

Complexity of detecting autocatalysis in chemical reaction networks

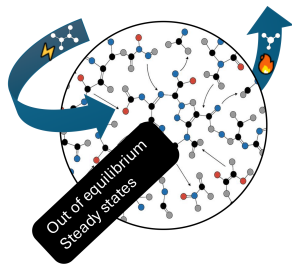
Denis Kuperberg
CNRS, LIP, ENS Lyon

Joint work with Sylvain Charlat, Thomas Kosc, Étienne Rajon

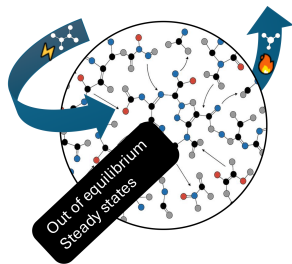
Combinatorics of Life Sciences
01/10/2025



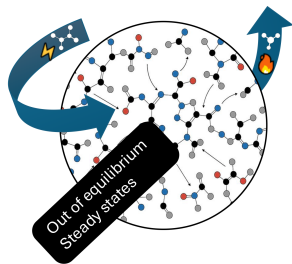
Origin of life



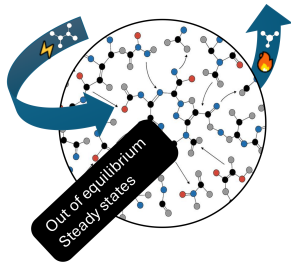
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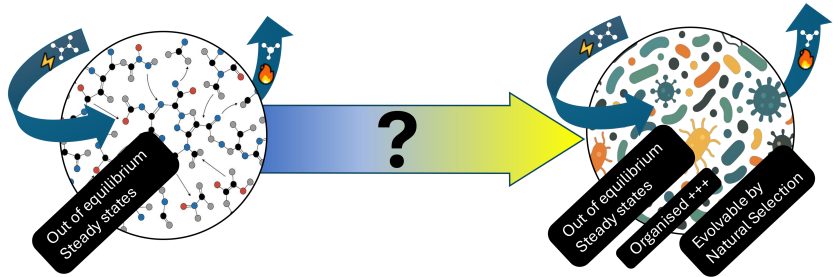
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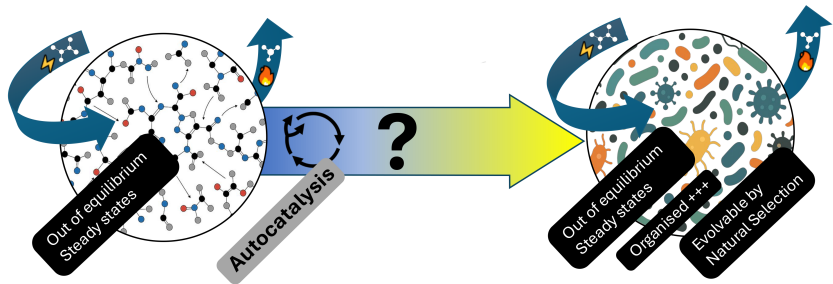
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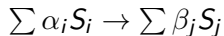


Reaction Networks

Reaction Network: $(\mathcal{S}, \mathcal{R})$

$\mathcal{S}$: species $(A, B, \dots)$

$\mathcal{R}$: reactions



Stoichiometric Matrix:

Rows: species $\mathcal{S}$

Columns: reactions $\mathcal{R}$

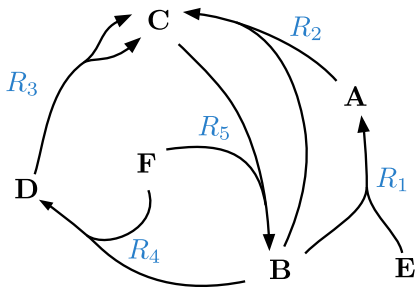
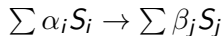
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$$M[i, j] = \beta_{ij} - \alpha_{ij}.$$

	R_1	R_2	R_3	R_4	R_5
A	1	-1	0	0	0
B	-1	-1	0	-1	1
C	0	1	2	0	-1
D	0	0	-1	1	0
E	-1	0	0	0	0
F	0	0	0	-1	-1

Using the stoichiometric matrix

Stoichiometric matrix

$$\begin{array}{c} \mathbf{A} \\ \mathbf{B} \\ \mathbf{C} \\ \mathbf{D} \\ \mathbf{E} \\ \mathbf{F} \end{array} \begin{array}{ccccc} R_1 & R_2 & R_3 & R_4 & R_5 \\ \left(\begin{array}{ccccc} 1 & -1 & 0 & 0 & 0 \\ -1 & -1 & 0 & -1 & 1 \\ 0 & 1 & 2 & 0 & -1 \\ 0 & 0 & -1 & 1 & 0 \\ -1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & -1 & 1 \end{array} \right) \end{array}$$

Flow vector

$$\begin{pmatrix} 2 \\ 1 \\ 0 \\ 1 \\ -2 \end{pmatrix} \begin{array}{l} R_1 \\ R_2 \\ R_3 \\ R_4 \\ R_5 \end{array}$$

Net production

$$= \begin{pmatrix} 1 \\ -6 \\ 3 \\ 1 \\ -2 \\ -3 \end{pmatrix} \begin{array}{l} \mathbf{A} \\ \mathbf{B} \\ \mathbf{C} \\ \mathbf{D} \\ \mathbf{E} \\ \mathbf{F} \end{array}$$

Autocatalysis

Autocatalytic core [Blokhuis, Lacoste, Nghe 2022]:

Submatrix N of M such that

Autonomy Each column and row contains coefs < 0 and > 0

Production $\exists \vec{v} \in \mathbb{R}^k$ such that $N \cdot \vec{v} \in (\mathbb{R}^{*+})^k$

Minimality N is minimal

Autocatalysis

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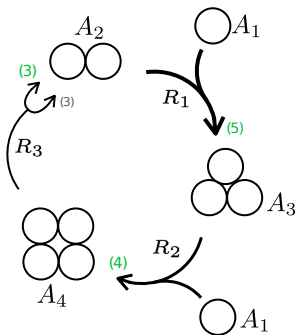
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Example:

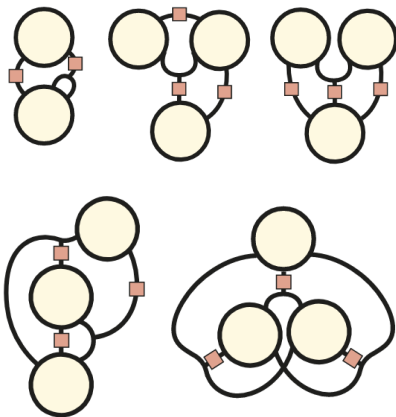


$$N: \begin{array}{ccc} & R_1 & R_2 & R_3 \\ \begin{array}{c} A_2 \\ A_3 \\ A_4 \end{array} & \begin{pmatrix} -1 & 0 & 2 \\ 1 & -1 & 0 \\ 0 & 1 & -1 \end{pmatrix} \end{array}$$

$$N \cdot \begin{pmatrix} 5 \\ 4 \\ 3 \end{pmatrix} = \begin{pmatrix} 1 \\ 1 \\ 1 \end{pmatrix}$$

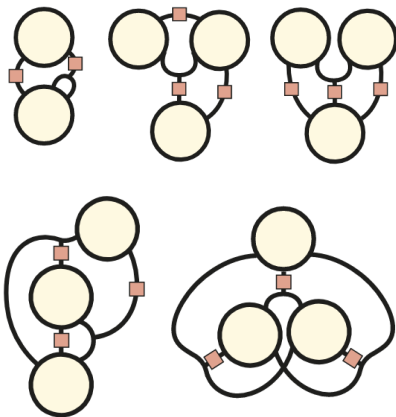
Classification of autocatalytic cores

[Blokhuys, Lacoste, Nghe 2022]



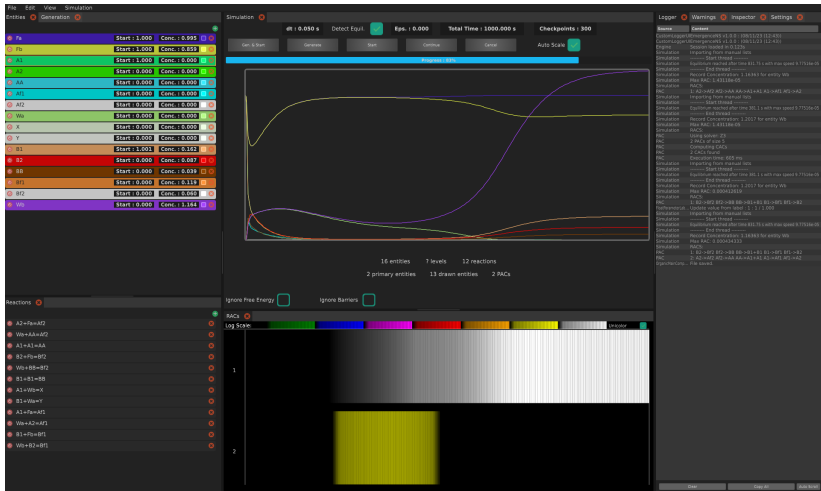
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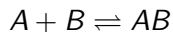


Goal: Find autocatalytic cores in the network, track their activity.

EmergeNS Software

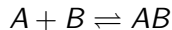


From concentrations to flows



How to compute flows ?

From concentrations to flows



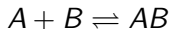
How to compute flows ? **Mass action law**

$$v_{\text{assoc}} = k_{\text{assoc}}[A][B]$$

$$v_{\text{dissoc}} = k_{\text{dissoc}}[AB]$$

$$\text{flow } v = v_{\text{assoc}} - v_{\text{dissoc}}$$

From concentrations to flows



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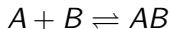
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Consistent core: Flow witness must be realistic :

Concentration vector $\vec{c} \rightsquigarrow$ flow vector $\vec{v}$ witnessing production.

From concentrations to flows



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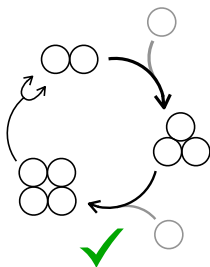
Compatible cores: share the same witness $\vec{v}$.

Results on thermodynamic realism

[Kosc, Kuperberg, Rajon, Charlat 2025]

Theorem 1:

Any core is consistent.

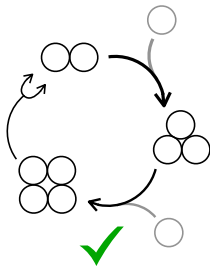


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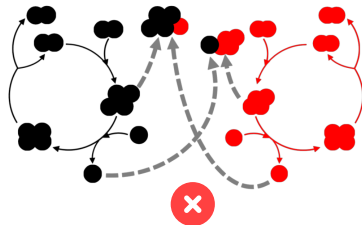
Theorem 1:

Any core is consistent.



Theorem 2:

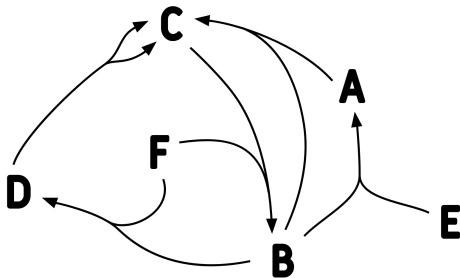
Compatible cores might be mutually inconsistent.



Detecting autocatalytic cores

Input: reaction network $(\mathcal{S}, \mathcal{R})$

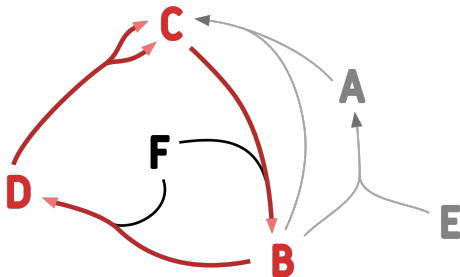
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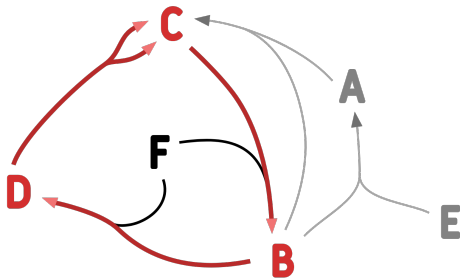
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Several variants:

Cycle: $\exists$ autocatalytic core

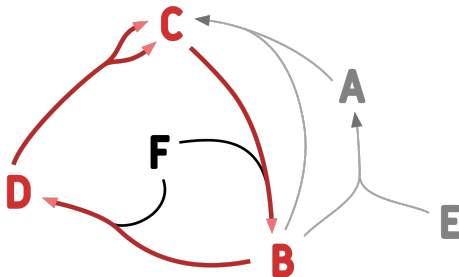
List: $\exists$ AC outside input list

Constrained: $\exists$ AC constraints on food/species.

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Do we allow irreversible reactions ?

Results

	Cycle	List	Constrained
Reversible	?	?	NP-c
Irreversible	NP-c	NP-c	NP-c

Reduction from SAT:

$$\begin{aligned} \varphi &= c_1 \wedge c_2 \wedge c_3 \\ c_1 &= x_1 \vee x_2 & c_2 &= x_1 \vee \bar{x}_2 & c_3 &= \bar{x}_1 \vee \bar{x}_2. \end{aligned}$$

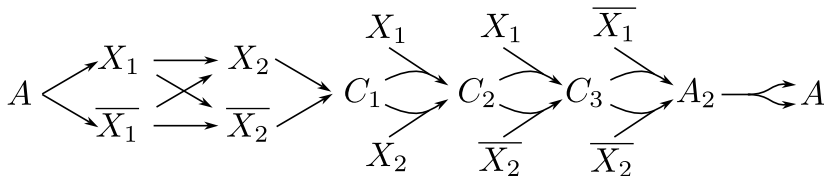
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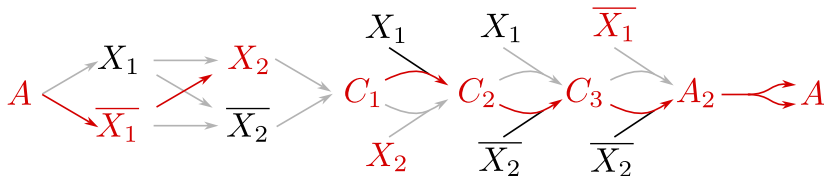
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Thank you !

