Modeling and analysis of dynamical distribution networks

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joint work with Bayu Jayawardhana, Shodhan Rao, Jay Wei

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Dynamical distribution networks are everywhere

Power networks, supply chains, gas distribution networks, biochemical reaction networks, · · ·.

**Network flow theory** is concerned with the static throughput aspects: what is the maximal throughput under flow capacity constraints?

On the other hand: **network dynamics** is usually focusing on closed systems: no inflows and outflows.

Clear need to merge static, optimal, **throughput analysis** with **dynamics**.

This talk:
(i) Flow control of distribution networks with unknown in/outflows.
(ii) Chemical reaction networks motivated by systems biology.
Outline

1. Flow control of distribution networks
2. Chemical reaction networks: basic structure
3. Detailed balanced mass action kinetics
4. Equilibrium analysis and stability
5. Open chemical reaction networks
6. Model reduction of chemical reaction networks
7. Conclusions and outlook
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Example: hydraulic network

- $x_i$ is fluid storage in $i$-th reservoir, $u_j$ is flow in $j$-th pipe.
- Dynamical equations

\[
\begin{bmatrix}
  \dot{x}_1 \\
  \dot{x}_2 \\
  \dot{x}_3 
\end{bmatrix} =
\begin{bmatrix}
  -1 & 0 & 1 \\
  1 & -1 & 0 \\
  0 & 1 & -1 
\end{bmatrix}
\begin{bmatrix}
  u_1 \\
  u_2 \\
  u_3 
\end{bmatrix}
\]

- $B$ is incidence matrix of the graph: $b_{ij} = -1$ if the $i$-th vertex is tail, or $+1$ if it is head of the $j$-th edge

\[\dot{x} = Bu\]
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With inflows and outflows

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-1 & 0 & 1 \\
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\end{bmatrix}
\begin{bmatrix}
u_1 \\
u_2 \\
u_3
\end{bmatrix} +
\begin{bmatrix}
0 \\
1 \\
-1
\end{bmatrix} d
\]

\(d = d_1 = d_2\) is necessary condition for existence of equilibrium. In general:

\[
\dot{x} = Bu + Ed, \quad \text{im } E \subset \text{im } B
\]

Since \(1^T B = 0\) this implies \(1^T E = 0\).
Port-Hamiltonian system defined on the graph

For any Hamiltonian $H(x)$ consider the port-Hamiltonian system

$$\dot{x} = Bu, \quad x \in \mathbb{R}^n \text{ (vertices)}, \quad u \in \mathbb{R}^m \text{ (edges)}$$

$$y = B^T \frac{\partial H}{\partial x}(x), \quad y \in \mathbb{R}^m \text{ (edges)}$$

satisfying the energy balance

$$\frac{dH}{dt} = y^T u$$

The control $u = -y$ results in

$$\frac{d}{dt} H = -\frac{\partial H^T}{\partial x}(x)BB^T \frac{\partial H}{\partial x}(x) \leq 0$$

For $H(x) = \frac{1}{2} \|x\|^2$ this is decentralized control $u = -B^T x$.

If the graph is connected then the system will converge to consensus

$$x_1 = x_2 = \cdots = x_n$$
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If the graph is connected then the system will converge to consensus

$$x_1 = x_2 = \cdots = x_n$$
Inflows and outflows

\[
\begin{align*}
\dot{x} &= Bu + Ed, \quad x \in \mathbb{R}^n, u \in \mathbb{R}^m \\
y &= B^T x, \quad y \in \mathbb{R}^m
\end{align*}
\]

Proportional output feedback is not sufficient anymore; we consider a proportional-integral controller structure

\[
\begin{align*}
\dot{x}_c &= y \\
u &= -y - x_c
\end{align*}
\]

The resulting closed loop is

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\begin{bmatrix}
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\begin{bmatrix}
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B^T & 0
\end{bmatrix}
\begin{bmatrix}
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x_c
\end{bmatrix} + 
\begin{bmatrix}
E \\
0
\end{bmatrix} d
\]

which is again a port-Hamiltonian system with total Hamiltonian

\[
\frac{1}{2}(\|x\|^2 + \|x_c\|^2)
\]
Inflows and outflows

\[ \dot{x} = Bu + Ed, \quad x \in \mathbb{R}^n, u \in \mathbb{R}^m \]
\[ y = B^T x, \quad y \in \mathbb{R}^m \]

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\frac{1}{2} (\|x\|^2 + \|x_c\|^2)
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Flow control of distribution networks

Inflows and outflows

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which is again a port-Hamiltonian system with total Hamiltonian

\[
\frac{1}{2} (\|x\|^2 + \|x_c\|^2)
\]
Theorem

Suppose the graph is connected, and \( \text{im } E \subset \text{im } B \). Then the trajectories of the closed-loop system for constant \( d \) will converge to an element of the set

\[
E = \{(x, x_c) \mid x = \alpha \mathbf{1}, \alpha \in \mathbb{R}, Bx_c = Ed\}
\]

with the limit value \( \alpha \) uniquely determined by the initial condition \( x(0) \).

Proof

Modified Hamiltonian can be used as Lyapunov function, i.e.

\[
V = \frac{1}{2}(\|x\|^2 + \|x_c - \bar{x}_c\|^2)
\]

\[
\frac{d}{dt} V = -x^T BB^T x \leq 0
\]

Conclusion follows by LaSalle’s invariance principle.
Theorem
Suppose the graph is connected, and $\text{im } E \subset \text{im } B$. Then the trajectories of the closed-loop system for constant $d$ will converge to an element of the set

$$\mathcal{E} = \{(x, x_c) \mid x = \alpha \mathbf{1}, \alpha \in \mathbb{R}, Bx_c = Ed\}$$

with the limit value $\alpha$ uniquely determined by the initial condition $x(0)$.

Proof
Modified Hamiltonian can be used as Lyapunov function, i.e.

$$V = \frac{1}{2}(\|x\|^2 + \|x_c - \bar{x}_c\|^2)$$

$$\frac{d}{dt} V = -x^T BB^T x \leq 0$$

Conclusion follows by LaSalle’s invariance principle.
Stability results can be extended to systems with flow constraints

\[ a_j \leq u_j \leq b_j, \quad j = 1, \ldots, m \]

If \( a_j < 0, \ b_j > 0 \) no main structural changes.

For \( a_j = 0, \ b_j > 0 \) (unidirectional flow) there are important changes.

See the papers quoted at the end of the talk, and a paper by J. Wei (to be submitted).
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3. Detailed balanced mass action kinetics
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Consider a chemical reaction network with \( m \) chemical species, among which \( r \) chemical reactions take place. The dynamics of the vector \( x \in \mathbb{R}_+^m \) of concentrations is given by the balance laws

\[
\dot{x} = Sv,
\]

where \( S \) is an \( m \times r \) matrix, called the stoichiometric matrix, consisting of (positive and negative) integer elements. For example, for the network consisting of two (reversible) reactions

\[
X_1 + 2X_2 \rightleftharpoons X_3 \rightleftharpoons 2X_1 + X_2
\]

we have

\[
S = \begin{bmatrix}
-1 & 2 \\
-2 & 1 \\
1 & -1
\end{bmatrix}
\]

The vector \( v \in \mathbb{R}^r \) are called the reaction fluxes, or reaction rates, whenever they are expressed as a function \( v(x) \).
The graph of complexes

Define the set of complexes as the union of all the different left- and right-hand sides (substrates and products) of all the reactions in the network. The expression of the $c$ complexes in terms of the $m$ chemical species defines an $m \times c$ matrix $Z$ called the complex stoichiometric matrix. The $\rho$-th column of $Z$ is the expression of the $\rho$-th complex in the $m$ chemical species.

For the network $X_1 + 2X_2 \rightleftharpoons X_3 \rightleftharpoons 2X_1 + X_2$ we have

$$Z = \begin{bmatrix} 1 & 0 & 2 \\ 2 & 0 & 1 \\ 0 & 1 & 0 \end{bmatrix}$$

All elements of the matrix $Z$ are non-negative integers.
Chemical reaction networks: basic structure

The complexes define the vertices of a **directed graph**, with edges corresponding to the reactions. The resulting graph is called the **graph of complexes**. In biochemical reaction networks $c, r$ are typically large. As before the complex graph is specified by its **incidence matrix** $B$: an $c \times r$ matrix with $(\rho, j)$-th element equal to $-1$ if vertex $\rho$ is the tail vertex of edge $j$ and $1$ if vertex $\rho$ is the head vertex of edge $j$, while $0$ otherwise. In the previous case

$$B = \begin{bmatrix} -1 & 0 \\ 1 & -1 \\ 0 & 1 \end{bmatrix}$$

**Basic relation**

$$S = ZB$$

Hence the dynamics $\dot{x} = Sv$ can be also written as

$$\dot{x} = ZBv,$$

with $Bv$ belonging to the space of complexes $\mathbb{R}^c$. 
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Arjan van der Schaft (Johann Bernoulli Institute Modeling and analysis of dynamical distribution networks)
The most basic model for specifying the reaction rates $v(x)$ is mass action kinetics. Consider the single reaction

$$X_1 + 2X_2 \rightleftharpoons X_3,$$

involving the three chemical species $X_1, X_2, X_3$ with concentrations $x_1, x_2, x_3$. In mass action kinetics the reaction is considered to be a combination of the forward reaction $X_1 + X_2 \rightarrow X_3$ with forward rate equation $v^+(x_1, x_2) = k^+ x_1 x_2^2$ and the reverse reaction $X_1 + X_2 \leftarrow X_3$, with rate equation $v^-(x_3) = k^- x_3$. The constants $k^+, k^-$ are called the forward and reverse reaction constants.

The net reaction rate given by mass action kinetics is thus

$$v(x_1, x_2, x_3) = k^+ x_1 x_2^2 - k^- x_3$$
In general, the mass action reaction rate of the $j$-th reaction, from a substrate complex $S_j$ to a product complex $P_j$, is given as

$$v_j(x) = k_j^+ \prod_{i=1}^{m} x_i^{Z_{is_j}} - k_j^- \prod_{i=1}^{m} x_i^{Z_{ip_j}}$$

where $Z_{i\rho}$ is the $(i, \rho)$-th element of the complex stoichiometric matrix $Z$, and $k_j^+, k_j^- \geq 0$ are the forward/reverse reaction constants of the $j$-th reaction.

**Crucial observation:** this can be also written as

$$v_j(x) = k_j^+ \exp (Z_{S_j}^T \Ln(x)) - k_j^- \exp (Z_{P_j}^T \Ln(x))$$

where $Z_{S_j}$ and $Z_{P_j}$ are the columns of the complex stoichiometric matrix $Z$ corresponding to the substrate and the product complex of the $j$-th reaction.

(The mapping $\Ln : \mathbb{R}_+^c \to \mathbb{R}^c$ is the element-wise natural logarithm.)
Detailed balanced mass action kinetics

Definition

A vector of concentrations $x^* \in \mathbb{R}_+^m$ is called a thermodynamic equilibrium if

$$\nu(x^*) = 0$$

Clearly, any thermodynamic equilibrium is an equilibrium of $\dot{x} = Sv(x)$, i.e., $Sv(x^*) = 0$, but not necessarily the other way around (since in general $S = ZB$ is not injective).

Basic paradigm from thermodynamics:

every well-defined chemical reaction network has a thermodynamic equilibrium

This corresponds to microscopic reversibility.
Necessary and sufficient conditions for the existence of a thermodynamic equilibrium are usually referred to as the Wegscheider conditions. Consider the \( j \)-th reaction from substrate \( S_j \) to product \( P_j \), described by mass action kinetics

\[
v_j(x) = k_j^+ \exp(Z_{S_j}^T \ln(x)) - k_j^- \exp(Z_{P_j}^T \ln(x))
\]

Then \( v(x^*) = 0 \) if and only if (detailed balance equations)

\[
k_j^+ \exp(Z_{S_j}^T \ln(x^*)) = k_j^- \exp(Z_{P_j}^T \ln(x^*)), \quad j = 1, \ldots, r
\]

Define the equilibrium constant \( K_j^{eq} \) of the \( j \)-th reaction as

\[
K_j^{eq} := \frac{k_j^+}{k_j^-}
\]

Then the detailed balance equations are equivalent to

\[
K_j^{eq} = \exp(Z_{P_j}^T \ln(x^*) - Z_{S_j}^T \ln(x^*)), \quad j = 1, \ldots, r
\]
Collecting all reactions this amounts to the vector equation

\[ K^{eq} = \text{Exp} \left( B^T Z^T \ln(x^*) \right) = \text{Exp} \left( S^T \ln(x^*) \right), \]

where \( K^{eq} \) is the \( r \)-dimensional vector with \( j \)-th element \( K_j^{eq}, j = 1, \ldots, r \), and \( \text{Exp} : \mathbb{R}^c \rightarrow \mathbb{R}^c_+ \) is the element-wise exponential function.

**Proposition**

*There exists a thermodynamic equilibrium \( x^* \in \mathbb{R}^m_+ \) if and only if \( k_j^+ > 0, k_j^- > 0 \), for all \( j = 1, \ldots, r \), and furthermore*

\[ \ln(K^{eq}) \in \text{im} S^T \]

**Hence all reactions should be reversible**, and in case \( S^T \) is not surjective, then the forward and reverse reaction constants should satisfy a **compatibility condition**! Such a network is called detailed balanced. It also follows that the set of all thermodynamic equilibria is equal to

\[ \mathcal{E} := \{ x^{**} \in \mathbb{R}^m_+ | S^T \ln(x^{**}) = S^T \ln(x^*) \} \]
Define for each reaction the (reaction) conductance

\[ \kappa_j(x^*) := k_j^+ \exp \left( Z_{S_j}^T \ln(x^*) \right) = k_j^- \exp \left( Z_{P_j}^T \ln(x^*) \right), \quad j = 1, \ldots, r \]

Then the reaction rate of the \( j \)-th reaction can be rewritten as

\[ v_j(x) = \kappa_j(x^*) \left[ \exp \left( Z_{S_j}^T \ln \left( \frac{x}{x^*} \right) \right) - \exp \left( Z_{P_j}^T \ln \left( \frac{x}{x^*} \right) \right) \right], \]

where for any vectors \( x, z \in \mathbb{R}^m \) the quotient vector \( \frac{x}{z} \in \mathbb{R}^m \) is defined elementwise.
Define the $r \times r$ diagonal matrix of conductances as

$$
\mathcal{K}(x^*) := \text{diag}(\kappa_1(x^*), \cdots, \kappa_r(x^*))
$$

It follows that the mass action reaction rate vector of a balanced reaction network can be written as

$$
\nu(x) = -\mathcal{K}(x^*) B^T \text{Exp} \left( Z^T \text{Ln} \left( \frac{x}{x^*} \right) \right),
$$

and thus the dynamics of a balanced reaction network takes the final form

$$
\dot{x} = -ZB\mathcal{K}(x^*) B^T \text{Exp} \left( Z^T \text{Ln} \left( \frac{x}{x^*} \right) \right), \quad \mathcal{K}(x^*) > 0
$$
The matrix $L := BK(x^*)B^T$ defines a weighted Laplacian matrix for the graph of complexes, with weights being the constants $\kappa_1(x^*), \cdots, \kappa_r(x^*)$. Structure of the equations is very similar to flow control distribution systems under the proportional output feedback $u = -K(x^*)y$. Thus we expect ‘convergence to consensus’.

The Laplacian matrix $L$ is an important tool for the analysis of the graph (algebraic graph theory). E.g., it will be key to the model reduction procedure discussed later on.

$K(x^*)$, and thus the Laplacian matrix $L$, is in principle dependent on the choice of the thermodynamic equilibrium $x^*$. However, this dependence is minor: for a connected complex graph the matrix $K(x^*)$ is, up to a positive multiplicative factor, independent of the choice of the thermodynamic equilibrium $x^*$. 
Thermodynamic interpretation

We may interpret

$$\mu(x) := RT \ln \left( \frac{x}{x^*} \right) = -RT \ln(x^*) + RT \ln(x)$$

as the vector of chemical potentials. Furthermore, $$\gamma(x) := Z^T \mu(x)$$, the complex thermodynamical affinity, acts as a ‘driving force’ for the reactions. Define the Gibbs’ free energy as

$$G(x) = RT x^T \ln \left( \frac{x}{x^*} \right) + RT (x^* - x)^T 1_m,$$

Then $$\frac{\partial G}{\partial x}(x) = RT \ln \left( \frac{x}{x^*} \right) = \mu(x)$$ and

$$\dot{x} = -ZB K(x^*) B^T \exp \left( Z^T \frac{\partial G}{\partial x}(x) \right), \quad \mu(x) = \frac{\partial G}{\partial x}(x)$$

Note that $$(RT) \ln(K^{eq}) = (RT) S^T \ln(x^*) = -B^T \gamma^o$$, and thus the equilibrium constants correspond to differences of the reference complex thermodynamical affinities of the substrate and product complexes.
All variables and relations are summarized in the following diagram

\[ v \in \mathcal{R} = \mathbb{R}^r \xrightarrow{B} \dot{y} \in \mathcal{C} = \mathbb{R}^c \xrightarrow{Z} \dot{x} \in \mathcal{M} = \mathbb{R}^m \]

\[ K(x^*) \quad | \quad \frac{\partial G}{\partial x}(x) \]

\[ v^* \in \mathcal{R}^* \xleftarrow{B^T} \gamma \in \mathcal{C}^* \xleftarrow{Z^T} \mu \in \mathcal{M}^* \]

\[ \text{Exp} \]

where \( \mu(x) = \frac{\partial G}{\partial x}(x) \).

Compared to other cases of physical network modeling a complication in the diagram is the map \( \text{Exp} : \mathcal{C}^* \rightarrow \mathcal{C}^* \), which introduces a discrepancy between \( v^* \) and \( \alpha := -B^T \gamma = -S^T \mu \).
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Consider a balanced chemical reaction network \( \dot{x} = Sv(x) = ZBv(x) \) governed by mass action kinetics, with thermodynamic equilibrium \( x^* \). Then all equilibria are thermodynamic equilibria, i.e., in

\[ \mathcal{E} := \{ x^{**} \in \mathbb{R}_+^m \mid S^T \ln(x^{**}) = S^T \ln(x^*) \} \]
Proof.

Denote for the \( j \)-th reaction the substrate complex by \( S_j \) and the product complex by \( P_j \). Let \( Z_{S_j} \) and \( Z_{P_j} \) denote the columns of the complex stoichiometric matrix \( Z \), corresponding to substrate complex \( S_j \) and product complex \( P_j \). Recall

\[
\mu(x) = \ln\left( \frac{x}{x^*} \right), \quad \gamma(x) := Z^T \mu(x), \quad \gamma_{S_j}(x) = Z_{S_j}^T \mu(x), \quad \gamma_{P_j}(x) = Z_{P_j}^T \mu(x)
\]

Suppose \( x^{**} \) is an equilibrium, i.e.,

\[
ZB \mathcal{K}(x^*) B^T \exp \left( Z^T \mu(x^{**}) \right) = 0.
\]

Then

\[
\mu^T(x^{**})ZB \mathcal{K}(x^*) B^T \exp \left( Z^T \mu(x^{**}) \right) = 0
\]

Denoting the columns of \( B \) by \( b_1, \cdots, b_r \), we have

\[
L = B \mathcal{K}(x^*) B^T = \sum_{j=1}^{r} \kappa_j(x^*) b_j b_j^T,
\]

while

\[
\mu^T(x^{**}) Z b_j = \mu^T(x^{**}) \left( Z_{P_j} - Z_{S_j} \right) = \gamma_{P_j}^T(x^{**}) - \gamma_{S_j}^T(x^{**}),
\]

\[
b_j^T \exp \left( Z^T \mu(x^{**}) \right) = \exp \left( \gamma_{P_j}^T(x^{**}) \right) - \exp \left( \gamma_{S_j}^T(x^{**}) \right)
\]
Proof.

It follows that

\[ 0 = \mu^T(x^{**})ZB\kappa(x^*)B^T\text{Exp}(Z^T\mu(x^{**})) = \sum_{j=1}^{r} [\gamma_{P_j}(x^{**}) - \gamma_{S_j}(x^{**})] \left[ \exp(\gamma_{P_j}(x^{**})) - \exp(\gamma_{S_j}(x^{**})) \right] \kappa_j(x^*) \]

Since the exponential function is strictly increasing and \(\kappa_j(x^*) > 0, j = 1, \ldots, r\), this implies that all terms in the summation are zero and thus

\[ \gamma_{P_j}(x^{**}) = \gamma_{S_j}(x^{**}), \quad j = 1, \ldots, r \]
\[ \exp(\gamma_{P_j}(x^{**})) = \exp(\gamma_{S_j}(x^{**})), \quad j = 1, \ldots, r \]

which implies

\[ B^T\text{Exp}(\gamma(x^{**})) = B^T\text{Exp}(Z^T\mu(x^{**})) = 0, \quad \text{and thus } v(x^{**}) = 0 \]
Theorem

Consider a balanced mass action reaction network. For every initial condition \( x_0 \in \mathbb{R}_+^m \) there exists a unique point \( x_\infty \in \mathcal{E} \) with \( x_\infty - x_0 \in \text{im } S \).

*If the network is persistent, the species concentration vector \( x \) starting from \( x(0) = x_0 \) converges for \( t \to \infty \) to \( x_\infty \).*
Proof.

There exists a unique $\mu \in \ker S^T$ such that $x^* \cdot \exp(\mu) - x_0 \in \text{im } S$. Define $x_\infty := x^* \cdot \exp(\mu) \in \mathbb{R}^m$.

It follows that $0 = S^T \mu = S^T \ln \left( \frac{x_\infty}{x^*} \right)$, that is, $x_\infty \in \mathcal{E}$. Furthermore, the function $G$ satisfies

$$G(x^*) = 0, \quad G(x) > 0, \quad \forall x \neq x^*,$$

while $\dot{G}(x) := \frac{\partial^T G}{\partial x}(x)Sv(x) = \frac{dG}{dt}(x)$ satisfies

$$\dot{G}(x) \leq 0 \quad \forall x \in \mathbb{R}^m, \quad \dot{G}(x) = 0 \text{ if and only if } x \in \mathcal{E}.$$

The convergence to $\mathcal{E}$ is equivalent to $B^T \gamma(x(t)) \to 0$ for $t \to \infty$. Thus the elements of $\gamma$ belonging to the same connected component of the complex graph converge to the same value (which is determined by $x_0$); similar to standard consensus algorithms.
Outline

1. Flow control of distribution networks
2. Chemical reaction networks: basic structure
3. Detailed balanced mass action kinetics
4. Equilibrium analysis and stability
5. Open chemical reaction networks
6. Model reduction of chemical reaction networks
7. Conclusions and outlook
Open balanced chemical reaction networks are given by

\[
\dot{x} = -ZB\mathcal{K}(x^*)B^T\exp\left(Z^T\ln\left(\frac{x}{x^*}\right)\right) + S_b\nu_b,
\]

\[
\mu_b = S_b^T\ln\left(\frac{x}{x^*}\right),
\]

which define an input-state-output system with inputs \(\nu_b\) (boundary fluxes) and outputs \(\mu_b\) (boundary potentials). It follows that

\[
\frac{d}{dt} G(x) = -\gamma^T(x)B\mathcal{K}(x^*)B^T\exp(\gamma(x)) + \mu_b^T\nu_b
\]

thus showing the passivity property

\[
\frac{d}{dt} G \leq \mu_b^T\nu_b
\]

What can we say about steady state behavior for constant \(\nu_b\) (similar to constant \(d\) for flow control distribution networks)?
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Proposition

Consider a directed graph with vertex set $\mathcal{V}$ and with weighted Laplacian matrix $L = BK(x^*)B^T$.

For any subset of vertices $\mathcal{V}_r \subset \mathcal{V}$ the Schur complement of $L$ with respect to the indices corresponding to $\mathcal{V}_r$ is well-defined, and is the weighted Laplacian matrix $\hat{L} = \hat{B}K(x^*)\hat{B}^T$ of a reduced directed graph with incidence matrix $\hat{B}$, whose vertex set is equal to $\mathcal{V} - \mathcal{V}_r$. 
Consider a balanced reaction network

\[ \Sigma : \dot{x} = -ZB\mathcal{K}(x^*)B^T \exp(Z^T \ln \left( \frac{x}{x^*} \right)) \]

Reduction is performed by deleting certain intermediate complexes in the complex graph, resulting in a reduced reaction network

\[ \hat{\Sigma} : \dot{x} = -\hat{Z}\hat{B}\hat{\mathcal{K}}(x^*)\hat{B}^T \exp(\hat{Z}^T \ln \left( \frac{x}{x^*} \right)), \quad \hat{\mathcal{K}}(x^*) > 0 \]

\( \hat{\Sigma} \) is again a balanced chemical reaction network governed by mass action kinetics, with a reduced number of complexes. The thermodynamic equilibrium \( x^* \) of the original reaction network \( \Sigma \) is also a thermodynamic equilibrium of the reduced network \( \hat{\Sigma} \).
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Conclusions and outlook

- Distribution networks are everywhere: clear need to combine network structure, dynamics, and throughput analysis.
- Current work is focusing on control under flow capacity constraints.
- Structured description of chemical reaction networks: dynamics is similar to mass-damper systems with nonlinear dampers.
- Framework can be extended from mass action kinetics to Michaelis-Menten kinetics (enzymatic reactions). Model reduction approach has been applied to a glycolysis network.
- Certainly for biochemical reaction networks the study of networks with external fluxes $v_b$ is essential: many open questions!
- We started to look at feedback loops from certain metabolites to the enzymes, corresponding e.g. to gene activity.
- Papers can be found on my homepage: www.math.rug.nl/~arjan