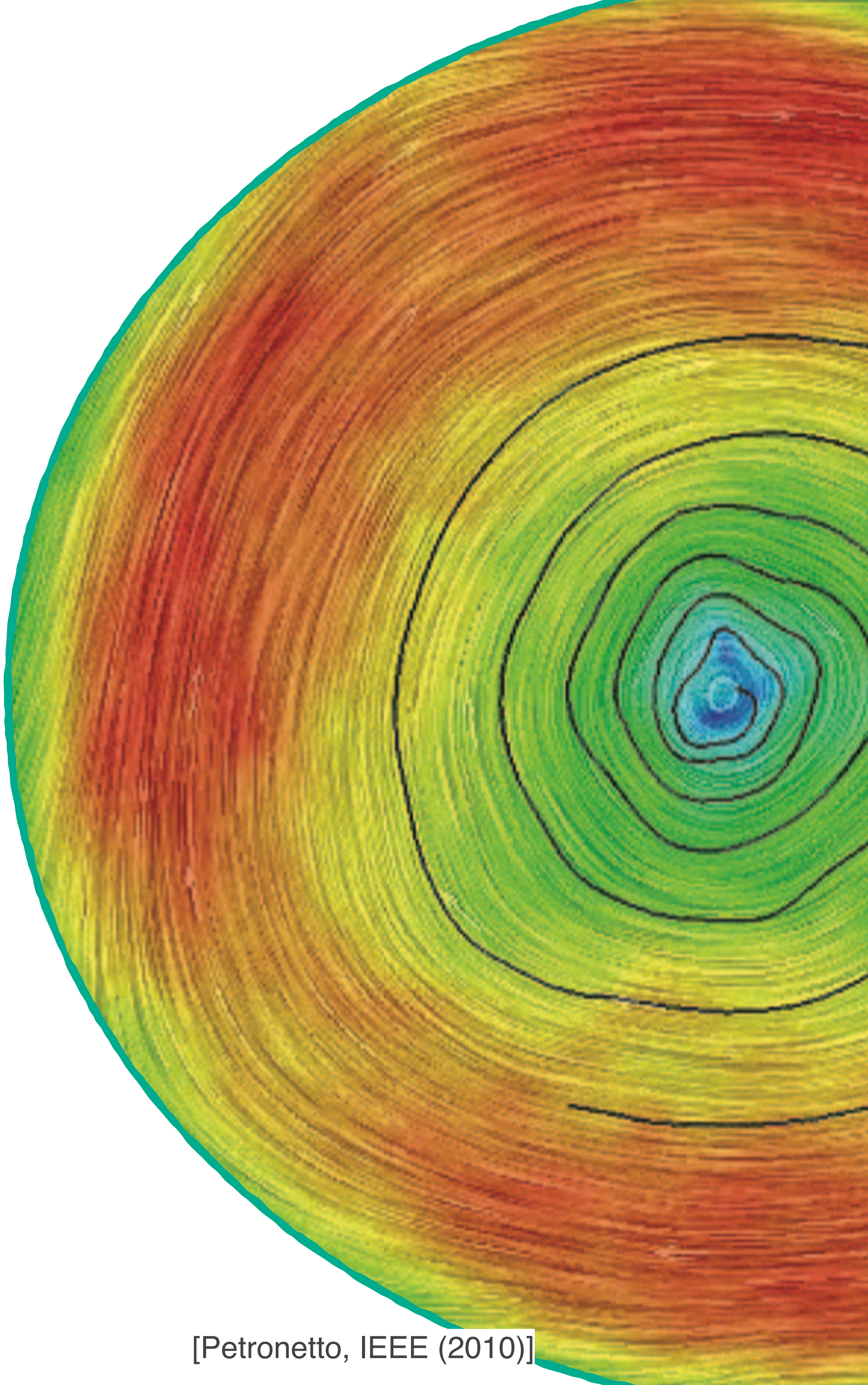
Schnakenberg without Schnakenberg

Sara Dal Cengio
LIPhy Grenoble

WOST III
31/05/22



[Petronetto, IEEE (2010)]

Identifying nonequilibrium forces

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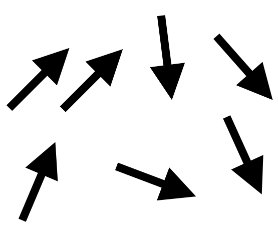
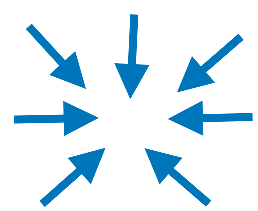
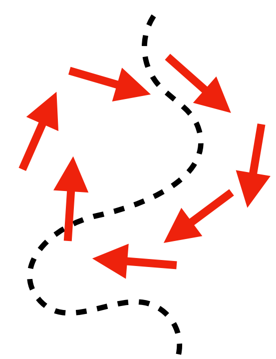
Helmholtz decomposition ($\mathbb{R}^2$, $\mathbb{R}^3$)

$$\mathbf{f} \quad = \quad -\nabla V \quad + \quad \nabla \times \mathbf{A}$$







Conservative Non-conservative

<u>In physics:</u> $\mathbf{f}_{\mathrm{nc}} = 0 \iff$ Equilibrium

Identifying nonequilibrium forces

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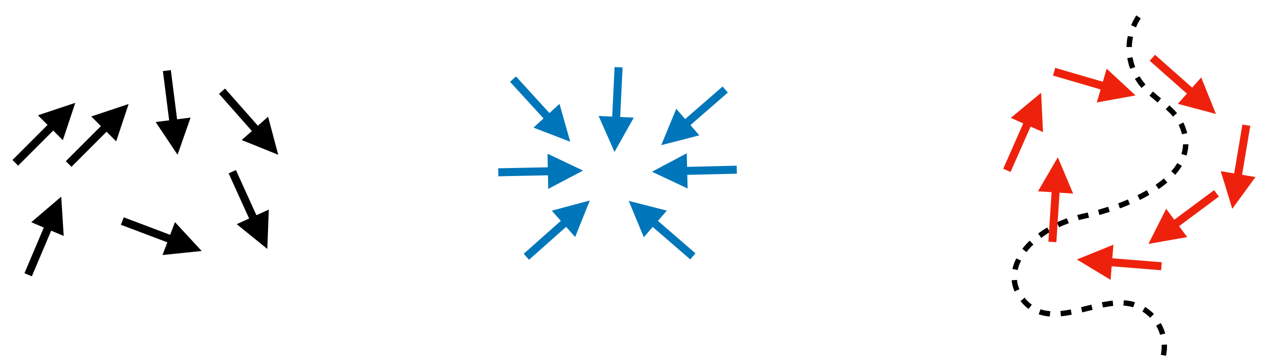

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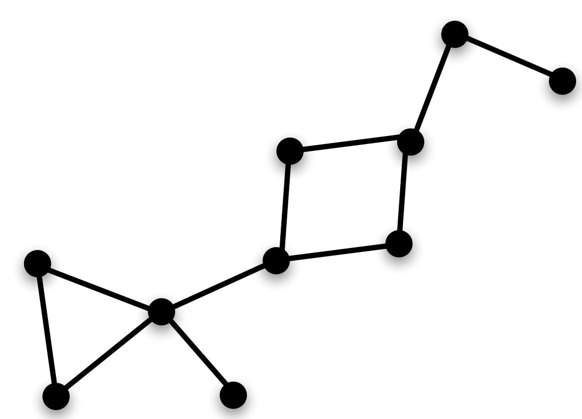
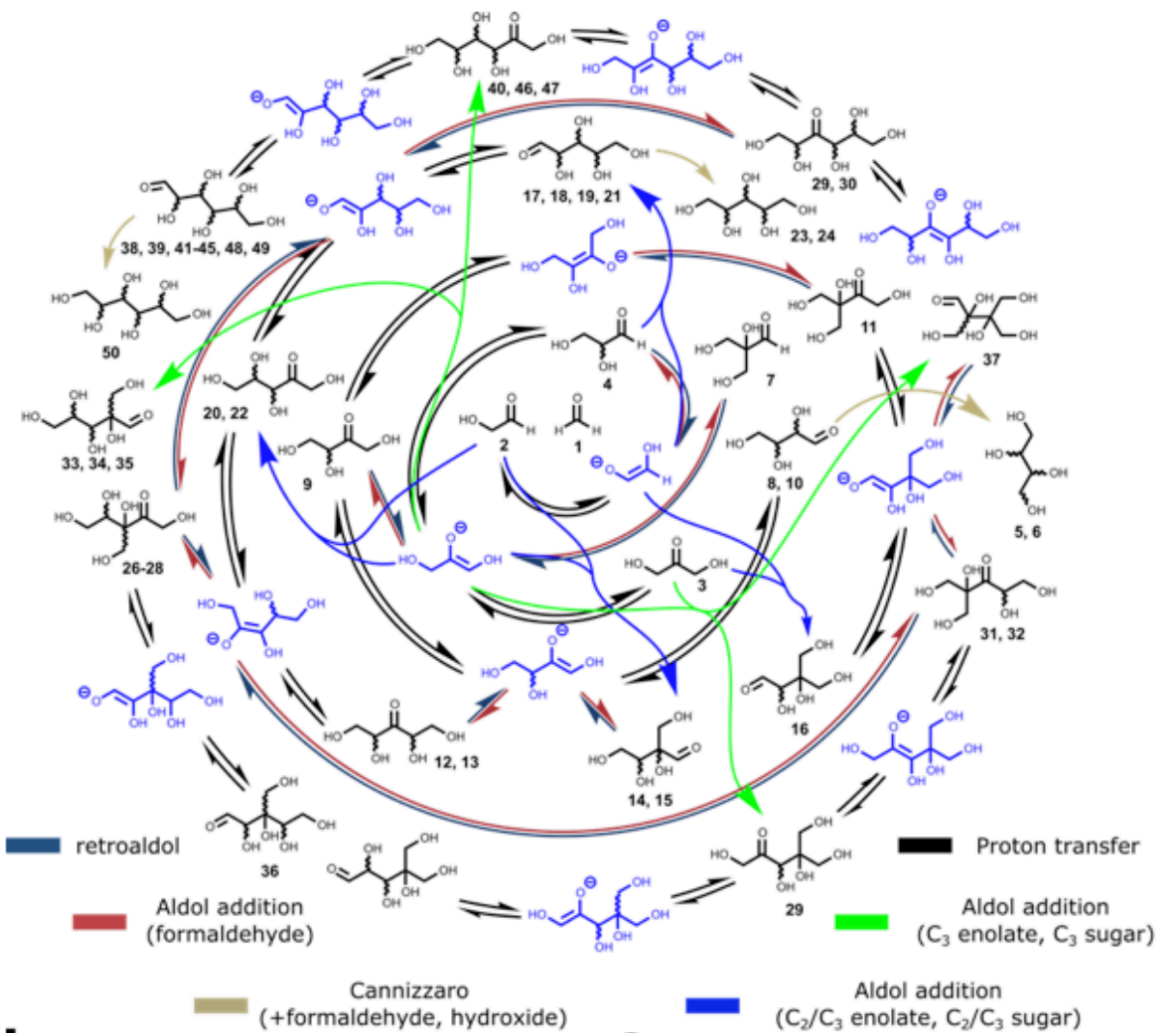


What if the space of configurations is a network?

Chemical reaction networks



Topological complexity

Biological functions

Nonequilibrium

[W. Robinson et al, preprint (2021)]

Chemical reaction networks

How to identify nonequilibrium (chemical) forces in complex topology?

Rev. Mod. Phys. (1976)

Network theory of microscopic and macroscopic behavior of master equation systems

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- Microscopic description: **population** dynamics
- Decomposition of forces based on **graph theory**
- Importance of **chemical cycles** for non-equilibrium steady states

Chemical reaction networks

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Problem: graph at the level of population is impractical!

Deterministic rate equations

- For large systems: evolution at the average level $$x_i \equiv \lim_{N,V\to\infty} \frac{N_i}{V}$$

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$\mathbb{S}$: Stoichiometric matrix encodes the topology

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  $\mathbb{S}$: Stoichiometric matrix encodes the topology

- Pair of current and affinity for each reaction ρ $$J_\rho(x)\,,\, A_\rho(x)$$

Noninteracting CRNs

Unimolecular reactions: $X_i \rightleftharpoons X_j$

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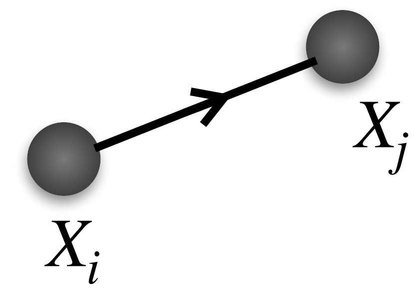
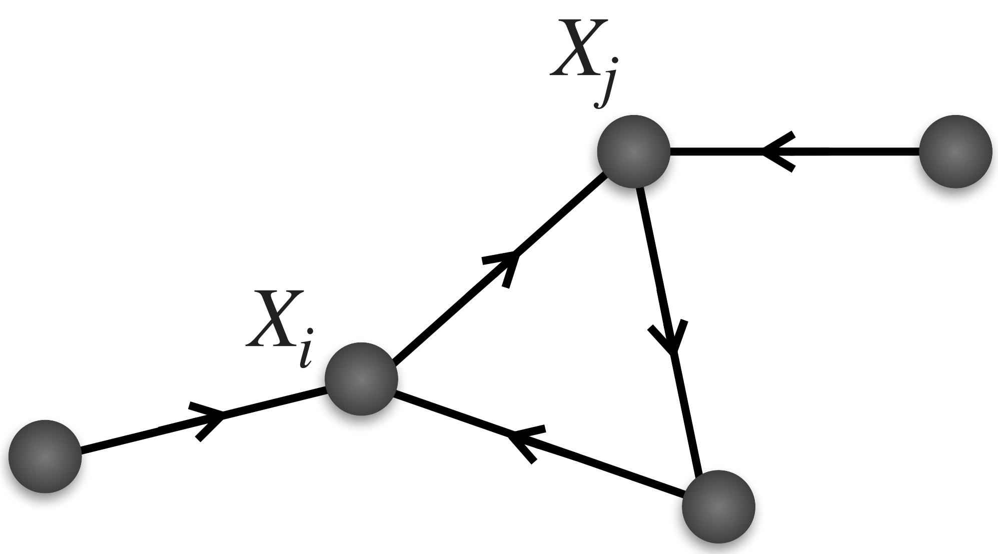




Planar graph representation:

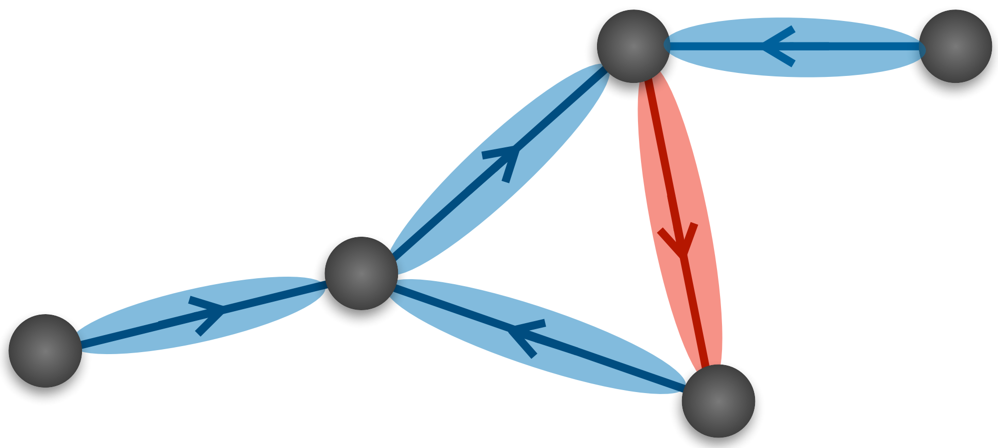
Nodes $\Longleftrightarrow$ Species

Edges $\Longleftrightarrow$ Reactions

$\neq$ graph at the population level!

Noninteracting CRNs

Unimolecular reactions: $X_i \rightleftharpoons X_j$



Choosing a spanning tree

Noninteracting CRNs

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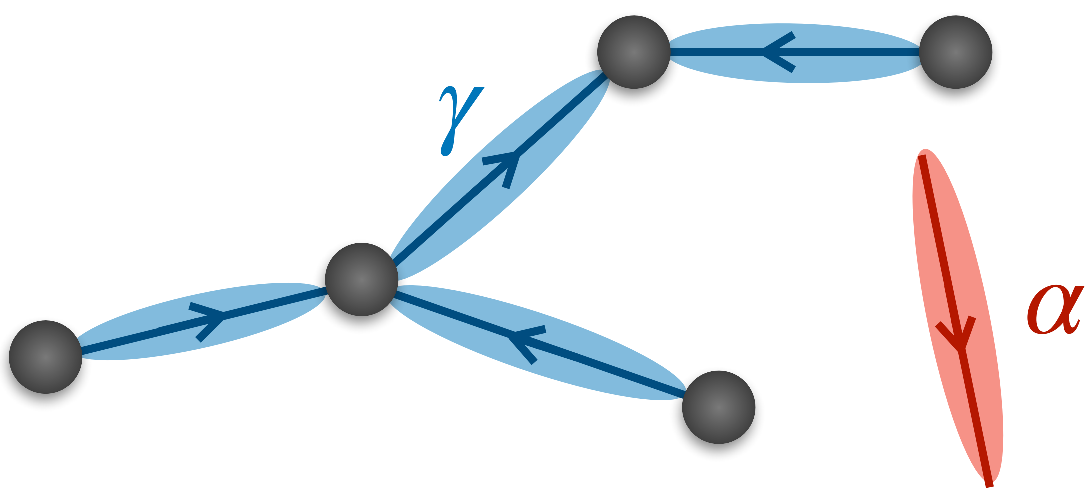
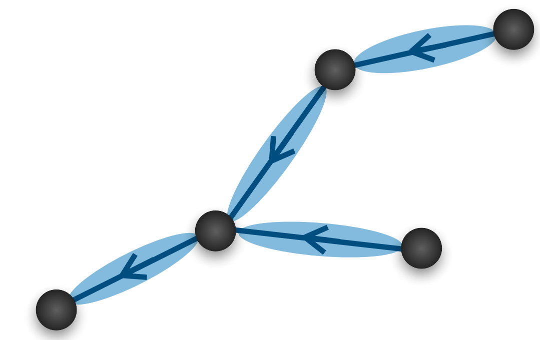
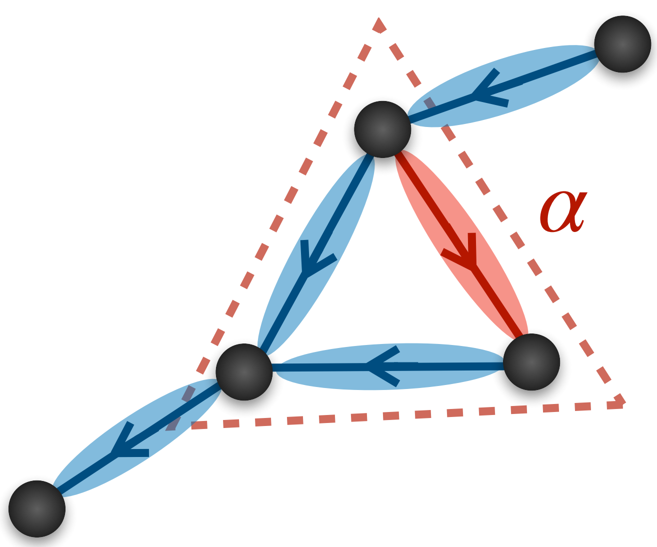


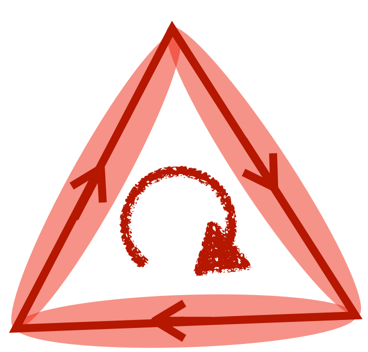
Choosing a spanning tree

Cycles & cocycles



Adding an edge back:

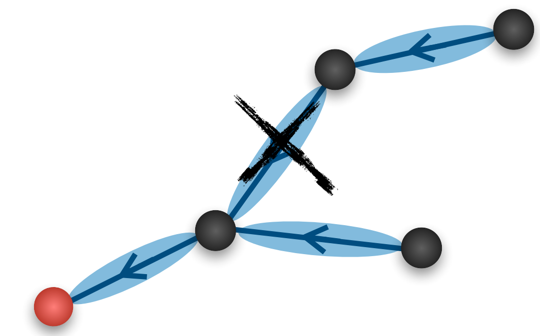




Cycle

$|c^{\alpha}\rangle$

Cycles & cocycles



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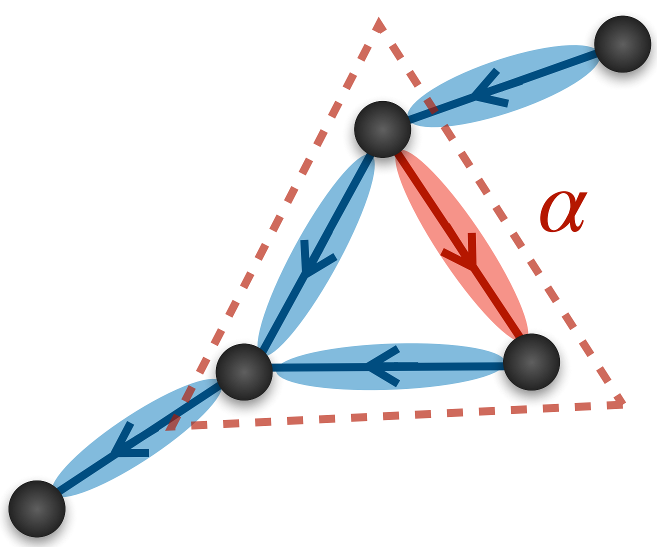

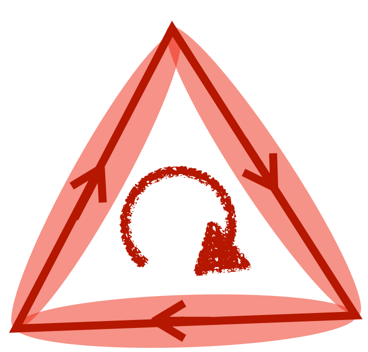

Cycle

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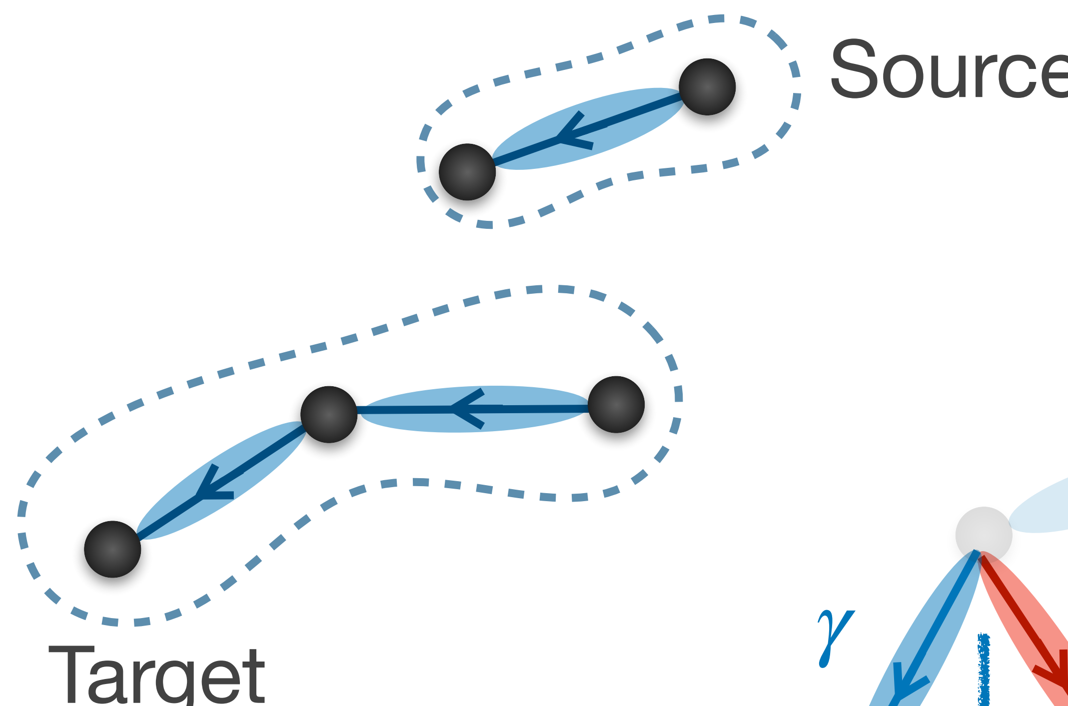
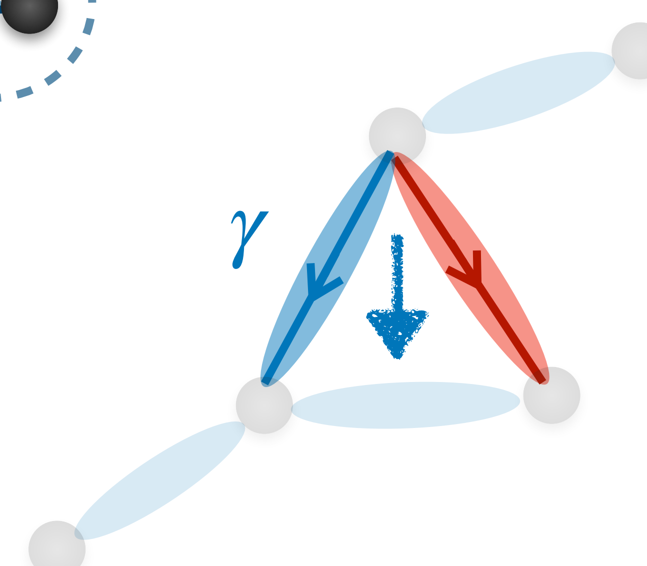
Removing a edge:

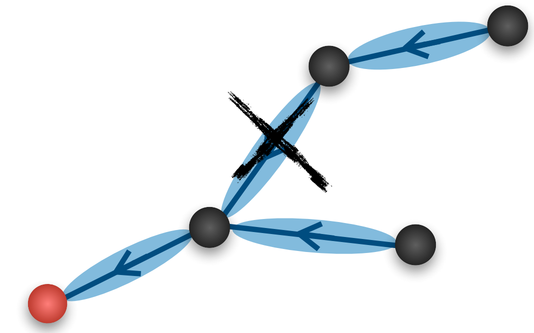


Cocycle

$|c^{\gamma}\rangle$



Cycles & cocycles

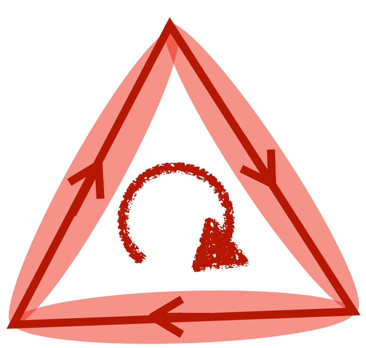


Adding an edge back:

Removing a edge:

How can they be used to decompose the chemical affinities?

Target



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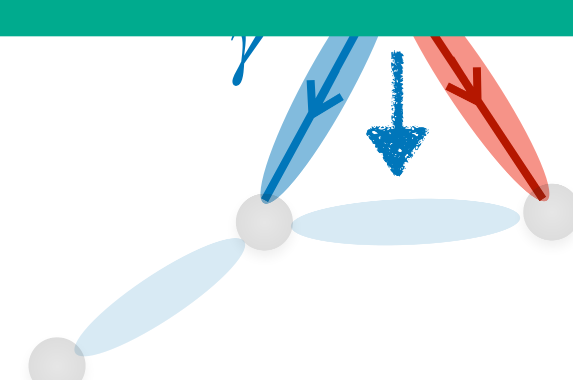
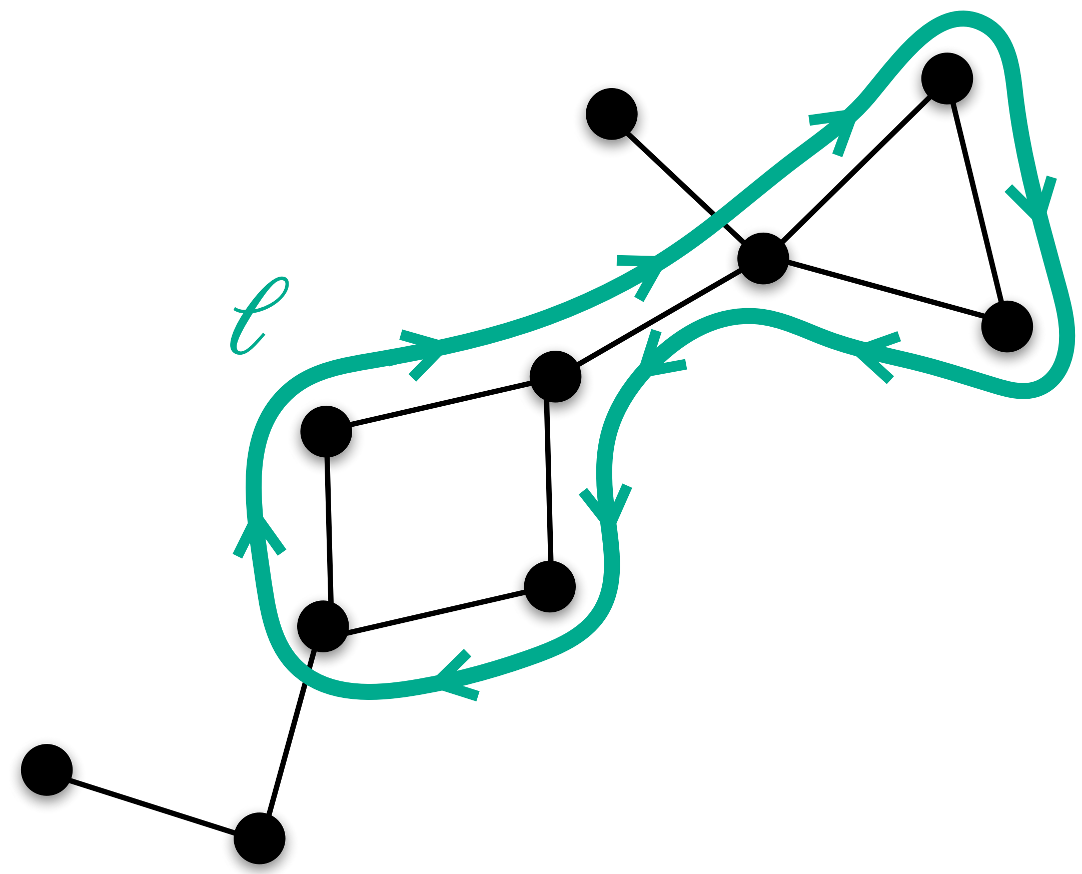


Non-conservative affinities

A generic loop on the graph is a linear combination of cycles



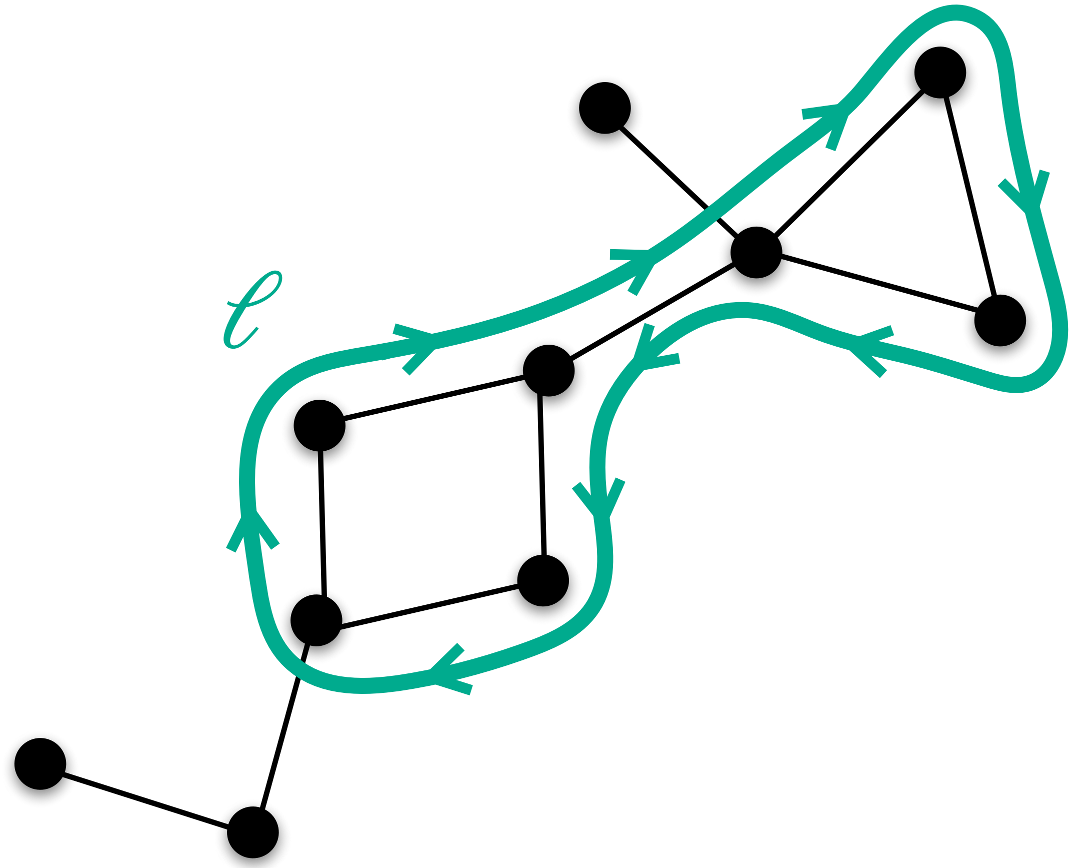
Non-conservative affinities

A <u>generic loop</u> on the graph is a linear combination of cycles

Circulation of the affinity:

$$\langle A \,|\, c^{\alpha} \rangle = A_{\alpha}$$

Non-conservative affinities



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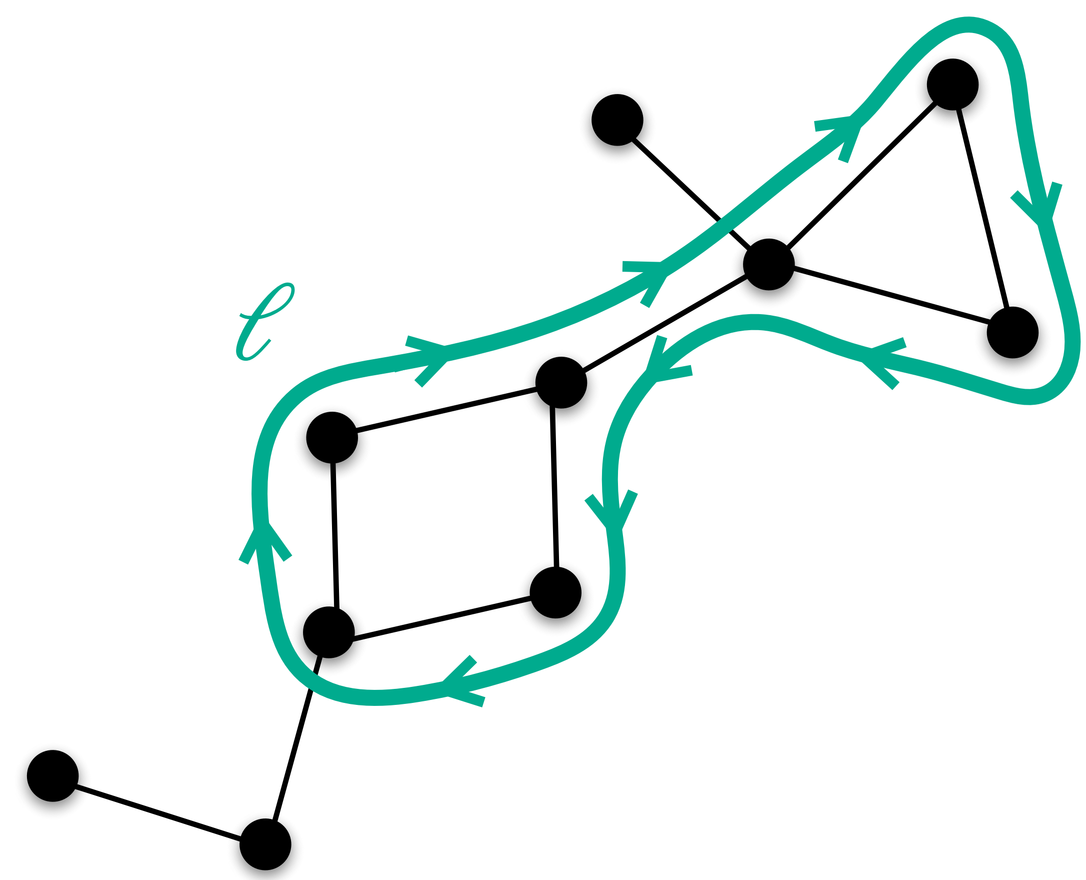


$A_{\alpha} = 0 \quad \forall \alpha \quad \Longleftrightarrow$ **Conservative affinity (KCL)**

[Schnakenberg]

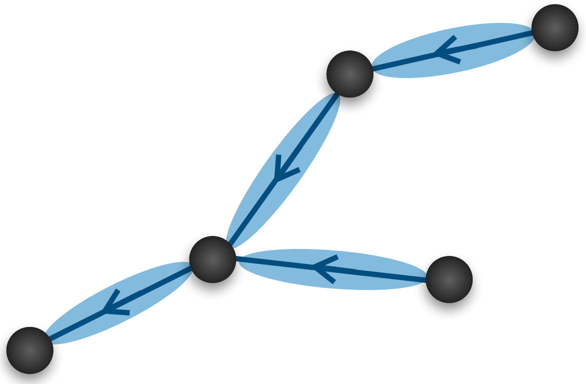
Conservative affinities

The cocycles form a basis for the conservative affinities

In the case of conservative dynamics:

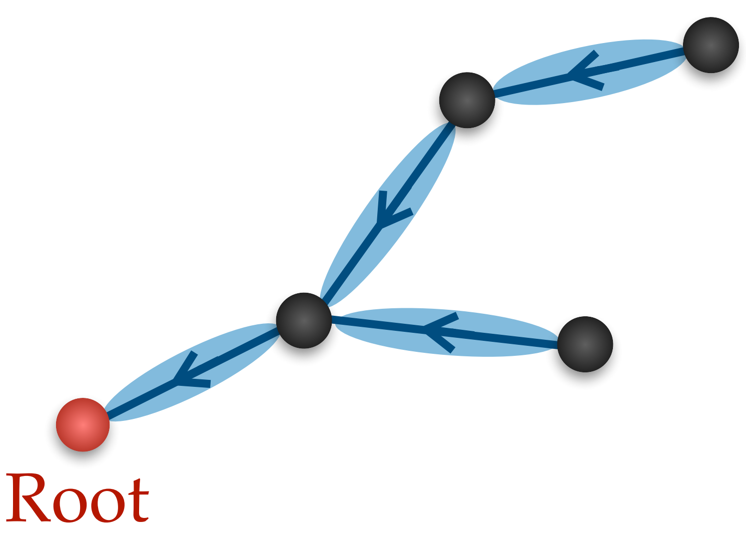
$$|A\rangle = \sum_\gamma A_\gamma |c^\gamma\rangle$$

Affinities of the reactions which form the spanning tree



[Polettini (2015)]

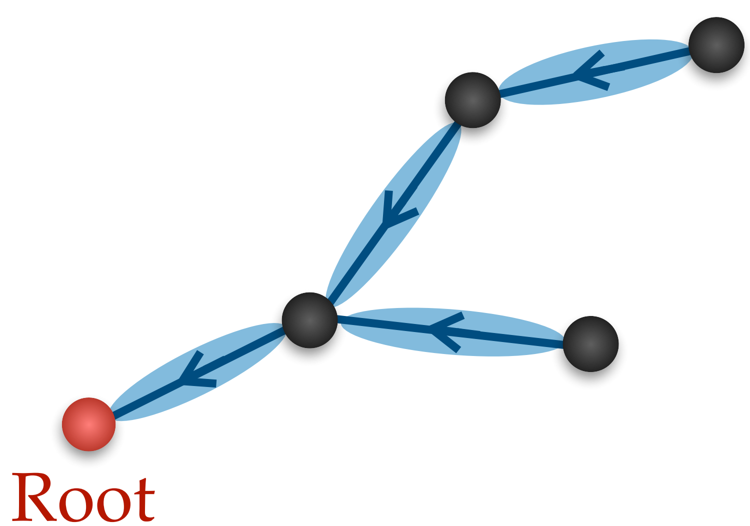
Conservative affinities



Integrating on the spanning tree:

$$G^{\top} = \begin{pmatrix} 1 & 0 & 0 & 0 & 0 \\ 1 & 1 & 0 & 0 & 0 \\ 1 & 1 & 1 & 0 & 0 \\ 1 & 1 & 1 & 1 & 0 \\ 1 & 1 & 0 & 0 & 1 \end{pmatrix}$$

Conservative affinities



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…Underlying potential landscape?

$$\sum_{[i\to \text{root}]} A_\gamma = \mu_i$$

Chemical potential

$$\sum_{[i\to \text{root}]} \log\left(\frac{k_\gamma^-}{k_\gamma^+}\right) = \mu_i^{\circ}$$

Standard chemical potential

A physical decomposition

From graph theory:

- A criterion for the affinity to be conservative
- A basis for the conservative affinities

A physical decomposition

From graph theory:

- A criterion for the affinity to be conservative
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$\{A_\gamma\}$ Complete set of conservative affinities

$\{A_\alpha\}$ Complete set of non-conservative affinities

Interacting CRNs

Example

$$2X_1 \rightleftharpoons X_2$$

$$X_2 + 2X_3 \rightleftharpoons 2X_4$$

$$X_4 \rightleftharpoons X_2 + X_5$$

$$X_4 \rightleftharpoons X_1 + X_3$$

Ex. Autocatalytic networks, epidemic dynamics…

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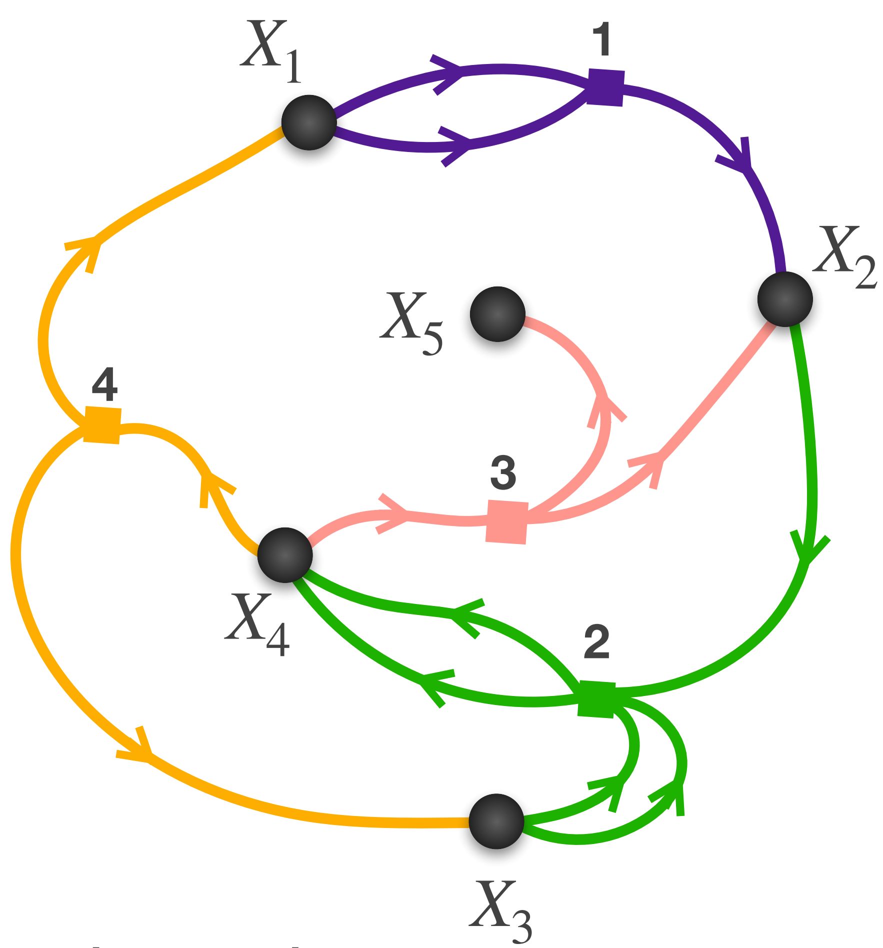
Hypergraph representation:



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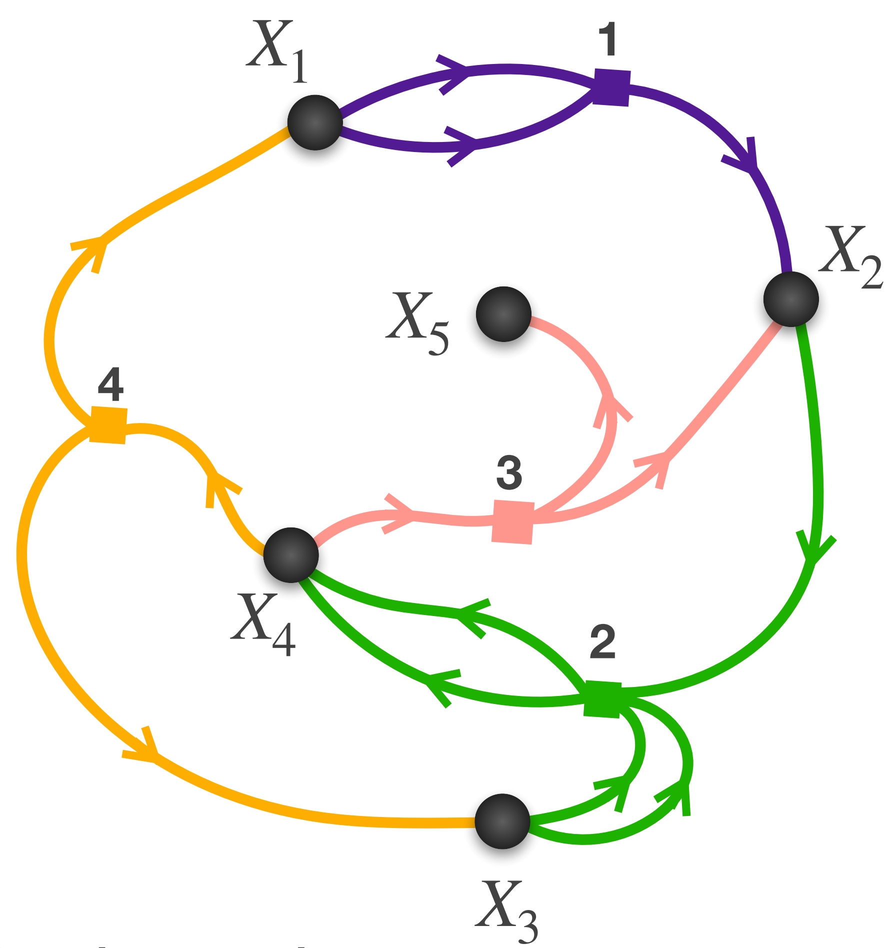


Ex. Autocatalytic networks, epidemic dynamics…

No longer a spanning tree… what about cycles and cocycles?

Gauss-Jordan elimination

Row reduced Echelon form for $\mathbb{S}$:

$$\mathrm{G}\,\mathbb{S} = \begin{pmatrix} \mathbf{1}_M & \mathbb{T} \\ 0 & 0 \end{pmatrix}$$

Algebraic tool

Gauss-Jordan elimination

Row reduced Echelon form for $\mathbb{S}$:

Fractional entries, unique

$$\mathrm{G}\,\mathbb{S} = \begin{pmatrix} \mathbf{1}_M & \mathbb{T} \\ 0 & 0 \end{pmatrix}$$

Algebraic tool

$$\Downarrow$$

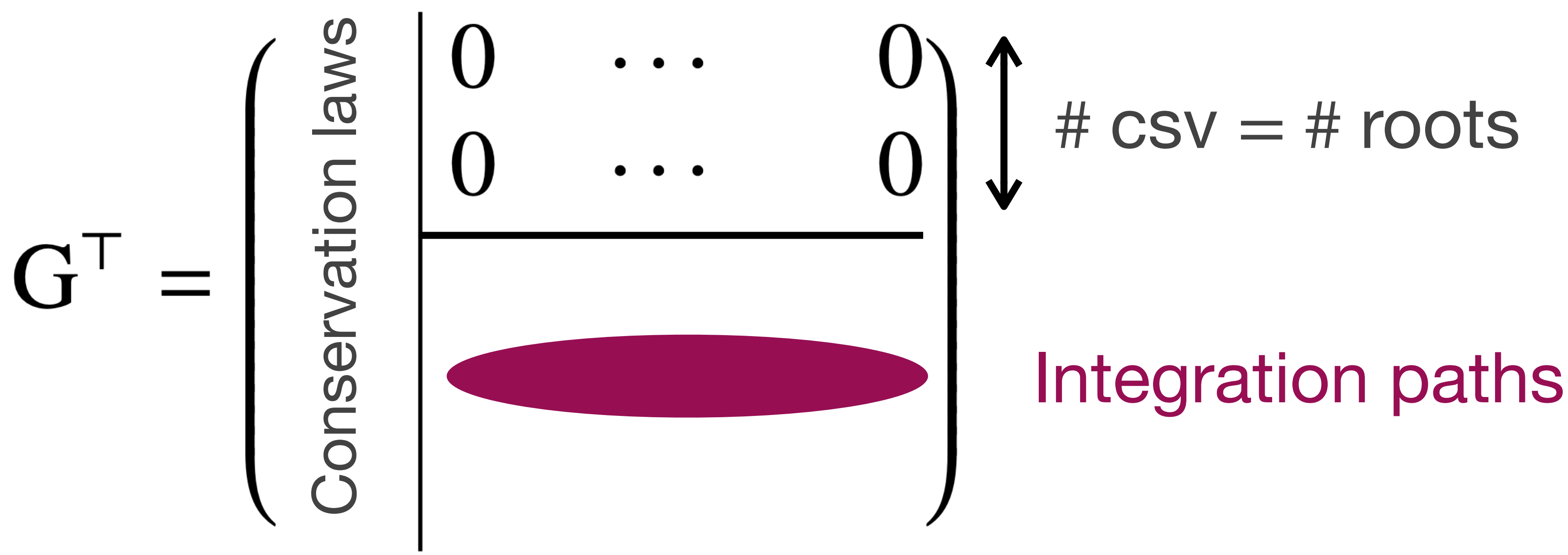
$$\big(\,|\,c^\gamma\rangle, |\,c^\alpha\rangle\big) = \begin{pmatrix} \mathbf{1}_M & -\mathbb{T} \\ \mathbb{T}^\top & \mathbf{1}_{\#\mathrm{cy}} \end{pmatrix}$$

$|\,c^\alpha\rangle$ Still a basis for Ker $\mathbb{S}$

$|\,c^\gamma\rangle$ Still a basis for Im $\mathbb{S}^\top$

Geometry of hypergraphs

Integrator operator on the hypergraph:



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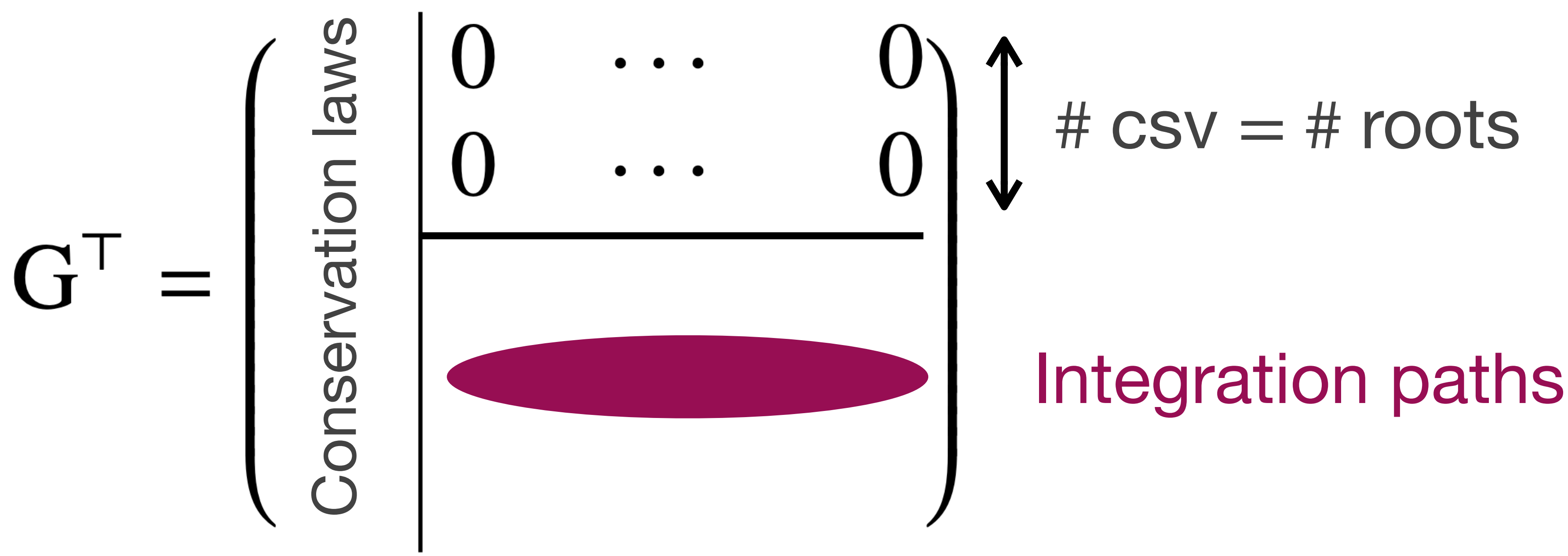
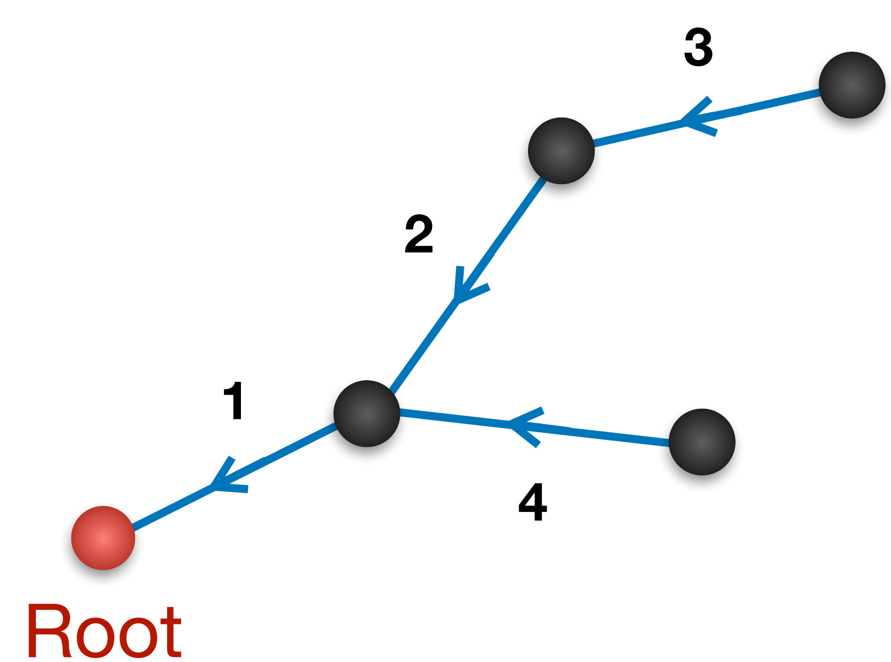


For the simple graph:

$$\begin{array}{l}
G^\top = \left(\begin{array}{c|cccc}
1 & 0 & 0 & 0 & 0 \\ \hline
1 & 1 & 0 & 0 & 0 \\
1 & 1 & 1 & 0 & 0 \\
1 & 1 & 1 & 1 & 0 \\
1 & 1 & 0 & 0 & 1
\end{array}\right)
\end{array}
\begin{array}{l} \text{1 root} \\ \\ \\ \\ \\ \end{array}$$

Mass conservation law



Geometry of hypergraphs

Integrator operator on the hypergraph:

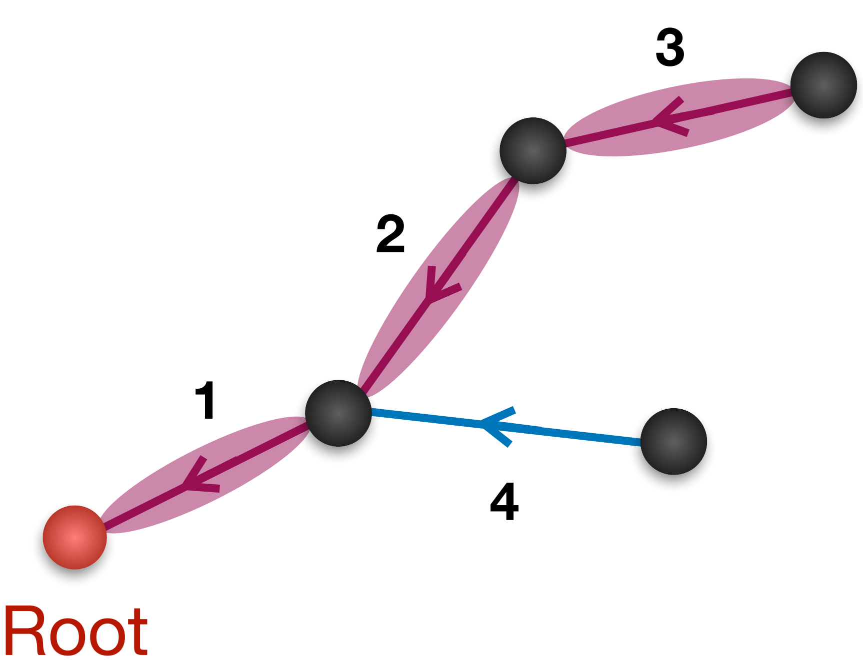
$$G^\top = \left(\begin{array}{c|ccc} & 0 & \cdots & 0 \\ \text{Conservation laws} & 0 & \cdots & 0 \\ \hline & & & \\ & & & \end{array}\right)$$

csv = # roots

Integration paths

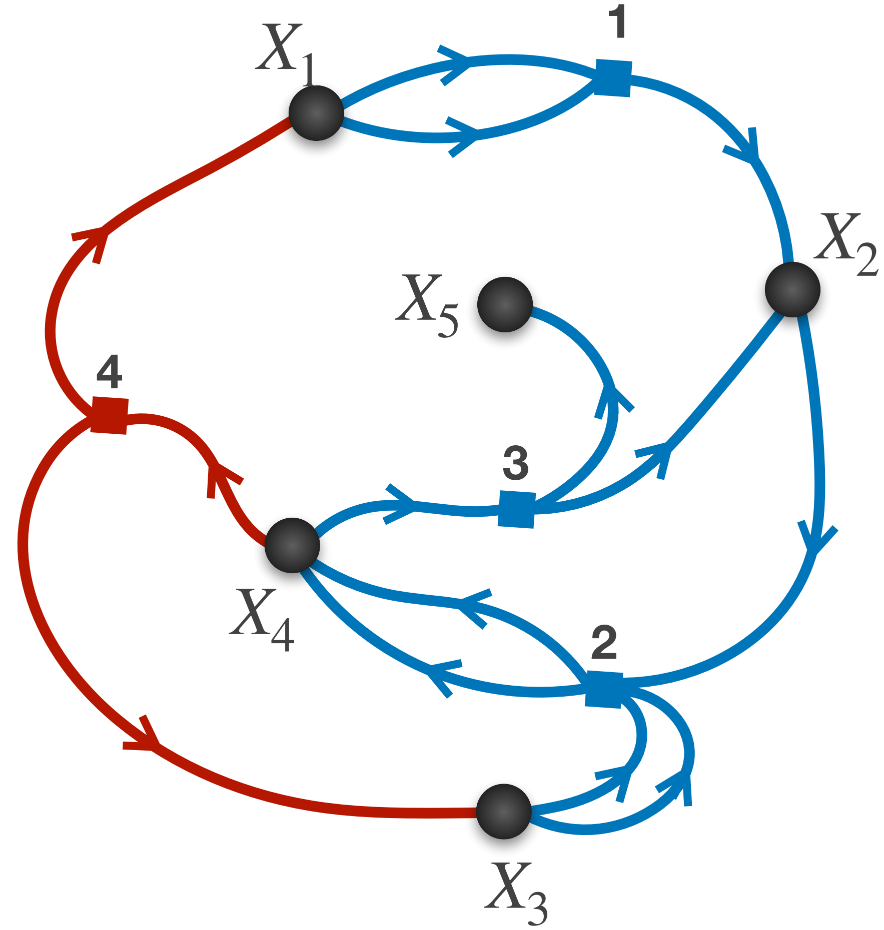
For the simple graph:

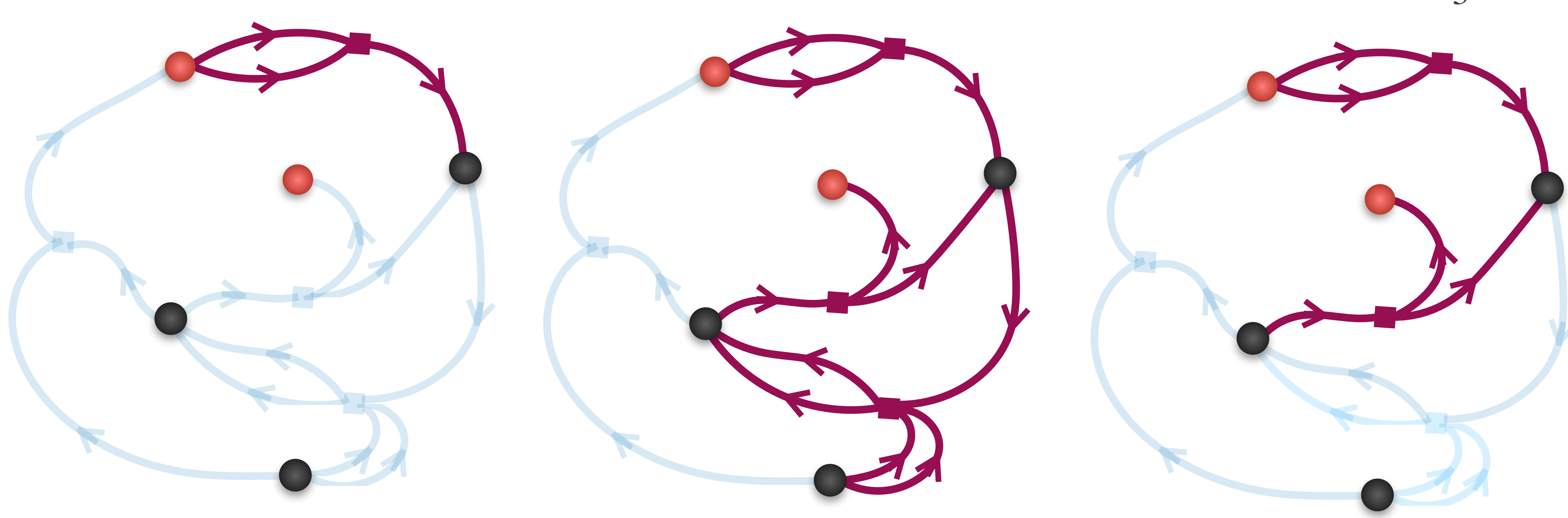
$$G^\top = \left(\begin{array}{c|cccc} 1 & 0 & 0 & 0 & 0 \\ \hline 1 & 1 & 0 & 0 & 0 \\ 1 & 1 & 1 & 0 & 0 \\ 1 & 1 & 1 & 1 & 0 \\ 1 & 1 & 0 & 0 & 1 \end{array}\right) \quad \gamma = 3$$



Geometry of hypergraphs

$$G^\top = \begin{pmatrix} 1 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 \\ 2 & 0 & 1 & 0 & 0 \\ 1 & 1 & 1/2 & -1/2 & -1 \\ 2 & 1 & 1 & 0 & -1 \end{pmatrix}$$





Onsager reciprocities

Natural framework to identify Onsager cross-couplings in linear response

Onsager reciprocities

Natural framework to identify Onsager cross-couplings in linear response

→ **Transient response in reversible dynamics:**

$$J_\gamma \equiv \langle c^\gamma | J \rangle = \langle c^\gamma | \Lambda | A \rangle = \langle c^\gamma | \Lambda | c^{\gamma'} \rangle \, A_{\gamma'}$$

Onsager reciprocities

Natural framework to identify Onsager cross-couplings in linear response

→ **Transient response in reversible dynamics:**

$$J_\gamma \equiv \langle c^\gamma | J \rangle = \langle c^\gamma | \Lambda | A \rangle = \underbrace{\langle c^\gamma | \Lambda | c^{\gamma'} \rangle}_{\text{Response matrix of relaxation}} A_{\gamma'}$$

M transient currents

M conservative affinities

Onsager reciprocities

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$$J_\gamma \equiv \langle c^\gamma | J \rangle = \langle c^\gamma | \Lambda | A \rangle = \langle c^\gamma | \Lambda | c^{\gamma'} \rangle \, A_{\gamma'}$$

→ **Steady-state response due to external drive (chemostatting)**

$$A_\alpha \equiv \langle c^\alpha | A \rangle = \langle c^\alpha | \Lambda^{-1} | J \rangle = \langle c^\alpha | \Lambda^{-1} | c^{\alpha'} \rangle J_{\alpha'}$$

Onsager reciprocities

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Non-conservative forces

Steady-state currents

Onsager reciprocities

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How are the two matrices related?

Onsager reciprocities

The two response matrices, after a change of variables:

$$L^{\mathrm{rel}} = \left(\begin{array}{c|c} \mathbf{1}_M + \tilde{\mathbb{T}}\tilde{\mathbb{T}}^\top & (0) \\ \hline (0) & \mathbf{0}_{\#\mathrm{cy}} \end{array}\right) \qquad L^{\mathrm{ext}} = \left(\begin{array}{c|c} \mathbf{0}_M & (0) \\ \hline (0) & \mathbf{1}_{\#\mathrm{cy}} + \tilde{\mathbb{T}}^\top\tilde{\mathbb{T}} \end{array}\right)$$

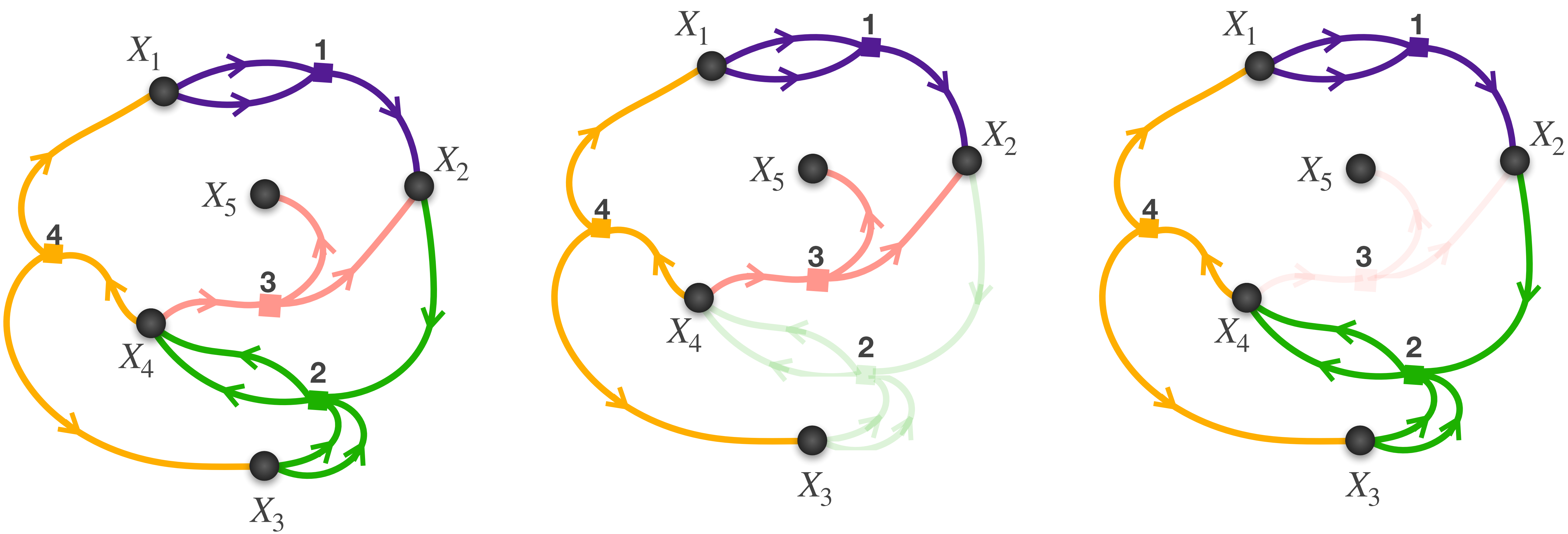
- Spectrum fully controls by the matrix $\mathbb{T}$
- They **share the same spectrum** up to the multiplicity of 0's and 1's eigenvalues
- Spectral Einstein relation

$L^{\mathrm{rel}} \Longleftrightarrow$ Noise matrix

$L^{\mathrm{ext}} \Longleftrightarrow$ Mobility

Beyond linear response

Response of the system to the suppression of a reaction?



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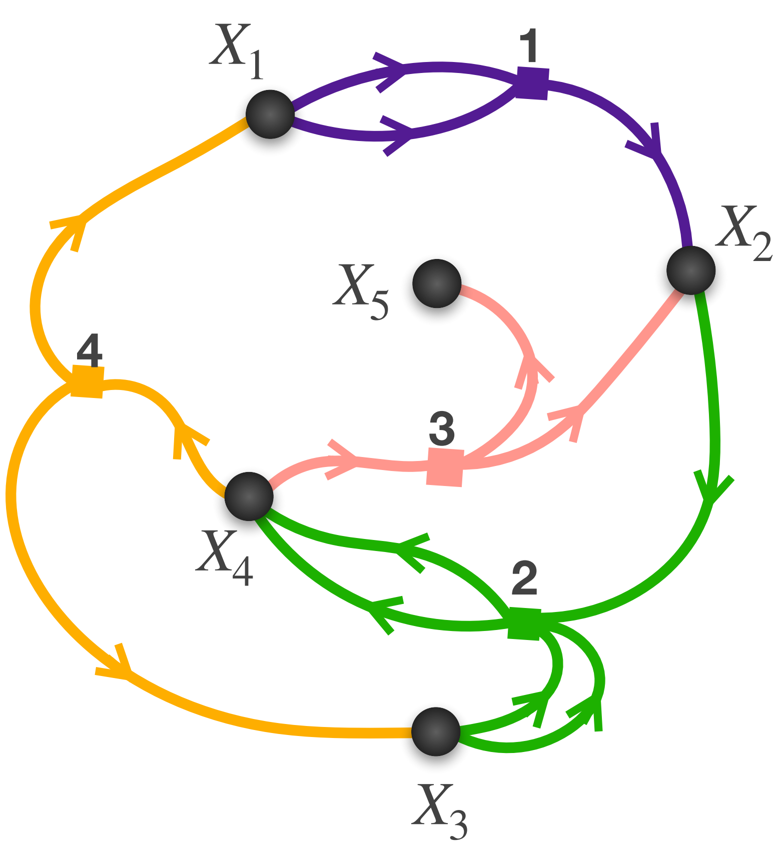
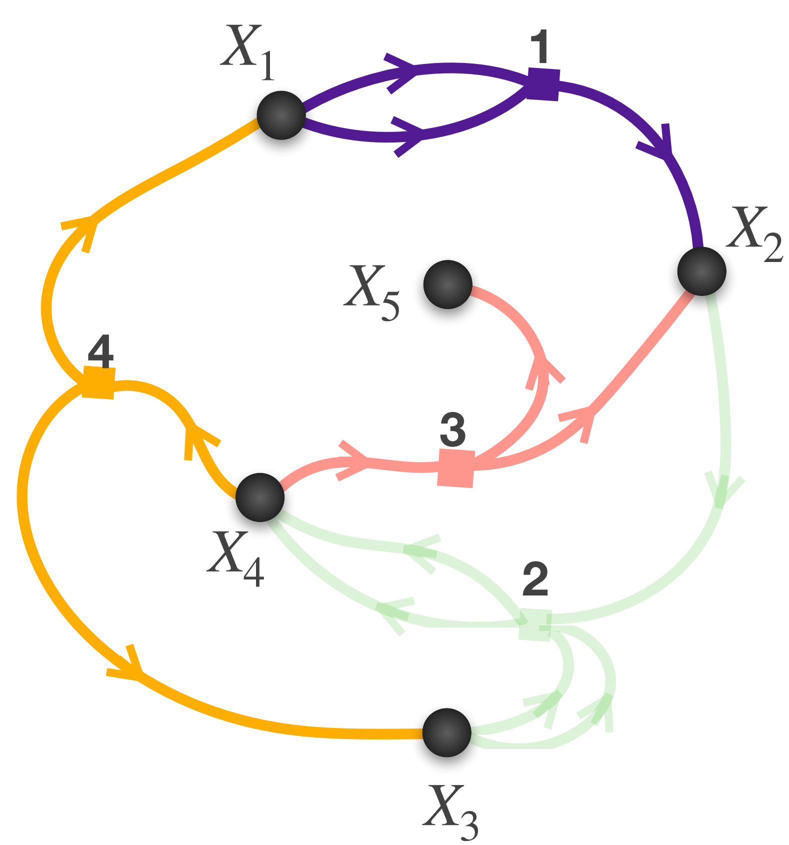
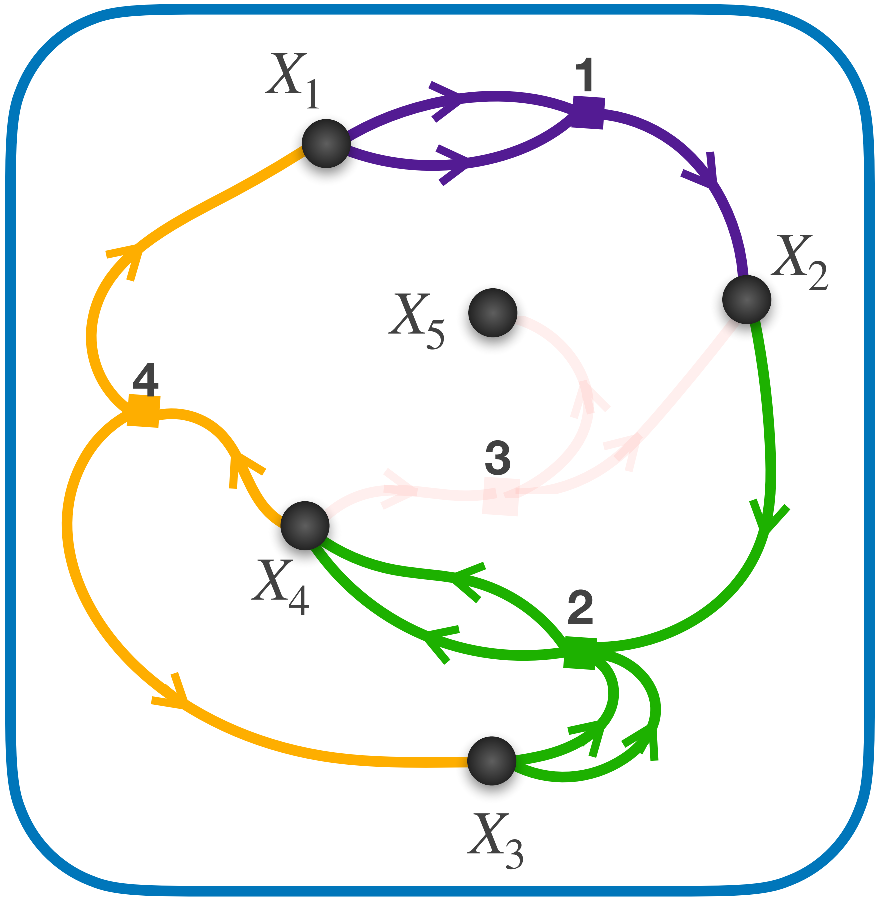


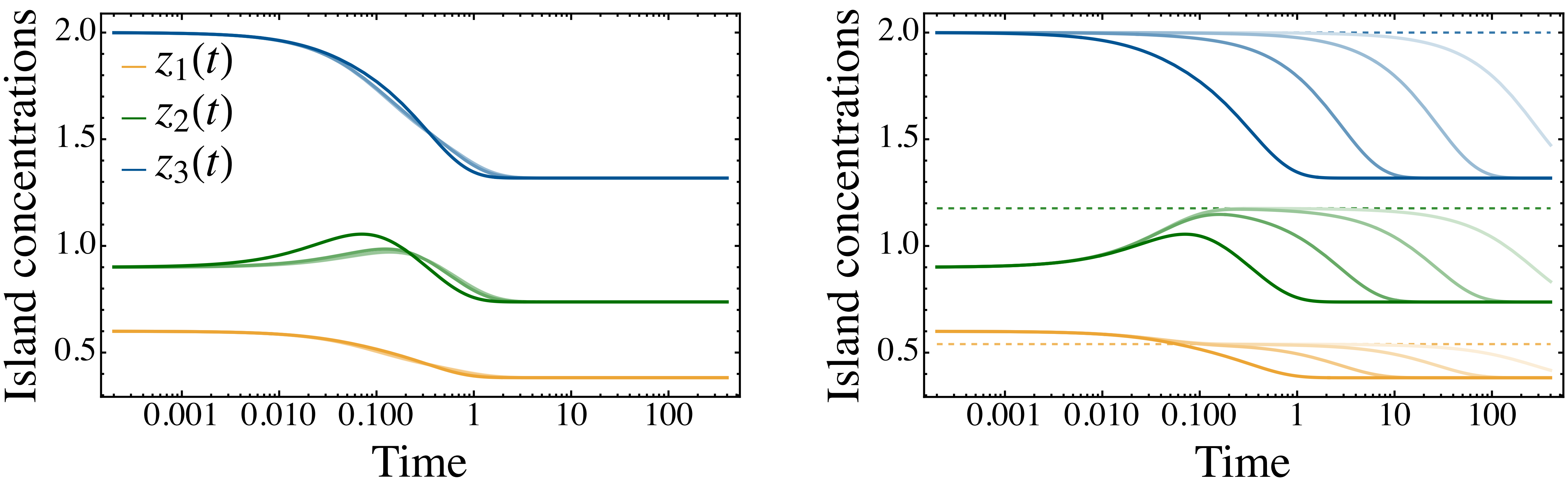




Reaction 3 is a cocycle,
i.e. a mode of relaxation

Beyond linear response

Emergent timescale in the relaxation by suppressing a cocycle



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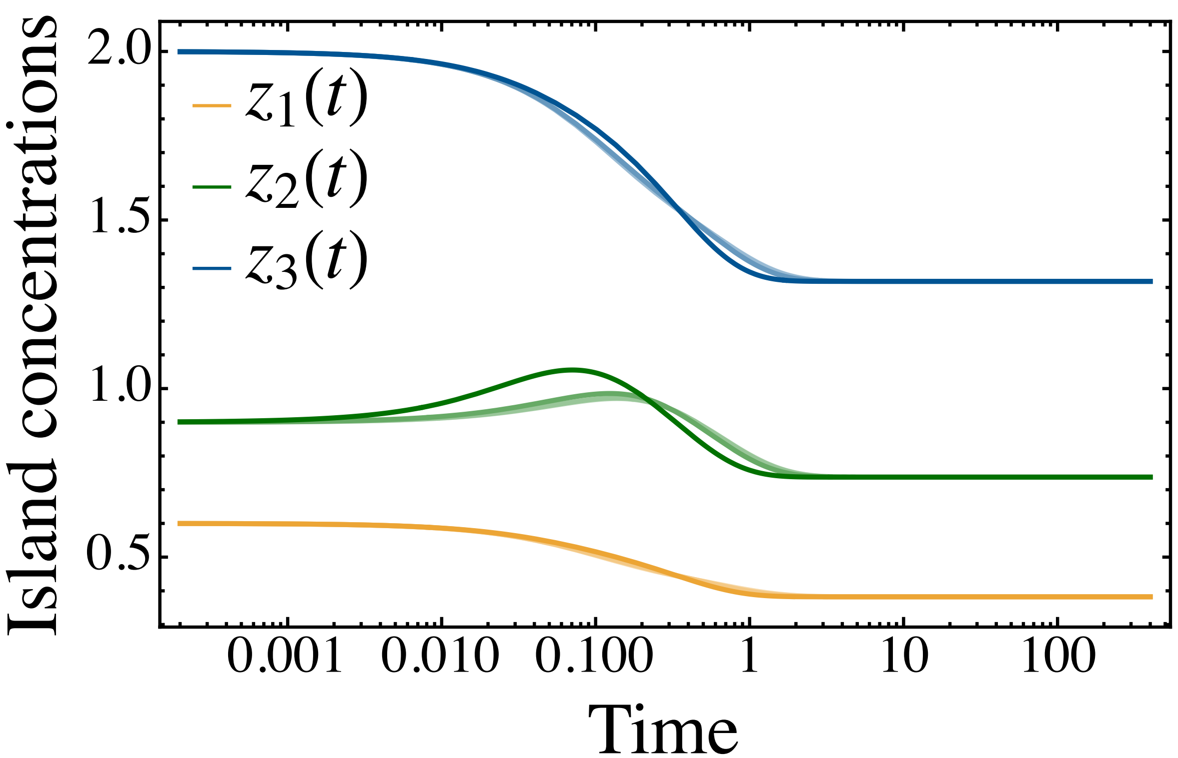
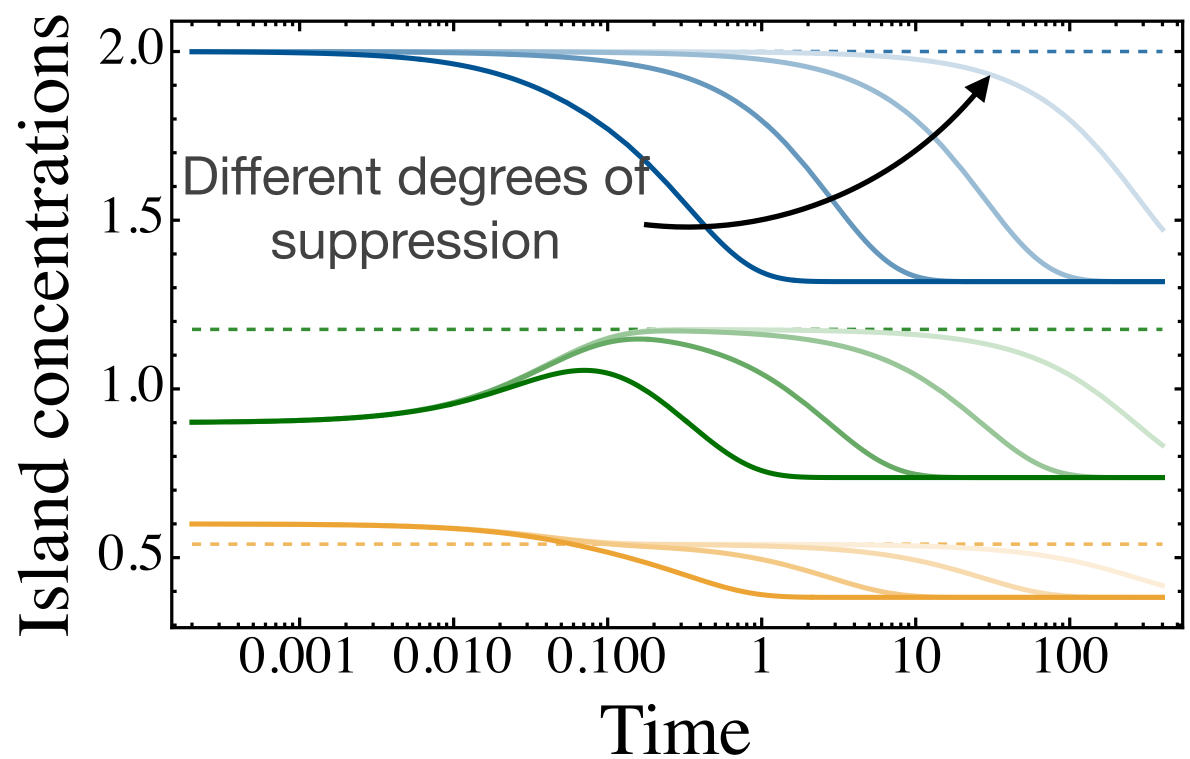
<u>Emergent timescale</u> in the relaxation by suppressing a cocycle





Dynamical control of complex CRNs?

Conclusions

Geometrically-informed decomposition of affinities and currents

Framework describing both relaxation and steady-state

Generalization to interacting CRNs using linear algebra

Application to linear and non-linear response

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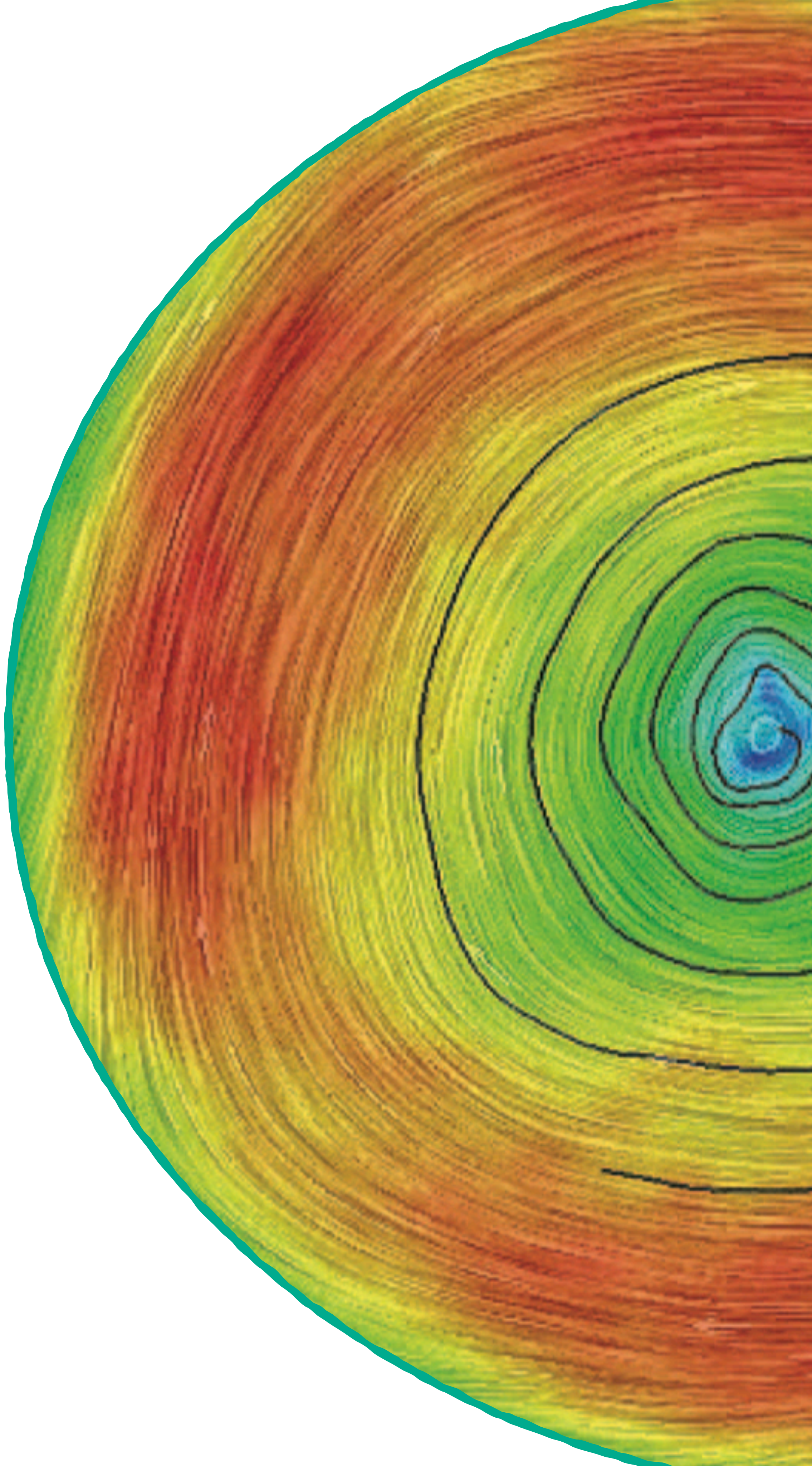
Collaborators: Vivien Lecomte, Matteo Polettini

Thank you!



Algebraic interpretation

Stoichiometric matrix encodes the topology of the network

$$\mathbb{S} = \begin{pmatrix} & & \\ & & \\ & & \end{pmatrix}$$

N species

R reactions

The cocycles are a basis for the coimage of the stoichiometric matrix

$$\mathrm{Im}\, \mathbb{S}^\top$$

The cycles are a basis for the kernel of the stoichiometric matrix

$$\mathrm{Ker}\, \mathbb{S}$$

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$\#\,\text{cocycles} = M = \text{Rank}\,\mathbb{S}$

The cycles are a basis for the kernel of the stoichiometric matrix

$\#\,\text{cycles} = R - M$