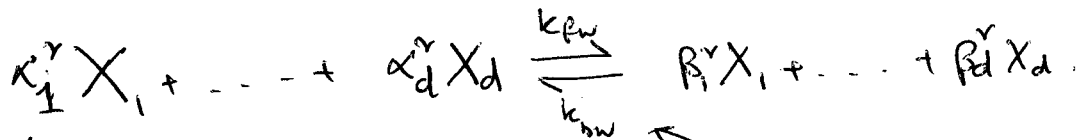


Chemical reaction networks.



↑
 $\in \mathbb{N}$, r -reactions (directed). $r = 1, \dots, R$. reaction can happen forward and backward.

k_{fw}^r - forward reaction rate
 k_{br}^r - backward reaction rate.

Two models: (I) Stochastic, discrete
 (II) deterministic, continuous.

(I) Stochastic model.

• observable $\underline{N} = (N_1, \dots, N_d) \in \{0, 1, \dots\}^d$.
 (N_i = number of particles of species X_i)

• $\underline{N}(t)$ evolves according to a ct. time. markov chain (ctmc).
 with rates:

$$(*) \text{ from } \underline{n} \text{ to } \underline{n} - \underline{\alpha}^r + \underline{\beta}^r : k_{fw}^r \cdot \prod_{i=1}^d \frac{n_i!}{(n_i - \alpha_i^r)!} \cdot \frac{1}{\text{vol}^{|\underline{\alpha}^r - \underline{\beta}^r|}}$$

$$(**) \text{ from } \underline{n} \text{ to } \underline{n} + \underline{\alpha}^r - \underline{\beta}^r : k_{br}^r \cdot \prod_{i=1}^d \frac{n_i!}{(n_i + \beta_i^r)!} \cdot \frac{1}{\text{vol}^{|\underline{\beta}^r - \underline{\alpha}^r|}}$$

let $\mu(t) \in \mathcal{P}(\mathbb{N}_0^d)$ be the law of $\underline{N}(t)$. Then, $\mu(t)$ satisfies the chemical master equation.

(II) deterministic model:

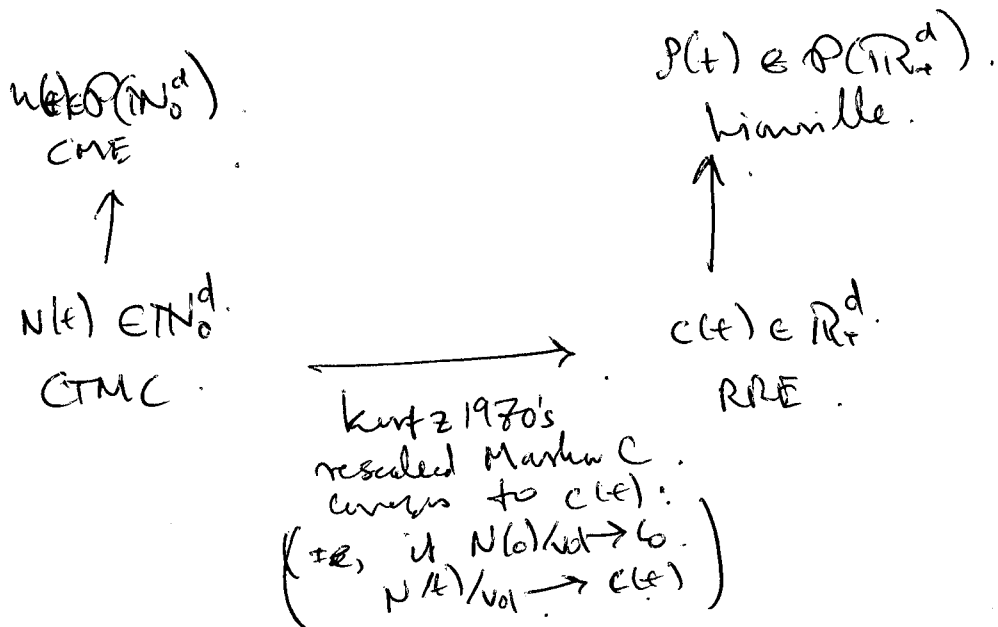
• observable $\underline{c} = (c_1, \dots, c_d) \in \mathbb{R}_+^d$; concentration of the species X_i .

• $\underline{c}(t)$ evolves according to reaction rate eqⁿ.

$$\dot{\underline{c}} = -\underline{R}(\underline{c}), \quad \dot{c}_i(t) = - \sum_{r=1}^R \left(k_{fw}^r \prod_{j=1}^d c_j(t)^{\alpha_j^r} - k_{br}^r \prod_{j=1}^d c_j(t)^{\beta_j^r} \right)$$

• let $p(t)$ be a prob measure $\in \mathcal{P}(\mathbb{R}_+^d)$
 be the law of $\underline{c}(t) \in \mathbb{R}_+^d$. Then,
 $p(t)$ evolves according to the Liouville eq:

$$\partial_t p(c) = \text{div}(p(c) R(c)).$$



• Gradient flows. Assum.

Assume $\exists \underline{c}^* := (c_1^*, \dots, c_d^*) \in \mathbb{R}_{>0}^d$ s.t.

$$k_{\alpha}^r := k_{\beta}^r \cdot \prod_{j=1}^d (c_j^*)^{\alpha_j^r} = k_{\beta}^r \cdot \prod_{j=1}^d (c_j^*)^{\beta_j^r} \quad \forall r=1, \dots, R.$$

Then CME, RRE, has gradient flow structures

• CME: $\dot{u} = -\mathcal{K}(u) DE(u)$. $E(u) = \text{Ent}(u|w^u)$.

$$(w^u)_n = e^{-V|c^*|} \cdot \frac{c_n^* V^{|\alpha|}}{n!} \quad \left(\begin{array}{l} \mathcal{K} - \text{pos. def. infinite} \\ \text{dim matrix} \\ \sim \text{inverse of Hessian} \\ \text{matrix.} \end{array} \right)$$

• RRE (Müller): $\dot{c} = k(c) DE(c)$. $E(c) = \text{Ent}(c|\underline{c}^*)$.

$$k(c) = \sum_r k_{\alpha}^r \theta\left(\frac{c^{\alpha^r}}{c_x^{\alpha^r}}, \frac{c^{\beta^r}}{c_x^{\beta^r}}\right) (\underline{\alpha}^r - \underline{\beta}^r) \otimes (c^{\alpha^r} - c^{\beta^r}).$$

$$E(c) = \sum_{i=1}^d c_i^* \ln\left(\frac{c_i}{c_i^*}\right), \quad \ln(t) = t \log_e |t| - t + 1.$$

• Kullback: $\dot{J} = -K(p) \nabla E(p), \quad E(p) = \int E(c) d\rho(c).$
 $(K(p) \nabla \rho)(c) = -\operatorname{div}(\rho(c) K(c) \nabla \eta(c)).$

Induced distance is \mathcal{W}_2 with underlying Riemann metric K^{-1} .

Set $\mathbb{F}_{\text{GME}}^*(\mu, \xi) = \frac{1}{2} \langle \xi, K(\mu) \xi \rangle, \quad \mu \in \mathcal{P}(\mathbb{N}_0^d), \quad \xi: \mathbb{N}_0^d \rightarrow \mathbb{R}.$

$$\begin{aligned} \mathbb{F}_{\text{MIO}}^*(\rho, \eta) &= \frac{1}{2} \langle \eta, K(\rho) \eta \rangle. \\ &= \frac{1}{2} \int \langle \nabla \eta(c), K(c) \nabla \eta(c) \rangle d\rho(c). \end{aligned} \quad \left| \begin{array}{l} \rho \in \mathcal{P}(\mathbb{R}_+^d). \\ \eta: \mathbb{R}_+^d \rightarrow \mathbb{R}. \end{array} \right.$$

Proof (M-Mielke) $\mathbb{F}_{\text{GME}}^* \xrightarrow{V \rightarrow \infty} \mathbb{F}_{\text{MIO}}^*$

Revisiting to the limit: " $\frac{1}{\sqrt{V}} \mathcal{E} \rightarrow \mathbb{E}$ ".

Recall: $\frac{1}{\sqrt{V}} \mathcal{E}(\mu) = \underbrace{\frac{1}{\sqrt{V}} \sum_{n \in \mathbb{N}_0^d} \mu_n \log \mu_n}_{\mathcal{E}_V^{\Delta}(\mu)} - \underbrace{\frac{1}{\sqrt{V}} \sum_n \mu_n \log w_n}_{\mathcal{E}_V^{\Sigma}(\mu)}.$

Study limit $V \rightarrow \infty, \mu_n \rightarrow \infty, \mu_n/V \rightarrow c_n.$

Sp. $\mu \in \mathcal{P}(\mathbb{N}_0^d)$ which approximates $\rho \in \mathcal{P}(\mathbb{R}_+^d).$

$$\mathcal{E}_V^{\Delta}(\mu) \approx \frac{1}{\sqrt{V}} \int \rho(c) \log \rho(c) - d \frac{\log V}{\sqrt{V}} \xrightarrow{\text{as } V \rightarrow \infty} 0.$$

Now, $-\frac{1}{\sqrt{V}} \log w_n^V = \sum_{i=1}^d \left[-\frac{n_i}{\sqrt{V}} \log \left(\frac{V c_i^*}{V} \right) + \frac{\log n_i!}{\sqrt{V}} + c_i^* \right]$

$$\approx E\left(\frac{\mu}{\sqrt{V}}\right).$$

(Shifting $\log n! \approx n \log n - n$.)

Thus: $\frac{1}{V} E(n) \approx \sum E\left(\frac{w}{V}\right) n_n \approx \int E(c) d\rho(c) = E(\rho)$.

\Rightarrow Lionille eq³ is a good approx to CME for large N .

∫ Lionille does not take volume into account. Can we find a better one which takes this into account. The gradient flow approach is suggestive in this direction.

First guess: set $\tilde{E}_V(\rho) = \int E(c) d\rho(c) + \frac{1}{V} \int \rho(c) \log \rho(c) \cdot dc$.

\Rightarrow associated gradient flow eq⁴.

$$\partial_t \rho = -K(\rho) D \tilde{E}_V(\rho).$$

(Fokker-Planck eq.).

~~A bet~~ (This only considers first term we throw away).

A better approx: \rightarrow Take into account term we throw away from using Sterling's formula in 2nd term.

$$\log n! \approx n \log n - n + \frac{1}{2} \log [2\pi(n + \frac{1}{6})].$$

$$\Rightarrow -\frac{1}{V} \log W_n^V \approx E\left(\frac{n}{V}\right) + \frac{1}{V} G_V\left(\frac{n}{V}\right).$$

$$G_V(c) = -\frac{1}{2} \sum_{\vec{v}} \log(2\pi(v c_i + \frac{1}{6})).$$

⇒ This leads to: $\mathbb{E}_v(\rho) = \mathbb{E}(\rho) + \frac{1}{v} \int \rho \log \rho + \frac{1}{v} \int G_v(c) d\rho(c)$

New equation:

$$\dot{\rho} = -\mathcal{K}(\rho) D \mathbb{E}(\rho).$$

$$\partial_t \rho = -\text{div} \left[\rho(c) R(c) + \frac{1}{v} \mathcal{K}(c) \nabla \rho(c) + \rho(c) A_v(c) \right].$$

where $A_v(c) = \frac{1}{2} \cdot \mathcal{K}(c) \left(\frac{1}{v c_i + \frac{1}{2}} \right)_{i=1, \dots, d}$.