Complexity of detecting autocatalysis in chemical reaction networks

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Joint work with Sylvain Charlat, Thomas Kosc, Étienne Rajon

Combinatorics of Life Sciences
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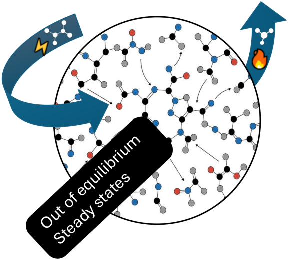
LABORATOIRE DE BIOMÉTRIE ET BIOLOGIE ÉVOLUTIVE

Origin of life



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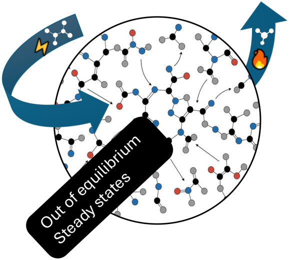

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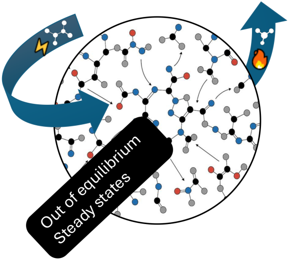

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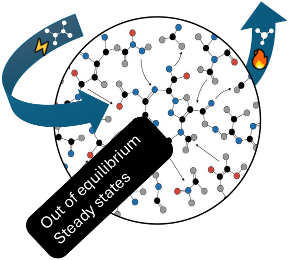

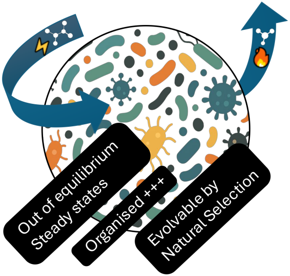

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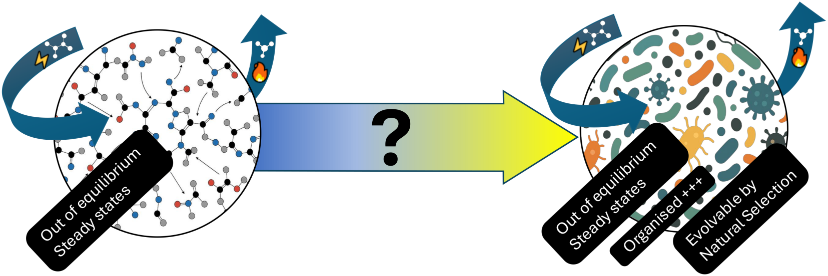

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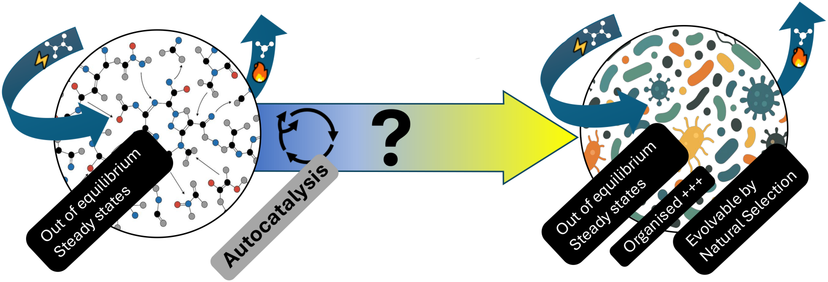

Reaction Networks

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

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

$\mathcal{R}$: reactions

$\sum \alpha_i S_i \to \sum \beta_j S_j$

Stoichiometric Matrix:

Rows: species $\mathcal{S}$

Columns: reactions $\mathcal{R}$

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

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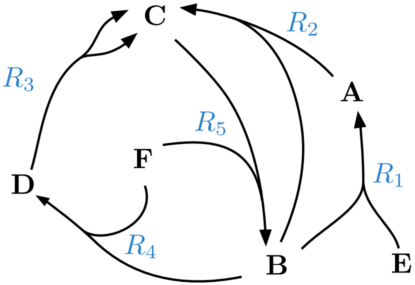

	R_1	R_2	R_3	R_4	R_5
A	1	−1	0	0	0
B	−1	−1	0	−1	1
C	0	1	2	0	−1
D	0	0	−1	1	0
E	−1	0	0	0	0
F	0	0	0	−1	−1

Using the stoichiometric matrix

Stoichiometric matrix · **Flow vector** = **Net production**

$$
\begin{array}{c} \\ \mathbf{A} \\ \mathbf{B} \\ \mathbf{C} \\ \mathbf{D} \\ \mathbf{E} \\ \mathbf{F} \end{array}
\begin{array}{c}
\begin{array}{ccccc} R_1 & R_2 & R_3 & R_4 & R_5 \end{array} \\
\begin{pmatrix}
1 & -1 & 0 & 0 & 0 \\
-1 & -1 & 0 & -1 & 1 \\
0 & 1 & 2 & 0 & -1 \\
0 & 0 & -1 & 1 & 0 \\
-1 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & -1 & 1
\end{pmatrix}
\end{array}
\cdot
\begin{pmatrix} 2 \\ 1 \\ 0 \\ 1 \\ -2 \end{pmatrix}
\begin{array}{c} R_1 \\ R_2 \\ R_3 \\ R_4 \\ R_5 \end{array}
=
\begin{pmatrix} 1 \\ -6 \\ 3 \\ 1 \\ -2 \\ -3 \end{pmatrix}
\begin{array}{c} \mathbf{A} \\ \mathbf{B} \\ \mathbf{C} \\ \mathbf{D} \\ \mathbf{E} \\ \mathbf{F} \end{array}
$$

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

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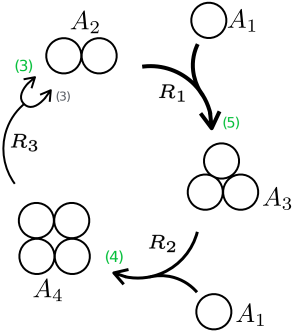
Example:

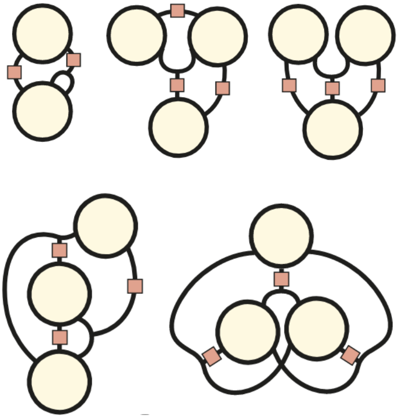


$$N: \quad \begin{array}{c} \\ A_2 \\ A_3 \\ A_4 \end{array} \begin{array}{c} \begin{array}{ccc} R_1 & R_2 & R_3 \end{array} \\ \begin{pmatrix} -1 & 0 & 2 \\ 1 & -1 & 0 \\ 0 & 1 & -1 \end{pmatrix} \end{array}$$

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

Classification of autocatalytic cores

[Blokhuis, Lacoste, Nghe 2022]



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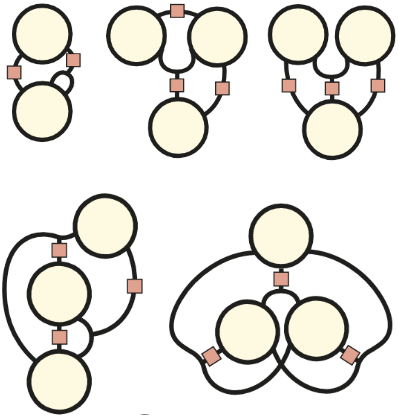
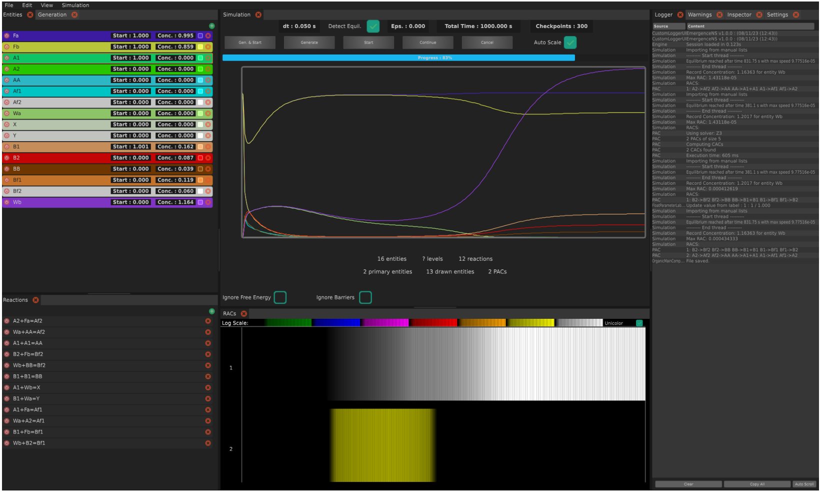


Goal: Find autocatalytic cores in the network, track their activity.

EmergeNS Software



From concentrations to flows

$$A + B \rightleftharpoons AB$$

How to compute flows ?

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

$$v_{\text{assoc}} = k_{\text{assoc}}[A][B]$$
$$v_{\text{dissoc}} = k_{\text{dissoc}}[AB]$$
$$\text{flow } v = v_{\text{assoc}} - v_{\text{dissoc}}$$

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Consistent core: Flow witness must be realistic :

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

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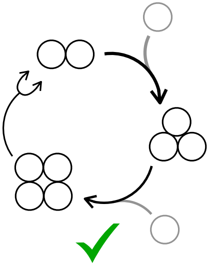
Compatible cores: share the same witness $\vec{v}$.

Results on thermodynamic realism

[Kosc, Kuperberg, Rajon, Charlat 2025]

Theorem 1:
Any core is consistent.



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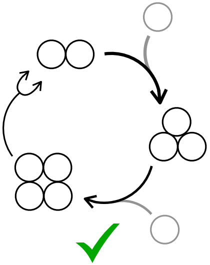
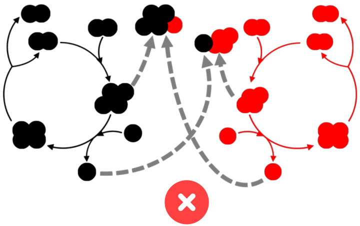


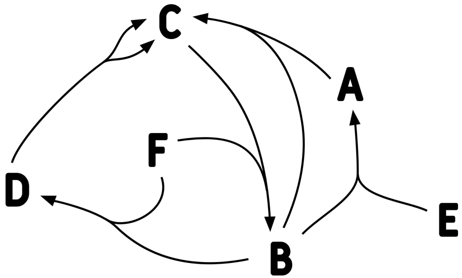
Theorem 2:
Compatible cores might be mutually inconsistent.



Detecting autocatalytic cores

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

Output: List of autocatalytic cores in the network.



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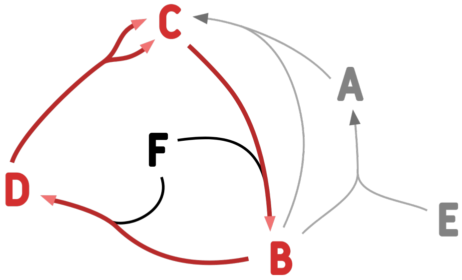

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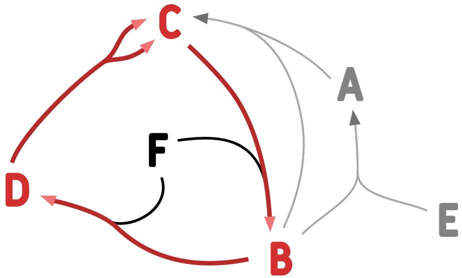

Several variants:

Cycle: $\exists$ autocatalytic core

List: $\exists$ AC outside input list

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

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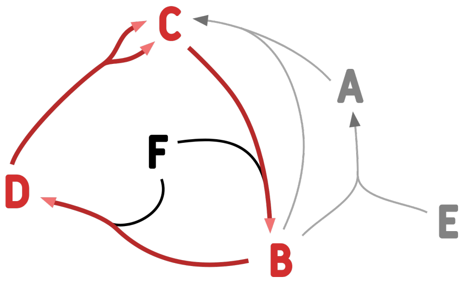

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Do we allow irreversible reactions ?

Results

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

Reduction from SAT:

$$\varphi = c_1 \wedge c_2 \wedge c_3$$

$$c_1 = x_1 \vee x_2 \qquad c_2 = x_1 \vee \overline{x}_2 \qquad c_3 = \overline{x}_1 \vee \overline{x}_2.$$

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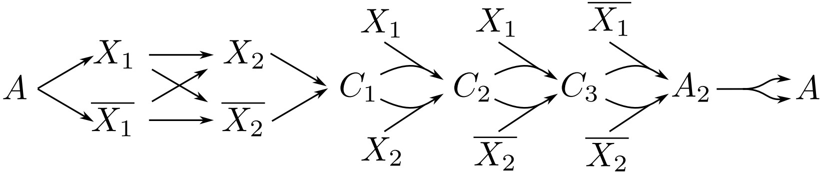

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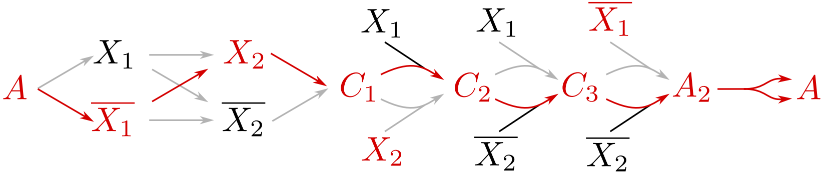

Thank you !