Formal reaction kinetics and related questions seminar series - December 3, 2024

Modeling and control of interconnected CRNs

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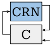
OUTLINE

- Open CRN Models
- Modeling Interconnected CRNs
- Passivity-based Control of CRNs
- Control of Interconnected CRNs

CRNs and Open CRN Models



The dynamic model of a Chemical Reaction Network (CRN) is built upon the following elements:

- *Species:* $\mathcal{S} := \{S_1 \dots S_n\}$ are constituent molecules undergoing (a series of) chemical reactions.
- *Complexes:* $\mathcal{C} := \{\mathcal{C}_1 \dots \mathcal{C}_m\}$ are formally linear combinations of the species, i.e. $\mathcal{C}_k := \sum_{i=1}^{n} \alpha_{k,i} S_i$, where $\alpha_{k,i}$ are non-negative integer stoichiometric coefficients.
- *Reactions:* $\mathcal{R} := \{\mathcal{R}_1 \dots \mathcal{R}_r\}$ where $\mathcal{R}_k : \ \mathcal{C}_i \to \mathcal{C}_j$. Here $\mathcal{C}_i$ is the reactant (or source) complex, and $\mathcal{C}_j$ is the product complex for $k = 1, \dots, r$.
- *Reaction rate coefficients:* $\kappa_k > 0$ that is associated to $\mathcal{R}_k$ for $k = 1, \dots, r$.

Dynamic CRN Model

Under the assumption of mass action law, the dynamic behavior of the species' chemical concentration ($\mathbf{x} = (x_i)^T \in \mathbb{R}^n_{>0}$) during the reactions is given:

$$\dot{\mathbf{x}} = Y A_\kappa \varphi(\mathbf{x}),\ \ \mathbf{x}(0) = \mathbf{x}_0 \in \mathbb{R}^n_{>0}$$

- $Y = [Y_{ij}] \in \mathbb{N}^{n \times m},\ Y_{ij} = \alpha_{ij}$ is the *complex composition matrix*
- $A_\kappa \in \mathbb{R}^{m \times m}$ is the so-called *Kirchhoff matrix* containing the reaction rate coefficients:

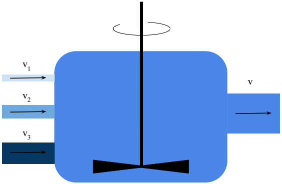
$$A_\kappa(i,j) = \begin{cases} \kappa_{ji}, & \text{for } j \neq i \\ -\sum_{\ell \neq j} \kappa_{j\ell}, & \text{if } j = i. \end{cases}$$

- $\varphi_j(\mathbf{x}) = \prod_{i=1}^n x_i^{\alpha_{ij}}$ for $j = 1, \ldots, m$ are *monomial functions*

Consider *constant volume* $\mathcal{V}$ in the reactor where the reactions take place:

$$\dot{\mathbf{x}} = YA_\kappa\varphi(\mathbf{x}) + \frac{1}{\mathcal{V}}(\mathrm{diag}(v_i)\mathbf{x}_I - v\mathbf{x}), \quad \text{where} \quad v = \sum_{i=1}^{n} v_i.$$

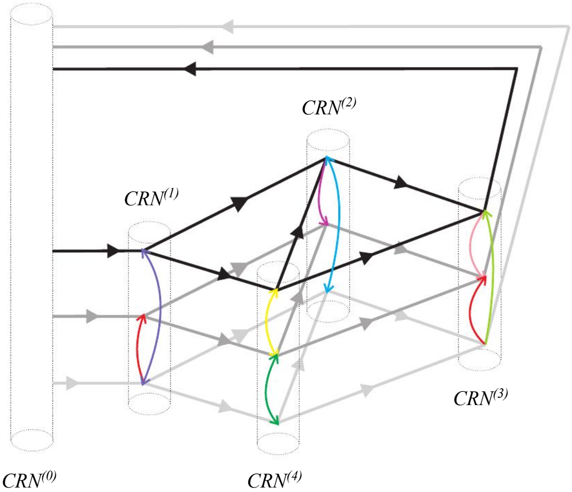
- $\mathbf{x}_I$ - concentration of inlet species
- v - volumetric flow rate

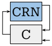


As follows we assume that $\mathcal{V} = 1$.

Physically Motivated Interconnections

Interconnected CRNs





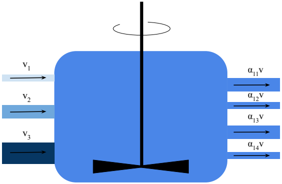
CRN Subsystem Model

The dynamics of the jth open CRN reads as:

$$\dot{\mathbf{x}}^{(j)} = Y^{(j)} A_\kappa^{(j)} \varphi^{(j)}(\mathbf{x}^{(j)}) + \sum_{\ell \in \mathcal{N}_I^{(j)}} \alpha_{\ell j} v_\ell \mathbf{x}^{(\ell)} - v_j \mathbf{x}^{(j)}$$

The outlet of the jth CRN is divided into fractions with the fraction coefficients α_{ji} and are fed into the neighboring CRNs.

$$\sum_{i \in \mathcal{N}_O^{(j)}} \alpha_{ji} = 1$$



Networks of CRNs

Let the *Kirchhoff convection matrix* of the interconnected CRN structure:

$$\mathbf{C}_\kappa = \begin{bmatrix} -v_1 & \alpha_{21}v_2 & \dots & \alpha_{N1}v_N \\ \alpha_{12}v_1 & -v_2 & \dots & \alpha_{N2}v_N \\ \dots & \dots & \dots & \dots \\ \alpha_{1N}v_1 & \alpha_{2N}v_2 & \dots & -v_N \end{bmatrix}$$

- Due to the definition of fraction coefficients, the column sum is zero, e.g. $\sum_{j=2}^{N} \alpha_{1j} = 0$.
- Due to the constant volume assumption, the row sum is zero, e.g. $\sum_{\ell=2}^{N} \alpha_{\ell 1} v_\ell = v_1$.

Subsystem models with *delay*:

$$\dot{\mathbf{x}}^{(j)} = Y^{(j)} A_{\kappa}^{(j)} \varphi^{(j)}(\mathbf{x}^{(j)}) + \sum_{\ell \in \mathcal{N}_I^{(j)}} \alpha_{\ell j} v_{\ell} \mathbf{x}_{Ti}^{(\ell)} - v_j \mathbf{x}^{(j)},$$

- Discrete delay: $x_{Ti}^{(\ell)} = x_i^{(\ell)}(t - T_{\ell j}), \quad T_{\ell j} > 0$ delay value.
- Distributed delay:

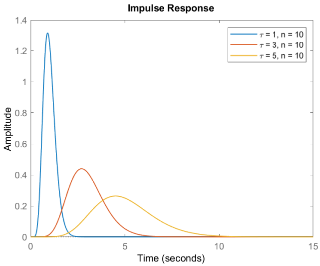
$$x_{Ti}^{(\ell)}(t) = \int_0^{\infty} g(\tau) x_i^{(\ell)}(t-\tau) d\tau = \int_{-\infty}^{t} g(t-\tau) x_i^{(\ell)}(t) d\tau$$

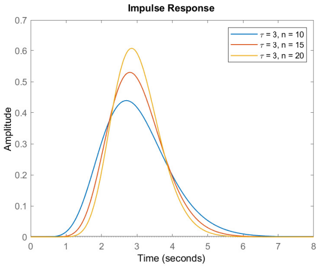
Here $g(\tau)$ is at least piece-wise continuous *kernel function* such that $\int_0^{\infty} g(\tau) d\tau = 1$.

Example: *Gamma-type kernel function*

$$g(t) = \frac{(n/T)^n e^{-nt/T}}{(n-1)!}$$

- T is a scaling parameter (time constant)
- n is a shape parameter (order of the system)





Let a single input – single output *Linear Time-Invariant* (LTI) system with state-space representation

$$\dot{\mathbf{x}}(t) = A\mathbf{x}(t) + Bu(t), \quad \mathbf{x}(0) = \mathbf{0}$$
$$y(t) = C\mathbf{x}(t)$$

where $\mathbf{x}(t) : \mathbb{R} \to \mathbb{R}^n$ are the time-dependent internal states, $y(t), u(t) : \mathbb{R} \to \mathbb{R}$ are the inputs and outputs respectively. The output of the LTI system:

$$y(t) = \int_0^t \underbrace{Ce^{A\tau}B}_{g(\tau)} u(t-\tau)d\tau$$

Here $g(t)$ is the output when the input is the Dirac-delta.

Approximation of Distributed Delay

The output of an LTI system:

$$y(t) = \int_0^t \underbrace{Ce^{A\tau}B}_{g(\tau)} u(t-\tau)d\tau$$

The distributed delay operator:

$$y(t) = \int_0^\infty g(\tau)u(t-\tau)d\tau$$

This suggests that LTI systems can be a (truncated) approximation of the distributed delay terms in dynamic models for a some types of kernel functions.

Example: *Gamma-type kernel function with* $n = 1$

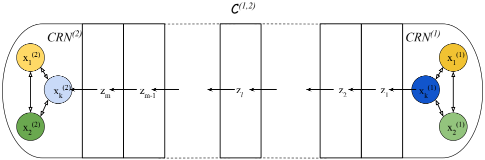
$$y(t) = \int_0^\infty \underbrace{\frac{1}{T} e^{-\tau/T}}_{g(\tau)} u(t-\tau) d\tau$$

The corresponding ODE:

$$\dot{y}(t) = v(u(t) - y(t))$$

Here $v = 1/T$ is the flow rate coefficient.

Example: *Linear chains*



$$\dot{z}_\ell = v(z_{\ell-1} - z_\ell) \qquad \dot{z}_1 = v(x_k^{(1)} - z_1)$$

The corresponding LTI approximate model is a *linear chain model* with the following terms

$$A = \begin{bmatrix} -v & 0 & \dots & 0 & 0 \\ v & -v & \dots & 0 & 0 \\ \dots & \dots & \dots & \dots & \\ 0 & 0 & \dots & v & -v \end{bmatrix} \quad B = \begin{bmatrix} v \\ 0 \\ \dots \\ 0 \end{bmatrix} \quad C^T = \begin{bmatrix} 0 \\ 0 \\ \dots \\ v \end{bmatrix}$$

Diffusive Interconnections

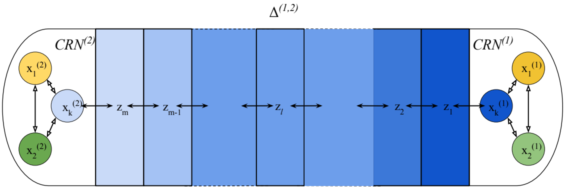
Let two CRNs be connected in the following way:

$$\dot{\mathbf{x}}^{(i)} = Y^{(i)} A_{\kappa}^{(i)} \varphi^{(i)}(\mathbf{x}^{(i)}) + \delta(\mathbf{x}^{(j)} - \mathbf{x}^{(i)})$$

$$\dot{\mathbf{x}}^{(j)} = Y^{(j)} A_{\kappa}^{(j)} \varphi^{(j)}(\mathbf{x}^{(j)}) + \delta(\mathbf{x}^{(i)} - \mathbf{x}^{(j)})$$

The interconnection flow is driven by the concentration (state) difference.
The interconnection term $\delta(\mathbf{x}^{(j)} - \mathbf{x}^{(i)})$ represents the simplest *static approximate diffusion model.*
The parameter $\delta > 0$ is the diffusion rate coefficient.

ODE model for *spatially discretized diffusion*



$$\dot{z}_\ell = \delta(z_{\ell-1} - z_\ell) + \delta(z_{\ell+1} - z_\ell)$$

$$\dot{z}_1 = \delta(z_2 - z_1) + \delta(x_k^{(1)} - z_1)$$

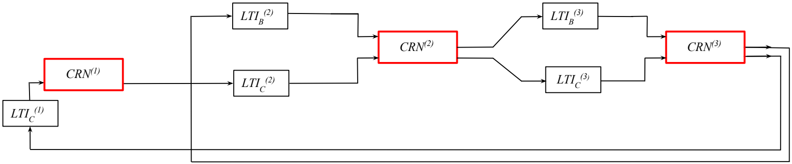
$$\dot{z}_m = \delta(z_{m-1} - z_m) + \delta(x_k^{(2)} - z_m)$$

ODE approximation: Two input – two output LTI system with the following terms

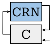
$$\dot{\mathbf{x}} = A\mathbf{x} + B\mathbf{u}, \quad \mathbf{x}(0) = \mathbf{x}_0$$
$$\mathbf{y} = C\mathbf{x}$$

$$A = \begin{bmatrix} -2\delta & \delta & \dots & 0 & 0 \\ \delta & -2\delta & \dots & 0 & 0 \\ \dots & \dots & \dots & \dots & \dots \\ 0 & 0 & \dots & \delta & -2\delta \end{bmatrix} B = \begin{bmatrix} \delta & 0 \\ 0 & 0 \\ \dots & \dots \\ 0 & \delta \end{bmatrix} C^T = \begin{bmatrix} \delta & 0 \\ 0 & 0 \\ \dots & \dots \\ 0 & \delta \end{bmatrix}$$

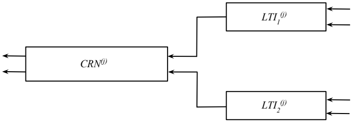
These cases (distributed delay, diffusion) motivate the analysis of such networks of CRNs in which the interconnections are LTI systems.



CRN Model of Interconnected CRNs



Interconnected CRNs by LTI elements



One directional case: a number of m species is transferred among the CRN subsystems.

$$CRN^{(j)} : \dot{\mathbf{x}}^{(j)} = Y^{(j)} A_\kappa^{(j)} \varphi^{(j)}(\mathbf{x}^{(j)}) + \sum_{\ell=1}^{m} F_\ell^{(j)} y_{I\ell}^{(j)} - H^{(j)} \mathbf{x}^{(j)}, \ \mathbf{x}^{(j)}(0) = \mathbf{x}_0^{(j)}$$

$$LTI_\ell^{(j)} : \begin{cases} y_{I\ell}^{(j)} = C_\ell^{(j)} \mathbf{x}_{I\ell}^{(j)} \\ \dot{\mathbf{x}}_{I\ell}^{(j)} = A_\ell^{(j)} \mathbf{x}_{I\ell}^{(j)} + \sum_{i \in \mathcal{N}_I^{(j)}} B_{i\ell}^{(j)} H_\ell^{(i)} \mathbf{x}^{(i)}, \quad \mathbf{x}_{I\ell}^{(j)}(0) = \mathbf{x}_{I\ell 0}^{(j)}. \end{cases}$$

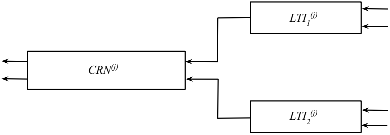
L. Márton, G. Szederkényi, K. M. Hangos, Modeling and control of networked kinetic systems with delayed interconnections, Journal of Process Control, Volume 130, 2023

Assumptions on Connecting LTI Models

- Motivated by the physical examples we assume that $A_\ell^{(j)}$ is Metzler and Hurwitz.
- The inflow rates are considered to be equal to the outflow rates both in the CRNs and LTI connecting subsystems. *Example:* The cumulative inflow rate in the open $CRN^{(j)}$ subsystem is equal to the outflow rate from this subsystem, i.e. the row sum of the matrix below is zero:

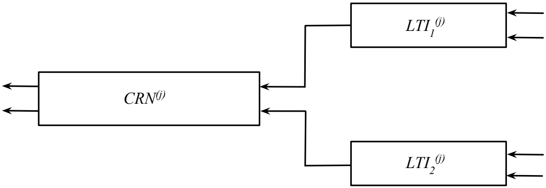
$$\left(F_1^{(j)} C_1^{(j)} \ldots F_\ell^{(j)} C_\ell^{(j)} \ldots F_m^{(j)} C_m^{(j)} \; -H^{(j)} \right)$$

The *extended subsystem* contains a CRN subsystem and the LTI connecting elements from its input neighborhood set.



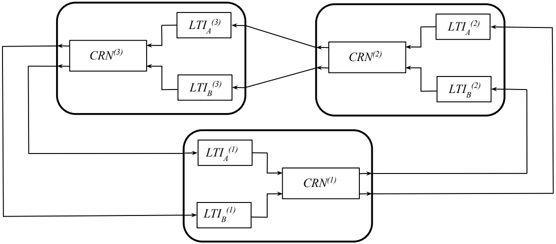
$$\underbrace{\begin{pmatrix} \dot{\mathbf{x}}^{(j)} \\ \dot{\mathbf{x}}_{I1}^{(j)} \\ \dot{\mathbf{x}}_{I2}^{(j)} \end{pmatrix}}_{\dot{\mathbf{X}}^{(j)}} = \underbrace{\begin{pmatrix} Y^{(j)} & O & O & I \\ O & I & O & O \\ O & O & I & O \end{pmatrix}}_{\mathbf{Y}^{(j)}} \underbrace{\begin{pmatrix} A_\kappa^{(j)} & O & O & O \\ O & A_1^{(j)} & O & O \\ O & O & A_2^{(j)} & O \\ O & F_1^{(j)} C_1^{(j)} & F_2^{(j)} C_2^{(j)} & -H^{(j)} \end{pmatrix}}_{\overline{\mathbf{A}}_\kappa^{(j)}} \underbrace{\begin{pmatrix} \varphi^{(j)}(\mathbf{x}^{(j)}) \\ \mathbf{x}_{I1}^{(j)} \\ \mathbf{x}_{I2}^{(j)} \\ \mathbf{x}^{(j)} \end{pmatrix}}_{\Phi^{(j)}(\mathbf{X}^{(j)})}$$

$$+ \underbrace{\begin{pmatrix} O & O & O & O \\ O & O & O & B_{1f}^{(j)} H_1^{(f)} \\ O & O & O & B_{2f}^{(j)} H_2^{(f)} \end{pmatrix}}_{\mathbf{B}_f^{(j)}} \underbrace{\begin{pmatrix} \varphi^{(f)}(\mathbf{x}^{(f)}) \\ \mathbf{x}_{I1}^{(f)} \\ \mathbf{x}_{I2}^{(f)} \\ \mathbf{x}^{(f)} \end{pmatrix}}_{\Phi^{(f)}(\mathbf{X}^{(f)})} + \underbrace{\begin{pmatrix} O & O & O & O \\ O & O & O & B_{1g}^{(j)} H_1^{(g)} \\ O & O & O & B_{2g}^{(j)} H_2^{(g)} \end{pmatrix}}_{\mathbf{B}_g^{(j)}} \underbrace{\begin{pmatrix} \varphi^{(g)}(\mathbf{x}^{(g)}) \\ \mathbf{x}_{I1}^{(g)} \\ \mathbf{x}_{I2}^{(g)} \\ \mathbf{x}^{(g)} \end{pmatrix}}_{\Phi^{(g)}(\mathbf{X}^{(g)})}$$



Generally, the open CRN model of an extended subsystem can be written in the following compact form:

$$\dot{\mathbf{X}}^{(j)} = \mathbf{Y}^{(j)} \overline{\mathbf{A}}_{\kappa}^{(j)} \Phi^{(j)}(\mathbf{X}^{(j)}) + \sum_{i \in \mathcal{N}_I^{(j)}} \mathbf{B}_i^{(j)} \Phi^{(i)}(\mathbf{X}^{(i)})$$

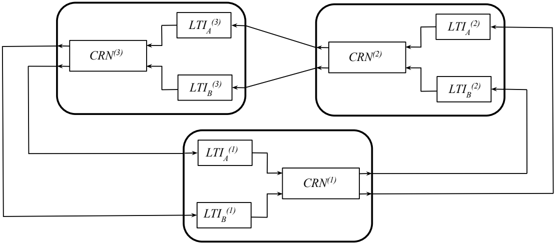


The state-space realization of the networks has the form:

$$\begin{pmatrix} \dot{\mathbf{X}}^{(1)} \\ \dot{\mathbf{X}}^{(2)} \\ \dot{\mathbf{X}}^{(3)} \end{pmatrix} = \begin{pmatrix} \mathbf{Y}^{(1)}\overline{\mathbf{A}}_\kappa^{(1)} & O & \mathbf{B}_3^{(1)} \\ \mathbf{B}_1^{(2)} & \mathbf{Y}^{(2)}\overline{\mathbf{A}}_\kappa^{(2)} & O \\ O & \mathbf{B}_2^{(3)} & \mathbf{Y}^{(3)}\overline{\mathbf{A}}_\kappa^{(3)} \end{pmatrix} \begin{pmatrix} \Phi^{(1)}(\mathbf{X}^{(1)}) \\ \Phi^{(2)}(\mathbf{X}^{(2)}) \\ \Phi^{(3)}(\mathbf{X}^{(3)}) \end{pmatrix}$$

Proposition: The matrices $\mathbf{B}_i^{(j)}$, can be factorized as:

$$\mathbf{B}_i^{(j)} = \mathbf{Y}^{(j)}\mathbf{B}_{Ei}^{(j)}, \quad \text{where} \quad \mathbf{B}_{Ei}^{(j)} = \begin{pmatrix} \mathbf{B}_i^{(j)} \\ O \end{pmatrix}$$

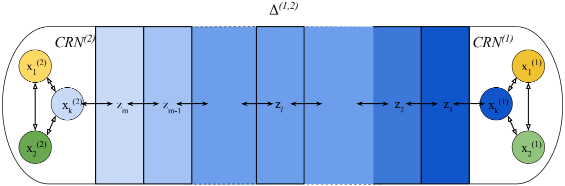


The dynamic network model can be rewritten in the form:

$$\underbrace{\begin{pmatrix} \dot{\mathbf{X}}^{(1)} \\ \dot{\mathbf{X}}^{(2)} \\ \dot{\mathbf{X}}^{(3)} \end{pmatrix}}_{\dot{\mathbf{X}}} = \underbrace{\begin{pmatrix} \mathbf{Y}^{(1)} & O & O \\ O & \mathbf{Y}^{(2)} & O \\ O & O & \mathbf{Y}^{(3)} \end{pmatrix}}_{\mathbf{Y}} \underbrace{\begin{pmatrix} \overline{\mathbf{A}}_\kappa^{(1)} & O & \mathbf{B}_{E3}^{(1)} \\ \mathbf{B}_{E1}^{(2)} & \overline{\mathbf{A}}_\kappa^{(2)} & O \\ O & \mathbf{B}_{E2}^{(3)} & \overline{\mathbf{A}}_\kappa^{(3)} \end{pmatrix}}_{\mathbf{A}_\kappa} \underbrace{\begin{pmatrix} \Phi^{(1)}(\mathbf{X}^{(1)}) \\ \Phi^{(2)}(\mathbf{X}^{(2)}) \\ \Phi^{(3)}(\mathbf{X}^{(3)}) \end{pmatrix}}_{\Phi(\mathbf{X})}$$

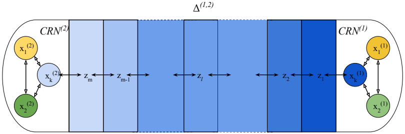
The model of the interconnected system has CRN form:

$$\dot{\mathbf{X}} = \mathbf{Y}\mathbf{A}_\kappa \Phi(\mathbf{X}).$$



$$\dot{z}_1 = \delta(z_2 - z_1) + \delta(x_k^{(1)} - z_1)$$
$$\dot{z}_m = \delta(z_{m-1} - z_m) + \delta(x_k^{(2)} - z_m)$$

The highlighted terms are included in the CRN models at the boundaries. Let the terms of the modified model be $(\overline{Y}^{(1)}, \overline{A}_{\kappa}^{(1)})$, and $(\overline{Y}^{(2)}, \overline{A}_{\kappa}^{(2)})$ respectively.



$$\mathbf{x} = \begin{bmatrix} \mathbf{x}^{(1)} \\ \mathbf{z} \\ \mathbf{x}^{(2)} \end{bmatrix} \quad \mathbf{Y} = \begin{bmatrix} \overline{Y}^{(1)} & 0 & 0 \\ 0 & I & 0 \\ 0 & 0 & \overline{Y}^{(2)} \end{bmatrix} \quad \mathbf{A}_\kappa = \begin{bmatrix} \overline{A}_\kappa^{(1)} & Q_{11} & 0 \\ Q_{12} & A_\Delta & Q_{21} \\ 0 & Q_{22} & \overline{A}_\kappa^{(2)} \end{bmatrix}$$

$$Q_{11} = \begin{bmatrix} 0 & 0 \\ \dots & \dots \\ 0 & \delta \end{bmatrix} \quad Q_{12} = \begin{bmatrix} 0 & \dots & 0 \\ 0 & \dots & \delta \end{bmatrix} \quad A_\Delta = \begin{bmatrix} -2\delta & \delta & \dots & 0 & 0 \\ \delta & -2\delta & \dots & 0 & 0 \\ \dots & \dots & \dots & \dots & \dots \\ 0 & 0 & \dots & \delta & -2\delta \end{bmatrix}$$

$$Q_{22} = \begin{bmatrix} 0 & 0 \\ \dots & \dots \\ \delta & 0 \end{bmatrix} \quad Q_{21} = \begin{bmatrix} 0 & \dots & \delta \\ 0 & \dots & 0 \end{bmatrix}$$

The global model of the interconnected system:

$$\dot{\mathbf{x}} = \mathbf{Y}\mathbf{A}_\kappa \varphi(\mathbf{x})$$

Control – Theory of Passive Systems

Let the open dynamic system:

$$\dot{\mathbf{x}} = \mathbf{f}(\mathbf{x}, \mathbf{u}), \quad \mathbf{x}(0) = \mathbf{x}_0$$
$$\mathbf{y} = \mathbf{h}(\mathbf{x})$$

- *Control problem*: Design $\mathbf{u}$ in the function of $\mathbf{y}$ such to achieve desired dynamic and steady-state proprieties for the (controlled) system states.
- Example: all the states remain bounded and the output converge to a prescribed constant *setpoint*.

$$\lim_{t \to \infty} \mathbf{y} = \mathbf{y}_{SP}$$

Let the same open dynamic system:

$$\dot{\mathbf{x}} = \mathbf{f}(\mathbf{x}, \mathbf{u}), \quad \mathbf{x}(0) = \mathbf{x}_0$$
$$\mathbf{y} = \mathbf{h}(\mathbf{x})$$

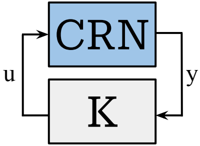
- Static *feedback control*:

$$\mathbf{u} = \mathbf{u}(\mathbf{y})$$

- Example: *linear control*

$$\mathbf{u} = -K\mathbf{y}, \quad K = (k_{ij})$$

- The controlled system is autonomous: $\dot{\mathbf{x}} = \mathbf{f}(\mathbf{x}, \mathbf{u}(\mathbf{h}(\mathbf{x})))$



Let a dynamic system

$$\dot{\mathbf{x}} = \mathbf{f}(\mathbf{x}), \quad \mathbf{x}(0) = \mathbf{x}_0,$$

Notions from Lyapunov's stability theory:

- Let $\mathbf{x}^*$ be an *equilibrium point* of the system, i.e. $\mathbf{f}(\mathbf{x}^*) = \mathbf{0}$
- The equilibrium point $\mathbf{x}^* = \mathbf{0}$ is *asymptotically stable* if $\forall \rho > 0 \; \exists r > 0$ such that $\|\mathbf{x}_0\| < r$ implies $\|\mathbf{x}(t)\| < \rho, \quad \forall t$ and $lim_{t \to \infty} \|\mathbf{x}(t)\| = 0$.
- *Lyapunov's direct method:* Let a *storage function* $S(\mathbf{x}) : \mathbb{R}^n \to \mathbb{R}$ assigned to the system such that $S(\mathbf{x}) > 0, \forall \mathbf{x} \neq 0$ and $S(\mathbf{0}) = 0$. If $\dot{S}(\mathbf{x}) < 0, \forall \mathbf{x} \neq 0$, then the system is asymptotically stable.
  Note that for uniform and global stability decrescency or radial unboundedness proprieties of S are required.

Let an *open* dynamic system

$$\dot{\mathbf{x}} = \mathbf{f}(\mathbf{x}, \mathbf{u}), \quad \mathbf{x}(0) = \mathbf{x}_0$$
$$\mathbf{y} = \mathbf{h}(\mathbf{x})$$

$\mathbf{u}, \mathbf{y} : \mathbb{R} \to \mathbb{R}^m$ are the (control) input and output vectors.

- The system is *passive* if $\exists \beta$ constant such that

$$\int_0^t \mathbf{y}^T \mathbf{u} d\tau \geq \beta \;\; \forall \; \mathbf{u}(t).$$

- If there exists a continuously differentiable storage function $S(\cdot) \geq 0$ such that

$$S(t) \leq \int_0^t \mathbf{y}^T \mathbf{u} d\tau + S(t=0) \;\; \text{or} \;\; \dot{S}(t) \leq \mathbf{y}^T \mathbf{u},$$

  then the system is passive.

Let an *input-affine* system:

$$\dot{\mathbf{x}} = \mathbf{f}(\mathbf{x}) + G(\mathbf{x})\mathbf{u}, \quad \mathbf{x}(0) = \mathbf{x}_0$$
$$\mathbf{y} = \mathbf{h}(\mathbf{x})$$

$G(\mathbf{x}) : \mathbb{R}^n \to \mathbb{R}^{n \times m}$ is a state-dependent input matrix.

- If there exists a continuously differentiable storage function $S(\cdot) \geq 0$, $S(\mathbf{0}) = 0$ such that

$$\frac{\partial S}{\partial \mathbf{x}} \mathbf{f}(\mathbf{x}) \leq 0$$
$$\text{and} \qquad \frac{\partial S}{\partial \mathbf{x}} G(\mathbf{x}) = \mathbf{h}(\mathbf{x})$$

  then the system is passive.

Let the dynamic system:

$$\dot{\mathbf{x}} = \mathbf{f}(\mathbf{x}, \mathbf{u}), \quad \mathbf{x}(0) = \mathbf{x}_0$$
$$\mathbf{y} = \mathbf{h}(\mathbf{x})$$

- The system is *zero state detectable* if $\mathbf{y} = \mathbf{0}$ and $\mathbf{u} = \mathbf{0}$ implies that the steady-state of $\mathbf{x} = \mathbf{0}$.
- If the system is zero state detectable and *passive*, then the linear diagonal control $\mathbf{u} = -K\mathbf{y}$ *asymptotically stabilizes* the equilibrium state $\mathbf{0}$. Here $K = \text{diag}(k_i),\ k_i > 0$.

Feedback Passivation

Let the input-affine system:

$$\dot{\mathbf{x}} = \mathbf{f}(\mathbf{x}) + G(\mathbf{x})\mathbf{u}, \quad \mathbf{x}(0) = \mathbf{x}_0$$
$$\mathbf{y} = \mathbf{h}(\mathbf{x})$$

- Let the control transformation:

$$\mathbf{u} = \mathbf{f}_p(\mathbf{x}) + G_p(\mathbf{x})\mathbf{u}_p$$

- The system with control:

$$\dot{\mathbf{x}} = \underbrace{\mathbf{f}(\mathbf{x}) + G(\mathbf{x})\mathbf{f}_p(\mathbf{x})}_{f_c(\mathbf{x})} + \underbrace{G(\mathbf{x})G_p(\mathbf{x})}_{G_c(\mathbf{x})}\,\mathbf{u}_p,$$
$$\mathbf{y} = \mathbf{h}(\mathbf{x})$$

- The selection of the output ($\mathbf{y}$) and the construction of the feedback transformation $\mathbf{u}$ called *feedback passivation*.

Passivity-based Control of CRNs

Complex Balanced CRNs

Let the CRN model

$$\dot{\mathbf{x}} = Y A_\kappa \varphi(\mathbf{x}),\ \mathbf{x}(0) = \mathbf{x}_0$$

- An equilibrium point of a CRN's dynamic model satisfies

$$Y A_\kappa \varphi(\mathbf{x}^*) = \mathbf{0}$$

- The CRN is called *complex balanced* if

$$A_\kappa \varphi(\mathbf{x}^*) = \mathbf{0}.$$

  i.e. the signed sum of incoming and outgoing reaction rates at equilibrium is zero for each complex.

- If the complex balanced property is satisfied for an equilibrium point, then it is fulfilled for all the other equilibrium points.

Let the open CRN model

$$\dot{\mathbf{x}} = Y A_\kappa \varphi(\mathbf{x}) + \mathbf{u}, \quad \mathbf{x}(0) = \mathbf{x}_0$$

The model is passive from the input $\mathbf{u}$ to the output

$$\mathbf{y} = \mathrm{Ln}(\mathbf{x}) - \mathrm{Ln}(\mathbf{x}^*)$$

with respect to the storage function

$$S(\mathbf{x}) = \sum_{i=1}^{n} \left[x_i \left(\ln \frac{x_i}{x_i^*} - 1 \right) + x_i^* \right].$$

if the CRN is complex balanced.

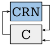
L. Márton, K. M. Hangos, G. Szederkényi, Disturbance Attenuation via Nonlinear Feedback for Chemical Reaction Networks, IFAC-PapersOnLine, Vol. 53, No. 2, 2020, pp 11497-11502.

Let the open CRN model

$$\dot{\mathbf{x}} = Y A_\kappa \varphi(\mathbf{x}) + B\mathbf{u} + \mathbf{d}, \quad \mathbf{x}(0) = \mathbf{x}_0$$

Here $\mathbf{d}$ is an unknown *disturbance* rate, B is the input matrix.
The control problem:

- Let a *setpoint* concentration $\mathbf{x}_{SP} > \mathbf{0}$ chosen from the equilibrium point set of the CRN.
- If $\mathbf{d} = \mathbf{0}$, design the control $\mathbf{u}$ such that $lim_{t\to\infty}\mathbf{x} = \mathbf{x}_{SP}$ or equivalently $\lim_{t\to\infty}\mathbf{y} = \lim_{t\to\infty}(\mathrm{Ln}(\mathbf{x}) - \mathrm{Ln}(\mathbf{x}_{SP})) = \mathbf{0}$.
- If $\mathbf{d} \neq \mathbf{0}$, ensure *disturbance attenuation*, i.e. “minimize” the effect of $\mathbf{d}$ on $\mathbf{y}$.



The control has a passivation feedback term and a setpoint tracking term:

$$\mathbf{u} = \mathbf{u}_p + \mathbf{u}_t$$

- The first term ($\mathbf{u}_p$) modifies the rate such that the dynamics of the controlled CRN “mimics” the dynamics of a complex balanced CRN with the same monomial vector.
- The second term ($\mathbf{u}_p$) ensures the setpoint tracking of the CRN in the presence of disturbances.

Design of Passivation Feedback $\mathbf{u}_p$

- First, design a reference Kirchhoff matrix $A_{\kappa ref}$ such that

$$A_{\kappa ref}\varphi(\mathbf{x}_{SP}) = \mathbf{0}$$

- Let the passivation feedback in the form:

$$\mathbf{u}_p = K_p \varphi(\mathbf{x})$$

- We can design such feedback iff

$$BB^{\dagger}Y\left(A_{\kappa ref} - A_{\kappa}\right) = Y\left(A_{\kappa ref} - A_{\kappa}\right)$$

- If the solvability condition holds, the solution is

$$K_p = B^{\dagger}Y\left(A_{\kappa ref} - A_{\kappa}\right) + \left(I - B^{\dagger}B\right)Z$$

- Let equilibrium state $\mathbf{x}^{(j)*} = (x_1^{(j)*} \; x_2^{(j)*} \; x_3^{(j)*})^T \in \mathbb{R}^3_{>0}$ and the vector of monomial functions:

$$\varphi^{(j)} : \mathbb{R}^3_{\geq 0} \to R^2_{\geq 0} \quad \varphi^{(j)}(\mathbf{x}^{(j)}) = \begin{pmatrix} x_1^{(j)} x_2^{(j)} \\ x_3^{(j)} \end{pmatrix}$$

- Let a diagonal matrix P_j in the form:

$$P_j = \begin{pmatrix} x_1^{(j)*} x_2^{(j)*} & 0 \\ 0 & x_3^{(j)*} \end{pmatrix}.$$

- Let $a_j > 0$ and

$$A_0^{(j)} = \begin{pmatrix} -1 & 1 \\ 1 & -1 \end{pmatrix}.$$

- The reference Kirchhoff matrix can be constructed as:

$$A_{\kappa ref}^{(j)} = a_j A_0^{(j)} P_j^{-1} = \begin{pmatrix} -\frac{a_j}{x_1^{(j)*} x_2^{(j)*}} & \frac{a_j}{x_3^{(j)*}} \\ \frac{a_j}{x_1^{(j)*} x_2^{(j)*}} & -\frac{a_j}{x_3^{(j)*}} \end{pmatrix}.$$

Setpoint Tracking Design ($\mathbf{u}_t$)

Let $\mathbf{u}_t = -K_t \mathbf{y} = -K_t \left(\mathrm{Ln}(\mathbf{x}) - \mathrm{Ln}(\mathbf{x}^*) \right)$.

- With this control, the CRN model has the form:

$$\dot{\mathbf{x}} = Y A_{\kappa ref} \varphi(\mathbf{x}) - K_t \mathbf{y} + \mathbf{d}.$$

- The time-derivative of the storage function satisfies

$$\dot{S} \leq \mathbf{y}^T (-K_t \mathbf{y} + \mathbf{d})$$

- If the controller gain matrix is chosen such that $k_t > \frac{1}{2}\left(1 + \frac{1}{\gamma}\right)$, where $\gamma > 0$ is the *prescribed disturbance attenuation level*, then the disturbance attenuation control objective $\int_0^t \mathbf{y}^T \mathbf{y} \leq \gamma \int_0^t \mathbf{d}^T \mathbf{d} + S(0)$ is achieved.

Realistic implementation of the control:

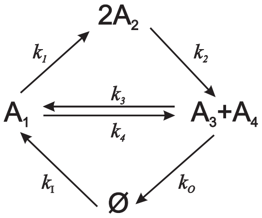
$$\mathbf{u} = \mathbf{u}_p + \mathbf{u}_t =: \mathrm{diag}(v_i)\mathbf{x}_I - v\mathbf{x}$$

The input concentration ($\mathbf{x}_I > \mathbf{0}$) is manipulated by the control mechanism.

Ensuring *positivity for* $\mathbf{x}_I$ *by manipulating the volumetric flow rate* v:

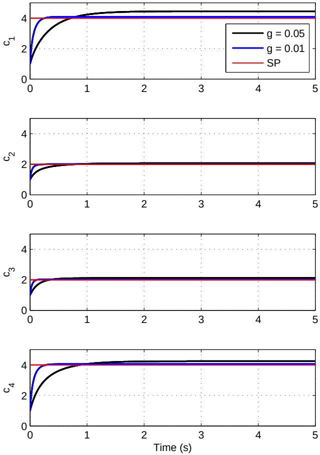
- Technical assumption 1: $0 < \varepsilon < x_i < x_M$
- Technical assumption 2: $-u_M < u_i < u_M$
- Design v_i such that $x_{Ii} = \frac{1}{v_i}(u_i + v x_i) > 0$ regardless of the sign of u_i.

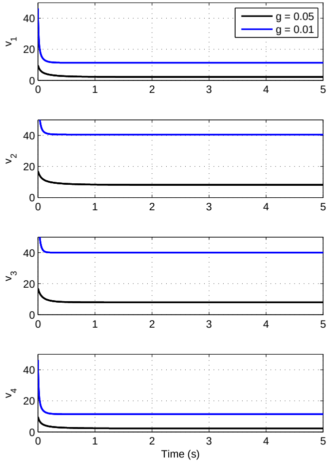
CRN with constant inflows and mass action kinetics outflows



$$\begin{pmatrix} \dot{x}_1 \\ \dot{x}_2 \\ \dot{x}_3 \\ \dot{x}_4 \end{pmatrix} = \underbrace{\begin{pmatrix} -(k_1+k_4) & 0 & k_3 \\ 2k_1 & -2k_2 & 0 \\ k_4 & k_2 & -k_3 \\ k_4 & k_2 & -k_3 \end{pmatrix}}_{M} \begin{pmatrix} x_1 \\ x_2^2 \\ x_3 x_4 \end{pmatrix} - \underbrace{\begin{pmatrix} 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & k_O \\ 0 & 0 & k_O \end{pmatrix}}_{K_O} \begin{pmatrix} x_1 \\ x_2^2 \\ x_3 c_4 \end{pmatrix} + \underbrace{\begin{pmatrix} k_I \\ k_I \\ 0 \\ 0 \end{pmatrix}}_{K_I \mathbf{1}} + \underbrace{\begin{pmatrix} v_1 x_{I1} - v x_1 \\ v_2 x_{I2} - v x_2 \\ v_3 x_{I3} - v x_3 \\ v_4 x_{I4} - v x_4 \end{pmatrix}}_{V\mathbf{x}_I - v\mathbf{x}}.$$

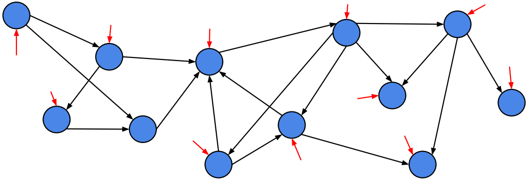
Simulation Results - Trajectories with Control




g = 0.05
g = 0.01
v1
v2
v3
v4
0
20
40
0
1
2
3
4
5
Time (s)

Control of Interconnected CRNs

Synchronization in Passive Networks

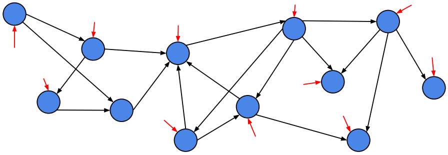


Let a network of subsystems

$$\dot{\mathbf{x}}^{(j)} = \mathbf{f}^{(j)}(\mathbf{x}^{(j)}) + G^{(j)}(\mathbf{x}^{(j)})\mathbf{u}^{(j)}, \quad \mathbf{x}^{(j)}(0) = \mathbf{x}_0^{(j)}$$
$$\mathbf{y}^{(j)} = \mathbf{h}^{(j)}(\mathbf{x}^{(j)})$$

The outputs of the network's subsystems are *synchronized* if

$$lim_{t\to\infty}\|\mathbf{y}^{(\ell)}(t) - \mathbf{y}^{(j)}(t)\| = 0, \quad \forall\ \ell, j$$



The network is synchronized if:

- All the subsystems are passive.
- The underlying graph of the network is strongly connected (there is a path from each vertex to each vertex)
- The inputs of the subsystems are:

$$\mathbf{u}^{(j)}(t) = k\left(\sum_{\ell\in\mathcal{N}_I^{(j)}} \mathbf{y}^{(\ell)}(t) - \mathbf{y}^{(j)}(t)\right), \quad k > 0$$

- CRN subsystem model:

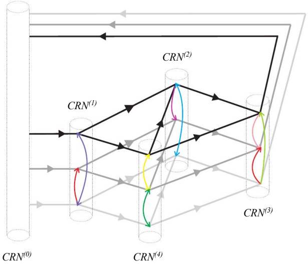
$$\frac{d\mathbf{x}^{(j)}}{dt} = Y^{(j)} A_{\kappa}^{(j)} \varphi^{(j)}(\mathbf{x}^{(j)}) + \underbrace{\sum_{\ell \in \mathcal{N}_{IN}^{(j)}} a_{\ell j} v_{\ell} \mathbf{x}^{(\ell)}(t - T_{\ell j})}_{Interconnection\ Inflow} + \underbrace{a_{Lj} v_j \mathbf{x}_C^{(j)}}_{Control\ Inflow} - \underbrace{v_{Oj} \mathbf{x}^{(j)}}_{Outflow} + \underbrace{\mathbf{d}^{(j)}}_{Disturbance}$$

- *Bounded disturbance* is assumed

$$\|\mathbf{d}^{(j)}\|_2 \leq d_M^{(j)}$$

- Network structure defined by the *Kirchhoff matrix*

$$\mathbf{C}_{\kappa} = \begin{bmatrix} -v_0 & \alpha_{10} v_1 & \dots & \alpha_{N0} v_N \\ \alpha_{01} v_0 & -v_1 & \dots & \alpha_{N1} v_N \\ \dots & \dots & \dots & \dots \\ \alpha_{0N} v_0 & \alpha_{1N} v_1 & \dots & -v_N \end{bmatrix}$$



The CRN network is connected through constant *inflows (raw material)* and constant *outflows (products)* to the *Environment*. Cumulative inflow rates are equal to cumulative outflow rates.

$$v_0 = \sum_{\ell=0}^{N} \alpha_{0l} v_\ell$$

Assume that the underlying graph of the interconnected system has such a *spanning tree* whose root is the Environment.

- Let the setpoint of the jth CRN be $\mathbf{x}_{SP}^{(j)}$ that belongs to the equilibrium point set of the jth CRN.

- Design the control input $\mathbf{x}_C$ for each CRN such to assure that

$$lim_{t\rightarrow\infty}\|\mathbf{y}^{(j)}(t)\| \leq \varepsilon, \ \ \forall\, \ell, j$$

where $\varepsilon > 0$ is a given *control precision* and
$\mathbf{y}^{(j)} = \mathrm{Ln}(\mathbf{x}^{(j)}) - \mathrm{Ln}(\mathbf{x}_{SP}^{(j)})$

L. Márton, G. Szederkényi, K. M. Hangos, Distributed control of interconnected Chemical Reaction Networks with delay, Journal of Process Control, Vol. 71, 2018, pp. 52-62

Let the control $\mathbf{x}_C^{(j)} = \mathbf{x}_p^{(j)} + \mathbf{x}_t^{(j)} + \mathbf{x}_{ff}^{(j)}$

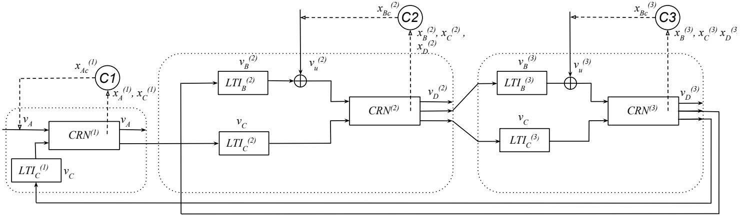
- $\mathbf{x}_p^{(j)} = K_p \varphi(\mathbf{x}^{(j)})$ - Local feedback to *ensure passivity.*
- $\mathbf{x}_t^{(j)} = -K_t \mathbf{y}^{(j)}$ - Setpoint tracking term.
- Feedforward term ($\mathbf{x}_{ff}^{(j)}$) - Compensates for the difference between the physical interconnections and passive outputs.

$$\mathbf{x}_{ff}^{(j)} = \frac{1}{\alpha_{Cj} v_j} \left(\sum_{\ell \in \mathcal{N}_{IN}^{(j)}} \alpha_{\ell j} v_\ell \left(\mathbf{y}^{(\ell)}(t - T_{\ell j}) - \mathbf{x}^{(\ell)}(t - T_{\ell j}) \right) - v_j \left(\mathbf{y}^{(j)} - \mathbf{x}^{(j)} \right) \right).$$

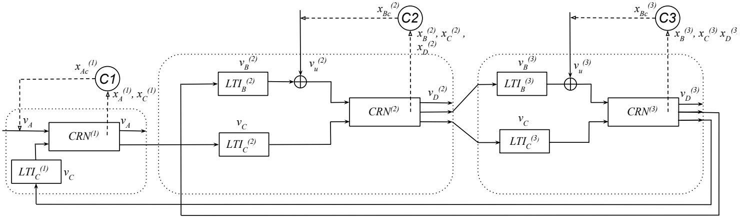
- Consider the Lyapunov-Krasovskii functional:

$$S_\Sigma = 2\sum_{j=0}^{N} S^{(j)} + \sum_{j=0}^{\mathcal{C}}\sum_{\ell=0}^{N} \alpha_{\ell j} v_\ell \int_{t-T_{\ell j}}^{t} \mathbf{y}^{(\ell)T}\mathbf{y}^{(\ell)} d\xi.$$

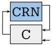
- If the controller gain matrix K_t is chosen such that $k_{ti} > 1 + \frac{d_{Mi}}{\varepsilon}$, it can be shown that $\dot{S}_\Sigma < 0$ for $\|\mathbf{y}^{(j)}(t)\| \geq \varepsilon$.



- The process system is designed to extract carbon dioxide (CO_2) from flue gases using lime hydrate ($Ca(OH)_2$).
- Unit 1 is for absorbing the carbon dioxide (specie A) in water that is in great excess and produces dissolved H_2CO_3 (carbonic acid - specie C): $A \xrightarrow{k^{(1)}} C$
- Units 2 and 3 realize a two-stage extractor where specie B (lime hydrate, $Ca(OH)_2$) and specie C (dissolved H_2CO_3) react to form specie D (rag-stone, $CaCO_3$): $B + C \xrightarrow{k} D$



- The control aim is to set the outflow concentration of specie C in $CRN^{(1)}$ high enough to consume most of the specie A (the carbon dioxide) in the inflow gas. Then we set the outflow concentration of specie C in $CRN^{(2)}$ and $CRN^{(3)}$ gradually smaller such that the resulting specie D can be safely withdrawn as a solid from these units.



Example ($CRN^{(2)}$):

- Control-oriented modeling

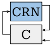
$$\left\{ \begin{array}{ll} \dot{x}_C^{(2)} &= -k^{(2)} x_B^{(2)} x_C^{(2)} + v_C y_{IC}^{(2)} - v_C x_C^{(2)} \\ \dot{x}_B^{(2)} &= -k^{(2)} x_B^{(2)} x_C^{(2)} + v_B^{(2)} y_{IB}^{(2)} - v_B^{(3)} x_B^{(2)} + v_u^{(2)} x_{Bc}^{(2)} \\ \dot{x}_D^{(2)} &= \ \ k^{(2)} x_B^{(2)} x_C^{(2)} - v_D^{(2)} x_D^{(2)} \end{array} \right. \quad , \quad v_B^{(2)} + v_u^{(2)} = v_B^{(3)}$$

- The steady-state value of the specie B can be computed in function of the prescribed steady-state values of specie C:

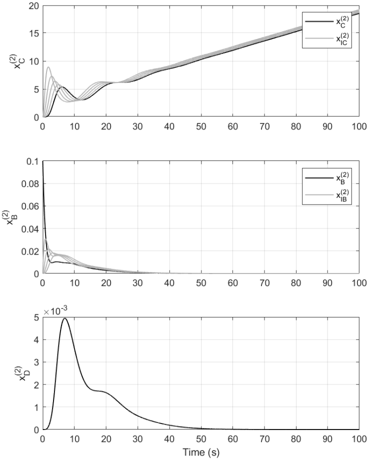
$$k^{(2)} x_{BSP}^{(2)} x_{CSP}^{(2)} = v_C (x_{CSP}^{(1)} - x_{CSP}^{(2)})$$

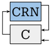
- The control input is the inlet concentration $x_{Bc}^{(2)}$:

$$x_{Bc}^{(2)} = \frac{v_D^{(2)}}{v_u^{(2)}} x_D^{(2)} + \frac{k_p^{(2)}}{v_u^{(2)}} \left(ln(x_{BSP}^{(2)}) - ln(x_B^{(2)}) \right) - \frac{v_B^{(2)}}{v_u^{(2)}} x_{BSP}^{(3)} + \frac{v_B^{(3)}}{v_u^{(2)}} x_{BSP}^{(2)}$$

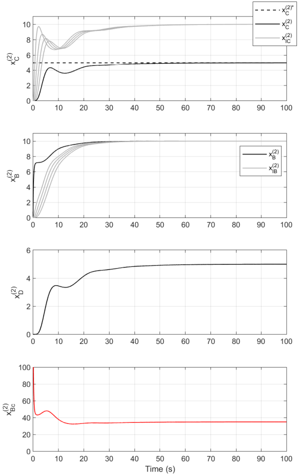


Non-controlled states in subsystem 2





Controlled states and control signal of subsystem 2



- The global models of some interconnected CRNs with physically motivated interconnections (distributed delay, diffusion) also have a CRN model form with mass-action kinetics. This can be explored for analysis and control of these systems.
- The passivity theory is a convenient approach to develop setpoint tracking controllers for CRNs in the presence of disturbances.
- The synchronization problem of passive systems can also be applied to develop control methods for interconnected CRNs.
- The passivity-based control design approach is also suitable to control interconnected Lotka-Volterra systems see e.g. DOI: 10.1088/1361-6544/abd52b