \tilde{S} = \operatorname{im}(-a,-b,c)^T = \ker \begin{pmatrix} c & 0 & a \\ 0 & c & b \end{pmatrix}$$

$$\sigma(S) = \left\{ \begin{pmatrix} - \\ - \\ + \end{pmatrix}, \begin{pmatrix} + \\ + \\ - \end{pmatrix}, \begin{pmatrix} 0 \\ 0 \\ 0 \end{pmatrix} \right\} = \sigma(\tilde{S}) \quad \text{and} \quad \begin{pmatrix} 1 \\ 1 \\ 2 \end{pmatrix} \in S^{\perp}$$

Minimal example

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For all $y \in \mathbb{R}^2_>$, $x^* \in \mathbb{R}^3_>$ and $a, b, c > 0$,

$$x_1^*\, \xi_1^c \begin{pmatrix} 1 \\ 0 \end{pmatrix} + x_2^*\, \xi_2^c \begin{pmatrix} 0 \\ 1 \end{pmatrix} + x_3^*\, \xi_1^a \xi_2^b \begin{pmatrix} 1 \\ 1 \end{pmatrix} = \begin{pmatrix} y_1 \\ y_2 \end{pmatrix}$$

has a unique solution $\xi \in \mathbb{R}^2_>$. (Birch's theorem: $a = b = c = 1$)

Injectivity of $\tilde{f}_{x^*}$

Injectivity

The polynomial map $\tilde{f}_{x^*}$ *is injective for all* $x^* > 0$*, if and only if* $\sigma(S) \cap \sigma(\tilde{S}^{\perp}) = \{0\}$.

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The polynomial map $\tilde{f}_{x^*}$ is injective for all $x^* > 0$, if and only if $\sigma(S) \cap \sigma(\tilde{S}^{\perp}) = \{0\}$.

Multistationarity

A weakly reversible reaction network with $\sigma(S) \cap \sigma(\tilde{S}^{\perp}) \neq \{0\}$ has the capacity for multiple complex balancing equilibria.

Injectivity of F_k

Unrestricted injectivity:

$$\tilde{f}_{x^*}(\xi) = W(x^* \circ \xi^{\tilde{W}})$$

$W \in \mathbb{R}^{d \times n}, \tilde{W} \in \mathbb{R}^{\tilde{d} \times n}$ with full rank $d, \tilde{d}$

Injectivity of F_k

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$$\tilde{f}_{x^*}(\xi) = W(x^* \circ \xi^{\tilde{W}})$$

$W \in \mathbb{R}^{d \times n}, \tilde{W} \in \mathbb{R}^{\tilde{d} \times n}$ with full rank $d, \tilde{d}$

$$\frac{\mathrm{d}x}{\mathrm{d}t} = F_k(x)$$

Injectivity on compatibility classes:

$$F_k(x) = N(k \circ x^V)$$

$N, V \in \mathbb{R}^{n \times r}$ possibly with linear dependencies

Result

Theorem

Let $F_k \colon \mathbb{R}^n_> \to \mathbb{R}^n \colon x \mapsto N(k \circ x^V)$, *where* $N, V \in \mathbb{R}^{n\times r}$ *and* $k \in \mathbb{R}^r_>$.
Further, let $S = \mathrm{im}(N)$ *and* $s = \mathrm{rank}(N)$.
The following statements are equivalent:

(inj) F_k *is injective on* $x' + S$, *for all* $x' \in \mathbb{R}^n_>$ *and* $k \in \mathbb{R}^r_>$.

(jac) *The Jacobian matrix* $J_{F_k}(x)$ *is injective on* S, *for all* $x \in \mathbb{R}^n_>$ *and* $k \in \mathbb{R}^r_>$.

(min) *For all subsets* $I \subseteq \{1, \ldots, n\}$, $J \subseteq \{1, \ldots, r\}$ *of cardinality* s, *the product* $\det(N_{I,J}) \det(V_{I,J})$ *either is zero or has the same sign as all other nonzero products, and moreover, at least one product is nonzero.*

(sig) $\sigma(\ker(N)) \cap \sigma(V^T(\Sigma(S^*))) = \emptyset$.

$S^* = S \setminus \{0\}$
$\Sigma(S) = \sigma^{-1}(\sigma(S))$, union of all orthants that S intersects

Descartes' rule of signs

Theorem

The number of positive real roots of a univariate real polynomial $f(x) = c_0 + c_1 x + \cdots + c_r x^r$ *is bounded above by the number of sign variations between consecutive nonzero coefficients.*

Descartes' rule of signs

Theorem

The number of positive real roots of a univariate real polynomial $f(x) = c_0 + c_1 x + \cdots + c_r x^r$ is bounded above by the number of sign variations between consecutive nonzero coefficients.

Partial multivariate generalization

Let $A, B \in \mathbb{R}^{n \times r}$ with full rank n.
Assume that for all subsets $J \subseteq \{1, \ldots, r\}$ of cardinality n, the product $\det(A_{[n],J}) \det(B_{[n],J})$ either is zero or has the same sign as all other nonzero products, and moreover, at least one product is nonzero.
Then, the system of n generalized polynomial equations in n unknowns

$$A\, x^B = y$$

has at most one positive solution $x \in \mathbb{R}^n_>$, for all $y \in \mathbb{R}^n$.

Sign vectors

Metabolic networks:

- stoichiometric models: thermodynamic feasibility
- kinetic models: enzyme allocation
  $\rightarrow$ constrained nonlinear optimization problem

Oriented matroids:

- elementary vectors
- sign vectors
- conformal sums

S. Müller, G. Regensburger, R. Steuer (2014). Enzyme allocation problems in kinetic metabolic networks: optimal solutions are elementary flux modes. *Journal of Theoretical Biology*, 347:182–190.

Publications

S. Müller and G. Regensburger (2014). Generalized mass-action systems and positive solutions of polynomial equations with real and symbolic exponents. *Computer Algebra in Scientific Computing, CASC 2014, Warsaw, Proceedings, LNCS, Springer.*

S. Müller, E. Feliu, G. Regensburger, C. Conradi, A. Shiu, A. Dickenstein (2013). Sign conditions for injectivity of generalized polynomial maps with applications to chemical reaction networks and real algebraic geometry. *arXiv:1311.5493 [math.AG]*.

S. Müller and G. Regensburger (2012). Generalized mass action systems: complex balancing equilibria and sign vectors of the stoichiometric and kinetic-order subspaces. *SIAM Journal on Applied Mathematics*, 72(6):1926–1947.

Thank you for your attention