Species Composition and Reversibility in Chemical Reaction Network Theory

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Species Composition: Theory and Applications

Species Composition: Theory and Applications

Reaction networks: examples

$$
\begin{array}{ccccc}
R & + & A & \rightleftharpoons & RA \\
+ & & & & + \\
B & & & & B \\
\downarrow\!\uparrow & & & & \downarrow\!\uparrow \\
RB & + & A & \rightleftharpoons & RAB
\end{array}
$$

$$
\begin{array}{l}
E + A \rightleftharpoons EA \rightarrow E + B \\
F + B \rightleftharpoons FB \rightarrow F + A
\end{array}
$$

$$
\begin{array}{ccc}
2A + B & \longrightarrow & C \\
\uparrow & & \downarrow \\
D & \longleftarrow & A + 2B
\end{array}
$$

Reaction Networks

Reaction networks: definition

Reaction network: $\mathscr{N} = (\mathscr{S}, \mathscr{C}, \mathscr{R})$

$\mathscr{S}$ = set of species; nonempty finite

$\mathscr{C}$ = set of complexes (nodes); nonempty finite $\subseteq \mathbb{Z}_{\geqslant 0}\mathscr{S}$

$\mathscr{R}$ = set of reactions $\subseteq \mathscr{C} \times \mathscr{C}$

Additional requirements:

No nonparticipating species

No nonparticipating complexes

No self-reacting complexes

Stoichiometric space

Stoichiometric space $\mathcal{S}$ of reaction network $\mathscr{N} = (\mathscr{S}, \mathscr{C}, \mathscr{R})$

The span in the species space $\mathbb{R}\mathscr{S}$ of the reaction vectors.

Dynamics evolutions stay within stoichiometric compatibility classes, which are the traces on $\mathbb{R}_{\geqslant 0}\mathscr{S}$ of the affine subspaces of $\mathbb{R}\mathscr{S}$ parallel to $\mathcal{S}$.

$\text{rank}(\mathscr{N}) := \dim \mathcal{S}$.

Stoichiometric space – an example

Simplest futile enzymatic cycle

$E + A \rightleftharpoons EA \to E + B$

$F + B \rightleftharpoons FB \to F + A$

Set of species: $\mathscr{S} = \{E, F, A, B, EA, FB\}$

Reactions; set $\mathscr{R}$	Reaction vectors; spanning $\mathcal{S}$ in $\mathbb{R}\mathscr{S}$
$E + A \to EA$	$EA - E - A$
$EA \to E + A$	$E + A - EA$
$EA \to E + B$	$E + B - EA$
$F + B \to FB$	$FB - F - B$
$FB \to F + B$	$F + B - FB$
$FB \to F + A$	$F + A - FB$

A basis for $\mathcal{S}$ (from a canonical construction):

$\{\ (A - B)/2\ ,\ EA - E - (A + B)/2\ ,\ FB - F - (A + B)/2\ \}$

Species Composition: Theory and Applications

Species composition

Species composition: definition

A species composition of length n for a reaction network $\mathscr{N} = (\mathscr{S}, \mathscr{C}, \mathscr{R})$ is any map from the species of set to the set of nonnegative nonzero n-tuples.

$$\mathscr{E} = (\mathscr{E}_1, \ldots, \mathscr{E}_n) : \mathscr{S} \to \mathbb{Z}^n_{\geqslant 0} \backslash \{0_n\}$$

The $\mathbb{R}$-linear extension

$$\tilde{\mathscr{E}} = \left(\tilde{\mathscr{E}}_1, \ldots, \tilde{\mathscr{E}}_n\right) : \mathbb{R}\mathscr{S} \to \mathbb{R}^n$$

gives rise to a sensible notion of composition of complexes (nodes).

Species compositions – Examples

$$R + A \rightleftharpoons RA$$
$$R + B \rightleftharpoons RB$$
$$RB + A \rightleftharpoons RAB$$
$$RA + B \rightleftharpoons RAB$$

X	$\mathscr{E}(X)$
R	$(1,0,0)$
A	$(0,1,0)$
B	$(0,0,1)$
RA	$(1,1,0)$
RB	$(1,0,1)$
RAB	$(1,1,1)$

$$E + A \rightleftharpoons EA \rightarrow E + B$$
$$F + B \rightleftharpoons FB \rightarrow F + A$$

X	$\mathscr{E}(X)$
E	$(1,0,0)$
F	$(0,1,0)$
A	$(0,0,1)$
B	$(0,0,1)$
EA	$(1,0,1)$
FB	$(0,1,1)$

$$2A + B \rightarrow C$$
$$C \rightarrow A + 2B$$
$$A + 2B \rightarrow D$$
$$D \rightarrow 2A + B$$

X	$\mathscr{E}(X)$
A	1
B	1
C	3
D	3

Notions associated with a composition $\mathscr{E}$

$\mathscr{E}$-elementary species X	:	$\mathscr{E}(X) = e_{n,i}$ for some $i = 1, \ldots, n$
$\mathscr{E}$-composite species Y	:	$\mathscr{E}(Y) \in \mathbb{Z}^n_{\geqslant 0} \backslash \{0_n, e_{n,1}, \ldots, e_{n,n}\}$
$\mathscr{E}$-isomeric species Z and Z'	:	$\mathscr{E}(Z) = \mathscr{E}(Z')$
$\mathscr{E}$-isomerism classes	:	Preimages of occurring compositions
$\mathscr{E}$-conservative reaction $Q \to Q'$	:	$\tilde{\mathscr{E}}(Q) = \tilde{\mathscr{E}}(Q')$
$\mathscr{E}$-conservative network	:	All reactions are $\mathscr{E}$-conservative
$\mathscr{E}$-conservation space	:	$\mathrm{Ker}\tilde{\mathscr{E}}$

A Couple of Trivial Results

- Reaction network is $\mathscr{E}$-conservative
  $\Leftrightarrow$ $\mathscr{E}$-conservation space Ker$\tilde{\mathscr{E}}$ $\supseteq$ stoichiometric space $\mathcal{S}$
- In an $\mathscr{E}$-conservative reaction network,
  stoichiometric isomerism $\Rightarrow$ $\mathscr{E}$-isomerism.
  - Stoichiometric isomerism:
    Two species X and Y are stoichiometrically isomeric if $Y - X \in \mathcal{S}$.
  - Example:
    $E + A \rightleftharpoons EA \rightarrow E + B$
    $F + B \rightleftharpoons FB \rightarrow F + A$
    Species A and B are stoichiometrically isomeric:
    $B - A = (E + B - EA) + (EA - E - A)$

Compositions and Conservative Networks – Examples

$$
\begin{array}{ccc}
R + A & \rightleftharpoons & RA \\
+ & & + \\
B & & B \\
\downarrow\uparrow & & \downarrow\uparrow \\
RB + A & \rightleftharpoons & RAB
\end{array}
$$

X	$\mathscr{E}(X)$
R	$(1, 0, 0)$
A	$(0, 1, 0)$
B	$(0, 0, 1)$
RA	$(1, 1, 0)$
RB	$(1, 0, 1)$
RAB	$(1, 1, 1)$

$$E + A \rightleftharpoons EA \rightarrow E + B$$
$$F + B \rightleftharpoons FB \rightarrow F + A$$

X	$\mathscr{E}(X)$
E	$(1, 0, 0)$
F	$(0, 1, 0)$
A	$(0, 0, 1)$
B	$(0, 0, 1)$
EA	$(1, 0, 1)$
FB	$(0, 1, 1)$

$$
\begin{array}{ccc}
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X	$\mathscr{E}(X)$
A	1
B	1
C	3
D	3

Core Composition

Core Composition Map $\mathscr{E}$ – definition

1. All expected $\mathscr{E}$-elementary species do occur, i.e. length n is not unneededly large. ($\tilde{\mathscr{E}}$ is surjective.)
2. $\mathscr{E}$-conservation space $\mathrm{Ker}\tilde{\mathscr{E}}$ $=$ stoichiometric space $\mathcal{S}$.

Near-Core Composition Map $\mathscr{E}$ – definition

1. All expected $\mathscr{E}$-elementary species do occur.
2. $\mathscr{E}$-conservation space $\mathrm{Ker}\tilde{\mathscr{E}}$ $\supseteq$ stoichiometric space $\mathcal{S}$, i.e. the network is $\mathscr{E}$-conservative.

Contention:

For a near-core composition $\mathscr{E}$, the quotient space $\boxed{\mathrm{Ker}\tilde{\mathscr{E}}/\mathcal{S}}$ embodies a deficiency of the network or the composition map.

Deficient $\neq$ Bad

Core Composition – Example and Counter Example

$$\begin{aligned} H + OH &\rightleftharpoons H_2O \\ C + 2O &\rightleftharpoons CO_2 \end{aligned}$$

X	$\mathscr{E}(X)$
H	$(1,0,0)$
C	$(0,1,0)$
O	$(0,0,1)$
OH	$(1,0,1)$
H_2O	$(2,0,1)$
CO_2	$(0,1,2)$

Sensible, but only near-core.

X	$\mathscr{E}'(X)$
H	$(1,0,0,0)$
C	$(0,1,0,0)$
O	$(0,0,1,0)$
OH	$(0,0,0,1)$
H_2O	$(1,0,0,1)$
CO_2	$(0,1,2,0)$

Not so sensible, yet core.

$$\mathrm{Ker}\tilde{\mathscr{E}} = \mathcal{S} \oplus \mathbb{R}\cdot(OH - O - H)$$

Stoichiometry does not reveal that *OH* is made of *O* and *H*.

Another Couple of Trivial Results

- If $\mathscr{E}$ is a near-core composition, then:

$$\begin{aligned}\dim \mathrm{Ker}\tilde{\mathscr{E}} &= \#\text{species} \\ &\quad - \#\text{isomerism\_classes\_elem\_species}\end{aligned}$$

  Note: #isomerism_classes_elem_species $= n$,
  where n is the length of composition map.

  Also: $\dim \mathrm{Ker}\tilde{\mathscr{E}} = \mathrm{rank}\mathscr{S} - \dim\left(\mathrm{Ker}\tilde{\mathscr{E}}/\mathcal{S}\right)$.

- If $\mathscr{E}$ is a core composition, then:

$$\begin{aligned}\text{HJF\_Deficiency} &= \#\text{complexes} \\ &\quad - \#\text{linkage\_classes} \\ &\quad - \#\text{species} \\ &\quad + \#\text{isomerism\_classes\_elem\_species}\end{aligned}$$

Species Composition: Theory and Applications

Why Yet Another Notion of Reversibility?

Motivation: Augment Chemical Reaction Network Theory with a notion of phenomenological non-graph-theoretic reversibility.

Example:

$$E + A \rightleftharpoons EA \rightarrow E + B$$

$$F + B \rightleftharpoons FB \rightarrow F + A$$

This futile enzymatic network is not reversible and not weakly reversible per CRNT.

Yet it models a reversible phenomenon.
Many scientists would simply call it reversible.

A categorization of reactions

Association or binding	$\sum_i n_i X_i \rightarrow Y$
Dissociation or unbinding	$Y \rightarrow \sum_i n_i X_i$
Isomerisation	$U \rightarrow V$
Do these really exist? Do they have a name?	$\sum_i a_i A_i \rightarrow \sum_j b_j B_j$

A categorization of species

Explicitly constructible	:	the target of a binding reaction
Explicitly destructible	:	the source of a dissociation reaction
Explicitly constructive	:	in the source of a binding reaction
Explicitly destructive	:	in target of a dissociation reaction

Each category extends with stoichiometric isomerism.

Constructive Networks

Constructive Network – definition

A reaction network is constructive if it admits a core composition.

- Terminology co-opted from
  Guy Shinar, Uri Alon and Martin Feinberg.
- In a constructive network, any core composition is universal among conserved compositions
  (in a category-theoretic sense).
- In a constructive network, notions of elementary, composite and isomeric species are independent of the choice of core composition.

Explicitly Constructive Networks

Explicitly Constructive Network – definition

- The network is constructive.
- Each composite species is
  - explicitly constructible, or
  - explicitly destructible, or
  - both.
- Each elementary species is
  - explicitly constructive, or
  - explicitly destructive, or
  - both.

Explicitly-Reversibly Constructive Networks

Explicitly-Reversibly Constructive Network – definition

- The network is constructive.
- Each composite species is both explicitly constructible and explicitly destructible.
- Each elementary species is both explicitly constructive and explicitly destructive.

A Theorem on Reversibility and Persistence

Stated casually

In a well-formed mass-action reaction network,
isomerism among the building blocks controls persistence.

A little more seriously

There is persistence if among the elementary species,

- there is no isomerism, or more generally
- each isomerism class is phenomenologically strongly connected. (Example: futility in enzymatic networks.)

Theorems on Reversibility and Persistence

Theorem

If
- a reaction network is explicitly-reversibly constructive, and
- there is no isomerism among elementary species, and
- the law of mass action is in effect,

then the reaction network is ("vacuously") persistent.

Theorem

If a mass-action binary enzymatic network is futile and cascaded, then it is ("vacuously") persistent.