Chemical Reaction Networks in a Laplacian Framework*

J. J. P. Veerman†‡, T. Whalen-Wagner§, Ewan Kummel¶

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Abstract

The study of the dynamics of chemical reactions, and in particular phenomena such as oscillating reactions, has led to the recognition that many dynamical properties of a chemical reaction can be predicted from graph theoretical properties of a certain directed graph, called a Chemical Reaction Network (CRN). In this graph, the edges represent the reactions and the vertices the reacting combinations of chemical substances.

In contrast with the classical treatment, in this work, we heavily rely on a recently developed theory of directed graph Laplacians to simplify the traditional treatment of the so-called deficiency zero systems of CRN theory. We show that much of the dynamics of these polynomial systems of differential equations can be understood by analyzing the directed graph Laplacian associated with the system. Beside the more concise mathematical treatment, this leads to considerably stronger results. In particular, (i) we show that our Laplacian deficiency zero theorem is markedly stronger than the traditional one and (ii) we derive simple equations for the locus of the equilibria in all (Laplacian) deficiency zero cases.

This paper is written in a way to make the material easily accessible to a mathematical audience. In particular, no knowledge of chemistry or physics is assumed.

Keywords. Laplacian, Chemical Reaction Network, Equilibrium, Stability.

1 Introduction

CRN's form a compelling area of study with many connections to other areas of mathematics. For example, recently, a wonderful introduction appeared highlighting the connection with algebraic geometry [9]. In this paper, we review the basic theory of Chemical Reaction Networks (CRN's) employing the recently developed formalism of directed graph Laplacians [7, 6, 21, 30, 31]. In the literature since the 1970's [16, 17, 10], this analysis has been based (for a variety of reasons) on the

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†Weizmann Institute of Science, Rehovot, Israel

‡Fariborz Maseeh Dept. of Math. and Stat., Portland State Univ., Portland, OR, USA; e-mail: veerman@pdx.edu

§Fariborz Maseeh Dept. of Math. and Stat., Portland State Univ., Portland, OR, USA; e-mail: tessaww@hushmail.com

¶Fariborz Maseeh Dept. of Math. and Stat., Portland State Univ., Portland, OR, USA; e-mail:ewan@pdx.edu

understanding of a different linear operator that, however, contains less information. The change to a Laplacian formulation allows us to give a more concise derivation of all the classical results of the zero deficiency theory with much less effort. Equally important is the fact that the Laplacian formulation gives stronger results, as we explain below. With this paper, we wish to make the material accessible to a mathematical audience. Thus we restrict our vocabulary to terms current in mathematics or at least mathematical graph theory.

Here is an overview of what we aim to achieve in this work. A chemical reaction network (or CRT) consists of a (often very large) collection of first order polynomial differential equations. First we formulate the *Laplacian* version of the zero deficiency condition (Definition 5.1) which essentially eliminates 'unobserved' chemical reactions. We assume this condition for the rest of the paper. We then prove the zero *Laplacian* deficiency theorem (Theorem 5.3), which says that there exists a strictly positive equilibrium if and only if the associated directed graph is componentwise strongly connected (or CSC, see Definition 3.7). Subsequently, we will prove that for every choice of certain constants of the motion (Definition 4.2), there is exactly one equilibrium (Theorem 6.4) and furthermore that this equilibrium is locally asymptotically stable (Theorem 7.3).

As mentioned, the Laplacian framework allows us not only to give more concise proofs but also leads to stronger results. We now describe the new aspects of this work. The Laplacian zero deficiency theorem is strictly stronger than its classical counterpart (Proposition 9.2) and in Section 9 we give a significant example of that. Using the Laplacian theory, we can in fact show that the existence of a positive equilibrium in any zero deficiency system is equivalent to the existence of an orbit in a compact subset of the open positive orthant (Theorem 5.4). For general zero deficiency systems, we derive simple equations that determine the locus of any equilibrium (Theorem 5.5). We give examples of this in Section 8. Finally, in some cases, the Laplacian method detects more constants of the motion than the traditional one (Proposition 9.1 and the remarks that follow it).

The first sporadic accounts of oscillating chemical reactions were published in the 19th century. At the time, they received very little attention, in part because known examples were difficult to reproduce and in part because of a belief among scientists that such behavior was impossible. When Bray [4] published the first detailed description of such a reaction in the 1920's, the consensus among his peers was that the behavior must be the result of experimental error. Indeed, 30 years later Belousov spent 8 years trying to publish a description of his famous reaction. His observations were eventually published in a non-peer reviewed journal (see [34] for details). Belousov's publication allowed other researchers to replicate his example, produce others, and eventually derive conditions needed for such reactions [35].

While the study of chemical reaction networks is at least old as the introduction of detailed balance for chemical reactions [33], the mathematical theory of chemical reaction networks began in earnest in the 1960's with the work of Aris [2] and achieved prominence in the 1970's with the work of Horn, Jackson, Feinberg, and others [10, 17, 16, 14], see also [13]. Since reaction rates are difficult to measure experimentally, this theory was in part motivated by the need to understand exotic behaviors of chemical reactions in a way that does not require knowing precise reaction rates. Examples of such behavior are oscillations and bi-stability. The landmark 1987 Feinberg paper [11] combines much of this early work into two theorems: the deficiency zero theorem which we discuss below, and an extension called the deficiency one theorem. In each case, the deficiency (Definition 5.1) of a reaction network is used to characterize the equilibria.

Probably the first papers in which a chemical reaction diagram, consisting of chemical com-

pounds connected by arrows, was explicitly treated as a directed graph was [26, 27]. It turns out that many notions in the theory of chemical reaction networks have direct parallels in the language of directed networks. Indeed, strictly from the perspective of dynamics, there is independent mathematical interest in the notion that the behavior of the highly non-linear system can be at least partly understood by the analysis of directed graphs. There are many recent papers [23, 24, 20] that make use of this interplay to derive new results. Other work [15, 8] specifically exploited the structure of directed graph Laplacians. However, they did so without the benefit of a clear, standardized theory describing such Laplacians.

This is an area of active on-going research. One focus of research is the global attractor conjecture, which asserts that if the associated directed graph is componentwise strongly connected in the zero deficiency case, then *every* initial condition in the open orthant converges to an equilibrium (see the remark after Theorem 7.3). This conjecture appears as early as [17], where it was mistakenly believed to be proved, and has been shown in certain cases [1]. The analysis of higher deficiency reaction networks is another active area of study [18, 22, 19]. Some results can be extended fairly easily to the deficiency one case as discussed in [13], but in general the behavior of higher deficiency networks is not well understood. Another important open question is that of "persistence". In general, a persistent reaction network is one in which all chemical concentrations have a positive lower bound for all positive time [5, 13]. One famous and, so far, unproved conjecture is that this holds for every network whose associated directed graph is componentwise strongly connected (independent of the deficiency) [25]. See also the comment after Theorem 5.4.

The original emphasis in reaction networks was biased towards controlling chemical reactions and therefore trying to ensure that exotic behavior does not arise. However, in recent years the promise of applying CRN theory to complex biological systems has shifted that interest towards seeking out and analyzing more complicated behaviors [15]. For instance, for the high deficiency case, it possible that reactions take place even though the associated linear system of reaction equations is at an equilibrium. For a collection of examples, we refer the reader to [13].

The outline of this paper is as follows. We first (Section 2) discuss some well-known preliminary results that we will need later, as well as some notation. In Section 3, we summarize the modern theory of directed graph Laplacians and its conclusions. Section 4 describes the mathematical definition of chemical reaction networks. Section 5 states and proves the zero deficiency theorem. In Sections 6 and 7, we prove that in zero deficient systems satisfying a certain connectedness property, each invariant subspace has a unique asymptotically stable equilibrium. In Section 8, we give a few examples of reaction networks designed to illustrate the theory. In Section 9, we compare our results and their classical counterparts and show that our results in some cases improve classical results.

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2 Preliminaries

In this section, we summarize some well-known results that we will need to use later and present some notation. The first two lemmas are standard results of linear algebra. Let $A : \mathbb{R}^n \to \mathbb{R}^m$ and $B : \mathbb{R}^e \to \mathbb{R}^n$ be linear maps and V and W (linear) subspaces of $\mathbb{R}^n$.

Lemma 2.1 *For linear subspaces V and W: $V^\perp \cap W^\perp = (V + W)^\perp$.*

Lemma 2.2 *For any matrix A we have:* $\operatorname{Ker} A = (\operatorname{Im} A^T)^\perp$*, where the orthogonal complement is in the domain of A.*

It follows that $\operatorname{Ker} A$ and $\operatorname{Im} A^T$ span the domain of A and so the sum of their dimensions equals n. $\dim \operatorname{Ker} A$ is referred to as the nullity of A and $\dim \operatorname{Im} A^T$ is equal to the rank of A.

Putting the previous lemmas together, we immediately see the following.

Proposition 2.3 *For any two matrices A and B:* $[\operatorname{Ker} A \cap \operatorname{Im} B]^\perp = \operatorname{Im} A^T + \operatorname{Ker} B^T$.

Proposition 2.4 *For any two matrices A and B:* $\dim [\operatorname{Ker} B \cap \operatorname{Im} A] = \dim \operatorname{Ker} BA - \dim \operatorname{Ker} A$.

Proof. To prove the equality, it is sufficient to show that the linear map $x \to Ax$ induces a bijection

$$\psi : \operatorname{Ker} BA / \operatorname{Ker} A \to \operatorname{Ker} A \cap \operatorname{Im} B\,.$$

Indeed, ψ is well-defined and injective, because for x and y in $\operatorname{Ker} BA$:

$$Ax = Ay \quad \Longleftrightarrow \quad A(y-x) = 0 \quad \Longleftrightarrow \quad y - x \in \operatorname{Ker} A\,.$$

Clearly ψ is surjective, because for any $z \in \operatorname{Ker} B \cap \operatorname{Im} A$, there is an x such that $z = Ax$. ∎

We will also need a few simple calculus lemmas.

Lemma 2.5 *For any $a > 0$ and $b > 0$, we have: $a(\ln a - \ln b) \geq a - b$. Equality iff $a = b$.*

Proof. The tangent line to $\ln x$ at $x = 1$ is above the graph of that function for all $x \neq 1$, and so $x - 1 \geq \ln x$. Substituting $x = b/a$ yields the result. ∎

Lemma 2.6 *For any $a > 0$ and $b > 0$, we have: $(a - b)(\ln a - \ln b) \geq 0$. Equality iff $a = b$.*

Proof. Lemma 2.5 implies $-b(\ln a - \ln b) \geq b - a$. Adding that inequality to the one in Lemma 2.5 proves the result. ∎

Lemma 2.7 *For any $x > 0$ and $z > 0$, there are $\mu_\pm \in \mathbb{R}$ such that $\forall \mu \notin [\mu_-, \mu_+]$: $xe^\mu - z\mu > x$.*

Proof. Taking the derivative of $f(\mu) := xe^\mu - z\mu$ shows that this function has a global minimum at $\mu^* = \ln z - \ln x$. Applying Lemma 2.5 to $f(\mu^*) = z - z(\ln z - \ln x)$ shows that $f(\mu^*) \leq z$. Finally, $\lim_{\mu \to \pm\infty} f(\mu) = +\infty$. ∎

Finally, we need a result from the theory of dynamical systems.

Definition 2.8 *A function $V : \mathcal{O} \subseteq \mathbb{R}^n \to \mathbb{R}$ where $\mathcal{O}$ is open, is called a Lyapunov function for the system $\dot{x} = f(x)$ in $\mathbb{R}^n$ if it is a continuously differentiable and satisfies that along a trajectory $\dot{V}(x(t)) := (\nabla V(x(t)), \dot{x}(t)) \leq 0$, where $(,)$ is the standard inner product, and ∇ the gradient, both in R^n.*

Definition 2.9 *The ω-limit set of x is the set of points y for which there is a sequence $t_n \to \infty$ so that* $\lim_{n\to\infty} x(t_n) = y$

Theorem 2.10 *[28] Let $V : \mathcal{O} \to \mathbb{R}$ be a Lyapunov function for the system $\dot{x} = f(x)$. The intersection of the ω-limit set of a point x and the set $\mathcal{O}$ is contained in the set where $(\nabla V(x(t)), \dot{x}(t)) = 0$.*

From now on, we will use the abbreviation $\dot{V}$ instead of the cumbersome $(\nabla V(x(t)), \dot{x}(t))$.

Finally, we mention some notation that will be used throughout this paper. Given vectors x and y in $\mathbb{R}^n$, we define $x \odot y$ as the vector whose components are $x_i y_i$. (This is also called the Hadamard product.) We write x/y for the vector whose components are $\frac{x_i}{y_i}$ ($y_i \neq 0$ for all i). The componentwise logarithm of x ($x_i > 0$ for all i) is denoted by $\operatorname{Ln} x$, while the componentwise exponential of x will be written as $\operatorname{Exp} x$. We write $x > 0$ when $x_i > 0$ for all i. Given a system of differential equations $\dot{x} = f(x)$, we will use the word *equilibrium* for a point x such that $f(x) = 0$.

3 Laplacians

Two things are important to bear in mind when working with *directed* graphs to model certain phenomena. First of all, directed graphs are used to model interactions that are not symmetric, i.e. the influence of x on y may not be the same as the influence of y on x. As a result, the Laplacian is usually not symmetric and its eigenvalues are not necessarily real. Another complicating factor is that different authors may choose opposite orientations of the edges. Below, we will use $G^{\urcorner}$ for the graph obtained from a graph G by reversing the orientation of all edges (compare Figures 3.1 and 3.2).

The conventions outlined in this section are taken from [6, 30, 31].

We now give a few of the basic facts of Laplacian dynamics in a directed, loopless[1] graph G. We assume that G has v vertices and e directed edges. The $v \times e$ matrix B is the *begin matrix* [29] such that $B_{ij} = 1$ if vertex i starts edge j and 0 otherwise. Similarly, the $v \times e$ *end matrix* [29] E is defined by $E_{ij} = 1$ if vertex i ends edge j and 0 otherwise. We use these matrices to define the boundary operator (or *incidence matrix* in graph theory texts) $\partial := E - B$. As an example, we exhibit the boundary operator associated the graph in Figure 3.1:

$$\partial = E - B = \begin{pmatrix} 1 & 1 & 0 & 0 & 0 & 0 & 0 & 0 \\ -1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & -1 & 1 & 0 & 0 \\ 0 & 0 & -1 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & -1 & 1 & 0 & 0 & 0 \\ 0 & -1 & 0 & 0 & 0 & 0 & 1 & -1 \\ 0 & 0 & 0 & 0 & 0 & -1 & -1 & 1 \end{pmatrix} \tag{3.1}$$

The *weight matrix* W is diagonal with (strictly) positive weights on the diagonal. The weights are equal to 1 in the *unweighted* case.

Definition 3.1 *[29] The* undirected *weighted Laplacian L (also called the Kirhhoff matrix) is given*

[1] A loop is an edge that starts and ends at the same vertex

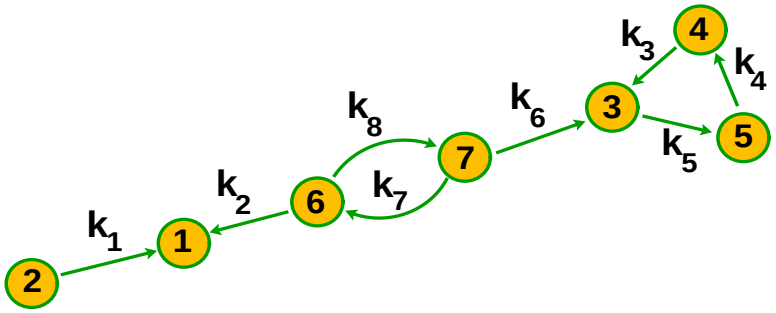

Figure 3.1: *An example of a directed network G. See also Section 8.*

by:

$$L \equiv \partial W \partial^T = (E-B)W(E-B)^T.$$

It is the sum of the in-degree *Laplacian* L_{in} *and the* out-degree *Laplacian* L_{out}.

$$L_{\text{in}} = EW(E-B)^T \qquad \text{and} \qquad L_{\text{out}} = -BW(E-B)^T.$$

Note that the out-degree Laplacian of G is the same as the in-degree Laplacian of $G^{\curlywedge}$.

As an example, we give the unweighted in- and out-degree Laplacian of the graph G in Figure 3.1. The ith row of L_{in} gives the vertices with edges coming *to* the ith vertex, while the the ith row of L_{out} gives the vertices with edges coming *from* the ith vertex.

$$L_{\text{in}} = \begin{pmatrix} \mathbf{2} & \mathbf{-1} & 0 & 0 & 0 & \mathbf{-1} & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \mathbf{2} & \mathbf{-1} & 0 & 0 & \mathbf{-1} \\ 0 & 0 & 0 & \mathbf{1} & \mathbf{-1} & 0 & 0 \\ 0 & 0 & \mathbf{-1} & 0 & \mathbf{1} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & \mathbf{1} & \mathbf{-1} \\ 0 & 0 & 0 & 0 & 0 & \mathbf{-1} & \mathbf{1} \end{pmatrix} \tag{3.2}$$

$$L_{\text{out}} = \begin{pmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ \mathbf{-1} & \mathbf{1} & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \mathbf{1} & 0 & \mathbf{-1} & 0 & 0 \\ 0 & 0 & \mathbf{-1} & \mathbf{1} & 0 & 0 & 0 \\ 0 & 0 & 0 & \mathbf{-1} & \mathbf{1} & 0 & 0 \\ \mathbf{-1} & 0 & 0 & 0 & 0 & \mathbf{2} & \mathbf{-1} \\ 0 & 0 & \mathbf{-1} & 0 & 0 & \mathbf{-1} & \mathbf{2} \end{pmatrix} \tag{3.3}$$

Remark: More generally, a Laplacian is a square matrix with non-negative diagonal and non-positive off-diagonal elements whose row-sums all give zero. It is easy to see that any such matrix can be written in the form stipulated by Definition 3.1.

Definition 3.2 *[6, 30, 31] Given a directed graph G.*
1) A vertex j is in the reachable set from the vertex i if $j = i$ or there is a directed path from i to j, $i \rightsquigarrow j$. The reachable set from i is called $R(i)$.

2) A reach *R is a maximal reachable set (i.e. one that is not* properly *contained in any other reachable set $R(j)$).*
3) A cabal *$C \subseteq R$ is the maximal (largest) set of vertices from which all of a reach R is reachable.*
4) The exclusive part H of a reach R is the set of vertices contained in R and in no other reach.
5) The common part $C = R - H$ is the set of vertices that R has in common with some other reach.

To illustrate these notions, consider the network of Figure 3.1. There are two reaches: $R_1 = \{2, 1\}$ and $R_2 = \{1, 6, 7, 3, 4, 5\}$. Their cabals are given by $B_1 = \{2\}$ (in R_1) and $B_2 = \{6, 7\}$ (in R_2). (We note that a cabal consisting of a single vertex as is the case in R_1 is often called a *leader*.) In R_1, only $H_1 = \{1\}$ is not shared by R_2, and so $C_1 = \{2\}$. Similarly, $H_2 = \{6, 7, 3, 4, 5\}$, while $C_2 = \{1\}$.

Definition 3.3 *[6, 30, 31] A* co-reach *is a reach in $G^{\curvearrowleft}$ and a* co-cabal *is a cabal in $G^{\curvearrowleft}$.*

Thus the *co-reaches* and *co-cabals* of G in Figure 3.1 can be found as the reaches and cabals of $G^{\curvearrowleft}$ in Figure 3.2. They are given by $R_1^{\curvearrowleft} = \{2, 1, 6, 7\}$ with cabal $B_1^{\curvearrowleft} = \{1\}$ and $R_2^{\curvearrowleft} = \{6, 7, 3, 4, 5\}$ with cabal $B_2^{\curvearrowleft} = \{3, 4, 5\}$.

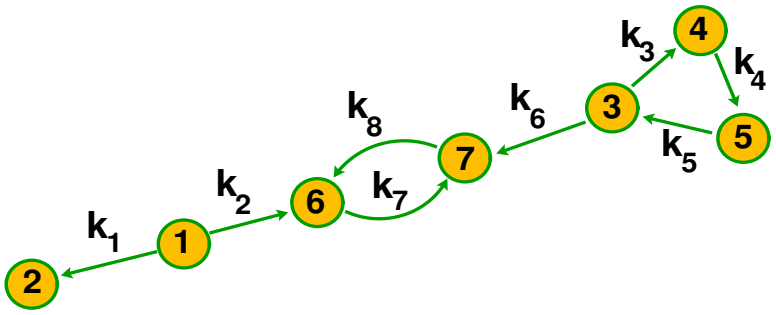

Figure 3.2: *The directed network $G^{\curvearrowleft}$ obtained from Figure 3.1 by reversing the orientation of the edges.*

In the following, the right kernel of a matrix A denotes the set of vectors x so that $Ax = 0$, while the left kernel is the set of (row) vectors y such that $yA = 0$.

Theorem 3.4 *[6, 30, 31] Let G be a digraph with reaches R_1,..., R_k. The eigenvalue 0 of L_{in} has geometric and algebraic multiplicity k. All other eigenvalues have negative real part.*

Theorem 3.5 *[6, 30, 31] Let G be a digraph with reaches R_1,..., R_k. The* column *vectors $\{\gamma_1, \cdots, \gamma_k\}$ form a basis for the* right *kernel of a Laplacian L_{in}, where:*

$$\begin{cases} \gamma_{m,j} = 1 & \text{if} \quad j \in H_m \quad \textit{(exclusive)} \\ \gamma_{m,j} \in (0,1) & \text{if} \quad j \in C_m \quad \textit{(common)} \\ \gamma_{m,j} = 0 & \text{if} \quad j \notin R_m \quad \textit{(not in reach)} \\ \sum_{m=1}^{k} \gamma_{m,j} = \mathbf{1} \end{cases}$$

Theorem 3.6 *[30, 31] Let G be a digraph with $k \geq 1$ reaches. The* row *vectors $\{\bar{\gamma}_1, \cdots, \bar{\gamma}_k\}$ form a basis for the* left *kernel of a Laplacian $L_{\rm in}$, where:*

$$\begin{cases} \bar{\gamma}_{m,j} > 0 & \text{if} \quad j \in B_m \quad \textit{(cabal)} \\ \bar{\gamma}_{m,j} = 0 & \text{if} \quad j \notin B_m \quad \textit{(not in cabal)} \\ \sum_{j=1}^{k} \bar{\gamma}_{m,j} = 1 \end{cases}$$

Later on, it will be of considerable importance that the vectors $\{\bar{\gamma}_1, \cdots, \bar{\gamma}_k\}$ have disjoint support (as opposed to the vectors $\{\gamma_1, \cdots, \gamma_k\}$) and so form an orthogonal basis of the left kernel. We note in passing that these null vectors form a basis for the space of stationary distributions in Markov chains [30, 31] and are related to the maximal spanning forests [7].

Definition 3.7 *For directed graphs, we distinguish* weakly connected components *– a maximal set of vertices for which there is an* undirected *path between every pair of vertices – from* strongly connected components *(SC's) – a maximal group of vertices for which there is a* directed *path between every pair of vertices.*

Definition 3.8 *A graph G is componentwise strongly connected (abbreviated to CSC) if every weak component is a strong component.*

Remark: One easily sees that the following statements are equivalent:
G is CSC,
$G^{\curlywedge}$ is CSC,
every reach of G (or $G^{\curlywedge}$) is strongly connected, and
every reach is a cabal.

Lemma 3.9 *For any G,* $\operatorname{Rank} \partial$ *(or* $\dim \operatorname{Im} \partial$*) equals the number of vertices minus the number of weak components. Furthermore,* $\operatorname{Nullity} \partial^T$ *(or* $\dim \operatorname{Ker} \partial^T$*) equals the number weak components.*

Proof. It is sufficient to prove this if G consists of one weak component. Suppose G is a weak component with v vertices and k reaches $\{R_i\}_1^k$. Note that since every edge has one endpoint and one begin point, $\partial^T \mathbf{1} = 0$. Lemma 2.2 and the remark following it now imply $\operatorname{Nullity} \partial^T + \operatorname{Rank} \partial = v$. Thus $\operatorname{Rank} \partial \leq v - 1$.

Choose an arbitrary vertex b as basepoint and let $r \neq b$ be any other vertex. By definition 3.7, there is an undirected path γ from b to r. Consider the directed edges e_i of γ. When γ traverses e_i in the positive direction, multiply e_i by $w_i = +1$, and in the other case by $w_i = -1$. The image under ∂ of $\sum w_i e_i$ is $r - b$. This shows that $\operatorname{Rank} \partial \geq v - 1$. The second statement follows from the first, because the remark after Lemma 2.2 says that the sum of the two dimensions must be v. ∎

Remark: This lemma is standard fare in algebraic graph theory [3] and, in fact, algebraic topology. In a nutshell, it is how the zeroth homology and cohomology groups are computed. To illustrate the procedure in the second paragraph of the proof, we turn to Figure 3.1. In that figure, denote the vertices marked with i by v_i and the edges marked with k_j by e_j. Choose, for example, basepoint $b = v_1$ and endpoint $r = v_7$. A path γ from b to r is given by $-e_2 + e_8$. Apply the boundary operator (read off from Figure 3.1 or using (3.1)) to get $\partial\gamma = -(v_1 - v_6) + (v_7 - v_6) = v_7 - v_1$.

4 Chemical Reaction Networks with Mass Action

The three basic ingredients of a CRN are:

$$\begin{cases} c \text{ "concentrations of molecules or similar chemical substances", each denoted by } x_i\,; \\ v \text{ vertices or "concentrations of reacting mixtures", each denoted by } v_i\,; \\ e \text{ directed edges or "reaction rates", each denoted by } e_i\,. \end{cases}$$

We then associate a linear vector space to each of these ingredients as follows. The column vectors $(x_1, \cdots, x_c)^T$ form the space $\mathbb{R}^c$. In the same way, vectors in the space $\mathbb{R}^v$ and $\mathbb{R}^e$ have components v_i and e_i, respectively. The begin and end matrices B and E defined in Section 3 correspond to linear transformations B and E from $\mathbb{R}^e$ to $\mathbb{R}^v$, whereas their transpose acts in the opposite direction.

The spaces $\mathbb{R}^v$ and $\mathbb{R}^e$ are used to compute rates of change of concentrations, not the concentrations themselves. As an example, look at the simple system consisting of the reaction $2H_2 + O_2 \to 2H_2O$. The x_i are the concentrations of, respectively, H_2, O_2, and H_2O. There are 2 vertices, v_1 denotes the concentration of the combination $2H_2 + O_2$ and v_2 that of $2H_2O$ and one edge (or reaction) $v_1 \xrightarrow{e_1} v_2$. While the concentration of $2H_2 + O_2$ is an ambiguous concept, the rate of change of that same quantity due to the reaction, is not.

Next, we describe the relationship between the reacting mixtures and the molecules. (Note that we are dropping the quotation marks.) The count of i-molecules in the jth vertex – or reacting mixture – equals S_{ij}. Put more simply, the jth column of S gives the composition of molecules in the jth vertex. Labeling both from left to right, the matrix S for the reaction given above, is:

$$S = \begin{pmatrix} 2 & 0 \\ 1 & 0 \\ 0 & 2 \end{pmatrix}\,.$$

This defines a linear transformation $S : \mathbb{R}^v \to \mathbb{R}^c$ whose matrix has entries that are *non-negative integers*. In a system with many simultaneous reactions, the rate of change in x_i (indicated by $\dot{x}_i$) equals the sum of the rates of change of those mixtures in which that molecule occurs. Thus

$$\dot{x} = S\dot{v} \qquad \text{or} \qquad \dot{x}_i = \sum_j S_{ij}\dot{v}_j\,. \tag{4.1}$$

Note that if the ith row of S is zero, then x_i is constant and we have a redundant equation. So without loss of generality, we assume that S has no zero rows.

The physical intuition behind a reaction $v_i \xrightarrow{e_\ell} v_j$ in a solution of chemicals is that the reaction rate is proportional to the probability that all the necessary molecules in v_i, the tail of the arrow e_ℓ, "meet" in some small volume (this is called the *mass action principle*). The probability that molecule r is present in some small volume is proportional to x_r, its concentration in the chemical mix. Assuming these probabilities are independent of one another, we see that the probability that all the right molecules of v_i are present in the small volume equals the product of all the concentrations of the molecules in v_i. This product is called $\psi_i(X)$, and these form a vector $\psi(x)$ in $\mathbb{R}^v$. With the above definition of S, we see that this product is proportional to $\prod_j x_j^{S_{ji}}$. We thus define a vector in vertex space $\mathbb{R}^v$ (using the convention that $0^0 := 1$):

$$\psi_i(x) \equiv \prod_j x_j^{S_{ji}} \qquad \text{or} \qquad \operatorname{Ln}\psi(x) = S^T \operatorname{Ln} x\,. \tag{4.2}$$

Next, we transform $\psi \in \mathbb{R}^v$ to the vector in the edge space $\mathbb{R}^e$ whose ℓth component is the reaction rate of the ℓth reaction $v_i \xrightarrow{e_\ell} v_j$. From the previous paragraph, we conclude that the rate of the ℓth reaction is proportional to $\psi_i(x)$, where the ith vertex is the tail (the begin point) of the ℓth directed edge. Thus using the begin matrix B of Section 3, we see that the reaction rates are proportional to

$$B^T\psi(x) \in \mathbb{R}^e.$$

In the chemical literature, this proportionality is (nearly) always expressed by a constant called k. It is important to note that this constant is associated with the ℓth reaction – or edge – and not with the reacting mixture – or begin vertex – of that reaction. Thus we weight the edges using an $e \times e$ diagonal matrix W whose ℓth diagonal element equals a (strictly) positive constant k_ℓ. The reaction rates are therefore given by

$$WB^T\psi(x) \in \mathbb{R}^e.$$

The reaction $v_i \xrightarrow{e_\ell} v_j$ adds to the concentration of mixture v_j and subtracts from the concentration of mixture v_i, both at the rate $k_\ell\psi_\ell$. Again, with the definitions of E and B of Section 3, we compute the rates of change of the concentration reacting mixtures $v \in \mathbb{R}^v$ as:

$$\dot{v} = (E - B)WB^T\psi(x) = \partial WB^T\psi(x) = -L_{\text{out}}^T\psi(x).$$

Finally, in chemical situations we can't necessarily measure or observe directly the concentrations of reacting mixtures. Rather, we observe the concentrations of the various molecules x_i. Applying (4.1) gives us the final form of the dynamical system in $\mathbb{R}^c$ associated to chemical reaction networks

$$\dot{x} = -SL_{\text{out}}^T\psi(x)\,. \tag{4.3}$$

Solutions of this system can also be derived from the solutions of the following system:

$$\dot{v} = -L_{\text{out}}^T\psi(Sv) \in \mathbb{R}^v, \tag{4.4}$$

where we used (4.1). Interestingly, the reverse is *not* necessarily true. A solution of (4.3) does *not* always determine a unique solution of (4.4). In fact, one of the problems that comes up in this type of system, is whether non-trivial reactions can take place even though $\dot{x} = 0$. From the above equations one can see that could happen if during these reactions $\dot{v} \in \operatorname{Ker} S$. This is of course impossible if $\operatorname{Ker} S \cap \operatorname{Im} L_{\text{out}}^T = 0$, as we will see in Section 5.

To summarize the whole framework schematically, here is a diagram of the transformations involved in (4.3).

$$\mathbb{R}^c \xleftarrow{S} \mathbb{R}^v \underbrace{\xleftarrow{\partial} \mathbb{R}^e \xleftarrow{W} \mathbb{R}^e \xleftarrow{B^T}}_{-L_{\text{out}}^T} \mathbb{R}^v \xleftarrow{\psi} \mathbb{R}^c. \tag{4.5}$$

The important step here is that we split these transformations into a non-linear part $\psi(x)$ and a linear part $-SL_{\text{out}}^T$. In the literature, however, since the revolutionary work done in the 1970's [16, 17, 10], the traditional split in treatment has been between $S\partial$ on the one hand and $WB^T\psi$ on the other. This was done, because the weights in W are the reaction rates and these are notoriously difficult to measure. In addition, of course, one did not have access to Theorems 3.5 and 3.6. And

so some of the linear transformations — to wit: WB^T in (4.5) — were lumped with the non-linear part ψ. What we exhibit in this work is the price paid for that choice.

Our next result is a reality check. Since concentrations cannot be negative, we want to make sure that the set $\mathbb{R}^c_+ = \{x \in \mathbb{R}^c \,|\, \forall i \,:\, x_i \geq 0\}$, also called the positive orthant, is forward invariant.

Proposition 4.1 *The positive orthant is forward invariant under the flow of* (4.3).

Proof. Suppose there is an orbit $x(t)$ of the flow defined by (4.3) that leaves the positive orthant. Let us say, for some $\epsilon > 0$, $x_j(t_1) = \epsilon$ and $x_j(t_2) = -\epsilon$ crossing the plane $x_j = 0$ at the point P. Then by continuity, all orbits with initial condition in some (small) neighborhood N of P of the plane $x_j = 0$, will leave the positive orthant. Thus the *flux* must satisfy

$$\int_N \left(-SL^T_{\text{out}}\psi(x) \cdot \hat{e}_j\right)\, dA < 0\,,$$

where $(,)$ denotes the standard inner product, $\hat{e}_j$ is the unit normal to $x_j = 0$ pointing *into* the positive orthant, and dA is the standard $(v-1)$-dimensional area form. To get the contradiction, it is therefore sufficient to show that if $x_j = 0$, then $\left(-SL^T_{\text{out}}\psi(x)\right)_j \geq 0$.

So suppose $x_j = 0$. Since S has no zero rows, there must be a i such that S_{ji} is a positive integer. From (4.2) we see that for all i such that then $S_{ji} > 0$, we have $\psi_i = 0$. The off-diagonal elements of $-L^T_{\text{out}}$ are non-negative, and so for these same i

$$\left(-L^T_{\text{out}}\psi\right)_i = \sum_j \left(-L^T_{\text{out}}\right)_{ij} \psi_j \geq 0.$$

Using again that S_{ji} is non-negative, we have

$$-\left(SL^T_{\text{out}}\psi\right)_j = \sum_i S_{ji}\left(-L^T_{\text{out}}\psi\right)_i \geq 0.$$

This proves the proposition. ∎

The preceding development shows that an out-degree Laplacian arises naturally in the analysis of CRNs. We will see that the algebraic results in Section 3 are of great use in this analysis. However to make use of them, we will need to adapt them to the out-degree Laplacian. Fortunately, this is extremely simple thanks to the dual relationship between the two, namely $L_{\text{out}}(G) = L_{\text{in}}(G^{\curvearrowleft})$ noted in definition 3.1. Theorems 3.4, 3.5, and 3.6 hold for L_{out} if we replace each instance of reach and cabal with the dual notions of co-reach and co-cabal.

It turns out that in the development of our theory, we do not use the fact that S is an integer matrix nor the fact that the Laplacian is out-degree. Hence in the next few sections, we consider the following slightly more general problem.

Remark: From now on, the matrix S is a non-negative matrix with no zero rows, $\psi : \mathbb{R}^c_+ \to \mathbb{R}^v_+$ is defined in (4.2) and L (the Laplacian) is $v \times v$ matrix with non-negative diagonal and non-positive off-diagonal elements whose row-sums all give zero. We consider the system given by (4.3).

Equation (4.3) implies that $\dot{x} \in \operatorname{Im} SL^T$. Thus the orthogonal projection of x to $\left(\operatorname{Im} SL^T\right)^\perp = \operatorname{Ker} LS^T$ is in fact a constant of the motion. This motivates the following definition.

Definition 4.2 *Let $P : \mathbb{R}^c_+ \to \operatorname{Ker} LS^T$ be the orthogonal projection. For $z \in \operatorname{Im} P$, let*

$$X_z := \{x \in \mathbb{R}^c_+ \,:\, P(x) = z\},,$$

These sets are invariant under the flow of (4.3) and will be referred to as invariant sets.

5 The Laplacian Zero Deficiency Theorem

We present two definition for the deficiency of a network. The fact that they are equal follows from Proposition 2.4.

Definition 5.1 *The Laplacian deficiency of a chemical reaction network is given by*

$$\delta_L \equiv \dim\left[\operatorname{Ker} S \cap \operatorname{Im} L^T\right] = \dim \operatorname{Ker} SL^T - \dim \operatorname{Ker} L^T\,.$$

Remark: Note that $\delta_L = 0$ means that $\operatorname{Ker} S \cap \operatorname{Im} L^T = \{0\}$, and thus $\dim \operatorname{Im} SL^T = \dim \operatorname{Im} L^T$.

This remark and theorems 3.5 and 3.6 motivate the following convention.

Definition 5.2 *Suppose a chemical reaction network (or CRN) has $\delta_L = 0$ and its graph has v vertices and k reaches. We will let $\{r_1, \cdots, r_{v-k}\}$ denote a basis of $\operatorname{Im} SL^T$.*

The next result shows that a 0 deficiency network has a strictly positive equilibrium if and only if it is CSC. In the two sections that follow we will refine this to show that if a 0 deficiency network is CSC, then every invariant set X_z (Definition 4.2) has a unique equilibrium (Theorem 6.4) and furthermore, that equilibrium is asymptotically stable (Theorem 7.3).

Theorem 5.3 (Laplacian Zero Deficiency Theorem) *Suppose a chemical reaction network (or CRN) has $\delta_L = 0$. Then the CRN has a (strictly) positive equilibrium if and only if G is CSC.*

Proof. We first prove $\Longrightarrow$. From equation (4.3) we see that the existence of a positive equilibrium together with $\delta_L = 0$ implies that there is a positive vector $\psi^* = \psi(x^*)$ such that $L^T\psi^* = 0$. From Theorem 3.6, we conclude that (recalling that k is the number of reaches)

$$\psi^* = \sum_{m=1}^{k} a_m \bar{\gamma}_m^T, \quad \text{and } \forall\, m,\, a_m > 0. \tag{5.1}$$

Furthermore, since $x^* > 0$, we have $\psi^* > 0$ and so from the form of the $\bar{\gamma}_m$, one notes that each reach must be a cabal, and thus (see remarks after Definition 3.8) a strong component. Thus G is CSC.

Now we prove $\Longleftarrow$. Suppose that every reach is a strong component, then using $\delta_L = 0$ we must show that (5.1) has a positive solution ψ^* with $x^* > 0$. By positivity, we can take the componentwise logarithm of both sides. We note that $\operatorname{Ln} \psi(x^*) = S^T \operatorname{Ln} x^*$. The logarithm of the right hand side of (5.1) can be written as

$$\operatorname{Ln} \sum_{m=1}^{k} a_m \bar{\gamma}_m^T = \sum_{m=1}^{k} (\ln a_m)\, \mathbf{1}_{\mathbf{R_m}} + \operatorname{Ln} \sum_{m=1}^{k} \bar{\gamma}_m^T,$$

where $\mathbf{1}_{\mathbf{R_m}}$ is the characteristic vector of the mth reach or (in this case) component. Note that $\sum_{m=1}^{k} \bar{\gamma}_m$ has all components positive by assumption. Thus from (5.1) we see that we need to solve x^* in

$$S^T \operatorname{Ln} x^* = \sum_{m=1}^{k} (\ln a_m)\, \mathbf{1}_{\mathbf{R_m}} + \operatorname{Ln} \sum_{m=1}^{k} \bar{\gamma}_m^T. \tag{5.2}$$

This can be re-arranged as

$$\operatorname{Ln} \sum_{m=1}^{k} \bar{\gamma}_m^T = S^T \operatorname{Ln} x^* - \sum_{m=1}^{k} (\ln a_m)\, \mathbf{1}_{\mathbf{R_m}}. \tag{5.3}$$

We observe that the first term of the right hand side ranges over $\operatorname{Im} S^T$ and the second over $\operatorname{Ker} L$. This has a solution if

$$\operatorname{Im} S^T + \operatorname{Ker} L = \mathbb{R}^v.$$

However, this is guaranteed by applying Proposition 2.3 to the zero deficiency condition. ∎

This is the analogue of the classical zero deficiency theorem. It can, however, be strengthened significantly with very little effort. Here we first show that once can weaken the existence of an positive equilibrium to the existence of an orbit $x(t)$ such that $\operatorname{Ln} x(t)$ is bounded. Secondly, even if the zero deficiency system is not CSC, we can still write down equations that determine all the equilibria of the dynamics in each X_z of Definition 4.2. In Sections 6 and 7, we will furthermore show existence and uniqueness as well as asymptotic stability of these equilibria.

Theorem 5.4 *Suppose a chemical reaction network (or CRN) has $\delta_L = 0$. Then the CRN has an orbit $x(t) > 0$ such that $\ln x_i(t)$ is bounded for all i if and only if G is CSC.*

Proof. $\Longleftarrow$ follows from Theorem 5.3. For the other direction, we compute

$$\frac{x(\tau) - x(0)}{\tau} = \frac{1}{\tau} \int_0^\tau \dot{x}\, dt = -\frac{1}{\tau} \int_0^\tau S L^T \psi(x(t))\, dt = -S L^T \frac{1}{\tau} \int_0^\tau \psi(x(t))\, dt. \tag{5.4}$$

The requirement on x_i implies that $F(\tau) := \frac{1}{\tau} \int_0^\tau \psi(x)\, dt$ has a compact range of the form $[\epsilon, \epsilon^{-1}]$ for some $\epsilon > 0$. Thus $F(n)$ must have a subsequence $F(n_i)$ convergent to some $F_\infty > 0$. On the other hand, the boundedness of x ensures that left hand side of (5.4) converges to 0 as τ tends to infinity. Thus for the subsequence $\{n_i\}$

$$0 = \lim_{i \to \infty} \frac{x(n_i) - x(0)}{n_i} = -S L^T F_\infty.$$

The remainder of the proof is as in the first part of Theorem 5.3 with F_∞ replacing ψ^*. ∎

Two comments are in order here. The first is that Theorems 5.3 and 5.4 imply that for a deficiency zero system S with associated graph G the following holds:

$$G \text{ is CSC} \Longleftrightarrow S \text{ has equilibrium} \Longleftrightarrow S \text{ admits orbit } x \text{ with } \operatorname{Ln} x \text{ bounded}.$$

In particular, for a (Laplacian) deficiency zero system, we have that that CSC implies that none of the concentrations x_i tend to zero. The persistence conjecture [11] says that this is true independently of the deficiency.

Theorem 5.5 *Suppose a chemical reaction network (or CRN) has $\delta_L = 0$ and its underlying graph has v vertices and k reaches. Then the equilibria in X_{z_0} (see Definition 4.2) must satisfy these v equations in v unknowns (the u_i and a_i):*

$$\psi\left(z_0 + \sum_{i=1}^{v-k} u_i r_i\right) = \sum_{m=1}^{k} a_m \bar{\gamma}_m^T \,,$$

where the r_i are and $\bar{\gamma}_m$ are given in Definition 5.2 and Theorem 3.6.

Proof. For deficiency zero systems, x^* is an equilibrium if and only if $\psi(x^*) \in \operatorname{Ker} L^T$. Using the basis of Theorem 3.6, this reads

$$\psi(x^*) = \sum_{m=1}^{k} a_m \bar{\gamma}_m^T \,.$$

Since X_{z_0} is given by $\left\{z_0 + \sum_{i=1}^{v-k} u_i r_i \mid z_0 \in \operatorname{Ker} LS^T, u_i \in \mathbb{R}\right\}$, the statement follows. ∎

6 Existence and Uniqueness of Equilibria

We will show that a CRN whose associated graph is CSC with zero Laplacian deficiency has *exactly* one positive equilibrium in each invariant set X_z (see Definition 4.2). Informally speaking, then, the set of equilibria forms a graph (as in: *is a function of*) over $\operatorname{Ker} LS^T$. The precise formulation is given below in Theorem 6.4. (See the last paragraph of the introduction for the notation.)

Lemma 6.1 *Given a CSC system with $\delta_L = 0$. Suppose $x^* > 0$ is an equilibrium. Then $x > 0$ is an equilibrium iff $\operatorname{Ln}[\psi(x)/\psi(x^*)] \in \operatorname{Ker} L$, which is equivalent to $\operatorname{Ln}[x/x^*] \in \operatorname{Ker} LS^T$.*

Proof. By our hypotheses, $x^* > 0$ is an equilibrium iff $\psi(x^*) = \sum_{i=1}^{k} a_i \bar{\gamma}_i^T$, with all $a_i > 0$. Similarly, the fact that $x > 0$ is an equilibrium is equivalent to $\psi(x) = \sum_{i=1}^{k} b_i \bar{\gamma}_i^T$, with all $b_i > 0$. Thus, given that $x^* > 0$ is an equilibrium, the same holds for x iff

$$\psi(x)/\psi(x^*) = \sum_{i=1}^{k} \frac{b_i}{a_i} \mathbf{1}_{\mathbf{R_i}} \iff \operatorname{Ln}[\psi(x)/\psi(x^*)] = \sum_{i=1}^{k} \ln \frac{b_i}{a_i} \mathbf{1}_{\mathbf{R_i}} \iff S^T \operatorname{Ln}[x/x^*] = \sum_{i=1}^{k} \ln \frac{b_i}{a_i} \mathbf{1}_{\mathbf{R_i}} \,,$$

where we used that $\operatorname{Ln} \psi = S^T \operatorname{Ln} x$. Using Theorem 3.5, we get $LS^T \operatorname{Ln}[x/x^*] = 0$, implying the lemma. ∎

Proposition 6.2 *Given a CSC system with $\delta_L = 0$. For every $z \in \operatorname{Ker} LS^T$, there exists $y \in \operatorname{Im} SL^T$ such that $x = y + z$ is a positive equilibrium.*

Proof. By Theorem 5.3, we may fix a positive equilibrium x^*. We also fix $z \in \operatorname{Ker} LS^T$. By Lemma 6.1, x is a positive equilibrium if (using the componentwise multiplication $\odot$) it can be written as $x = x^* \odot \operatorname{Exp} \mu$ with $\mu \in \operatorname{Ker} LS^T$. Thus it is sufficient to show that there is a $\mu^* \in \mathbb{R}^c$ so that $y := (x^* \odot \operatorname{Exp} \mu^* - z)$ is orthogonal to $\operatorname{Ker} LS^T$ (i.e. is in $\operatorname{Im} SL^T$), for then $x = z + y$ is a positive equilibrium. Thus we wish to prove that given x^* and z,

$$\exists\, \mu^* \in \operatorname{Ker} LS^T \quad \text{such that} \quad \forall v \in \operatorname{Ker} LS^T \;:\; (x^* \odot \operatorname{Exp} \mu^* - z, v) = 0, \tag{6.1}$$

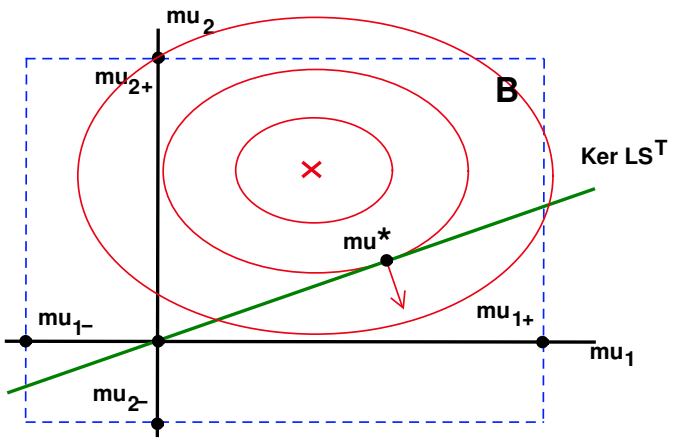

Figure 6.1: $g(\mu) = (x_1 e^{\mu_1} - z_1\mu_1) + (x_1 e^{\mu_1} - z_1\mu_1)$. $g(\mu) > \sum_{i=1}^{c} x_i^*$ *outside the box and* $g(0) = \sum_{i=1}^{c} x_i^*$. *Therefore* g *restricted to* $\operatorname{Ker} LS^T$ *has a minimum inside the box* B.

where $(,)$ stands for the usual inner product. We settle this by defining a smooth function $g(\mu)$ whose gradient ∇g with respect to μ equals $x^* \odot \operatorname{Exp} \mu - z$ and which has a minimum at μ^*, so that $\nabla g(\mu^*) = 0$.

To accomplish this, fix x^* and z as above and define $g : \mathbb{R}^c \to \mathbb{R}$ by setting

$$g(\mu) = (x^*, \operatorname{Exp} \mu) - (z, \mu)\,.$$

This function is a sum of c one-dimensional functions described in Lemma 2.7. This Lemma implies that there is a box $B = [\mu_{1,-}, \mu_{1,+}] \times \cdots \times [\mu_{c,-}, \mu_{c,+}] \subseteq \mathbb{R}^c$ so that

$$\forall \mu \notin B \;:\; g(\mu) > \sum_{i=1}^{c} x_i^* = g(0)\,.$$

See Figure 6.1. Therefore the set C defined by

$$C \equiv \left\{ \mu \in \operatorname{Ker} LS^T \;\middle|\; g(\mu) \le g(0) \right\} \tag{6.2}$$

is non-empty (as it contains 0), closed (by continuity of g), and bounded.

Now we restrict g to $\operatorname{Ker} LS^T$. Since $0 \in \operatorname{Ker} LS^T$, the continuous function g assumes its minimum in $\operatorname{Ker} LS^T$ at a point μ^*. Since g is also differentiable, at $\mu = \mu^*$, we must have

$$\forall v \in \operatorname{Ker} LS^T \;:\; 0 = (\nabla g(\mu^*), v) = \lim_{\epsilon \to 0} \frac{g(\mu^* + \epsilon v) - g(\mu^*)}{\epsilon} = (x^* \odot \operatorname{Exp} \mu^* - z, v)\,,$$

which establishes equation (6.1), thereby proving the proposition. ∎

Proposition 6.3 *Given a CSC system with* $\delta_L = 0$. *For every* $z \in \operatorname{Ker} LS^T$, *there exists* at most one $y \in \operatorname{Im} SL^T$ *such that* $x = y + z$ *is a positive equilibrium.*

Proof. Suppose that we have y and u both satisfying the requirements. Then by Lemma 6.1,

$$\operatorname{Ln}(z + y) - \operatorname{Ln}(z + u) \in \operatorname{Ker} LS^T,$$

and by hypothesis y and u in $\operatorname{Im} SL^T$, so

$$(z+y)-(z+u) \in \operatorname{Im} SL^T.$$

By Lemma 2.2, the two are orthogonal. Taking the inner product of the two differences gives

$$((z+y)-(z+u), \operatorname{Ln}(z+y) - \operatorname{Ln}(z+u)) = 0.$$

Lemma 2.6 then shows that $z+y = z+u$, and therefore $y = u$. ∎

Putting the last two propositions together immediately gives the main result of this section.

Theorem 6.4 *For a CSC system with $\delta_L = 0$ we have the following. For every $z \in \operatorname{Ker} LS^T$, there is a unique $y \in \left(\operatorname{Ker} LS^T\right)^\perp = \operatorname{Im} SL^T$ such that $x = y + z$ is a positive equilibrium.*

Proof. Proposition 6.2 proves existence and Proposition 6.3 proves uniqueness. ∎

Definition 6.5 *Suppose G is CSC with $\delta_L = 0$. The unique positive equilibrium of the flow of (4.3) restricted to the invariant sets X_z (see Definition 4.2) will be denoted by x^*_z.*

7 Convergence to Equilibria

For the definition of Lyapunov functions and their use, we refer the reader to Definitions 2.8 and 2.9 and Theorem 2.10.

The existence of Lyapunov functions depends crucially on the following remarkable result. In the following proposition and proof, we often refer to $\psi(x^*)$ where x^* is an equilibrium. To avoid cluttering the formulas, we abbreviate $\psi(x^*)$ as ψ^*.

Proposition 7.1 *Let L be the in-degree or out-degree Laplacian. Suppose that there is a $\psi^* > 0$ so that $\psi^{*T} L = 0$. Then the associated graph is CSC and for all $\psi > 0$*

$$\psi^T L (\operatorname{Ln}\psi - \operatorname{Ln}\psi^*) = (\psi - \psi^*)^T L (\operatorname{Ln}\psi - \operatorname{Ln}\psi^*) \geq 0.$$

Equality holds if and only if on every strong component C_i there is a constant $c_i > 0$ such that

$$\psi|_{C_i} = c_i \psi^*|_{C_i}.$$

Proof. Let $\psi^* > 0$ and $\psi^{*T} L = 0$. We start by observing that Theorem 3.6 implies that then every vertex is in a cabal and so the associated graph is CSC (see Definition 3.8 and the remark following it). Now we write

$$\psi^T L (\operatorname{Ln}\psi - \operatorname{Ln}\psi^*) = \psi^T L \operatorname{Ln}(\psi/\psi^*)$$

in terms of a sum over its edges. For every directed edge, let w_{ij} be the weight of the edge $j \to i$ if L is in-degree Laplacian, and $i \to j$ if L is an out-degree Laplacian. Denote by $\sum_{edges}$ the sum over all directed edges. We obtain that $\psi^T L \operatorname{Ln}(\psi/\psi^*)$ equals

$$\begin{aligned}\sum_{edges} w_{ij}\psi_i \left(\ln \psi_i/\psi_i^* - \ln \psi_j/\psi_j^*\right) &= \sum_{edges} \psi_i^* w_{ij} \;\; \psi_i/\psi_i^* \left(\ln \psi_i/\psi_i^* - \ln \psi_j/\psi_j^*\right) \\ &\geq \sum_{edges} \psi_i^* w_{ij} \;\; \left(\psi_i/\psi_i^* - \psi_j/\psi_j^*\right) = \psi^{*T} L (\psi/\psi^*).\end{aligned}$$

The inequality follows from Lemma 2.5 (plus the fact that all non-zero weights are positive). By assumption, ψ^{*T} is in the left kernel of L, and so the last expression gives zero.

Lemma 2.5 also implies the necessary and sufficient condition for equality. To be precise, that lemma asserts that the condition for equality in the above formula is that on each edge the value of (ψ/ψ^*) at the head equals its value at the tail. Therefore (ψ/ψ^*) is constant (and positive) on every strong component. ∎

Proposition 7.2 *Given a Laplacian L with $\delta_L = 0$ that has a strictly positive equilibrium x^*. Then the ω-limit set of a positive point x is bounded and is contained in the union of the boundary of $\mathbb{R}^c_+$ and the set of positive equilibria.*

Remark: Note that x^* in the proposition is an equilibrium.

Proof. We will first show that $V : \mathbb{R}^c_+ \to \mathbb{R}$ in (7.1) defined by

$$V(x) = V(x_1, \cdots, x_c) := \sum_{i=1}^{c} \int_{x_i^*}^{x_i} \ln(s/x_i^*)\, ds \tag{7.1}$$

is a Lyapunov function (Definition 2.8) for (4.3). V is clearly continuously differentiable. In the interest of brevity, we write $\dot{V}$ for $(\nabla V(x(t)), \dot{x}(t))$. To show that $\dot{V} \leq 0$, we observe

$$\begin{aligned} \dot{V} &= \dot{x}^T \mathrm{Ln}\,(x/x^*) = -\left(SL^T\psi(x)\right)^T \mathrm{Ln}(x/x^*) \\ &= -\psi^T L S^T \mathrm{Ln}(x/x^*) = -\psi^T L\, \mathrm{Ln}(\psi/\psi^*) = -\psi^T L\, \mathrm{Ln}(\psi - \mathrm{Ln}\psi^*)\,. \end{aligned}$$

Note from (4.2) that $x > 0$ implies $\psi(x) > 0$. It now follows from the first part of Proposition 7.1 that $\dot{V}(x(t)) \leq 0$. The second part of Proposition 7.1 says that $\dot{V}(x) = 0$ iff $\mathrm{Ln}\,[\psi/\psi^*]$ is constant on strong components. Theorem 3.5 implies that then $\mathrm{Ln}\,[\psi/\psi^*]$ is a right null vector of L. From Lemma 6.1 we conclude that then $\dot{V}(x) = 0$ implies that x is an equilibrium.

Thus by Theorem 2.10, the ω-limit set of an initial condition may be unbounded, may contain boundary points of the orthant, and may contain equilibrium points. We rule out the first possibility (unbounded) by showing that trajectories are bounded. Each integral in the sum of (7.1) has the form $I_{x_i^*}(x_i) = \int_{x_i^*}^{x_i} \ln s - \ln x_i^*\, ds$, we have

$$I_{x_i^*}(x_i) = \int_{x_i^*}^{x_i} \ln s - \ln x_i^*\, ds = [s \ln s - s - s \ln x_i^*]_{x_i^*}^{x_i} = x_i(\ln x_i - \ln x_i^*) - (x_i - x_i^*) \geq 0\,.$$

The final inequality here follows from Lemma 2.5. Thus each of the integrals in (7.1) is non-negative. Furthermore, on the one hand, $\dot{V} \leq 0$ and so $V(x(t)) \leq V(x(0))$, and on the other,

$$I_{x_i^*}(x_i) = \int_{x_i^*}^{x_i} \ln s - \ln x_i^*\, ds = x_i(\ln x_i - \ln x_i^* - 1) + x_i^* \tag{7.2}$$

tends to infinity if $x_i \to \infty$. This proves that orbits are bounded. ∎

Remark: We have required that the system satisfies $\delta_L = 0$. This is used to ensure that for any positive equilibrium x^*, we have $\psi(x^*) = \sum_{i=1}^{k} a_i \bar{\gamma}_i^T$. If we *start* with the assumption that there is an equilibrium of that form, the hypothesis $\delta_L = 0$ is not necessary.

Theorem 7.3 *Suppose G is CSC with $\delta_L = 0$. The unique equilibrium x_z^* in X_z (Definition 6.5) is asymptotically stable in X_z. The ω-limit set (Definition 2.9) of any positive initial condition either equals that equilibrium or is a bounded set contained in the boundary of the positive orthant.*

Proof. Existence and uniqueness of x_z^* in X_z follow from Theorem 6.4. Given *any* positive equilibrium x^* and consider the function V in (7.1). Thus V is a sum of integrals as exhibited in (7.2):

$$V(x) = \sum_{i=1}^{c} I_{x_i^*}(x_i)\,.$$

Now $I_{x_i^*}(x_i)$ has a minimum 0 achieved at $x_i = x_i^*$. On the boundary ∂X_z of X_z, at least one of the x_i must be zero. Thus, since $I_{x_i^*}(0) = x_i^*$, V restricted to ∂X_z is greater than or equal to $\min_i x_i^*$. So if we choose an initial condition $x(0)$ such that $V(x(0)) < \min_i x_i^*$, then the fact that $V(x)$ is a Lyapunov function (see the proof of Proposition 7.2) prevents $x(t)$ from having limit points in ∂X_z. Thus by Proposition 7.2, the ω-limit set is contained in the set of equilibria. But by Theorem 6.4, the equilibrium is unique. Thus every orbit with $V(x(0)) < \min_i x_i^*$ converges to the unique equilibrium, which therefore is asymptotically stable. ■

Remark: This proof says that the basin (in X_z) of attraction of the equilibrium x_z^* contains the set $\{x \in X_z \,:\, V(x) < \min_i x_i^*\}$ where V is given by (7.1) and (7.2). This gives us a way to get *some* estimate of the basin of attraction of x_z in X_z. Recall that the global attractor conjecture (see Section 1) says that in this case all positive initial conditions converge to the equilibrium.

8 Examples

Example 1: We consider the following simple system taken from wikipedia's "Chemical reaction network theory" entry:

$$\begin{array}{lrcl} \text{Reaction 1:} & 2\,H_2 + O_2 & \to & 2\,H_2O \\ \text{Reaction 2:} & C + O_2 & \to & CO_2 \end{array}$$

The vertices of the network are:

$$v_1 \leftrightarrow 2\,H_2 + O_2\,,\ v_2 \leftrightarrow 2\,H_2O\,,\ v_3 \leftrightarrow C + O_2\,,\ v_4 \leftrightarrow CO_2\,.$$

The graph G for this system is given in Figure 8.1. Now we set x_i equal to concentration of following

Figure 8.1: *The directed network G of example 1.*

molecules ($[H_2]$ denotes the concentration of H_2 in chemistry notation).

$$x_1 = [H_2]\,,\ x_2 = [O_2]\,,\ x_3 = [H_2O]\,,\ x_4 = [C]\,,\ x_5 = [CO_2]\,.$$

We assume that all molecules are always mixed uniformly so that the mass action principle applies. That principle says that in reaction 1, the increase of the number of x_3 molecules is proportional to twice the product of x_2 and the square of x_1. The (positive) reaction constant is denoted by k_1. Notice that the increase of x_3 molecules must equal the decrease of the x_1 molecules. Reasoning like this we get the following system of equations.

$$\begin{array}{rcl} \dot{x}_1 &=& -2k_1x_1^2x_2 \\ \dot{x}_2 &=& -k_1x_1^2x_2 - k_2x_2x_4 \\ \dot{x}_3 &=& 2k_1x_1^2x_2 \\ \dot{x}_4 &=& -k_2x_2x_4 \\ \dot{x}_5 &=& k_2x_2x_4 \end{array} \tag{8.1}$$

We will now illustrate our methods and main results using this example. Setting up the Laplacian as defined in Section 3 and S as in Section 4, we get

$$L_{\text{out}} = \begin{pmatrix} k_1 & -k_1 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & k_2 & -k_2 \\ 0 & 0 & 0 & 0 \end{pmatrix} \qquad \text{and} \qquad S = \begin{pmatrix} 2 & 0 & 0 & 0 \\ 1 & 0 & 1 & 0 \\ 0 & 2 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{pmatrix}.$$

One computes

$$-SL_{\text{out}}^T = \begin{pmatrix} -2k_1 & 0 & 0 & 0 \\ -k_1 & 0 & -k_2 & 0 \\ 2k_1 & 0 & 0 & 0 \\ 0 & 0 & -k_2 & 0 \\ 0 & 0 & k_2 & 0 \end{pmatrix} \qquad \text{and} \qquad \operatorname{Ln}\psi = S^T \operatorname{Ln} x = \operatorname{Ln} \begin{pmatrix} x_1^2x_2 \\ x_3^2 \\ x_2x_4 \\ x_5 \end{pmatrix}.$$

Writing out equation 4.3, we obtain (8.1) again.

Starting with Section 4, one derives with a little computational effort that the range of SL_{out}^T is spanned by

$$\begin{pmatrix} 1 & 1/2 & -1 & 0 & 0 \end{pmatrix}^T \qquad \text{and} \qquad \begin{pmatrix} 0 & 1 & 0 & 1 & -1 \end{pmatrix}^T,$$

while the kernel of $L_{\text{out}}S^T$ is spanned by

$$\begin{pmatrix} 1 & 0 & 1 & 0 & 0 \end{pmatrix}^T \quad , \quad \begin{pmatrix} 1/2 & -1 & 0 & 1 & 0 \end{pmatrix}^T \qquad \text{and} \qquad \begin{pmatrix} -1/2 & 1 & 0 & 0 & 1 \end{pmatrix}^T.$$

Definition 4.2 and the remark prior to it now imply that the orthogonal projections to the latter are preserved by the flow. Thus

$$c_3 = x_1 + x_3 \quad , \quad c_4 = \tfrac{1}{2}x_1 - x_2 + x_4 \qquad \text{and} \qquad c_5 = -\tfrac{1}{2}x_1 + x_2 + x_5$$

are constants of the motion. The dynamics of the system can therefore be described in terms of the variables

$$u_1 = x_1 + \tfrac{1}{2}x_2 - x_3 \qquad \text{and} \qquad u_2 = x_2 + x_4 - x_5$$

plus the constants c_1, c_2, c_3. The conversion is laborious and the resulting equations are not particularly illuminating, so we leave this as an exercise.

Moving to Section 5, it is not hard to see that $\delta = 0$. Since the graph is not CSC, Theorem 5.3 implies that there is no (strictly) positive equilibrium. In this case, this is reasonably clear from inspecting (8.1). It is even easier to see from the reactions themselves that eventually some of the substances at the left hand of the reactions must run out. Since the associated graph (Figure 3.1) is not CSC, Sections 6 and 7 do not apply.

For the system at hand, we use the above constants of the motion and set x_1 and x_2 to be our independent variables to obtain the equations of Theorem 5.5. Writing the kernel of L_{out} as $\begin{pmatrix} 0 & a_1 & 0 & a_2 \end{pmatrix}^T$ and eliminating x_3, x_4, and x_5 in favor of the constants c_i, we obtain an equilibrium if and only if

$$\begin{array}{rcl} x_1^2 x_2 & = & 0 \\ (c_3 - x_1)^2 & = & a_1 \\ x_2(c_4 - \frac{1}{2}x_1 + x_2) & = & 0 \\ c_5 + \frac{1}{2}x_1 - x_2 & = & a_2 \end{array}$$

And thus given the constants c_i, we can solve for x_1 , x_2, a_1, and a_2.

Example 2: Consider the out-degree Laplacian L_{out} of the graph G in Figure 3.1. For simplicity, we set all $k_i = 1$. The matrix we obtain was given in equation (3.3). This example was chosen to give the same Laplacian as the examples in [30, 31]; its left and right kernels can be found in those papers. In particular, the (right) kernel (Theorem 3.5) of L_{out} is spanned by

$$\gamma_1 = \begin{pmatrix} 0 & 0 & 1 & 1 & 1 & \frac{1}{3} & \frac{2}{3} \end{pmatrix}^T \quad \text{and} \quad \gamma_2 = \mathbf{1} - \gamma_1 = \begin{pmatrix} 1 & 1 & 0 & 0 & 0 & \frac{2}{3} & \frac{1}{3} \end{pmatrix}^T .$$

The left kernel (Theorem 3.6) of L_{out} is spanned by

$$\bar{\gamma}_1 = \begin{pmatrix} 1 & 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix} \quad \text{and} \quad \bar{\gamma}_2 = \begin{pmatrix} 0 & 0 & \frac{1}{3} & \frac{1}{3} & \frac{1}{3} & 0 & 0 \end{pmatrix}.$$

Let S be given by, for example,

$$S = \begin{pmatrix} 0 & 0 & 3 & 3 & 3 & 1 & 2 \\ 1 & 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 2 & 0 & 3 & 0 & 0 & 0 \\ 0 & 0 & 3 & 0 & 0 & 0 & 2 \\ 0 & 0 & 3 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 3 & 0 & 0 \end{pmatrix}$$

One again computes

$$-SL_{\text{out}}^T = \begin{pmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 & 0 \\ 0 & -2 & 0 & -3 & 3 & 0 & 0 \\ 0 & 0 & -3 & 3 & 0 & 2 & -1 \\ 0 & 0 & -3 & 3 & 0 & -2 & 4 \\ 0 & 0 & 3 & 0 & -3 & 0 & 0 \end{pmatrix} \quad \text{and} \quad \psi = \begin{pmatrix} x_2 \\ x_2 x_3^2 \\ x_1^3 x_4^3 x_5^3 \\ x_1^3 x_3^3 \\ x_1^3 x_6^3 \\ x_1 x_5 \\ x_1^2 x_4^2 \end{pmatrix} \tag{8.2}$$

The evolution equations become

$$\begin{array}{rcl} \dot{x}_1 & = & 0 \\ \dot{x}_2 & = & x_1 x_5 \\ \dot{x}_3 & = & -2x_2 x_3^2 - 3x_1^3 x_3^3 + 3x_1^3 x_6^3 \\ \dot{x}_4 & = & -3x_1^3 x_4^3 x_5^3 + 3x_1^3 x_3^3 + 2x_1 x_5 - x_1^2 x_4^2 \\ \dot{x}_5 & = & -3x_1^3 x_4^3 x_5^3 + 3x_1^3 x_3^3 - 2x_1 x_5 + 4x_1^2 x_4^2 \\ \dot{x}_6 & = & 3x_1^3 x_4^3 x_5^3 - 3x_1^3 x_6^3 \end{array} \tag{8.3}$$

Note that the second of these equations implies that there is no positive equilibrium at all! It is possible to show directly that the positive orthant is invariant, but it is much more involved than in the previous example. The kernel of the matrix $L_{\text{out}}S^T$ is spanned by $(1,0,0,0,0,0)^T$ and so in this example the only linear conserved quantity is the value of x_1. It is clear from equation (8.3) that it is conserved, though it would take some work to directly verify that there are no other linear ones.

One confirms (by tedious computation or using symbolic manipulator like MAPLE) that $\operatorname{Ker} SL_{\text{out}}^T = \operatorname{Ker} L_{\text{out}}^T$. Thus the Laplacian deficiency (Definition 5.1) of this system is zero. There is no strictly positive equilibrium, and Theorem 5.3 says that in this is equivalent to G not being CSC. This can be directly verified from Figure 3.1. Better yet, Theorem 5.4 implies that there is no orbit such that for all i, $\ln x_i(t)$ is bounded. The orbit of a positive initial condition must approach the boundary of the orthant or infinity (or both).

In fact, we can use Theorem 5.5 to find the equilibria. Let $\{e_i\}$ denote the standard basis of $\mathbb{R}^v$. Since $\operatorname{Ker} L_{\text{out}}S^T$ is spanned by e_1, we can choose $\{r_2 = e_2, \cdots, r_7 = e_7\}$ as its orthogonal complement. Setting $x_1 = c$ (constant) and using the above expressions for $\bar{\gamma}_1$ and $\bar{\gamma}_2$, the equations for the equilibria become:

$$\begin{pmatrix} u_2 \\ u_2u_3^2 \\ c^3u_4^3u_5^3 \\ c^3u_3^3 \\ c^3u_6^3 \\ cu_5 \\ cu_4^2 \end{pmatrix} = \begin{pmatrix} a_1 \\ 0 \\ a_2/3 \\ a_2/3 \\ a_2/3 \\ 0 \\ 0 \end{pmatrix} .$$

Let us assume that $c > 0$, Then $u_4 = u_5 = 0$. It follows that $a_2 = 0$, and therefore $u_3 = u_6 = 0$. The solutions are $u_1 = c$ and $u_2 = a_1$. One checks directly from (8.3) that $x = (c, d, 0, 0, 0, 0)^T$ are indeed equilibria.

One may object that we have overly simplified by setting all the k_i in Figure 3.1 equal to 1. However, the general conclusions are independent of the k_i. The Laplacian for the general case is

$$L_{\text{out}} = \begin{bmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ -k_1 & k_1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & k_5 & 0 & -k_5 & 0 & 0 \\ 0 & 0 & -k_3 & k_3 & 0 & 0 & 0 \\ 0 & 0 & 0 & -k_4 & k_4 & 0 & 0 \\ -k_2 & 0 & 0 & 0 & 0 & k_2 + k_8 & -k_8 \\ 0 & 0 & -k_6 & 0 & 0 & -k_7 & k_7 + k_6 \end{bmatrix} .$$

Performing the same computations, one shows that the deficiency is still zero, there is one linear constant of the motion, and the equations for the equilibria can still be written out. The main difference is that the one linear constant of the motion now cannot easily be read off from the differential equations, because it depends in a fairly complicated way on the k_i. This, in turn, complicates the form of the equations for the equilibria. Nonetheless, all this can be computed easily using a symbolic manipulator.

Section 6 and 7 assume that G is CSC, and so these have no further implications for this

particular example.

9 Comparison with Classical Results

We briefly compare our formulation of the main results concerning zero deficiency systems — Theorems 5.3, 5.4, 5.5, 6.4, and 7.3 — with their formulation in the literature and show that some of our results are *strictly* stronger than their classical counterparts. For this we briefly return to the context of actual chemical reactions (and to the notation L_{out} for the Laplacian). Recall the equation (4.3), governing this type of system

$$\dot{x} = -SL_{\text{out}}^T\psi(x) = S\partial\, WB^T\psi(x).$$

The only nonlinear term is the function ψ. So the split in treatment between it and the linear terms seems very reasonable. However, as explained by equation (4.5), the traditional split in treatment has been between $S\partial$ on the one hand[2] and $WB^T\psi$ on the other. Thus where we find that $\mathbb{R}^c$ is stratified by invariant affine spaces X_z of Definition 4.2), the traditional stratification is by the sets where the projection to $(\operatorname{Im} S\partial)^T = \operatorname{Ker} \partial^T S^T$ is constant. Though both are invariant sets, these sets are *not* the same! We give examples below.

Summarizing, our Theorems 5.3 and Theorems 6.4 and 7.3 imply the classical results. All we need to do is to make the following replacements:

$$\begin{array}{rcl}
\delta_L = \dim \operatorname{Ker} SL_{\text{out}}^T - \dim \operatorname{Ker} L_{\text{out}}^T & \text{becomes} & \delta = \dim \operatorname{Ker} S\partial - \dim \operatorname{Ker} \partial \\
\operatorname{Ker} L_{\text{out}}S^T \quad \text{and} \quad \operatorname{Im} SL_{\text{out}}^T & \text{becomes} & \operatorname{Ker} \partial^T S^T \quad \text{and} \quad \operatorname{Im} S\partial \\
X_z & \text{becomes} & \{x_0 + V \,:\, V = \operatorname{Im} S\partial\}\,.
\end{array}$$

The following proposition shows that the orthogonal projection onto $\operatorname{Ker} L_{\text{out}}S^T$ gives *as many or more* constants of the motion as the projection onto $\operatorname{Ker} \partial^T S^T$ (see Definition 4.2).

Proposition 9.1 $\operatorname{Ker} \partial^T S^T \subseteq \operatorname{Ker} L_{\text{out}}S^T$.

Proof. This becomes clear once we write L_{out} in full (Definition 3.1):

$$\operatorname{Ker} \partial^T S^T \subseteq \operatorname{Ker} L_{\text{out}}S^T = \operatorname{Ker} BW\partial^T S^T\,. \qquad \blacksquare$$

In example 2 of Section 8, there is a linear conserved quantity, namely $x_1 = c$. As mentioned, this is picked up by our method because $(1, 0, \cdots, 0)^T$ spans the kernel of $\operatorname{Ker} L_{\text{out}}S^T$. However, the classical theory does not pick up this constant. Indeed, one checks that the matrix $\partial = E - B$ is given by

$$\partial = \begin{pmatrix}
-1 & -1 & 0 & 0 & 0 & 0 & 0 & 0 \\
1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & -1 & -1 & 0 & 1 \\
0 & 0 & 0 & 0 & 0 & 1 & -1 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 1 & -1 \\
0 & 1 & 1 & -1 & 0 & 0 & 0 & 0 \\
0 & 0 & -1 & 1 & 1 & 0 & 0 & 0
\end{pmatrix}$$

[2]The matrix $S\partial$ is called the *stoichiometry matrix* in the literature.

Using the same matrix S as before, one obtains that $\operatorname{Ker}\partial^T S^T = \{0\}$. Thus the classical method does not "see" this constant of the motion.

The next proposition shows that if $\delta = 0$, then $\delta_L = 0$. However, in the case of CSC graphs, the two are equivalent. Thus Theorem 5.3 is equivalent to the traditional zero deficiency theorem for these graphs.

Proposition 9.2 *$\delta_L \leq \delta$ with equality if G is CSC.*

Proof. According to Proposition 2.3, we have

$$[\operatorname{Ker} S \cap \operatorname{Im}\partial]^{\perp} = \operatorname{Im} S^T + \operatorname{Ker}\partial^T.$$

This evidently implies that

$$\delta = \dim\left[\operatorname{Ker} S \cap \operatorname{Im}\partial\right] = v - \dim\left[\operatorname{Im} S^T + \operatorname{Ker}\partial^T\right],$$

where v is the dimension of the vertex space (see Section 4). Similarly, we obtain that

$$\delta_L = v - \dim\left[\operatorname{Im} S^T + \operatorname{Ker} BW\partial^T\right],$$

where we have used that $L_{\text{out}} = -BW\partial^T$. The inequality follows from $\operatorname{Ker}\partial^T \subseteq \operatorname{Ker} BW\partial^T$.

When G is CSC, Lemma 3.9 and Theorem 3.5 imply that in addition the dimensions of $\operatorname{Ker}\partial^T$ and $\operatorname{Ker} BW\partial^T = \operatorname{Ker} L_{\text{out}}$ are equal. Thus the two sets must be equal. ∎

Similarly, one proves of course that for CSC graphs, the dimensions of $\operatorname{Ker} L_{\text{out}}S^T$ and $\operatorname{Im} SL_{\text{out}}^T$ are the same as those of $\operatorname{Ker}\partial^T S^T$ and $\operatorname{Im} S\partial$ and so on.

For non-CSC graphs the situation is different as the following simple example shows. Consider the stargraph with 3 outgoing edges from the central vertex. It is easy to see that

$$L_{\text{out}}^T = \begin{pmatrix} 3 & 0 & 0 & 0 \\ -1 & 0 & 0 & 0 \\ -1 & 0 & 0 & 0 \\ -1 & 0 & 0 & 0 \end{pmatrix} \qquad \partial = \begin{pmatrix} -1 & -1 & -1 \\ 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{pmatrix}.$$

The values on the diagonal of the edge weighting matrix W do not matter, so we can take them to be 1. Suppose further that

$$S = \begin{pmatrix} 2 & 1 & 1 & 1 \end{pmatrix}.$$

Since we have

$$SL_{\text{out}}^T = \begin{pmatrix} 3 & 0 & 0 & 0 \end{pmatrix} \qquad \text{and} \qquad S\partial = \begin{pmatrix} -1 & -2 & -2 & -2 \end{pmatrix},$$

it follows that in this example $\delta_L = 0$, while $\delta = 2$. The obvious generalization to the stargraph with k outgoing edges will give $\delta_L = 0$, while $\delta = k - 1$. This shows that the traditional deficiency can be made arbitrarily larger than the Laplacian one.

A much more interesting example of the difference between the Laplacian deficiency δ_L and the traditional deficiency δ is an example that plays an important role in the so-called deficiency one theorem where the additivity of the deficiency is required. We refer to [12] for the details of that

theorem. This example is based on the work [32]. Consider the graph in Figure 9.1 where the matrix S is given by

$$S = \begin{pmatrix} 1 & 0 & 0 & 0 & 0 & 1 \\ 1 & 0 & 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 1 \\ 0 & 0 & 0 & 0 & 1 & 0 \end{pmatrix}.$$

Thus for example, $\psi_3 = x_2 x_4$ (the 3rd column of S) with our usual notation. That means that the

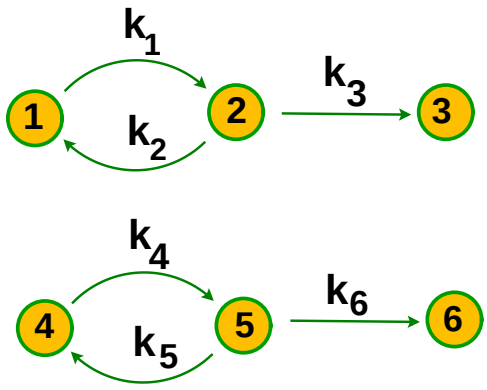

Figure 9.1: *A directed network G with $\delta_L = 0$ and $\delta = 1$.*

end of the 3rd reaction (or the 3rd vertex) vertex should be labelled $X_2 + X_4$, where X_2 and X_4 represent the molecules for which x_2 and x_4 represent the concentrations. For convenience, we list the two relevant matrices.

$$L_{\text{out}} = \begin{pmatrix} k_1 & -k_1 & 0 & 0 & 0 & 1 \\ -k_2 & k_2 + k_3 & -k_3 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & k_4 & -k_4 & 0 \\ 0 & 0 & 0 & -k_5 & k_5 + k_6 & -k_6 \\ 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix} \quad \text{and}$$

$$\partial = \begin{pmatrix} -1 & 1 & 0 & 0 & 0 & 0 \\ 1 & -1 & -1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & -1 & 1 & 0 \\ 0 & 0 & 0 & 1 & -1 & -1 \\ 0 & 0 & 0 & 0 & 0 & 1 \end{pmatrix}.$$

If one does the required computations, whose verification we leave as an exercise, it becomes clear that $\delta_L = 0$, while $\delta = 1$. Since the graph has two identical weak components, the latter cannot be

additive over weak components. Since that is a condition of the traditional deficiency one theorem, this system is outside the scope of both theorems. However, it still falls within the scope of our Laplacian zero deficiency theorem.

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