Hidden Hamiltonian Systems in Chemical Reaction Networks

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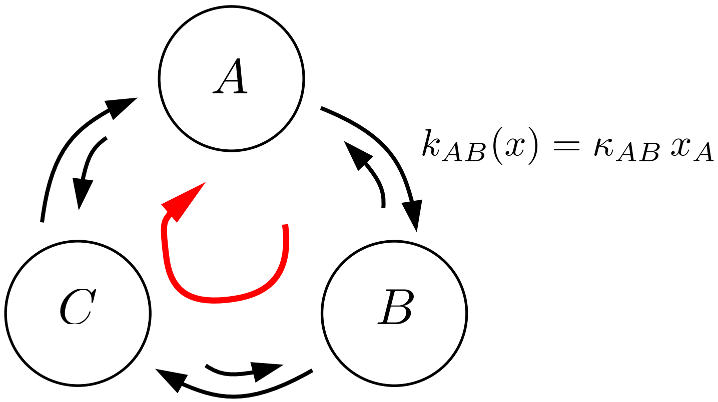
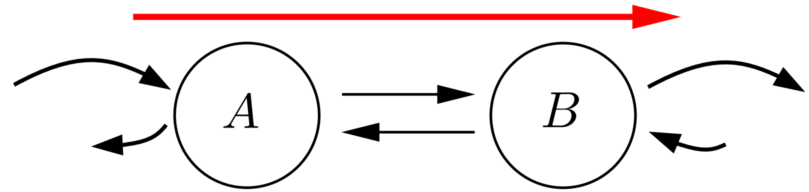
Non-equilibrium systems

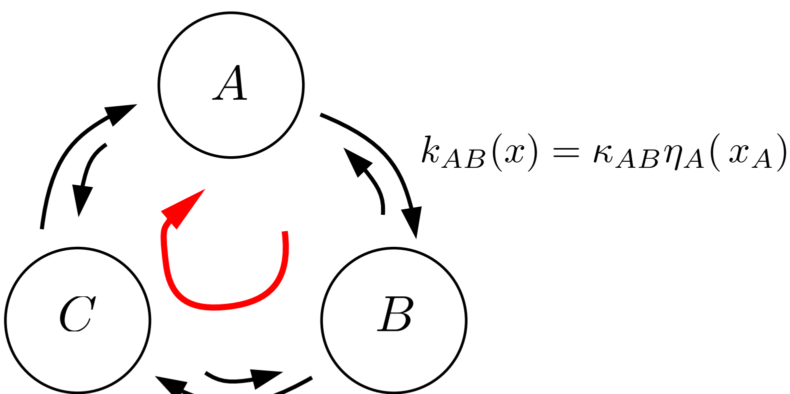
Monomolecular



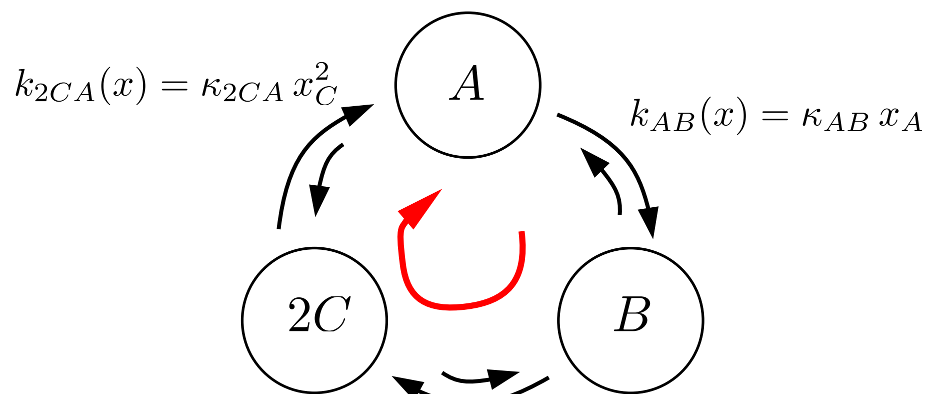
Boundary-driven systems



Zero-range



Chemical reactions



Flux Reaction Rate Equation

- Reversible network,
  (every forward reaction r has a backward reaction $\mathrm{bw}(r)$)
- At least 3 connected complexes in a loop,
  (else always detailed balance)
- Γ stoichiometric matrix for forward reactions,
- $j_r(t)$ net reaction flux (forward – backward).

$\dot{x}(t) = \Gamma j(t),$	continuity equation (CE)
$j(t) = k_{\mathrm{fw}}(x(t)) - k_{\mathrm{bw}}(x(t)).$	reaction rate equation (RRE)

$$\begin{cases} \dot{x}(t) = \Gamma j(t), \\ j(t) = k_{\mathrm{fw}}(x(t)) - k_{\mathrm{bw}}(x(t)). \end{cases}$$

Goal:
1. derive response relation $j(t) = \nabla\Psi^*\big(x(t), F(x(t))\big),$
2. decompose forces $F(x) = F^{\mathrm{sym}}(x) + F^{\mathrm{asym}}(x),$
3. study dynamics of $\dot{x}(t) = \Gamma\nabla\Psi^*\big(x(t), F^{\mathrm{sym}}(x(t))\big),$
4. study dynamics of $\dot{x}(t) = \Gamma\nabla\Psi^*\big(x(t), F^{\mathrm{asym}}(x(t))\big).$

1. Response relation

Kurtz limit: stochastic $\left(X^n(t), J^n(t)\right) \xrightarrow{n\to\infty} \left(x(t), j(t)\right),$ deterministic RRE

Large deviations: $\mathbb{P}\big((X^n, J^n) \approx (x,j)\big) \overset{n\to\infty}{\sim} e^{-n\int_0^T \mathcal{L}(x(t),j(t))\,dt},$

Known but not very nice

$$\mathcal{L}(x,j) \begin{cases} = 0, & j = k_{\text{fw}}(x) - k_{\text{bw}}(x), \\ > 0, & \text{otherwise.} \end{cases}$$

Th. [Onsager, Machlup 1953, Bertini et al 2002, Mielke, Peletier, R. 2014, R. 2018].

$\exists!$ $F(x)$ and convex dual non-negative potentials $\Psi(x,\cdot), \Psi^*(x,\cdot)$ such that:

$$\mathcal{L}(x,j) = \Psi(x,j) + \Psi^*(x, F(x)) - F(x)\cdot j.$$

Hence for the typical flux:

$$k_{\text{fw}}(x) - k_{\text{bw}}(x) = j = \nabla_\zeta \Psi^*\big(x, F(x)\big).$$

Force-response relation!

Specifically for reaction networks:

$$F_r(x) = \frac{1}{2}\log\frac{k_r(x)}{k_{\text{bw}(r)}(x)}, \qquad \Psi^*(x,\zeta) := 2\sum_{r\,\text{fw}} \sqrt{k_r(x)k_{\text{bw}}(r)}\big(\cosh(\zeta_r) - 1\big).$$

2. Decomposing the force

Th. [Bertini et al 2002, Mielke, Peletier, R. 2014, R. 2018, R., Zimmer 2021].
If the *stochastic* system $X^n(t)$ is in detailed balance w.r.t. invariant measure

$$\Pi^n(x) \overset{n\to\infty}{\sim} e^{-n\mathcal{V}(x)}$$

for some nonnegative „quasipotential" $\mathcal{V}$, then

$$F(x) = -\frac{1}{2}\Gamma^{\mathsf{T}}\nabla\mathcal{V}(x).$$

If *not* in detailed balance, we define:

$$F^{\text{sym}}(x) := -\frac{1}{2}\Gamma^{\mathsf{T}}\nabla\mathcal{V}(x), \qquad F^{\text{asym}}(x) := F(x) - F^{\text{sym}}(x).$$

steady state of (RRE)

Th. [Patterson, R., Sharma 2024]. For mass-action kinetics:
stochastic system $X^n(t)$ in Complex Balance $\iff$ $\mathcal{V}(x) = \mathrm{RelEnt}(x \mid \pi)$.

Th. [Anderson, Craciun, Kurtz 2010, Gao, Liu 2022]. For mass-action kinetics:
stochastic system $X^n(t)$ in Complex Balance $\iff$ $\Pi^n(x) = \prod_i \frac{(n\pi_i)^{nx_i}}{(nx_i)!}e^{-n\pi_i}$.

3. Symmetric flow

Set $F^{\mathrm{asym}}(x) = 0$. Corresponds to Detailed Balance!

$$
\begin{aligned}
\dot{x}(t) &= \Gamma \nabla \Psi^* \big(x(t), F^{\mathrm{sym}}(x(t))\big) \\
&= \Gamma \nabla \Psi^* \big(x(t), -\tfrac{1}{2}\Gamma^{\mathsf{T}} \nabla \mathcal{V}(x(t))\big)
\end{aligned}
$$

Interpreted as a gradient flow of $\mathcal{V}$.

All solutions move towards the minimiser π of $\mathcal{V}$.

Mielke, Peletier, R. 2013,
Mielke, Patterson, Peletier, R. 2014,
Peletier, Rossi, Savaré,Tse 2022,
Peletier, Schlichting 2023,
Hraivoronska, Tse 2023,
...

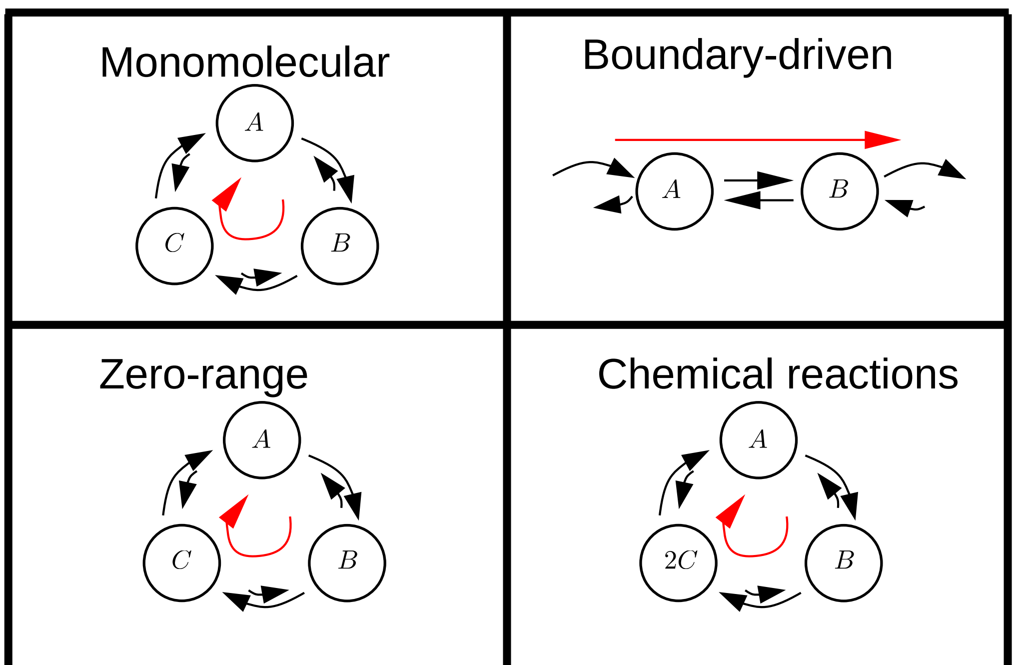
4. Antisymmetric flow

Set $F^{\text{sym}}(x) = 0$.
Corresponds to shutting down entropy!

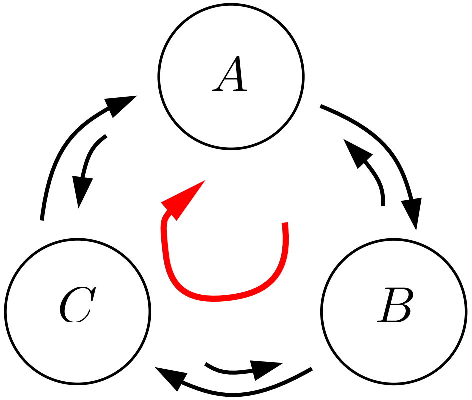
$$\dot{x}(t) = \Gamma \nabla \Psi^* \big(x(t), F^{\text{asym}}(x(t)) \big)$$

Nothing known in general!

Look at specific examples:



Monomolecular



$$F_r(x) = F_{ij}(x) = \frac{1}{2} \log \frac{\kappa_{ij} x_i}{\kappa_{ji} x_j},$$

$$F_{ij}^{\mathrm{sym}}(x) = \frac{1}{2} \log \frac{\pi_j x_i}{\pi_i x_j},$$

$$F_{ij}^{\mathrm{asym}}(x) = \frac{1}{2} \log \frac{\kappa_{ij} \pi_i}{\kappa_{ji} \pi_j}.$$

full flow:

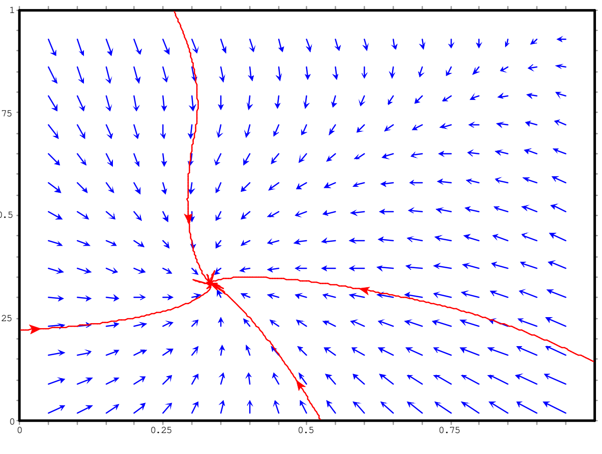
$$\dot{x}(t) = \kappa^{\mathsf{T}} x(t)$$

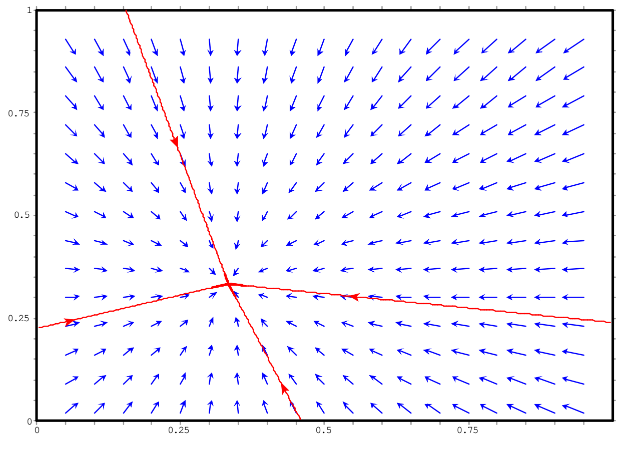
symmetric flow:

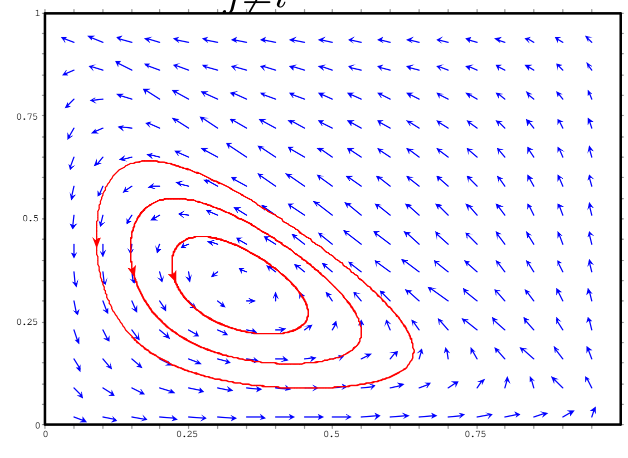
$$\dot{x}(t) = \bar{\kappa}^{\mathsf{T}} x(t)$$

antisymmetric flow:

$$\dot{x}_i(t) = \sum_{j \neq i} A_{ij} \sqrt{x_i(t) x_j(t)}$$



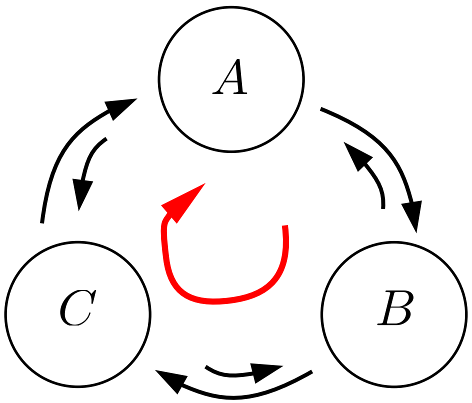




$$\bar{\kappa}_{ij} := \sqrt{\frac{\pi_j \kappa_{ij} \kappa_{ji}}{\pi_i}},$$

$$A_{ij} := \kappa_{ji} \sqrt{\frac{\pi_j}{\pi_i}} - \kappa_{ij} \sqrt{\frac{\pi_i}{\pi_j}}.$$

Zero-range

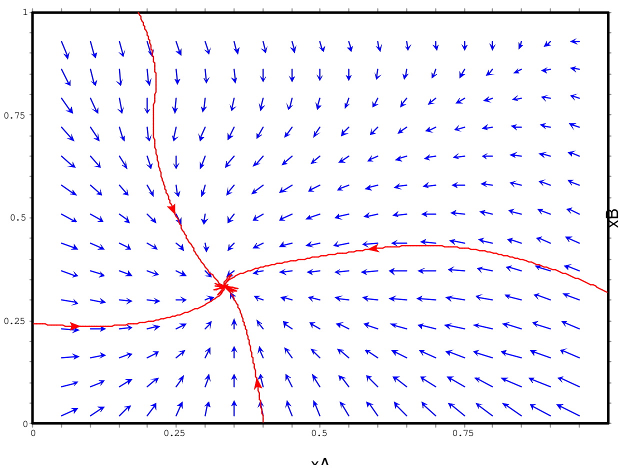


$$F_r(x) = F_{ij}(x) = \frac{1}{2}\log\frac{\kappa_{ij}\pi_i\eta_i(x_i/\pi_i)}{\kappa_{ji}\pi_j\eta_j(x_j/\pi_j)},$$

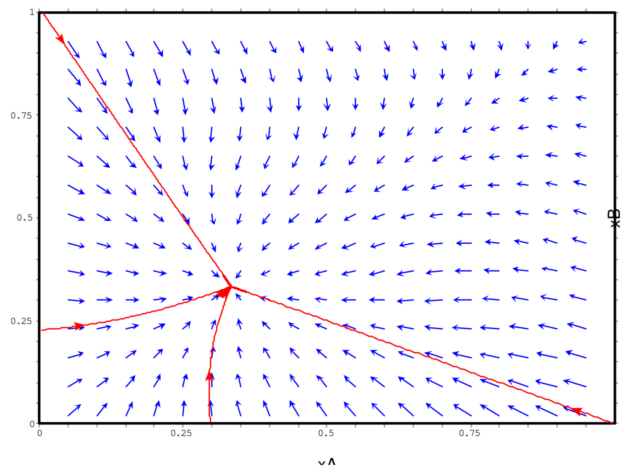
$$F_{ij}^{\mathrm{sym}}(x) = \frac{1}{2}\log\frac{\eta_i(x_i/\pi_i)}{\eta_j(x_j/\pi_j)},$$

$$F_{ij}^{\mathrm{asym}}(x) = \frac{1}{2}\log\frac{\kappa_{ij}\pi_i}{\kappa_{ji}\pi_j}.$$

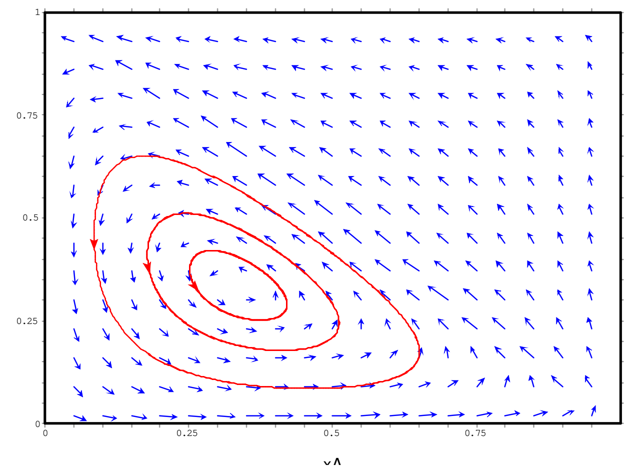
full flow:



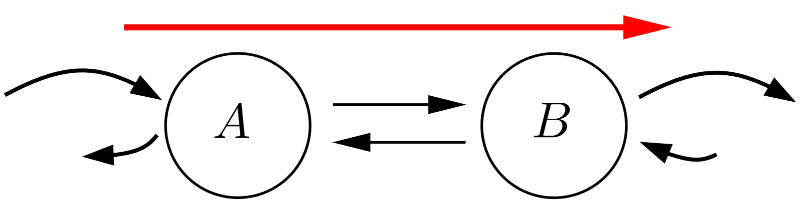
symmetric flow:



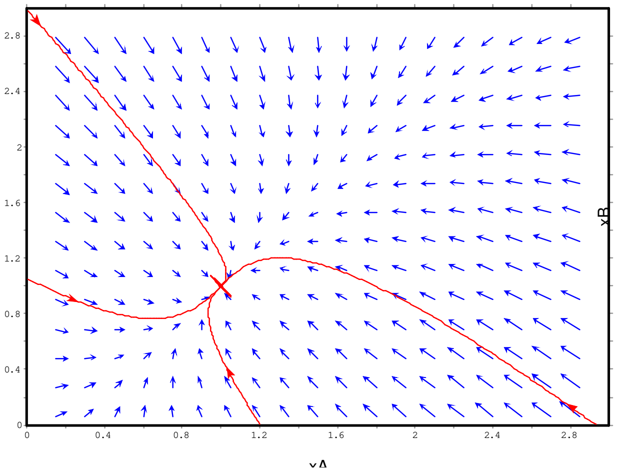
antisymmetric flow:



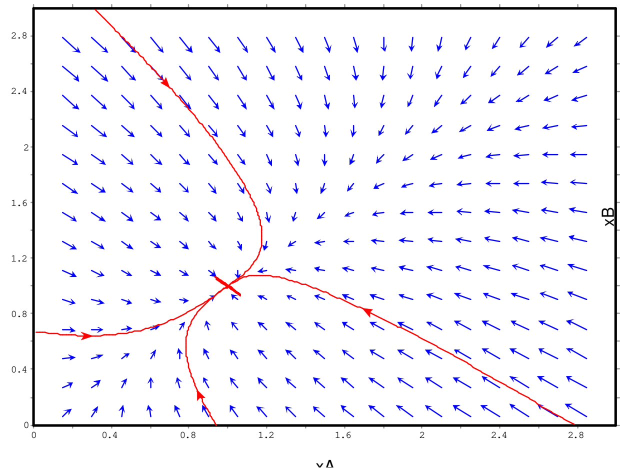
Boundary-driven systems



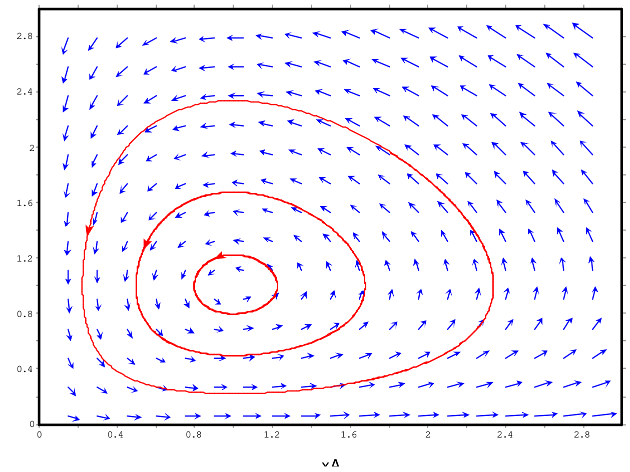
full flow:



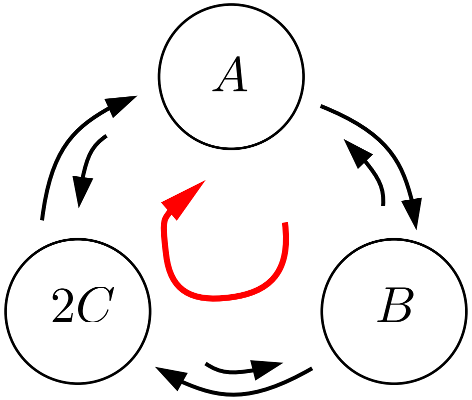
symmetric flow:



antisymmetric flow:



Complex-balance mass-action

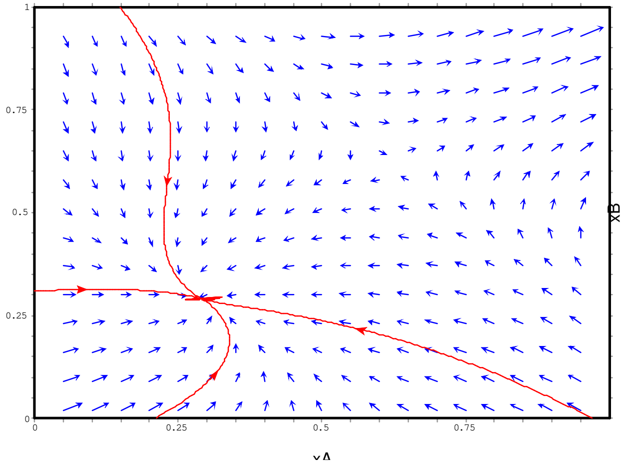


$$F_r(x) = \frac{1}{2}\log\frac{\kappa_r x^{\alpha^{(r)}}}{\kappa_{\mathrm{bw}(r)} x^{\alpha^{\mathrm{bw}(r)}}},$$

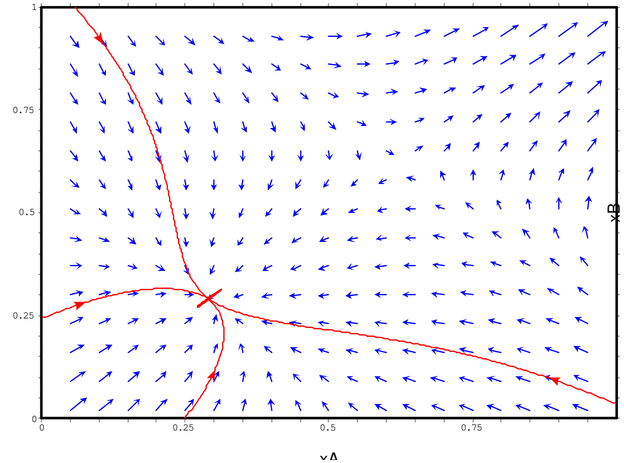
$$F_r^{\mathrm{sym}}(x) = \frac{1}{2}\log\frac{(x/\pi)^{\alpha^{(r)}}}{(x/\pi)^{\alpha^{\mathrm{bw}(r)}}},$$

$$F_r^{\mathrm{asym}}(x) = \frac{1}{2}\log\frac{\kappa_r \pi^{\alpha^{(r)}}}{\kappa_{\mathrm{bw}(r)} \pi^{\alpha^{\mathrm{bw}(r)}}},$$

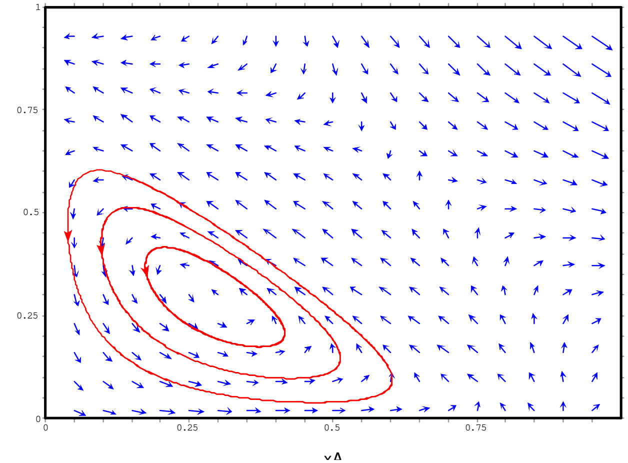
full flow:



symmetric flow:



antisymmetric flow:



Hamiltonian systems

Th. [Patterson, R., Sharma 2024, R., Sharma 2022, R. 2024]. For:

- Monomolecular reactions,
- Zero-range process,
- Mono/Zero-range with open boundaries,

the antisymmetric flow $\dot{x}(t) = \Gamma\nabla\Psi^*\big(x(t), F^{\mathrm{asym}}(x(t))\big) = \mathbb{J}(x(t))\nabla\mathcal{E}(x(t))$

is a **Hamiltonian** system.

Antisymmetric flow for

- complex-balance mass-action:

$$\dot{x}(t) = \sum_{r\,\mathrm{fw}} (\alpha_{\mathrm{bw}(r)} - \alpha_r)\big(\kappa_r \pi^{\frac{\alpha^{(r)} - \alpha^{\mathrm{bw}(r)}}{2}} - \kappa_{\mathrm{bw}(r)} \pi^{\frac{\alpha^{\mathrm{bw}(r)} - \alpha^{(r)}}{2}}\big) x(t)^{\frac{\alpha^{(r)} + \alpha^{\mathrm{bw}(r)}}{2}}.$$

Always periodic orbits?

Hamiltonian system?

Byproduct: entropy production

Along the flow of the RRE:

$$0 = \mathcal{L}(x,j) = \Psi(x,j) + \Psi^*(x, F(x)) - F(x)\cdot j$$

$$= \Psi(x,j) + \Psi^*(x, F^{\text{sym}}(x) + F^{\text{asym}}) - F^{\text{sym}}(x)\cdot j - F^{\text{asym}}(x)\cdot j$$

„generalised orthogonality“

$$= \underbrace{\Psi(x,j) + \Psi^*(x, F^{\text{asym}}) - F^{\text{asym}}(x)\cdot j}_{\geq 0} + \underbrace{\tilde{\Psi}^*(x, F^{\text{asym}})}_{\geq 0} - \underbrace{F^{\text{sym}}(x)\cdot j}_{= -\frac{1}{2}\Gamma^{\mathsf{T}}\nabla\mathcal{V}(x)\cdot j}$$

$$= -\tfrac{1}{2}\nabla\mathcal{V}(x)\cdot\Gamma j$$

$$= -\tfrac{1}{2}\nabla\mathcal{V}(x)\cdot\dot{x}$$

$$= -\tfrac{1}{2}\frac{d}{dt}\mathcal{V}(x)$$

and so $\displaystyle\frac{d}{dt}\mathcal{V}(x) \leq 0.$

(R., Zimmer 2021, Patterson, R., Sharma 2024)

Consistent with :

„3 faces of 2nd law“ (Freitas, Esposito 2021), and
„Lyupunov functions“ (Anderson, Craciun, Gopalkrishnan, Wiuf 2015).