Chemical Engineering Science, Vol. 42, No. 10, pp. 2229–2268, 1987.
Printed in Great Britain.

0009–2509/87 $3.00 + 0.00
Pergamon Journals Ltd.

REVIEW ARTICLE NUMBER 25

CHEMICAL REACTION NETWORK STRUCTURE AND THE STABILITY OF COMPLEX ISOTHERMAL REACTORS—I. THE DEFICIENCY ZERO AND DEFICIENCY ONE THEOREMS

MARTIN FEINBERG
Department of Chemical Engineering, University of Rochester, Rochester, NY 14627, U.S.A.

(*Received* 3 *February* 1986; *accepted* 19 *August* 1986)

Abstract—The dynamics of complex isothermal reactors are studied in general terms with special focus on connections between reaction network structure and the capacity of the corresponding differential equations to admit unstable behavior. As in some earlier work, the principal results rely on a classification of reaction networks by means of an easily computed non-negative integer index called the deficiency. This index often provides nontrivial information about the kind of dynamics that can be expected. Part of the previously reported Deficiency Zero Theorem is substantially generalized by the Deficiency One Theorem. The foundation is laid for a companion article containing a theory of multiple steady states generated by reaction networks of deficiency one.

CONTENTS

1. INTRODUCTION

It has been known for a long time that *nonisothermal* reactors with very simple chemistry can exhibit unstable behavior. Although detailed theoretical study of these reactors is not entirely straightforward, the analysis is at least made tractable by the presence of relatively few dependent variables (temperature and species concentrations) in the governing system of differential equations.

Somewhat more recent has been the growing awareness that *isothermal* reactors can also exhibit unstable (and sometimes very wild) behavior when the underlying chemistry is suitably intricate. By now there is no shortage of experiments indicating pathological behavior in complex isothermal reactors, nor is there any shortage of model studies showing how certain "play" chemical systems (often unrealistic) can give rise to instabilities in an isothermal setting.

It is entirely understandable that, at the outset, theoretical studies of unstable isothermal reactors should have focused on unrealistic chemical models involving only two or three species. The fact is that not much is known *in general* about large systems of nonlinear differential equations in many dependent variables, and so there is a limit to how much one can bring from the mathematical literature directly to the analysis of a reactor involving, say, seven or eight species.

Nevertheless, simple model studies have their uses. At the very least, they indicate that differential equations of the kind that arise in the description of more realistic systems do indeed have the capacity to admit varieties of unstable behavior observed in experiments. More importantly, simple model studies provide clear, well-worked examples that must be "fit" by any comprehensive theory of isothermal reactor behavior.

But it should also be said that the uses of simple model studies are limited. It is not immediately apparent how even a comprehensive library of "small" examples could provide much help in the study of a realistic isothermal reactor with truly complex chemistry.

If instabilities in real isothermal reactors arise from complexity in the underlying chemistry, then we must ultimately confront the fact that the differential equations describing these reactors will themselves be complex, involving many species and many chemical reactions. To make matters worse, the general shape of the governing equations will change markedly as we proceed from the study of a reactor with a given chemistry to the study of another reactor with a very different chemistry.

Whatever the difficulties might be, it would seem that we must begin to understand the behavior of complex isothermal reactors in a systematic way. If there is an absence of incisive results appropriate for the study of large systems of nonlinear differential equations *in general*, then we have little choice but to develop *special* theory tailored precisely to those systems of differential equations that arise in the study of complex isothermal reactors.

This is the aim of *chemical reaction network theory*. At least in rough terms, the central premise of chemical reaction network theory might be described in the following way: Although the governing differential equations vary markedly from one chemical system to another, the equations themselves are determined in a rather precise way by the underlying network of chemical reactions. Thus, one can hope to draw firm connections between aspects of reaction network structure and the variety of dynamics that might be admitted by the corresponding system of differential equations.

In particular, one would like results of such a theory to satisfy two conditions: First, *they should not be inherently limited in their applicability to "small" systems involving very few reactions among very few species* and, second, *they should be useful to practicing chemists and engineers who, while not necessarily conversant with modern mathematics, have a need to understand complex reactors in a systematic way.*

There should be no misconception about the questions chemical reaction network theory tries to address.

In an initial approach to the understanding of an isothermal laboratory reactor, say one which has exhibited instability, a chemist or engineer usually has very little certainty about the chemical reactions that are actually occurring, much less about precise values of rate constants that are associated with those reactions. (The common assumption is that rate functions are of mass action type.) Thus, in an initial attempt to model the reactor, a presumption about the reactions occurring might lead to the formulation of differential equations, but parameters (rate constants) appearing in these equations usually cannot be filled in with any great confidence. In the absence of detailed knowledge of the rate constants, it is reasonable to ask whether the resulting differential equations *have the capacity* to admit certain kinds of qualitative behavior (e.g. multiple steady states, unstable steady states, sustained composition oscillations)—that is, whether there can even exist rate constant values such that the differential equations resulting from a presumed chemistry admit behavior of a specified kind. In this way one can determine whether a postulated chemistry (taken with mass action kinetics) could, for example, even begin to account for sustained composition oscillations or multiple steady states that might have been observed.

Thus, a central concern of chemical reaction network theory becomes the classification of reaction networks according to the variety of dynamics (i.e. the variety of phase portraits) the corresponding differential equations might possibly admit. When the kinetics is presumed to be mass action, our initial concern will not be with the detailed behavior associated with a particular set of rate constants. Rather, we shall be interested in knowing for a given network whether the corresponding differential equations can, for at least some rate constant values, admit qualitative behavior of a specified kind. In other words, the basic object of study, at least initially, is the reaction network itself, not the reaction network taken with a *particular* assignment of rate constants.

This is the first in a series of articles in which we shall try, in an informal way, to make some results in chemical reaction network theory available to potential users of the theory. To some extent, this article will serve as an introduction to the series. It will provide a backdrop against which future articles can be better understood. By far the most important results contained in this article are the Deficiency Zero Theorem and the Deficiency One Theorem. These will be found in Section 6. Everything else here amounts either to preparation for the theorem statements or to further elaboration on the theorems themselves.

In Section 2 we discuss aspects of reaction network structure; in particular, we provide some vocabulary that will be of importance not only in this article but in future articles as well. In Section 3 we tentatively restrict our attention to closed homogeneous reactors. In that context we indicate how, once a reaction network is assigned a kinetics, the differential equations that govern the species concentrations can be written in vectorial terms. This will provide some "geometric" insight into the way solutions of the equations behave. In Section 4 we broaden our discussion to include open reactors. The central idea there is that, to a great extent, open reactors can be accommodated within the framework established in Section 3 for closed reactors, provided we model contributions of feed and effluent streams by means of certain "pseudoreactions". By enlarging our conception of reaction networks to include such pseudoreactions we can discuss both open and closed reactors in a common mathematical setting. In Section 5 we begin our discussion of the connections between reaction network structure and the nature of solutions to the corresponding differential equations. The connections drawn in Section 5 are not very penetrating, but they are essential precursors to the far deeper results given in Section 6. In Section 6 we state the principal results of this article. Section 7 gives an indication of the problems that future articles will address.

Remark 1.A. *Readers who wish to do so can proceed directly from Section* 5.2 *to Section* 6. *In Section* 6 *all passages labeled "Remark" can also be passed over*. This course of action is especially recommended for readers who are approaching results in chemical reaction network theory for the first time. The omitted material, while worth knowing, is of secondary importance.

We should say at the outset that no theorem given here is limited in its applicability to "small" reaction networks; indeed, the theorems have the capacity to deliver information about networks containing hundreds of species and hundreds of reactions. On the other hand, we shall frequently (but not always) employ small networks in examples designed for illustrative purposes, and it will sometimes happen that in these examples the chemistry is unrealistic, perhaps involving trimolecular reactions. It should be clearly understood that the examples were chosen, not out of disdain for "real" chemistry, but rather out of a desire to give simple, easily assimilated illustrations involving very few species. (The need to study networks that are inconsistent with conservation of mass is explained in Section 4.)

Finally, we wish to call attention to a comprehensive survey by Bruce Clarke of some results in chemical reaction network theory (Clarke, 1980). Moreover, a written version of a lecture by E. Beretta provides an introduction to some interesting ideas about the relationship between reaction network structure and the nature of eigenvalues associated with the linearization of the corresponding differential equations near a steady state (Beretta, 1981).

2. SOME ASPECTS OF REACTION NETWORK STRUCTURE

Chemists sometimes assert that, strictly speaking, all reactions should be considered reversible. This is to say that whenever a reaction is deemed to occur, its reverse should be deemed to occur as well, even if the occurrence rate of the reverse reaction is very small.

For the purpose of modelling, however, one often neglects the occurrence of reactions that are regarded to proceed at very small rates. Our interest here is in properties of reaction network *models*, be they accurate or merely approximate descriptions of whatever chemical systems one might wish to consider. For this reason we shall want to study not only networks in which each reaction is reversible but also networks containing reactions that are regarded to be irreversible. This will complicate our discussion of reaction network structure somewhat, but the resulting theory will have a substantially broader range.

Our aim in this section is to provide a vocabulary with which reaction network structure can be discussed. Some of the terms introduced here will not find use until Section 5, but there are two reasons for locating most of our vocabulary in one place. First, there is a close relationship between some of the terms, and it is advantageous to have them appear in close proximity. Second, this section will also provide the essential vocabulary for a companion article (Feinberg, 1988). Many of the aspects of reaction network structure discussed here were also discussed in (Feinberg, 1980), but we shall need some additional ideas as well.

Our introduction of terminology will be casual, relying more on examples than on formal definitions. [Formal definitions can be found in (Feinberg, 1979, 1986).] At least at the outset our discussion will focus on network (2.1). In that network, as in all our examples, distinct chemical species are designated $A_1, A_2, \ldots$, the way in which species are numbered playing no substantive role.

$$A_1 + A_2 \rightleftarrows A_3 \rightarrow A_4 + A_5 \rightleftarrows A_6$$

$$\begin{tikzcd}
2A_1 \arrow[r] & A_2 + A_7 \arrow[d, shift left] \\
& A_8 \arrow[ul] \arrow[u, shift left]
\end{tikzcd} \tag{2.1}$$

We shall use the symbol N to denote the number of species in a network under consideration. Thus, for network (2.1) $N = 8$. By $\mathbb{R}^N$ we shall mean the usual vector space of N-tuples of real numbers. The standard basis for $\mathbb{R}^N$ will be denoted $\{\mathbf{e}_1, \mathbf{e}_2, \ldots, \mathbf{e}_N\}$, where

$$\begin{aligned} \mathbf{e}_1 &= [1,0,0,\ldots,0] \\ \mathbf{e}_2 &= [0,1,0,\ldots,0] \\ &\vdots \\ \mathbf{e}_N &= [0,0,0,\ldots,1]. \end{aligned} \tag{2.2}$$

2.1. *The complexes of a network*

The *complexes* of a network are the objects that appear before and after the reaction arrows (Horn and Jackson, 1972). Thus the set of complexes for network (2.1) is $\{A_1 + A_2, A_3, A_4 + A_5, A_6, 2A_1, A_2 + A_7, A_8\}$. *We shall reserve the symbol n to denote the number of distinct complexes in a network.* For network (2.1) $n = 7$.

Given a network with N species, we shall associate with each complex a vector in $\mathbb{R}^N$: Consider network (2.1), for which $N = 8$. With complex $A_1 + A_2$ we associate the vector $\mathbf{e}_1 + \mathbf{e}_2$ $(= [1,1,0,\ldots,0])$ in $\mathbb{R}^8$; with complex A_3 we associate the vector $\mathbf{e}_3$ $(= [0,0,1,0,\ldots,0])$; with complex $A_4 + A_5$ we associate the vector $\mathbf{e}_4 + \mathbf{e}_5$ $(= [0,0,0,1,1,0,0,0])$; with complex $2A_1$ we associate the vector $2\mathbf{e}_1$ $(= [2,0,\ldots,0])$; and so on. In this way we obtain the set of *complex vectors* for network (2.1).

In general, for a network with N species and n distinct complexes we obtain a set of n complex vectors in $\mathbb{R}^N$. These we shall usually designate by the symbols $\mathbf{y}_1, \mathbf{y}_2, \ldots, \mathbf{y}_n$, the manner in which complexes are numbered playing no essential role. We shall sometimes find it convenient to blur the distinction between a complex and its vectorial representation so that we can refer to "the complex $\mathbf{y}_i$".

The idea of *the stoichiometric coefficient of a species within a complex* should be familiar: For example, in network (2.1) the stoichiometric coefficients of species A_1 and A_2 in complex $A_1 + A_2$ are each one, while the stoichiometric coefficients of species $A_3, A_4, \ldots, A_8$ are each zero; the stoichiometric coefficient of species A_1 in complex $2A_1$ is two, while the stoichiometric coefficients of $A_2, \ldots, A_8$ within that complex are all zero; and so on. *We denote by y_{iL} the stoichiometric coefficient of species A_L in the ith complex.* This is just the Lth component of the complex vector $\mathbf{y}_i$. It will be understood that the stoichiometric coefficients of the species within the various complexes are all nonnegative numbers.

Hereafter we shall write $\mathbf{y}_i \to \mathbf{y}_j$ (or the abbreviation $i \to j$) to indicate the reaction whereby complex $\mathbf{y}_i$ reacts to complex $\mathbf{y}_j$. Later on we shall denote the set of reactions in a network by the symbol $\mathscr{R}$.

2.2. *The reaction vectors for a network*

Consider a reaction network with N species. With each reaction of the network we associate a *reaction vector* in $\mathbb{R}^N$ obtained by subtracting the "reactant" complex vector from the "product" complex vector. That is, for the reaction $\mathbf{y}_i \to \mathbf{y}_j$ the corresponding reaction vector is $\mathbf{y}_j - \mathbf{y}_i$.

Consider network (2.1), for which $N = 8$. For reaction $A_1 + A_2 \to A_3$ the corresponding reaction vector in $\mathbb{R}^8$ is $\mathbf{e}_3 - (\mathbf{e}_1 + \mathbf{e}_2) = [-1,-1,1,0,\ldots,0]$. The vector corresponding to reaction $2A_1 \to A_2 + A_7$ is $\mathbf{e}_2 + \mathbf{e}_7 - 2\mathbf{e}_1 = [-2,1,0,0,0,0,1,0]$. The complete set of reaction vectors for network (2.1) is displayed in (2.3).

$$\begin{aligned} &\{\mathbf{e}_3 - (\mathbf{e}_1 + \mathbf{e}_2), \mathbf{e}_1 + \mathbf{e}_2 - \mathbf{e}_3, \mathbf{e}_4 + \mathbf{e}_5 - \mathbf{e}_3, \\ &\mathbf{e}_6 - (\mathbf{e}_4 + \mathbf{e}_5), \mathbf{e}_4 + \mathbf{e}_5 - \mathbf{e}_6, \mathbf{e}_2 + \mathbf{e}_7 - 2\mathbf{e}_1, \\ &\mathbf{e}_8 - (\mathbf{e}_2 + \mathbf{e}_7), \mathbf{e}_2 + \mathbf{e}_7 - \mathbf{e}_8, 2\mathbf{e}_1 - \mathbf{e}_8\}. \end{aligned} \tag{2.3}$$

2.3. *The rank of a reaction network*

Recall that a set of vectors $\{\mathbf{x}_1, \mathbf{x}_2, \ldots, \mathbf{x}_k\}$ in $\mathbb{R}^N$ is said to be *linearly dependent* if there exist numbers $\alpha_1, \alpha_2, \ldots, \alpha_k$, not all zero, such that

$$\alpha_1 \mathbf{x}_1 + \alpha_2 \mathbf{x}_2 + \ldots + \alpha_k \mathbf{x}_k = \mathbf{0}. \tag{2.4}$$

Otherwise the set $\{\mathbf{x}_1, \ldots, \mathbf{x}_k\}$ is said to be *linearly independent.*

We shall say that a reaction network has *rank s* (where s is a positive integer) if there exists a linearly independent set of s reaction vectors for the network and there exists no linearly independent set of $s+1$ reaction vectors. That is, the rank of a network is the number of elements in the largest linearly independent set of reaction vectors for the network. *We shall reserve the symbol s to denote the rank of a reaction network.*

Consider, for example, network (2.1). The set of five reaction vectors

$$\begin{aligned} \{\mathbf{e}_3 - (\mathbf{e}_1 + \mathbf{e}_2), \mathbf{e}_4 + \mathbf{e}_5 - \mathbf{e}_3, \mathbf{e}_6 - (\mathbf{e}_4 + \mathbf{e}_5), \\ \mathbf{e}_2 + \mathbf{e}_7 - 2\mathbf{e}_1, 2\mathbf{e}_1 - \mathbf{e}_8\} \end{aligned} \tag{2.5}$$

is linearly independent, but any set of six reaction vectors for network (2.1) is linearly dependent. Thus, the rank of network (2.1) is five, and for it we write $s = 5$.

Remark 2.3.A. For readers who would like a formal procedure to determine the rank of a reaction network we can give the following prescription: Consider a network with N species and r reactions. The reaction vectors for the network are N-tuples, and these can be listed, one under another, to form an $r \times N$ matrix. The rank of the network is then precisely the rank of this matrix, which can be computed by standard methods in matrix theory—for example, by using elementary row operations to reduce the matrix to echelon form. [See (Lang, 1986), pp. 115–122.] The formal procedure described here for calculating the rank of a reaction network is hardly the most efficient. Once we have a little more language available we will be in a position to indicate how the rank of a reaction network can be calculated in a simpler fashion (Remark 2.4.A).

2.4. *The linkage classes of a reaction network*

The display shown in (2.1) is an example of what we call a *standard reaction diagram*: Each complex is written just once, and then arrows are drawn to indicate a "reacts to" relation in the set of complexes. A display of this kind brings out clearly the manner in which the various complexes are "linked" by reaction arrows.

For example, it is evident that the diagram (2.1) is composed of two separate "pieces"—one containing the complexes $\{A_1+A_2, A_3, A_4+A_5, A_6\}$, the other containing the complexes $\{2A_1, A_2+A_7, A_8\}$. Disregarding the directions in which reaction arrows point, we note that complexes in the set $\{A_1+A_2, A_3, A_4+A_5, A_6\}$ are linked to each other, however indirectly, but not to any other complex. Similarly, complexes in the set $\{2A_1, A_2+A_7, A_8\}$ are linked to each other but not to any other complex. We say that the sets $\{A_1+A_2, A_3, A_4+A_5, A_6\}$ and $\{2A_1, A_2+A_7, A_8\}$ are the *linkage classes* of network (2.1). *The symbol ℓ will be used to indicate the number of linkage classes in a network*; thus, for network (2.1) $\ell = 2$.

The number of linkage classes for a network and the linkage classes themselves are readily determined by a glance at the network's standard reaction diagram. The number of linkage classes is simply the number of separate "pieces" of which the diagram is composed. A linkage class is then identified with the set of complexes appearing in one such piece.

A few more examples might be helpful. For network (2.6) $\ell = 3$.

$$\begin{gathered} A_1 \rightleftarrows 2A_2 \rightleftarrows A_3 \\ 2A_3 \rightleftarrows A_4 \\ A_1+A_2 \rightleftarrows A_5 \end{gathered} \tag{2.6}$$

The linkage classes are $\{A_1, 2A_2, A_3\}$, $\{2A_3, A_4\}$ and $\{A_1+A_2, A_5\}$. For network (2.7) $\ell = 1$. The only linkage class is $\{A_1, A_2+A_3, A_4\}$.

$$\begin{tikzcd} A_1 \arrow[rr, shift left] & & A_2+A_3 \arrow[ll, shift left] \\ & A_4 \arrow[ul] \arrow[ur] & \end{tikzcd} \tag{2.7}$$

For network (2.8) $\ell = 2$. The linkage classes are $\{A_1, 2A_2, A_3, A_4, A_5+A_6\}$ and $\{2A_1, A_7\}$.

$$\begin{tikzcd} A_1 \arrow[r, shift left] & 2A_2 \arrow[l, shift left] \arrow[r] \arrow[d, shift left] & A_4 \arrow[r, shift left] & A_5+A_6 \arrow[l, shift left] \\ & A_3 \arrow[u, shift left] & & \\ 2A_1 \arrow[r] & A_7 & & \end{tikzcd} \tag{2.8}$$

In preparation for the next remark we emphasize that here we regard a linkage class to be merely a *set of complexes*. Although the reaction arrows in a specified network determine its linkage classes, the linkage classes themselves are merely sets of complexes devoid of any arrow structure.

Remark 2.4.A. Now that we have available the idea of a linkage class we can state a simple but useful fact, proof of which amounts to a fairly straightforward exercise in elementary linear algebra: *Any two reaction networks with the same complexes and the same linkage classes also have the same rank.*

For example, networks (2.1), (2.9) and (2.10) have the same rank since

$$\begin{gathered} A_1+A_2 \rightarrow A_3 \leftarrow A_4+A_5 \leftarrow A_6 \\ 2A_1 \rightarrow A_2+A_7 \rightarrow A_8 \end{gathered} \tag{2.9}$$

$$\begin{tikzcd} A_1+A_2 & A_3 \arrow[l] \arrow[r] \arrow[d] & A_4+A_5 \\ & A_6 & \\ 2A_1 & A_8 \arrow[l] \arrow[r] & A_2+A_7 \end{tikzcd} \tag{2.10}$$

all three networks have the same complexes and all three have the same linkage classes, $\{A_1+A_2, A_3, A_4+A_5, A_6\}$ and $\{2A_1, A_2+A_7, A_8\}$. *Thus, to determine the rank of network* (2.1) *it suffices to determine the rank of either of the simpler networks* (2.9) *or* (2.10).

Note that network (2.1) contains nine reactions while networks (2.9) and (2.10) each contain only five. Determination of the rank of network (2.1) by the formal procedure described in Remark 2.3.A requires that one calculate the rank of a 9×8 matrix; on the other hand, determination of the rank of network (2.9) or of network (2.10) requires that one study a smaller 5×8 matrix.

From the definition of the rank of a network it follows immediately that a network's rank cannot exceed the number of reactions in the network. Thus, even before we calculate the rank of network (2.1), we can determine that its rank cannot exceed *five*: The rank of network (2.1) is the same as the rank of network (2.9), which contains only five reactions.

It should be clear from the discussion so far that *the precise nature of the reaction arrows in a network affects the rank of the network only insofar as the reaction arrows determine the linkage classes of the network.* Given only the complexes of a network and a specification of how they are partitioned into linkage classes, we can calculate the rank of the network without knowing precisely how the complexes are joined by reaction arrows. To do this, we need only determine the rank of *any* reaction network formed from the specified complexes, these being joined by reaction arrows in such a way that the specified linkage classes are obtained. If there are n complexes and ℓ linkage classes, it is not difficult to see that a network constructed according to these specifications need contain only $n-\ell$ reactions, in which case its rank cannot exceed $n-\ell$. But then the rank of the original network could not exceed $n-\ell$ either, no matter how many reactions that network contained.

In this way we can see that, for any reaction network,

$$n - \ell - s \geqslant 0, \tag{2.11}$$

where n is the number of complexes in the network, ℓ is the number of linkage classes in the network and s is the rank of the network.

2.5. *The deficiency of a reaction network*

For each reaction network we can calculate a non-negative integer index, δ, defined by the formula

$$\delta = n - \ell - s, \tag{2.12}$$

where again n is the number of complexes in the network, ℓ is the number of its linkage classes and s is the rank of the network. The index δ is called the *deficiency* of the network. That the deficiency of every network is non-negative follows from the discussion in Remark 2.4.A.

Remark 2.5.A. From the assertion at the beginning of Remark 2.4.A it follows easily that *any two reaction networks with the same complexes and the same linkage classes also have the same deficiency.* (Two such networks have the same rank; it is obvious that they also have the same number of complexes and the same number of linkage classes.) Thus, *the precise nature of the reaction arrows in a network affects the deficiency of the network only insofar as the reaction arrows determine the linkage classes of the network.*

It will be instructive to calculate the deficiencies of some networks we have already encountered.

For network (2.1) $n = 7$, $\ell = 2$ and $s = 5$; thus, for network (2.1) $\delta = 7-2-5 = 0$. From Remark 2.5.A it follows immediately that networks (2.9) and (2.10) also have deficiencies of zero. For network (2.6) $n = 7$, $\ell = 3$ and $s = 4$; thus $\delta = 7-3-4 = 0$. For network (2.7) $n = 3$, $\ell = 1$ and $s = 2$; thus $\delta = 3-1-2 = 0$. For network (2.8) $n = 7$, $\ell = 2$, $s = 5$, and $\delta = 7-2-5 = 0$.

All the deficiencies calculated so far have been zero. There do, however, exist networks of positive deficiency. Consider, for example, network (2.13).

$$\begin{gathered} A_1 \rightleftarrows A_2 \rightleftarrows A_3 \\ A_1 + A_2 \rightleftarrows 2A_3 \end{gathered} \tag{2.13}$$

Clearly, $n = 5$, $\ell = 2$, and it is easy to determine that $s = 2$. Thus, for network (2.13) we have $\delta = 5-2-2 = 1$. For network (2.14) $n = 4$, $\ell = 1$

$$\begin{tikzcd} 2A_1 \arrow[r, shift left] & A_3 \arrow[l, shift left] \arrow[r, shift left] \arrow[d, shift left] & 2A_2 \arrow[l, shift left] \\ & A_1 + A_2 \arrow[u, shift left] & \end{tikzcd} \tag{2.14}$$

and $s = 2$, whereupon $\delta = 4-1-2 = 1$. In order to provide a counter-example to a seemingly plausible conjecture, Horn and Jackson (1972) studied the dynamics associated with the "play" network (2.15). For this network $n = 4$,

$$\begin{tikzcd} 3A_1 \arrow[r] & A_1 + 2A_2 \arrow[d] \\ 2A_1 + A_2 \arrow[u] & 3A_2 \arrow[l] \end{tikzcd} \tag{2.15}$$

$\ell = 1$ and $s = 1$; thus, $\delta = 4-1-1 = 2$. (Network (2.15) will, for us, serve as a counter-example to a conjecture somewhat different from the one studied by Horn and Jackson.)

2.6. *The rank and the deficiency of a linkage class*

In our discussion of the linkage classes of a reaction network we indicated that the standard reaction diagram for the network can be regarded to be composed of a number of separate "pieces". Thus, for example, the diagram (2.1) is composed of two pieces:

$$A_1 + A_2 \rightleftarrows A_3 \rightarrow A_4 + A_5 \rightleftarrows A_6 \tag*{(2.1)$_1$}$$

and

$$\begin{tikzcd} 2A_1 \arrow[rr] & & A_2 + A_7 \arrow[dl, shift left] \\ & A_8 \arrow[ul] \arrow[ur, shift left] & \end{tikzcd} \tag*{(2.1)$_2$}$$

We can, if we wish, view each such "piece" in a reaction network as a little network unto itself and calculate for each its own rank and deficiency. If, for a network with ℓ pieces, we number the pieces from 1 to ℓ in some arbitrary fashion, we can then designate by n_θ the number of complexes in the θth piece and by s_θ the rank of the θth piece. The deficiency of the θth piece is then given by the formula

$$\delta_\theta = n_\theta - 1 - s_\theta, \tag{2.16}$$

since each piece, viewed as a network by itself, has just one linkage class.

Consider, for example, network (2.1). For the piece displayed as (2.1)$_1$ we have $n_1 = 4$ and $s_1 = 3$ so that $\delta_1 = 4-1-3 = 0$. For the piece displayed as (2.1)$_2$ we have $n_2 = 3$ and $s_2 = 2$ so that $\delta_2 = 3-1-2 = 0$.

Rather than refer to the rank or the deficiency of a "piece" of a reaction network, we shall find it more convenient to refer instead to the *rank of a linkage class* or to *the deficiency of a linkage class.* Thus, we shall refer to the rank or deficiency of linkage class $\{A_1 + A_2, A_3, A_4 + A_5, A_6\}$ in network (2.1) rather than to the rank or deficiency of "piece (2.1)$_1$". Recall that here we regard a linkage class to be a set of complexes devoid of any arrow structure. Nevertheless, there is no ambiguity in our terminology: From the discussion in Remarks 2.4.A and 2.5.A it should be clear that, to calculate the rank and deficiency of a particular piece of a reaction network, it is enough to know *only* the set of complexes appearing in that piece; the result of the calculation is not affected by the precise way in which reaction arrows hold the piece together.

Remark 2.6.A. To understand the hypothesis of Theorem 6.2 in Section 6 [and of the somewhat narrower Theorem 6.1 in (Feinberg, 1980)], readers unacquainted with the rudiments of linear algebra should know that *the rank of a reaction network need not be the same as the sum of the ranks of its linkage classes.* And from this it follows that *the deficiency of a reaction network need not be the same as the sum of the deficiencies of its linkage classes.*

Consider, for example, network (2.13). For the first linkage class, $\{A_1, A_2, A_3\}$, we have $n_1 = 3$ and $s_1 = 2$ so that $\delta_1 = 3-1-2 = 0$. For the second linkage class, $\{A_1 + A_2, 2A_3\}$, we have $n_2 = 2$ and $s_1 = 1$ so that $\delta_2 = 2-1-1 = 0$. Recall that, for the entire network, $n = 5$, $\ell = 2$ and $s = 2$ so that $\delta = 5-2-2 = 1$. Clearly, $s < s_1 + s_2$ and $\delta > \delta_1 + \delta_2$.

Readers familiar with rudimentary linear algebra will see immediately that the rank of a reaction network cannot exceed the sum of the ranks of its linkage classes and, from (2.12) and (2.16), that the deficiency of a reaction network cannot be less than the sum of the deficiencies of its linkage classes.

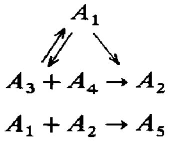
In all the aspects of reaction network structure discussed so far the precise way in which complexes are joined by reaction arrows has played a very marginal role. In particular, the *directions* in which the arrows point do not affect the linkage classes, rank or deficiency of a network, nor do they affect the rank or deficiency of an individual linkage class. Now, however, we shall consider important aspects of network structure in which the directions of reaction arrows play a crucial role.

2.7. *Reversibility and weak reversibility*

By a *reversible* network we shall mean, as usual, one in which each reaction is accompanied by its reverse. For example, networks (2.6), (2.13) and (2.14) are reversible, but networks (2.1), (2.7), (2.8), (2.9), (2.10) and (2.15) are not reversible.

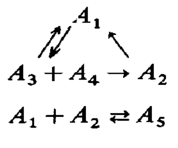
In reaction network theory it often turns out that assertions which hold true for reversible networks are just as easily proved for networks satisfying a weaker condition: We shall say that a network is *weakly reversible* if, whenever there exists a directed arrow pathway (consisting of one or more reaction arrows) "pointing" from one complex to another, there also exists a directed arrow pathway "pointing" from the second complex back to the first.

For example, network (2.17) is *not* weakly reversible. There is a directed arrow pathway from complex $A_3 + A_4$ to complex A_2 but no directed arrow pathway from A_2 back to $A_3 + A_4$. Similarly, there exists a directed arrow pathway from $A_1 + A_2$ to A_5 but no directed arrow pathway from A_5 back to $A_1 + A_2$.



(2.17)

On the other hand, network (2.18) *is* weakly reversible. As in network (2.17) there is a directed arrow pathway from $A_3 + A_4$ to A_2, but now there is a directed arrow pathway from A_2 back to $A_3 + A_4$ (via A_1). As in (2.17) there is a directed arrow pathway from $A_1 + A_2$ to A_5, but now there is a directed arrow pathway from A_5 back to $A_1 + A_2$. By checking all other pairs of complexes in (2.18), one can confirm that the network is weakly reversible. Clearly, network (2.18) is not reversible.



(2.18)

Networks (2.6), (2.13), (2.14) and (2.15) are also weakly reversible, but networks (2.1), (2.7), (2.8), (2.9) and (2.10) are not.

It should be clear that *every reversible network is also weakly reversible.* Thus, *any theorem statement about weakly reversible networks applies to reversible networks as a special case.*

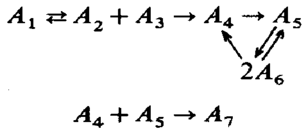
2.8. *The strong linkage classes of a reaction network*

Recall from Section 2.3 that the standard reaction diagram for a reaction network induces a partition of its set of complexes into subsets called linkage classes. Each complex is a member of one and only one linkage class. Recall also that the linkage classes of a network are not affected by the *directions* in which the reaction arrows point.

We shall need to study a somewhat more refined partition of the complexes, one which *is* affected by the directions of the reaction arrows. We shall partition the set of complexes into *strong linkage classes* (Feinberg and Horn, 1977); each complex will be a member of one and only one strong linkage class.

To begin, we say that two *different* complexes in a reaction network are *strongly linked* if there exists a directed arrow pathway pointing from one complex to the other *and* a directed arrow pathway pointing from the second complex back to the first. Moreover, for reasons that will soon become apparent, we adopt the convention that *every complex is strongly linked to itself.*

Consider, for example, network (2.19). Complex A_4 is strongly linked to complex $2A_6$ since there is a directed arrow pathway from A_4 to $2A_6$ (via complex A_5) *and* a directed arrow pathway from $2A_6$ back to A_4. Similarly, A_4 is strongly linked to A_5, and A_5 is strongly linked to $2A_6$. Complexes A_1 and $A_2 + A_3$ are also strongly linked. Complex A_1 is not strongly linked to complex $2A_6$: Although there is a directed arrow pathway from A_1 to $2A_6$ (via complexes $A_2 + A_3$, A_4 and A_5), there is no directed arrow pathway from $2A_6$ back to A_1. The only complex strongly linked to $A_4 + A_5$ is itself; the same is true of complex A_7.



(2.19)

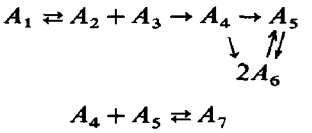
By a *strong linkage class* in a reaction network we mean a set of complexes with the following property: Every pair of complexes within the set is strongly linked, and no complex in the set is strongly linked to a complex that is not in the set. For each reaction network we can determine (uniquely) its strong linkage classes by inspecting the corresponding reaction diagram.

For network (2.19) the strong linkage classes are $\{A_1, A_2 + A_3\}$, $\{A_4, A_5, 2A_6\}$, $\{A_4 + A_5\}$ and $\{A_7\}$. Note that $\{A_5, 2A_6\}$ is *not* a strong linkage class: although complexes A_5 and $2A_6$ are strongly linked, they are both strongly linked to A_4—a complex that lies outside the set $\{A_5, 2A_6\}$. Note also that complex $A_4 + A_5$ is strongly linked to itself but not to any other complex;

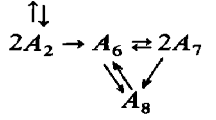
thus $\{A_4 + A_5\}$ is a strong linkage class, as is $\{A_7\}$. The convention adopted earlier—that each complex is strongly linked to itself—ensures that every complex will reside in a strong linkage class.

A few more examples might be helpful.

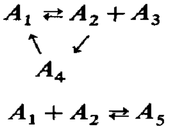
Network (2.20) has the same complexes and linkage classes as network (2.19), but its strong linkage classes are different from those of (2.19). The strong linkage classes of network (2.20) are $\{A_1, A_2 + A_3\}$, $\{A_4\}$, $\{A_5, 2A_6\}$ and $\{A_4 + A_5, A_7\}$.


(2.20)

For network (2.21) the strong linkage classes are $\{A_1, 2A_2\}$, $\{A_3 + A_4, A_5\}$ and $\{A_6, 2A_7, A_8\}$.


(2.21)

The strong linkage classes of network (2.22) are $\{A_1, A_2 + A_3, A_4\}$ and $\{A_1 + A_2, A_5\}$. Note that these are also the linkage classes of network (2.22).


(2.22)

Remark 2.8.A. It should be clear that every strong linkage class in a reaction network lies entirely within a linkage class. For example, the strong linkage class $\{A_4, A_5, 2A_6\}$ in network (2.19) is contained within the linkage class $\{A_1, A_2 + A_3, A_4, A_5, 2A_6\}$. Moreover, each linkage class is the union of strong linkage classes. For example, in network (2.19) the linkage class $\{A_1, A_2 + A_3, A_4, A_5, 2A_6\}$ is the union of the strong linkage classes $\{A_1, A_2 + A_3\}$ and $\{A_4, A_5, 2A_6\}$.

It might of course happen that a linkage class in a network is also a strong linkage class; consider, for example, linkage class $\{A_4 + A_5, A_7\}$ in network (2.20). Note that *both* linkage classes in the weakly reversible network (2.22) are also strong linkage classes. In fact, it is easy to see that *the weakly reversible networks are precisely those for which each linkage class is also a strong linkage class.*

2.9. *The terminal strong linkage classes of a reaction network*

By a *terminal strong linkage class* in a reaction network we mean a strong linkage class containing no complex that reacts to a complex in a different strong linkage class (Feinberg and Horn, 1977). In rough terms, a strong linkage class is terminal if there is no exit from it along a directed arrow pathway.

Recall that the strong linkage classes of network (2.19) are $\{A_1, A_2 + A_3\}$, $\{A_4, A_5, 2A_6\}$, $\{A_4 + A_5\}$ and $\{A_7\}$. The terminal strong linkage classes are $\{A_4, A_5, 2A_6\}$ and $\{A_7\}$. The strong linkage class $\{A_1, A_2 + A_3\}$ is not terminal because complex $A_2 + A_3$ reacts to complex A_4, which is not a member of $\{A_1, A_2 + A_3\}$. Similarly, the strong linkage class $\{A_4 + A_5\}$ is not terminal because $A_4 + A_5$ reacts to A_7, which is not a member of $\{A_4 + A_5\}$.

We shall reserve the symbol t to denote the number of terminal strong linkage classes in a reaction network. Thus, for network (2.19) $t = 2$. For network (2.20) the terminal strong linkage classes are $\{A_5, 2A_6\}$ and $\{A_4 + A_5, A_7\}$ so that $t = 2$. The terminal strong linkage classes of network (2.21) are $\{A_3 + A_4, A_5\}$ and $\{A_6, 2A_7, A_8\}$, and again $t = 2$.

Recall that we denote by ℓ the number of linkage classes in a network. It is not hard to see that each linkage class must contain *at least* one terminal strong linkage class.† Thus, for every reaction network we have

$$t \geqslant \ell. \tag{2.23}$$

That inequality might in fact hold in (2.23) is demonstrated by network (2.21) for which $t = 2$ and $\ell = 1$. On the other hand, for networks (2.19) and (2.20) we have $t = \ell = 2$.

It is instructive to consider the weakly reversible network (2.22). The linkage classes are $\{A_1, A_2 + A_3, A_4\}$ and $\{A_1 + A_2, A_5\}$. Recall that these are the *strong* linkage classes as well. Moreover, it is easy to see that each strong linkage class is also a *terminal* strong linkage class.

In fact, *the weakly reversible networks are precisely those for which the linkage classes, strong linkage classes, and terminal strong linkage classes coincide. Thus $t = \ell$ for every weakly reversible network* (*and, in particular, for every reversible network*). On the other hand, the set of networks for which $t = \ell$ is obviously far larger than the set of weakly reversible networks. [Recall networks (2.19) and (2.20). For both networks $t = \ell$, but neither is weakly reversible.]

Remark 2.9.A. We indicated earlier that, in chemical reaction network theory, assertions which can be proved for reversible networks can often be proved just as easily for weakly reversible networks. At least with respect to certain issues, weakly reversible networks are particularly nice to study because, for them, the linkage classes and terminal strong linkage classes coincide. It sometimes turns out that proofs about weakly reversible networks rely not so much on the fact that the linkage classes and terminal strong linkage classes coincide but, rather, on the fact that the *number* of linkage classes is identical to the *number* of terminal strong linkage classes. For this reason some assertions that hold true for weakly reversible networks also hold

---

†Although we have not said as much explicitly, it is presumed here that all networks under consideration have a finite number of complexes.

true for the more general class of networks which have the property that $t = \ell$. Theorem 6.2, for example, contains an assertion that holds true not only for weakly reversible networks satisfying a certain algebraic condition but also for all networks of the $t = \ell$ class satisfying that same condition.

It should be kept in mind that the class of networks for which $t = \ell$ includes the class of weakly reversible networks and, in particular, the class of reversible networks. Thus, any theorem about networks of the $t = \ell$ class holds true for weakly reversible networks (and for reversible networks in particular).

3. REACTION NETWORKS, KINETICS AND THE CORRESPONDING DIFFERENTIAL EQUATIONS

A chemical reaction network, taken together with a specification of reaction rate functions, gives rise to a system of ordinary differential equations, usually nonlinear. In this section we shall indicate how these equations can be formulated in vectorial terms, for then certain elementary geometrical connections between reaction network structure and the nature of solutions to the equations will become more transparent. Once these connections are understood, we shall be in a position to pose sharper, more incisive questions.

Throughout this section the picture we shall keep in mind is that of a *closed* homogeneous isothermal reactor of constant volume. *Our focus on closed reactors is merely temporary*; it is intended to lay the groundwork for the next section. There we shall consider reactors that are *open* to the exchange of material with the environment, and we shall indicate how ideas discussed here carry over to certain open reactors as well, provided our conception of reaction networks is suitably broadened.

Consider, then, a closed homogeneous (well-stirred) isothermal reactor of constant volume, and suppose that the chemistry within the reactor is believed to be reasonably well-modelled by a reaction network in which the set of species is $\{A_1, A_2, \ldots, A_N\}$. We denote by c_L the (instantaneous) molar concentration of species A_L in the reactor, $L = 1, 2, \ldots, N$. It is, of course, understood that each c_L is non-negative (but not necessarily positive). The (instantaneous) *composition* of the mixture in the reactor is identified with the vector $\mathbf{c} = [c_1, c_2, \ldots, c_N]$ in $\mathbb{R}^N$. Eventually, we shall want to write a differential equation that describes the way in which the composition vector evolves in time.

We denote by $\mathbb{P}^N$ the positive orthant of $\mathbb{R}^N$ and by $\bar{\mathbb{P}}^N$ the non-negative orthant of $\mathbb{R}^N$. That is,

$$\mathbb{P}^N := \{[x_1, x_2, \ldots, x_N] \in \mathbb{R}^N | x_L > 0,\ L = 1, 2, \ldots, N\} \qquad (3.1)$$

and

$$\bar{\mathbb{P}}^N := \{[x_1, x_2, \ldots, x_N] \in \mathbb{R}^N | x_L \geqslant 0,\ L = 1, 2, \ldots, N\}. \qquad (3.2)$$

Note that composition vectors are members of $\bar{\mathbb{P}}^N$ (but not necessarily $\mathbb{P}^N$). Moreover, the complex vectors introduced in Section 2.1 are also members of $\bar{\mathbb{P}}^N$.

Our discussion of reaction rate functions will be facilitated once we have available a little more terminology.

Remember that a composition state of the reactor under consideration might be such that the molar concentrations of certain species in the set $\{A_1, A_2, \ldots, A_N\}$ are zero. By the *support of a composition vector* $\mathbf{c}$, denoted supp $\mathbf{c}$, we shall mean the set of species that are actually present in the reactor when the reactor is in composition state $\mathbf{c}$. That is,

$$\text{supp } \mathbf{c} := \{A_L | c_L > 0\}. \qquad (3.3)$$

Note that for each $\mathbf{c}$ in $\mathbb{P}^N$ we have supp $\mathbf{c} = \{A_1, A_2, \ldots, A_N\}$.

Recall from Section 2.1 that we designate the set of complexes in a reaction network by $\{\mathbf{y}_1, \mathbf{y}_2, \ldots, \mathbf{y}_n\}$, blurring the distinction between a complex and its vectorial representation in $\mathbb{R}^N$. By *the support of complex* $\mathbf{y}_i$, denoted supp $\mathbf{y}_i$, we shall mean the set of all species that have non-zero stoichiometric coefficients in complex $\mathbf{y}_i$. That is,

$$\text{supp } \mathbf{y}_i := \{A_L | y_{iL} > 0\}, \qquad (3.4)$$

where, it will be recalled, y_{iL} is the stoichiometric coefficient of species A_L in complex $\mathbf{y}_i$. Thus, for example, the support of complex $A_1 + A_2$ (or of the vector corresponding to complex $A_1 + A_2$) is $\{A_1, A_2\}$; the support of complex $2A_1$ is $\{A_1\}$; the support of complex $2A_5 + A_6$ is $\{A_5, A_6\}$. In other words, the support of a complex is simply the set of species "appearing in" that complex (with non-zero stoichiometric coefficients).

The terminology given in (3.3) and (3.4) will help us to state and discuss a natural restriction that will be placed upon reaction rate functions. It will also be of some use in Sections 5.3 and 6.1, where we shall discuss, in a qualitative way, the relationship between reaction network structure and the location of steady states and cyclic composition trajectories in $\bar{\mathbb{P}}^N$.

3.1. *Kinetics for a reaction network*

We have presumed that the chemistry in the reactor under consideration is reasonably well-modelled by a certain reaction network. To formulate differential equations that describe how the various species concentrations evolve in time, we must first specify how the instantaneous occurrence rates of the individual reactions in the network depend upon the instantaneous composition state of the reactor

By a *kinetics* for a reaction network with N species we shall mean an assignment to each reaction, $\mathbf{y}_i \to \mathbf{y}_j$, of a *rate function*, $\mathscr{K}_{i \to j}(\cdot)$, that has domain $\bar{\mathbb{P}}^N$ and that takes non-negative values. The non-negative number $\mathscr{K}_{i \to j}(\mathbf{c})$ is the *rate of reaction* $\mathbf{y}_i \to \mathbf{y}_j$ *at composition* $\mathbf{c}$ (per unit reactor volume).

We shall hereafter require of a kinetics that the rate functions have the following properties: For each reaction, $\mathbf{y}_i \rightarrow \mathbf{y}_j$, in the network

(K.1) $\mathscr{K}_{i\rightarrow j}(\cdot)$ is continuously differentiable

and

(K.2) $\mathscr{K}_{i\rightarrow j}(\mathbf{c}) > 0$ if and only if supp $\mathbf{y}_i$ is contained in supp $\mathbf{c}$.

The second condition serves to describe precisely those compositions at which reaction $\mathbf{y}_i \rightarrow \mathbf{y}_j$ proceeds at *non-zero* rate (however slowly). In words, condition (K.2) requires of the rate function $\mathscr{K}_{i\rightarrow j}(\cdot)$ that the reaction $\mathbf{y}_i \rightarrow \mathbf{y}_j$ proceed at non-zero rate in a homogeneous mixture of a specified composition if and only if that composition is such that all species appearing in the *reactant* complex $\mathbf{y}_i$ are actually present in the mixture. (For example, the reaction $A_1 + A_2 \rightarrow A_3$ proceeds at non-zero rate in a homogeneous mixture of composition $\mathbf{c}$ if and only if c_1 and c_2 are both nonzero.) Recall that supp $\mathbf{c}$ is just the set of those species appearing in the network which have nonzero molar concentrations at composition $\mathbf{c}$. Recall also that supp $\mathbf{y}_i$ is the set of species appearing in complex $\mathbf{y}_i$; these are the "ingredients" required for the occurrence of reaction $\mathbf{y}_i \rightarrow \mathbf{y}_j$. Thus, to say that the set supp $\mathbf{y}_i$ is contained in the set supp $\mathbf{c}$ is to say that, at composition $\mathbf{c}$, all ingredients required for the occurrence of reaction $\mathbf{y}_i \rightarrow \mathbf{y}_j$ are, in fact, available.

Remark 3.1.A. For each composition $\mathbf{c}$ in $\mathbb{P}^N$—that is, for each composition at which *all* species concentrations are nonzero—we have supp $\mathbf{c} = \{A_1, A_2, \ldots, A_N\}$, and the support of *every* complex is contained in supp $\mathbf{c}$. Thus, condition (K.2) requires that, at each composition in $\mathbb{P}^N$, *all* reactions proceed at non-zero rate and are, in effect, "switched on".

Remark 3.1.B. We do not take the position here that the only rate functions one should ever study are those which conform to conditions (K.1) and (K.2). Rather, we regard those conditions to be natural ones that are likely to be respected in a wide variety of kinetic models. In fact, for some of the results stated later, conditions (K.1) and (K.2) can be relaxed. [For example, some results require only that all reactions are "switched on" at each composition in $\mathbb{P}^N$; this is implied by but is weaker than condition (K.2).] We have uniformly imposed conditions (K.1) and (K.2) at the outset in order to avoid the more fussy presentation that would result from an attempt to draw every conclusion from the weakest possible hypothesis.

Our primary (but not exclusive) interest will be in reaction systems for which the rate functions are of the standard mass action form. A kinetics for a network is *mass action* if, for each reaction $\mathbf{y}_i \rightarrow \mathbf{y}_j$ of the network, there exists a positive *rate constant*, $k_{i\rightarrow j}$, such that

$$\mathscr{K}_{i\rightarrow j}(\mathbf{c}) \equiv k_{i\rightarrow j} \prod_{L=1}^{N} (c_L)^{y_{iL}}. \tag{3.5}$$

Recall that y_{iL} is the stoichiometric coefficient of species A_L in complex $\mathbf{y}_i$. Thus, with mass action kinetics, the rate of each reaction is proportional to the product of all the molar species concentrations, each raised to a power given by the corresponding stoichiometric coefficient in the *reactant* complex.

By a *reaction system* we shall mean a reaction network taken together with a kinetics. By a *mass action system* we shall mean a reaction system for which the kinetics is mass action.

3.2. *The differential equations for a reaction system*

We have supposed that the chemistry in the reactor under consideration is well-modelled by a particular network of chemical reactions, and we now suppose also that the network has associated with it a kinetics which describes the way in which rates of the various reactions depend upon the composition state of the reactor. Our aim now is to write a (vector) differential equation that describes the way in which the composition evolves in time.

We formulate the (vector) differential equation for a reaction system as follows:

$$\boxed{\dot{\mathbf{c}} = \sum_{\mathscr{R}} \mathscr{K}_{i\rightarrow j}(\mathbf{c})\,(\mathbf{y}_j - \mathbf{y}_i), \quad \mathbf{c} \in \bar{\mathbb{P}}^N} \tag{3.6}$$

The overdot indicates differentiation with respect to time. The symbol $\mathscr{R}$ denotes the set of reactions in the underlying network, and its presence under the summation sign is intended to indicate that the sum is taken over all reactions $\mathbf{y}_i \rightarrow \mathbf{y}_j \in \mathscr{R}$.

The vector differential equation (3.6) encodes a system of N scalar equations, one for each species in the network. The N component equations of (3.6) are

$$\dot{c}_L = \sum_{\mathscr{R}} \mathscr{K}_{i\rightarrow j}(\mathbf{c})\,(y_{jL} - y_{iL}), \quad L = 1,2,\ldots,N. \tag{3.7}$$

Note that, for reaction $\mathbf{y}_i \rightarrow \mathbf{y}_j \in \mathscr{R}$, the number $y_{jL} - y_{iL}$ is the difference between the stoichiometric coefficient of species A_L in the product complex $\mathbf{y}_j$ and its stoichiometric coefficient in the reactant complex $\mathbf{y}_i$. This is just the *net* number of molecules of species A_L produced with each occurrence of reaction $\mathbf{y}_i \rightarrow \mathbf{y}_j$. Thus (3.7) asserts that, at composition $\mathbf{c}$, the rate of change of the molar concentration of species A_L is obtained by summing the reaction occurrence rates, each weighted by the net number of molecules of A_L produced with every occurrence of the corresponding reaction. For reactors of the kind under consideration, this is precisely the idea one normally uses to formulate a system of differential equations governing the species concentrations.

For a mass action system equation (3.6) takes the form

$$\boxed{\dot{\mathbf{c}} = \sum_{\mathscr{R}} k_{i\rightarrow j} \left(\prod_{L=1}^{N} c_L^{y_{iL}} \right) (\mathbf{y}_j - \mathbf{y}_i).} \tag{3.8}$$

By a *steady state* of a reaction system we shall mean a composition $\mathbf{c}^* \in \bar{\mathbb{P}}^N$ such that

$$\mathbf{0} = \sum_{\mathscr{R}} \mathscr{K}_{i \to j}(\mathbf{c}^*)\,(\mathbf{y}_j - \mathbf{y}_i). \tag{3.9}$$

By a *positive steady state* we shall mean a steady state in $\mathbb{P}^N$—that is, a steady state at which all species concentrations are positive.

4. OPEN REACTORS: WHY STUDY "PECULIAR" REACTION NETWORKS?

In the balance of this article the reader will see that we sometimes study reaction networks which, at first glance, seem incompatible with the conservation of mass. In particular, the reader will encounter reactions such as $A_L \to 2A_L$ or even $0 \to A_L$ ("zero reacts to A_L"). It is our purpose in this section to explain not only why it makes sense to study such peculiar networks but also why it is essential that we do so.

At least for *closed* reactors of the kind discussed in Section 3, it is clear that the shape of the governing differential equations is strongly influenced by the nature of the underlying reaction network. Equation (3.6) makes this connection explicit even for arbitrary kinetics. In fact, when the kinetics is mass action, (3.8) tells us that the governing differential equations are, apart from rate constant values, determined *completely* by the underlying reaction network. Thus, it is reasonable to try to develop a broad, incisive theory of equation (3.6)—and, in particular, of its mass action version, (3.8)—that ties qualitative aspects of composition dynamics directly to reaction network structure.

Let us suppose that such a program could be realized. We would nevertheless have to remember that equations (3.6) and (3.8) were formulated with *closed* reactors in mind. Thus it would seem that even a comprehensive theory of these equations would be unable to address questions about the dynamics of *open* reactors. In particular, equations (3.6) and (3.8) were constructed to take account of composition changes due *only* to the occurrence of chemical reactions. They took no account of the possibility that material might be continuously added to or removed from the reactor vessel.

Yet, there is a way in which important categories of open reactors *can* be accommodated within the framework of equations (3.6) and (3.8). In very rough terms, one incorporates into a reaction network certain *pseudoreactions* designed to account for the effect of feed and effluent streams on composition changes within the reactor vessel. These pseudoreactions are assigned rate functions in such a way that (3.6), written for the *augmented* reaction system, reduces precisely to the system of equations one would normally write to describe the particular open reactor under study.

In this way any theory developed for equations (3.6) and (3.8) can be applied directly to the study of open reactors. Suppose, for example, that we could develop theory that ties the capacity of equation (3.6) to admit multiple steady states directly to the structure of the underlying reaction network. Then such a theory might give information about the possibility of multiple steady states in a particular open reactor, *provided it is understood that the reaction network of interest is the augmented one constructed to model not only the effects of true chemical reactions but also the effects of feed and effluent streams.* That is, we would use the theory to tie properties of differential equations written for an open system directly to the structure of the network constructed to model that open system. The crucial idea is that *the model network (taken together with its assigned kinetics) should, when inserted into* (3.6), *give rise to precisely those differential equations one would normally write for the particular open reactor under study.*

Procedures for constructing networks designed to model open systems have been discussed elsewhere—see, for example Horn and Jackson, 1972; Feinberg and Horn, 1974; Feinberg, 1977, 1980. An understanding of these procedures is essential if the theory we shall present is to be applied to open reactors. For this reason we are providing here some easily generalized examples to indicate how important categories of open reactors can be described in reaction network terms. We begin with a remark.

Remark 4.A. (*The Zero Complex*). We shall be employing "pseudoreactions" of the form $0 \to A_L$ (zero reacts to A_L) and $A_L \to 0$ (A_L reacts to zero). The symbol "0" denotes the *zero complex*, which we shall understand to be a complex in which the stoichiometric coefficient of every species is zero. Thus, the complex vector associated with the zero complex is just the zero vector in $\mathbb{R}^N$, where N is the number of species in the entire network. The reaction vector in $\mathbb{R}^N$ associated with the reaction $0 \to A_L$ therefore becomes $\mathbf{e}_L - \mathbf{0} = \mathbf{e}_L$, while the reaction vector associated with the reaction $A_L \to 0$ is $\mathbf{0} - \mathbf{e}_L = -\mathbf{e}_L$.

Suppose that we assign *mass action* kinetics to a network containing the reaction $0 \to A_L$, and suppose that the rate constant for this reaction is α. Then from (3.5) it follows that the rate of reaction $0 \to A_L$ is

$$\alpha (c_1)^0 (c_2)^0 \ldots (c_N)^0 = \alpha.$$

In other words, the reaction $0 \to A_L$ proceeds at a *constant* rate α (independent of composition). A similar observation can be made for any reaction of the form $\mathbf{0} \to \mathbf{y}_j$.

Finally, we note from (3.4) that *the support of the zero complex is the empty set.* Since the empty set is a subset of every set, it follows from condition (K.2) imposed in Section 3 that, even when the kinetics is not mass action, a reaction of the form $\mathbf{0} \to \mathbf{y}_j$ proceeds at *nonzero* rate at *every* composition. That is, there is no composition at which a reaction of the form $\mathbf{0} \to \mathbf{y}_j$ is "switched off".

We are now in a position to show how, by modifying the network of "true" chemical reactions, the differential equations for certain classical categories of open reactors can be brought within the framework of equation (3.6). In all the examples given here we shall be concerned exclusively with mass action kinetics, and so we shall in fact be dealing with equation (3.8), the mass action version of (3.6). For the sake of clarity we have chosen examples involving fairly simple chemistry, but the reader should have no difficulty in seeing how the same strategy can be implemented for open reactors in which the chemistry is more intricate (and in which the kinetics is not necessarily mass action).

4.1. *Homogeneous continuous flow stirred tank reactors*

Consider an isothermal homogeneous continuous flow stirred tank reactor subject to the usual constant density assumption. The only reactions occurring within the reactor vessel are those given in (4.1). The kinetics for (4.1) is mass action with rate constants as indicated.

$$A_1 + A_2 \underset{\beta}{\overset{\alpha}{\rightleftarrows}} A_3. \tag{4.1}$$

Species A_1 and A_2 are carried in the feed stream at constant molar concentrations c_1^f and c_2^f, respectively. The reciprocal of the residence time is ξ. The dynamical equations for the molar concentrations of A_1, A_2, and A_3 within the reactor are given in (4.2).

$$\begin{aligned} \dot{c}_1 &= \xi(c_1^f - c_1) + \beta c_3 - \alpha c_1 c_2 \\ \dot{c}_2 &= \xi(c_2^f - c_2) + \beta c_3 - \alpha c_1 c_2 \\ \dot{c}_3 &= -\xi c_3 + \alpha c_1 c_2 - \beta c_3. \end{aligned} \tag{4.2}$$

Clearly, these are *not* the equations that would emerge from (3.8), *written for the mass action system displayed in* (4.1); in particular, terms in (4.2) resulting from the presence of the feed and effluent streams would be absent.

On the other hand, the differential equations given in (4.2) are *precisely* those that would emerge from (3.8), *written for the mass action system depicted in* (4.3). The pseudoreactions $A_1 \rightarrow 0$, $A_2 \rightarrow 0$ and $A_3 \rightarrow 0$

$$\begin{tikzcd} & & A_1 \arrow[d, shift right, "\xi"'] \\ A_1 + A_2 \arrow[r, shift left, "\alpha"] & A_3 \arrow[l, shift left, "\beta"] \arrow[r, "\xi"] & 0 \arrow[u, shift right, "\xi c_1^f"'] \arrow[d, shift left, "\xi c_2^f"] \\ & & A_2 \arrow[u, shift left, "\xi"] \end{tikzcd} \tag{4.3}$$

are adjoined to the network (4.1) of true chemical reactions in order to model removal of the three species from the reactor vessel by the effluent stream. Note that the rate constant for each of these (first order) reactions is taken to be ξ, the reciprocal of the residence time. Similarly, the pseudoreactions $0 \rightarrow A_1$ and $0 \rightarrow A_2$ are adjoined to the network of true chemical reactions in order to model the addition of A_1 and A_2 to the reactor vessel by the feed stream. The rate constants assigned to these (zeroth order) reactions are ξc_1^f and ξc_2^f, respectively.

Since the differential equations given in (4.2) derive from (4.3) via (3.8), it should be clear that any theory of (3.8) that connects dynamics to reaction network structure becomes applicable to the study of (4.2), *once it is understood that the reaction network of real interest is that given in* (4.3).

It should also be clear how any homogeneous continuous flow stirred tank reactor of the kind considered here can be similarly modelled in reaction network terms.

4.2. *Continuous flow stirred tank reactors involving heterogeneous catalysis*

The situation here is very much like that for homogeneous CFSTRs. There is, however, a difference between the two cases which seems innocuous but which turns out to be rather important (Remark 4.2.A).

Consider an isothermal chamber that is continuously fed a gaseous mixture containing species A, B and an inert carrier (say argon). In the chamber is a solid surface containing active catalyst sites. Species A and B bind to these sites and also desorb from them. Adsorbed A and B react on the surface to form a product, C, which desorbs from the surface and enters the gas phase. A gaseous mixture of A, B, C and inert carrier is continuously withdrawn from the chamber. The gas phase in the chamber and the catalyst surface are each presumed to have a spatially homogeneous composition at all times. Moreover, the volumetric flow rates of the feed and effluent streams are presumed to be equal to each other and time-invariant. (It is supposed that the feed and effluent streams are composed largely of inert gas.)

The chemistry within the chamber (including adsorption and desorption steps) is regarded to be adequately reflected in the reaction diagram (4.4).

$$\begin{aligned} &A_1 + A_4 \underset{\beta}{\overset{\alpha}{\rightleftarrows}} A_5 \\ &A_2 + A_4 \underset{\varepsilon}{\overset{\gamma}{\rightleftarrows}} A_6 \\ &A_5 + A_6 \overset{\nu}{\rightarrow} A_3 + 2A_4. \end{aligned} \tag{4.4}$$

In (4.4) gas phase A, B and C are denoted by A_1, A_2, and A_3, respectively. The symbol A_4 denotes an unoccupied catalyst site, while A_5 and A_6 denote catalyst sites occupied by species A and B, respectively. Rates of the reactions in (4.4) are presumed to be governed by mass action kinetics with rate constants as indicated. (Rates and concentrations are understood to be on a per reactor volume basis. Conversion factors involving the catalyst surface area per unit reactor volume are understood to be absorbed in the rate constants.)

The species concentrations are presumed to be governed by the system of differential equations displayed in (4.5). The symbols c_1^f and c_2^f denote the (fixed) concentrations of A_1 and A_2 (i.e. A and B) in the feed stream, and the symbol ξ denotes the reciprocal of the residence time associated with the gaseous feed and effluent streams.

$$
\begin{aligned}
\dot{c}_1 &= \xi(c_1^f - c_1) - \alpha c_1 c_4 + \beta c_5 \\
\dot{c}_2 &= \xi(c_2^f - c_2) - \gamma c_2 c_4 + \varepsilon c_6 \\
\dot{c}_3 &= -\xi c_3 + \nu c_5 c_6 \\
\dot{c}_4 &= -\alpha c_1 c_4 + \beta c_5 - \gamma c_2 c_4 + \varepsilon c_6 + 2\nu c_5 c_6 \\
\dot{c}_5 &= \alpha c_1 c_4 - \beta c_5 - \nu c_5 c_6 \\
\dot{c}_6 &= \gamma c_2 c_4 - \varepsilon c_6 - \nu c_5 c_6.
\end{aligned}
\tag{4.5}
$$

Note that the equations given in (4.5) are *not* those one would obtain from (3.8), written for the mass action system depicted in (4.4). In particular, the system (4.4) would not give rise to terms in (4.5) that account for the presence of the feed and effluent streams.

However, (4.5) is *precisely* what would be obtained if (3.8) were written for the "augmented" mass action system displayed in (4.6). The pseudoreactions $A_1 \to 0$, $A_2 \to 0$ and $A_3 \to 0$, each taken with rate constant ξ, account for the presence of the effluent stream, while the pseudoreactions $0 \to A_1$ and $0 \to A_2$, taken with the indicated rate constants, account for the presence of A_1 and A_2 in the feed stream.

$$
\begin{array}{c}
A_1 \\
\xi \downarrow\uparrow \xi c_1^f \\
A_3 \xrightarrow{\xi} 0 \\
\xi \uparrow\downarrow \xi c_1^f \\
A_2 \\
\\
A_1 + A_4 \underset{\beta}{\overset{\alpha}{\rightleftarrows}} A_5 \\
\\
A_2 + A_4 \underset{\varepsilon}{\overset{\gamma}{\rightleftarrows}} A_6 \\
\\
A_5 + A_6 \xrightarrow{\nu} A_3 + 2A_4.
\end{array}
\tag{4.6}
$$

Because the differential equations in (4.5) derive from (4.6) via (3.8), any theory of (3.8) that connects dynamics to reaction network structure becomes applicable to the study of (4.5), *provided it is kept in mind that the network of interest is* (4.6), *not* (4.4).

The CFSTR described here was studied in (Lyberatos *et al.*, 1984).

Remark 4.2.A. There is a physical distinction between homogeneous CFSTRs and CFSTRs involving heterogeneous catalysis that turns out to have important mathematical implications.

In the case of *homogeneous* CFSTRs every species present in the reactor vessel is also in the effluent stream. Thus, when such a reactor is modelled in reaction network terms, one must adjoint to the network of true chemical reactions a pseudoreaction of the form $A_L \to 0$ for *each* species in the network. When there are several bimolecular complexes in the network of true chemical reactions, the addition of such a large number of pseudoreactions will generally result in a network of deficiency two or more.

In the case of CFSTRs involving heterogeneous catalysis the situation is somewhat different. Only *certain* species are in the effluent stream—i.e., those present in the fluid phase. Thus, there are relatively few pseudoreactions that need be adjoined to the true chemical reactions. Even when the surface chemistry (including adsorption–desorption steps) is moderately complicated, the deficiency of the resulting model network often turns out to be *one*. (For network (4.6) $n = 10$, $\ell = 4$ and $s = 5$ so $\delta = 10 - 4 - 5 = 1$.)

Thus, theory developed specifically for deficiency *one* networks often serves to give very useful information about CFSTRs involving heterogeneous catalysis. On the other hand, the study of *homogeneous* CFSTRs with even moderately complicated chemistry generally requires somewhat different ideas.

4.3. *Reactors with certain species concentrations regarded constant*

We consider here a model biochemical reactor studied in (Edelstein, 1970). The reactor contains a homogeneous mixture maintained at constant volume and temperature. The reactions indicated in (4.7) occur within the mixture.

$$
\begin{gathered}
A_1 + A_4 \underset{\beta}{\overset{\rho}{\rightleftarrows}} 2A_1 \\
A_1 + A_2 \underset{\varepsilon}{\overset{\gamma}{\rightleftarrows}} A_3 \underset{\mu}{\overset{\theta}{\rightleftarrows}} A_2 + A_5.
\end{gathered}
\tag{4.7}
$$

They are intended to represent an autocatalytic production of A_1 accompanied by an enzymatic degradation of A_1, species A_2 playing the role of the enzyme. The kinetics is mass action with rate constants as indicated. We suppose that A_4 and A_5 are added to or removed from the reactor in such a way as to maintain their concentrations at *constant* values c_4^* and c_5^*, respectively. Otherwise there is no transport of material into or out of the reactor.

The dynamical equations for the five species are those shown in (4.8). Note that these are *not* the differential equations that would be obtained from (3.8), written for the mass action system depicted in (4.7). In particular, the equations for $\dot{c}_4$ and $\dot{c}_5$ would be rather different from those given in (4.8).

$$
\begin{aligned}
\dot{c}_1 &= \rho c_4^* c_1 - \beta c_1^2 - \gamma c_1 c_2 + \varepsilon c_3 \\
\dot{c}_2 &= -\gamma c_1 c_2 + (\varepsilon + \theta) c_3 - \mu c_5^* c_2 \\
\dot{c}_3 &= \gamma c_1 c_2 - (\varepsilon + \theta) c_3 + \mu c_5^* c_2 \\
\dot{c}_4 &= 0 \\
\dot{c}_5 &= 0.
\end{aligned}
\tag{4.8}
$$

On the other hand, the first three equations in (4.8)—the only ones of real interest—are *precisely* those that would be obtained if (3.8) were written for the mass action system shown in (4.9). Thus, if we had available a general theory of (3.8) that draws connections between dynamics and reaction network structure, the theory could be used in a study of the Edelstein system, provided we understand the network of interest to be (4.9) rather than (4.7).

$$\begin{gathered} A_1 \underset{\beta}{\overset{\rho c_4^*}{\rightleftarrows}} 2A_1 \\ A_1 + A_2 \underset{\varepsilon}{\overset{\gamma}{\rightleftarrows}} A_3 \underset{\mu c_5^*}{\overset{\theta}{\rightleftarrows}} A_2 \end{gathered} \tag{4.9}$$

Our passage from network (4.7) to network (4.9) is readily generalized to other reactors in which certain species concentrations are regarded to be constant. One "strips away" from the network of true chemical reactions those species having time-invariant concentrations; and, when the kinetics is mass action, one modifies the rate constants as in the example. As the example indicates, the resulting "stripped down" network might appear to be incompatible with the conservation of mass.

Remark 4.3.1. We regarded the Edelstein reactor to be open, species A_4 and A_5 having been added to or removed from the reactor in such a way as to maintain their concentrations constant within the reacting mixture. In fact, it is difficult to see how such controlled addition and removal could be easily managed.

Nevertheless, there is a practical situation which, in purely formal terms, is closely approximated by a picture of the kind we painted in our discussion of the Edelstein system. Suppose, for example, that the Edelstein reactions (4.7) take place in a *closed* reactor, and suppose also that, in the reactor, the concentrations of A_4 and A_5 are initially much greater than those of A_1, A_2, and A_3. Then, on some reasonable time scale, we would not expect the concentrations of A_4 and A_5 to experience much variation, for there is not enough A_1, A_2 or A_3 available to affect the supply of A_4 and A_5 in an appreciable way. On that time scale we would expect the dynamics of c_1, c_2 and c_3 to be well-described by the first three equations in (4.8), where c_4^* and c_5^* are the (approximately) constant concentrations of A_4 and A_5. Again, these equations derive from (3.8) written for the mass action system (4.9).

Remark 4.3.2. The zero complex might arise not only in the study of continuous flow stirred tank reactors but also in the study of reactors in which certain species concentrations are regarded constant. Suppose, for example, that a "true" chemical reaction of the form

$$A_3 \xrightarrow{k} A_1 + A_2 \tag{4.10}$$

takes place in a homogeneous reactor in which the concentration of A_3 is deemed to have the constant value c_3^*. Suppose also that the kinetics is mass action and that reaction (4.10) has a rate constant k. Then, in the corresponding "stripped" network, reaction (4.10) would be replaced by

$$0 \xrightarrow{kc_3^*} A_1 + A_2 \tag{4.11}$$

with the indicated rate constant.

The examples considered in this section should make clear how, by admitting "peculiar" reaction networks for consideration, we might bring theory developed for equations (3.6) and (3.8) directly to the study of important categories of open reactors. With this in mind, we shall here-after regard *any* reaction network as a legitimate object of study, whether or not it is compatible with mass conservation. In effect, we shall seek to develop theory sufficiently broad as to accommodate whatever reaction network models might arise in applications.

5. SOME ELEMENTARY PROPERTIES OF THE DIFFERENTIAL EQUATIONS FOR A REACTION SYSTEM

For an arbitrary reaction system (not necessarily mass action) there are certain elementary inferences that can be drawn from the differential equation (3.6). We shall draw these inferences here in preparation for the deeper (and far less transparent) results stated in Section 6. Throughout this section it should be kept in mind that we interpret eq. (3.6) in its broadest sense. That is, the underlying reaction network might consist in part of pseudoreactions designed to model open reactors of the kind discussed in Section 4. Thus, assertions made here about eq. (3.6) will be applicable to open reactors, provided that (3.6) is understood to be written for a reaction system constructed, as in Section 4, to describe the particular open reactor under study.

5.1. *The accumulation rate of an absent species is not negative*

If, at a particular composition $\mathbf{c} \in \bar{\mathbb{P}}^N$, species A_L is absent from the reactor (i.e. if $c_L = 0$), equation (3.6) should conform to the obvious physical requirement that, at composition $\mathbf{c}$, the derivative $\dot{c}_L$ should be non-negative. As we show in Appendix I, equation (3.6) already ensures that $\dot{c}_L \geqslant 0$ whenever $c_L = 0$ (see also Fife, 1979.)

5.2. *Stoichiometric compatibility*

Even if we cannot solve (3.6) for a specified reaction system, we can nevertheless make some simple qualitative deductions about the way in which the composition vector moves through $\bar{\mathbb{P}}^N$. Regardless of the kinetics, the underlying reaction network already imposes restrictions on the way composition trajectories can look. In particular, a trajectory that passes through composition $\mathbf{c} \in \bar{\mathbb{P}}^N$ can eventually reach composition $\mathbf{c}' \in \bar{\mathbb{P}}^N$ only if the pair $\{\mathbf{c}', \mathbf{c}\}$ is compatible with "stoichiometrical" conditions the network imposes. In very rough terms, composition trajectories are not generally free to wander through $\bar{\mathbb{P}}^N$ in an arbitrary fashion because the reaction network itself, through equation (3.6), restricts the directions in which the "velocity vector" $\dot{\mathbf{c}}$ can point. This is a simple idea we need to develop.

By the *stoichiometric subspace* for a reaction network with N species we mean the set of vectors in $\mathbb{R}^N$ consisting of all possible linear combinations of the reaction vectors for the network. That is, $\gamma \in \mathbb{R}^N$ is a member of the stoichiometric subspace if and only if there exist a set of numbers, $\{\alpha_{i\to j}\}_{i\to j \in \mathscr{R}}$, such that

$$\gamma = \sum_{\mathscr{R}} \alpha_{i\to j}(\mathbf{y}_j - \mathbf{y}_i). \qquad (5.1)$$

It is easy to see that the stoichiometric subspace contains the zero vector of $\mathbb{R}^N$ and also every reaction vector. The stoichiometric subspace is a linear subspace of $\mathbb{R}^N$; in fact, it is the smallest linear subspace of $\mathbb{R}^N$ containing all the reaction vectors. From elementary considerations in linear algebra it follows that *the dimension of the stoichiometric subspace for a reaction network is equal to what we called the rank of the network in Section* 2.3.

Hereafter we denote the stoichiometric subspace for a given network by the symbol S. Thus, with S denoting the rank of the network, we have

$$s = \dim S. \qquad (5.2)$$

Some simple examples might be helpful.

Consider the simple network (5.3). Here $N = 2$. The reaction vectors are $2\mathbf{e}_2 - \mathbf{e}_1$ ($= [-1,2]$) and $\mathbf{e}_1 - 2\mathbf{e}_2$ ($= [1,-2]$). The rank of network (5.3) is clearly one, and so the stoichiometric subspace for the network is one-dimensional. It is a line in $\mathbb{R}^2$ that passes through the origin and through the points $[-1,2]$ and $[1,-2]$. The stoichiometric subspace for network (5.3) is depicted in Fig. 1 as the line labeled S.

$$A_1 \rightleftarrows 2A_2. \qquad (5.3)$$

For network (5.4) $N = 3$. The reaction vectors are $\mathbf{e}_2 - 2\mathbf{e}_1$ ($= [-2,1,0]$), $2\mathbf{e}_1 - \mathbf{e}_3$ ($= [2,0,-1]$), $\mathbf{e}_2 - \mathbf{e}_3$ ($= [0,1,-1]$) and $\mathbf{e}_3 - \mathbf{e}_2$ ($= [0,-1,1]$). The rank of network (5.4) is easily determined to be two, and so the stoichiometric subspace for the network is two-dimensional. It is a plane in $\mathbb{R}^3$ that passes through the origin and through the points $[-2,1,0]$, $[2,0,-1]$, $[0,1,-1]$ and $[0,-1,1]$. The stoichiometric subspace for network (5.4) is depicted in Fig. 1 as the plane labeled S.

$$\begin{tikzcd} 2A_1 \arrow[r] & A_2 \arrow[d, shift left] \\ & A_3 \arrow[ul] \arrow[u, shift left] \end{tikzcd} \qquad (5.4)$$

The dynamical significance of the stoichiometric subspace becomes clear when we inspect equation (3.6), written for an arbitrary reaction system. For *any* composition $\mathbf{c}$, the corresponding value of $\dot{\mathbf{c}}$ given by (3.6) is a linear combination of the reaction vectors for the underlying reaction network. This is to say that the "velocity vector" $\dot{\mathbf{c}}$ invariably lies in the stoichiometric subspace that the reaction vectors generate.

Thus, for a reaction system in which the underlying network is (5.3), values of $\dot{\mathbf{c}}$ given by (3.6) always point along the line labeled S in Fig. 1. With the velocity $\dot{\mathbf{c}}$ constrained to point along the line S, it is fairly obvious that a composition trajectory for (3.6) that begins at an initial composition $\mathbf{c}(0)$ must lie on a line in Fig. 1 which passes through $\mathbf{c}(0)$ and is parallel to the line S.

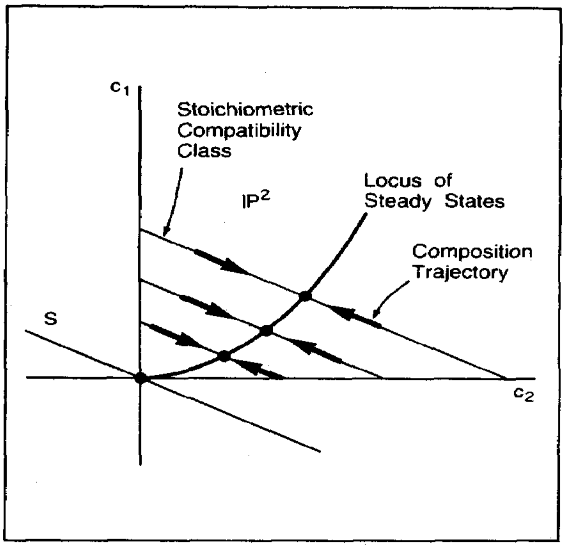


Fig. 1. The stoichiometric subspace, stoichiometric compatibility classes, and composition trajectories for network (5.3). The locus of steady states depicted is for mass action kinetics.

For a reaction system in which the underlying network is (5.4), values of $\dot{\mathbf{c}}$ given by (3.6) always point along the plane labeled S in Fig. 2. In this case, we should expect a composition trajectory for (3.6) that begins at composition $\mathbf{c}(0)$ to lie entirely on a plane in Fig. 2 which passes through $\mathbf{c}(0)$ and is parallel to the plane S.

We can examine the general situation by performing an integration of equation (3.6) along a hypothetical solution. Consider equation (3.6), written for an arbitrary reaction system, and suppose that the equation has a solution $\mathbf{c}(\cdot)$ which contains in its domain the

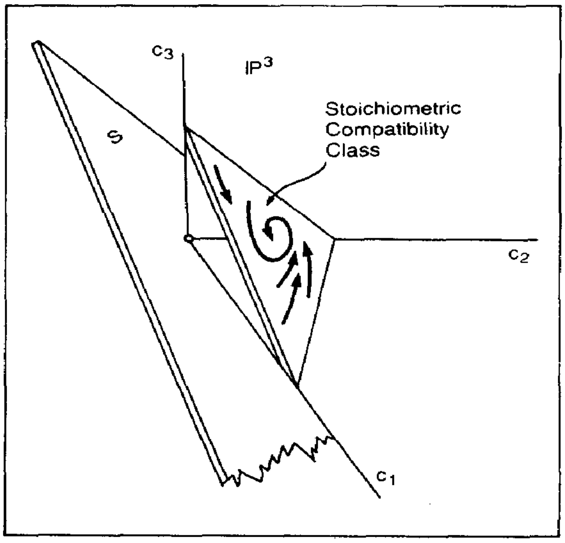


Fig. 2. The stoichiometric subspace, a stoichiometric compatibility class and some composition trajectories for network (5.4).

time interval $[0,T]$. If, along this solution, we integrate (3.6) up to some time $t \in [0,T]$, we obtain

$$\mathbf{c}(t) - \mathbf{c}(0) = \sum_{\mathscr{R}} \left[\int_0^t \mathscr{K}_{i \to j}(\mathbf{c}(\tau))\,\mathrm{d}\tau \right] (\mathbf{y}_j - \mathbf{y}_i). \qquad (5.5)$$

Thus, $\mathbf{c}(t) - \mathbf{c}(0)$ is a linear combination of the reaction vectors for the underlying network and so must be a member of the stoichiometric subspace generated by them. The point here is that *two compositions can lie on the same composition trajectory only if their difference lies in the stoichiometric subspace.*

Our consideration of networks (5.3) and (5.4) suggests that a composition trajectory governed by eq. (3.6) should be contained entirely within a parallel of the stoichiometric subspace for the underlying reaction network. In fact, this will follow immediately from (5.5) once we make precise the notion of "a parallel of the stoichiometric subspace".

Suppose that $S \subset \mathbb{R}^N$ is the stoichiometric subspace for a network and that $\mathbf{c} \in \bar{\mathbb{P}}^N$ is a composition. By *the parallel of* S *containing* $\mathbf{c}$, denoted $\mathbf{c} + S$, we mean the set of vectors in $\mathbb{R}^N$ obtained by adding $\mathbf{c}$ to all vectors of S. That is,

$$\mathbf{c} + S := \{\mathbf{c} + \gamma \in \mathbb{R}^N \mid \gamma \in S\}. \qquad (5.6)$$

In rough terms, $\mathbf{c} + S$ is the set of vectors in $\mathbb{R}^N$ obtained by a parallel shift of S up to the point $\mathbf{c}$. It is not difficult to see that a composition $\mathbf{c}'$ lies in the parallel $\mathbf{c} + S$ if and only if $\mathbf{c}' - \mathbf{c}$ lies in S. When this condition is satisfied, the parallel $\mathbf{c}' + S$ is identical to the parallel $\mathbf{c} + S$.

Now we consider once again a solution $\mathbf{c}(\cdot)$ of eq. (3.6) which contains in its domain the time interval $[0,T]$. For each $t \in [0,T]$, the right side of (5.5) lies in the stoichiometric subspace, S, for the underlying reaction network. Thus, for each $t \in [0,T]$, we have from (5.5) that $\mathbf{c}(t) = \mathbf{c}(0) + \gamma(t)$, where $\gamma(t)$ is a member of S. This is to say that, for all $t \in [0,T]$, $\mathbf{c}(t)$ lies in the parallel $\mathbf{c}(0) + S$. In other words, *a trajectory beginning at* $\mathbf{c}(0)$ *lies entirely in the parallel of* S *containing* $\mathbf{c}(0)$. In fact, specification of any point along a trajectory serves to specify the parallel of S containing the trajectory.

With these considerations in mind, we say that two compositions, $\mathbf{c} \in \bar{\mathbb{P}}^N$ and $\mathbf{c}' \in \bar{\mathbb{P}}^N$, for a reaction system are *stoichiometrically compatible* if $\mathbf{c}' - \mathbf{c}$ lies in S, the stoichiometric subspace for the underlying reaction network. Thus, $\mathbf{c}'$ and $\mathbf{c}$ are stoichiometrically compatible if and only if they lie in the same parallel of S. We can partition the set of all possible compositions ($\bar{\mathbb{P}}^N$) into *stoichiometric compatibility classes*, each of which is obtained by taking the intersection of a parallel of S with $\bar{\mathbb{P}}^N$. In particular, the stoichiometric compatibility class containing composition $\mathbf{c} \in \bar{\mathbb{P}}^N$ is just the set

$$(\mathbf{c} + S) \cap \bar{\mathbb{P}}^N.$$

In language we now have available, we can say that a composition trajectory for (3.6) which passes through the composition $\mathbf{c}$ must lie entirely in the stoichiometric compatibility class containing $\mathbf{c}$.

We can also partition the set of all *positive* compositions ($\mathbb{P}^N$) into *positive stoichiometric compatibility classes*, each of which is obtained by taking the intersection of a parallel of S with $\mathbb{P}^N$. In particular, the positive stoichiometric compatibility class containing composition $\mathbf{c} \in \mathbb{P}^N$ is the set

$$(\mathbf{c} + S) \cap \mathbb{P}^N.$$

In Fig. 1 the stoichiometric compatibility classes generated by network (5.3) are those parts of lines parallel to line S that lie in $\bar{\mathbb{P}}^2$, the first quadrant of $\mathbb{R}^2$ (including its boundary). The positive stoichiometric compatibility classes are those parts of lines parallel to line S that lie in $\mathbb{P}^2$, the interior of the first quadrant.

In Fig. 2 the stoichiometric compatibility class depicted for network (5.4) is a triangular region obtained by intersecting a parallel of the plane labeled S with $\bar{\mathbb{P}}^3$, the non-negative orthant of $\mathbb{R}^3$. The interior of the triangle is a positive stoichiometric compatibility class.

In both figures, the composition trajectories depicted lie entirely within stoichiometric compatibility classes.

Our understanding of stoichiometric compatibility classes will help us pose sharper questions. It is instructive to consider a simple mass action system for which the underlying reaction network is (5.3). We designate the rate constants α and β as in (5.7). The two component

$$A_1 \underset{\beta}{\overset{\alpha}{\rightleftarrows}} 2A_2 \qquad (5.7)$$

equations of the vector eq. (3.8) take the form

$$\begin{aligned} \dot{c}_1 &= -\alpha c_1 + \beta c_2^2 \\ \dot{c}_2 &= 2\alpha c_1 - 2\beta c_2^2. \end{aligned} \qquad (5.8)$$

Thus, a composition $[c_1, c_2]$ is a steady state precisely when

$$c_1 = \frac{\beta}{\alpha} c_2^2. \qquad (5.9)$$

The locus of steady state compositions is the parabola shown in Fig. 1. To ask in an unqualified way whether this trivial mass action system admits multiple steady states is to ask a question which is not suitably refined, for obviously there are an infinite number of steady states.

Our usual interest will be in the nature of the dynamics *within a stoichiometric compatibility class.* If we ask whether the mass action system (5.7) admits multiple steady states *within a stoichiometric compatibility class,* it is apparent from Fig. 1 that the answer is no. In fact, regardless of the values that the rate constants take, the mass action system (5.7) admits *precisely one* steady state within each positive stoichiometric compatibility class. For a specified family of reaction systems, the question we shall generally try to answer is this: *Can the corresponding differential equations admit multiple steady states within a positive stoichiometric compatibility class?*

We shall also have some interest in the asymptotic stability of positive steady states. In rough terms, we shall want to know whether a positive steady state $\mathbf{c}^*$ has the property that all composition trajectories beginning sufficiently close to $\mathbf{c}^*$ remain close to $\mathbf{c}^*$ and, moreover, approach $\mathbf{c}^*$ as a limit.

Here again, Fig. 1 indicates that questions about asymptotic stability must be posed with some care. Suppose that $\mathbf{c}^*$ is a point along the steady state parabola in Fig. 1. Now consider a trajectory beginning at a composition $\mathbf{c}^0$ which is arbitrarily close to $\mathbf{c}^*$ but which lies in a different stoichiometric compatibility class. Such a trajectory will not approach $\mathbf{c}^*$ as a limit; rather, it will approach the steady state in the stoichiometric compatibility class containing $\mathbf{c}^0$. Thus, without some qualification of our notion of asymptotic stability, no steady state displayed in Fig. 1 is asymptotically stable.

Remember, however, that our interest is in the dynamics *within* a stoichiometric compatibility class. With this in mind, we shall regard a steady state $\mathbf{c}^*$ to be asymptotically stable if all composition trajectories beginning sufficiently close to $\mathbf{c}^*$ *and in the stoichiometric compatibility class containing* $\mathbf{c}^*$ remain close to $\mathbf{c}^*$ and approach $\mathbf{c}^*$ as a limit. In this sense, every steady state along the parabola in Fig. 1 is asymptotically stable. *This is the sense in which we shall understand asymptotic stability hereafter.*

Remark 5.2.A. The stoichiometric compatibility classes depicted in Figs 1 and 2 are bounded; that is, they do not "go out to infinity". It should be understood, however, that unbounded stoichiometric compatibility classes do arise naturally in the study of open systems.

Consider, for example, the reaction system constructed to model the simple three-species CFSTR discussed in Section 4.1. The underlying network (4.3) has a rank of three, and so the corresponding stoichiometric subspace is a three-dimensional linear subspace of $\mathbb{R}^3$. Thus, the stoichiometric subspace is *all* of $\mathbb{R}^3$. In this case, there is but one stoichiometric compatibility class, the entire non-negative orthant of $\mathbb{R}^3$. The only positive stoichiometric compatibility class is the interior of the non-negative orthant of $\mathbb{R}^3$.

In the case of the Edelstein network (4.9), the stoichiometric subspace is a two-dimensional linear subspace of $\mathbb{R}^3$ containing the entire A_1 axis. In this case, typical stoichiometric compatibility classes look like rectangles in $\bar{\mathbb{P}}^3$ that extend out to infinity in a direction parallel to the A_1 axis. (See Fig. 4.1 in Feinberg, 1980.)

In (Horn and Jackson, 1972) it is shown that all stoichiometric compatibility classes generated by a reaction network are bounded if and only if the network satisfies a certain conservation condition, in effect that there exists a vector in $\mathbb{P}^N$ which is orthogonal to every reaction vector. (In that article, stoichiometric compatibility classes are called *reaction simplices.*)

Remark 5.2.B. In the spirit of Remarks 2.4.A and 2.5.A we make the following observation: It is not hard to show that any two reaction networks with the same complexes and the same linkage classes give rise to the same stoichiometric subspace. It follows that the precise nature of the reaction arrows in a network affect the stoichiometric subspace (and, therefore, the stoichiometric compatibility classes) only insofar as the reaction arrows determine the linkage classes of the network.

Remark 5.2.C. Although the preceding discussion of stoichiometric compatibility will be adequate for our purposes, it was somewhat incomplete. The central idea was that, for an arbitrary reaction system, the "velocity vector" $\dot{\mathbf{c}}$ given by (3.6) is always a linear combination of the reaction vectors for the underlying reaction network and so must lie in the stoichiometric subspace generated by them. In fact, we could have said more.

Because the individual reaction rate functions in (3.6) take non-negative values, we might have observed that $\dot{\mathbf{c}}$ must always be representable as a linear combination of the reaction vectors in which the scalar multipliers are *non-negative.* Moreover, for each index $m \in \{1, 2, \ldots, n\}$, multipliers in (3.6) of the form $\mathscr{K}_{m \to j}(\mathbf{c})$ are either *all* positive or are *all* zero according to whether $\operatorname{supp} \mathbf{y}_m$ is or is not contained in $\operatorname{supp} \mathbf{c}$. [Recall condition (K.2) in Section 3.1.] In other words, $\dot{\mathbf{c}}$ is always a *special* kind of linear combination of the reaction vectors.

This idea is developed in Appendix III, where we make the sharpened observation that $\dot{\mathbf{c}}$ always points along what we call the *stoichiometric cone* generated by the reaction network. For a given network the stoichiometric cone is contained in and might be smaller than the stoichiometric subspace. We show, however, that for reaction systems in which we shall have most interest—those that admit *positive* steady states—the stoichiometric cone and the stoichiometric subspace actually coincide. Thus, for such systems there is nothing gained from the sharpened observation that $\dot{\mathbf{c}}$ points along the stoichiometric cone.

In Appendix IV we discuss another, more substantive, way in which we might have refined our discussion of the nature of composition trajectories. There it is shown that, for mass action systems, the velocity vector $\dot{\mathbf{c}}$ invariably points along what is called the *kinetic subspace* (Feinberg and Horn, 1977). The kinetic subspace is a linear subspace that is contained in and *might* be *smaller* than the stoichiometric subspace. When the kinetic subspace is, in fact, smaller than the stoichiometric subspace, one can make sharper statements about the way composition trajectories look. It turns out, however, that for mass action systems in which the underlying reaction network is of the $\ell = \ell$ variety (i.e. each linkage class contains just one terminal strong linkage class), the stoichiometric and kinetic subspaces actually *coincide.* This is not usually true for networks of the $\ell > \ell$ variety. Appendix IV will perhaps help explain why some of our results are confined to the $t = \ell$ case and why, for networks of the $t > \ell$ variety one should actually pose more refined questions than those we address here. Appendix IV will also help explain why mass action models that derive from $t > \ell$ networks are often structurally unstable.

Readers who wish to do so can proceed to Section 6 without loss of continuity. In this case, passages labeled "Remark" in Section 6 should also be omitted.

5.3. *Some elementary observations about steady states and cyclic composition trajectories*

Suppose that, for a given reaction system, $\mathbf{c}^* \in \bar{\mathbb{P}}^N$ is a steady state. Then (3.6) reduces to

$$\mathbf{0} = \sum_{\mathscr{R}} \mathscr{K}_{i \to j}(\mathbf{c}^*)(\mathbf{y}_j - \mathbf{y}_i). \tag{5.10}$$

If $\mathbf{c}^*$ is a *positive* steady state—that is, if $\mathbf{c}^*$ lies in $\mathbb{P}^N$, then all the $\mathscr{K}_{i \to j}(\mathbf{c}^*)$ in (5.10) are positive numbers (Remark 3.1.A). For a reaction system to admit a positive steady state it is therefore *necessary* that the reaction vectors for the underlying network satisfy the following condition (Feinberg, 1977): There exists a set of positive numbers $\{\alpha_{i \to j}\}_{i \to j \in \mathscr{R}}$ such that

$$\mathbf{0} = \sum_{\mathscr{R}} \alpha_{i \to j}(\mathbf{y}_j - \mathbf{y}_i). \tag{5.11}$$

When this condition is satisfied we say that the reaction vectors are *positively dependent*.

Remark 5.3.A. For every weakly reversible network (in particular for every reversible network) the reaction vectors are positively dependent. For a reversible network it is easy to see that (5.11) can be satisfied by taking $\alpha_{i \to j} = 1$ for every reaction. More generally, for an arbitrary weakly reversible network one can choose positive $\alpha_{i \to j}$ satisfying (5.11) as follows: Find in the network a set of directed reaction cycles such that each reaction appears in at least one cycle. Choose $\alpha_{i \to j}$ to be the number of cycles from among this set in which reaction $\mathbf{y}_i \to \mathbf{y}_j$ appears. To see that (5.11) will be satisfied, note that, for each of the cycles selected, we can write an equation which asserts that the sum of the reaction vectors for the cycle will equal the zero vector. After summing the resulting set of equations, we obtain (5.11) with the $\alpha_{i \to j}$ as chosen above.

Remark 5.3.B. For any network with positively dependent reaction vectors there exists *some* set of rate constants such that the corresponding mass action differential equation (3.8) admits a positive steady state. In fact, suppose that, for the network, $\{\alpha_{i \to j}\}_{i \to j \in \mathscr{R}}$ is a set of positive numbers satisfying (5.11) and suppose that $\mathbf{c}^* \in \mathbb{P}^N$ is any (positive) composition. If we assign to the network a set of rate constants $\{k_{i \to j}\}_{i \to j \in \mathscr{R}}$ chosen to satisfy

$$k_{i \to j} \prod_{L=1}^{N} (c_L^*)^{y_{iL}} = \alpha_{i \to j}, \quad \forall\, i \to j \in \mathscr{R}, \tag{5.12}$$

it follows from (3.8) and (5.11) that $\mathbf{c}^*$ is a positive steady state for the resulting mass action system.

On the other hand, for a network with positively dependent reaction vectors it is *not* necessarily true that *every* assignment of rate constants results in a mass action system for which there exists a positive steady state. Consider, for example, the simple mass action system (5.13)

$$2A_1 \underset{k}{\overset{1}{\rightleftarrows}} A_1 + A_2 \xrightarrow{1} 2A_2 \tag{5.13}$$

with rate constants as indicated. The three reaction vectors—$\mathbf{e}_1 + \mathbf{e}_2 - 2\mathbf{e}_1 = [-1, 1]$, $2\mathbf{e}_1 - (\mathbf{e}_1 + \mathbf{e}_2) = [1, -1]$, and $2\mathbf{e}_2 - (\mathbf{e}_1 + \mathbf{e}_2) = [-1, 1]$—are easily seen to be positively dependent. Written for the system (5.13), the component equations of (3.8) reduce to

$$\begin{aligned} \dot{c}_1 &= -c_1^2 + (k-1)c_1c_2 \\ \dot{c}_2 &= c_1^2 - (k-1)c_1c_2. \end{aligned} \tag{5.14}$$

For $k > 1$ it is easy to see that (5.14) admits positive steady states (i.e. steady states with $c_1 > 0, c_2 > 0$). For $k \leqslant 1$, however, there are no positive steady states at all.

Clearly, then, positive dependence of the reaction vectors is *necessary* for the existence of a positive steady state and is, in fact, sufficient to ensure the existence of *some* rate constants for which the corresponding mass action equations admit a positive steady state. But our example demonstrates that positive dependence of the reaction vectors is not, by itself, sufficient to ensure that positive steady states exist for *every* assignment of rate constants.

We make this point in order to emphasize that general questions concerning *existence* (let alone uniqueness) of positive steady states for reaction systems can be rather difficult. It is only at the shallowest level that positive dependence of the reaction vectors comes into play. If the reaction vectors *are* positively dependent (as is the case whenever the underlying network is reversible or, more generally, weakly reversible), there remain serious analytical problems that must be confronted. In particular, it is no simple matter to determine whether an intricate network with positively dependent reaction vectors has the property that the corresponding mass action differential equations admit a positive steady state *regardless* of values the rate constants take. In effect, one must study a large system of polynomial equations in which a large number of variables (species concentrations) and a large number of unspecified parameters (rate constants) appear.

Nevertheless, in Section 6 we shall be able to describe a broad class of reaction networks for which the corresponding mass action equations invariably admit positive steady states, regardless of values of the rate constants.

Although our emphasis will be on the existence and uniqueness of positive steady states for a reaction system, we should say something about steady states in which one or more species concentrations are zero. It follows from condition (K.2) in Section 3.1 that, at such a steady state, certain reactions will have zero rate and will, in effect, be "switched off". Indeed, if we specify only the set of species with zero concentration, condition (K.2) indicates precisely which reactions have zero rate and which have positive rate—that is, which reactions are "switched off" and which are "switched on".

In fact, for a given reaction system, we shall see that there are only certain combinations of species that can have zero concentration at a steady state; and, consequently, there are only certain combinations of reactions that can be switched on or off. Quite apart from the precise nature of the kinetics, the underlying network itself imposes restrictions on the various combinations of species that might be present or absent in a particular steady state.

Proposition 5.3.1 below describes such a restriction; proof is provided in Appendix II. Recall from Section 3 that if $\mathbf{c}^*$ is a composition, then supp $\mathbf{c}^*$ is the set of all species with *nonzero* concentrations at composition $\mathbf{c}^*$. Recall also that if $\mathbf{y}_i$ is a complex, then supp $\mathbf{y}_i$ is the set of all species appearing in that complex. Thus, to say that supp $\mathbf{y}_i$ is contained in supp $\mathbf{c}^*$ is to say that, at composition $\mathbf{c}^*$, all species appearing in complex $\mathbf{y}_i$ have nonzero concentrations.

In effect, Proposition 5.3.1 asserts that if $\mathbf{c}^*$ is a steady state in which certain species are present, then certain other species must be present as well.

Proposition 5.3.1. *Suppose that, for a given reaction system (not necessarily mass action), the differential eq. (3.6) admits a steady state* $\mathbf{c}^*$. *Moreover, suppose that* $\mathbf{y}_i$ *and* $\mathbf{y}_j$ *are complexes in the underlying reaction network such that there exists a directed reaction pathway leading from* $\mathbf{y}_i$ *to* $\mathbf{y}_j$. *If* supp $\mathbf{y}_i$ *is contained in* supp $\mathbf{c}^*$, *then* supp $\mathbf{y}_j$ *is also contained in* supp $\mathbf{c}^*$. *In particular,* supp $\mathbf{c}^*$ *either contains the supports of all complexes within a given strong linkage class or else it contains the support of none of them.*

Proposition 5.3.1 will serve as a backdrop for some sharper results contained in Section 6.

Remark 5.3.C. By virtue of condition (K.2) in Section 3.1, Proposition 5.3.1 gives information about the various combinations of reactions that might be switched on or off at a steady state.

Suppose that, for a particular reaction system, $\mathbf{y}_i \rightarrow \mathbf{y}_p$ and $\mathbf{y}_j \rightarrow \mathbf{y}_q$ are reactions in the underlying network, and suppose also that there exists a directed reaction pathway leading from complex $\mathbf{y}_i$ to complex $\mathbf{y}_j$. Then if, at some steady state, reaction $\mathbf{y}_i \rightarrow \mathbf{y}_p$ is switched on, it must be the case that reaction $\mathbf{y}_j \rightarrow \mathbf{y}_q$ is also switched on.

In fact, the last sentence in Proposition 5.3.1 leads to the following observation: Let Λ denote the set of all complexes comprising a particular strong linkage class. At a steady state, either *all* reactions in the set

$$\{\mathbf{y}_i \rightarrow \mathbf{y}_j \in \mathscr{R} : y_i \in \Lambda\}$$

are switched on or else *all* are switched off. In particular, if the underlying reaction network is weakly reversible, then, at a steady state, either *all* reactions connecting complexes in a given linkage class are switched on or else *all* are switched off.

Remark 5.3.D. It is perhaps worth making explicit mention of reaction systems in which the underlying network contains the zero complex. At least with respect to issues under discussion here, the crucial fact about the zero complex is that *its support is the empty set*. Thus, for *any composition* $\mathbf{c}$, we have that supp $\mathbf{0}$ is contained in supp $\mathbf{c}$ (Remark 4.A). From Proposition 5.3.1 it then follows that if $\mathbf{c}^*$ is *any* steady state and if $\mathbf{y}_j$ is a complex such there exists a directed reaction pathway leading from the zero complex to $\mathbf{y}_j$, supp $\mathbf{y}_j$ must be contained in supp $\mathbf{c}^*$.

In fact, we might also observe that Proposition 5.3.1 tells us immediately that steady state operation of a CFSTR cannot result in the *complete* conversion of any species in the feed, no matter what reactions are occurring within the reactor vessel and no matter what rate functions [subject to condition (K.2)] are associated with those reactions. This result emerges from Proposition 5.3.1 in the following way: In the sense of Sections 4.1 and 4.2, the differential equations for the CFSTR can be viewed to derive from a reaction system in which the underlying network contains a reaction of the form $0 \rightarrow A_L$ for each species A_L in the feed. Thus if A_L is a species in the feed, the network clearly has the property that there exists a directed reaction pathway leading from the zero complex to complex A_L (the support of which is simply $\{A_L\}$). Now if the reactor vessel (and hence the effluent stream) has a steady state composition $\mathbf{c}^*$, Proposition 5.3.1 requires that $\{A_L\}$ be contained in supp $\mathbf{c}^*$; that is, c_L^* must be (strictly) positive.

Remark 5.3.E. Proposition 5.3.1 certainly does not exhaust all that we can say about the relationship between the support of a steady state composition for a reaction system and the supports of the various complexes in the underlying network. In fact, we can easily generalize the observations we made earlier about *positive* steady states: If $\mathbf{c}^* \in \bar{\mathbb{P}}^N$ is a (not necessarily positive) steady state, then in equation (5.10), $\mathscr{K}_{i \rightarrow j}(\mathbf{c}^*)$ is positive or zero depending upon whether supp $\mathbf{y}_i$ is or is not contained in supp $\mathbf{c}^*$. In eq. (5.10), therefore, we can simply disregard all reactions that are switched off at composition $\mathbf{c}^*$ and then observe that the reaction vectors corresponding to the remaining reactions must be positively dependent. That is, *if* $\mathbf{c}^* \in \bar{\mathbb{P}}^N$ *is a steady state then the set*

$$\{\mathbf{y}_j - \mathbf{y}_i \in \mathbb{R}^N \mid \mathbf{y}_i \rightarrow \mathbf{y}_j \in \mathscr{R}, \text{ supp } \mathbf{y}_i \subset \text{supp } \mathbf{c}^*\}$$

must be positively dependent. In fact, this simple idea underlies the proof of Proposition 5.3.1.

Finally, we shall make a few elementary observations about cyclic composition trajectories. To a great extent these will parallel our observations about steady states.

Suppose that the differential equation (3.6) for a given reaction system admits a periodic solution. In particular, suppose that, for the system, the corresponding differential equation (3.6) admits a solution $\mathbf{c}(\cdot)$ which contains in its domain the time interval $[0, T]$ and which has the property that $\mathbf{c}(0) = \mathbf{c}(T)$. Then, by taking $t = T$ in (5.5), we obtain

$$\mathbf{0} = \sum_{\mathscr{R}} \left[\int_0^T \mathscr{K}_{i \to j}(\mathbf{c}(\tau))\, d\tau \right] (\mathbf{y}_j - \mathbf{y}_i). \tag{5.15}$$

Now if, at some instant $\tau \in [0, T]$, $\mathbf{c}(\tau)$ lies $\mathbb{P}^N$, it follows from conditions (K.1) and (K.2) imposed on rate functions in Section 3.1 that each of the integrals in (5.15) is positive. In this way we can see that for the existence of a cyclic composition trajectory which passes through $\mathbb{P}^N$ it is again *necessary* that the reaction vectors for the underlying network be positively dependent (Feinberg, 1977).

As with steady states, we can also ask about the nature of cyclic composition trajectories that lie entirely on the boundary of $\bar{\mathbb{P}}^N$. In effect, Proposition 5.3.1 restricted the regions on the boundary of $\bar{\mathbb{P}}^N$ in which steady states can lie. Proposition 5.3.2 below will restrict the regions on the boundary of $\bar{\mathbb{P}}^N$ in which cyclic composition trajectories can lie.

We shall say that *a cyclic composition trajectory for a reaction system has support* Γ (*where* Γ *is a subset of* $\{A_1, \ldots, A_N\}$) *if, for every composition* $\mathbf{c}$ *along the trajectory,* supp $\mathbf{c} = \Gamma$. This is to say that, at each composition $\mathbf{c}$ along the trajectory, $c_L > 0$ if species A_L is contained in Γ and $c_L = 0$ if A_L is not contained in Γ.

Remark 5.3.F. If we say that a cyclic composition trajectory has support Γ, we are implicitly asserting that all compositions along the trajectory have the *same* support. But if this were not the case, at least one species concentration would be positive, then vanish, and then become positive again—all in finite time. When the differential equation (3.6) has the property that to each initial condition there corresponds a unique solution, it can be shown that no species becomes extinct in finite time. Conditions imposed on rate functions in Section 3.1 are sufficient to ensure uniqueness of solutions.

The following proposition is proved in Appendix II.

Proposition 5.3.2. *Suppose that, for a reaction system (not necessarily mass action), the differential eq.* (3.6) *admits a cyclic composition trajectory with support* Γ. *Moreover, suppose that* $\mathbf{y}_i$ *and* $\mathbf{y}_j$ *are complexes in the underlying reaction network such that there exists a directed reaction pathway leading from* $\mathbf{y}_i$ *to* $\mathbf{y}_j$. *If* supp $\mathbf{y}_i$ *is contained in* Γ, *then* supp $\mathbf{y}_j$ *is also contained in* Γ. *In particular,* Γ *either contains the supports of all complexes within a given strong linkage class or else it contains the support of none of them.*

In a sense, Proposition 5.3.2 subsumes Proposition 5.3.1, for we can regard a steady state $\mathbf{c}^*$ to be a (trivial) cyclic composition trajectory corresponding to the (trivially) periodic solution $\mathbf{c}(\cdot)$ such that $\mathbf{c}(t) = \mathbf{c}^*$ for all t. In this case, we would identify Γ with supp $\mathbf{c}^*$. As a consequence of Proposition 5.3.2, it is not difficult to see how the remarks following Proposition 5.3.1 can be recast in terms of cyclic composition trajectories.

In Section 6 we shall see how Propositions 5.3.1 and 5.3.2 can be substantially sharpened for reaction systems in which the underlying network has a deficiency of zero.

5.4. *Independent subnetworks*

Some reaction networks lend themselves to decomposition into smaller networks which, at least with respect to *certain* issues, can be studied separately. Decompositions of the kind described here are suggested by rudimentary algebraic considerations.

We begin by reviewing some elementary linear algebra. Suppose that U is a linear subspace of $\mathbb{R}^N$ and that $U_1, U_2, \ldots, U_p$ are linear subspaces of U. We say that U is the *sum* of $U_1, U_2, \ldots, U_p$ if every vector $\mathbf{x}$ in U has a representation of the form

$$\mathbf{x} = \mathbf{x}_1 + \mathbf{x}_2 + \ldots + \mathbf{x}_p, \quad \mathbf{x}_\theta \in U_\theta, \quad \theta = 1, 2, \ldots, p. \tag{5.16}$$

In this case we write

$$U = U_1 + U_2 + \ldots + U_p. \tag{5.17}$$

We say that U is the *direct sum* of $U_1, U_2, \ldots, U_p$ if U is the sum of $U_1, U_2, \ldots, U_p$ and, in addition, (5.18) holds *only* if $\mathbf{x}_\theta = \mathbf{0}$, $\theta = 1, 2, \ldots, p$.

$$\mathbf{0} = \mathbf{x}_1 + \mathbf{x}_2 + \ldots + \mathbf{x}_p, \ \mathbf{x}_\theta \in U_\theta, \ \theta = 1, 2, \ldots, p. \tag{5.18}$$

In this special case we write

$$U = U_1 \oplus U_2 \oplus \ldots \oplus U_p. \tag{5.19}$$

For our purposes, the crucial fact is this: *If* U *is the sum of* $U_1, U_2, \ldots, U_p$, *then* U *is the direct sum of* $U_1, U_2, \ldots, U_p$ *if and only if the dimensions of these subspaces satisfy the equation*

$$\dim U = \sum_{\theta=1}^{p} \dim U_\theta. \tag{5.20}$$

Now consider a reaction network with N species. As before, we denote by $\mathscr{R}$ the set of all reactions in the network. Recall that the stoichiometric subspace generated by these reactions is the linear subspace $S \subset \mathbb{R}^N$ consisting of all possible linear combinations of the corresponding reaction vectors. That is, members of S are those vectors in $\mathbb{R}^N$ which are representable in the form

$$\sum_{\mathscr{R}} \alpha_{i \to j} (\mathbf{y}_j - \mathbf{y}_i), \tag{5.21}$$

where the $\alpha_{i \to j}$ are arbitrary real numbers.

Suppose that we now partition the set $\mathscr{R}$ of reactions in some arbitrary way into (disjoint) subsets $\mathscr{R}_1, \mathscr{R}_2, \ldots, \mathscr{R}_p$. For example, we can partition the reactions in network (5.22)

$$\begin{tikzcd} & A_1 \arrow[r, shift left] \arrow[d, shift right] & 2A_1 \arrow[l, shift left] \\ A_1 + A_2 \arrow[r, shift left] & A_3 \arrow[u, shift right] \arrow[l, shift left] \arrow[r, shift left] & A_2 \arrow[l, shift left] \end{tikzcd} \tag{5.22}$$

into two disjoint subsets:

$$A_1 \rightleftarrows A_3 \tag{5.23$_1$}$$

and

$$\begin{gathered} A_1 \rightleftarrows 2A_1 \\ A_1 + A_2 \rightleftarrows A_3 \rightleftarrows A_2. \end{gathered} \tag{5.23$_2$}$$

As this example makes clear, a partition of the set of reactions into subsets $\mathscr{R}_1, \mathscr{R}_2, \ldots, \mathscr{R}_p$ amounts to a decomposition of the "parent network" into p "subnetworks" having no reaction in common. As in the example, it may happen that one or more of the subnetworks contains fewer species than the parent network. We shall nevertheless continue to regard the reaction vectors for each subnetwork to be members of $\mathbb{R}^N$, where N is the number of species in the parent network.

We can associate with the θth subnetwork its own stoichiometric subspace $S_\theta \subset \mathbb{R}^N$, defined to be the set of all linear combinations of its reaction vectors. That is, S_θ is the linear subspace of $\mathbb{R}^N$ consisting of all vectors of the form

$$\sum_{\mathscr{R}_\theta} \alpha_{i \to j} (\mathbf{y}_j - \mathbf{y}_i), \tag{5.24}$$

where the $\alpha_{i \to j}$ are arbitrary real numbers. Moreover, in the sense of Section 2.3, we can associate with the θth subnetwork its own rank, s_θ. In fact, just as in (5.2) we have

$$s_\theta = \dim S_\theta, \quad \theta = 1, 2, \ldots, p. \tag{5.25}$$

It is easy to see that the stoichiometric subspace, S, for the parent network is the sum of the stoichiometric subspaces generated by the separate subnetworks with reaction sets $\mathscr{R}_1, \mathscr{R}_2, \ldots, \mathscr{R}_p$. That is,

$$S = S_1 + S_2 + \ldots + S_p. \tag{5.26}$$

Moreover, the sum is *direct* precisely when the rank, s, of the parent network is equal to the sum of the ranks of the individual subnetworks. That is,

$$S = S_1 \oplus S_2 \oplus \ldots \oplus S_p \tag{5.27}$$

if and only if

$$s = s_1 + s_2 + \ldots + s_p. \tag{5.28}$$

This follows immediately from (5.2), (5.25) and the condition for direct summing given in (5.20). Note that for network (5.22) $s = 3$, while for the two subnetworks (5.23)$_1$ and (5.23)$_2$ we have $s_1 = 1$ and $s_2 = 2$. Thus, the stoichiometric subspace for network (5.22) is the *direct* sum of the stoichiometric subspaces generated separately by the subnetworks (5.23)$_1$ and (5.23)$_2$.

We shall introduce next the idea of an "independent subnetwork". Consider a network with reaction set $\mathscr{R}$, and consider also a subnetwork with reaction set $\mathscr{R}' \subset \mathscr{R}$. By the subnetwork *complementary* to the given subnetwork we mean the subnetwork with reaction set $\mathscr{R}'' = \mathscr{R} \setminus \mathscr{R}'$. Roughly speaking, this is just the subnetwork we would obtain from the parent network after deletion of all reactions in the given subnetwork.

We say that the given subnetwork is an *independent subnetwork* of the parent network if

$$s = s' + s'', \tag{5.29}$$

where s is the rank of the parent network, s' is the rank of the given subnetwork and s'' is the rank of its complement. Condition (5.29) is equivalent to

$$S = S' \oplus S'', \tag{5.30}$$

where S is the stoichiometric subspace of the parent network, S' is the stoichiometric subspace generated by the given subnetwork, and S'' is the stoichiometric subspace generated by the complementary subnetwork. It is evident that the complement of an independent subnetwork is also an independent subnetwork.

For example, the (complementary) subnetworks (5.23)$_1$ and (5.23)$_2$ of network (5.22) are both independent subnetworks since the sum of their ranks is equal to the rank of the parent network. On the other hand,

$$A_1 \rightleftarrows 2A_1 \tag{5.31}$$

is *not* an independent subnetwork of (5.22): Its complement is

$$\begin{tikzcd} & A_1 \arrow[d, shift left] \\ A_1 + A_2 \arrow[r, shift left] & A_3 \arrow[u, shift left] \arrow[l, shift left] \arrow[r, shift left] & A_2. \arrow[l, shift left] \end{tikzcd} \tag{5.32}$$

The rank of (5.31) is one, the rank of (5.32) is three, and the rank of the parent network (5.22) is three. Thus, (5.29) is not satisfied. Clearly, (5.32) is not an independent subnetwork of (5.22) either.

It is not difficult to show that, if the set of reactions in a network is partitioned into p subsets, then (5.28) and, therefore, (5.27) hold if and only if each of the resulting p subnetworks is an independent subnetwork.

As we shall now see, the related ideas of subnetwork independence and direct summing have simple and rather obvious implications in the study of steady states. These same ideas have only slightly less obvious implications in the study of cyclic composition trajectories.

Consider a network with reaction set $\mathscr{R}$, and suppose that $\{\alpha_{i \to j}\}_{i \to j \in \mathscr{R}}$ is a set of numbers such that

$$\mathbf{0} = \sum_{\mathscr{R}} \alpha_{i \to j} (\mathbf{y}_j - \mathbf{y}_i). \tag{5.33}$$

Now suppose that the reaction set is partitioned into subsets $\mathscr{R}_1, \mathscr{R}_2, \ldots, \mathscr{R}_p$. Clearly, (5.33) is equivalent to

$$\mathbf{0} = \sum_{\theta=1}^{p} \left[\sum_{\mathscr{R}_\theta} \alpha_{i \to j} (\mathbf{y}_j - \mathbf{y}_i) \right]. \tag{5.34}$$

Now that the θth bracketed term in (5.34) is of the form

(5.24) and so is a member of S_θ, the stoichiometric subspace for the θth subnetwork. *If the partition is such that* (5.28)*—and, therefore,* (5.27)*—hold, the definition of a direct sum requires that each of the p terms in* (5.34) *be separately equal to the zero vector*; that is, we must have

$$\mathbf{0} = \sum_{\mathscr{R}_\theta} \alpha_{i\to j}(\mathbf{y}_j - \mathbf{y}_i), \quad \theta = 1, 2, \ldots, p. \tag{5.35}$$

Remark 5.4.A. Consider a network with reaction set $\mathscr{R}$, and suppose that $\{\alpha_{i\to j}\}_{i\to j\in\mathscr{R}}$ is a set of numbers such that

$$\mathbf{0} = \sum_{\mathscr{R}} \alpha_{i\to j}(\mathbf{y}_j - \mathbf{y}_i).$$

Then for any *independent* subnetwork, say with reaction set $\mathscr{R}'$, the numbers $\{\alpha_{i\to j}\}_{i\to j\in\mathscr{R}'}$ must in fact satisfy

$$\mathbf{0} = \sum_{\mathscr{R}'} \alpha_{i\to j}(\mathbf{y}_j - \mathbf{y}_i). \tag{5.36}$$

This is a simple consequence of the discussion above and the fact that the partition of $\mathscr{R}$ into $\mathscr{R}'$ and $\mathscr{R}'' = \mathscr{R}\backslash\mathscr{R}'$ satisfies (5.29).

The implications of these ideas in the study of steady states are immediate. Consider a reaction system with reaction set $\mathscr{R}$ and kinetics $\{\mathscr{K}_{i\to j}(\cdot)\}_{i\to j\in\mathscr{R}}$. If $\mathbf{c}^*$ is a steady state we have

$$\mathbf{0} = \sum_{\mathscr{R}} \mathscr{K}_{i\to j}(\mathbf{c}^*)(\mathbf{y}_j - \mathbf{y}_i). \tag{5.37}$$

From the discussion above it follows that, if the reaction set is partitioned into subsets $\mathscr{R}_1, \mathscr{R}_2, \ldots, \mathscr{R}_p$ such that (5.28) holds, we must have

$$\mathbf{0} = \sum_{\mathscr{R}_\theta} \mathscr{K}_{i\to j}(\mathbf{c}^*)(\mathbf{y}_j - \mathbf{y}_i), \quad \theta = 1, 2, \ldots, p. \tag{5.38}$$

We can view the θth eq. in (5.38) as an assertion that $\mathbf{c}^*$ is, in fact, a steady state for the "reaction subsystem" with reactions $\mathscr{R}_\theta$ and kinetics $\{\mathscr{K}_{i\to j}(\cdot)\}_{i\to j\in\mathscr{R}_\theta}$. In other words, *when the reactions in the parent network are partitioned in such a way that* (5.28) *is satisfied, any steady state for the parent reaction system must be a steady state for each of the resulting reaction subsystems viewed separately.*

Remark 5.4.B. Suppose that $\mathbf{c}^*$ is a steady state for a reaction system with reaction set $\mathscr{R}$ and kinetics $\{\mathscr{K}_{i\to j}(\cdot)\}_{i\to j\in\mathscr{R}}$. From (5.37) and Remark 5.4.A it follows that for any *independent* subnetwork, say with reaction set $\mathscr{R}'$, we must have

$$\mathbf{0} = \sum_{\mathscr{R}'} \mathscr{K}_{i\to j}(\mathbf{c}^*)(\mathbf{y}_j - \mathbf{y}_i). \tag{5.39}$$

In other words, $\mathbf{c}^*$ *must be a steady state for the "independent reaction subsystem" with reactions* $\mathscr{R}'$ *and kinetics* $\{\mathscr{K}_{i\to j}(\cdot)\}_{i\to j\in\mathscr{R}'}$.

Remark 5.4.C. For a reaction subsystem with reaction set $\mathscr{R}'$ we continue to view the rate functions $\{\mathscr{K}_{i\to j}(\cdot)\}_{i\to j\in\mathscr{R}'}$ as having domain $\bar{\mathbb{P}}^N$, where N is the number of species in the parent network, even when the subnetwork corresponding to $\mathscr{R}'$ contains fewer than N species. These functions nevertheless constitute a kinetics for the subnetwork to the extent that conditions (K.1) and (K.2) in Section 3.1 remain satisfied.

Direct summing and subnetwork independence also have simple implications in the study of cyclic composition trajectories. Suppose that a network with reaction set $\mathscr{R}$ is endowed with a kinetics such that the differential eq. (3.6) for the resulting reaction system admits a cyclic composition trajectory. In particular suppose that, for the reaction system, $\mathbf{c}(\cdot)$ is a solution of (3.6) which contains in its domain the time interval $[0, T]$ and which has the property that $\mathbf{c}(0) = \mathbf{c}(T)$. From the discussion in Section 5.3 it follows that (5.15) must hold:

$$\mathbf{0} = \sum_{\mathscr{R}} \left[\int_0^T \mathscr{K}_{i\to j}(\mathbf{c}(\tau))\,\mathrm{d}\tau\right](\mathbf{y}_j - \mathbf{y}_i). \tag{5.15}$$

If $\mathscr{R}$ is partitioned into subsets $\mathscr{R}_1, \mathscr{R}_2, \ldots, \mathscr{R}_p$ in such a way that (5.28) is satisfied, considerations of the kind discussed earlier lead to the conclusion that

$$\mathbf{0} = \sum_{\mathscr{R}_\theta} \left[\int_0^T \mathscr{K}_{i\to j}(\mathbf{c}(\tau))\,\mathrm{d}\tau\right](\mathbf{y}_j - \mathbf{y}_i),$$
$$\theta = 1, 2, \ldots, p. \tag{5.40}$$

In other words, *when* (5.28) *is satisfied, the periodic solution* $\mathbf{c}(\cdot)$ *of the differential equation for the parent reaction system must be such as to satisfy an equation of the form* (5.15) *for each reaction subsystem separately.* (This is *not* to say that the differential equations for the separate reaction subsystems must each admit a nonconstant cyclic composition trajectory if the differential equation for the parent reaction system admits a nonconstant cyclic composition trajectory.)

Remark 5.4.D. Suppose that the differential equation (3.6) for a reaction system with reaction set $\mathscr{R}$ and kinetics $\{\mathscr{K}_{i\to j}(\cdot)\}_{i\to j\in\mathscr{R}}$ admits a periodic solution $\mathbf{c}(\cdot)$ such that $\mathbf{c}(0) = \mathbf{c}(T)$. From (5.15) and Remark 5.4.A it follows that for any *independent* subnetwork, say with reaction set $\mathscr{R}'$, we must have

$$\mathbf{0} = \sum_{\mathscr{R}'} \left[\int_0^T \mathscr{K}_{i\to j}(\mathbf{c}(\tau))\,\mathrm{d}\tau\right](\mathbf{y}_j - \mathbf{y}_i). \tag{5.41}$$

In other words, the periodic solution $\mathbf{c}(\cdot)$ *must satisfy an equation of the form* (5.15) *written separately for the "independent reaction subsystem" with reaction set* $\mathscr{R}'$ *and kinetics* $\{\mathscr{K}_{i\to j}(\cdot)\}_{i\to j\in\mathscr{R}'}$.

As we shall see, the simple Remarks 5.4.B and 5.4.D usually find use in the following way: One might wish to study the steady states or the possibility of (nonconstant) cyclic composition trajectories for a large and intricate reaction system about which little can be said at first glance. But there might be embedded in the reaction system an independent reaction subsystem for which theorems of the kind presented in Section 6 give information. In this case one often can, with great effect, "carry up" that information to the study of the parent system.

It is rather surprising that one can sometimes work in just the opposite way. It might happen that one is confronted with a reaction system about which little can be said. But it might also happen that the given reaction system can be embedded as an independent reaction subsystem in a larger reaction system for which available theorems give information. In this case that information can be "carried down" to the study of the original reaction system. We shall see how this works in Remark 6.2.B.

Remark 5.4.E. In preparation for Section 6, there is one special and elementary kind of partition we should consider. For a reaction network with ℓ linkage classes, we can certainly partition the full set of reactions into subsets $\mathscr{R}_1, \mathscr{R}_2, \ldots, \mathscr{R}_\ell$, where $\mathscr{R}_\theta$ is simply the subset of reactions joining complexes in the θth linkage class. For example, the set of reactions in the network

$$\begin{array}{c} A_1 \rightarrow 2A_2 \\ A_1 + A_3 \rightleftarrows A_4 \\ \nwarrow \quad \swarrow \\ A_2 + A_5 \end{array} \tag{5.42}$$

can be partitioned into two subsets,

$$A_1 \rightarrow 2A_2 \tag{5.43$_1$}$$

and

$$\begin{array}{c} A_1 + A_3 \rightleftarrows A_4 \\ \nwarrow \quad \swarrow \\ A_2 + A_5 \end{array} \tag{5.43$_2$}$$

Such a partition simply amounts to a partition of the parent network into ℓ subnetworks which, in the sense of Section 2.4, are the separate "pieces" of which the parent network is composed. In this case the subnetworks not only have no reaction in common, *they also have no complex in common.*

For partitions of this *special* kind, the condition

$$s = s_1 + s_2 + \ldots + s_\ell \tag{5.44}$$

is easily seen to be equivalent to the condition

$$\delta = \delta_1 + \delta_2 + \ldots + \delta_\ell, \tag{5.45}$$

where δ is the deficiency of the parent network and δ_θ is, in the sense of Section 2.6, the deficiency of the θth linkage class. *Thus,* (5.45) *is equivalent to the condition that the stoichiometric subspace for the parent network be the direct sum of the stoichiometric subspaces corresponding to the separate linkage classes.* When (5.45) is satisfied, each separate "piece" of the parent network amounts to an independent subnetwork.

As we shall see, condition (5.45) plays a part in the statement of the Deficiency One Theorem given in Section 6 [just as it did in the statement of the narrower version of the theorem given in (Feinberg, 1980).] In light of the preceding discussion, the role of condition (5.45) should be fairly evident: To a great extent, the direct summing ensured by (5.45) reduces the study of steady states for the parent reaction system to the study of steady states for the independent reaction subsystems associated with the separate linkage classes.

For an *arbitrary* partition of the full set of reactions into p subsets it will not necessarily be true that the condition

$$s = \sum_{\theta=1}^{p} s_\theta \tag{5.46}$$

is equivalent to the condition

$$\delta = \sum_{\theta=1}^{p} \delta_\theta, \tag{5.47}$$

where δ is the deficiency of the parent network and δ_θ is the deficiency of the θth subnetwork computed separately. In fact, it is obvious that (5.46) and (5.47) are equivalent if and only if the partition is such that

$$n - \ell = \sum_{\theta=1}^{p} (n_\theta - \ell_\theta), \tag{5.48}$$

where n and ℓ are the number of complexes and the number of linkage classes in the parent network, and n_θ and ℓ_θ are the number complexes and the number of linkage classes in the θth subnetwork. For the special partition described at the beginning of this remark (5.48) is satisfied trivially.

6. PRINCIPAL THEOREMS

In this section we shall state two theorems. Both give immediate and rather incisive qualitative information about nonlinear differential equations for what might be extremely intricate reaction systems. Use of these theorems requires only that one be familiar with those aspects of reaction network structure we have discussed so far. In particular, one should know how to calculate the rank and deficiency of a network.

The *Deficiency Zero Theorem* has been discussed elsewhere (see, for example Feinberg and Horn, 1974; Horn, 1973; Feinberg, 1977, 1980). Here we shall elaborate further on special properties of deficiency zero networks, and we shall indicate how knowledge of these properties can be of some use even in the study of networks with nonzero deficiency. Moreover, our discussion of the Deficiency Zero Theorem will set the stage for what we shall call the *Deficiency One Theorem.*

A version of the Deficiency One Theorem, restricted to weakly reversible networks, was stated in (Feinberg, 1980). Here we shall state a substantially more general version. Just as the Deficiency Zero Theorem sets the stage for the Deficiency One Theorem, the Deficiency One Theorem will, in turn, provide a backdrop for additional theory contained in a companion article (Feinberg, 1988).

Use of both theorems will be illustrated in several examples. In our consideration of examples we shall not always write out the differential equations corresponding to the particular reaction system under study. *It should be remembered, however, that these equations are generally quite complex.* Indeed, it is rather remarkable that the Deficiency Zero and Deficiency One Theorems provide incisive information about extremely complicated systems of differential equations *that one need not even write out.* When the equations are displayed, our purpose is to remind readers that these theorems do, in fact, address questions which would otherwise be extraordinarily difficult.

6.1. *The Deficiency Zero Theorem*

Reaction networks of deficiency zero can be extremely intricate, involving hundreds of species and hundreds of reactions. Nevertheless, there is quite a bit one can say about properties of differential equations that derive from deficiency zero networks. For the sake of clarity we shall not attempt to provide one comprehensive theorem containing all that can be said. We prefer instead to begin by stating a "basic" theorem containing the most essential information. Then we shall be in a position to indicate how this "basic" theorem can be fleshed out further.

Ideas underlying the proof of the Deficiency Zero Theorem can be found in Horn and Jackson (1972), Horn (1972), Feinberg (1972) and Feinberg (1977). A complete account of the proof can be found in Feinberg (1979).

In very rough terms, the Deficiency Zero Theorem asserts that, at least when the kinetics is mass action, one should not expect "exotic" behavior (e.g. multiple positive steady states, unstable positive steady states, periodic composition trajectories) to result from differential equations that derive from a deficiency zero network, no matter how intricate the network might be.

Theorem 6.1.1. (*The Deficiency Zero Theorem*): *For any reaction network of deficiency zero the following statements hold true:*

(i) *If the network is not weakly reversible then, for arbitrary kinetics* (*not necessarily mass action*), *the differential equations for the corresponding reaction system cannot admit a positive steady state* (i.e. *a steady state in* $\mathbb{P}^N$).

(ii) *If the network is not weakly reversible then, for arbitrary kinetics* (*not necessarily mass action*), *the differential equations for the corresponding reaction system cannot admit a cyclic composition trajectory along which all species concentrations are positive.*

(iii) *If the network is weakly reversible then, for mass action kinetics* (*but regardless of the positive values the rate constants take*), *the differential equations for the corresponding reaction system have the following properties: There exists within each positive stoichiometric compatibility class* precisely one *steady state; that steady state is asymptotically stable; and there is no nontrivial cyclic composition trajectory along which all species concentrations are positive.*

Remark 6.1.A. Proofs of parts (i) and (ii) of the Deficiency Zero Theorem are sufficiently simple that we can give a brief explanation of the underlying ideas. In Sections 5.3 we argued that, in order for the differential equations of a reaction system to admit either a steady state in $\mathbb{P}^N$ or a cyclic composition trajectory that passes through $\mathbb{P}^N$, it is *necessary* that the reaction vectors for the underlying network be positively dependent. This is true regardless of the deficiency of the network. To prove parts (i) and (ii) of the Deficiency Zero Theorem one shows that, *for a deficiency zero network that is not weakly reversible, the set of reaction vectors cannot be positively dependent.*

Use of the Deficiency Zero Theorem will be illustrated with some examples.

We shall begin by recalling network (2.1), and we shall suppose for the sake of discussion that the network is given mass action kinetics. The resulting mass action system is described by a rather intricate system of eight coupled polynomial differential equations in eight species concentration. We can ask whether this system admits a positive steady state or a cyclic composition trajectory along which all species concentrations are positive.

$$A_1 + A_2 \rightleftarrows A_3 \rightarrow A_4 + A_5 \rightleftarrows A_6$$

$$\begin{tikzcd}[column sep=small] 2A_1 \arrow[rr] & & A_2 + A_7 \arrow[dl, shift right] \\ & A_8 \arrow[ul] \arrow[ur, shift right] & \end{tikzcd} \qquad (2.1)$$

The Deficiency Zero Theorem answers the question immediately: In Section 2.5 we established that the deficiency of network (2.1) is *zero*. Moreover, the network is not weakly reversible. Thus, from parts (i) and (ii) of the theorem we can quickly conclude that, *no matter what the rate constants might be, the differential equations for the corresponding mass action system cannot admit a positive steady state, nor can they admit a cyclic composition trajectory along which all species concentrations are positive.* In fact, this same conclusion follows from the theorem even if the kinetics is not mass action.

We consider next a weakly reversible version of network (2.1), displayed as (6.1). Again we shall suppose that the kinetics is mass action with rate constants as indicated by Greek letters alongside the corresponding reaction arrows:

$$A_1 + A_2 \underset{\beta}{\overset{\alpha}{\rightleftarrows}} A_3 \underset{\varepsilon}{\overset{\gamma}{\rightleftarrows}} A_4 + A_5 \underset{\theta}{\overset{\eta}{\rightleftarrows}} A_6$$

$$\begin{tikzcd}[column sep=small] 2A_1 \arrow[rr, "\kappa"] & & A_2 + A_7 \arrow[dl, shift right, "\lambda"'] \\ & A_8 \arrow[ul, "\nu"] \arrow[ur, shift right, "\mu"'] & \end{tikzcd} \qquad (6.1)$$

The corresponding differential equations are displayed in (6.2):

$$\begin{aligned}
\dot{c}_1 &= -\alpha c_1 c_2 + \beta c_3 - 2\kappa c_1^2 + \nu c_8 \\
\dot{c}_2 &= -\alpha c_1 c_2 + \beta c_3 + \kappa c_1^2 - \lambda c_2 c_7 + \mu c_8 \\
\dot{c}_3 &= \alpha c_1 c_2 + \varepsilon c_4 c_5 - (\gamma + \beta) c_3 \\
\dot{c}_4 &= \gamma c_3 + \theta c_6 - (\varepsilon + \eta) c_4 c_5 \\
\dot{c}_5 &= \gamma c_3 + \theta c_6 - (\varepsilon + \eta) c_4 c_5 \\
\dot{c}_6 &= \eta c_4 c_5 - \theta c_6 \\
\dot{c}_7 &= \kappa c_1^2 + \mu c_8 - \lambda c_2 c_7 \\
\dot{c}_8 &= \lambda c_2 c_7 - (\mu + \nu) c_8 .
\end{aligned} \tag{6.2}$$

We now ask the following questions: *Does the system* (6.2) *admit a positive steady state? Does it admit multiple positive steady states? Does it admit an unstable positive steady state? Does it admit a periodic composition trajectory along which all species concentrations are positive?* Each answer might, of course, depend on the particular values of the rate constants. Each question, studied on an *ad hoc* basis, would be extremely difficult.

Yet the Deficiency Zero Theorem again answers *all* the questions immediately: The deficiency of network (6.1), like that of network (2.1), is *zero*. (In fact, since both networks have the same complexes and the same linkage classes, Remark 2.5.A tells us that both networks have the same deficiency.) Unlike network (2.1), however, network (6.1) is weakly reversible. Thus, part (iii) of the theorem tells us that, *regardless* of the (positive) values the rate constants take, the answers to the questions posed above are *yes*, *no*, *no* and *no*.

It is instructive to consider the well-studied "Brusselator" (Glansdorff and Prigogine, 1971), which (in the sense of Section 4.3) is modelled by network (6.3). When the kinetics is mass action with rate constants as

$$\begin{gathered}
0 \underset{\beta}{\overset{\alpha}{\rightleftarrows}} A_1 \xrightarrow{\gamma} A_2 \\
2A_1 + A_2 \xrightarrow{\varepsilon} 3A_1
\end{gathered} \tag{6.3}$$

indicated in (6.3), the corresponding differential equations are those shown in (6.4). For certain values of the rate constants these equations admit an unstable *positive* steady state and a cyclic composition trajectory in the positive orthant. There is, however, no contradiction of parts (i) and (ii) of the Deficiency Zero Theorem: The deficiency of network (6.3) is *one* ($n = 5$, $\ell = 2$, and $s = 2$; $\delta = 5 - 2 - 2 = 1$).

$$\begin{aligned}
\dot{c}_1 &= \alpha - (\beta + \gamma) c_1 + \varepsilon c_1^2 c_2 \\
\dot{c}_2 &= \gamma c_1 - \varepsilon c_1^2 c_2 .
\end{aligned} \tag{6.4}$$

It is interesting to see how the Deficiency Zero Theorem distinguishes between two apparently similar mass action systems.

Recall the Edelstein network, which was discussed in Section 4.3 and which we repeat here as (6.5). With rate constants as indicated in (6.5)

$$\begin{gathered}
A_1 \underset{\beta}{\overset{\alpha}{\rightleftarrows}} 2A_1 \\
A_1 + A_2 \underset{\varepsilon}{\overset{\gamma}{\rightleftarrows}} A_3 \underset{\eta}{\overset{\theta}{\rightleftarrows}} A_2
\end{gathered} \tag{6.5}$$

the corresponding mass action differential equations become those shown in (6.6). For certain values of the rate constants these equations admit *three* steady states in a positive stoichiometric compatibility class, one of which is *unstable*. The Deficiency Zero Theorem, part (iii), is not contradicted: The deficiency of network (6.5) is *one* ($n = 5$, $\ell = 2$ and $s = 2$; $\delta = 5 - 2 - 2 = 1$).

$$\begin{aligned}
\dot{c}_1 &= \alpha c_1 - \beta c_1^2 - \gamma c_1 c_2 + \varepsilon c_3 \\
\dot{c}_2 &= -\gamma c_1 c_2 + (\varepsilon + \theta) c_3 - \eta c_2 \\
\dot{c}_3 &= \gamma c_1 c_2 + \eta c_2 - (\varepsilon + \theta) c_3 .
\end{aligned} \tag{6.6}$$

On the other hand, consider the very similar mass action system given in (6.7). The corresponding system of differential equations is given in (6.8).

$$\begin{gathered}
A_1 \underset{\beta}{\overset{\alpha}{\rightleftarrows}} 2A_1 \\
A_1 + A_2 \underset{\varepsilon}{\overset{\gamma}{\rightleftarrows}} A_3 \underset{\eta}{\overset{\theta}{\rightleftarrows}} 2A_2 .
\end{gathered} \tag{6.7}$$

Although these are similar to the equations given in (6.6), the dynamical situation is rather different: The deficiency of network (6.6) is *zero* ($n = 5$, $\ell = 2$ and $s = 3$). In this case, part (iii) of the Deficiency Zero Theorem tells us that, *no matter what positive values the rate constants take, the system* (6.8) *admits precisely one positive steady state and that steady state is asymptotically stable.*

$$\begin{aligned}
\dot{c}_1 &= \alpha c_1 - \beta c_1^2 - \gamma c_1 c_2 + \varepsilon c_3 \\
\dot{c}_2 &= -\gamma c_1 c_2 + (\varepsilon + 2\theta) c_3 - 2\eta c_2^2 \\
\dot{c}_3 &= \gamma c_1 c_2 + \eta c_2^2 - (\varepsilon + \theta) c_3 .
\end{aligned} \tag{6.8}$$

These examples should make clear that the "basic" Deficiency Zero Theorem already provides rather incisive information about qualitative properties of differential equations that derive from deficiency zero networks. Now, in a series of remarks, we shall indicate how this information can be sharpened.

Remark 6.1.B. (*The Nature of Steady States for Deficiency Zero Networks*). The Deficiency Zero Theorem tells us that a reaction system that derives from a deficiency zero network which is *not* weakly reversible cannot admit a *positive* steady state. Whatever steady states do exist must be on the boundary of $\bar{\mathbb{P}}^N$, where at least certain species concentrations are zero. As it is stated, however, the theorem tells us nothing about where on the boundary of $\bar{\mathbb{P}}^N$ steady states might lie.

It might be recalled, however, that Proposition 5.3.1 gives some information: Suppose that $\mathbf{c}^*$ is a steady state, say on the boundary of $\bar{\mathbb{P}}^N$, and suppose also that $\mathbf{y}_i$ and $\mathbf{y}_j$ are complexes of the network such that there exists a directed reaction pathway leading from $\mathbf{y}_i$ to $\mathbf{y}_j$.

Then, if supp $\mathbf{y}_i$ is contained in supp $\mathbf{c}^*$, it must be the case that supp $\mathbf{y}_j$ is also contained in supp $\mathbf{c}^*$. This is to say that if *all* species appearing in complex $\mathbf{y}_i$ have nonzero concentrations at composition $\mathbf{c}^*$, it must *also* be the case that *all* species appearing in complex $\mathbf{y}_j$ have nonzero concentrations at composition $\mathbf{c}^*$. Although this is helpful information, Proposition 5.3.1 never quite tells us in unconditional terms that a particular complex *cannot* have its support contained entirely in the support of $\mathbf{c}^*$.

It should be remembered, however, that Proposition 5.3.1 was written for networks of *arbitrary* deficiency. If we restrict our attention to networks of deficiency *zero* there is much more that can be said. Proof of the following proposition can be found in (Feinberg, 1979).

Proposition 6.1.2. *Consider a reaction system (not necessarily mass action) for which the underlying reaction network has a deficiency of zero. If* $\mathbf{c}^*$ *is a steady state of the corresponding differential equations and* $\mathbf{y}_i$ *is a complex in the network, then* supp $\mathbf{c}^*$ *contains* supp $\mathbf{y}_i$ *only if* $\mathbf{y}_i$ *is a member of a terminal strong linkage class. If* supp $\mathbf{c}^*$ *contains* supp $\mathbf{y}_i$, *then* supp $\mathbf{c}^*$ *also contains the support of each complex in the terminal strong linkage class to which* $\mathbf{y}_i$ *belongs.*

The last sentence of this proposition is already implied by Proposition 5.3.1; it is included only for the sake of completeness. What is new here is that, if the deficiency of the network is *zero* and if $\mathbf{c}^*$ is a steady state, then supp $\mathbf{c}^*$ *cannot* contain the support of *any* complex which does not lie in a terminal strong linkage class. That is, if $\mathbf{y}_i$ is a complex that does *not* lie in a terminal strong linkage class then, at composition $\mathbf{c}^*$, *at least one species appearing in complex* $\mathbf{y}_i$ *must have a concentration of zero.*

It is easy to see that Proposition 6.1.2 implies (and sharpens) part (ii) of the Deficiency Zero Theorem: A network which is not weakly reversible must contain at least one complex that does not lie in a terminal strong linkage class. If the network has a deficiency of zero, any steady state that exists must be characterized by the absence of one or more species appearing in that "nonterminal" complex. Thus, there can be no *positive* steady state.

An example might be helpful. We shall consider a reaction system (not necessarily mass action) for which the underlying network is given by (2.1), and we shall use Proposition 6.1.2 to determine where in $\bar{\mathbb{P}}^N$ steady states might lie. The terminal strong linkage classes are $\{A_4 + A_5, A_6\}$ and $\{2A_1, A_2 + A_7, A_8\}$. The complexes that do *not* lie in terminal strong linkage classes are $A_1 + A_2$ and A_3. Thus, if $\mathbf{c}^*$ is a steady state, Proposition 6.1.2 tells us that supp $\mathbf{c}^*$ *cannot* contain the support of complex $A_1 + A_2$ $(= \{A_1, A_2\})$ or the support of complex A_3 $(= \{A_3\})$. Thus, $c_3^* = 0$, and we must also have $c_1^* = 0$ or $c_2^* = 0$ (or both). With this information in hand, we can apply the last sentence of Proposition 6.1.2 to determine that c_1^* and c_8^* must be zero; moreover, the only combinations of species that might have positive concentrations at composition $\mathbf{c}^*$ are $\{A_4\}$, $\{A_5\}$, $\{A_4, A_5, A_6\}$, $\{A_2, A_4\}$, $\{A_2, A_5\}$, $\{A_2, A_4, A_5, A_6\}$, $\{A_4, A_7\}$, $\{A_5, A_7\}$ and $\{A_4, A_5, A_6, A_7\}$.

Proposition 6.1.2. has an immediate consequence when taken in conjunction with condition (K.2) imposed on rate functions in Section 3.1: *At a steady state of a reaction system for which the underlying network has a deficiency of zero, the only reactions that might be "switched on" are those that join complexes contained in a terminal strong linkage class; moreover, if one reaction joining complexes in a particular terminal strong linkage class is switched on, then all reactions joining complexes in that terminal strong linkage class are switched on.*

It is interesting to note that if a deficiency zero network has the property that each terminal strong linkage class is trivial (i.e. consists of a single complex) then, no matter what the kinetics might be, the only steady states that can exist are those at which *all* reactions are "switched off". There are still other deficiency zero networks that admit only steady states at which all reactions are switched off. Network (6.9) provides a simple example. In fact, consider any deficiency zero network with the following property: There exists in each nontrivial terminal strong linkage class a complex containing a species that also appears alone (without any other species) in a complex that does not belong to a terminal strong linkage class. It is then an easy consequence of Proposition 6.1.2 that,

$$\begin{gathered} 2A_1 \to A_2 \\ A_1 + A_3 \rightleftarrows A_4 \end{gathered} \tag{6.9}$$

no matter what kinetics is assigned to the network, the differential equations for the corresponding reaction system can admit *only* steady states at which *all* reactions are switched off. [For example, in network (6.9) the only nontrivial terminal strong linkage class is $\{A_1 + A_3, A_4\}$. The complex $A_1 + A_3$ contains a species, A_1, that appears alone in the "nonterminal" complex $2A_1$.]

There is another interesting consequence of Proposition 6.1.2: *Consider a deficiency zero network that contains the zero complex, and suppose that the zero complex does not lie in a terminal strong linkage class. Then, no matter what kinetics is assigned to the network, the differential equations for the resulting reaction system admit no steady states at all.* To see this, suppose that $\mathbf{c}^*$ is a steady state. Proposition 6.1.2 requires that the support of the zero complex *not* lie in supp $\mathbf{c}^*$. But the support of the zero complex is the empty set, which *is* contained in supp $\mathbf{c}^*$ (Remark 5.3.D). Thus we have a contradiction. [Note that the mass action system (6.3) *does* admit a steady state even though the underlying network contains a "nonterminal" zero complex. That network has a deficiency of *one*.]

Lest it be supposed that the content of Proposition 6.1.2 is intuitively obvious, we emphasize that the proposition becomes *false* if the deficiency zero condition is omitted from its hypothesis. For example, it is easy to assign a kinetics (in fact, a mass action kinetics) to the *deficiency one* network (6.10) such that the differential equations for the resulting reaction system admit a positive steady state. The support of that steady state is $\{A_1, A_2, A_3\}$, which—in contradiction to what Proposition 6.1.2 would require—

$$\begin{gathered} A_1 \rightarrow 2A_1 \\ A_1 + A_2 \rightleftarrows A_3 \rightleftarrows A_2 \end{gathered} \tag{6.10}$$

contains the support of the "nonterminal" complex A_1. On the other hand, the slightly different network (6.11) has a deficiency of zero. From Proposition 6.1.2 it follows easily that, no matter what kinetics is assigned to network (6.11), the *only* steady state the resulting reaction system admits is one for which the concentrations of all three species are *zero*. Thus, any intuition that purports to render Proposition 6.1.2 obvious must be sufficiently refined as to distinguish between the different situations for the very similar networks (6.10) and (6.11).

$$\begin{gathered} A_1 \rightarrow 2A_1 \\ A_1 + A_2 \rightleftarrows A_3 \rightleftarrows 2A_2 \end{gathered} \tag{6.11}$$

Remark 6.1.C. (*The Possibility and Nature of Cyclic Composition Trajectories for Deficiency Zero Networks*). The Deficiency Zero Theorem does not *entirely* preclude the possibility that nontrivial composition cycles might be admitted by a reaction system for which the underlying reaction network has a deficiency of zero. In particular, the theorem does not preclude the possibility that, with *some* kinetics (not necessarily mass action), there might be cyclic composition trajectories that lie entirely on the boundary of $\bar{\mathbb{P}}^N$. It is interesting to consider where on the boundary of $\bar{\mathbb{P}}^N$ nontrivial cyclic composition trajectories might lie.

Proposition 5.3.2 already gives some information. Recall from Section 5.3 that we say that a cyclic composition trajectory has support Γ (where Γ is a subset of the species in the network) if, for every composition $\mathbf{c}$ along the trajectory, $\operatorname{supp} \mathbf{c} = \Gamma$. Should a reaction system admit a cyclic composition trajectory with support Γ, Proposition 5.3.2 asserts that Γ cannot be an arbitrary set of species but, rather, must bear a certain relationship to the structure of the underlying reaction network: Suppose that $\mathbf{y}_i$ and $\mathbf{y}_j$ are complexes such that there exists a directed reaction pathway leading from $\mathbf{y}_i$ to $\mathbf{y}_j$; then, if *all* species appearing in complex $\mathbf{y}_i$ are contained in Γ, it must *also* be the case that *all* species appearing in complex $\mathbf{y}_j$ are contained in Γ. Thus, Proposition 5.3.2 tells us that there are only certain parts of the boundary of $\bar{\mathbb{P}}^N$ on which a cyclic composition trajectory might lie.

Proposition 5.3.2 was written for networks of *arbitrary* deficiency. If our attention is restricted to networks of deficiency *zero*, we can say much more—in effect that Γ can contain the support of only certain complexes. Proof of the following proposition can be found in (Feinberg, 1979).

Proposition 6.1.3. *Consider a reaction system (not necessarily mass action) for which the underlying reaction network has a deficiency of zero. If the corresponding differential equations admit a cyclic composition trajectory with support Γ and if $\mathbf{y}_i$ is a complex in the network, then Γ contains the support of $\mathbf{y}_i$ only if $\mathbf{y}_i$ is a member of a terminal strong linkage class. If Γ contains the support of $\mathbf{y}_i$, then Γ also contains the support of each complex in the terminal strong linkage class to which $\mathbf{y}_i$ belongs.*

Proposition 6.1.3 implies (and sharpens) part (ii) of the Deficiency Zero Theorem: A network which is not weakly reversible must contain at least one complex that does not lie in a terminal strong linkage class. If a cyclic trajectory could exit in $\mathbb{P}^N$, its support would contain *all* the species in the network and would therefore contain the support of *every* complex in the network, even the "nonterminal" ones, in contradiction to Proposition 6.1.3.

In fact, Proposition 6.1.3 tells us something more about deficiency zero networks: Suppose that, for some assignment of a kinetics, the corresponding differential equations admit a cyclic composition trajectory on the boundary of $\bar{\mathbb{P}}^N$, and suppose that the trajectory has support Γ. Because Γ cannot contain the support of *any* complex that does not lie in a terminal strong linkage class, condition (K.2) in Section 3.1 implies that *the trajectory must lie entirely in a part of the boundary of $\bar{\mathbb{P}}^N$ in which the only reactions that might be "switched on" are those that connect complexes belonging to a terminal strong linkage class.* Moreover, condition (K.2) and Proposition 6.1.3 tells us that *if, along the trajectory, even one reaction connecting complexes in a particular terminal strong linkage class is "switched off" then all reactions connecting complexes in that terminal strong linkage class are "switched off"*.

Now we shall suppose that a deficiency zero network endowed with some kinetics admits a nontrivial cyclic composition trajectory on the boundary of $\bar{\mathbb{P}}^N$, and we shall examine the nature of the subnetwork consisting of those reactions that are switched on along the trajectory. From the discussion in the preceding paragraph it is easy to see that this subnetwork is *weakly reversible*: Its complexes are those that lie in certain terminal strong linkage classes of the original network, and the reactions in the subnetwork are precisely those in the original network that connect these complexes to each other. Moreover, it is not difficult to show that *any subnetwork of a deficiency zero network is itself a network of deficiency zero*. Thus, the subnetwork consisting of those reactions that are switched on along the trajectory *is weakly reversible and has a deficiency of zero.*

We already know that a deficiency zero network taken with *mass action* kinetics cannot generate a nontrivial cyclic composition trajectory in the *interior* of $\bar{\mathbb{P}}^N$. We are now in a position to argue that a deficiency zero network taken with mass action kinetics cannot generate *any* nontrivial cyclic composition trajectory, even on the boundary of $\bar{\mathbb{P}}^N$.

Suppose on the contrary that, for some assignment of rate constants, the corresponding system of differential equations could admit a nontrivial cyclic composition trajectory, say with support Γ, on the boundary of $\bar{\mathbb{P}}^N$. Renumbering the species if necessary, we shall presume that $\Gamma = \{A_1, A_2, \ldots, A_M\}$, where $M < N$. Thus, the trajectory lies in the relative interior of the set

$$\{\mathbf{c} \in \bar{\mathbb{P}}^N : c_L = 0, L = M+1, \ldots, N\}. \tag{6.12}$$

From previous arguments we know that, in the relative interior of (6.12), the reactions that are switched on constitute a deficiency zero weakly reversible subnetwork of the original network, and it is clear that these reactions neither produce nor consume any species in the set $\{A_{M+1}, \ldots, A_N\}$. Moreover, these are the only reactions that might be switched on anywhere in (6.12). Thus, the set (6.12) is an invariant set of compositions. We can regard the dynamics there to be generated by a mass action system for which the underlying reaction network contains only species $\{A_1, \ldots, A_M\}$ and is a weakly reversible deficiency zero subnetwork of the original network. [In fact, we can identify (6.12) with $\bar{\mathbb{P}}^M$ and its relative interior with $\mathbb{P}^M$.] But for such a system the Deficiency Zero Theorem, part *(iii)*, precludes the possibility of a nontrivial cyclic composition trajectory along which the concentrations of species $A_1, \ldots, A_M$ are positive. This contradicts what we supposed.

There is an additional observation we can make about deficiency zero networks, one which is independent of the precise nature of the associated kinetics: *Consider a deficiency zero network that contains the zero complex and suppose that the zero complex does not lie in a terminal strong linkage class.* Then, no matter what kinetics is assigned to the network, *the differential equations for the resulting reaction system cannot admit a nontrivial cyclic composition trajectory.* (If such a trajectory could exist, Proposition 6.1.3 would require that its support *not* contain the support of the zero complex. But the support of the zero complex is the empty set.) Despite the presence of a "nonterminal" zero complex, the mass action system (6.3) *does* admit a nontrivial cyclic composition trajectory (for certain rate constant values). However, the deficiency of the network in (6.3) is *one*.

Remark 6.1.D. (*Independent Subnetworks of Deficiency Zero*). Here we shall indicate how results about deficiency zero networks can sometimes give information about networks of nonzero deficiency. The basic idea is this: It sometimes happens that a network of nonzero deficiency has imbedded within it a deficiency zero subnetwork which, in the sense of Section 5.4, is independent. In this case we can combine what we know about special properties of independent subnetworks with what we know about networks of deficiency zero.

It will be instructive to study a simple example. Consider network (6.13), which we shall presume to be endowed with a kinetics (not necessarily mass action). We shall want to determine where in $\bar{\mathbb{P}}^N$ steady states for

$$\begin{array}{ccccc} & & A_1 & \rightleftarrows & 2A_1 \\ & & \downarrow & & \\ A_1 + A_2 & \rightleftarrows & A_3 & \rightleftarrows & A_2 \end{array} \tag{6.13}$$

the corresponding reaction system might lie. It is easy to confirm that the deficiency of network (6.13) is *one* ($n = 5$, $\ell = 1$, $s = 3$). At first glance, our results about deficiency zero networks would appear to give no information at all.

Note, however, that networks $(6.13)_1$ and $(6.13)_2$ are (complementary) *independent* subnetworks of (6.13): The rank of (6.13) is three, while the ranks of $(6.13)_1$ and $(6.13)_2$ are one and two, respectively. Note also that the deficiency of subnetwork $(6.13)_1$ is *zero*. [The deficiency of $(6.13)_2$ is one.]

$$A_1 \rightarrow A_3 \qquad (6.13)_1$$

$$\begin{array}{c} A_1 \rightleftarrows 2A_1 \\ A_1 + A_3 \rightleftarrows A_3 \rightleftarrows A_2 . \end{array} \qquad (6.13)_2$$

Now suppose that a reaction system derived from network (6.13) admits a steady state $\mathbf{c}^*$. From Remark 5.4.B it follows that $\mathbf{c}^*$ *must be a steady state for each of the separate "reaction subsystems" corresponding to the independent subnetworks* $(6.13)_1$ *and* $(6.13)_2$. From Proposition 6.1.2 it follows that any steady state for network $(6.13)_1$ must be characterized by the absence of species A_1. Thus, the steady state $\mathbf{c}^*$ for the "parent" reaction system [derived from network (6.13)] must *also* be such that $c_1^* = 0$. With this information in hand, we can invoke Proposition 5.3.1 for the (deficiency one) network (6.13) to deduce that c_2^* and c_3^* are also both zero. Thus, no matter what kinetics is assigned to network (6.13), the only steady state is (0, 0, 0).

Our formal use of Proposition 5.3.1 to deduce that species A_1 must be absent in any steady state for the trivial network $(6.13)_1$ was, of course, unnecessary; in this case Proposition 5.3.1 merely told us the obvious. But the example should make clear how Proposition 5.3.1 can be applied to a perhaps more complicated deficiency zero independent subnetwork to give information about steady states for an even more complicated parent network of nonzero deficiency. In fact, ideas used in the study of our example provide the basis for the following proposition:

Proposition 6.1.4. *Suppose that* $\mathbf{c}^*$ *is a steady state for a reaction system, and suppose also that the underlying reaction network contains an independent subnetwork of deficiency zero. If* $\mathbf{y}_j$ *is a complex in that subnetwork, then* supp $\mathbf{c}^*$ *contains* supp $\mathbf{y}_j$ *only if* $\mathbf{y}_j$ *lies in a terminal strong linkage class of the subnetwork. Moreover, if* $\mathbf{y}_j$ *does not lie in a terminal strong linkage class of the subnetwork and if* $\mathbf{y}_i$ *is a complex in the parent network such that there exists in the parent network a directed reaction pathway leading from* $\mathbf{y}_i$ *to* $\mathbf{y}_j$, *then* supp $\mathbf{c}^*$ *does not contain* supp $\mathbf{y}_i$.

(The last sentence of the proposition is an easy consequence of the preceding sentence and Proposition 5.3.1.)

It should be kept in mind that the "parent" network in Proposition 6.1.4 need not have a deficiency of zero and that the kinetics need not be mass action. In rough terms, the proposition says that, if $\mathbf{y}_j$ is a "nonterminal" complex in an independent deficiency zero subnetwork of the parent network, then, in any steady state for the parent system, there must be an absence of at least one species appearing in complex $\mathbf{y}_j$. Moreover, if in the *parent* network there is a directed reaction pathway leading from complex $\mathbf{y}_i$ to complex $\mathbf{y}_j$, then, in any steady state for the parent system, there must also be an absence of at least one species appearing in complex $\mathbf{y}_i$.

Just as Proposition 6.1.4 broadens the use of Proposition 6.1.2, the following proposition broadens the use of Proposition 6.1.3.

Proposition 6.1.5. *Suppose that the differential equations for a reaction system admit a cyclic composition trajectory with support* Γ, *and suppose also that the underlying reaction network contains an independent subnetwork of deficiency zero. If* $\mathbf{y}_j$ *is a complex in that subnetwork, then* Γ *contains* supp $\mathbf{y}_j$ *only if* $\mathbf{y}_j$ *lies in a terminal strong linkage class of the subnetwork. Moreover, if* $\mathbf{y}_j$ *does not lie in a terminal strong linkage class of the subnetwork and if* $\mathbf{y}_i$ *is a complex in the parent network such that there exists in the parent network a directed reaction pathway leading from* $\mathbf{y}_i$ *to* $\mathbf{y}_j$, *then* Γ *does not contain* supp $\mathbf{y}_i$.

Arguments behind Proposition 6.1.5 are similar to those underlying Proposition 6.1.4. In the study of cyclic composition trajectories, Remark 5.4.D plays the role formerly played by Remark 5.4.B in the study of steady states.

Remark 6.1.E. (*The Possibility of an Approach to the Boundary of* $\bar{\mathbb{P}}^N$ *from the Interior of* $\bar{\mathbb{P}}^N$). Consider a mass action system for which the underlying reaction network is weakly reversible and has a deficiency of zero. The Deficiency Zero Theorem ensures that there is precisely one steady state in each positive stoichiometric compatibility class; that steady state is asymptotically stable; and there are no nontrivial cyclic composition trajectories in $\mathbb{P}^N$. This suggests that a trajectory which begins at a positive composition, say $\mathbf{c}^0$, will ultimately evolve toward the (unique) steady state in the positive stoichiometric compatibility class containing the initial composition $\mathbf{c}^0$. As it is stated, however, the Deficiency Zero Theorem does not quite ensure that this will be the case.

It is conceivable that there might, for example, exist a (*nonpositive*) steady state on the boundary of $\bar{\mathbb{P}}^N$ which lies in the stoichiometric compatibility class containing $\mathbf{c}^0$ and that the trajectory beginning at $\mathbf{c}^0$ might evolve toward this steady state as a limit with increasing time. The Deficiency Zero Theorem does *not* say that there is only one steady state that is stoichiometrically compatible with $\mathbf{c}^0$; rather, it ensures that there is precisely one *positive* steady state that is stoichiometrically compatible with $\mathbf{c}^0$.

There is no question that one can construct examples of weakly reversible deficiency zero networks which, when taken with mass action kinetics, admit two or more steady states—one on the interior of $\bar{\mathbb{P}}^N$ and one or more on the boundary of $\bar{\mathbb{P}}^N$—such that all lie in the same stoichiometric compatibility class. It is not known, however, whether one can construct an example of this kind for which a trajectory beginning at a positive composition approaches (as a limit with increasing time) a steady state on the boundary of $\bar{\mathbb{P}}^N$.

We conjecture that no such examples exist. In fact, we conjecture that, for *any* weakly reversible network (not necessarily deficiency zero) taken with mass action kinetics, the corresponding differential equations have the property that no composition trajectory beginning with all species concentrations positive evolves in increasing time toward a limit in which one or more species concentrations are zero. (It is easy to construct counterexamples if the kinetics is not required to be mass action.)

Even in the absence of a proof of this conjecture, we can still make a simple but useful observation: *If, for a reaction system, there exist a steady state on the boundary of* $\bar{\mathbb{P}}^N$, *it is not necessarily true that this steady state is stoichiometrically compatible with any* positive *composition.* (In other words, the stoichiometric compatibility class containing the steady state might not intersect $\mathbb{P}^N$.) If not, it follows from the discussion in Section 5.2 that the steady state cannot be approached by any trajectory originating in $\mathbb{P}^N$; such an approach is precluded *on stoichiometric grounds* no matter what the kinetics might be. In fact, there exists a wide variety of reaction systems for which no steady state on the boundary of $\bar{\mathbb{P}}^N$ is stoichiometrically compatible with a positive composition.

Consider, for example, the very simple network (6.14).

$$A_1 + A_2 \rightleftarrows A_3. \tag{6.14}$$

The stoichiometric subspace, S, for the network is just the line in $\mathbb{R}^3$ that passes through the origin and contains the reaction vectors $[-1, -1, 1]$ and $[1, 1, -1]$; that is, the stoichiometric subspace consists of all vectors in $\mathbb{R}^3$ of the form $[\alpha, \alpha, -\alpha]$, where α is any number. It is apparent that, regardless of the kinetics, the composition $\mathbf{c}^* = [1, 0, 0]$ is a steady state. The parallel of S containing $\mathbf{c}^*$ (i.e. $\mathbf{c}^* + S$) is the set of all vectors in $\mathbb{R}^3$ of the form

$$[1, 0, 0] + [\alpha, \alpha, -\alpha] = [1 + \alpha, \alpha, -\alpha],$$

where α is any number. It is easy to see that this set does not intersect the interior of $\bar{\mathbb{P}}^3$. In fact, $\mathbf{c}^* + S$ intersects $\bar{\mathbb{P}}^3$ in precisely one point, $\mathbf{c}^*$. (The line $\mathbf{c}^* + S$ just "grazes" the non-negative orthant at the boundary point $\mathbf{c}^*$.) Thus, the stoichiometric compatibility class containing $\mathbf{c}^*$ consists only of the composition $\mathbf{c}^*$, and there is certainly no positive composition (i.e. a composition in $\mathbb{P}^3$) that is stoichiometrically compatible with $\mathbf{c}^*$. In fact, as far as steady states on the boundary of $\bar{\mathbb{P}}^3$ are concerned, there is nothing special about the steady state $[1, 0, 0]$. It is easy to confirm that, regardless of the kinetics, all points in $\bar{\mathbb{P}}^3$ along the c_1-axis and along the c_2-axis are steady states, and none of these is stoichiometrically compatible with a composition in the interior of $\bar{\mathbb{P}}^3$.

The example we have just considered is a simple one. Even for more intricate networks (not necessarily of deficiency zero) it often happens that approach to a steady state on the boundary of $\bar{\mathbb{P}}^N$ from the interior of $\bar{\mathbb{P}}^N$ can be precluded on stoichiometric grounds alone. It should be kept in mind that Propositions 5.3.1, 6.1.2 and 6.1.4 give a good picture of the nature of the support of a steady state on the boundary of $\bar{\mathbb{P}}^N$. This information is helpful when taken in conjunction with the following observation: *Consider a reaction network with stoichiometric subspace S, and suppose that* $\mathbf{c}^*$ *is a point on the boundary of* $\bar{\mathbb{P}}^N$. *Then the stoichiometric compatibility class containing* $\mathbf{c}^*$ *fails to intersect the interior of* $\bar{\mathbb{P}}^N$ *if and only if there exists a nonzero vector in* $\bar{\mathbb{P}}^N$ *which is orthogonal to* S *and has support disjoint from* supp $\mathbf{c}^*$. (By the support of a vector $\mathbf{M}$ in $\bar{\mathbb{P}}^N$ we mean, as before, the set of species for which the corresponding components of $\mathbf{M}$ are nonzero; that is supp $\mathbf{M} = \{A_L : M_L > 0\}$.) Proof of the "if" part of this statement—the part of real interest here—is easy.

Returning to the example above, we note that the support of the steady state $\mathbf{c}^* = [1, 0, 0]$ is the set $\{A_1\}$. The vector $\mathbf{M} = [0, 1, 1]$ is orthogonal to the stoichiometric subspace for network (6.14) and has support $\{A_2, A_3\}$, which is disjoint from supp $\mathbf{c}^*$. Thus, as we argued above, the stoichiometric compatibility class containing $\mathbf{c}^*$ does not intersect the interior of $\bar{\mathbb{P}}^3$.

6.2. *The Deficiency One Theorem*

We are now in a position to state the second of our two major theorems. To some extent, the Deficiency One Theorem generalizes information given by the Deficiency Zero Theorem, part (iii). Unlike part (iii) of the Deficiency Zero Theorem, the Deficiency One Theorem gives no *dynamical* information: it addresses only issues connected with the uniqueness (and existence) of positive steady states. On the other hand, the Deficiency One Theorem gives information for a much broader class of networks. Moreover, it paves the way for a still broader theory that is described in a companion article (Feinberg, 1988).

In order to clarify the sense in which the Deficiency One Theorem generalizes information given by the Deficiency Zero Theorem, we shall find it useful to characterize deficiency zero networks in a different (and seemingly awkward) way. Recall from Section 2.6 that we can calculate not only the deficiency of a reaction network as a whole but also the deficiency of each of its linkage classes. Recall also that the deficiency of the entire network need not be the same as the sum of the deficiencies computed for the linkage classes separately (Remark 2.6.A). *The deficiency zero networks are precisely those that satisfy both of the following conditions: First, the deficiency of each linkage class is zero; and, second, the deficiency of the entire network is equal to the sum of the deficiencies of the individual linkage classes.*

Thus, some of the information given by part (iii) of the Deficiency Zero Theorem can be phrased differently: *Consider a mass action system for which the underlying reaction network is weakly reversible and has ℓ linkage classes. Moreover, suppose that the deficiency of the entire network and the deficiencies of the individual linkage classes satisfy the following conditions:*

(i) $\delta_\theta = 0, \ \theta = 1, 2, \ldots, \ell$

(ii) $\sum_{\theta=1}^{\ell} \delta_\theta = \delta.$

Then, no matter what (positive) values the rate constants take, the corresponding differential equations admit precisely one steady state in each positive stoichiometric compatibility class.

In part, the Deficiency One Theorem asserts that this statement remains true even when condition (i) is replaced by the far weaker requirement that the deficiencies of the individual linkage classes be no greater than *one*! (Hence the name attached to the theorem.)

In fact, the theorem does more.

For networks of deficiency zero that are *not* weakly reversible we know from the Deficiency Zero Theorem, part (i), that there can be no positive steady states at all; and so, for such networks, it is pointless to ask whether there can be multiple steady states within a positive stoichiometric compatibility class. Networks of nonzero deficiency present a very different situation. For them, weak reversibility is not a precondition for the existence of a positive steady state. Thus, for networks of nonzero deficiency, the issue of multiple positive steady states becomes a serious one even in the absence of weak reversibility.

With respect to the preclusion of multiple positive steady states, the Deficiency One Theorem not only relaxes the deficiency requirements given in the statement above, *it also replaces the weak reversibility condition by the far milder condition that each linkage class contain no more than one terminal strong linkage class.* (Recall that weakly reversible networks are merely very special examples of networks satisfying this milder condition on reaction arrow structure.)

Although the following statement of the Deficiency One Theorem substantially broadens the statement given in (Feinberg, 1980), it is still not the most general version we can give. Later on we shall indicate how the hypothesis can be weakened even further. Proof of the theorem will be found in (Feinberg, 1986).

Theorem 6.2.1. (*The Deficiency One Theorem*): *Consider a mass action system for which the underlying reaction network has ℓ linkage classes, each containing just one terminal strong linkage class. Suppose that the deficiency of the network and the deficiencies of the* *individual linkage classes satisfy the following conditions:*

(i) $\delta_\theta \leqslant 1, \quad \theta = 1, 2, \ldots, \ell$

(ii) $\sum_{\theta=1}^{\ell} \delta_\theta = \delta.$

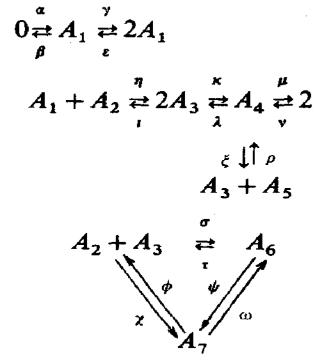
Then, no matter what (positive) values the rate constants take, the corresponding differential equations can admit no more than one steady state within a positive stoichiometric compatibility class. If the network is weakly reversible, the differential equations admit precisely one steady state in each positive stoichiometric compatibility class.

For networks having just one linkage class condition (ii) is satisfied trivially. Thus, we have an immediate corollary.

Corollary 6.2.2. *A mass action system for which the underlying reaction network has just one linkage class can admit multiple steady states within a positive stoichiometric compatibility class only if the deficiency of the network or the number of its terminal strong linkage classes exceeds one.*

Some examples will help demonstrate how Deficiency One Theorem can be used.

Consider network (6.15) taken with mass action kinetics. The rate constants are indicated by Greek letters alongside the corresponding reaction arrows. The differential equations for the resulting mass action system are displayed in (6.16).



(6.15)

$$\begin{aligned}
\dot{c}_1 &= \alpha + (\gamma - \beta)c_1 - \varepsilon c_1^2 - \eta c_1 c_2 + \iota c_3^2 \\
\dot{c}_2 &= -\eta c_1 c_2 + \iota c_3^2 + \tau c_6 + \phi c_7 - (\chi + \sigma) c_2 c_3 \\
\dot{c}_3 &= 2\eta c_1 c_2 - 2(\kappa + \iota) c_3^2 + (2\lambda + \xi) c_4 - \rho c_3 c_5 \\
\dot{c}_4 &= \kappa c_3^2 + \rho c_3 c_5 + \nu c_5^2 - (\lambda + \mu + \xi) c_4 \qquad (6.16) \\
\dot{c}_5 &= (2\mu + \xi) c_4 - 2\nu c_5^2 - \rho c_3 c_5 \\
\dot{c}_6 &= \sigma c_2 c_3 + \omega c_7 - (\tau + \psi) c_6 \\
\dot{c}_7 &= \chi c_2 c_3 + \psi c_6 - (\phi + \omega) c_7 .
\end{aligned}$$

We now ask two questions: Does the system (6.16) admit a *positive* steady state *regardless* of values of the rate constants? Can there exist values of the rate constants such that the system (6.16) admits *multiple* positive steady states (in a stoichiometric compatibility class)?

Studied on an *ad hoc* basis, these are far from easy questions. Each requires examination of a system of eight polynomial algebraic equations in eight unknowns (species concentrations), and in those equations there are eighteen unspecified parameters (rate constants).

It happens that the Deficiency One Theorem provides answers very quickly: the deficiency of the first linkage class, $\{0, A_1, 2A_1\}$, is one ($n_1 = 3$, $s_1 = 1$; $\delta_1 = 3 - 1 - 1 = 1$). The deficiency of the second linkage class,

$$\{A_1 + A_2, 2A_3, A_4, A_3 + A_5, 2A_5\},$$

is also one ($n_2 = 5, s_2 = 3; \delta_2 = 5 - 1 - 3 = 1$). And the deficiency of the third linkage class, $\{A_2 + A_3, A_6, A_7\}$, is zero ($n_3 = 3$, $s_3 = 2$; $\delta_3 = 3 - 1 - 2 = 0$). Thus, condition (i) of the Deficiency One Theorem is satisfied. Moreover, the deficiency of the entire network is two ($n = 11$, $\ell = 3$, $s = 6$; $\delta = 11 - 3 - 6 = 2$, and so condition (ii) is also satisfied ($\delta_1 + \delta_2 + \delta_3 = 2 = \delta$). The network is weakly reversible (in fact, reversible). Therefore we can assert that, *no matter what (positive) values the rate constants take, the system* (6.16) *admits precisely one steady state in each positive stoichiometric compatibility class.* The answers to the two questions posed above are *yes* and *no*.

The example we have just considered demonstrates that the Deficiency One Theorem can actually give information for networks of deficiency two or more. On the other hand, we shall see that there are deficiency one networks for which the theorem gives no information. It should be kept in mind that the name of the theorem refers not to the deficiency of the entire network but rather to the deficiencies of the individual linkage classes.

It should also be kept in mind that the hypothesis of the theorem requires that a network under consideration satisfy *three* conditions: Not only must conditions (i) and (ii) be satisfied but also the condition that each linkage class contain just one terminal strong linkage class. By means of examples we can show that the theorem—in particular, the statement regarding *uniqueness* of positive steady states—becomes false if any of the three conditions is omitted from the hypothesis.

We shall first demonstrate that we cannot drop the requirement that each linkage class contain no more than one terminal strong linkage class. For this purpose network (6.17) provides the simplest (and in some ways the most pathological) example. With rate constants as indicated

$$2A_1 \xleftarrow{\alpha} A_1 + A_2 \xrightarrow{\beta} 2A_2 \qquad (6.17)$$

alongside the reaction arrows, the corresponding mass action differential equations are those shown in (6.18). It is easy to see that, when the rate constants are unequal, there are no positive steady states. On the other hand, when the rate constants are equal, *every composition is a steady state.*

$$\begin{aligned} \dot{c}_1 &= (\alpha-\beta)c_1c_2 \\ \dot{c}_2 &= (\beta-\alpha)c_1c_2. \end{aligned} \tag{6.18}$$

In this case, *there are an infinite number of steady states in each positive stoichiometric compatibility class.* Since there is only one linkage class in network (6.17), condition (ii) of the Deficiency One Theorem is satisfied trivially. The deficiency of the network (and therefore of the sole linkage class) is *one* ($n = 3$, $\ell = 1$, $s = 1$); thus, condition (i) is satisfied as well. Note, however, that there are *two* terminal strong linkage classes, $\{2A_1\}$ and $\{2A_2\}$, residing in a single linkage class. This example makes clear that we cannot expect the conclusion of the Deficiency One Theorem to hold in a general way if we drop the requirement that each linkage class contain no more than one terminal strong linkage class.

Remark 6.2.A. Recall that we denote by t the number of terminal strong linkage classes in a network and by ℓ the number of linkage classes. For networks having the property that $t > \ell$, there are good reasons to expect that there should be more than one positive steady state in a stoichiometric compatibility class if, in that stoichiometric compatibility class, there are any positive steady states at all. These reasons are discussed in Appendix IV. (See also the discussion at the end of Remark 5.2.C.)

With regard to the uniqueness of positive steady states, it is reasonable to conjecture that condition (i) might be superfluous to the conclusions given by the Deficiency One Theorem. Such a conjecture would be *false*: In (Horn and Jackson, 1972) it was shown that there exist rate constants for network (6.19) such that the corresponding mass action differential equations

$$\begin{tikzcd} 3A_1 \arrow[r] & A_1+2A_2 \arrow[d] \\ 2A_1+A_2 \arrow[u] & 3A_2 \arrow[l] \end{tikzcd} \tag{6.19}$$

admit *three* steady states in each positive stoichiometric compatibility class. Note that the network is weakly reversible (so that $t = \ell$) and, moreover, there is only one linkage class so that condition (ii) is satisfied trivially. Recall, however, that at the end of Section 2.5 we calculated the deficiency of network (6.19) to be *two*; thus, condition (i) of the Deficiency One Theorem is not satisfied. The example demonstrates that, at least with respect to the uniqueness of positive steady states, condition (i) cannot be dropped from the hypothesis of the theorem.

We have now demonstrated that, as far as the uniqueness of positive steady states is concerned, we cannot drop condition (i) or the $t = \ell$ condition from the hypothesis of the Deficiency One Theorem. It remains to be shown that we cannot drop condition (ii) either. For this purpose we return to the Edelstein system (Section 4.3). Once again we display the network along with the corresponding system of mass action differential equations:

$$\begin{gathered} A_1 \underset{\beta}{\overset{\alpha}{\rightleftarrows}} 2A_1 \\ A_1 + A_2 \underset{\varepsilon}{\overset{\gamma}{\rightleftarrows}} A_3 \underset{\eta}{\overset{\theta}{\rightleftarrows}} A_2 \end{gathered} \tag{6.20}$$

$$\begin{aligned} \dot{c}_1 &= \alpha c_1 - \beta c_1^2 - \gamma c_1 c_2 + \varepsilon c_3 \\ \dot{c}_2 &= -\gamma c_1 c_2 + (\varepsilon+\theta)c_3 - \eta c_2 \\ \dot{c}_3 &= \gamma c_1 c_2 + \eta c_2 - (\varepsilon+\theta)c_3. \end{aligned} \tag{6.21}$$

It was shown in (Edelstein, 1970) that, for certain values of the rate constants, there exist positive stoichiometric compatibility classes containing *three* steady states. [A sketch of the locus of steady states is given in (Feinberg, 1980).] The network is reversible, and so each linkage class contains just one terminal strong linkage class; in fact, the linkage classes and terminal strong linkage classes coincide. Moreover, it is easy to calculate that the deficiency of each linkage class is *zero*, so condition (i) is satisfied. On the other hand, the deficiency of the entire network is *one* ($n = 5$, $\ell = 2$, $s = 2$; $\delta = 5-2-2 = 1$). Thus, *condition (ii) is not* satisfied. The Edelstein example therefore demonstrates that, with respect to the uniqueness of positive steady states, condition (ii) cannot be dropped from the hypothesis of the Deficiency One Theorem.

Remark 6.2.B. In our discussion of the Deficiency Zero Theorem we indicated how, by changing a single stoichiometric coefficient in the Edelstein network, we could obtain a mass action system which, unlike the Edelstein system, cannot give rise to multiple positive steady states no matter what values the rate constants take. It is interesting to study a different perturbation of the Edelstein network, one which leaves all the complexes intact but which involves more reactions. Consider network (6.22). We shall suppose the kinetics to be mass action with rate constants as indicated alongside

$$\begin{tikzcd} & A_1 \arrow[r, shift left, "\alpha"] \arrow[d, shift left, "\sigma"] & 2A_1 \arrow[l, shift left, "\beta"] \\ A_1 + A_2 \arrow[r, shift left, "\gamma"] & A_3 \arrow[l, shift left, "\varepsilon"] \arrow[r, shift left, "\theta"] \arrow[u, shift left, "\tau"] & A_2 \arrow[l, shift left, "\eta"] \end{tikzcd} \tag{6.22}$$

the corresponding reactions arrows. The corresponding differential equations are displayed in (6.23). We shall ask whether—as was the case with the Edelstein system—there can exist values of the rate constants such that

$$\begin{aligned} \dot{c}_1 &= (\alpha-\sigma)c_1 - \beta c_1^2 - \gamma c_1 c_2 + (\varepsilon+\tau)c_3 \\ \dot{c}_2 &= -\gamma c_1 c_2 + (\varepsilon+\theta)c_3 - \eta c_2 \\ \dot{c}_3 &= \gamma c_1 c_2 + \eta c_2 - (\varepsilon+\theta+\tau)c_3 + \sigma c_1 \end{aligned} \tag{6.23}$$

(6.23) admits multiple positive steady states. Corollary 6.2.2 tells us immediately that the answer is *no*, even when the rate constants for the two added reactions are arbitrarily small: The deficiency of the (reversible) network (6.22), like that of network (6.20), is *one* ($n = 5$,

$\ell = 1$, $s = 3$; $\delta = 5-1-3 = 1$), *but now there is just one linkage class.* [In this case the dimension of the stoichiometric subspace is three, so it coincides with $\mathbb{R}^3$. There is only one positive stoichiometric compatibility class, the entire positive orthant of $\mathbb{R}^3$. The Deficiency One Theorem tells us that, no matter what positive values the rate constants take, the system (6.23) admits precisely one steady state in $\mathbb{P}^3$.]

We should also mention that it is possible to construct rate constants for network (6.22) such that the corresponding system of mass action differential equations admits a cyclic composition trajectory in $\mathbb{P}^3$ and, moreover, has the property that the sole positive steady state is unstable. This example demonstrates that we cannot expect all weakly reversible networks satisfying the conditions of the Deficiency One Theorem to have the *dynamical* properties guaranteed by part (iii) of the Deficiency Zero Theorem.

It should be remembered that the Deficiency One Theorem gives information not only about the uniqueness of positive steady states but also about their *existence.* The theorem asserts that, for any mass action system such that the underlying reaction network is *weakly reversible* and satisfies conditions (i) and (ii), the corresponding differential equations actually admit a steady state in each positive stoichiometric compatibility class *no matter what (positive) values the rate constants take.* This is far from easy to prove. (Recall the discussion in Remark 5.3.B.)

It is easy to construct examples of networks which are not weakly reversible (but which otherwise obey all the conditions in the Deficiency One Theorem) such that the corresponding mass action differential equations admit no positive steady states regardless of what values the rate constants take. (Any deficiency zero network that is not weakly reversible will suffice. There are other examples as well.)

In fact, there are examples of networks which are not weakly reversible (but which otherwise obey the conditions of the Deficiency One Theorem) such that the corresponding mass action equations admit positive steady states for some values of the rate constants *but not for others.* Recall our discussion of network (5.13), which satisfies all three conditions in the Deficiency One Theorem. When the rate constants are those indicated in (5.13) there are no positive steady states for $k \leqslant 1$; on the other hand, for $k > 1$ there is precisely one steady state in each positive stoichiometric compatibility class.

Is is also interesting to note that there are examples of networks which are not weakly reversible and which have the property that, for *all* values of the rate constants, the corresponding mass action differential equations admit steady states in *some* positive stoichiometric compatibility classes *but not in others.* Consider network (6.24) taken with mass action kinetics.

$$\begin{aligned} &A_2 \xrightarrow{\alpha} A_1 \\ &A_1 + 2A_2 \xrightarrow{\beta} 3A_2. \end{aligned} \tag{6.24}$$

The corresponding differential equations are given in (6.25). It is easy to see that there are steady states along the entire c_1 axis in $\bar{\mathbb{P}}^2$.

$$\begin{aligned} \dot{c}_1 &= \alpha c_2 - \beta c_1 c_2^2 \\ \dot{c}_2 &= -\alpha c_2 + \beta c_1 c_2^2. \end{aligned} \tag{6.25}$$

On the other hand, the positive steady states lie along a hyperbola in $\mathbb{P}^2$ described by eq. (6.26). It is clear from the phase portrait given in Fig. 3 that there are steady states in the positive stoichiometric

$$c_1 c_2 = \frac{\alpha}{\beta} \tag{6.26}$$

compatibility classes far from the origin but not in those close to the origin. This qualitative picture persists no matter what positive values one chooses for α and β. Note that there are positive stoichiometric compatibility classes containing *two* steady states. Thus, network (6.24) cannot satisfy the three sufficient conditions for uniqueness given by the Deficiency One Theorem. In fact, the deficiency of the entire network is *one,* while the deficiencies of the linkage classes are each *zero*; therefore condition (ii) is not satisfied.

We shall close this section with two remarks, both related to properties of independent subnetworks (Section 5.4).

Remark 6.2.C. (*More on the Existence of Positive Steady States*). We wish to show how the Deficiency One Theorem, when taken together with simple ideas introduced in Section 5.4, can be used to give information even for networks that fail to satisfy the hypothesis of the theorem. By way of example we shall consider the following question: *Does the system* (6.21) *of mass action equations for the Edelstein network* (6.20) *admit a positive steady state no matter what (positive) values the rate constants take?* At first glance it would appear that

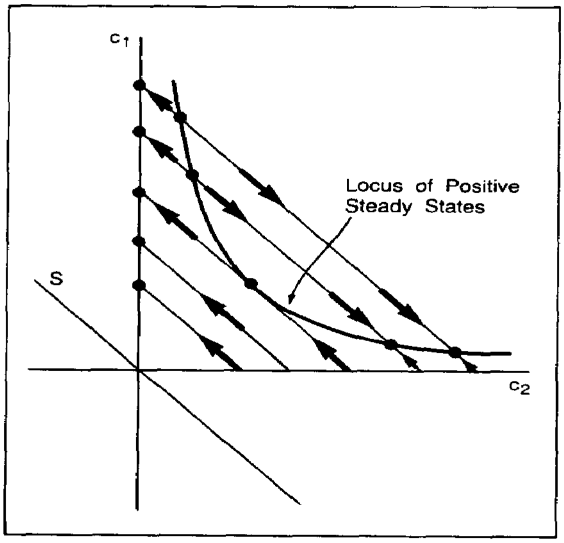


Fig. 3. A phase portrait for system (6.25)

the Deficiency One Theorem gives no information because, as we have seen, network (6.20) does not satisfy condition (ii).

But there is an observation we can make: It was established in Section 5.4 that the Edelstein network is an *independent* subnetwork of the larger network (6.22). Moreover, network (6.22) is reversible (and therefore weakly reversible) and satisfies both conditions (i) and (ii) of the Deficiency One Theorem. Thus, the theorem tells us that, *no matter what rate constants are assigned to network* (6.22), the corresponding system (6.23) of mass action equations admit a *positive* steady state. Since the Edelstein network is an *independent* subnetwork of (6.22), it follows from Remark 5.4.B that this steady state is *also* a (positive) steady state of the smaller system of equations (6.22). It should be clear, then, that the answer to the question posed above is *yes*.

This example demonstrates how we can sometimes answer questions about a network by "embedding" it as an independent subnetwork in a larger network for which we have information; that information is then "carried down" from the larger network to the smaller one.

Remark 6.2.D. (*A More General Version of the Deficiency One Theorem*). The role played by condition (ii) in the Deficiency One Theorem is, to some extent, explained by Remark 5.4.E and the discussion preceding Remark 5.4.B. Condition (ii) ensures that the stoichiometric subspace for the entire network is the *direct* sum of the stoichiometric subspaces generated by the ℓ linkage classes separately; each of the ℓ "pieces" comprising the network is an independent subnetwork. In this case, any steady state for the mass action system generated by the entire network must be a steady state for each of the mass action subsystems generated by the disjoint "pieces" of which the network is composed. Thus, when condition (ii) is satisfied, the set of steady states for the parent reaction system amounts to the intersection of the steady state sets for ℓ reaction subsystems corresponding to the individual linkage classes. In rough terms, then, proof of the theorem reduces to a study of steady state sets for the indicated reaction subsystems, each subnetwork having just one linkage class, just one terminal strong linkage class, and a deficiency no greater than one.

For networks that fail to satisfy the conditions of the Deficiency One Theorem it sometimes happens that we can still effect a decomposition of the parent network into *independent* subnetworks satisfying the following conditions:

(a) Each subnetwork contains just one linkage class and just one terminal strong linkage class.
(b) None of the subnetworks has a deficiency greater than one.

In this case the conclusions of the Deficiency One Theorem remain true: *If the network is given mass action kinetics then, regardless of the rate constant values, the corresponding differential equations admit at most one steady state in any positive stoichiometric compatibility class. Moreover, if the network is weakly reversible there exists precisely one steady state in each positive stoichiometric compatibility class.* (Recall that for a decomposition of the parent network into p subnetworks, the subnetworks are all independent if and only if

$$s = \sum_{\theta=1}^{p} s_\theta, \tag{6.27}$$

where s is the rank of the parent network and s_θ is the rank of the θth subnetwork.)

Network (6.28) provides a contrived but very simple example. There is just one linkage class, and it is easy to calculate that the deficiency of

$$0 \rightleftarrows A_1 \rightleftarrows 2A_1 \rightleftarrows A_1 + A_2 \rightleftarrows 2A_2 \tag{6.28}$$

the network is *two* ($n = 5$, $\ell = 1$, $s = 2$; $\delta = 5 - 1 - 2 = 2$). Clearly, condition (i) of the Deficiency One Theorem is *not* satisfied. On the other hand, network (6.28) can be partitioned into two subnetworks, $(6.28)_1$ and $(6.28)_2$.

$$0 \rightleftarrows A_1 \rightleftarrows 2A_1 \qquad (6.28)_1$$

$$2A_1 \rightleftarrows A_1 + A_2 \rightleftarrows 2A_2. \qquad (6.28)_2$$

In fact, these are *independent* subnetworks since the rank of each is easily calculated to be *one*, while the rank of the parent network is *two*; thus, (6.27) is satisfied. Moreover, the deficiency of each subnetwork is *one* so that condition (b) above is satisfied; and it is easy to see that condition (a) is satisfied as well. We can therefore conclude that, no matter what rate constants are assigned to network (6.28), the corresponding mass action equation admit precisely one positive steady state. [There is just one positive stoichiometric compatibility class for network (6.28)—the entire positive quadrant of $\mathbb{R}^2$.]

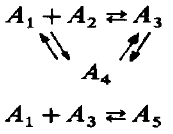
Although we could have written the Deficiency One Theorem to reflect the more general ideas contained in this remark, we chose to sacrifice a small amount of breadth in favor of a simpler theorem statement.

7. OUTLOOK

The Deficiency Zero and Deficiency One Theorems take us a long way toward a systematic understanding of connections between reaction network structure and the nature of solutions to the corresponding differential equations. Quite apart from the detailed information they give, these results tell us that a theory of large and intricate reaction networks is indeed possible, that the differential equations arising from reaction networks have sufficiently special structure as to permit proof of rather deep theorems about them.

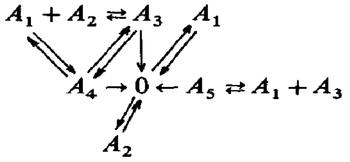
On the other hand, the theorems given here leave important practical questions unanswered.

Networks of high deficiency arise naturally in the study of *homogeneous* continuous flow stirred tank reactors, in particular when the "true" chemistry involves several bimolecular reactions. Consider for example a homogeneous CFSTR in which the "true" chemical reactions are those depicted in (7.1).



(7.1)

Species $A_1, \ldots, A_5$ are all in the effluent stream, and we shall suppose that only species A_1 and A_2 are carried in the feed. In the sense of Section 4.1, the network we would construct to model the reactor is that shown in (7.2).



(7.2)

The deficiency of network (7.2) is readily calculated to be *two* ($n = 8, \ell = 1, s = 5; \delta = 8 - 1 - 5 = 2$). It is easy to see that the Deficiency One Theorem gives no information about the capacity of the reactor to admit multiple positive steady states.

In view of their practical importance it is clear that complex homogeneous CFSTRs require understanding. It is also clear that, in studying them, we shall often find ourselves in a situation of the kind presented by our example: Because *every* species in the reactor is also in the effluent stream, a large number of pseudoreactions of the form $A_L \rightarrow 0$ must be adjoined to the true chemical reactions, and this will usually result in a network outside the class for which the Deficiency One Theorem gives information.

But it is also evident that networks that derive from the study of *homogeneous* CFSTRs have a *special* structure, characterized by the presence of a reaction of the form $A_L \rightarrow 0$ for *every* species appearing in the network. Thus, in the absence of a general theory of high deficiency networks, it makes sense to attempt development of *special* theory tailored specifically to those networks that arise in the study of homogeneous CFSTRs. Work has already been done along these lines, and we expect to make the results available in a series of articles devoted exclusively to problems associated with continuous flow stirred tank reactors.

It should also be understood that, even when we restrict our attention to mass action kinetics, networks with high deficiency are not the only ones for which the theorems given here may fail to yield information. Consider, for example, the class of networks of deficiency *one* having the property that each linkage class contains just one terminal strong linkage class. Within this class, the networks which fail to satisfy the hypothesis of the Deficiency One Theorem are precisely those for which each linkage class has a deficiency of *zero* (in which case condition (ii) is not satisfied).

Deficiency one networks of this kind arise naturally in the study of systems of the Edelstein type (Section 4.3) in which certain species concentrations are regarded to be time-invariant. More important from an engineering perspective is that *they often arise in the study of continuous flow stirred tank reactors involving heterogeneous catalysis* (Remark 4.2.A). In fact, network (4.6), which derived from our study of a heterogeneous CFSTR, is problematic: It has a deficiency of one and each linkage class has just one terminal strong linkage class, but the deficiency of each linkage class is *zero*. The Deficiency One Theorem therefore gives no information about the capacity of corresponding mass action equations to admit multiple steady states.

Thus, it is especially important that we have available theory tailored specifically to deficiency *one* networks, even those which fail to satisfy condition (ii) of the Deficiency One Theorem. This is the subject of a companion article (Feinberg, 1988).

Acknowledgments—The work described here was supported by a grant from the National Science Foundation. The author is grateful for a visit to the University of Minnesota's Institute for Mathematics and its Applications and also for stimulating discussions with his students, V. Dabholkar, D. Rumschitzki, P. Schlosser and M. Yue.

NOTATION

$A_1, A_2, \ldots, A_N$	chemical species
c_L	molar concentration of species A_L
$\mathbf{c}$	composition vector
$\mathbf{e}_1, \mathbf{e}_2, \ldots, \mathbf{e}_N$	standard basis for $\mathbb{R}^N$
$k_{i \rightarrow j}$	rate constant for reaction $i \rightarrow j$
$\mathcal{K}_{i \rightarrow j}(\cdot)$	rate function for reaction $i \rightarrow j$
K	the kinetic subspace (Appendix IV)
ℓ	number of linkage classes in a network
n	number of complexes in a network
n_θ	number of complexes in the θth linkage class (or in the θth subnetwork in Section 5.4)
N	number of species in a network
$\mathbb{P}$	positive real numbers
$\mathbb{P}^N$	positive orthant of $\mathbb{R}^N$
$\bar{\mathbb{P}}^N$	non-negative orthant of $\mathbb{R}^N$
$\mathbb{R}^N$	standard vector space of N-tuples
$\mathcal{R}$	set of reactions in a network
$\mathcal{R}_{i \rightarrow}$	set of reactions in a network having $\mathbf{y}_i$ as the reactant complex
$\mathcal{R}_{\rightarrow i}$	set of reactions in a network having $\mathbf{y}_i$ as the product complex
$\mathcal{R}_\theta$	set of reactions in the θth subnetwork
s	the rank of a reaction network (or, equivalently, the dimension of the stoichiometric subspace)
s_θ	the rank of the θth linkage class (or of the θth subnetwork in Section 5.4)
S	the stoichiometric subspace for a network
S_θ	the stoichiometric subspace for the θth subnetwork
supp $\mathbf{c}$	support of a composition vector, defined in (3.3)

supp $\mathbf{y}_i$	support of complex $\mathbf{y}_i$, defined in (3.4)
ℓ	the number of terminal strong linkage classes in a network
$\mathbf{y}_i$	the ith complex vector in a reaction network
y_{iL}	the stoichiometric coefficient of species A_L complex $\mathbf{y}_i$

Greek letters

Γ	the support of a cyclic composition trajectory (Section 5.3)
δ	the deficiency of a network
δ_θ	the deficiency of the θth linkage class (or of the θth subnetwork in Section 5.4)

REFERENCES

Beretta, E., 1981, Stability problems of chemical networks, in *Nonlinear Differential Equations: Invariance, Stability and Bifurcations* (Edited by P. de Mottoni and L. Salvadori), pp. 11–27. Academic Press, New York.

Clarke, B. L., 1980, Stability of complex reaction networks. *Adv. Chem. Phys.* **42**, 1–213.

Edelstein, B., 1970, A biochemical model with multiple steady states and hysteresis. *J. Theor. Biol.* **29**, 57–62.

Feinberg, M., 1972, Complex balancing in general kinetic systems. *Arch. Rational Mech. Anal.* **49**, 187–194.

Feinberg, M., 1977, Mathematical aspects of mass action kinetics. *Chemical Reactor Theory: A Review* (Edited by L. Lapidus and N. Amundson), pp. 1–78. Prentice-Hall, Englewood Cliffs, N.J.

Feinberg, M., 1979, Lectures on Chemical Reaction Networks, unpublished written versions of lectures given at the Mathematics Research Center, University of Wisconsin.

Feinberg, M., 1980, Chemical oscillations, multiple equilibria and reaction network structure, in *Dynamics and Modelling of Reactive Systems* (Edited by W. Stewart, W. H. Ray and C. Conley), pp. 59–130. Academic Press, New York.

Feinberg, M., 1986, The existence and uniqueness of steady states for some chemical reaction networks of positive deficiency, to appear in *Arch. Rational Mech. Anal.*

Feinberg, M., 1988, Chemical reaction network structure and the stability of complex isothermal reactors—II. Multiple steady states for networks of deficiency one. *Chem. Engng Sci.* (in press).

Feinberg, M. and Horn, F. J. M., 1974, Dynamics of open chemical systems and the algebraic structure of the underlying reaction network. *Chem. Engng Sci.* **29**, 775–787.

Feinberg, M. and Horn, F. J. M., 1977, Chemical mechanism structure and the coincidence of the stoichiometric and kinetic subspaces. *Arch. Rational Mech. Anal.* **66**, 83–97.

Fife, P., 1979, Mathematical aspects of reacting and diffusing systems. Lecture Notes in Biomathematics No. 28, Springer, Berlin, pp. 24–37.

Glansdorff, P. and Prigogine, I., 1971, *The Thermodynamic Theory of Structure, Stability and Fluctuations*, pp. 232–242. Wiley-Interscience, New York.

Horn, F. J. M., 1972, Necessary and sufficient conditions for complex balancing in chemical kinetics. *Arch. Rational Mech. Anal.* **49**, 172–186.

Horn, F. J. M., 1973, On a connexion between stability and graphs in chemical kinetics, I. Stability and the reaction diagram, II. Stability and the complex graph. *Proc. R. Soc.* **A334**, 299–330.

Horn, F. J. M. and Jackson, R., 1972, General mass action kinetics. *Arch. Rational Mech. Anal.* **47**, 81–116.

Lang, S., 1986, *Introduction to Linear Algebra*, second edition. Springer, Berlin.

Lyberatos, G., Kuszta, B. and Bailey, J. E., 1984, Steady-state multiplicity and bifurcation analysis via the Newton polyhedron approach. *Chem. Engng Sci.* **39**, 947–960.

APPENDIX I. PROOF THAT $\dot{c}_L \geqslant 0$ WHEN $c_L = 0$

Suppose that $\mathbf{c} \in \bar{\mathbb{P}}^N$ is a composition such that $c_L = 0$—i.e. such that species A_L is not contained in supp **c**. We wish to show that, at composition **c**, the value of $\dot{c}_L$ given by eq. (3.6) is non-negative. The Lth component of the vector equation (3.6) is

$$\dot{c}_L = \sum_{\mathscr{R}} \mathscr{K}_{i \to j}(\mathbf{c})\,(y_{jL} - y_{iL}). \tag{I.1}$$

From (K.2) in Section 3.1 it follows that $\mathscr{K}_{i \to j}(\mathbf{c}) = 0$ when supp $\mathbf{y}_i$ is not contained is supp **c**—*in particular when* $y_{iL} > 0$. (When $y_{iL} > 0$, supp $\mathbf{y}_i$ contains the species A_L, which by supposition is not contained in supp **c**. In this case supp $\mathbf{y}_i$ is not contained in supp **c**.) Therefore, (I.1) reduces to

$$\dot{c}_L = \sum_{\mathscr{R}} \mathscr{K}_{i \to j}(\mathbf{c})\, y_{jL}. \tag{I.2}$$

Each y_{jL} in (I.2) is non-negative (Section 2.1) as is each $\mathscr{K}_{i \to j}(\mathbf{c})$ (Section 3.1). Thus (I.2) implies that $\dot{c}_L$ is non-negative.

Remark. Suppose that **c** is a composition such that $c_L = 0$. From (I.2) and condition (K.2) in Section 3.1 it follows that $\dot{c}_L$ is *positive* if and only if the network under consideration contains a reaction $\mathbf{y}_i \to \mathbf{y}_j$ such that supp $\mathbf{y}_i \subset$ supp **c** and $A_L \in$ supp $\mathbf{y}_j$.

APPENDIX II. PROOFS OF PROPOSITIONS 5.3.1 AND 5.3.2

We begin with a useful lemma.

Lemma II.1. *Suppose that* $\Omega \subset \{A_1, A_2, \ldots, A_N\}$ *is a fixed subset of the species in a reaction network, and suppose also that there exists for the network a set of non-negative numbers* $\{\alpha_{p \to q}\}_{p \to q \in \mathscr{R}}$ *satisfying both of the following conditions:*

(i) $\alpha_{p \to q} > 0$ *if and only if* supp $\mathbf{y}_p \subset \Omega$

(ii) $\sum_{\mathscr{R}} \alpha_{p \to q}(\mathbf{y}_q - \mathbf{y}_p) = \mathbf{0}$.

If $\mathbf{y}_i \to \mathbf{y}_j$ *is a reaction in the network and* supp $\mathbf{y}_i$ *is contained in* Ω, *then* supp $\mathbf{y}_j$ *is also contained in* Ω.

Proof. Suppose that $\mathbf{y}_i \to \mathbf{y}_j$ is a reaction in the network with supp $\mathbf{y}_i \subset \Omega$. In this case the set

$$\mathscr{R}' := \{\mathbf{y}_p \to \mathbf{y}_q \in \mathscr{R} : \text{supp } \mathbf{y}_p \subset \Omega\}$$

is not empty. From (i) it follows that (ii) can be written

$$\sum_{\mathscr{R}'} \alpha_{p \to q}(\mathbf{y}_q - \mathbf{y}_p) = \mathbf{0}, \tag{II.1}$$

where each of the $\alpha_{p \to q}$ in (II.1) is *positive*.

We want to show that supp $\mathbf{y}_j$ is contained in Ω. Suppose not. Then supp $\mathbf{y}_j$ contains a species A_L that is not contained in Ω. This implies that $y_{jL} > 0$ and that $y_{pL} = 0$ for each $\mathbf{y}_p$ such that supp $\mathbf{y}_p \subset \Omega$. Thus, the Lth component of the vector eq. (II.1) reduces to

$$\sum_{\mathscr{R}'} \alpha_{p \to q}\, y_{qL} = 0. \tag{II.2}$$

Note that each term in the sum of the left of (II.2) is non-negative. In particular, the term $\alpha_{i \to j}\, y_{jL}$ is positive. Thus (II.2) cannot hold, and we have a contradiction.

Lemma II.2. *Suppose that* Ω *is a fixed subset of the species in a reaction network and that there exists for the network a set of non-negative numbers* $\{\alpha_{p \to q}\}_{p \to q \in \mathscr{R}}$ *satisfying conditions* (i) *and* (ii) *in Lemma* II.1. *Suppose also that* $\mathbf{y}_i$ *and* $\mathbf{y}_j$ *are complexes* *in the network such that there exists a directed reaction pathway leading from* $\mathbf{y}_i$ *to* $\mathbf{y}_j$. *If* supp $\mathbf{y}_i$ *is contained in* Ω, *then* supp $\mathbf{y}_j$ *is also contained in* Ω.

Proof. Suppose that supp $\mathbf{y}_i$ is contained in Ω. If $\mathbf{y}_i$ reacts directly to $\mathbf{y}_j$, Lemma II.1 implies that supp $\mathbf{y}_j$ is also contained in Ω. On the other hand if there exists in the network a chain of reactions leading from $\mathbf{y}_i$ to $\mathbf{y}_j$, say

$$\mathbf{y}_i \to \mathbf{y}_1 \to \mathbf{y}_2 \to \dots \to \mathbf{y}_m \to \mathbf{y}_j,$$

then Lemma II.1. can be applied sequentially along the chain to show that supp $\mathbf{y}_1 \subset \Omega$, supp $\mathbf{y}_2 \subset \Omega, \dots,$ supp $\mathbf{y}_j \subset \Omega$.

Remark II.A. If complexes $\mathbf{y}_i$ and $\mathbf{y}_j$ lie in the same strong linkage class, there exists in the network a directed reaction pathway leading from $\mathbf{y}_i$ to $\mathbf{y}_j$ *and* a directed reaction pathway leading from $\mathbf{y}_j$ to $\mathbf{y}_i$. Thus, under the conditions of Lemma II.2, the supports of *both* $\mathbf{y}_i$ and $\mathbf{y}_j$ are contained in Ω or else the support of *neither* is contained in Ω.

To prove Proposition 5.3.1 we consider a reaction network endowed with kinetics $\{\mathscr{K}_{p\to q}(\cdot)\}_{p\to q\in\mathscr{R}}$, and we suppose that this reaction system admits a steady state $\mathbf{c}^*$; that is,

$$\sum_{\mathscr{R}} \mathscr{K}_{p\to q}(\mathbf{c}^*)\,(\mathbf{y}_q - \mathbf{y}_p) = 0. \tag{II.3}$$

Note that $\mathscr{K}_{p\to q}(\mathbf{c}^*)$ is non-negative and is positive if and only if supp $\mathbf{y}_p$ is contained in supp $\mathbf{c}^*$. [Recall (K.2) in Section 3.1.] Thus, in Lemma II.2 we can identify Ω with supp $\mathbf{c}^*$ and each $\alpha_{p\to q}$ with $\mathscr{K}_{p\to q}(\mathbf{c}^*)$. Proposition 5.3.1 then follows from Lemma II.2 and Remark II.A.

To prove Proposition 5.3.2 we consider a reaction network endowed with kinetics $\{\mathscr{K}_{p\to q}(\cdot)\}_{p\to q\in\mathscr{R}}$, and we suppose that the corresponding differential eq. (3.6) admits a cyclic composition trajectory with support Γ. In particular we suppose that (3.6) admits a solution $\mathbf{c}(\cdot)$ (containing in its domain the time interval $[0, T]$) such that $\mathbf{c}(0) = \mathbf{c}(T)$ and such that supp $\mathbf{c}(t) = \Gamma$ for all $t \in [0, T]$. Integration of (3.6) over the time interval $[0, T]$ gives

$$\mathbf{0} = \sum_{\mathscr{R}} \left[\int_0^T \mathscr{K}_{p\to q}(\mathbf{c}(t))\,\mathrm{d}t\right](\mathbf{y}_q - \mathbf{y}_p). \tag{II.4}$$

Note that each of the integrals in (II.4) is non-negative; and, from (K.1) and (K.2) in Section 3.1,

$$\int_0^T \mathscr{K}_{p\to q}(\mathbf{c}(t))\,\mathrm{d}t > 0 \text{ if and only if supp } \mathbf{y}_p \subset \Gamma. \tag{II.5}$$

Thus, in Lemma II.2 we can take $\Omega = \Gamma$ and

$$\alpha_{p\to q} = \int_0^T \mathscr{K}_{p\to q}(\mathbf{c}(t))\,\mathrm{d}t, \quad \forall p\to q \in \mathscr{R}.$$

Proposition 5.3.2 then follows from Lemma II.2 and Remark II.4.

APPENDIX III. THE STOICHIOMETRIC CONE

The dynamical significance of the stoichiometric subspace resulted from our observation that, for each $\mathbf{c} \in \bar{\mathbb{P}}^N$, the corresponding value of $\dot{\mathbf{c}}$ given by (3.6) is a linear combination of the reaction vectors for the network under consideration. In particular, from (5.5) it followed that if composition $\mathbf{c}'$ follows composition $\mathbf{c}$ along a solution of (3.6), then $\mathbf{c}' - \mathbf{c}$ must also be a linear combination of the reaction vectors.

There are somewhat sharper observations we might have made. From the properties of a kinetics given in Section 3.1 it follows that, at a particular composition $\mathbf{c} \in \bar{\mathbb{P}}^N$, multipliers of the reaction vectors in (3.6) are in fact *non-negative* numbers with $\mathscr{K}_{i\to j}(\mathbf{c})$ *positive* precisely when supp $\mathbf{y}_i$ is contained in supp $\mathbf{c}$. Thus, at each composition $\mathbf{c}$, the corresponding value of $\dot{\mathbf{c}}$ given by (3.6) is a *special* kind of linear combination of the reaction vectors. Similarly, in (5.5) the integrals multiplying the reaction vectors are *non-negative* numbers, the integral corresponding to reaction $\mathbf{y}_i \to \mathbf{y}_j$ being *positive* if and only if, for some $\tau \in [0, t]$, supp $\mathbf{y}_i$ is contained in supp $\mathbf{c}(\tau)$. Again, the right side of (5.5) is a special kind of linear combination of the reaction vectors.

Recall that the stoichiometric subspace for a network is the set of *all* linear combinations of the reaction vectors. That is, $\gamma \in \mathbb{R}^N$ is a member of the stoichiometric subspace if and only if there exists a set of numbers, $\{\alpha_{i\to j}\}_{i\to j\in\mathscr{R}}$, such that

$$\gamma = \sum_{\mathscr{R}} \alpha_{i\to j}(\mathbf{y}_j - \mathbf{y}_i). \tag{III.1}$$

Here the $\alpha_{i\to j}$ can be positive, negative or zero.

By the *stoichiometric cone* for a network we shall mean the set of vectors in $\mathbb{R}^N$ defined as follows: $\gamma \in \mathbb{R}^N$ is a member of the stoichiometric cone if and only if there exists a set of *non-negative* numbers, $\{\alpha_{i\to j}\}_{i\to j\in\mathscr{R}}$ satisfying (III.1) and the additional condition that, for each index $m \in \{1, 2, \dots, n\}$, numbers in the set $\{\alpha_{i\to j}: i = m]$ are either *all* positive or *all* zero. (This last condition amounts to a requirement that the $\alpha_{i\to j}$ corresponding to reactions having a common reactant complex are all positive or else are all zero.) Clearly the stoichiometric cone for a network is contained in *and might be smaller than* the stoichiometric subspace for the network.

From equation (3.6), written for an arbitrary reaction system, it is apparent that, at each $\mathbf{c} \in \bar{\mathbb{P}}^N$, the corresponding value of $\dot{\mathbf{c}}$ is an element of the stoichiometric cone for the underlying reaction network. This sharpens our earlier observation that $\dot{\mathbf{c}}$ must invariably lie in the stoichiometric subspace. Similarly, if composition $\mathbf{c}'$ follows composition $\mathbf{c}$ along a solution to (3.6), it follows from (5.5) that the composition change $\mathbf{c}' - \mathbf{c}$ must also be a member of the stoichiometric cone. This sharpens our observation that $\mathbf{c}' - \mathbf{c}$ must lie in the stoichiometric subspace.

Although these sharpened observations are worth making in general, it turns out that they are often inconsequential. It happens that for a very large class of reaction networks (including all weakly reversible networks) the stoichiometric cone actually *coincides* with the stoichiometric subspace.

In fact, *the stoichiometric cone and the stoichiometric subspace coincide for any network having the property that the reaction vectors are positively dependent.* To prove the claim it is enough to show that, for a network with positively dependent reaction vectors, any vector in the stoichiometric subspace also lies in the stoichiometric cone. Suppose that γ is a member of the stoichiometric subspace. Then there exists a set of (not necessarily non-negative) numbers, $\{\alpha'_{i\to j}\}_{i\to j\in\mathscr{R}}$, such that

$$\gamma = \sum_{\mathscr{R}} \alpha'_{i\to j}(\mathbf{y}_j - \mathbf{y}_i). \tag{III.2}$$

If the reaction vectors are positively dependent there exists a set of *positive* numbers, $\{\beta_{i\to j}\}_{i\to j\in\mathscr{R}}$, such that

$$\mathbf{0} = \sum_{\mathscr{R}} \beta_{i\to j}(\mathbf{y}_j - \mathbf{y}_i). \tag{III.3}$$

After multiplying both sides of (III.3) by a suitably large positive number, we can add the result to (III.2) to obtain a representation of γ in the form

$$\gamma = \sum_{\mathscr{R}} \alpha_{i\to j}(\mathbf{y}_j - \mathbf{y}_i),$$

where each $\alpha_{i\to j}$ is *positive.* Thus γ is contained in the stoichiometric cone.

Our primary interest will be in reaction systems that have the capacity to admit a positive steady state. In Section 5.3 we argued that, for a reaction system to admit a positive steady state, it is necessary that the reaction vectors be positively dependent. Thus, for reaction systems in which we shall have most interest, there is no real distinction between the stoichiometric cone and the stoichiometric subspace.

APPENDIX IV. THE KINETIC SUBSPACE: WHY NETWORKS OF THE $\ell > \ell$ VARIETY ARE PROBLEMATICAL

In Appendix III we indicated how observations made in Section 5.2 could be sharpened. However we also indicated that, while the sharpened observations are worth making in general, they are of little consequence for any reaction system that has the capacity to admit a positive steady state.

In this appendix we shall discuss another, more subtle, way *in which the discussion given in Section 5.2 might have been* made more incisive. It will turn out that the sharpened observations we shall make here *are* of importance, but only for networks of the $\ell > \ell$ variety—that is, only for networks having the property that at least one each linkage class contains two or more terminal strong linkage classes.

Moreover, this appendix will help to explain why mass action models deriving from $\ell > \ell$ networks often carry a kind of degeneracy (related to structural instability) which, to some extent, makes them unsuited for the description of real chemical systems. In particular, such models will often give rise to phase portraits which are quite different from those generated by "nearby" mass action models deriving from $\ell = \ell$ networks. For example, certain dramatic phenomena exhibited by $\ell > \ell$ models can be perturbed away by making all reactions reversible, even when rate constants for the added reverse reactions are taken to be vanishingly small. Phenomena of this kind should not be taken too seriously, and it would be unwise to place much credence in models that generate them.

The following example will help give some sense of the kind of pathology that networks of the $\ell > \ell$ variety can exhibit.

Consider the mass action system displayed in (IV.1). The underlying network has two linkage classes ($\{A_1, A_2, A_3\}$, $\{A_2 + A_3, 2A_1\}$) and three terminal strong linkage classes ($\{A_2\}, \{A_3\}, \{2A_1\}$). Thus, we have $\ell > \ell$.

$$A_2 \xleftarrow{k} A_1 \xrightarrow{1} A_3$$
$$A_2 + A_3 \xrightarrow{1} 2A_1 \tag{IV.1}$$

It is not difficult to determine that the stoichiometric subspace is two-dimensional. The stoichiometric subspace and a typical stoichiometric compatibility class are depicted in Fig. 4.

The mass action differential equations corresponding to (IV.1) are given in (IV.2). It is easy to confirm that for $k \neq 1$ there are no positive steady states at all. On the other hand, when $k = 1$ positive steady states do exist and, in fact, each positive stoichiometric compatibility class contains an *infinite* number of steady states. (See Fig. 4.)

$$\begin{aligned} \dot{c}_1 &= -(k+1)c_1 + 2c_2c_3 \\ \dot{c}_2 &= kc_1 - c_2c_3 \\ \dot{c}_3 &= c_1 - c_2c_3. \end{aligned} \tag{IV.2}$$

In other words, the very special value $k = 1$ leads not only to the existence of positive steady states but also to an "explosion" of steady states within each positive stoichiometric compatibility class. If at least one of the reactions $A_2 \rightarrow A_1$ or $A_3 \rightarrow A_1$ is added to the network shown in (IV.1), the resulting $\ell = \ell$ network does not give rise to this phenomenon. No matter what rate constants are assigned to the reactions, the corresponding mass action differential equations admit at most one steady state in each positive stoichiometric compatibility class.

We can begin to understand the degenerate behavior exhibited in the $k = 1$ case once we indicate how the discussion in Section 5.2 lends itself to sharpening. Our attention hereafter will be restricted to mass action systems, and so our focus will be entirely on dynamics given by equation (3.8). Because (3.8) is merely a special version of (3.6), all the observations made in Section 5.2 apply in particular to systems governed by (3.8): For each $\mathbf{c} \in \bar{\mathbb{P}}^N$, the corresponding value of $\dot{\mathbf{c}}$ is a *linear combination of the reaction vectors and so* must lie in the stoichiometric subspace generated by them. Moreover, composition trajectories compatible with (3.8) are constrained to lie entirely in stoichiometric compatibility classes.

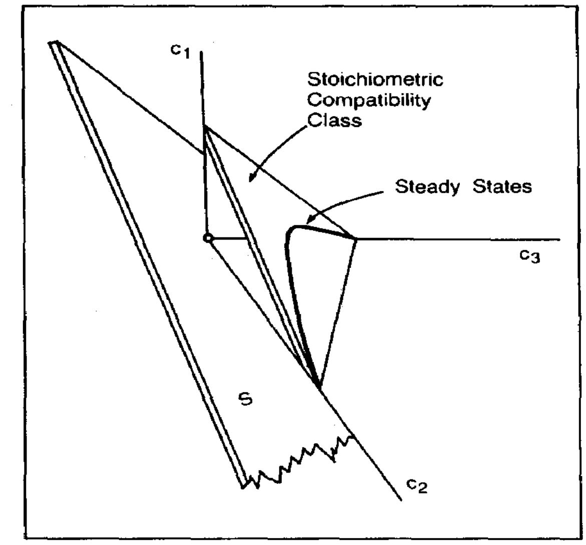


Fig. 4. The stoichiometric subspace and a stoichiometric compatibility class for the network shown in (IV.1). (The steady state locus is for $k = 1$.)

To see how these observations can be sharpened we shall need some additional notation. For a particular mass action system we let $\mathscr{R}_{i\rightarrow}$ denote the set of all reactions in the underlying networking having $\mathbf{y}_i$ as the reactant complex. That is,

$$\mathscr{R}_{i\rightarrow} := \{\mathbf{y}_m \rightarrow \mathbf{y}_j \in \mathscr{R} : m = i\}. \tag{IV.3}$$

It is easy to see that equation (3.8) can be rewritten in the following way:

$$\dot{\mathbf{c}} = \sum_{i=1}^{n} \left[\prod_{L=1}^{N} (c_L)^{y_{iL}} \right] \left[\sum_{\mathscr{R}_{i\rightarrow}} k_{i\rightarrow j} (\mathbf{y}_j - \mathbf{y}_i) \right]. \tag{IV.4}$$

(When a particular complex $\mathbf{y}_i$ appears in the network as a product but never as a reactant, the set $\mathscr{R}_{i\rightarrow}$ is empty. *In this case we shall understand the sum over* $\mathscr{R}_{i\rightarrow}$ *in* (IV.4) *to be the zero vector.*) Letting

$$\mathbf{d}_i := \sum_{\mathscr{R}_{i\rightarrow}} k_{i\rightarrow j} (\mathbf{y}_j - \mathbf{y}_i), \quad i = 1, 2, \ldots, n, \tag{IV.5}$$

we can rewrite (IV.4) in the form

$$\dot{\mathbf{c}} = \sum_{i=1}^{n} \left[\prod_{L=1}^{N} (c_L)^{y_{iL}} \right] \mathbf{d}_i. \tag{IV.6}$$

By the *kinetic subspace*, denoted K, for a mass action system we shall mean the linear subspace of $\mathbb{R}^N$ consisting of all linear combinations of the set $\{\mathbf{d}_1, \mathbf{d}_2, \ldots, \mathbf{d}_n\}$. When (3.8) is recast as (IV.6) it becomes apparent that, *for each* $\mathbf{c} \in \bar{\mathbb{P}}^N$, *the corresponding value of* $\dot{\mathbf{c}}$ *lies in the kinetic subspace.* Since each $\mathbf{d}_i$ is a linear combination of reaction vectors, it follows easily that *the kinetic subspace is contained in* (*and might be smaller than*) *the stoichiometric subspace generated by the underlying reaction network.*

At this point there is an important observation we need to make: *Although the stoichiometric subspace is completely determined by the reaction vectors for the underlying network, the nature of the kinetic subspace depends not only on the reaction vectors but also may be influenced by the particular* *values of the rate constants.* (Note that the rate constants enter the definition of the $\mathbf{d}_i$ vectors, which in turn generate the kinetic subspace.) Thus, *the kinetic and stoichiometric subspaces might coincide for certain values of the rate constants while, for other values of the rate constants, the kinetic subspace might in fact be smaller than the stoichiometric subspace.* In particular, *when the kinetic subspace is smaller than the stoichiometric subspace, its orientation in* $\mathbb{R}^N$ *will generally be influenced by rate constant values.*

Example: We can illustrate these ideas by returning to the mass action system displayed in (IV.1). The stoichiometric subspace is the two-dimensional linear subspace of $\mathbb{R}^N$ spanned by the reaction vectors

$$\{\mathbf{e}_2-\mathbf{e}_1,\ \mathbf{e}_3-\mathbf{e}_1,\ 2\mathbf{e}_1-(\mathbf{e}_2+\mathbf{e}_3)\}. \tag{IV.7}$$

On the other hand, the kinetic subspace is the linear subspace of $\mathbb{R}^N$ spanned by the set (IV.5). In the case of the mass action system (IV.1), members of (IV.5) corresponding to the complexes $\{A_1,\ A_2,\ A_3,\ A_2+A_3,\ 2A_1\}$ are, respectively,

$$\{k(\mathbf{e}_2-\mathbf{e}_1)+(\mathbf{e}_3-\mathbf{e}_1),\ \mathbf{0},\ \mathbf{0},\ 2\mathbf{e}_1-(\mathbf{e}_2+\mathbf{e}_3),\ \mathbf{0}\}. \tag{IV.8}$$

For $k \neq 1$ the span of the set (IV.8) is two-dimensional and coincides with the span of the set (IV.7). When $k = 1$, however, the span of the set (IV.8) is one-dimensional; it is a line in $\mathbb{R}^N$ containing the vector $2\mathbf{e}_1-(\mathbf{e}_2+\mathbf{e}_3)$. Thus, the mass action system (IV.1) has the property that for all $k \neq 1$ the kinetic and stoichiometric subspaces coincide. For the special value $k = 1$ the kinetic subspace is a one-dimensional linear subspace of the (two-dimensional) stoichiometric subspace. (See Fig. 5.)

If, for a particular mass action system, the kinetic subspace is in fact smaller than the stoichiometric subspace, then the observation that $\dot{\mathbf{c}}$ invariably lies in the kinetic subspace clearly amounts to a sharpening of our earlier observation that $\dot{\mathbf{c}}$ always lies in the stoichiometric subspace.

In fact, when K is smaller than S we can also sharpen our observation that each composition trajectory is contained entirely in a stoichiometric compatibility class:

For each composition $\mathbf{c} \in \bar{\mathbb{P}}^N$, we denote by $\mathbf{c}+K$ the parallel of K containing $\mathbf{c}$. That is,

$$\mathbf{c}+K:=\{\mathbf{c}+\gamma \in \mathbb{R}^N : \gamma \in K\}. \tag{IV.9}$$

In rough terms, $\mathbf{c}+K$ is the set in $\mathbb{R}^N$ resulting from a parallel shift of the linear subspace K up to the vector $\mathbf{c}$.

Since the "velocity vector" $\dot{\mathbf{c}}$ given by (IV.6) always points along the linear subspace K, it is not difficult to see that a trajectory beginning at composition $\mathbf{c}(0)$ must lie entirely in the parallel of K containing $\mathbf{c}(0)$. [The argument can be made by a formal integration of (IV.6) along a solution just as we integrated (3.6) in Section 5.2 to show that each trajectory is contained entirely in a parallel of S.] In other words, if one composition is to evolve to another, it is necessary that the two compositions be compatible at least to the extent that both lie in the same parallel of K.

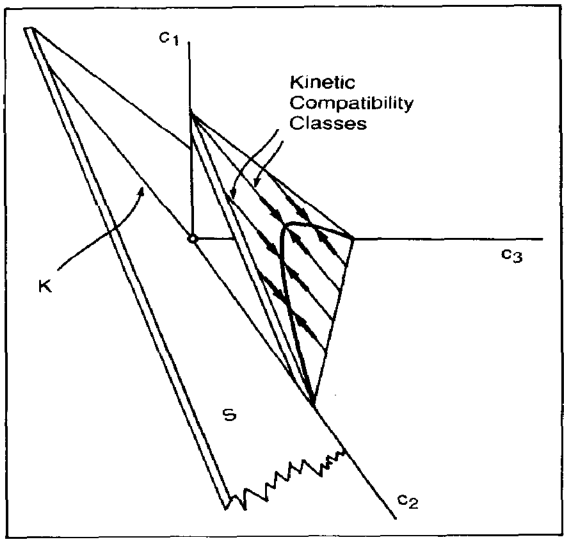


Fig. 5. The kinetic subspace and some kinetic compatibility classes for the mass action system (IV.1) with $k = 1$.

With this in mind, we can regard the set of all possible compositions (i.e. $\bar{\mathbb{P}}^N$) to be partitioned into the various parallels of K. These we call the *kinetic compatibility classes* for the mass action system under consideration. In particular, the *kinetic compatibility class containing composition* $\mathbf{c}$ is the set

$$(\mathbf{c}+K)\cap\bar{\mathbb{P}}^N.$$

This is just that part of the parallel of K containing $\mathbf{c}$ that lies in the non-negative orthant of $\mathbb{R}^N$. Two compositions belong to the same kinetic compatibility class if and only if their difference lies in K.

In language we now have available, we can say that *a composition trajectory for* (3.8) *which begins in a particular kinetic compatibility class must be contained entirely within that kinetic compatibility class.* When the kinetic subspace is smaller than the stoichiometric subspace, this sharpens our observation that a trajectory beginning in a particular stoichiometric compatibility class must lie entirely within it, for then the kinetic compatibility classes are much smaller objects than the stoichiometric compatibility classes. In fact, each stoichiometric compatibility class contains and is 'stratified" into kinetic compatibility classes.

Example: We return once again to the mass action system (IV.1), letting $k = 1$. Recall that, in this very special case, the kinetic subspace is a line in $\mathbb{R}^N$ which lies in the two-dimensional stoichiometric subspace and which contains the vector $2\mathbf{e}_1-(\mathbf{e}_2+\mathbf{e}_3)$. Both the kinetic and stoichiometric subspaces are depicted in Figure 5, where they are labeled K and S respectively. The stoichiometric compatibility class formerly depicted in Fig. 4 is shown again in Fig. 5, where we indicate how, for the case $k = 1$, the stoichiometric compatibility class is stratified into an infinite number of kinetic compatibility classes. As Fig. 5 is intended to suggest, a composition trajectory beginning in a particular kinetic compatibility class lies entirely within it.

Figure 5 is instructive. It suggests why, *when the kinetic subspace for a mass action system is smaller than the stoichiometric subspace, a stoichiometric compatibility class containing at least one positive steady state will usually contain an infinite number of positive steady states.* Suppose, for example, that a certain stoichiometric compatibility class contains a positive steady state $\mathbf{c}^*$. The stoichiometric compatibility class is stratified into an infinite number of kinetic compatibility classes, one of which contains $\mathbf{c}^*$. Under fairly mild conditions (given by the implicit function theorem) we should expect a steady state (close to $\mathbf{c}^*$) in each kinetic compatibility class lying sufficiently nearby the kinetic compatibility class containing $\mathbf{c}^*$. (In fact, it is reasonable to expect entire phase portraits within nearby kinetic compatibility classes to resemble the phase portrait in the kinetic compatibility class containing $\mathbf{c}^*$.)

We turn now to consideration of circumstances under which a mass action system can have the property that the kinetic subspace is, in fact, smaller than the stoichiometric subspace. In particular, we shall make precise the role played by the $t > \ell$ condition.

[†] In that article the formal definition of a linkage class is improperly constructed and does not carry the meaning intended. The definition should read, for example, as in (Feinberg, 1979, 1986). Nevertheless, the examples given in the article make clear the intent of the definition.

The relationship between the kinetic and stoichiometric subspaces is examined in (Feinberg and Horn, 1977).† There it is shown that, *for any reaction network such that each linkage class contains just one terminal strong linkage, the kinetic and stoichiometric subspaces coincide no matter what values the rate constants take. In other words, for all mass action systems such that the underlying network is of the* $\ell = t$ *variety (in particular, for all mass action systems such that the underlying network is weakly reversible), there is no real distinction between the kinetic and stoichiometric subspace*. It is this fact that makes networks for which $\ell = t$ relatively easy to study.

Now consider a mass action system for which the underlying reaction network is of the $\ell > t$ variety. In (Feinberg and Horn, 1977) it is also shown that *if* $\ell - t$ *is greater than the deficiency of the network, then the kinetic subspace is smaller than the stoichiometric subspace no matter what values the rate constants take.* In particular, if the network has a deficiency of zero, then the difference in the dimensions of S and K is exactly equal to $\ell - t$.

On the other hand, if $\ell - t$ is positive but *not* greater than the deficiency of the network, it may happen that, for certain values of the rate constants, K is smaller than S while, for other values of the rate constants, S and K actually coincide.

In fact, results in (Feinberg and Horn, 1977) are easily extended to show the following: If $\ell - t$ is positive and greater than *or equal to* the deficiency of the network, then, *for any set of rate constants such that the corresponding differential equations admit a positive steady state*, the kinetic subspace is *smaller* than the stoichiometric subspace. (In this case a stoichiometric compatibility class containing at least one positive steady state will usually contain an infinite number of positive steady states.)

As a corollary we can observe that, for any $\ell > t$ deficiency *one* network, *the kinetic subspace is smaller than the stoichiometric subspace whenever the rate constants are such that the corresponding differential equations admit a positive steady state* (and, in this case, a stoichiometric compatibility class containing a positive steady state will usually contain an infinite number of them).

Example: Consider the mass action system shown in (IV.1). For the underlying reaction network $\ell = 3$, $t = 2$, and the deficiency of the network is readily calculated to be *one*. Thus we have $\ell - t = \delta$. For $k \neq 1$ there are no positive steady states, and the kinetic and stoichiometric subspaces happen to coincide. For $k = 1$ there exist positive steady states, and the kinetic subspace is in fact smaller than the stoichiometric subspace.

Our emphasis throughout the main body of this article has been on the relationship between reaction network structure and the nature of phase portraits (e.g. the number of positive steady states, the asymptotic stability of positive steady states) within *stoichiometric* compatibility classes. More refined questions for mass action systems might instead have focused on the nature of phase portraits within *kinetic* compatibility classes. Note, for example, that the stoichiometric compatibility class depicted in Fig. 5 contains an infinite number of positive steady states, while each of the kinetic compatibility classes contains at most one. Note also that each of the positive steady states is *asymptotically* stable relative to initial conditions in the same kinetic compatibility class but *not* relative to initial conditions in the same stoichiometric compatibility class.

It should be kept in mind, however, that the distinction between kinetic and stoichiometric compatibility classes arises *only* for mass action models in which the underlying reaction network is of the $\ell > t$ variety. It follows, then, that *the distinction disappears completely in the presence of extremely small perturbations in the model.* For example, by adding reactions (with very small rate constants) such as to make all of the original reactions reversible, the original network can be perturbed to one of the $\ell = t$ variety. (The same result can often be achieved without making all reactions reversible.) The point here is that, while $\ell > t$ networks hold some interest, *dynamical peculiarities arising from a distinction between the kinetic and stoichiometric subspaces carry with them a kind of structural instability*; they disappear under small perturbations of the model.

Remark. In Appendix III we observed that, for any reaction system, the instantaneous value of $\dot{\mathbf{c}}$ must lie not only in the stoichiometric subspace but also in the stoichiometric cone. For mass action systems we can sharpen this observation as follows: From eq. (IV.6) it is apparent that $\dot{\mathbf{c}}$ must be of the form

$$\sum_{i=1}^{n} \alpha_i \mathbf{d}_i \tag{IV.10}$$

where each of the α_i is *non-negative*. By the *kinetic cone* we mean the set in $\mathbb{R}^N$ consisting of all vectors expressible in this form. Thus $\dot{\mathbf{c}}$ must lie not only in the kinetic subspace but also in the kinetic cone. It is easy to show, however, that the kinetic subspace and the kinetic cone coincide when the set $\{\mathbf{d}_1, \mathbf{d}_2, \ldots, \mathbf{d}_n\}$ is positively dependent—that is, when there exist positive numbers $\beta_1, \beta_2, \ldots, \beta_n$ such that

$$\sum_{i=1}^{n} \beta_i \mathbf{d}_i = \mathbf{0}.$$

Moreover, it is easy to see from eq. (IV.6) that the set $\{\mathbf{d}_1, \mathbf{d}_2, \ldots, \mathbf{d}_n\}$ will be positively dependent for any mass action system that admits a positive steady state.