

# Species Composition and Reversibility in Chemical Reaction Network Theory

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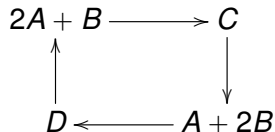
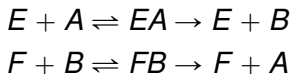
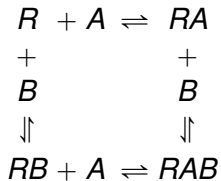
# Species Composition: Theory and Applications

- 1 Reaction Networks
- 2 Species Composition
- 3 Reversibility

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# Reaction networks: examples



# Reaction Networks

## Reaction networks: definition

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

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

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

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

Additional requirements:

No nonparticipating species

No nonparticipating complexes

No self-reacting complexes

# Stoichiometric space

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

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

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

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

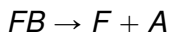
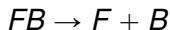
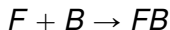
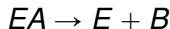
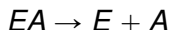
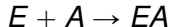
## Stoichiometric space – an example

Simplest futile enzymatic cycle

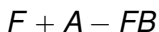
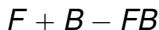
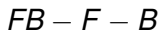
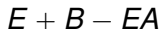
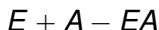
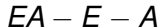


Set of species:  $\mathcal{S} = \{E, F, A, B, EA, FB\}$

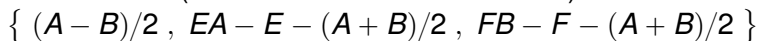
Reactions; set  $\mathcal{R}$



Reaction vectors; spanning  $\mathcal{S}$  in  $\mathbb{R}\mathcal{S}$



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



# Species Composition: Theory and Applications

- 1 Reaction Networks
- 2 Species Composition**
- 3 Reversibility



# Species composition

## Species composition: definition

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

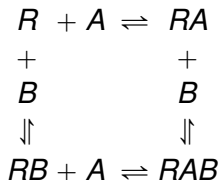
$$\mathcal{E} = (\mathcal{E}_1, \dots, \mathcal{E}_n) : \mathcal{S} \rightarrow \mathbb{Z}_{\geq 0}^n \setminus \{0_n\}$$

The  $\mathbb{R}$ -linear extension

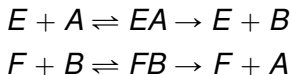
$$\tilde{\mathcal{E}} = (\tilde{\mathcal{E}}_1, \dots, \tilde{\mathcal{E}}_n) : \mathbb{R}\mathcal{S} \rightarrow \mathbb{R}^n$$

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

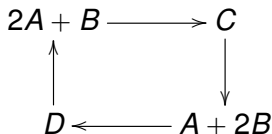
# Species compositions – Examples



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



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



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

## Notions associated with a composition $\mathcal{E}$

- $\mathcal{E}$ -elementary species  $X$  :  $\mathcal{E}(X) = \mathbf{e}_{n,i}$  for some  $i = 1, \dots, n$
- $\mathcal{E}$ -composite species  $Y$  :  $\mathcal{E}(Y) \in \mathbb{Z}_{\geq 0}^n \setminus \{\mathbf{0}_n, \mathbf{e}_{n,1}, \dots, \mathbf{e}_{n,n}\}$
- $\mathcal{E}$ -isomeric species  $Z$  and  $Z'$  :  $\mathcal{E}(Z) = \mathcal{E}(Z')$
- $\mathcal{E}$ -isomerism classes : Preimages of occurring compositions
- $\mathcal{E}$ -conservative reaction  $Q \rightarrow Q'$  :  $\tilde{\mathcal{E}}(Q) = \tilde{\mathcal{E}}(Q')$
- $\mathcal{E}$ -conservative network : All reactions are  $\mathcal{E}$ -conservative
- $\mathcal{E}$ -conservation space :  $\text{Ker} \tilde{\mathcal{E}}$

# A Couple of Trivial Results

- Reaction network is  $\mathcal{E}$ -conservative  
 $\Leftrightarrow \mathcal{E}$ -conservation space  $\text{Ker} \tilde{\mathcal{E}} \supseteq$  stoichiometric space  $\mathcal{S}$
- In an  $\mathcal{E}$ -conservative reaction network,  
 stoichiometric isomerism  $\Rightarrow \mathcal{E}$ -isomerism.

- Stoichiometric isomerism:

Two species  $X$  and  $Y$  are stoichiometrically isomeric if  
 $Y - X \in \mathcal{S}$ .

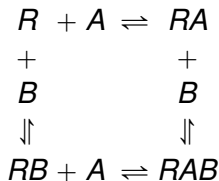
- Example:



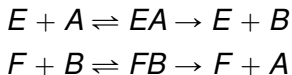
Species  $A$  and  $B$  are stoichiometrically isomeric:

$$B - A = (E + B - EA) + (EA - E - A)$$

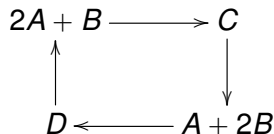
# Compositions and Conservative Networks – Examples



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



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



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

# Core Composition

## Core Composition Map $\mathcal{E}$ – definition

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

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

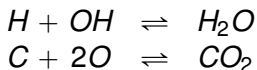
- 1 All expected  $\mathcal{E}$ -elementary species do occur.
- 2  $\mathcal{E}$ -conservation space  $\text{Ker} \tilde{\mathcal{E}} \supseteq$  stoichiometric space  $\mathcal{S}$ , i.e. the network is  $\mathcal{E}$ -conservative.

### Contention:

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

### Deficient $\neq$ Bad

# Core Composition – Example and Counter Example



$X$	$\mathcal{E}(X)$
$H$	(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.

$X$	$\mathcal{E}'(X)$
$H$	(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.

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

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

## Another Couple of Trivial Results

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

$$\dim \text{Ker} \tilde{\mathcal{E}} = \begin{array}{l} \# \text{species} \\ - \# \text{isomerism\_classes\_elem\_species} \end{array}$$

Note:  $\# \text{isomerism\_classes\_elem\_species} = n$ ,  
 where  $n$  is the length of composition map.

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

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

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



# Species Composition: Theory and Applications

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# Why Yet Another Notion of Reversibility?

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

**Example:**



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.