

# Computing sign vector conditions for existence and uniqueness of equilibria of chemical reaction networks

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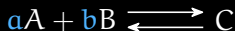
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## Chemical reaction network

Weighted directed graph  $1 \xrightleftharpoons[k_{21}]{k_{12}} 2$  rate constants  $k_{12}, k_{21} > 0$

Stoichiometric complexes:

Kinetic complexes:



MAK:  $a = b = 1$

GMAK:  $a, b \in \mathbb{R}$

$$\frac{d}{dt} \begin{pmatrix} x_A \\ x_B \\ x_C \end{pmatrix} = k_{12} x_A^a x_B^b \begin{pmatrix} -1 \\ -1 \\ 1 \end{pmatrix} + k_{21} x_C \begin{pmatrix} 1 \\ 1 \\ -1 \end{pmatrix}$$

Existence of (unique) equilibrium?

Stoichiometric subspace:

Kinetic-order subspace:

$$S = \text{im} \begin{pmatrix} -1 & -1 & 1 \end{pmatrix}^\top$$

$$\tilde{S} = \text{im} \begin{pmatrix} -a & -b & 1 \end{pmatrix}^\top$$

MAK:  $S = \tilde{S}$

## Deficiency zero theorem

### Theorem (Feinberg, Horn, Jackson 1972)

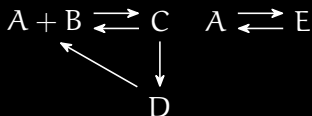
*For CRN with MAK, there is unique complex-balanced, asymptotically stable equilibrium in every stoichiometric class and for all rate constants iff  $\delta = 0$  and network weakly reversible.*

(Stoichiometric) deficiency:

$$\delta = m - l - \dim S,$$

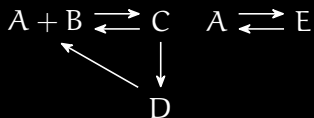
$m$  complexes,  $l$  connected components

Stoichiometric complexes:



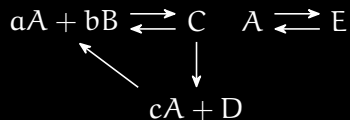
- Weakly reversible
- $m = 5, l = 2$
- $S = ?$

## Stoichiometric and kinetic deficiency



$$S = \text{im} \begin{pmatrix} 1 & 1 & -1 & 0 & 0 \\ 0 & 0 & -1 & 1 & 0 \\ 1 & 0 & 0 & 0 & -1 \end{pmatrix}^T$$

$$\begin{aligned}
 \delta &= m - l - \dim S \\
 &= 5 - 2 - 3 = 0
 \end{aligned}$$



$$\tilde{S} = \text{im} \begin{pmatrix} a & b & -1 & 0 & 0 \\ c & 0 & -1 & 1 & 0 \\ 1 & 0 & 0 & 0 & -1 \end{pmatrix}^T$$

$$\begin{aligned}
 \tilde{\delta} &= m - l - \dim \tilde{S} \\
 &= 5 - 2 - 3 = 0
 \end{aligned}$$

- Perturb from MAK ( $S = \tilde{S}$ )?

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

## Sign vectors

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

$$x \in \mathbb{R}^n: \quad \text{sign}(x) \in \{-, 0, +\}^n$$

$$S \subseteq \mathbb{R}^n: \quad \text{sign}(S) = \{\text{sign}(x) : x \in S\} \subseteq \{-, 0, +\}^n$$

$$\left. \begin{array}{l} 0 < - \\ 0 < + \end{array} \right\} \rightsquigarrow \text{partial order on } \{-, 0, +\}^n$$

$$\text{Closure:} \quad \overline{\text{sign}(S)} = \{\tau \in \{-, 0, +\}^n : \tau \leq \rho \text{ for some } \rho \in \text{sign}(S)\}$$

$$\overline{\left\{ \begin{pmatrix} + \\ 0 \end{pmatrix}, \begin{pmatrix} - \\ + \end{pmatrix} \right\}} = \left\{ \begin{pmatrix} 0 \\ 0 \end{pmatrix}, \begin{pmatrix} + \\ 0 \end{pmatrix}, \begin{pmatrix} 0 \\ + \end{pmatrix}, \begin{pmatrix} - \\ 0 \end{pmatrix}, \begin{pmatrix} - \\ + \end{pmatrix} \right\}$$

- Compute sign vectors?

## Computing sign vectors

$$S = \text{im} \begin{pmatrix} 1 & 1 & -1 & 0 & 0 \\ 0 & 0 & -1 & 1 & 0 \\ 1 & 0 & 0 & 0 & -1 \end{pmatrix}^T$$

$$\text{sign}(S) = ?$$

$$S = \ker(W), \quad W = \begin{pmatrix} 1 & 0 & 1 & 1 & 1 \\ 0 & 1 & 1 & 1 & 0 \end{pmatrix}$$

| I         | $\det(W_I)$ | chirotope |
|-----------|-------------|-----------|
| $\{1,2\}$ | 1           | +         |
| $\{1,3\}$ | 1           | +         |
| $\{1,4\}$ | 1           | +         |
| $\{1,5\}$ | 0           | 0         |
| $\{2,3\}$ | -1          | -         |
| $\{2,4\}$ | -1          | -         |
| $\vdots$  | $\vdots$    | $\vdots$  |

Support minimal elements (cocircuits) in  $\text{sign}(S)$

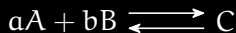
$$\begin{pmatrix} 0 \\ 0 \\ + \\ - \\ 0 \end{pmatrix}, \begin{pmatrix} 0 \\ + \\ - \\ 0 \\ + \end{pmatrix}, \begin{pmatrix} 0 \\ + \\ 0 \\ - \\ + \end{pmatrix}, \begin{pmatrix} + \\ 0 \\ 0 \\ 0 \\ - \end{pmatrix}, \begin{pmatrix} + \\ + \\ 0 \\ - \\ 0 \end{pmatrix}, \begin{pmatrix} + \\ + \\ - \\ 0 \\ 0 \end{pmatrix}, \dots \in \text{sign}(S)$$

- Chirotopes determine all cocircuits
- Cocircuits determine all sign vectors
- Implementation
- Package for SageMath

## Robust deficiency zero theorem

### Theorem (robust $\delta = \tilde{\delta} = 0$ theorem)

*For CRN with GMAK, there is unique complex-balanced equilibrium in every stoichiometric class, for all rate constants, and all small perturbations of kinetic orders iff  $\delta = \tilde{\delta} = 0$ , network weakly reversible, and  $\text{sign}(S) \subseteq \overline{\text{sign}(\tilde{S})}$*



$$S = \text{im} \begin{pmatrix} -1 & -1 & 1 \end{pmatrix}^\top$$

$$\tilde{S} = \text{im} \begin{pmatrix} -a & -b & 1 \end{pmatrix}^\top$$

$$\text{sign}(S) = \left\{ \begin{pmatrix} 0 \\ 0 \\ 0 \end{pmatrix}, \begin{pmatrix} + \\ + \\ - \end{pmatrix}, \begin{pmatrix} - \\ - \\ + \end{pmatrix} \right\}$$

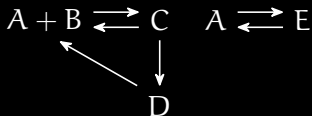
- $\text{sign}(\tilde{S})$ ?  $a, b$ ?

## Closure condition

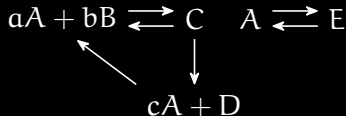
### Proposition

$S = \ker(W)$ ,  $\tilde{S} = \ker(\tilde{W})$ . The following are equivalent:

- (1)  $\text{sign}(S) \subseteq \overline{\text{sign}(\tilde{S})}$
- (2) (a) For all  $I$ ,  $\det(W_I) \neq 0 \Rightarrow \det(W_I) \det(\tilde{W}_I) > 0$ ; or  
 (b) For all  $I$ ,  $\det(W_I) \neq 0 \Rightarrow \det(W_I) \det(\tilde{W}_I) < 0$ .  
 $I \subseteq \{1, \dots, n\}$  with  $|I| = d$



$$W = \begin{pmatrix} 1 & 0 & 1 & 1 & 1 \\ 0 & 1 & 1 & 1 & 0 \end{pmatrix}$$



$$\tilde{W} = \begin{pmatrix} 1 & 0 & a & a-c & 1 \\ 0 & 1 & b & b & 0 \end{pmatrix}$$

- Unique equilibrium? – Find conditions on  $a, b, c$ .

## Closure condition – Maximal minors

Show: For all  $I$ ,  $\det(W_I) \neq 0 \Rightarrow \det(W_I) \det(\widetilde{W}_I) > 0$ .

$$W = \begin{pmatrix} 1 & 0 & 1 & 1 & 1 \\ 0 & 1 & 1 & 1 & 0 \end{pmatrix}$$

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

| $I$        | $\det(W_I)$ | $\det(\widetilde{W}_I)$ |         |
|------------|-------------|-------------------------|---------|
| $\{1, 2\}$ | 1           | 1                       | ✓       |
| $\{1, 3\}$ | 1           | $b$                     | $b > 0$ |
| $\{1, 5\}$ | 0           | 0                       | ✓       |
| $\{2, 3\}$ | -1          | $-a$                    | $a > 0$ |
| $\{2, 4\}$ | -1          | $c - a$                 | $c < a$ |
| $\{3, 4\}$ | 0           | $bc$                    | ✓       |
| $\vdots$   | $\vdots$    | $\vdots$                |         |

```
sage: W = matrix([[1, 0, 1, 1, 1],
....:             [0, 1, 1, 1, 0]])
sage: var('a, b, c')
sage: Wt = matrix([[1, 0, a, a - c, 1],
....:             [0, 1, b, b, 0]])
sage: from sign_vector_conditions import *
sage: condition_closure_minors(W, Wt)
{a > 0, a - c > 0, b > 0}
```

# Uniqueness

## Theorem

*For CRN with GMAK, there is at most one complex-balanced equilibrium in every stoichiometric class and for all rate constants iff*

$$\text{sign}(S) \cap \text{sign}(\tilde{S}^\perp) = \{0\}.$$

$$S = \text{im} \begin{pmatrix} -1 & -1 & 1 \end{pmatrix}^\top \quad \tilde{S} = \text{im} \begin{pmatrix} -a & -b & 1 \end{pmatrix}^\top$$

```
sage: S = matrix([[ -1, -1, 1]])
sage: var('a, b');
sage: St = matrix([[ -a, -b, 1]])
sage: from sign_vectors.oriented_matroids import *
sage: covectors_from_matrix(S, kernel=False)
{(000), (--+), (++-)}
sage: assume(a > 0, b > 0)
sage: covectors_from_matrix(St, kernel=True)
{(000), (+-+), (---), (-+0), (-+-), (+0+), (-++),
 (-0-), (+++), (+--), (0++), (0--), (+-0)}
```

- What about general  $a, b \in \mathbb{R}$ ?

## Uniqueness – Maximal minors

### Corollary

Let  $S = \ker(W)$ ,  $\tilde{S} = \ker(\tilde{W})$ . The following are equivalent:

- (1)  $\text{sign}(S) \cap \text{sign}(\tilde{S}^\perp) = \{0\}$
- (2) Exactly one of the following holds:
  - (a) For all  $I \subseteq \{1, \dots, n\}$  with  $|I| = d$ ,  $\det(W_I) \det(\tilde{W}_I) \geq 0$ .
  - (b) For all  $I \subseteq \{1, \dots, n\}$  with  $|I| = d$ ,  $\det(W_I) \det(\tilde{W}_I) \leq 0$ .

$$S = \text{im} \begin{pmatrix} -1 & -1 & 1 \end{pmatrix}^\top \quad \tilde{S} = \text{im} \begin{pmatrix} -a & -b & 1 \end{pmatrix}^\top$$

$$W = \begin{pmatrix} 1 & 0 & 1 \\ 0 & 1 & 1 \end{pmatrix} \quad \tilde{W} = \begin{pmatrix} 1 & 0 & a \\ 0 & 1 & b \end{pmatrix}$$

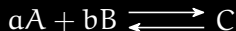
| I          | $\det(W_I)$ | $\det(\tilde{W}_I)$ |              |
|------------|-------------|---------------------|--------------|
| $\{1, 2\}$ | 1           | 1                   | $\checkmark$ |
| $\{1, 3\}$ | 1           | b                   | $b \geq 0$   |
| $\{2, 3\}$ | -1          | -a                  | $a \geq 0$   |

## Multistationarity

### Corollary

*Weakly reversible generalized mass-action system has capacity for multiple complex-balanced equilibria iff*

$$\text{sign}(S) \cap \text{sign}(\tilde{S}^\perp) \neq \{0\}.$$



| I          | $\det(W_I)$ | $\det(\tilde{W}_I)$ |
|------------|-------------|---------------------|
| $\{1, 2\}$ | 1           | 1                   |
| $\{1, 3\}$ | 1           | b                   |
| $\{2, 3\}$ | -1          | -a                  |

$$\rightsquigarrow a < 0 \text{ or } b < 0$$

## Exactly one equilibrium

### Theorem ( $\delta = \tilde{\delta} = 0$ theorem)

*For a CRN with GMAK, there is a unique complex-balanced equilibrium in every stoichiometric class and for all rate constants iff  $\delta = \tilde{\delta} = 0$ , network weakly reversible and*

- (1)  $\text{sign}(S) \cap \text{sign}(\tilde{S}^\perp) = \{0\}$ ;
- (2) *for every non-zero  $\tilde{\tau} \in \text{sign}(\tilde{S}^\perp)_\oplus$ , there is non-zero  $\tau \in \text{sign}(S^\perp)_\oplus$  such that  $\tau \leq \tilde{\tau}$ ; and*
- (3)  $(S, \tilde{S})$  *is non-degenerate.*

- Recursive algorithm
- Implementation

# Outlook

- SageMath packages
  - Sign vectors, oriented matroids, elementary vectors  
[https://github.com/MarcusAichmayr/sign\\_vectors](https://github.com/MarcusAichmayr/sign_vectors)
  - Sign vector conditions for chemical reaction networks  
(not yet public)