Reaction Networks, Species Composition, and Reversibility

an effort to utilize the intersection of chemical reaction network theory and the chemical principle of molecular composition

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Species Composition: Theory and Applications

Species Composition: Theory and Applications

Reaction networks – examples

$$
\begin{array}{ccccc}
R & + A & \rightleftharpoons & RA \\
+ & & & + \\
B & & & B \\
\downharpoonleft\upharpoonright & & & \downharpoonleft\upharpoonright \\
RB & + A & \rightleftharpoons & RAB
\end{array}
$$

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

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

Reaction networks defined

Definition – broad and generous

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 $\mathcal{S}$: the span in $\mathbb{R}\mathscr{S}$ of the reaction vectors

Species composition

Species composition map of length n (or simply composition)

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

Sensible notion of composition of complexes (nodes) with $\mathbb{R}$-linear extension $\tilde{\mathscr{E}} = \left(\tilde{\mathscr{E}}_1, \ldots, \tilde{\mathscr{E}}_n\right) : \mathbb{R}\mathscr{S} \to \mathbb{R}^n$

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	:	$\mathrm{Ker}\tilde{\mathscr{E}}$

Compositions and Conservative Networks – Examples

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

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	$(0,1,1)$

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

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

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.

  Example: In “usual” enzymatic networks,
  substrates and products must be $\mathscr{E}$-isomeric.

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.
2. $\mathscr{E}$-conservation space $\text{Ker}\tilde{\mathscr{E}} \; = \;$ 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 $\text{Ker}\tilde{\mathscr{E}} \; \supseteq \;$ stoichiometric space $\mathcal{S}$ i.e. the network is $\mathscr{E}$-conservative.

Contention:

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

Deficient $\neq$ Bad

Core Composition – Example and Counter Example

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

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:

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

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

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

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

Species Composition: Theory and Applications

Reversibility and Persistence

Observation: In the literature instances of non-persistence and non-obvious persistence always involve networks with isomerism among the building blocks.

Theorem

If

- a reaction network is explicitly-reversibly constructive, and
- there is no isomerism among elementary species, and
- the Law of Mass Action kinetics is in effect,

then the reaction network is (vacuously) persistent.

Casual formulation: In a “well-formed” mass-action network, the absence of isomerism among the building blocks is sufficient (but not necessary) for persistence.

Why Yet Another Notion of Reversibility?

Motivation: Incorporate phenomenological non-graph-theoretic reversibility.

Example:
Enzyme-catalyzed interconversion of substrate and product.

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

Not reversible in any graph-theoretic sense, yet reversible as a phenomenon.

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 (target of a binding reaction), or
  - explicitly destructible (source of a dissociation reaction), or
  - both.
- Each elementary species is
  - explicitly constructive (in source of a binding reaction), or
  - explicitly destructive (in target of a dissociation reaction), 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.

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 kinetics is in effect,

then the reaction network is (vacuously) persistent.

Basic Message:
Isomerism is a key influential factor in (non-)persistence.