Thermodynamics of Open Chemical Reaction Networks

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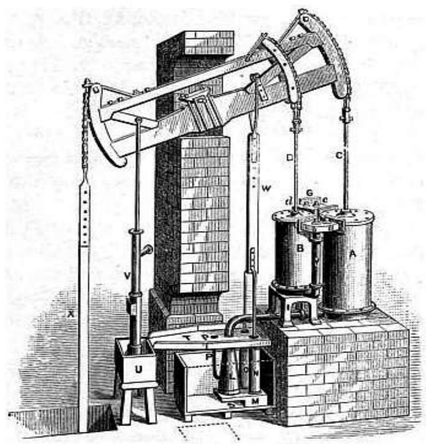
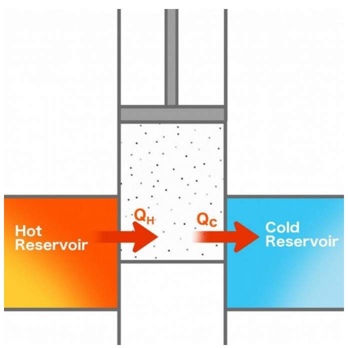
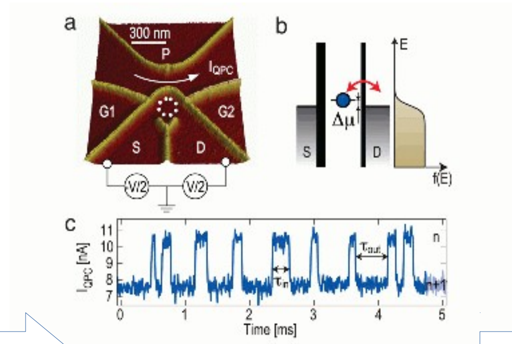
Harvard, November 13, 2019

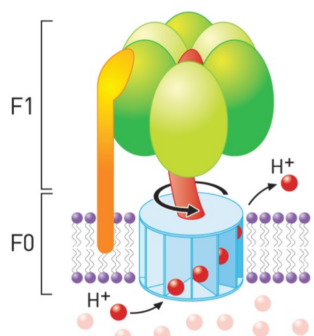
Motivation





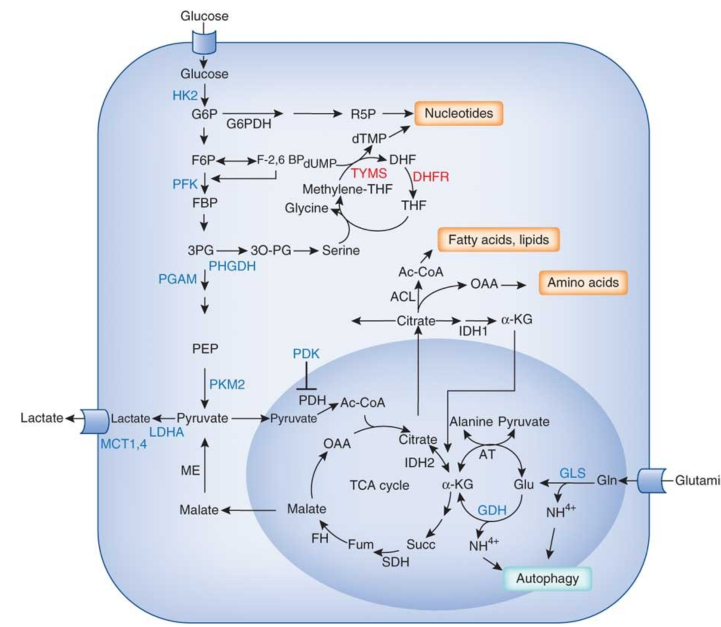
Classical thermodynamics





Stochastic thermodynamics

Cell Metabolism



Thermodynamics of Chemical Reaction Networks

“[Thermodynamics] is the only physical theory of universal content which I am convinced will never be overthrown, within the framework of applicability of its basic concepts.” A. Einstein

Outline

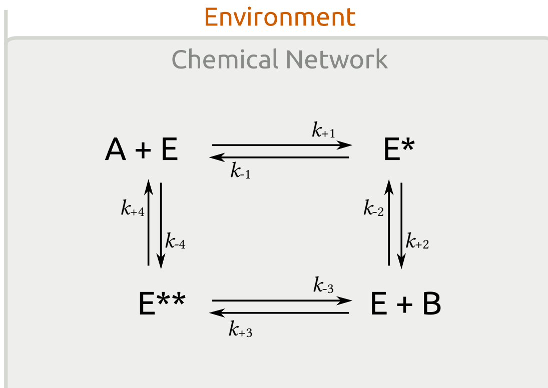
- Deterministic Dynamics of Open CNRs
- Thermodynamics of Open CRNs
    - First and Second Law
    - Role of Topology
- Reaction-Diffusion
- Concluding Remarks

Dynamics of Closed CRNs

$$\boldsymbol{\nu}_+ \cdot \mathbf{Z} \underset{\mathbf{k}_-}{\overset{\mathbf{k}_+}{\rightleftharpoons}} \boldsymbol{\nu}_- \cdot \mathbf{Z}$$

Stoichiometric matrix

$$\boldsymbol{\nu}_- - \boldsymbol{\nu}_+ =: \mathbb{S}$$



$$\mathbb{S} = \begin{array}{c c} \begin{array}{cccc} 1 & 2 & 3 & 4 \end{array} & \\ \begin{pmatrix} -1 & 1 & -1 & 1 \\ 1 & -1 & 0 & 0 \\ 0 & 0 & 1 & -1 \\ -1 & 0 & 0 & 1 \\ 0 & 1 & -1 & 0 \end{pmatrix} & \begin{array}{l} \mathrm{E} \\ \mathrm{E}^* \\ \mathrm{E}^{**} \\ \mathrm{A} \\ \mathrm{B} \end{array} \end{array}$$

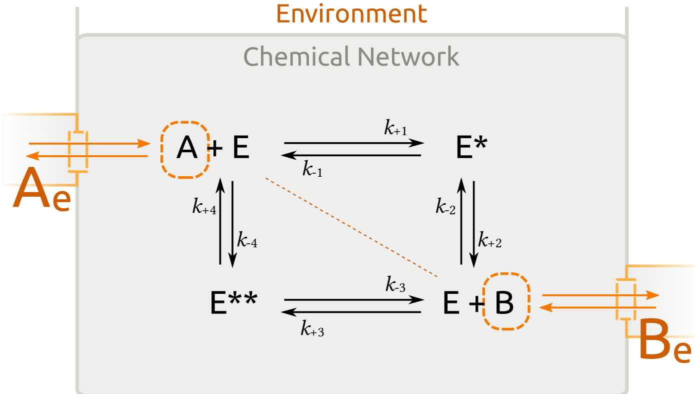
Rate equations $$\mathrm{d}_t[\mathbf{Z}] = \boxed{\mathbb{S}\,\mathbf{J}}$$

Reactions

Ideal Dilute Solution + Elementary Reactions
= Mass action kinetics

$$\begin{cases} \mathbf{J} = \mathbf{J}_+ - \mathbf{J}_- \\ \mathbf{J}_\pm = \mathbf{k}_\pm [\mathbf{Z}]^{\cdot \boldsymbol{\nu}_\pm} \end{cases}$$

Dynamics of Open CRNs



$$\boldsymbol{\nu}_+ \cdot \mathbf{Z} \underset{\mathbf{k}_-}{\overset{\mathbf{k}_+}{\rightleftharpoons}} \boldsymbol{\nu}_- \cdot \mathbf{Z}$$

Stoichiometric matrix

$$\boldsymbol{\nu}_- - \boldsymbol{\nu}_+ =: \mathbb{S} = \begin{pmatrix} \mathbb{S}^X \\ \mathbb{S}^Y \end{pmatrix}$$

$$[\mathbf{Z}] = \begin{pmatrix} [\mathbf{X}] \\ [\mathbf{Y}] \end{pmatrix} \begin{array}{l} \text{Internal} \\ \text{Chemostatted} \end{array}$$

$$\mathbb{S} = \begin{pmatrix} -1 & 1 & -1 & 1 \\ 1 & -1 & 0 & 0 \\ 0 & 0 & 1 & -1 \\ \hline -1 & 0 & 0 & 1 \\ 0 & 1 & -1 & 0 \end{pmatrix} \begin{array}{l} \mathbb{S}^X \\ \\ \\ \mathbb{S}^Y \\ \\ \end{array}$$

Rate equations

$$d_t [\mathbf{X}] = \mathbb{S}^X \mathbf{J}$$

$$d_t [\mathbf{Y}] = \mathbb{S}^Y \mathbf{J} + \mathbf{I}$$

Reactions Exchange

Autonomous CRNs $d_t [\mathbf{Y}] = 0$

Thermodynamics of CRNs

Enthalpy of formation

Entropy of formation

Ideal Dilute Solutions

Local equilibrium

$$\boldsymbol{\mu} = \underbrace{\boldsymbol{h}^\circ - \overbrace{\mathrm{T}\boldsymbol{s}^\circ + \mathrm{RT}\ln[\mathbf{Z}]}}_{\boldsymbol{\mu}^\circ}$$

$\boldsymbol{\mu}^\circ$ Standard-state chemical potential

Local Detailed Balance

$$\boxed{\ln \frac{\mathbf{k}_+}{\mathbf{k}_-} = -\frac{\boldsymbol{\mu}^\circ \cdot \mathbb{S}}{\mathrm{RT}}}$$

Elementary Reactions

"0th law of Thermodynamics": Closed CRN relax to equilibrium

$$\mathbf{J}^{\mathrm{eq}} = \mathbf{J}_+^{\mathrm{eq}} - \mathbf{J}_-^{\mathrm{eq}} = 0$$

detailed-balance

First and Second Law

CRN Enthalpy:

$$\mathsf{H} = \boldsymbol{h}^\circ \cdot [\mathbf{Z}]$$

CRN Entropy:

$$\mathsf{S} = \left(\boldsymbol{s}^\circ - \mathsf{R}\ln[\mathbf{Z}]\right) \cdot [\mathbf{Z}] + \underbrace{\mathsf{R}[\mathsf{Z}]}^{\text{total concentration}}$$

1^{st} law
Enthalpy Balance

$$\boxed{\mathrm{d}_t \mathsf{H} = \boldsymbol{h}^\circ \cdot \mathbb{S}\mathbf{J} + \boldsymbol{h}_{\mathsf{Y}} \cdot \mathbf{I} = \underbrace{\boldsymbol{h}^\circ \cdot \mathbb{S}\mathbf{J} + \mathsf{T}\boldsymbol{s}_{\mathsf{Y}} \cdot \mathbf{I}}_{\text{Heat Flow } \dot{\mathsf{Q}}} + \overbrace{\boldsymbol{\mu}_{\mathsf{Y}} \cdot \mathbf{I}}^{\text{Chemical Work } \dot{W}_{\text{chem}}}}$$

2^{nd} law
Entropy Balance

$$\boxed{\dot{\Sigma} = \mathrm{d}_t \mathsf{S} \underbrace{- \dot{\mathsf{Q}}/\mathsf{T}}_{\text{Entropy change in (thermal \& chemical) reservoirs}}}$$

Entropy production:
(total entropy change)

$$\mathsf{T}\dot{\Sigma} = -\boldsymbol{\mu} \cdot \mathbb{S}\,\mathbf{J} = (\mathbf{J}_+ - \mathbf{J}_-) \cdot \mathsf{RT} \ln \frac{\mathbf{J}_+}{\mathbf{J}_-} \geqslant 0$$

[Rao & Esposito, *Phys. Rev. X* **6**, 041064 (2016)]

Work principle: Equilibrium of Closed CRN

Non-Eq. Gibbs free energy $G = H - TS$

$$\boxed{T\dot{\Sigma} = \dot{W}_{\mathrm{chem}} - d_t G \geqslant 0}$$

$$G = G_{\mathrm{eq}} + RT\, \underbrace{\mathcal{L}\left([\mathbf{Z}] \middle| [\mathbf{Z}]_{\mathrm{eq}}\right)}_{\text{"Relative entropy"}}$$

Equilibrium of closed CRN

$$= [\mathbf{Z}] \cdot \ln \frac{[\mathbf{Z}]}{[\mathbf{Z}]_{\mathrm{eq}}} - ([Z] - [Z]_{\mathrm{eq}}) \geqslant 0$$

In a closed CRN, $W_{\mathrm{chem}} = 0$, G is minimized by the dynamics until the CRN reaches equilibrium

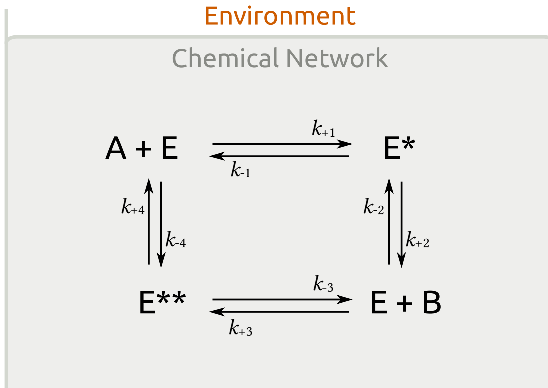
[Rao & Esposito, *Phys. Rev. X* **6**, 041064 (2016)]

Conservation Laws & Cycles in Closed CRNs

Conservation Laws: $\boldsymbol{\ell}_\lambda \cdot \mathbb{S} = 0$

$$\mathrm{L}_\lambda = \boldsymbol{\ell}_\lambda \cdot [\mathbf{Z}]$$

Cycles: $\mathbb{S}\, \mathbf{c}_\alpha = 0$



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\end{array}
\begin{array}{l} \\ \mathrm{E} \\ \mathrm{E}^* \\ \mathrm{E}^{**} \\ \mathrm{A} \\ \mathrm{B} \end{array}$$

$$\boldsymbol{\ell}_1 = \begin{pmatrix} 1 & 1 & 1 & 0 & 0 \end{pmatrix}$$

$$\mathrm{L}_1 = [\mathrm{E}] + [\mathrm{E}^*] + [\mathrm{E}^{**}]$$

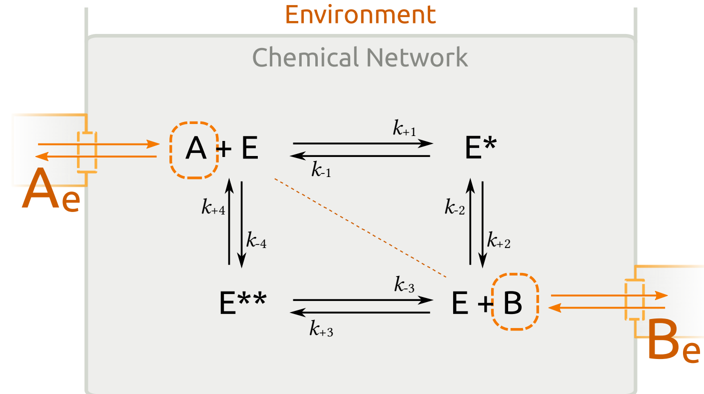
$$\boldsymbol{\ell}_2 = \begin{pmatrix} 0 & 1 & 1 & 1 & 1 \end{pmatrix}$$

$$\mathrm{L}_2 = [\mathrm{E}^*] + [\mathrm{E}^{**}] + [\mathrm{A}] + [\mathrm{B}]$$

$$\mathbf{c} = \begin{pmatrix} 1 & 1 & 1 & 1 \end{pmatrix}^{\mathrm{T}}$$

Conservation Laws & Cycles in Open CRNs

$$\mathbb{S} = \begin{pmatrix} -1 & 1 & -1 & 1 \\ 1 & -1 & 0 & 0 \\ 0 & 0 & 1 & -1 \\ \hline -1 & 0 & 0 & 1 \\ 0 & 1 & -1 & 0 \end{pmatrix} \begin{array}{l} \mathbb{S}^X \\ \\ \mathbb{S}^Y \end{array}$$



Opening may break some conservation laws

$\lambda \to \lambda_b, \lambda_u$ unbroken: $\ell_1 = (1 \quad 1 \quad 1 \mid 0 \quad 0)$ $L_1 = [E] + [E^*] + [E^{**}]$

$\ell_{\lambda_b} \cdot \mathbb{S}^X \neq 0$ broken: $\cancel{\ell_2 = (0 \quad 1 \quad 1 \mid 1 \quad 1)}$ $L_2 = [E^*] + [E^{**}] + [A] + [B]$

Opening may create emergent cycles

$$\begin{cases} \mathbb{S}^X \mathbf{c}_\epsilon = 0 \\ \mathbb{S}^Y \mathbf{c}_\epsilon \neq 0 \end{cases}$$

$\mathbf{c} = (1 \quad 1 \quad 1 \quad 1)^T$

emergent: $\mathbf{c}_\epsilon = (1 \quad 1 \quad 0 \quad 0)^T$

$$\boxed{\#Y = \#\lambda_b + \#\mathbf{c}_\epsilon} \qquad Y \to Y_b, Y_f$$

1	=	1	+	0
2	=	1	+	1
2	=	2	+	0

[Polettini & Esposito, *J. Chem. Phys.* **141**, 024117 (2014)]

Entropy Production shaped by Topology

$$\boxed{\# = \#Y - \#\lambda_b}$$

Fundamental Forces

$$\boldsymbol{\mu}_{Y_f} - \mathbb{L}\boldsymbol{\mu}_{Y_b}$$

Emergent Cycle Affinities

$$-\boldsymbol{\mu}_Y \cdot \mathbb{S}^Y \, \mathbf{c}_\epsilon$$

$$\mathcal{F}_{Y_f} \cdot \mathbf{I}_{Y_f} = \mathcal{A}_\epsilon \cdot \mathcal{J}_\epsilon$$

$$\boxed{T\dot{\Sigma} = \dot{W}_d + \dot{W}_{nc} - d_t\mathcal{G} \geqslant 0}$$

Nonconservative Work

Driving Work

$$\dot{W}_d = -\sum_{\lambda_b} \left[\partial_t f_{\lambda_b}(\boldsymbol{\mu}_{Y_b})\right] L_{\lambda_b}$$

NonEq semigrand Gibbs free energy

$$\mathcal{G} = G - \sum_{\lambda_b} f_{\lambda_b}(\boldsymbol{\mu}_{Y_b}) \, L_{\lambda_b}$$

[Falasco, Rao & Esposito, *Phys. Rev. Lett.* **121**, 108301 (2018)]

$$\boxed{T\dot{\Sigma} = \dot{W}_{\mathrm{d}} + \dot{W}_{\mathrm{nc}} - \mathrm{d}_t \mathcal{G} \geqslant 0}$$

Some special class of CRNs

Detailed Balanced CRNs: $\mathcal{F}_{Y_f}\ ,\ \mathcal{A}_{\epsilon} = 0 \longrightarrow \dot{W}_{\mathrm{nc}} = 0$

DB & autonomous: $T\dot{\Sigma} = -\mathrm{d}_t \mathcal{G} \geqslant 0$ Relaxation to Eq.: $\mathcal{G}$ minimized by dynamics

Non-Eq. Steady State: (autonomous) $T\dot{\Sigma} = \mathcal{F}_{Y_f} \cdot \mathbf{I}_{Y_f} = \mathcal{A}_{\epsilon} \cdot \mathcal{J}_{\epsilon} \geqslant 0$ $\#Y - \#\lambda_b$ Force-Flux pairs

Work principle

$$\mathcal{G} = \mathcal{G}_{\mathrm{eq}} + RT\,\underbrace{\mathcal{L}\left([\mathbf{X}]\middle|[\mathbf{X}]_{\mathrm{eq}}\right)}_{\geqslant 0}$$

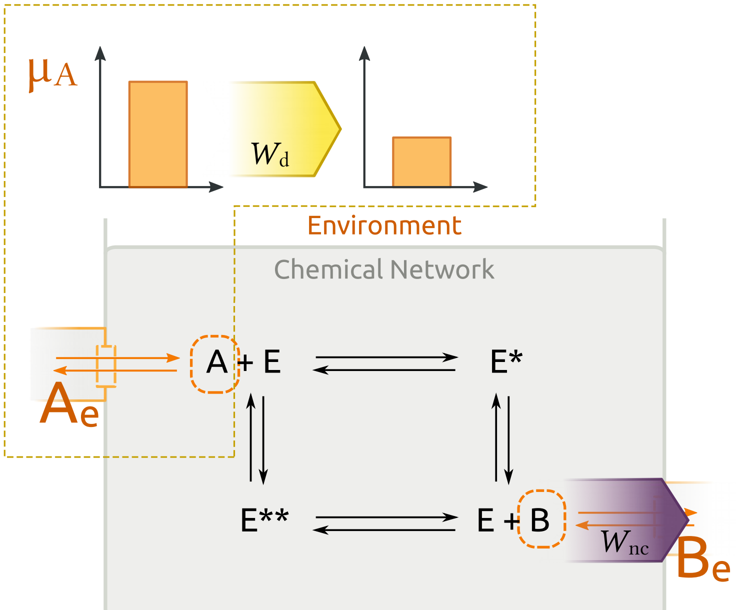
$\mathcal{G}_{\mathrm{eq}}$: Equilibrium of open CRN

$$\boxed{W_{\mathrm{d}} + W_{\mathrm{nc}} \geqslant \Delta\mathcal{G}_{\mathrm{eq}} + \mathcal{L}\left([\mathbf{X}]\middle|[\mathbf{X}]_{\mathrm{eq}}\right)} \longrightarrow$$

Minimal work to generate a Non-Eq distribution

[Falasco, Rao & Esposito, *Phys. Rev. Lett.* **121**, 108301 (2018)]

Example



$$L_b = [E^*] + [E^{**}] + [A] + [B]$$

$$T\dot{\Sigma} = \underbrace{\dot{W}_d}_{\substack{\text{Driving Work} \\ -[\partial_t \mu_A] L_b}} + \underbrace{\dot{W}_{nc}}_{\substack{\text{Nonconservative Work} \\ (\mu_B - \mu_A) I_B}} - d_t \underbrace{\mathcal{G}}_{\substack{\text{Noneq. semigrand Gibbs free energy} \\ \mathcal{G} = G - \mu_A L_b}} \geqslant 0$$

Adding Diffusion

Reaction—Diffusion Equations

$$\mathrm{d}_t[\mathbf{X}]_{\mathbf{r}} = \boxed{-\nabla \cdot \mathbf{J}^{X}_{\mathbf{r}}} + \boxed{\mathbb{S}^{X}\mathbf{j}_{\mathbf{r}}}$$

$$\mathrm{d}_t[\mathbf{Y}]_{\mathbf{r}} = \boxed{-\nabla \cdot \mathbf{J}^{Y}_{\mathbf{r}}} + \boxed{\mathbb{S}^{Y}\mathbf{j}_{\mathbf{r}}} + \boxed{\mathbf{I}_{\mathbf{r}}}$$

Diffusion Reactions Exchange

Mass-action kinetics

$$\mathbf{j}^{\pm}_{\mathbf{r}} = \mathbf{k}_{\pm}[\mathbf{Z}]_{\mathbf{r}}^{\circ\boldsymbol{\nu}_{\pm}}$$

Diffusion: Fick's Law

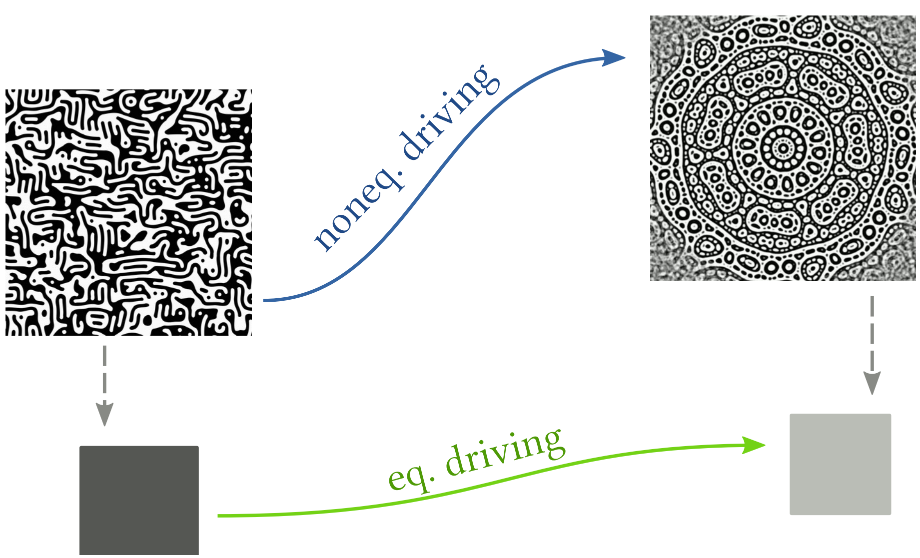
$$\mathbf{J}_{\mathbf{r}} = -\mathbb{D}\nabla[\mathbf{Z}]_{\mathbf{r}}$$

Diffusion coefficients

$$\boxed{\mathcal{W}_{\mathrm{d}} + \mathcal{W}_{\mathrm{nc}} = \Delta\mathcal{G}_{\mathrm{eq}} + RT\,\Delta\mathcal{L} + T\Sigma}$$

$$\geqslant 0$$

$$= \int_{\mathcal{V}} \mathrm{d}\mathbf{r} \left[[\mathbf{Z}]_{\mathbf{r}} \circ \ln \frac{[\mathbf{Z}]_{\mathbf{r}}}{[\mathbf{Z}]_{\mathrm{eq}}} - \left([\mathrm{Z}]_{\mathbf{r}} - [\mathrm{Z}]_{\mathrm{eq}}\right) \right] \geqslant 0$$



Spacial structuring takes work:

$$\mathcal{L}\left([\mathbf{Z}]_{\mathrm{patt}} \middle| [\mathbf{Z}]_{\mathrm{eq}}\right) \geqslant \mathcal{L}\left([\bar{\mathbf{Z}}] \middle| [\mathbf{Z}]_{\mathrm{eq}}\right)$$

[Falasco, Rao & Esposito, *Phys. Rev. Lett.* **121**, 108301 (2018)]

Final remarks

The big issue of coarse graining

Non-Eq. thermodynamics needs to describe **all** the degrees of freedom that are out-of-equilibrium must be described. We need coarse graining strategies which preserves thermodynamic consistency.

Ex: Coarse-graining Biocatalysts [Wachtel, Rao & Esposito, *New J. Phys.* **20** 042002 (2018)]

Useful?

- Performance of energy storage and energy conversion (from molecular motors to metabolic networks)

  Ex: Driven synthesis [Penocchio, Rao & Esposito, *Nature Communications*, **10** 3865 (2019)]

- Cost of Chemical Information Processing

  Ex: Turing patterns [Falasco, Rao & Esposito, *Phys. Rev. Lett.* **121**, 108301 (2018)]

  Chemical waves [Avanzini, Falasco & Esposito, arXiv:1904.08874]

Stochasticity?

Stochastic Thermodynamics of CRNs (nonlinear) [Rao & Esposito, *J. Chem. Phys.* **149**, 245101 (2018)]

Thermo at stochastic vs deterministic level: yes at steady state for complex balanced CRNs
[Polettini, Wachtel & Esposito, *J. Chem. Phys.* **143**, 184103 (2015)]

Phase transitions [Lazarescu, Cossetto, Falasco & Esposito, *J. Chem. Phys.* **151**, 064117 (2019)]