Network Analysis of Biochemical Reactions in Complex Environments

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Abstract

We present extensions to Chemical Reaction Network Theory which are relevant to biochemical modelling. We show that a weakly reversible chemical reaction network has a bounded absorbing set if mass is conserved in all reaction steps that do not involve explicit inflows or outflows—an assumption that is fulfilled by many biochemical networks. This result provides a qualitative criterion to establish that a biochemical network will not diverge by checking structural properties of the graph of the reaction network. It can also be used to characterise certain bifurcations from stationary to oscillatory behaviour. In addition, we provide a deficiency-zero-like theorem for reactions under dimensionally-restricted conditions as experienced in the cellular environment. Under these conditions, the law of mass action does not strictly apply and reactions can be described by power-law kinetics. We illustrate our results with applications to some simple biological examples.

Notation

\[ x_i \] \quad \text{ith entry of vector } x \in \mathbb{R}^n
\[ A_{(i,j)} \] \quad (i, j)\text{th entry of matrix } A \in \mathbb{R}^{n \times n}
\[ A \geq 0 \ (A > 0) \] \quad \text{nonnegative (positive) definite matrix}
\[ \mathbb{R}_+^n, \mathbb{R}_+^n \} \quad \{ x \in \mathbb{R}^n : x > 0 \}, \{ x \in \mathbb{R}^n : x \geq 0 \}
\[ \text{diag}(A), A \in \mathbb{R}^{n \times n} \] \quad \text{a vector of length } n, \text{ where } \text{diag}(A)_i = A_{(i,i)}
\[ \text{diag}(x), x \in \mathbb{R}^n \] \quad \text{a matrix } \in \mathbb{R}^{n \times n}, \text{ where } \text{diag}(x)_{(i,i)} = x_i \text{ and } \text{diag}(x)_{(i,j) \neq i} = 0

1 Introduction

When modelling biochemical systems, precise parameter values are often difficult to obtain. On the other hand, there is a wealth of qualitative information which is usually summarised in terms of biochemical network diagrams. Analytical methods that do not rely on quantitative parameters can be extremely useful to enhance our understanding of the system dynamics. Feinberg’s Chemical Reaction Network Theory (CRNT) [1] is the classic example of such a methodology. In this paper we provide extensions to CRNT that are appropriate to biochemical networks. We show that a weakly reversible chemical reaction network has a bounded absorbing set if we assume that mass is conserved in all reaction steps that do not involve explicit inflows or outflows (Theorem 3.7). Additionally, we provide a deficiency-zero-like theorem (Theorem 4.2) for reactions under dimensionally-restricted conditions as are normally experienced in the cellular environment. We conclude with a brief set of biological examples to illustrate our results.

2 Chemical Reaction Networks Obeying Mass Action Kinetics

Chemical reaction networks with mass action kinetics are the standard tool to describe many processes in biochemistry. An illustrative example is the Michaelis-Menten mechanism for

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enzymatic chemical reactions:

\[ \begin{align*}
E + S & \xrightleftharpoons[k_{-1}]{k_1} C \xrightleftharpoons[k_{-2}]{k_2} E + P,
\end{align*} \]  

(1)

where \( S \) denotes the substrate, \( E \) the enzyme, \( C \) the intermediate complex, and \( P \) the product. If we assume that the system is homogeneous, well-stirred and three-dimensional, the dynamics of the reaction network (1) can be described through a set of nonlinear ordinary differential equations given by the law of mass action. This can be compactly written as:

\[
\dot{x} = f(x) = YA_{\kappa}\Psi(x), \quad \ln \Psi(x) = Y^T \ln x,
\]  

(2)

where \( x \in \mathbb{R}_+^n \) denotes the vector of concentrations of species; \( \Psi(x) \in \mathbb{R}_+^m \) is the vector of complexes (the 'nodes' in the network); \( A_{\kappa} \in \mathbb{R}^{m \times m} \) is the kinetic matrix; and \( Y \in \mathbb{R}^{n \times m} \) is the stoichiometric matrix. For the Michaelis-Menten Reaction (1):

\[
x = \begin{bmatrix} [E] \\ [S] \\ [C] \\ [P] \end{bmatrix}, \quad A_{\kappa} = \begin{bmatrix} -k_1 & k_{-1} & 0 & 0 \\ k_1 & -(k_{-1} + k_2) & k_{-2} & 0 \\ 0 & k_2 & -k_{-2} & 0 \\ 0 & 0 & 0 & 1 \end{bmatrix}, \quad Y = \begin{bmatrix} 1 & 0 & 1 & 0 \\ 1 & 0 & 0 & 1 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 \end{bmatrix}, \quad \text{and} \quad \Psi(x) = \begin{bmatrix} [E][S] \\ [C] \\ [P] \end{bmatrix},
\]

where \([\cdot]\) denotes concentration.

The following definitions are standard in CRNT [1] and will be used subsequently:

**Definition 2.1.** A linkage class is a closed set of complexes that are linked through reactions. The number of linkage classes is \( \ell \) (in Fig. 1, \( \ell = 4 \) in (a) and \( \ell = 1 \) in (b)). Each class corresponds to a submatrix of \( A_{\kappa} \).

**Definition 2.2.** A chemical reaction network is weakly reversible if there is a directed reaction path from any complex to any other within the same linkage class. This implies that every submatrix of \( A_{\kappa} \) associated with a linkage class is irreducible.

**Definition 2.3.** Let \( q = \text{rank}(YA_{\kappa}) \). Then, the deficiency of a chemical reaction network is given by: \( \delta = \dim A_{\kappa} - q - \ell = m - q - \ell \geq 0 \).

**Definition 2.4.** Let \( s = n - q \). Then, if \( s > 0 \) and the following constraint holds

\[
p_r^T \dot{x} = 0 \Rightarrow p_r^T x = \gamma, \quad x \in \mathbb{R}_+^n, \gamma \in \mathbb{R}, \, p_r \in \mathbb{R}^n, \, p_r \neq 0, \, r \in \{1, \ldots, s\},
\]

(3)

then the set of \( s \) linearly independent vectors \( p_r \) defines the admissible subspace in \( \mathbb{R}^n \).

The central results of CRNT [1] are: (i) the Deficiency Zero Theorem, which guarantees that, for all positive parameter values, there exists a unique positive and stable equilibrium point if and only if the chemical reaction network is of deficiency zero and weakly reversible; (ii) the Deficiency One Theorem, which guarantees that, for all positive parameter values, there exists (at most) one positive equilibrium point if the network is (not) weakly reversible, the deficiency of each linkage class \( \leq 1 \) and their sum equals the deficiency of the network.

### 3 Boundedness of a Class of Weakly Reversible Chemical Reaction Networks

We start with two definitions and a lemma regarding the dynamics of the network:
Definition 3.1. If there exists a $p >> 0$ such that $p^T Y A_\kappa = 0$, the chemical reaction network is said to be conservative. Note that if a chemical reaction network is conservative, the origin is Lyapunov stable, since, for $x \neq 0$, $V = p^T x > 0$ is a Lyapunov function with $\dot{V} = p^T Y A_\kappa \Psi(x) = 0$.

Definition 3.2. A dynamical system $f(x)$ is said to be dissipative if it possesses a bounded absorbing set. The bounded set $B_0$ is absorbing if for any bounded set $B \in \mathbb{R}^n$ there exists a $t_0 = t_0(B)$ such that $x(B) \in B_0$ for $t > t_0$. Furthermore, there exists a scalar $\gamma \geq 0$ and a Lyapunov function $V(x)$ such that $\dot{V}(x) < 0$, if $\|x\| \geq \gamma$.

Lemma 3.3. If a dynamical system is a chemical reaction network (2), then $\dot{x}_i|_{x_i=0} \geq 0$, $\forall i$.

This lemma implies that solutions remain nonnegative if the initial conditions are nonnegative and we can therefore restrict our analysis to the nonnegative orthant, the space of realistic solution trajectories.

Assumption 3.4. We assume chemical reaction networks with mass action kinetics in which only elementary reactions occur. This means that bimolecular reactions are the reactions of highest order, a well-justified assumption for ‘real’ biochemical reaction networks. To introduce our next assumption, consider the following change of notation. Let $Y A_\kappa = \begin{bmatrix} 0 & \hat{Y} \end{bmatrix} \begin{bmatrix} 0 & u \\ \hat{A}_\kappa \end{bmatrix}$, then the system (2) can be written as $\dot{x} = f(x) = \hat{Y}(u + \hat{A}_\kappa \hat{\Psi}(x)) = \hat{u} + A(x)x$. Without loss of generality, let also

$$\hat{A}_\kappa = \text{diag}([\hat{A}_{\kappa_1} \hat{A}_{\kappa_2} \cdots \hat{A}_{\kappa_\ell}]^T),$$  \hspace{1cm} (4)

then $\hat{Y} = [\hat{Y}_1 \hat{Y}_2 \cdots \hat{Y}_\ell]$, where $\ell$ is the number of linkage classes. We assume that for the chemical reaction network there exists a $p >> 0$ such that for each $i$ the elements of $p^T \hat{Y}_i$ are identical, $i \in \{1, \ldots, \ell\}$. Most biochemical networks fulfil this requirement, which means that mass is conserved in all reaction steps that do not involve explicit inflows or outflows. An example of a reaction that violates this requirement is: $X \rightarrow 2X$ ($\dot{x} = x$). This also implies that the network is conservative if $u = 0$; and that $p^T Y \hat{A}_\kappa << 0$ if $u \neq 0$ and the network is weakly reversible.

Under these assumptions, we prove now that a weakly reversible network with inputs is dissipative, hence, ultimately bounded.

Lemma 3.5. If the chemical reaction network is weakly reversible, $\text{rank}(\hat{Y} \hat{A}_\kappa) = \text{rank}(Y A_\kappa)$.

Proof. Let $\hat{A}_{\kappa_1}$ and $\hat{Y}_1$ be defined as in equation (4), and $\hat{A}_{\kappa_1} \in \mathbb{R}^{m_1 \times m_1}$ the submatrix representing the component of the chemical network that is connected to the source. Note that there is only one such component if the network is weakly reversible and that in this case $\hat{A}_{\kappa_1}$ is nonsingular. Let $u^T = [u_1 \ 0 \ \cdots \ 0]$. By Sylvester’s inequality: $\text{rank}(\hat{Y}_1) + \text{rank}(\hat{A}_{\kappa_1}) - m_1 \leq \text{rank}(\hat{Y}_1 \hat{A}_{\kappa_1}) \leq \text{min}\{\text{rank}(\hat{Y}_1), \text{rank}(\hat{A}_{\kappa_1})\} \Rightarrow \text{rank}(\hat{Y}_1) \leq \text{rank}(\hat{Y}_1 \hat{A}_{\kappa_1}) \leq \text{min}\{\text{rank}(\hat{Y}_1), \ m_1\} \Rightarrow \text{rank}(\hat{Y}_1 \hat{A}_{\kappa_1}) = \text{rank}(\hat{Y}_1)$. Furthermore, $\text{rank}(\hat{Y}_1) + \text{rank}([u_1 \ \hat{A}_{\kappa_1}]) - m_1 \leq \text{rank}(\hat{Y}_1[u_1 \ A_{\kappa_1}]) \leq \text{min}\{\text{rank}(\hat{Y}_1), \text{rank}([u_1 \ A_{\kappa_1}])\} \Rightarrow \text{rank}(\hat{Y}_1) \leq \text{rank}(\hat{Y}_1[u_1 \ A_{\kappa_1}]) \leq \text{min}\{\text{rank}(\hat{Y}_1), \ m_1\} \Rightarrow \text{rank}(\hat{Y}_1[u_1 \ A_{\kappa_1}]) = \text{rank}(\hat{Y}_1)$. Finally, this implies that $\text{rank}(Y A_\kappa) = \text{rank}(\hat{Y} \hat{A}_\kappa)$ if the chemical reaction network is weakly reversible.

Lemma 3.6. If the chemical reaction network is weakly reversible and matrix $A(x)$ is nonsingular for all $x$, the chemical reaction network is dissipative.
Proof. First, a nonsingular $A(x)$ implies that $u \neq 0$. Next, if, for all $x$, $A(x)$ is nonsingular, there exists a $p >> 0$ such that $p^T Y A_k = 0$, which implies that $x_i \neq \infty$ for all $i$. If $u \neq 0$, let $\text{rank}(Y) = q (q \leq n)$. Next, $\text{rank}(f(x)) = q$ by Lemma 3.5 if the chemical reaction network is weakly reversible. Furthermore, note that if a chemical reaction network is dissipative then $x_i \neq \infty$ for all $i$. However, let us assume $x_i = \infty$ for some $i$. Then, neither $x_i$ or $2x_i$ can form a complex. Otherwise, there exists a $j$ such that $\Psi_j(x)$ is either $x_i$ or $x_i^2$, and $x_i = \infty$ would mean that there exists a chemical reaction network $x = p^T x > 0$ such that $\dot{V}(x) = p^T Y (u + A_k \Psi(x)) < 0$ if $\|x\| > \gamma > 0$, which would establish dissipativity. This implies that there exists some $k$ such that $x_i + x_k$ form a complex, $x_k = 0$ and $x_i x_k$ is constant. Thus, there exists a matrix $A(x)$ representing the network that is singular. Therefore, there exists a vector $v \neq 0$ such that $v^T Y = 0$, which implies that $q < n$. Next, let $s = n - q$. Then, if the chemical reaction network is weakly reversible, there exist $s$ vectors $v_r \neq 0$ such that $v_r^T Y = 0$, $r \in \{1, \ldots, s\}$; note that if the network is not weakly reversible, it is not necessarily true that there exist $s$ such vectors. This implies that we can reduce the chemical reaction network until $n_{\text{reduced}} = q$ and $A(x)$ is nonsingular. However, by Lemma 3.6 this means that the chemical reaction network is dissipative, which contradicts our assumption that $x_i = \infty$ for some $i$. Therefore, $x_i \neq \infty$ for all $i$ if the network is weakly reversible. 

Remark 3.8. By Theorem 3.7, a weakly reversible network is either conservative or dissipative.

4 Chemical Reaction Networks under Dimensionally-Restricted Conditions

The cell can be hardly described as a vessel containing a well-mixed macroscopic solution of chemicals. Furthermore, many key reactions occur at interfaces (e.g., extracellular or cytosolic signal molecules with receptors on the membrane) or take place directly under reduced dimensions (e.g., enzymatic reactions in the membrane or along the filaments of the cytoskeleton). Following Savageau [2], equation (2) can be modified to represent chemical reaction networks in spatially constrained environments by assuming an empirical power-law approximation:

$$\dot{x} = Y A_k \Psi(x), \quad \ln \Psi(x) = G^T \ln x, \quad G - Y \geq 0.$$ 

Here, a zero entry in matrix $Y$ implies a corresponding zero entry in matrix $G$. Furthermore, we assume that monomolecular reactions (i.e., structural changes of a molecule or its breaking down) remain of power 1 even under dimensionally-restricted conditions. This implies that for $Y \in \mathbb{R}_{+}^{n \times m}$ and $G \in \mathbb{R}_{+}^{p \times m}$, where $e^T = [1, \ldots, 1]$ and $e \in \mathbb{R}^n$:

$$Y_{(i,j)} = 0 \Leftrightarrow G_{(i,j)} = 0; \quad (e^T Y)_i = 1 \Leftrightarrow (e^T G)_i = 1; \quad (e^T Y)_i = 2 \Leftrightarrow (e^T G)_i \geq 2. \quad (5)$$

Lemma 4.1. If (5) holds for all $i, j$ then Theorem 3.7 also applies to weakly reversible chemical reaction networks with the power-law approximation.

In the following, we prove local asymptotic stability of the fixed point $x_{eq} \in \mathbb{R}_+^n$ of a chemical reaction network with the power-law approximation, if $x_{eq}$ is such that $A_k \Psi(x_{eq}) = 0$ and there exists a diagonal matrix $D > 0$ such that $G = D Y$. Note that if the chemical reaction network has deficiency zero then $A_k \Psi(x_{eq}) = 0$. 

Theorem 3.7. Under the assumptions stated in Assumption 3.4, if a chemical reaction network is weakly reversible then $x_i \neq \infty$ for all $i$. 

Proof. First, a nonsingular $A(x)$ implies that $u \neq 0$. Next, if, for all $x$, $A(x)$ is nonsingular, there exists a $p >> 0$ such that $p^T Y A_k = 0$, which implies that $x_i \neq \infty$ for all $i$. If $u \neq 0$, let $\text{rank}(Y) = q (q \leq n)$. Next, $\text{rank}(f(x)) = q$ by Lemma 3.5 if the chemical reaction network is weakly reversible. Furthermore, note that if a chemical reaction network is dissipative then $x_i \neq \infty$ for all $i$. However, let us assume $x_i = \infty$ for some $i$. Then, neither $x_i$ nor $2x_i$ can form a complex. Otherwise, there exists a $j$ such that $\Psi_j(x)$ is either $x_i$ or $x_i^2$, and $x_i = \infty$ would mean that there exists a chemical reaction network $x = p^T x > 0$ such that $\dot{V}(x) = p^T Y (u + A_k \Psi(x)) < 0$ if $\|x\| > \gamma > 0$, which would establish dissipativity. This implies that there exists some $k$ such that $x_i + x_k$ form a complex, $x_k = 0$ and $x_i x_k$ is constant. Thus, there exists a matrix $A(x)$ representing the network that is singular. Therefore, there exists a vector $v \neq 0$ such that $v^T Y = 0$, which implies that $q < n$. Next, let $s = n - q$. Then, if the chemical reaction network is weakly reversible, there exist $s$ vectors $v_r \neq 0$ such that $v_r^T Y = 0$, $r \in \{1, \ldots, s\}$; note that if the network is not weakly reversible, it is not necessarily true that there exist $s$ such vectors. This implies that we can reduce the chemical reaction network until $n_{\text{reduced}} = q$ and $A(x)$ is nonsingular. However, by Lemma 3.6 this means that the chemical reaction network is dissipative, which contradicts our assumption that $x_i = \infty$ for some $i$. Therefore, $x_i \neq \infty$ for all $i$ if the network is weakly reversible. 

Remark 3.8. By Theorem 3.7, a weakly reversible network is either conservative or dissipative.
Theorem 4.2. A deficiency-zero-like theorem for power law kinetics. The fixed point $x_{eq} \in \mathbb{R}^n_+$ of a chemical reaction network with power-law kinetics, where $x_{eq}$ is such that $A_{eq}\Psi(x_{eq}) = 0$ and there exists a diagonal matrix $D > 0$ such that $G = DY$, is locally asymptotically stable.

Proof. The Jacobian at $x = x_{eq}$ is: $J = Y\hat{A}_nY^TD[\text{diag}(x_{eq})]^{-1}$, where $\hat{A}_n = A_{eq}\text{diag}(\Psi(x_{eq}))$, $J \in \mathbb{R}^{n \times n}$, $Y \in \mathbb{R}^{n \times m}$, $A_{eq} \in \mathbb{R}^{m \times m}$, and $\Psi(x_{eq}) \in \mathbb{R}^m$. Note that $e^T\hat{A}_n = 0$, $\hat{A}_n e = 0$, where $e^T = [1, \ldots, 1]$, and $e \in \mathbb{R}^m$. Furthermore, $r^T\hat{A}_nr \leq 0$, since $\hat{A}_n$ is an M-matrix and $\hat{A}_{n(i,i)} = \sum_{j=1,j\neq i}^m \hat{A}_{n(i,j)} = \sum_{j=1,j\neq i}^m \hat{A}_{n(j,i)}$, for all $i,j$, where $r \in \mathbb{R}^m$. Now, if $Y\hat{A}_nY^T < 0$, then with

$$P = [\text{diag}(x_{eq})]D^{-1} = D^{-1}[\text{diag}(x_{eq})] > 0$$

the following (Lyapunov) inequality holds

$$Y\hat{A}_nY^TD[\text{diag}(x_{eq})]^{-1}P + P[\text{diag}(x_{eq})]^{-1}DY\hat{A}_nY^T < 0.$$ 

This implies local asymptotical stability of the fixed point. To see that $Y\hat{A}_nY^T < 0$, let $Y_{eq}\Psi(x) = Y(u + A_{eq}\Psi(x))$. Then, $\partial(Y_{eq}\Psi(x))/\partial x = \partial(Y\hat{A}_n\Psi(x))/\partial x$ and either (7) holds with $Y$ replaced by $Y_{eq}$, and $\hat{A}_n$ replaced by $A_{eq}\text{diag}(\Psi(x_{eq}))$, or otherwise $s > 0$, where $s = n - q$. In this case, there exist $s$ linearly independent vectors $p_r$ such that the set of constraints given by equation (3) holds for the chemical reaction network, $r \in \{1, \ldots, s\}$. Furthermore, equation (3) holds also for the linearised system $\dot{x} = Jx$. Hence, if we consider the following Lyapunov function $V(x) = \frac{1}{2}(x - x_{eq})^TP(x - x_{eq})$, $x \neq x_{eq}$ and $P$ as in (6), then $\dot{V}(x) = 0$ only if $x - x_{eq} = p_r$. In this case, $p_r^T(x - x_{eq}) = \gamma - \gamma = p_r^Tp_r = 0$, which is a contradiction, since $p_r \neq 0$, $\forall r$. Thus, $V(x) < 0$ and $x_{eq}$ is locally asymptotically stable. \qed

5 Conclusions and Application to Biological Examples

In this paper, we have shown that a weakly reversible chemical reaction network has a bounded absorbing set under certain realistic conditions. This result provides a qualitative criterion to establish that a biochemical network will not diverge. This is directly relevant to the stationary behaviour of a chemical system but can also be used to characterise certain bifurcations from stationary to oscillatory behaviour (see Section 5.1). Furthermore, we have provided a deficiency-zero-like theorem for reactions under dimensionally-restricted conditions, as experienced in the cellular environment, where the law of mass action does not strictly apply. We now briefly illustrate these results with applications to simple biological examples.

5.1 A Chemical Oscillator

Consider the system in Figure 1. By Theorem 3.7, all variables of the chemical reaction network are bounded. Thus, let $x_4$ and $x_5$ take any positive value $< \infty$. Then, the corresponding network (Figure 1b) with $ax_4 = \alpha$ and $ex_5 = \varepsilon$ is of deficiency one, and the dynamical system in Figure 1c admits a unique positive equilibrium point for all positive parameter values. Our Theorem 3.7 also guarantees, that if the equilibrium is unstable, then the system exhibits oscillatory behaviour. This transition can be easily explored in parameter space via the Ruth-Hurwitz criterion.
5 Conclusions and Application to Biological Examples

(a) \[ x_4 \xrightarrow{\frac{u_4}{d_4}} 0 \quad \xrightarrow{\frac{d_5}{u_5}} x_5 \]
\[ x_1 \xrightarrow{\frac{c}{d}} x_3 \xrightarrow{\frac{k}{h}} x_2 \]
\[ x_1 + x_4 \xrightarrow{\frac{u}{b}} 2x_1 \]
\[ x_1 + x_2 \xrightarrow{\frac{g}{e}} x_3 + x_5 \]

(b) \[ \dot{x}_1 = -(\alpha + c)x_1 - bx_2^2 + (d + \varepsilon)x_3 - gx_1x_2 \]
\[ \dot{x}_2 = -hx_2 + (k + \varepsilon)x_3 - gx_1x_2 \]
\[ \dot{x}_3 = -(d + k + \varepsilon)x_3 + hx_2 + cx_1 + gx_1x_2 \]

(c) \[ x_1 + x_2 \xrightarrow{\frac{g}{c}} x_3 \xrightarrow{\frac{k}{h}} x_2 \]

Fig. 1: A chemical oscillator. By Theorem 3.7 and the Ruth-Hurwitz criterion, the system in (c) exhibits oscillations, e.g., if \( \alpha = 100; b, c, d = 0.1; g, h = 1; k = 100; \varepsilon < 354. \)

5.2 Signalling systems: Kinetic Proofreading and the EnvZ/OmpR system

Kinetic proofreading schemes have been proposed to model certain signalling cascades [3]. The corresponding biochemical reaction network (Figure 2) is weakly reversible and of deficiency zero. Thus, it has a unique stable equilibrium solution and periodic solutions cannot exist under mass action kinetics. Even if the reactions do not obey the law of mass action due to the volume exclusion effects or to macromolecular obstacles, Theorem 4.2 states that an equilibrium point under power law kinetics is locally asymptotically stable. Note also that the system is conservative independently of the kinetics.

Fig. 2: A kinetic proofreading scheme [3]. A signaling cascade where \( R \) is the receptor, \( L \) the ligand and the \( S_i \) are signal elements.

Another example is the two-component EnvZ/OmpR signaling system (Figure 3), which regulates OmpR-P and the expression of porins OmpF and OmpC in E. Coli [4]. The chemical reaction network is also of deficiency zero and by Theorem 4.2 the equilibrium point is locally asymptotically stable when taken with either mass action kinetics or the power-law approximation. Again, this system is conservative independently of the kinetics.

Fig. 3: A model of the EnvZ/OmpR two-component circuit [4].

References