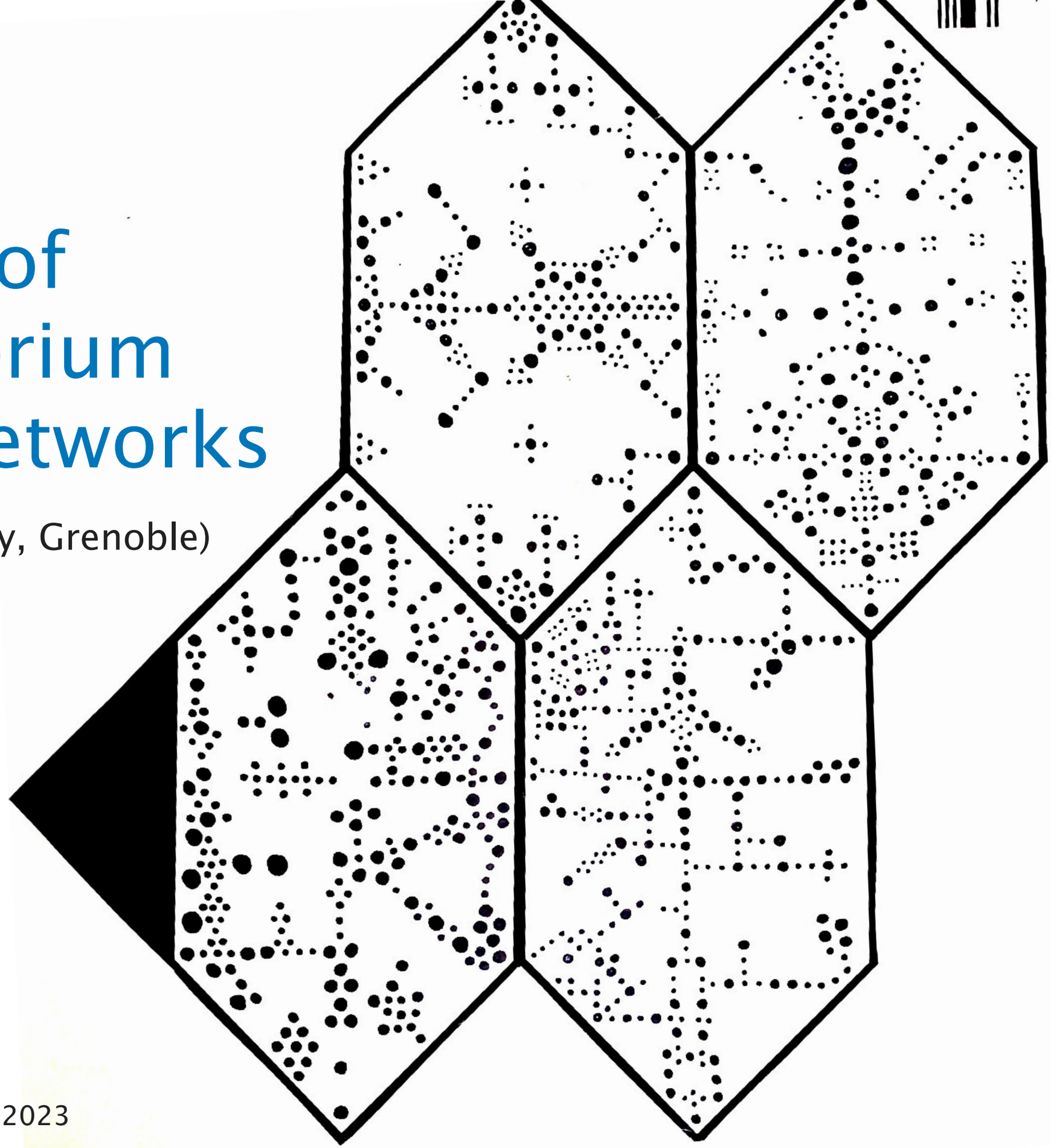
Geometry of nonequilibrium reaction networks

Sara Dal Cengio (LIPhy, Grenoble)

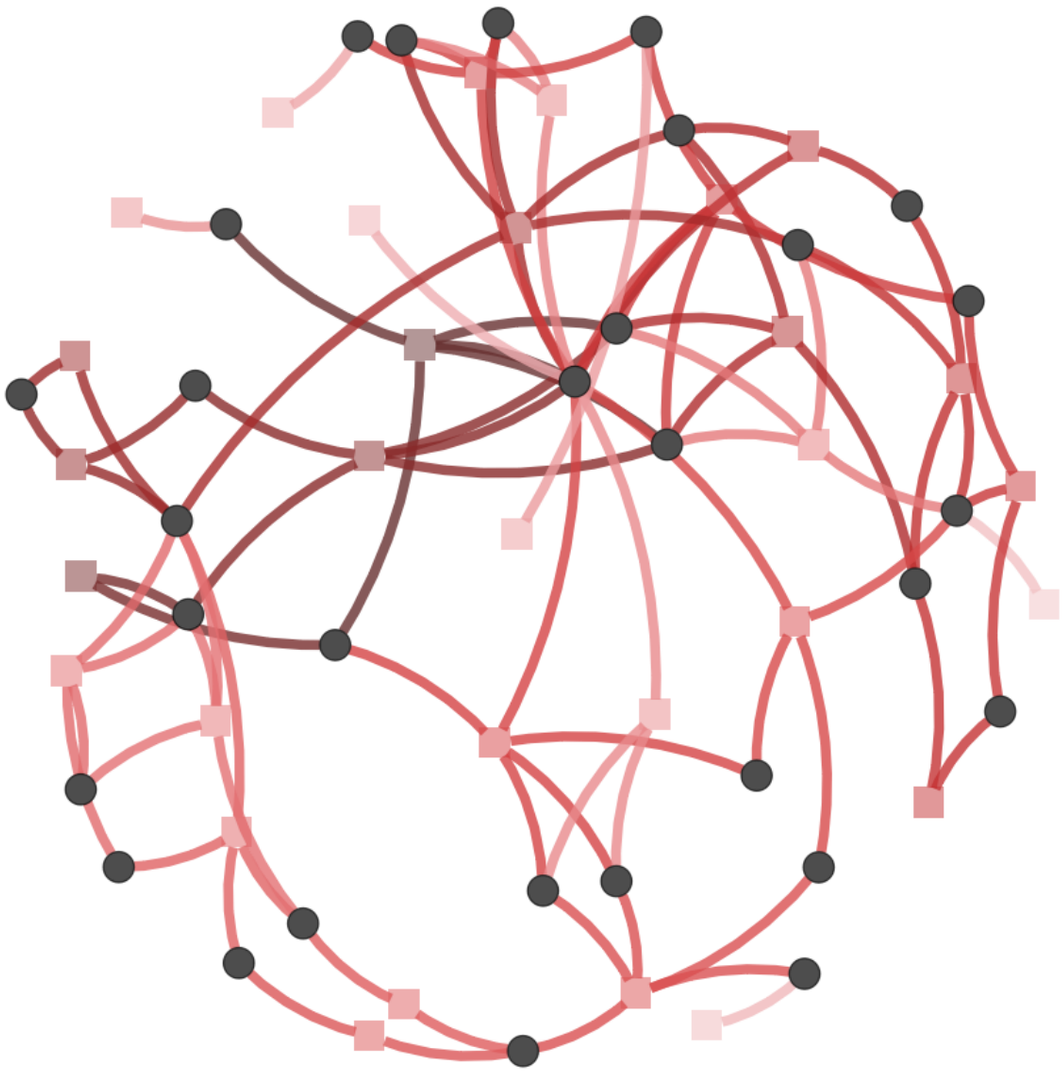


Cologne, summer solstice 2023

Questions

● = species

■ = reaction



red blood cell

reaction network

Questions

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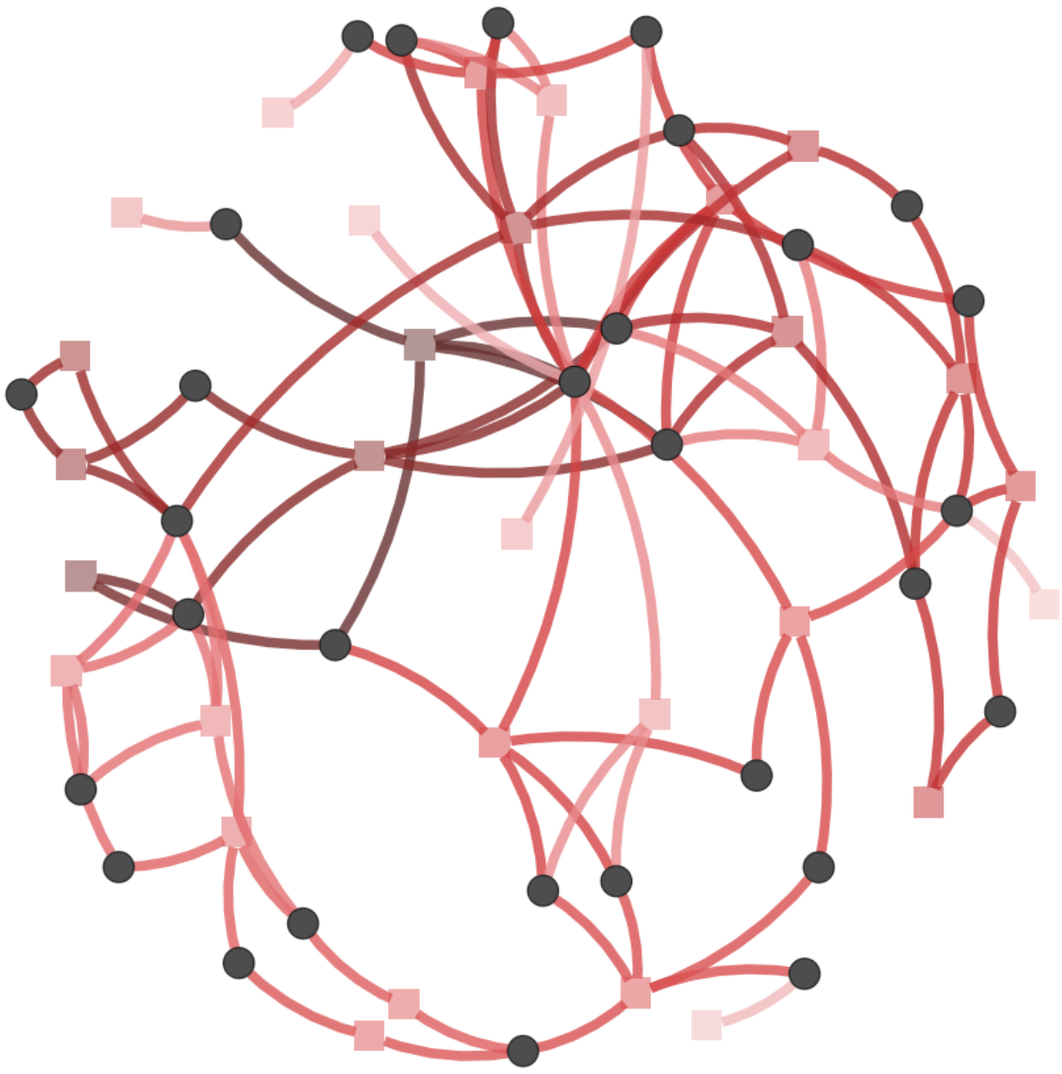
■ = reaction



red blood cell

reaction network

✳ How to characterize the nonequilibrium drive and dynamics?

✳ How to understand their geometrical features?

Statement of the problem

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

Hill-Schnakenberg approach:
[Schakenberg, Rev mod Phys 1976]

- Microscopic description (**population** level)
- Based on tools from **graph theory**
- Role of **cycles** for nonequilibrium steady state

Statement of the problem

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

But:

- Graph at the population level is impractical.
  - **Macroscopic** description?
- Steady-state picture only.
  - What about the **transient**?

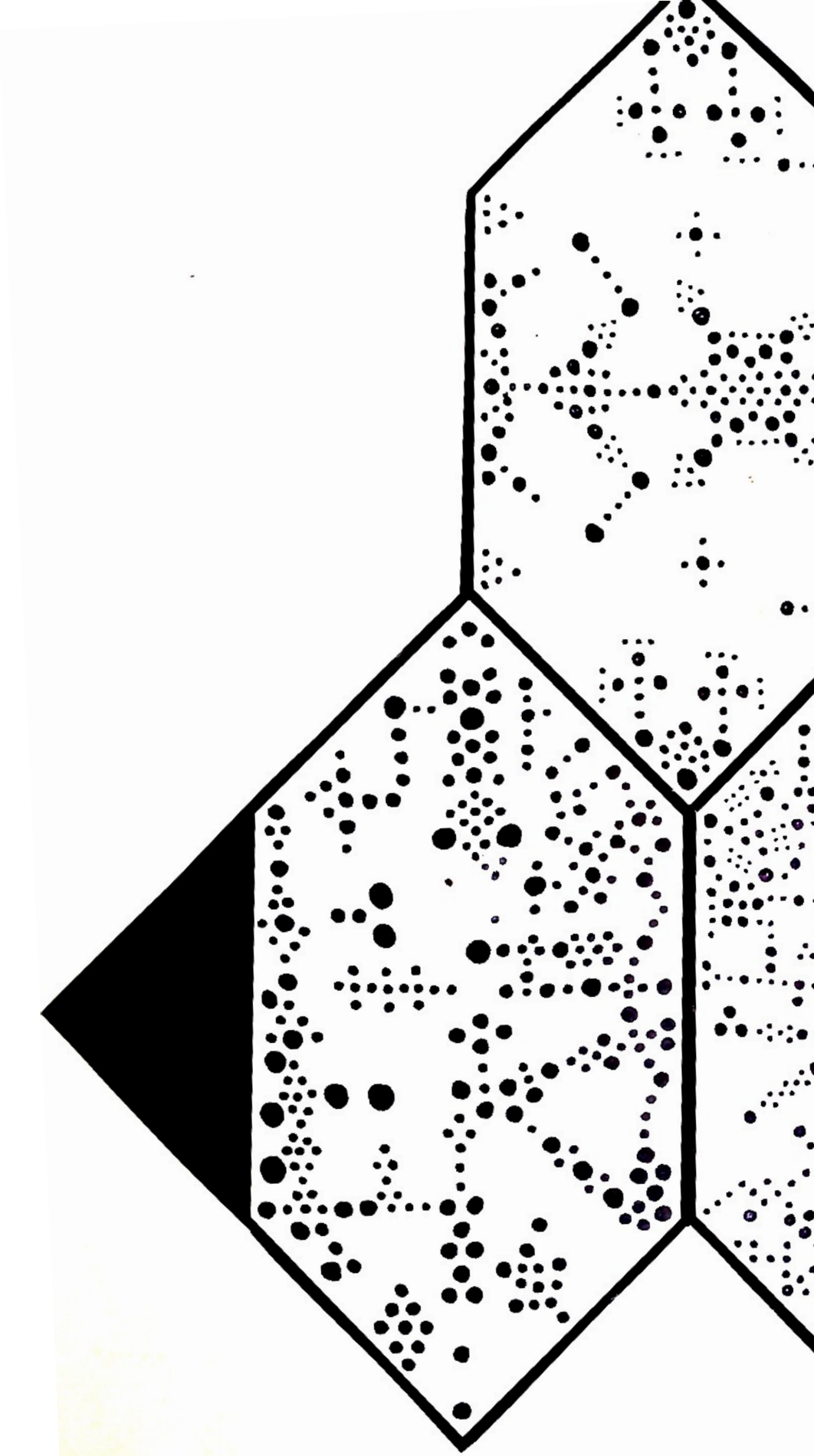
Outline

- Introduction

- **Non-interacting** networks
  - Graph theory
  - Geometry and algebra

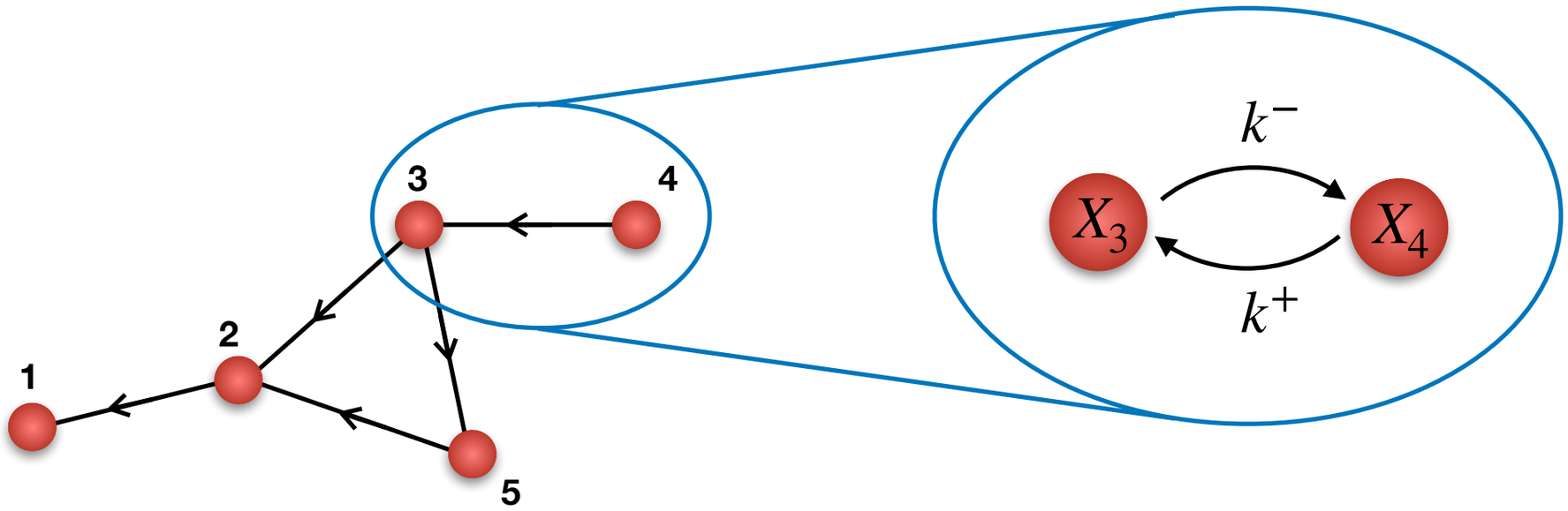
- **Interacting** networks
  - Algebra
  - Geometry

- Application
  - Metabolic reconstruction



Noninteracting networks: graph representation

Unimolecular reactions: $X_i \rightleftharpoons X_j$ (E.g. Markov chains)



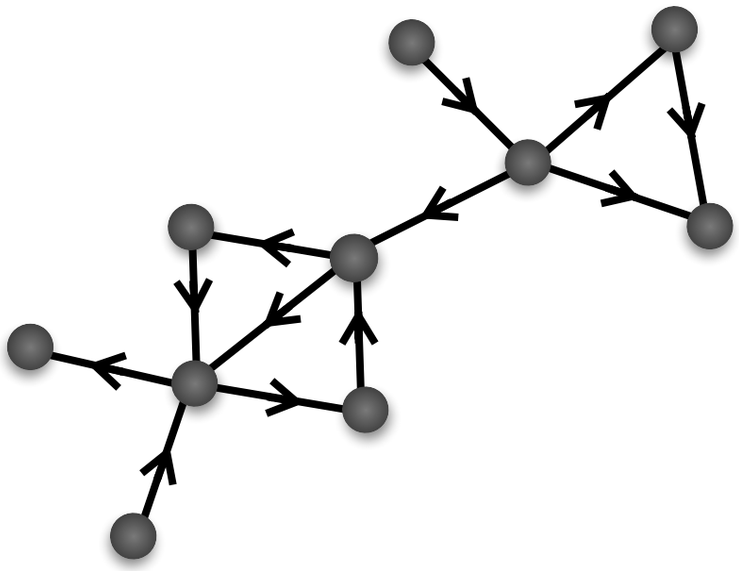
Oriented **graph** representation:

N nodes/species

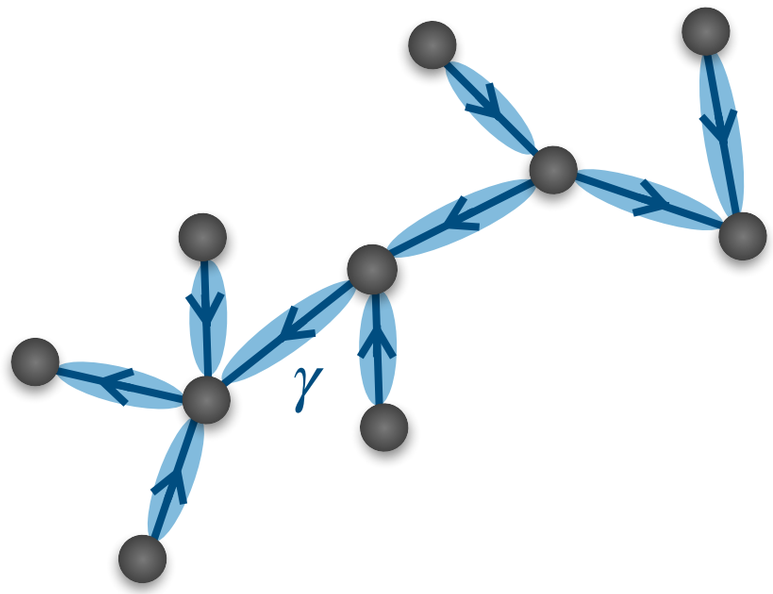
R edges/reactions

Elements of graph theory

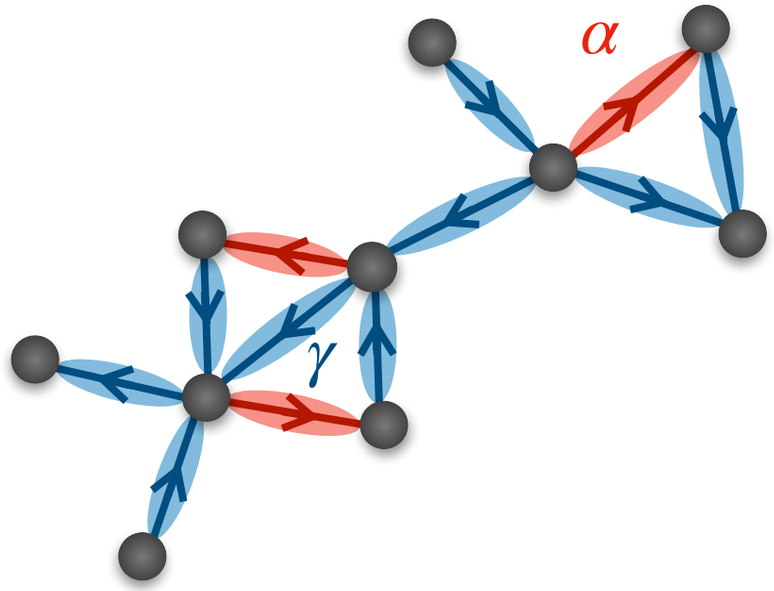
Oriented graph



Spanning tree



Chords & cochords



Connected graph: N nodes/species, R edges/reactions

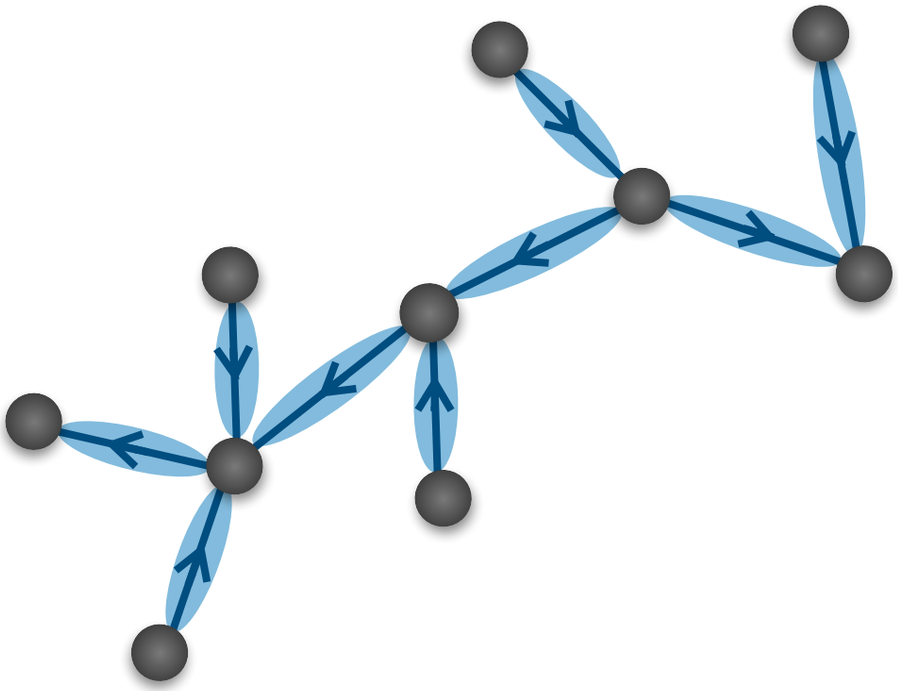
Spanning tree: $M = N - 1$ independent reactions

Cochords: reactions that belong to the tree, indexed by γ

Chords: reactions that do **not** belong to the tree, indexed by α

Elements of graph theory

Adding a **chord** back to the spanning tree…



Elements of graph theory

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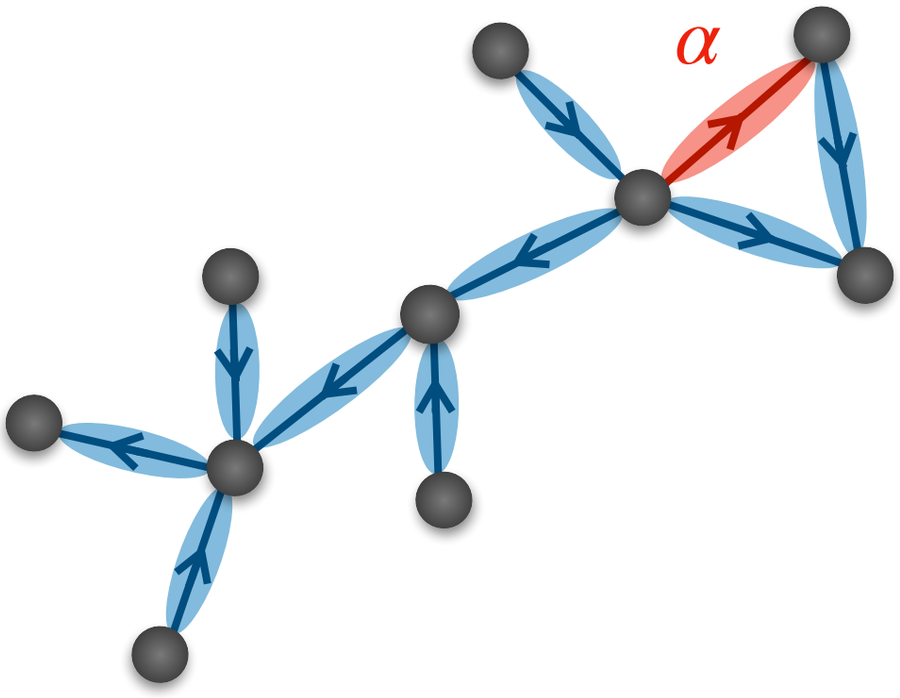

Elements of graph theory

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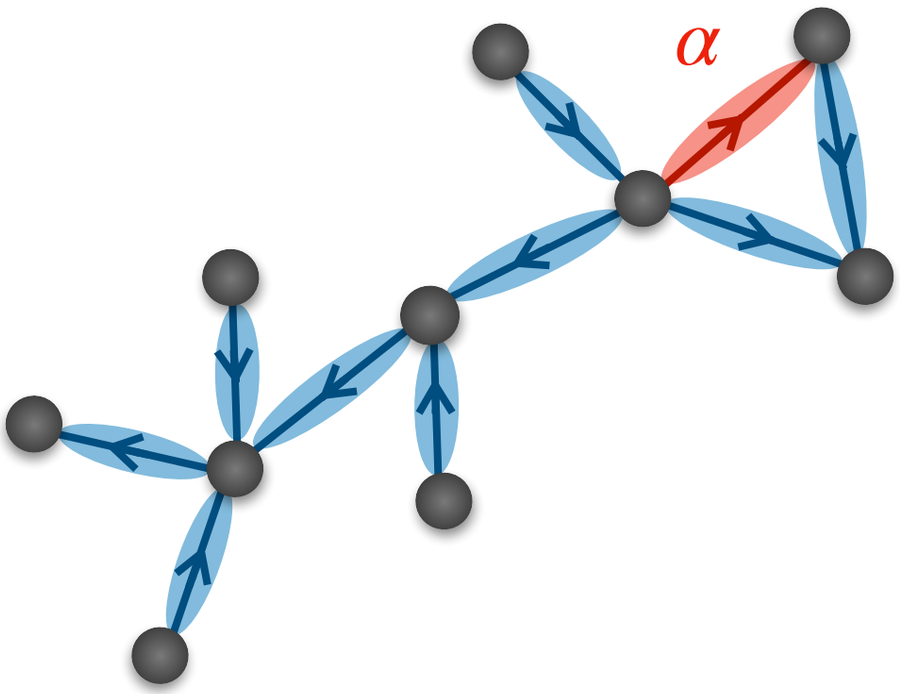
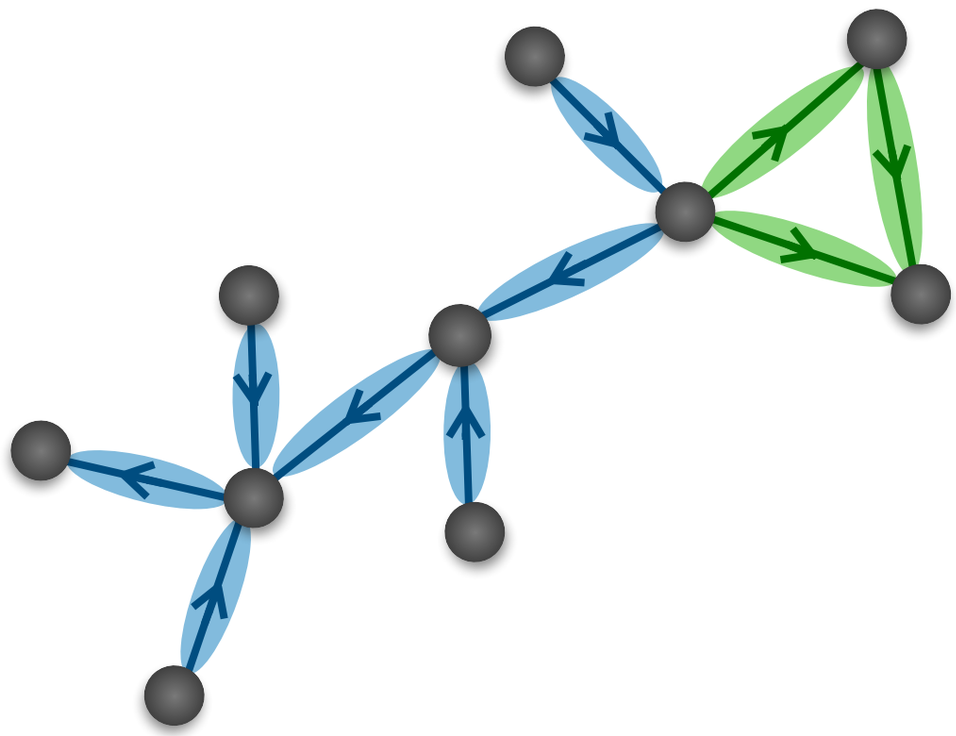
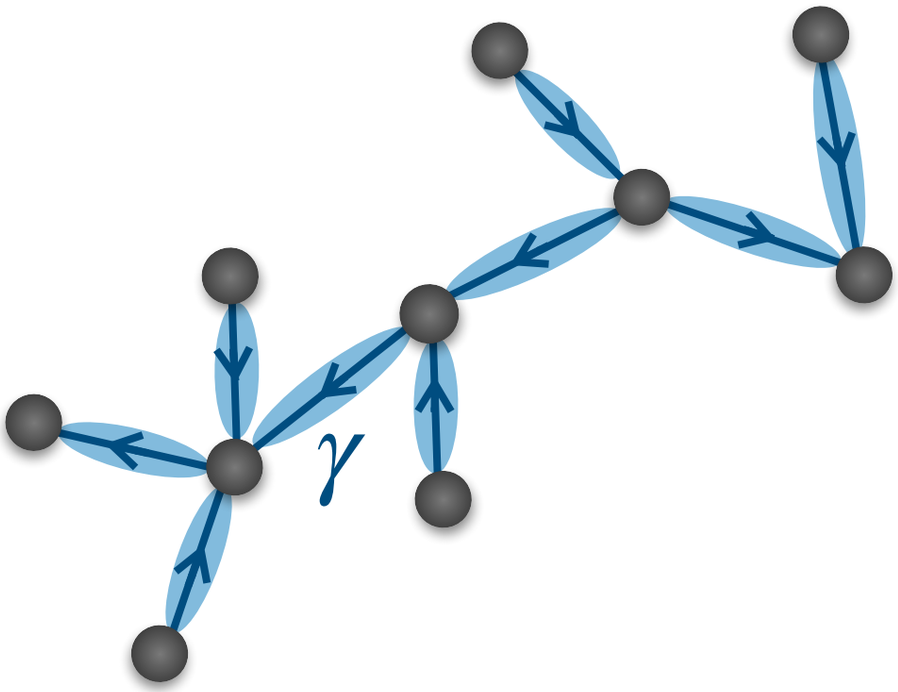




Cycle: applying its reactions leaves the system unchanged, indexed by α

Elements of graph theory

Removing a **cochord** from the spanning tree…



Elements of graph theory

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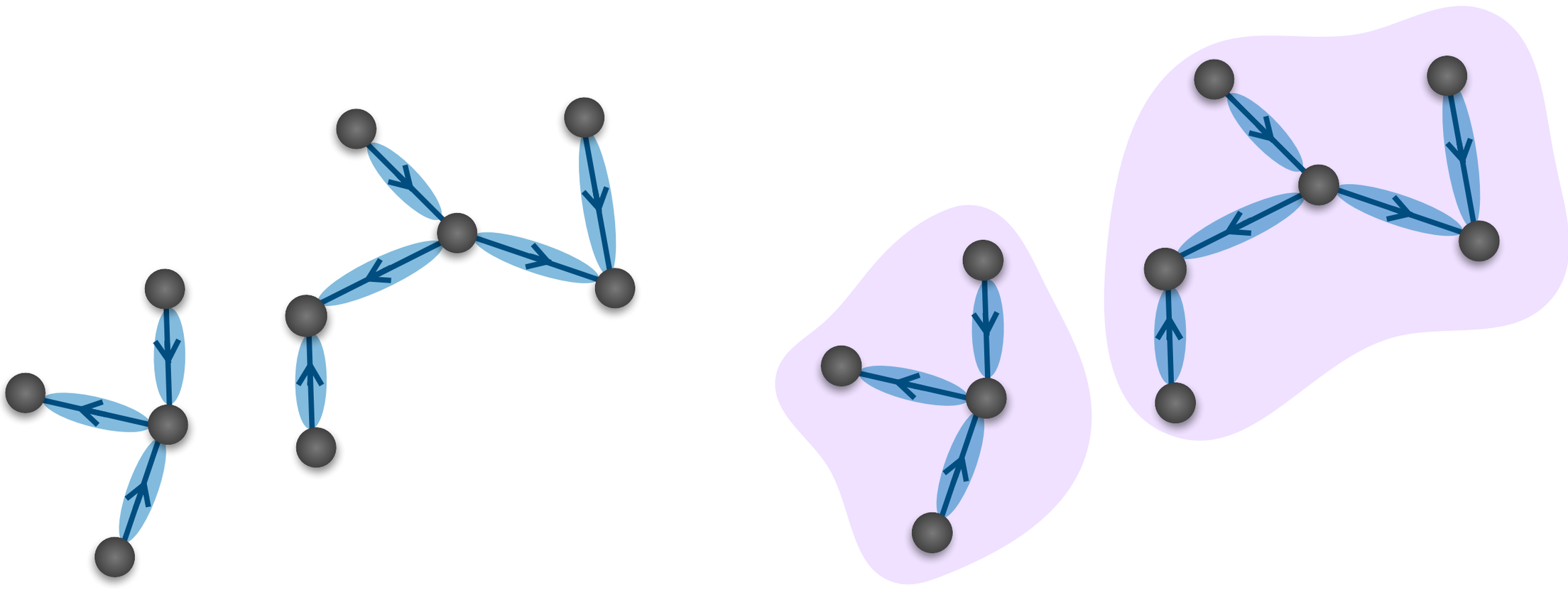
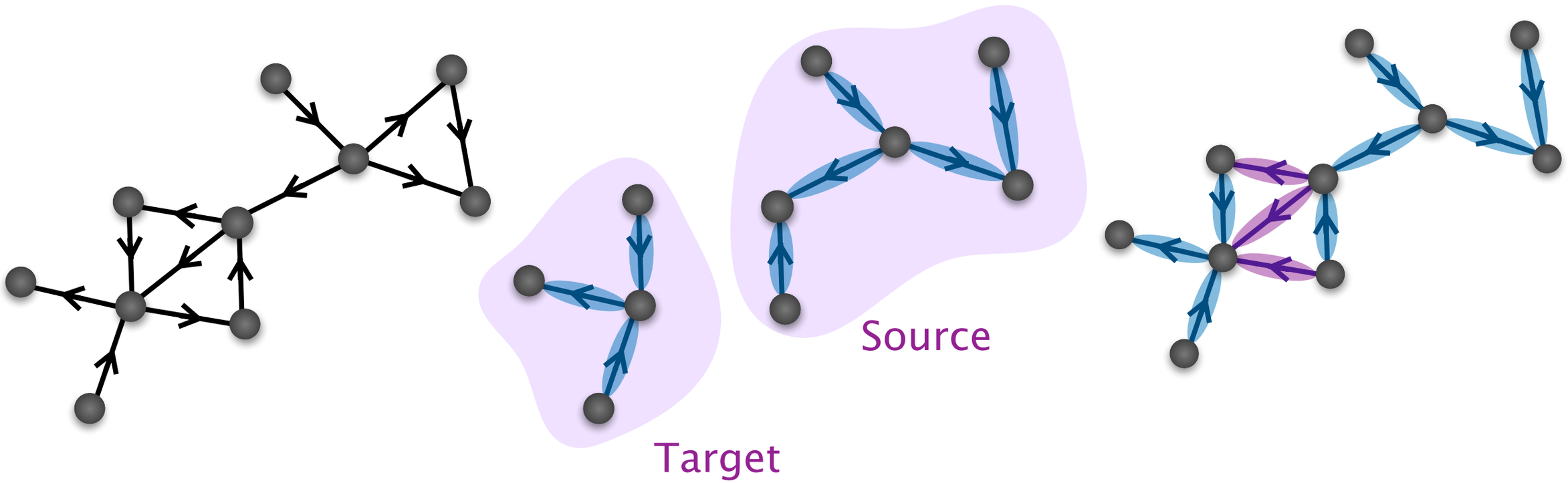


The tree is split in two **islands**

Elements from graph theory

Removing a **cochord** from the spanning tree…



Cocycle: all edges connecting the two islands, indexed by γ

Algebraic tools

Average behavior: concentration $x_i \equiv \lim_{n,\Omega\to\infty} \frac{n_i}{\Omega}$

Rate equation: $\boxed{\partial_t \boldsymbol{x}(t) = \mathbb{S}\,\boldsymbol{J}(\boldsymbol{x})}$

Stoichiometric matrix $\mathbb{S}$ $(N \times R)$ encodes the **topology**

Algebraic tools

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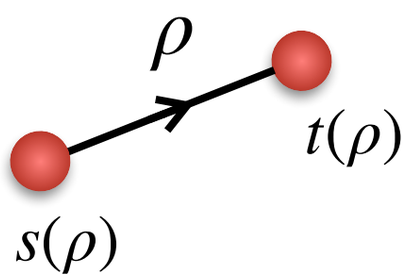
Rate equation: $\boxed{\partial_t \boldsymbol{x}(t) = \mathbb{S}\,\boldsymbol{J}(\boldsymbol{x})}$

Stoichiometric matrix $\mathbb{S}$ $(N \times R)$ encodes the **topology**

Unimolecular reaction ρ:

$$X_{s(\rho)} \underset{k_\rho^-}{\overset{k_\rho^+}{\rightleftharpoons}} X_{t(\rho)}$$



$$\mathbb{S} = \begin{pmatrix} +1 & 0 & 0 & 0 & 0 \\ -1 & +1 & 0 & +1 & 0 \\ 0 & -1 & +1 & 0 & -1 \\ 0 & 0 & -1 & 0 & 0 \\ 0 & 0 & 0 & -1 & +1 \end{pmatrix}$$

$\mathbb{S}$: discrete divergence

$\mathbb{S}^\top$: discrete gradient

Algebraic tools

Average behavior: concentration $x_i \equiv \lim_{n,\Omega\to\infty} \frac{n_i}{\Omega}$

Rate equation: $\boxed{\partial_t \boldsymbol{x}(t) = \mathbb{S}\,\boldsymbol{J}(\boldsymbol{x})}$

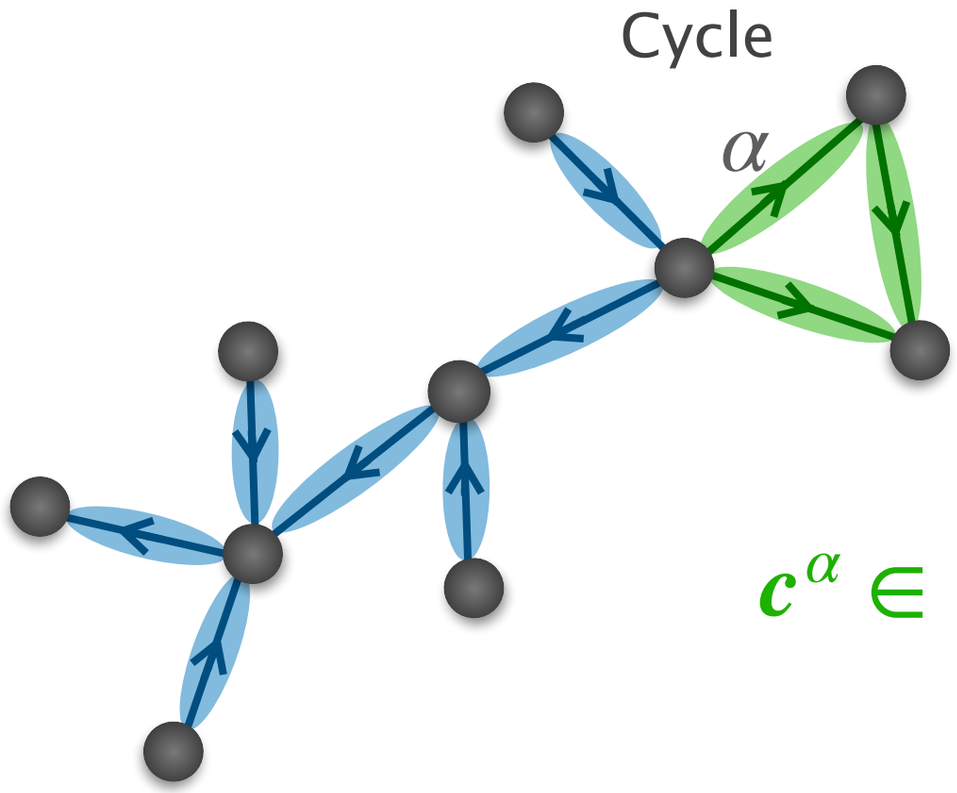
Stoichiometric matrix $\mathbb{S}$ $(N \times R)$ encodes the **topology**

- **Current** of ρ : $J_\rho(\boldsymbol{x}) = k_\rho^+ \boldsymbol{x}^{t(\rho)} - k_\rho^- \boldsymbol{x}^{s(\rho)} = k_\rho^+ \boldsymbol{x}^{s(\rho)} \left[1 - e^{-A_\rho(\boldsymbol{x})}\right]$

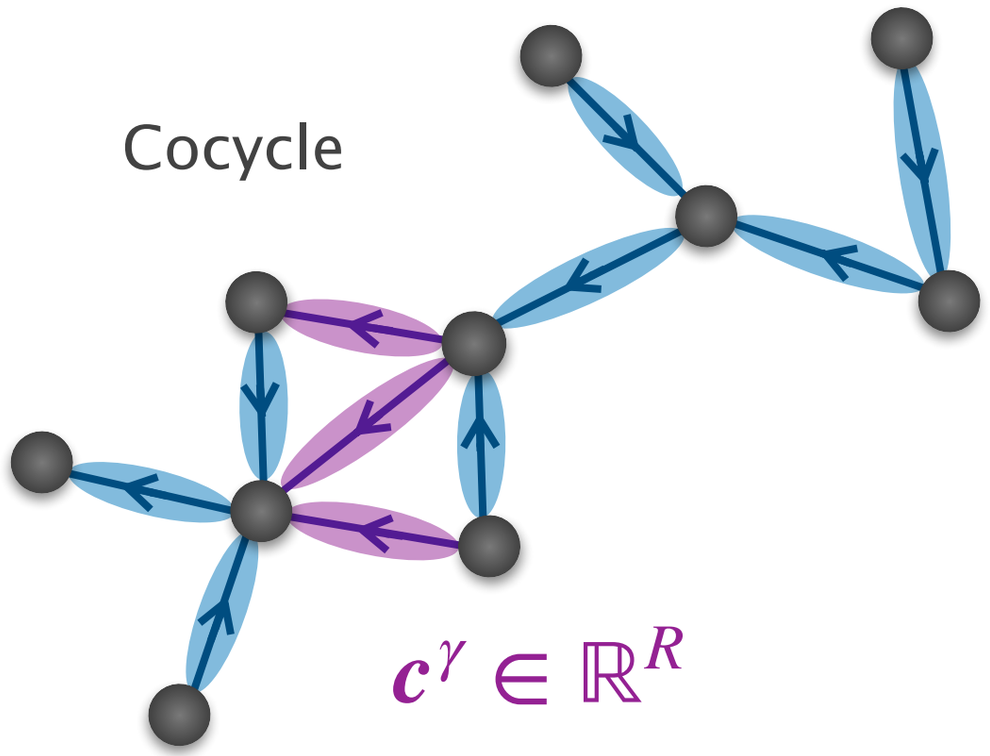
- **Affinity** (or **force**) of ρ : $A_\rho(\boldsymbol{x}) = \log\left(\frac{j_\rho^+(\boldsymbol{x})}{j_\rho^-(\boldsymbol{x})}\right) = \log\left(\frac{k_\rho^+}{k_\rho^-}\boldsymbol{x}^{-\mathbb{S}_\rho}\right)$

Equilibrium steady-state: $A_\rho(x^{\mathrm{eq}}) = 0$, $J_\rho(x^{\mathrm{eq}}) = 0$

Algebraic representation of cycles & cocycles

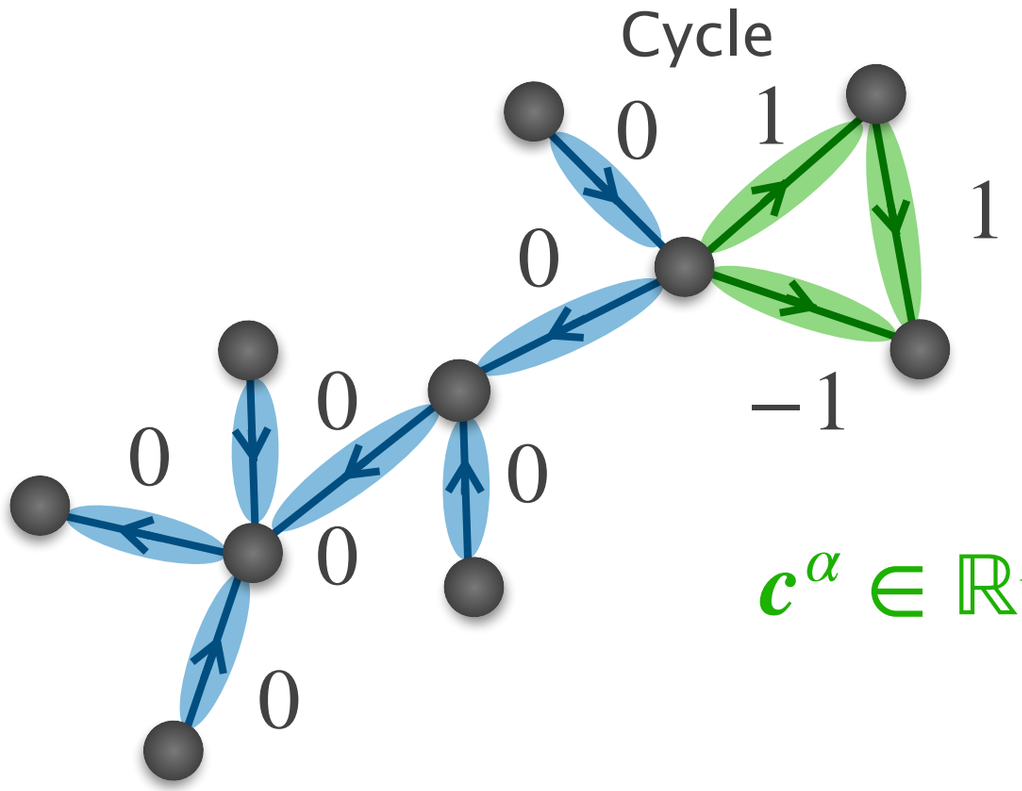


$\boldsymbol{c}^{\alpha} \in \mathbb{R}^{R}$



$\boldsymbol{c}^{\gamma} \in \mathbb{R}^{R}$

Algebraic representation of cycles & cocycles



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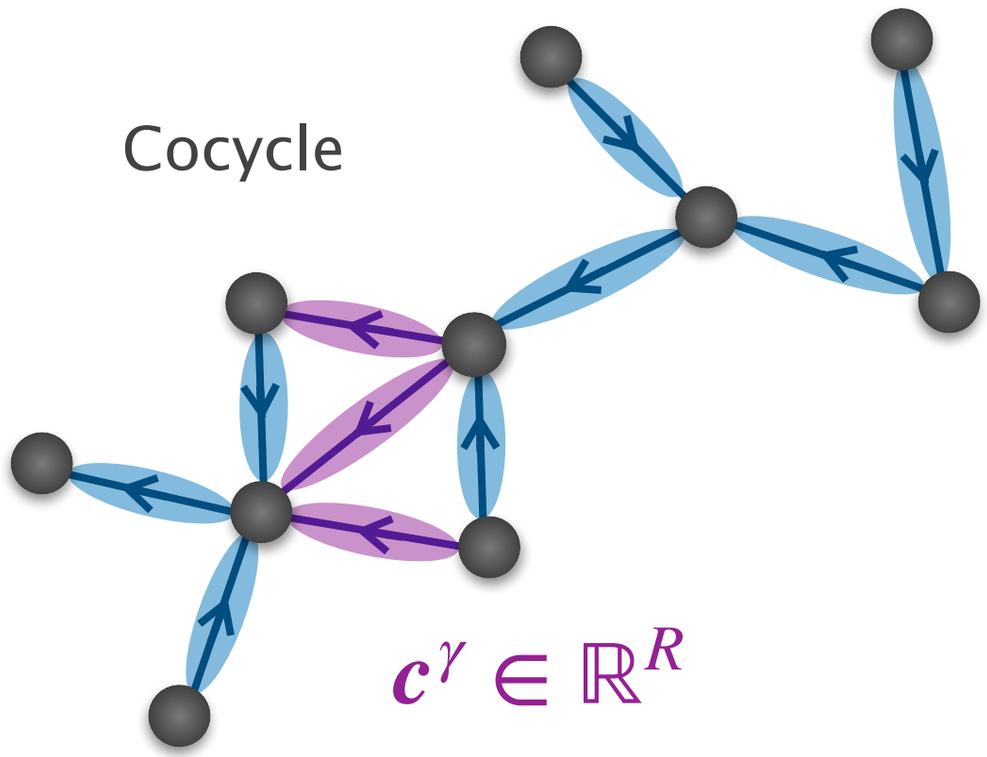


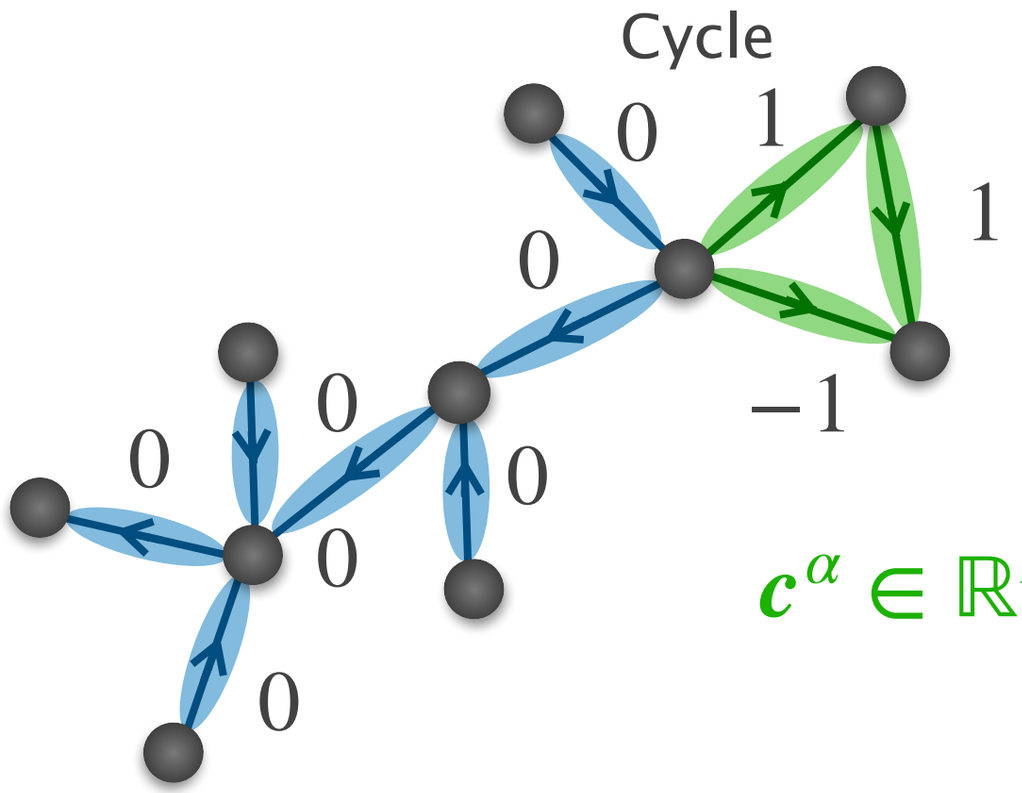
$\boldsymbol{c}^{\gamma} \in \mathbb{R}^{R}$

Algebraic $R - M$ **cycles** and M **cocycles**:

($M = \operatorname{Rank} \mathbb{S}$)

$$\left(\ldots, \boldsymbol{c}^{\alpha}, \ldots\right) = \begin{pmatrix} -\mathbb{T} \\ \mathbf{1}_{R-M} \end{pmatrix} \qquad \left(\ldots, \boldsymbol{c}^{\gamma}, \ldots\right) = \begin{pmatrix} \mathbf{1}_{M} \\ \mathbb{T}^{\mathsf{T}} \end{pmatrix}$$

Algebraic representation of cycles & cocycles



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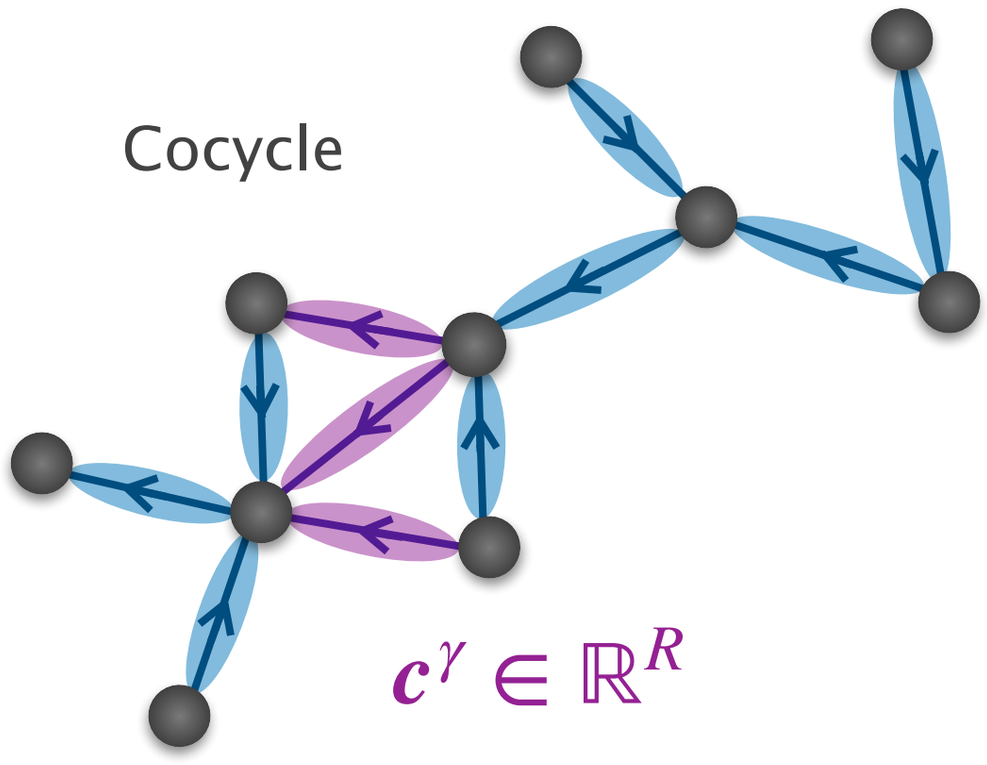

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Non-trivial duality: **same matrix** $\mathbb{T}$ with $(\pm 1, 0)$ entries

Algebraic representation of cycles & cocycles

$$\left(\ldots, \boldsymbol{c}^{\alpha}, \ldots\right) = \begin{pmatrix} -\mathbb{T} \\ \mathbf{1}_{R-M} \end{pmatrix} \qquad \left(\ldots, \boldsymbol{c}^{\gamma}, \ldots\right) = \begin{pmatrix} \mathbf{1}_{M} \\ \mathbb{T}^{\mathsf{T}} \end{pmatrix}$$

- All **independent** vectors
- **Orthogonal** families: $\boldsymbol{c}^{\alpha} \cdot \boldsymbol{c}^{\gamma} = 0$

Orthogonal vector spaces:

$$\text{span}\,\{\boldsymbol{c}^{\alpha}\} = \text{Ker}\,\mathbb{S}$$
$$\text{span}\,\{\boldsymbol{c}^{\gamma}\} = \text{Im}\,\mathbb{S}^{\mathsf{T}}$$

Rank-nullity thm: $\text{Im}\,\mathbb{S}^{\mathsf{T}} \oplus \text{Ker}\,\mathbb{S} = \mathbb{R}^{R}$ $\qquad \text{Ker}\,\mathbb{S} \perp \text{Im}\,\mathbb{S}^{\mathsf{T}}$

A physical decomposition of chemical forces

Reminder: $\partial_t \boldsymbol{x}(t) = \mathbb{S}\boldsymbol{J}(\boldsymbol{x})$ with $J_\rho(\boldsymbol{x}) = k^+ \boldsymbol{x}^{s(\rho)} \left[1 - e^{-A_\rho(\boldsymbol{x})}\right]$

The affinity (chemical force) is decomposed as:

$$\boldsymbol{A} = \sum_\gamma A^c_\gamma \boldsymbol{c}^\gamma + \sum_\alpha A^e_\alpha \boldsymbol{e}^\alpha$$

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Cycle affinities: $A^e_\alpha = \boldsymbol{c}^\alpha \cdot \boldsymbol{A}$ (Graph: sum along a cycle)

Condition for the affinity to be **conservative**:

$$\forall \alpha\,,\ A^e_\alpha = 0 \Leftrightarrow \boldsymbol{A} \in \mathrm{Im}\,\mathbb{S}^\top \Leftrightarrow \boldsymbol{A} = -\,\mathbb{S}^\top \boldsymbol{V}$$

For electric circuits, it is **Kirchhoff voltage law**

A physical decomposition of chemical forces

Reminder: $\partial_t \boldsymbol{x}(t) = \mathbb{S}\boldsymbol{J}(\boldsymbol{x})$ with $J_\rho(\boldsymbol{x}) = k^+ \boldsymbol{x}^{s(\rho)} \left[1 - e^{-A_\rho(\boldsymbol{x})}\right]$

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$$A = \underbrace{\sum_\gamma A^c_\gamma \boldsymbol{c}^\gamma}_{\text{Conservative}} + \underbrace{\sum_\alpha A^e_\alpha \boldsymbol{e}^\alpha}_{\text{Non-conservative}} \qquad (\star)$$

Hence: $(\star)$ is a Helmholtz–Hodge decomposition (on graph)

Cocycles are a basis for conservative affinities

A physical decomposition of chemical forces

Reminder: $\partial_t \boldsymbol{x}(t) = \mathbb{S}\boldsymbol{J}(\boldsymbol{x})$ with $J_\rho(\boldsymbol{x}) = k^+ \boldsymbol{x}^{s(\rho)} \left[1 - e^{-A_\rho(\boldsymbol{x})}\right]$

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Notice that for the (stochastic) molecular dynamics:

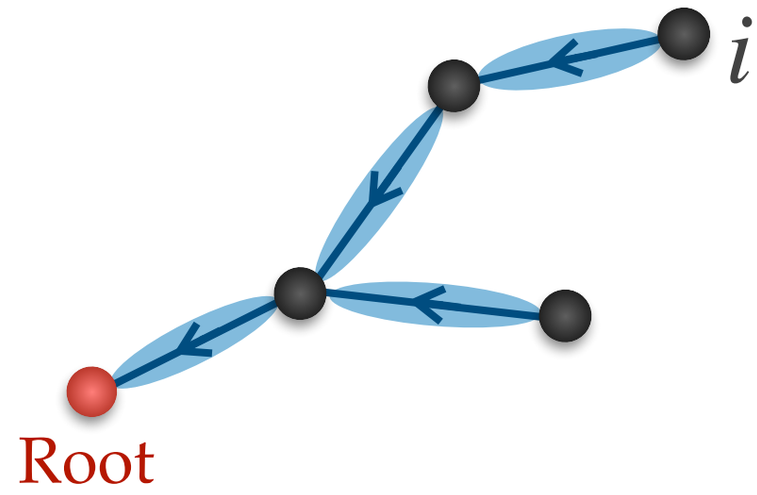
$\forall \alpha\,,\ A^e_\alpha = 0 \Leftrightarrow$ The dynamics is reversible (**Kolmogorov**)

Geometry of affinities – and of cocycles

How to integrate conservative forces

$$\boldsymbol{A}_{\text{pot}} = \sum_{\gamma} A_{\gamma}^{c} \boldsymbol{c}^{\gamma} = -\,\mathbb{S}^{\mathsf{T}} \boldsymbol{V}$$

in order to obtain the potential $\boldsymbol{V}$?



By integrating along the spanning tree

$$V_i[A_{\gamma}^{c}] = \sum_{1 \le \gamma \le M} \left(\mathbb{G}^{\mathsf{T}}\right)_{is(\gamma)} A_{\gamma}^{c}$$

$$= \text{sum of affinities } A_{\gamma}^{c} \text{ between root and node } i$$

Geometry of affinities – and of cocycles

How to integrate conservative forces

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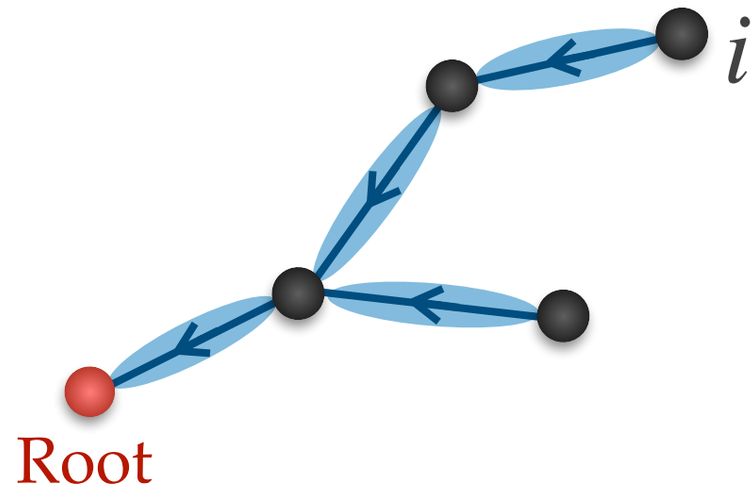
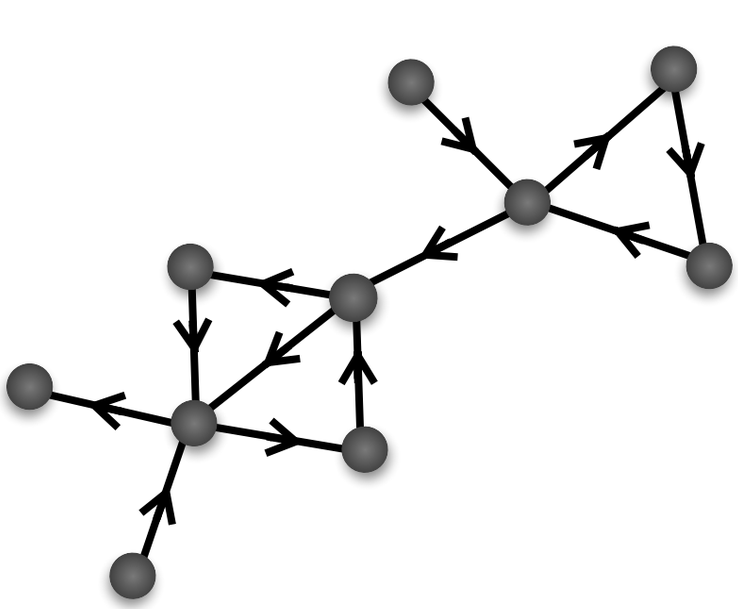
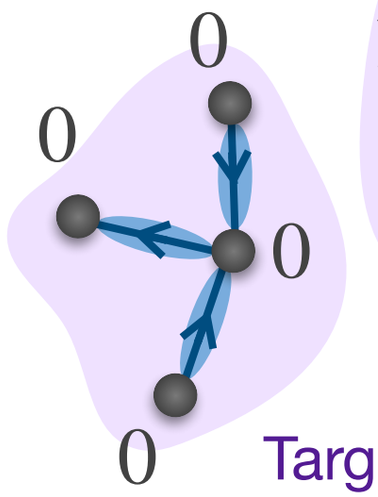


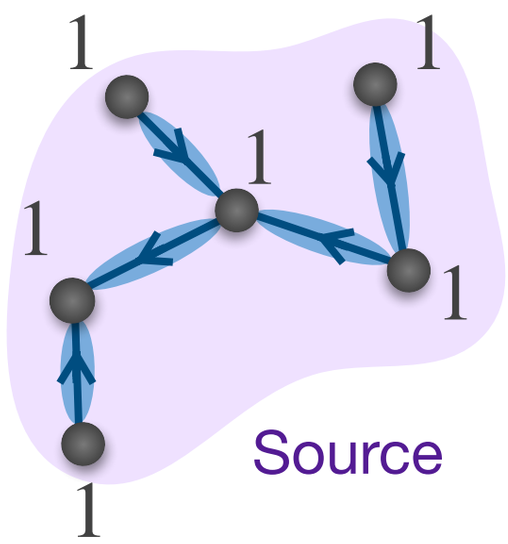
$\mathbb{G}^{\mathsf{T}}$ plays the role of **inverse** (or Green function) for $\mathbb{S}^{\mathsf{T}}$

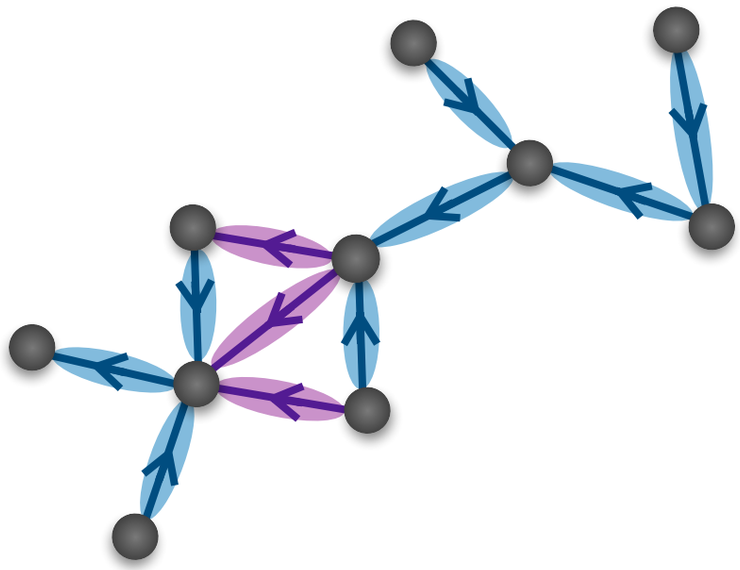
$$-\mathbb{S}^{\mathsf{T}}\,\mathbb{G}^{\mathsf{T}} = \begin{pmatrix} \mathbf{0} & \mathbf{1}_{M} \\ \mathbf{0} & \mathbb{T} \end{pmatrix}$$

Geometry of affinities – and of cocycles









Build a **characteristic potential** $v_i^\gamma = \delta_{i \in \text{ source island}}$

$\Rightarrow$ $c^\gamma =$ gradient of potential between the source and target islands

$= -\mathbb{S}^\mathsf{T} v^\gamma$

Each column is an emergent conservation law

$$\mathbb{G}^\mathsf{T} = \begin{pmatrix} & | & \\ & | & \\ & | & \end{pmatrix}$$

A physical decomposition of currents

Reminder: $\partial_t \boldsymbol{x}(t) = \mathbb{S}\,\boldsymbol{J}(\boldsymbol{x})$ with $J_\rho(\boldsymbol{x}) = k^+ \boldsymbol{x}^{s(\rho)} \left[1 - e^{-A_\rho(\boldsymbol{x})}\right]$

The current is decomposed as:

$$\boldsymbol{J} = \sum_\gamma J^e_\gamma \boldsymbol{e}^\gamma + \sum_\alpha J^c_\alpha \boldsymbol{c}^\alpha$$

Note the difference with: $\boldsymbol{A} = \sum_\gamma A^c_\gamma \boldsymbol{c}^\gamma + \sum_\alpha A^e_\alpha \boldsymbol{e}^\alpha$

A physical decomposition of currents

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Cycle component: in steady state $\mathbb{S}\boldsymbol{J}^* = 0$

$$\boldsymbol{J}^* = \sum_\alpha J^{c,*}_\alpha \boldsymbol{c}^\alpha$$

Cycles are a basis for stationary currents

For electric circuits, this is **Kirchhoff current law**

A physical decomposition of currents

Reminder: $\partial_t \boldsymbol{x}(t) = \mathbb{S}\boldsymbol{J}(\boldsymbol{x})$ with $J_\rho(\boldsymbol{x}) = k^+ \boldsymbol{x}^{s(\rho)} \left[1 - e^{-A_\rho(\boldsymbol{x})}\right]$

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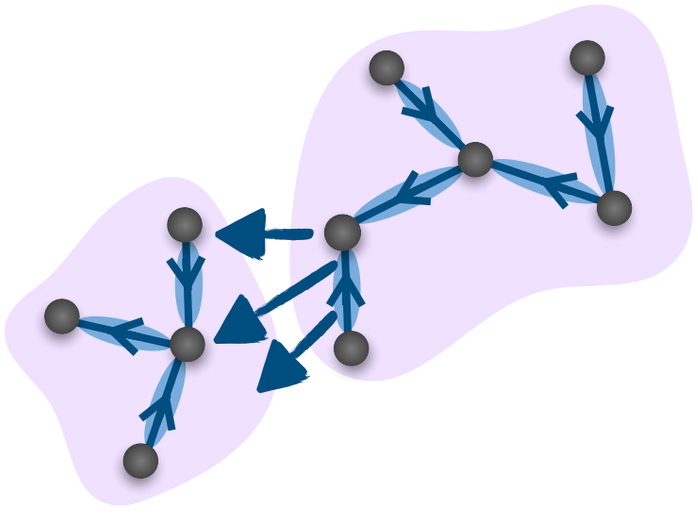


Tidal component: $J^e_\gamma = \boldsymbol{c}^\gamma \cdot \boldsymbol{J}$ (Graph: sum along a cocycle)

$=$ outward flux from the island $\boldsymbol{v}^\gamma$

Tidal currents are transient, they control relaxation to steady state

From graphs to hypergraphs

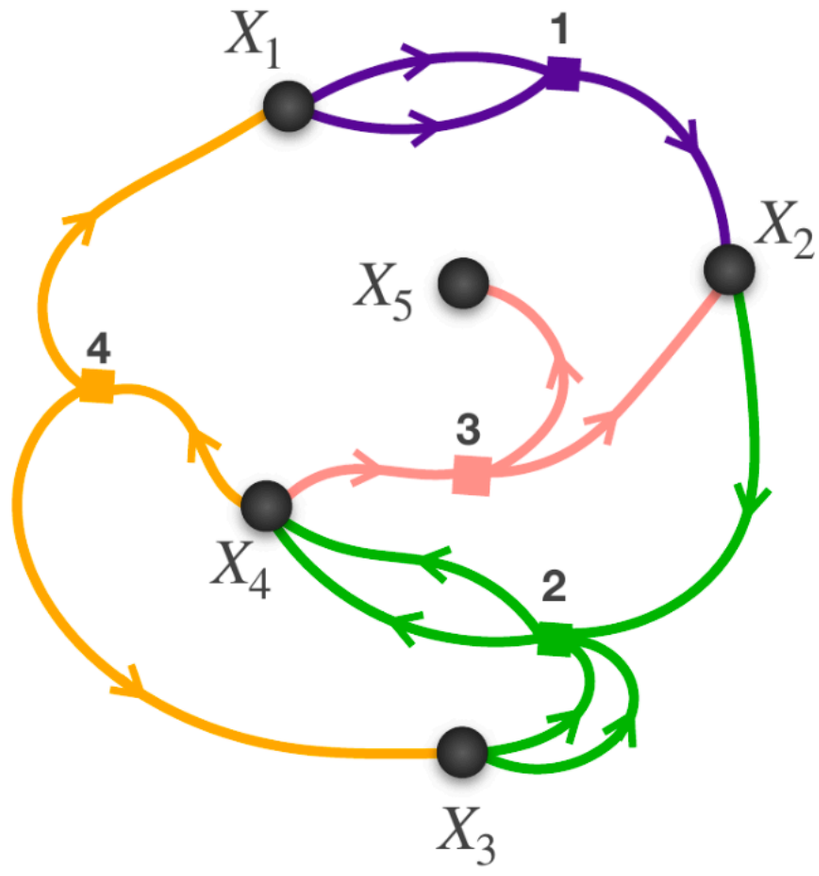
Interacting reaction networks

$$2X_1 \rightleftharpoons X_2$$

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

$$X_4 \rightleftharpoons X_2 + X_5$$

$$X_4 \rightleftharpoons X_1 + X_3$$



Graph theory cannot be used anymore (no spanning tree, no cocycles)

How to proceed?

From graphs to hypergraphs

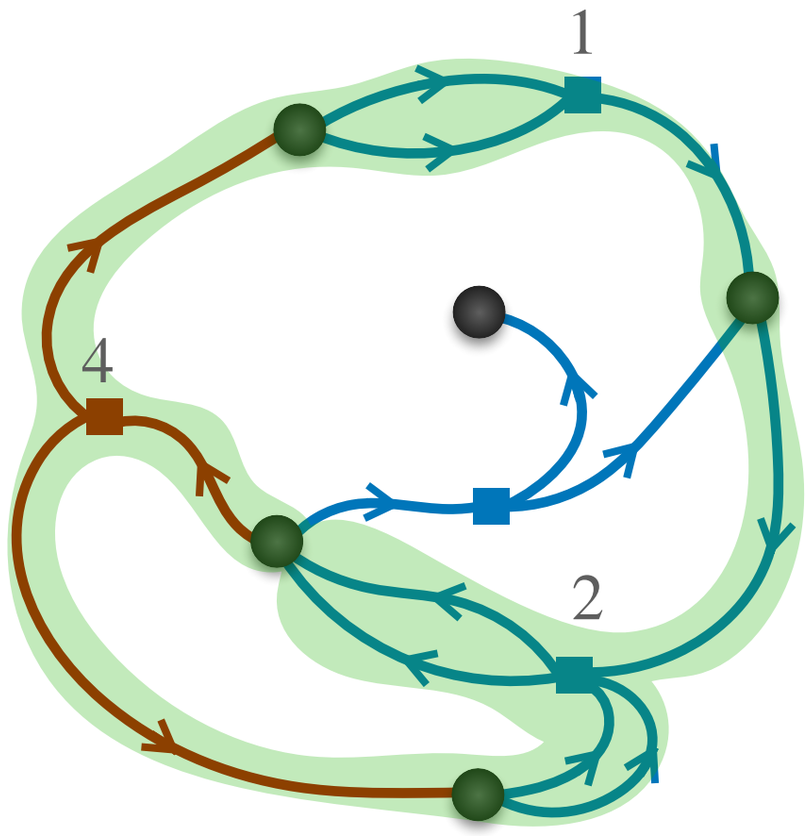
$$2X_1 \overset{1}{\rightleftharpoons} X_3$$

$$X_3 + 2X_4 \overset{2}{\rightleftharpoons} 2X_5$$

$$X_5 \overset{3}{\rightleftharpoons} X_2 + X_3$$

$$X_5 \overset{4}{\rightleftharpoons} X_1 + X_4$$

$$\mathbb{S} = \begin{pmatrix} -2 & 0 & 0 & +1 \\ 0 & 0 & +1 & 0 \\ +1 & -1 & +1 & 0 \\ 0 & -2 & 0 & +1 \\ 0 & +2 & -1 & -1 \end{pmatrix}$$



Cycles: weighted set of reactions leaving the system unchanged

In this example: $\boldsymbol{c} = (1/2 \;\; 1/2 \;\; 0 \;\; 1)^{\mathsf{T}}$ spans the Ker $\mathbb{S}$

What about cocycles?

An algebraic construction

Upon an adequate reordering of reactions and species

Row reduction in echelon form $\Rightarrow$ $\exists$ invertible matrix $\mathbb{G}$:

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

$(M = \mathrm{Rank}\,\mathbb{S})$

Purely algebraic tool

Same relation as before

$\Rightarrow$ **Key equation** to build generalized cycles/cocycles

$\mathbb{T}$ uniquely defined, with **fractional** entries (instead of $\pm 1, 0$)

An algebraic construction

Upon an adequate reordering of reactions and species

Row reduction in echelon form $\Rightarrow$ $\exists$ invertible matrix $\mathbb{G}$:

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

$(M = \mathrm{Rank}\,\mathbb{S})$

Purely algebraic tool

Non-canonical basis in the reaction space:

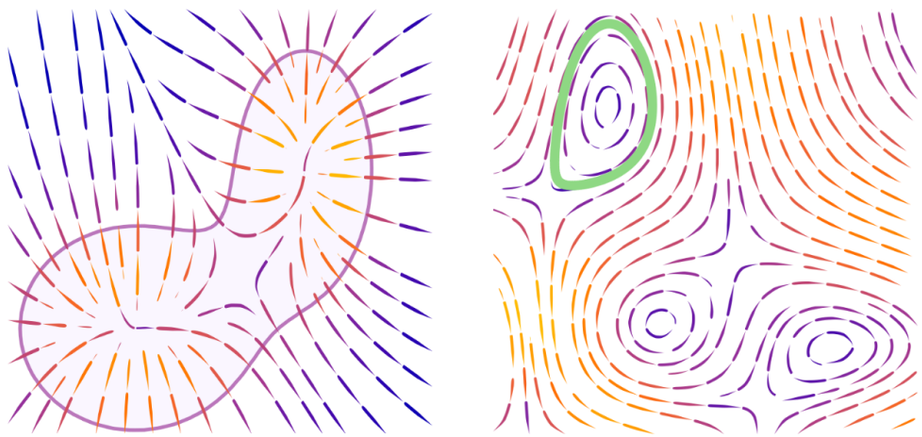
$$\left(\boldsymbol{c}^{\gamma}, \boldsymbol{c}^{\alpha}\right) = \begin{pmatrix} \mathbf{1}_M & -\mathbb{T} \\ \mathbb{T} & \mathbf{1}_{R-M} \end{pmatrix}$$

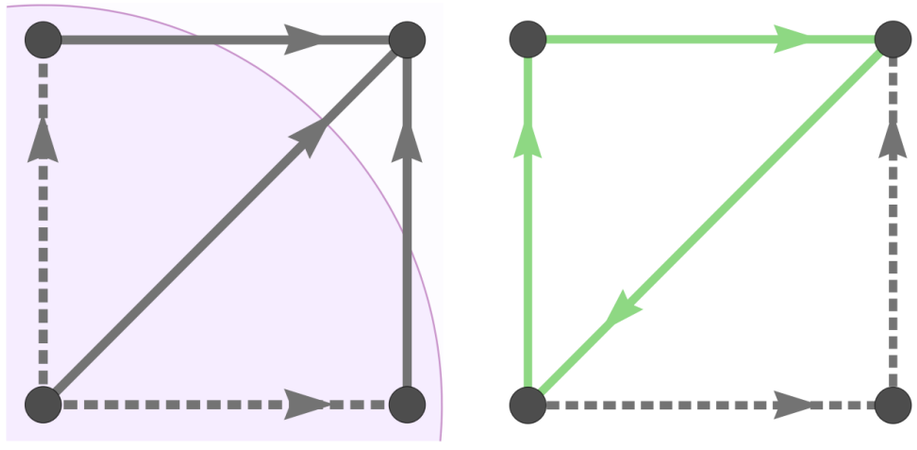
$\mathrm{span}\,\{\boldsymbol{c}^{\alpha}\} = \mathrm{Ker}\,\mathbb{S}$

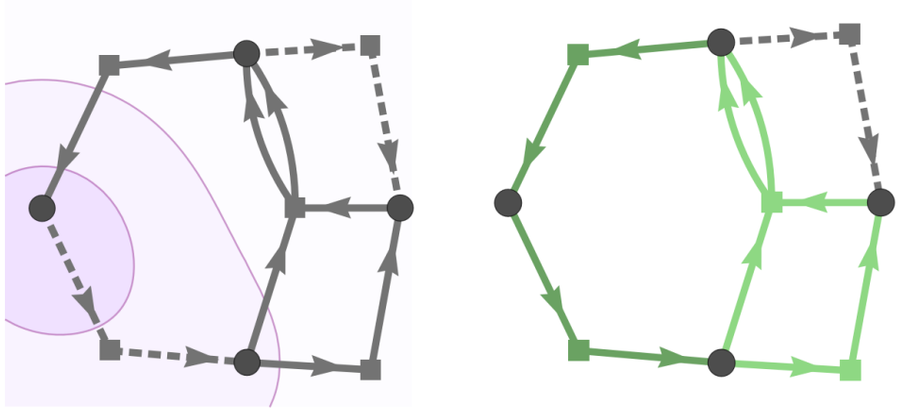
$\mathrm{span}\,\{\boldsymbol{c}^{\gamma}\} = \mathrm{Im}\,\mathbb{S}^{\mathsf{T}}$

M cocycles $\quad R - M$ cycles

Generalized cycles and cocycles







Physical decomposition for forces and currents

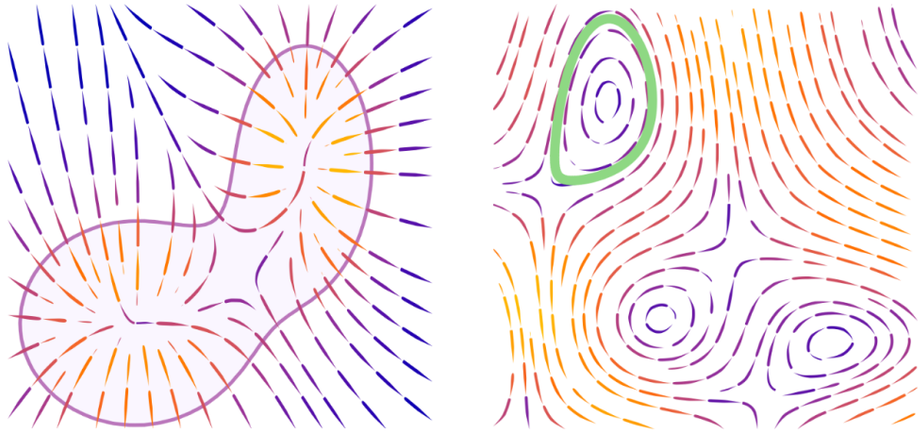
$$\boldsymbol{A} = \sum_{\gamma} A^{c}_{\gamma}\, \boldsymbol{c}^{\gamma} + \sum_{\alpha} A^{e}_{\alpha}\, \boldsymbol{e}^{\alpha}$$

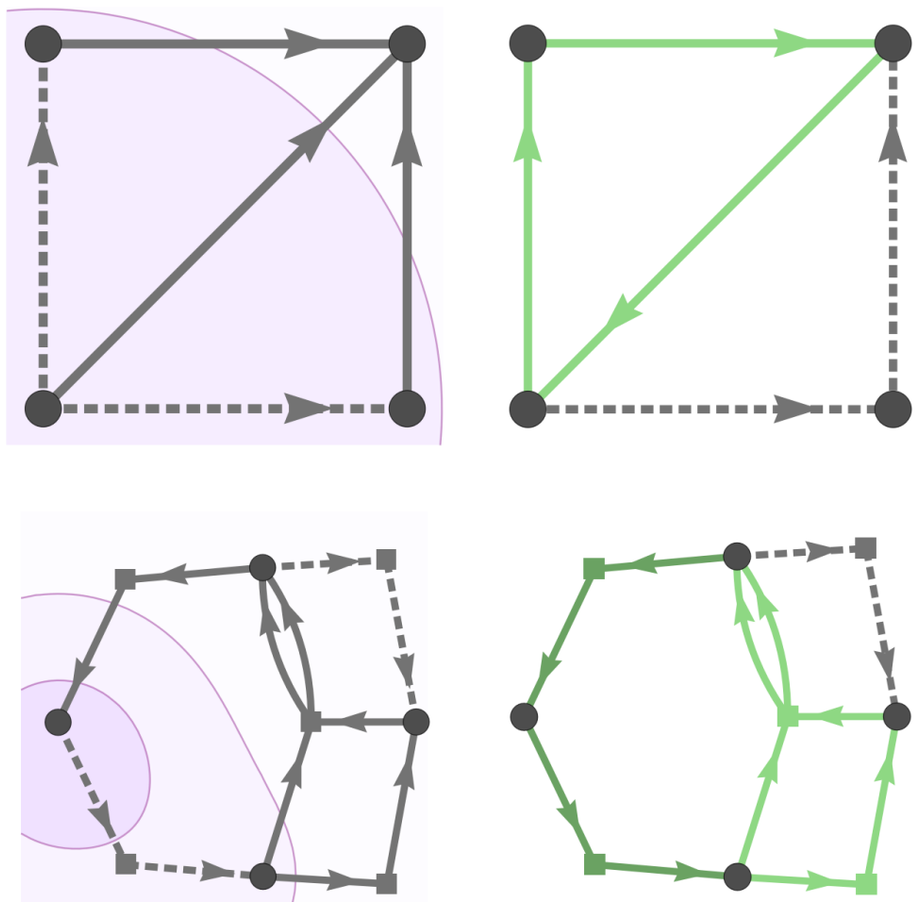
$$\boldsymbol{J} = \sum_{\gamma} J^{e}_{\gamma}\, \boldsymbol{e}^{\gamma} + \sum_{\alpha} J^{c}_{\alpha}\, \boldsymbol{c}^{\alpha}$$

Cocycles = basis for conservative forces, support for tidal currents

Cycles = basis for stationary currents, support for non-conservative forces

Their geometry





Characteristic island/
emergent civ laws

$$\mathbb{G}^{\top} = \begin{pmatrix} & \\ \text{csv} & \begin{matrix} 0 & \cdots\cdots & 0 \\ 0 & \cdots\cdots & 0 \end{matrix} \\ \hline \text{laws} & \\ & \\ & \end{pmatrix} \begin{matrix} \uparrow \\ N-M \\ \downarrow \\ \\ \uparrow \\ M \\ \downarrow \end{matrix}$$

Integration paths

Application on metabolic reconstruction

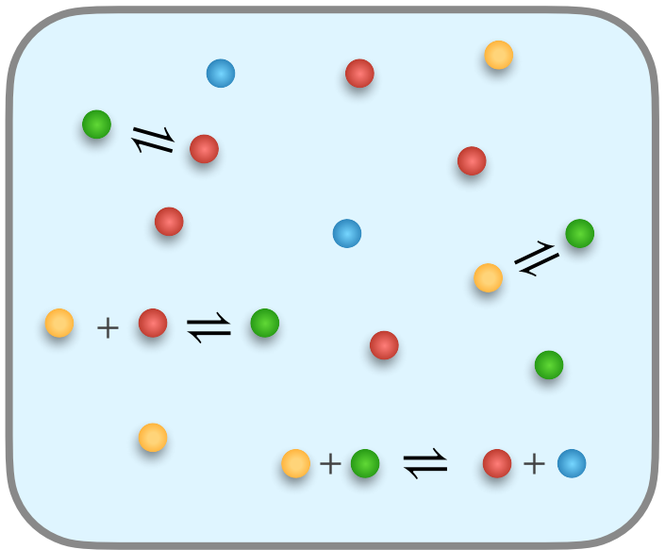
Thermodynamic feasibility or KVL

- A closed system eventually relaxes to equilibrium with $(J_\rho\ , A_\rho) = 0 \ \ \forall \rho$
- A nonzero A_ρ generates nonzero J_ρ of the same sign, s.t. $\dot{s}(t) = \sum J_\rho A_\rho \geq 0$

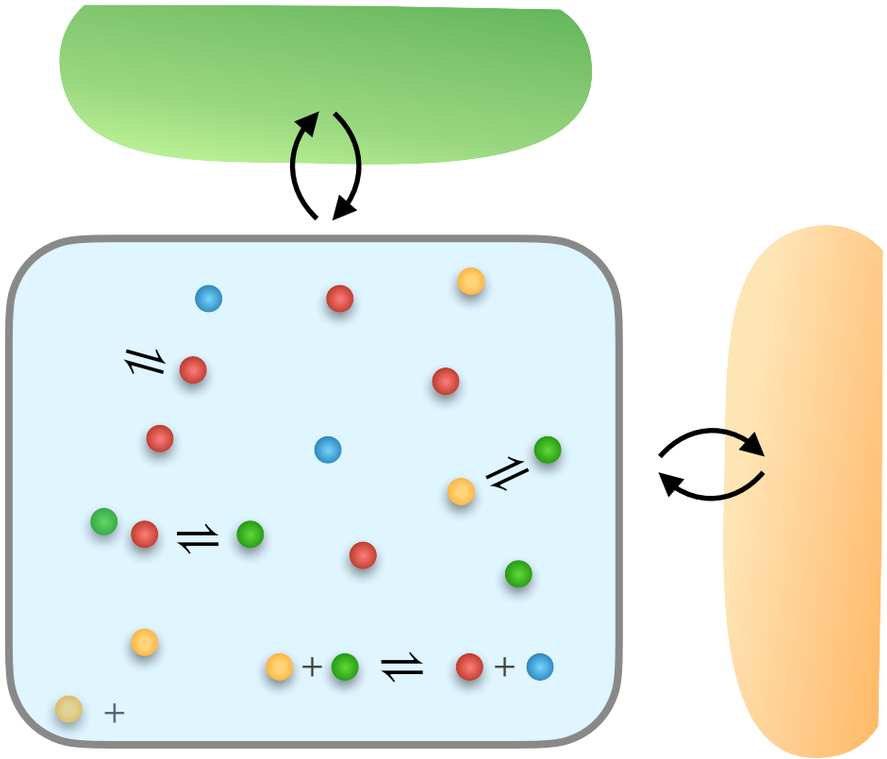
In the absence of chemostatting, affinities are conservative

$$\boldsymbol{A} = \sum_\gamma A_\gamma^c \boldsymbol{c}^\gamma = -\,\mathbb{S}^\top \boldsymbol{V}$$

$\boldsymbol{c}^\alpha \cdot \boldsymbol{A} = 0 \ \forall \alpha$ for all internal cycles

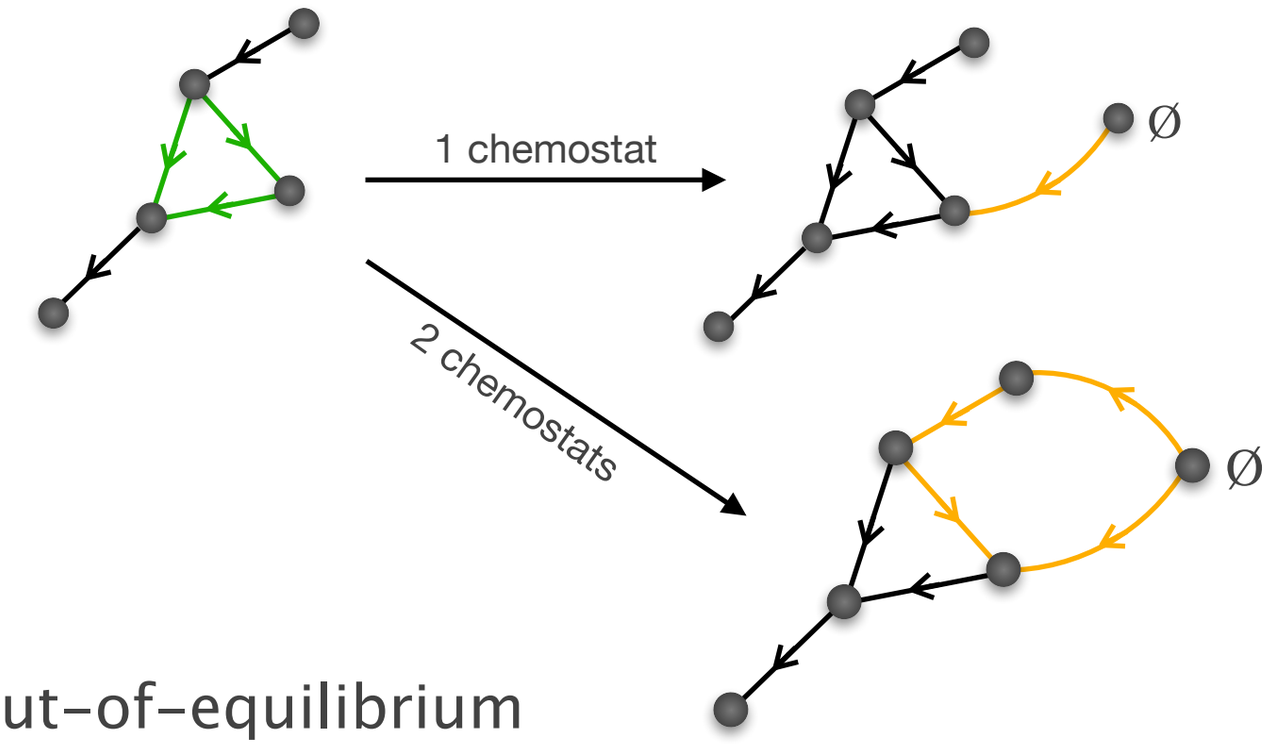


Thermodynamic feasibility or KVL



Open system

Adding chemostatting reactions $\emptyset \rightleftharpoons Y_i$
(may) introduce new emergent cycles



Emergent cycles drive the system out-of-equilibrium

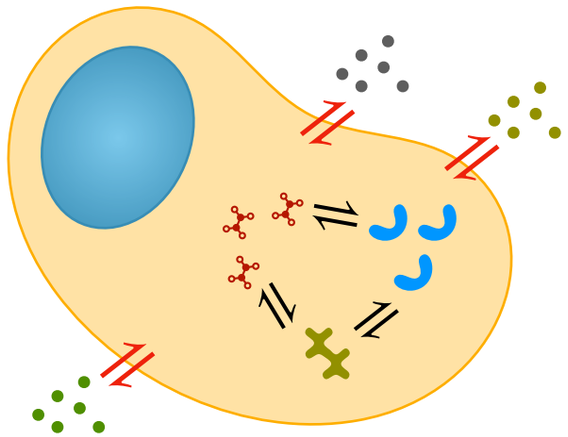
Even if the system is open, internal constraints are still there

$\boldsymbol{c}^{\alpha} \cdot \boldsymbol{A} = 0 \; \forall \alpha$ for all internal cycles

Metabolic reconstruction

Genome-based metabolic networks: stoichiometry is known

Experimentally one has access to some external exchange currents



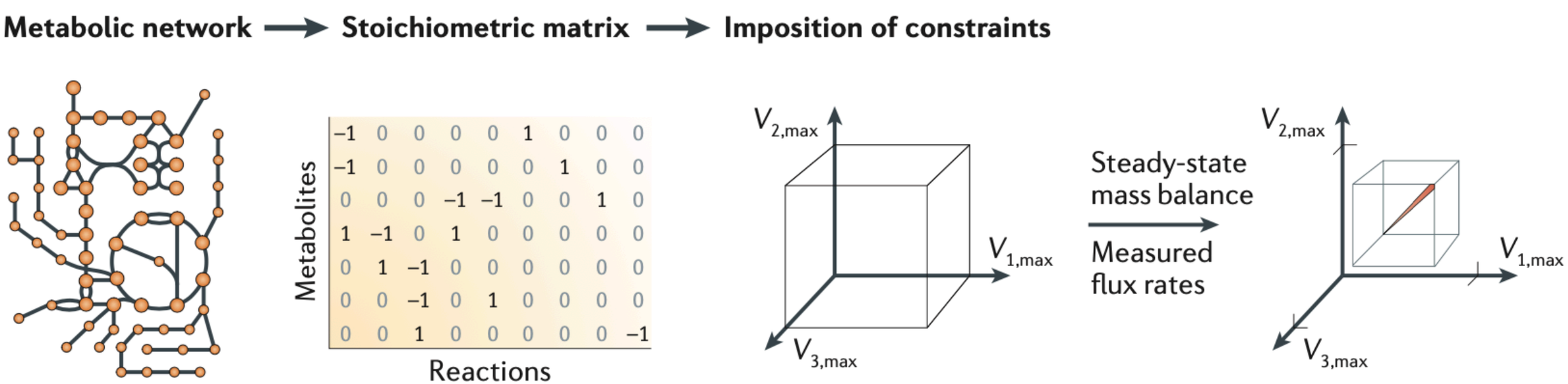
$\boldsymbol{J}^{\text{ext}}$: known exchange currents

$\boldsymbol{J}$: Unknown internal metabolic currents

Q: How to reconstruct the internal currents $\boldsymbol{J}$ in the cell?

$$\mathbb{S}_X \boldsymbol{J} = -\mathbb{S}_Y \boldsymbol{J}^{\text{ext}}$$ (Rate equation at stationarity)

Constrained-based models



[Nature Reviews Genetics 15, (2) 107–120 (2014)]

- Flux Balance Analysis (FBA): optimizing some cellular objective function under the hypothesis of stationarity
- Unbiased sampling via MCMC of the solution space + currents bounds

Imposing thermodynamic feasibility is hard

A geometric approach to reconstruction

Recalling the current decomposition: $\boldsymbol{J} = \sum_{\gamma} J^e_{\gamma} \boldsymbol{e}^{\gamma} + \sum_{\alpha} J^c_{\alpha} \boldsymbol{c}^{\alpha}$

With $J^e_{\gamma} \equiv \boldsymbol{c}^{\gamma} \cdot \boldsymbol{J}$

and $J^c_{\alpha} \equiv \boldsymbol{e}^{\alpha} \cdot \boldsymbol{J}$

$$\begin{pmatrix} \boldsymbol{J}^e \\ \boldsymbol{J}^c \end{pmatrix} = \begin{pmatrix} \mathbb{G}_M \mathbb{S}_Y \boldsymbol{J}^{\text{ext}} \\ \text{function}(\boldsymbol{J}^{\text{ext}}) \end{pmatrix}$$

- The cocycle currents are not constrained by thermodynamic feasibility
- $R - M$ Cycle currents are the one affected by thermodynamic feasibility

A geometric approach to reconstruction

Using the linear regime approximation: $J_\rho = \Lambda_\rho A_\rho$ with $\Lambda_\rho > 0$

$$\begin{pmatrix} \boldsymbol{J}^e \\ \boldsymbol{J}^c \end{pmatrix} = \begin{pmatrix} \mathbb{G}_M \mathbb{S}_Y \boldsymbol{J}^{\text{ext}} \\ \mathbb{L}_P^{-1} \mathbb{T}^\top \Lambda_M^{-1} \mathbb{G}_M \mathbb{S}_Y \boldsymbol{J}^{\text{ext}} \end{pmatrix}$$

With Λ diagonal and positive

$$(\Lambda)_{\rho\rho} \equiv \Lambda_\rho$$

With $\mathbb{L}_P = \Lambda_{R-M}^{-1} + \mathbb{T}^\top \Lambda_M^{-1} \mathbb{T}$
positive-definite and symmetric

In the linear regime, the Λ_ρ's are the equilibrium chemical conductivities and $\mathbb{L}_P$ is the Onsager response matrix

A geometric approach to reconstruction

Using the linear regime approximation: $J_\rho = \Lambda_\rho A_\rho$ with $\Lambda_\rho > 0$

$$\begin{pmatrix} \boldsymbol{J}^e \\ \boldsymbol{J}^c \end{pmatrix} = \begin{pmatrix} \mathbb{G}_M \mathbb{S}_Y \boldsymbol{J}^{\text{ext}} \\ \mathbb{L}_P^{-1} \mathbb{T}^\top \Lambda_M^{-1} \mathbb{G}_M \mathbb{S}_Y \boldsymbol{J}^{\text{ext}} \end{pmatrix}$$

With Λ diagonal and positive

$$(\Lambda)_{\rho\rho} \equiv \Lambda_\rho$$

With $\mathbb{L}_P = \Lambda_{R-M}^{-1} + \mathbb{T}^\top \Lambda_M^{-1} \mathbb{T}$ positive-definite and symmetric

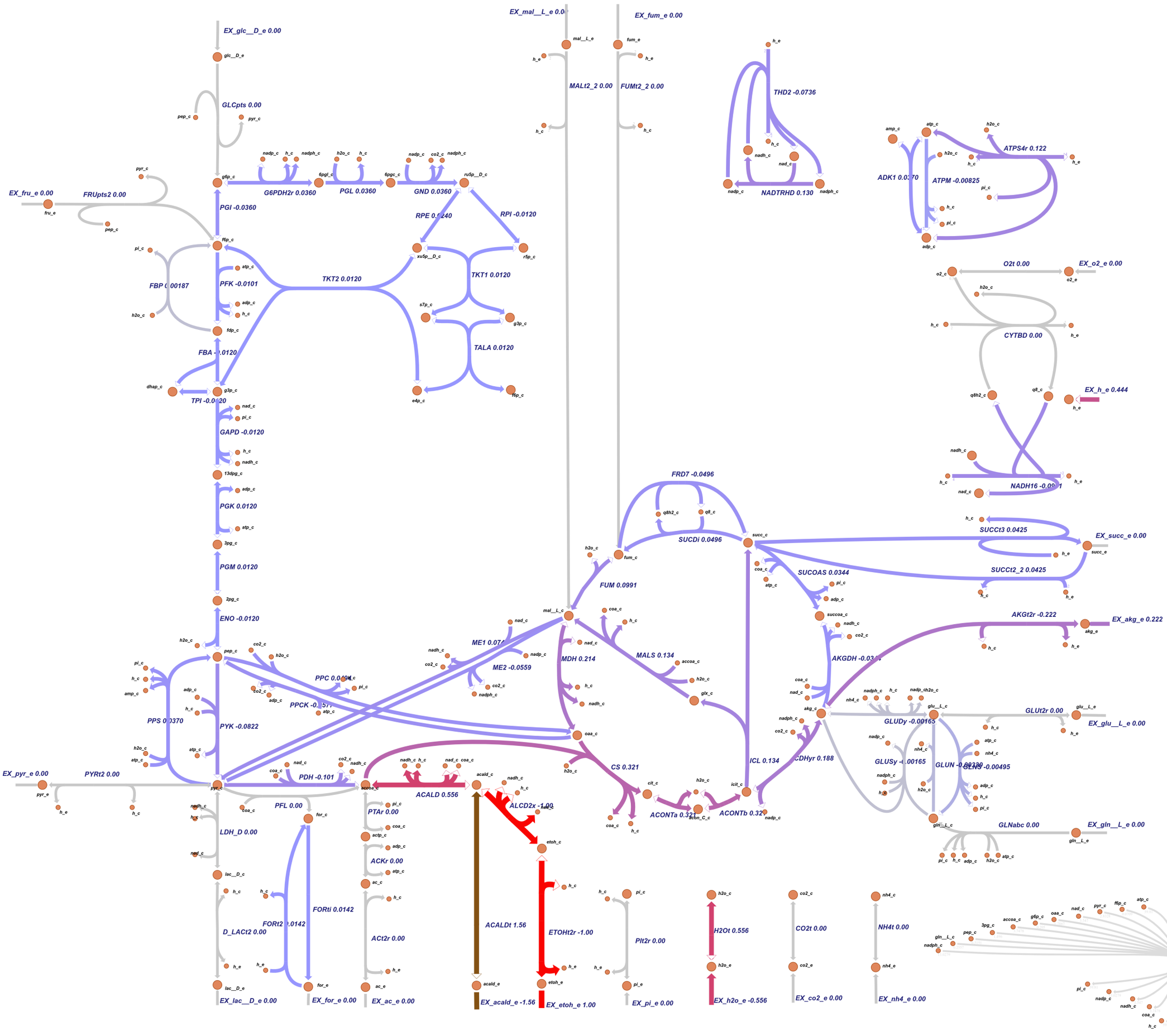
For metabolic reconstruction, the Λ_ρ's are the free parameters which parametrize the space of feasible solutions

$\# \Lambda_\rho =$ # reactions which belongs to internal chemical cycles

Outlook

Working with Delphine Ropers (INRIA) for application to the metabolism of Escherichia Coli

79 internal currents $\boldsymbol{J}$, 15 external (fixed) currents $\boldsymbol{J}^{\mathrm{ext}}$, 12 internal cycles $\boldsymbol{c}^{\alpha}$


EX_glc__D_e 0.00
GLCpts 0.00
G6PDH2r 0.0360
PGL 0.0360
GND 0.0360
EX_fru_e 0.00
FRUpts2 0.00
PGI -0.0360
RPE 0.0240
RPI -0.0120
FBP -0.00187
PFK -0.0101
TKT2 0.0120
TKT1 0.0120
TALA 0.0120
FBA -0.0120
TPI -0.0120
GAPD -0.0120
PGK 0.0120
PGM 0.0120
ENO -0.0120
PPS 0.0370
PYK -0.0822
PPC 0.0094
PPCK -0.0571
ME1 0.074
ME2 -0.0559
PDH -0.101
PFL 0.00
LDH_D 0.00
PTAr 0.00
ACKr 0.00
ACt2r 0.00
FORti 0.0142
FORt2 0.0142
D_LACt2 0.00
EX_pyr_e 0.00
PYRt2 0.00
EX_lac__D_e 0.00
EX_for_e 0.00
EX_ac_e 0.00
EX_mal__L_e 0.00
EX_fum_e 0.00
MALt2_2 0.00
FUMt2_2 0.00
FUM 0.0991
FRD7 -0.0496
SUCDi 0.0496
MDH 0.214
MALS 0.134
CS 0.321
ACONTa 0.321
ACONTb 0.32
ICL 0.134
SUCOAS 0.0344
AKGDH -0.03
SUCCt3 0.0425
SUCCt2_2 0.0425
EX_succ_e 0.00
AKGt2r -0.222
EX_akg_e 0.222
GLUDy -0.00165
GLUSy -0.00165
GLUN -0.00339
GLNS -0.00495
GLUt2r 0.00
EX_glu__L_e 0.00
GLNabc 0.00
EX_gln__L_e 0.00
THD2 -0.0736
NADTRHD 0.130
ATPS4r 0.122
ATPM -0.00825
ADK1 0.0170
O2t 0.00
EX_o2_e 0.00
CYTBD 0.00
EX_h_e 0.444
NADH16 -0.00
ACALD 0.556
ALCD2x -1.00
ACALDt 1.56
ETOHt2r -1.00
EX_acald_e -1.56
EX_etoh_e 1.00
Plt2r 0.00
EX_pi_e 0.00
H2Ot 0.556
EX_h2o_e -0.556
CO2t 0.00
EX_co2_e 0.00
NH4t 0.00
EX_nh4_e 0.00
BIOMASS_Ecoli_core_w_GAM (nd)

Outlook

Working with Delphine Ropers (INRIA) for application to the metabolism of Escherichia Coli

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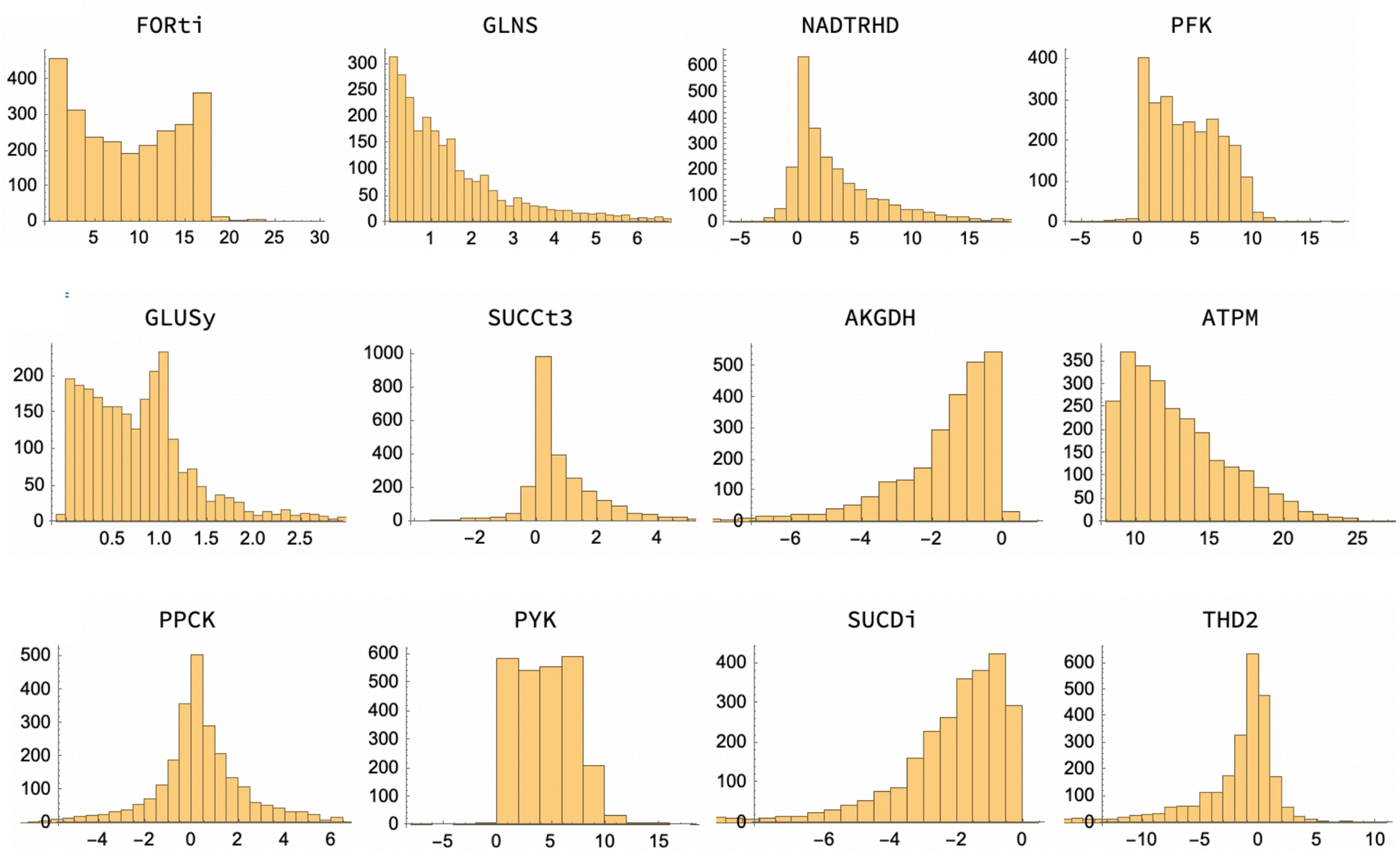

Outlook

Working with Delphine Ropers (INRIA) for application to the metabolism of Escherichia Coli

79 internal currents $\boldsymbol{J}$, 15 external (fixed) currents $\boldsymbol{J}^{\text{ext}}$, 12 internal cycles $\boldsymbol{c}^{\alpha}$

- A criterion to check thermodynamical feasibility given a set of currents $\boldsymbol{J}$. Applications?
- How to incorporate bounds on internal currents systematically in our approach?
- How do these bounds relate to thermodynamic feasibility?
- Comparison with other algorithms like cycle-free flux?

Thank you!

Sara Dal Cengio
Vivien Lecomte
Matteo Polettini

Soon to appear in PRX