Computing Sign Vector Conditions for Complex-Balanced Equilibria of Chemical Reaction Networks

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MAK vs. GMAK

- Reversible reaction (rate constants $k_{1\to2}, k_{2\to1} > 0$):

$$1 \underset{k_{2\to1}}{\overset{k_{1\to2}}{\rightleftarrows}} 2$$

- Stoichiometric and kinetic-order complexes:

$$1\mathsf{A} + 1\mathsf{B} \rightleftarrows \mathsf{C} \qquad a\mathsf{A} + b\mathsf{B} \rightleftarrows \mathsf{C}$$

- MAK: $a = b = 1$ GMAK: $a, b \in \mathbb{R}$

$$\frac{\mathrm{d}x}{\mathrm{d}t} = k_{1\to2}\, x_1^a x_2^b \begin{pmatrix} -1 \\ -1 \\ 1 \end{pmatrix} + k_{2\to1}\, x_3 \begin{pmatrix} 1 \\ 1 \\ -1 \end{pmatrix}$$

Generalized Mass-Action Systems

- **Generalized mass-action system** $(G_k, y, \widetilde{y})$ given by:
  - Directed graph $G = (V, E)$,
  - Edge labels $k \in \mathbb{R}^E_>$ (**rate constants** $k_{i\to i'} > 0$),
  - $y\colon V \to \mathbb{R}^n$ (**stoichiometric complex** for each vertex),
  - $\widetilde{y}\colon V \to \mathbb{R}^n$ (**kinetic-order complex** for each vertex).
- Network **weakly reversible**: Every reaction belongs to cycle.
- ODE system for **concentrations** $x \in \mathbb{R}^n_\geq$ (n species):

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

- Positive **complex-balanced equilibrium** (CBE): Steady state $x \in \mathbb{R}^n_>$ with $A_k\, x^{\widetilde{Y}} = 0$ (A_k **graph Laplacian**)
- Incidence matrix I_E of G
- **Stoichiometric subspace** $\mathcal{S} = \operatorname{im}(Y I_E)$
- **Kinetic-order subspace** $\widetilde{\mathcal{S}} = \operatorname{im}(\widetilde{Y} I_E)$

$$\text{MAK: } \mathcal{S} = \widetilde{\mathcal{S}} \quad (\text{“coefficients = exponents”})$$

- **Deficiency** (m complexes, l connected components):

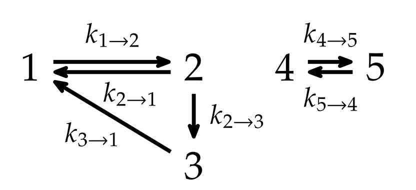
$$\delta = m - l - \dim \mathcal{S},$$

Theorem (Deficiency zero theorem, Horn, Jackson, Feinberg 1972)

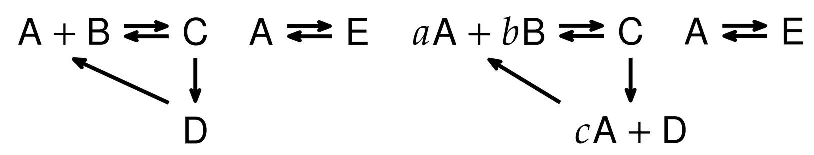
For CRN with MAK, there is unique positive CBE in every stoichiometric class, and for all rate constants iff $\delta = 0$ and network weakly reversible.

Example

- Directed graph:



- Stoichiometric and kinetic-order complexes:



- ODE system for concentrations $x \in \mathbb{R}^5_\geq$:

$$\frac{\mathrm{d}x}{\mathrm{d}t} = \underbrace{\begin{pmatrix} 1&0&0&1&0\\ 1&0&0&0&0\\ 0&1&0&0&0\\ 0&0&1&0&0\\ 0&0&0&0&1 \end{pmatrix}}_{Y} \underbrace{\begin{pmatrix} -k_{1\to2} & k_{2\to1} & k_{3\to1} & 0 & 0\\ k_{1\to2} & -k_{2\to1}-k_{2\to3} & 0 & 0 & 0\\ 0 & k_{2\to3} & -k_{31} & 0 & 0\\ 0 & 0 & 0 & -k_{4\to5} & k_{5\to4}\\ 0 & 0 & 0 & k_{4\to5} & -k_{5\to4} \end{pmatrix}}_{A_k} \underbrace{\begin{pmatrix} x_1^a x_2^b\\ x_3\\ x_1^c x_4\\ x_1\\ x_5 \end{pmatrix}}_{x^{\widetilde{Y}}}$$

- Stoichiometric and kinetic-order subspaces:

$$\mathcal{S} = \operatorname{im} \begin{array}{c} \mathsf{A}\\ \mathsf{B}\\ \mathsf{C}\\ \mathsf{D}\\ \mathsf{E} \end{array} \begin{pmatrix} -1&0&-1\\ -1&0&0\\ 1&-1&0\\ 0&1&0\\ 0&0&1 \end{pmatrix}, \quad \widetilde{\mathcal{S}} = \operatorname{im} \begin{pmatrix} -a&c&-1\\ -b&0&0\\ 1&-1&0\\ 0&1&0\\ 0&0&1 \end{pmatrix}$$

- Deficiencies:

$$\delta = m - l - \dim \mathcal{S} = 5 - 2 - 3 = 0, \qquad \widetilde{\delta} = m - l - \dim \widetilde{\mathcal{S}} = 5 - 2 - 3 = 0$$

- Kernel matrices ($\mathcal{S} = \ker P$ and $\widetilde{\mathcal{S}} = \ker \widetilde{P}$):

$$P = \begin{pmatrix} 1&0&1&1&1\\ 0&1&1&1&0 \end{pmatrix}, \qquad \widetilde{P} = \begin{pmatrix} 1&0&a&a-c&1\\ 0&1&b&b&0 \end{pmatrix}$$

Crash Course on Sign Vectors

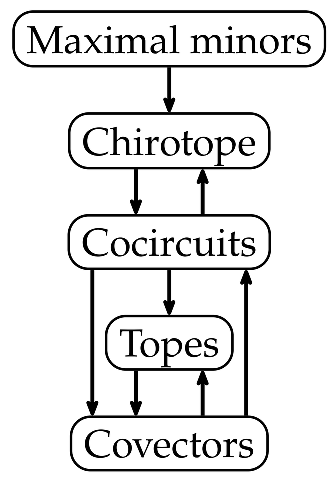
- **Sign vector**: Element in $\{-, 0, +\}^n$

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

- $\mathcal{S} \subseteq \mathbb{R}^n$: $\operatorname{sign}(\mathcal{S}) = \{\operatorname{sign} x \mid x \in \mathcal{S}\} \subseteq \{-, 0, +\}^n$
- **Covectors**: Elements in $\operatorname{sign}(\mathcal{S})$
- **Cocircuits**: Support-minimal covectors
- **Topes**: Support-maximal covectors
- **Maximal minor**: Determinant of max. submatrix
- **Chirotope**: Signs of maximal minors
- Partial order $\leq$ on $\{-, 0, +\}^n$ by $0 \leq -, +$

Computing $\operatorname{sign}(\ker P)$: $P = \begin{pmatrix} 1&0&1&1&1\\ 0&1&1&1&0 \end{pmatrix}$

J	$\det P_J$	chirotope
$\{1,2\}$	1	$+$
$\{1,3\}$	1	$+$
$\{1,4\}$	1	$+$
$\{1,5\}$	0	0
$\{2,3\}$	-1	$-$
$\{2,4\}$	-1	$-$
$\{2,5\}$	-1	$-$
$\{3,4\}$	0	0
$\{3,5\}$	-1	$-$
$\{4,5\}$	-1	$-$



Robust Deficiency Zero Theorem

- **Closure**: $\mathcal{A}^{\downarrow} = \{\pi \mid \pi \leq \rho \text{ for a } \rho \in \mathcal{A}\}$

Theorem (Robust $\delta = \widetilde{\delta} = 0$ theorem)

For CRN with GMAK, there is unique positive CBE in every stoichiometric class, for all rate constants, and all small perturbations of kinetic orders iff $\delta = \widetilde{\delta} = 0$, network weakly reversible, and

(CC) $\operatorname{sign}(\mathcal{S}) \subseteq \operatorname{sign}(\widetilde{\mathcal{S}})^{\downarrow}$.

Proposition (Closure condition)

The following are equivalent:

(CC) $\operatorname{sign}(\mathcal{S}) \subseteq \operatorname{sign}(\widetilde{\mathcal{S}})^{\downarrow}$.

(CC^t) *For every tope $\tau \in \operatorname{sign}(\mathcal{S})$, there is a tope $\widetilde{\tau} \in \operatorname{sign}(\widetilde{\mathcal{S}})$ with $\tau \leq \widetilde{\tau}$.*

(CC^m) *There is an $\varepsilon = \pm 1$ such that for all subsets $J \subseteq \{1, \dots, n\}$ with $|J| = r$,*

$$\det P_J \neq 0 \quad \text{implies} \quad \varepsilon \det P_J \det \widetilde{P}_J > 0.$$

Example

- (CC), (CC^t) and (UC) only for fixed a, b and c.

$\rightarrow$ Use (CC^m) and (UC^m) instead!

J	$\det P_J$	$\det \widetilde{P}_J$	(CC^m)	(UC^m)
$\{1,2\}$	1	1	✓	✓
$\{1,3\}$	1	b	$b > 0$	$b \geq 0$
$\{1,4\}$	1	b	$b > 0$	$b \geq 0$
$\{1,5\}$	0	0	✓	✓
$\{2,3\}$	-1	$-a$	$a > 0$	$a \geq 0$
$\{2,4\}$	-1	$c - a$	$c < a$	$c \leq a$
$\{2,5\}$	-1	-1	✓	✓
$\{3,4\}$	0	bc	✓	✓
$\{3,5\}$	-1	$-b$	$b > 0$	$b \geq 0$
$\{4,5\}$	-1	$-b$	$b > 0$	$b \geq 0$

- (CC) holds iff $a > 0$, $b > 0$ and $a > c$.
- (UC) holds iff $a \geq 0$, $b \geq 0$ and $a \geq c$.

Uniqueness

Theorem

For CRN with GMAK, there is at most one positive CBE in every stoichiometric class and for all rate constants iff

(UC) $\operatorname{sign}(\mathcal{S}) \cap \operatorname{sign}(\widetilde{\mathcal{S}}^{\perp}) = \{0\}$.

Corollary (Uniqueness condition)

The following are equivalent:

(UC) $\operatorname{sign}(\mathcal{S}) \cap \operatorname{sign}(\widetilde{\mathcal{S}}^{\perp}) = \{0\}$.

(UC^m) *Exactly one of the following holds:*

- $\det P_J \det \widetilde{P}_J \geq 0$ *for all* $J \subseteq \{1, \dots, n\}$ *with* $|J| = r$.
- $\det P_J \det \widetilde{P}_J \leq 0$ *for all* $J \subseteq \{1, \dots, n\}$ *with* $|J| = r$.

Unique Existence

- **Nonnegative sign vectors**: $\mathcal{A}_{\oplus} = \mathcal{A} \cap \{0, +\}^n$

Theorem ($\delta = \widetilde{\delta} = 0$ theorem)

For a CRN with GMAK, there is unique positive CBE in every stoichiometric class and for all rate constants iff $\delta = \widetilde{\delta} = 0$, network weakly reversible and

(UC) $\operatorname{sign}(\mathcal{S}) \cap \operatorname{sign}(\widetilde{\mathcal{S}}^{\perp}) = \{0\}$.

(FC) *For every nonzero $\widetilde{\pi} \in \operatorname{sign}(\widetilde{\mathcal{S}}^{\perp})_{\oplus}$, there is nonzero $\pi \in \operatorname{sign}(\mathcal{S}^{\perp})_{\oplus}$ with $\pi \leq \widetilde{\pi}$.*

(NDC) *$(\mathcal{S}, \widetilde{\mathcal{S}})$ is nondegenerate.*

Definition

A pair $(\mathcal{S}, \widetilde{\mathcal{S}})$ is ***degenerate*** *if there exists a $z \in \widetilde{\mathcal{S}}^{\perp}$ such that:*

(DC1^c) *There is a nonempty set of cocircuits $\mathcal{D} \subseteq \operatorname{sign}(\mathcal{S})_{\oplus}$ such that:*

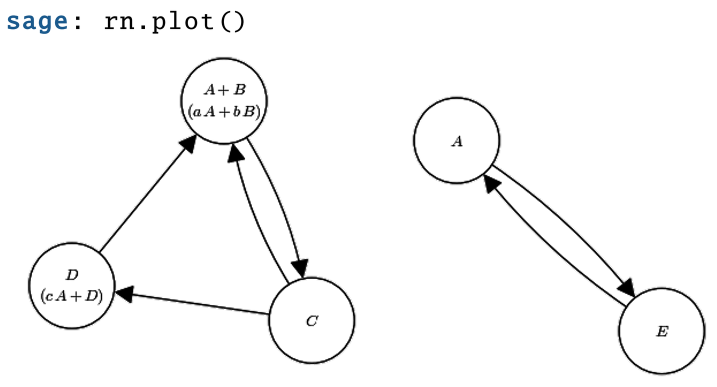
- *For all $\sigma \in \mathcal{D}$ and for all $i, j \in \operatorname{supp} \sigma$, we have $z_i = z_j > 0$.*
- *For all $i \notin \bigcup_{\sigma\in\mathcal{D}} \operatorname{supp} \sigma$, we have $z_i \leq 0$.*

(DC2^c) *For every cocircuit $\sigma \in \operatorname{sign}(\mathcal{S}^{\perp})_{\oplus}$, we have $\operatorname{supp} \sigma \not\subseteq \operatorname{supp} z$.*

- Recursive algorithm to check (NDC)

SageMath Example

```
sage: from sign_crn import *
sage: species("A, B, C, D, E")  sage: var("a, b, c")
(A, B, C, D, E)                 (a, b, c)
sage: rn = ReactionNetwork()
sage: rn.add_complexes([(0, A + B, a*A + b*B), ..., (4, E)])
sage: rn.add_reactions([(0, 1), (1, 0), (1, 2), ..., (4, 3)])
sage: rn.plot()
```




```
sage: rn.ode_rhs()
(-k_0_1*x_A^a*x_B^b + k_2_0*x_A^c*x_D - k_3_4*x_A + k_1_0*x_C +
   k_4_3*x_E, ..., k_3_4*x_A - k_4_3*x_E)
sage: rn.stoichiometric_matrix  sage: rn.kinetic_order_matrix
[-1  1  0  1 -1  1]             [-a   a   c  a-c  -1   1]
[-1  1  0  1  0  0]             [-b   b   0   b    0   0]
[ 1 -1 -1  0  0  0]             [ 1  -1  -1   0    0   0]
[ 0  0  1 -1  0  0]             [ 0   0   1  -1    0   0]
[ 0  0  0  0  1 -1]             [ 0   0   0   0    1  -1]
sage: rn.deficiency_stoichiometric
0
sage: rn.deficiency_kinetic_order
0
sage: rn.is_weakly_reversible()
True
sage: rn.has_robust_cbe()         sage: rn.has_at_most_one_cbe()
[{a > 0, b > 0, a - c > 0}]       [{a >= 0, b >= 0, a - c >= 0}]
sage: rn(a=2, b=1, c=1).has_exactly_one_cbe()
True
```

References

[1] M. S. Aichmayr. “Computing Circuits and Sign Vectors with Applications to Linear Inequality Systems and Reaction Networks”. Submitted. PhD thesis. University of Kassel, Germany, 2026.

[2] M. S. Aichmayr. “SignVectors: a SageMath Package for Oriented Matroids”. Submitted. 2026.

[3] M. S. Aichmayr, S. Müller, and G. Regensburger. “A SageMath package for elementary and sign vectors with applications to chemical reaction networks”. In: *Mathematical software—ICMS 2024*. Vol. 14749. LNCS. Springer, Cham, 2024, pp. 155–164.

[4] S. Müller, J. Hofbauer, and G. Regensburger. “On the bijectivity of families of exponential/generalized polynomial maps”. In: *SIAM Journal on Applied Algebra and Geometry* 3 (2019), pp. 412–438.

SageMath Packages

Sign vectors, oriented matroids:
https://github.com/MarcusAichmayr/sign_vectors

Sign vector conditions for CRNs:
https://github.com/MarcusAichmayr/sign_crn