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The Existence and Uniqueness of Steady States for a Class of Chemical Reaction Networks

MARTIN FEINBERG

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1. Introduction

My purpose here is to draw some general relationships between the structure of a chemical reaction network and the nature of the set of equilibrium states for the corresponding system of nonlinear ordinary differential equations.

An example will illustrate the way in which a system of ordinary differential equations is induced by a chemical reaction network: We consider a closed* vessel containing a fluid mixture in which chemical reactions occur among species labeled A, B, C, D and E. The mixture is stirred continuously. The stirring is sufficiently effective as to render the temperature and the molar concentrations of all species uniform throughout the mixture. Moreover, the temperature and the volume of the mixture are kept time-invariant by external means. On the other hand, the composition of the mixture may experience temporal variation resulting from the occurrence of chemical reactions.

We suppose that the chemical reactions occurring within the mixture are reasonably well reflected in the diagram

$$\begin{array}{ccc} & & \mathrm{A} \rightleftarrows 2\mathrm{B} \\ & \nwarrow \quad \swarrow & \\ \mathrm{A} + \mathrm{C} & & \rightleftarrows \mathrm{D} \\ & \searrow \quad \nearrow & \\ & \mathrm{B} + \mathrm{E}, & \end{array} \tag{1.1}$$

which indicates that a molecule of A can decompose into two molecules of B, that two molecules of B can react to form one molecule of A, that a molecule of A can react with a molecule of C to form a molecule of D, and so on.

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* The theory contained here is, in fact, applicable to reactors open to the transport of material. (See the comments following Definition 2.1.) The closed reactor considered in this introductory discussion was chosen to provide the simplest possible context in which I might indicate how a chemical reaction network gives rise to a system of differential equations.

Our interest is in the evolution of the mixture composition. By an instantaneous mixture composition we mean a specification for each species of a (non-negative) molar concentration. The molar concentrations (in moles per unit volume) of the individual species at time t are denoted $c_A(t)$, $c_B(t)$, $c_C(t)$, $c_D(t)$, and $c_E(t)$. The mixture composition at time t is denoted $c(t)$. (For the moment it suffices to view $c(t)$ as a "vector of molar concentrations". I will soon be more precise about the vector space in which $c(t)$ resides.)

In order to write differential equations that govern the species concentrations, it will be necessary to have information about the occurrence rates of the individual chemical reactions. It is generally supposed that the occurrence rate of each reaction depends in its own way on the instantaneous mixture composition. Thus we presume, for example, the existence of a non-negative real-valued *rate function* $\mathscr{K}_{A\to 2B}(\cdot)$ such that $\mathscr{K}_{A\to 2B}(c)$ is the instantaneous occurrence rate (per unit mixture volume) of reaction $A \to 2B$ when the instantaneous mixture composition is c. A *kinetics* for a reaction network is an assignment of such a rate function to each reaction in the network.

Once a kinetics is associated with reaction network (1.1), we can determine the rate at which the molar concentration of species A changes when the mixture composition is c: The reaction $A \to 2B$ has an occurrence rate $\mathscr{K}_{A\to 2B}(c)$, and with each occurrence there is a *loss* of *one* molecule of A. On the other hand, the reaction $2B \to A$ has an occurrence rate $\mathscr{K}_{2B\to A}(c)$, and each occurrence results in the *gain* of *one* molecule of A. Note also that reaction $A + C \to D$ results in a loss of one molecule of A, while the reactions $D \to A + C$ and $B + E \to A + C$ each result in the gain of one molecule of A. Thus, we write

$$\dot{c}_A = -\mathscr{K}_{A\to 2B}(c) + \mathscr{K}_{2B\to A}(c) - \mathscr{K}_{A+C\to D}(c) + \mathscr{K}_{D\to A+C}(c) + \mathscr{K}_{B+E\to A+C}(c).$$

In a similar way we can write a differential equation for the rate of change of the molar concentration of species B: When the mixture composition is c, the occurrence rate of reaction $A \to 2B$ is $\mathscr{K}_{A\to 2B}(c)$, and each occurrence results in a *gain* of *two* molecules of B. On the other hand, the reaction $2B \to A$ has an occurrence rate $\mathscr{K}_{2B\to A}(c)$, and each occurrence results in a *loss* of *two* molecules of B. The reaction $D \to B + E$ results in a *gain* of *one* molecule of B, while the reaction $B + E \to A + C$ results in a *loss* of *one* molecule of B. Thus, we write

$$\dot{c}_B = 2\mathscr{K}_{A\to 2B}(c) - 2\mathscr{K}_{2B\to A}(c) + \mathscr{K}_{D\to B+E}(c) - \mathscr{K}_{B+E\to A+C}(c).$$

Continuing in this way, we can write a system of ordinary differential equations that governs the mixture composition:

$$\begin{aligned}
\dot{c}_A &= -\mathscr{K}_{A\to 2B}(c) + \mathscr{K}_{2B\to A}(c) - \mathscr{K}_{A+C\to D}(c) + \mathscr{K}_{D\to A+C}(c) + \mathscr{K}_{B+E\to A+C}(c),\\
\dot{c}_B &= 2\mathscr{K}_{A\to 2B}(c) - 2\mathscr{K}_{2B\to A}(c) + \mathscr{K}_{D\to B+E}(c) - \mathscr{K}_{B+E\to A+C}(c),\\
\dot{c}_C &= -\mathscr{K}_{A+C\to D}(c) + \mathscr{K}_{D\to A+C}(c) + \mathscr{K}_{B+E\to A+C}(c),\\
\dot{c}_D &= -\mathscr{K}_{A+C\to D}(c) + \mathscr{K}_{D\to A+C}(c) - \mathscr{K}_{D\to B+E}(c),\\
\dot{c}_E &= \mathscr{K}_{D\to B+E}(c) - \mathscr{K}_{B+E\to A+C}(c).
\end{aligned} \tag{1.2}$$

My focus here is almost exclusively on *mass-action* kinetics. When the kinetics for a reaction network is of mass-action type, the rate function for each reaction is determined (up to a multiplicative positive constant) by the reaction itself. In rough terms, the idea behind mass-action kinetics is this: For a reaction such as $A \to 2B$ it is presumed that the occurrence rate is proportional to c_A, the molar concentration of species A. On the other hand, for a reaction such as $A + C \to D$ it is presumed that the occurrence rate is proportional to the product $c_A c_C$, which is deemed to reflect the likelihood of an encounter between a molecule of A and a molecule of C. Similarly, the occurrence rate of a reaction such as $2B \to A$ is regarded to be proportional to $(c_B)^2$. When the kinetics is of mass-action type, the rate functions for the reactions in network (1.1) are of the kind shown in (1.3).

$$\begin{aligned} &\mathscr{K}_{A\to 2B}(c) = \alpha c_A,\ \mathscr{K}_{2B\to A}(c) = \beta(c_B)^2,\ \mathscr{K}_{A+C\to D}(c) = \gamma c_A c_C, \\ &\mathscr{K}_{D\to B+E}(c) = \varepsilon c_D,\ \mathscr{K}_{D\to A+C}(c) = \delta c_D,\ \mathscr{K}_{B+E\to A+C}(c) = \xi c_B c_E. \end{aligned} \tag{1.3}$$

The positive numbers α, β, γ, ε, δ and ξ are *rate constants* for the corresponding reactions. My focus here is on *isothermal* reactors, but it should be kept in mind that values of the rate constants generally change from one operating temperature to another. The precise values that the rate constants actually take of course depend upon the chemical nature of the various species participating in the reactions. When a reaction network is endowed with mass-action kinetics, it is customary to adorn the reaction diagram, as in (1.4), with rate constants (or symbols for them) alongside the corresponding reaction arrows.

$$\begin{array}{ccc} & \overset{\alpha}{\underset{\beta}{\rightleftarrows}} & \\ A & & 2B \\ & \overset{\rho}{\underset{\delta}{\rightleftarrows}} & \\ A + C & & D \\ {\scriptstyle\xi}\nwarrow & & \swarrow{\scriptstyle\varepsilon} \\ & B + E & \end{array} \tag{1.4}$$

When the kinetics is of mass-action type, the system of differential equations given in (1.2) reduces to the system shown in (1.5).

$$\begin{aligned} \dot{c}_A &= -\alpha c_A + \beta(c_B)^2 - \gamma c_A c_C + \delta c_D + \xi c_B c_E, \\ \dot{c}_B &= 2\alpha c_A - 2\beta(c_B)^2 + \varepsilon c_D - \xi c_B c_E, \\ \dot{c}_C &= -\gamma c_A c_C + \delta c_D + \xi c_B c_E, \\ \dot{c}_D &= \gamma c_A c_C - (\delta + \varepsilon) c_D, \\ \dot{c}_E &= \varepsilon c_D - \xi c_B c_E. \end{aligned} \tag{1.5}$$

What should emerge from this example is the idea that there is a rather precise formalism governing the passage from a mass-action system (such as that depicted in (1.4)) to the corresponding system of polynomial differential equations. In

particular, it should be noted that *the equations are completely determined (up to values of the rate constants) by the reaction network itself.*

Thus, we are presented with the possibility that reaction-network structure might be connected in a precise way with the variety of phase portraits that the corresponding differential equations can admit (as the rate constants vary). In other words, *we might hope to develop theory with which it becomes feasible to inspect a diagram such as that shown in* (1.1) *and then draw conclusions about the existence (or non-existence) of rate constants such that qualitative phenomena of a specified kind derives from the corresponding mass-action differential equations.*

Such theory already exists. In fact, it is already possible to inspect network (1.1) and conclude *almost immediately* that, *no matter what positive values the rate constants take*, the system (1.5) behaves in a certain way: There is *precisely one* equilibrium (in each positive stoichiometric compatibility class*), the equilibrium is asymptotically stable, and there are no nontrivial periodic orbits along which all species concentrations are positive.

These results are consequences of the *Deficiency-Zero Theorem*, which gives precisely the same information for all networks in a rather large and easily described class. This theorem will be reviewed in Section 4 when we have more vocabulary at our disposal. Here it suffices to say that networks are classified by means of an easily computed non-negative integer index called the *deficiency*. When the deficiency of a network is zero (as is the case for network (1.1)), a certain kind of stable behavior is ensured for the corresponding mass-action differential equations. This stability persists for all positive values of the rate constants.

Networks of nonzero deficiency are not nearly as well understood. For some, in fact, there exist rate constants such that the corresponding mass-action differential equations admit behavior that is rather wild.

I wish to show, however, that there is an easily delineated class of networks, which includes (but is significantly larger than) the class described by the Deficiency Zero Theorem, for which *certain* conclusions of the theorem continue to obtain. In particular, I wish to describe a class of networks — some extraordinarily complicated — which have the property that, no matter what (positive) values the rate constants take, the corresponding system of mass-action equations can admit no more than one equilibrium (within a positive stoichiometric compatibility class). Thus, whatever other interesting features might be contained in phase portraits for such networks, the presence of multiple positive equilibria is excluded.

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* The notion of stoichiometric compatibility class will be discussed more fully in Section 3. In rough terms, stoichiometric compatibility classes are natural equivalence classes induced in the set of all possible compositions by the reaction network under study (independent of any kinetics the network might carry). No matter what kinetics is assigned to the network, the stoichiometric compatibility classes remain invariant under the flow given by the corresponding differential equations.

Notation. In the next section I will make formal the idea of a reaction network. Here it suffices to say that I regard a reaction network to be specified by three sets: The first is the set of *species* — {A, B, C, D, E} in network (1.1). The second is the set of *complexes*; these are the objects that appear before and after the reaction arrows — {A, 2B, A + C, D, B + E} in (1.1). Finally, there is the set of *reactions*, specified by a "reacts to" relation in the set of complexes. It is clear that these sets are tied to one another. For example, it is natural to view the complexes as members of the vector space generated by the species. In fact, I shall draw upon vector spaces generated not only by the species but also by the complexes and by the reactions. The following notation is offered with this in mind.

The real numbers are denoted by $\mathbb{R}$, the positive real numbers by $\mathbb{P}$, and the non-negative real numbers by $\bar{\mathbb{P}}$. Throughout this discussion of notation, the symbol I denotes a finite (index) set.

By *the vector space generated by the set* I, denoted $\mathbb{R}^I$, I mean the usual vector space of real-valued functions with domain I. The subset of $\mathbb{R}^I$ consisting of those functions that take exclusively positive [non-negative] values is denoted $\mathbb{P}^I$ [$\bar{\mathbb{P}}^I$].

When x is an element of $\mathbb{R}^I$, the symbol x_i is almost always used to denote the number assigned by x to $i \in I$. If x and y are elements of $\mathbb{R}^I$, the symbol xy denotes the element of $\mathbb{R}^I$ defined by

$$(xy)_i = x_i y_i \quad \forall i \in I.$$

When x is an element of $\mathbb{R}^I$, the symbol e^x denotes the element of $\mathbb{P}^I$ defined by

$$(e^x)_i = \exp(x_i) \quad \forall i \in I.$$

When z is an element of $\mathbb{P}^I$, the symbol $\ln z$ denotes the element of $\mathbb{R}^I$ defined by

$$(\ln z)_i = \ln z_i \quad \forall i \in I.$$

The *support* of an element $x \in \mathbb{R}^I$ (denoted $\operatorname{supp} x$) is defined as follows:

$$\operatorname{supp} x := \{i \in I: x_i \neq 0\}.$$

When J is a subset of I, the symbol ω_J denotes the characteristic function on J; that is, ω_J is the element of $\mathbb{R}^I$ such that

$$(\omega_J)_i = \begin{cases} 1 & \text{if } i \in J \\ 0 & \text{if } i \notin J \end{cases}.$$

In particular, if J is the singleton $\{j\}$, then $\omega_{\{j\}}$ is the element of $\mathbb{R}^I$ such that

$$(\omega_{\{j\}})_i = \begin{cases} 1 & \text{if } i = j \\ 0 & \text{if } i \neq j \end{cases}.$$

In this case I write ω_j *in place of the more formal* $\omega_{\{j\}}$.*

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* Although x_j is a *number* (the value assigned to j by $x \in \mathbb{R}^I$), ω_j is a *vector* in $\mathbb{R}^I$. No confusion should result if it is remembered that a subscripted ω is *always* a member of a vector space of the kind $\mathbb{R}^I$.

The *standard basis* for $\mathbb{R}^I$ is the set

$$\{\omega_i \in \mathbb{R}^I : i \in I\}.$$

Note that for each $x \in \mathbb{R}^I$ we have the representation

$$x = \sum_{i \in I} x_i \omega_i.$$

When the set I carries no algebraic structure it is sometimes useful to replace the symbol ω_i by i itself. Thus, for example, the symbols $i + j$ and $2i$ become abbreviations for the vectors $\omega_i + \omega_j$ and $2\omega_i$ in $\mathbb{R}^I$. *I adopt this convention when (and only when) the set in question is the set $\mathscr{S}$ of chemical species.* If, as in our example, $\mathscr{S} = \{A, B, C, D, E\}$, we can then regard the symbol A + B as an abbreviation for $\omega_A + \omega_B \in \mathbb{R}^{\mathscr{S}}$, the symbol 2B as an abbreviation for $2\omega_B \in \mathbb{R}^{\mathscr{S}}$, and so on. In this way we can view the *complexes* in a network — the objects that appear before and after the reaction arrows — as members of the vectors space $\mathbb{R}^{\mathscr{S}}$ (in fact, as members of the cone $\bar{\mathbb{P}}^{\mathscr{S}}$). This will prove to be convenient.

The *standard scalar product* in $\mathbb{R}^I$ is defined as follows: If x and z are elements of $\mathbb{R}^I$, then

$$x \cdot z = \sum_{i \in I} x_i z_i.$$

With respect to the standard scalar product, the standard basis for $\mathbb{R}^I$ is orthonormal. Unless stated otherwise, $\mathbb{R}^I$ is understood to carry the standard scalar product.

2. Reaction Network Structure

In this section I provide a vocabulary with which reaction network structure can be discussed. Once this vocabulary is in place, I will be in a position to draw relationships between the structure of a reaction network and qualitative properties of the corresponding mass-action differential equations.

The first definition serves to make formal what I mean by a chemical reaction network. Recall that the *complexes* of a reaction network are the objects appearing before and after the reaction arrows. Recall also that the complexes are identified with vectors in $\mathbb{R}^{\mathscr{S}}$, where $\mathscr{S}$ is the set of species in the network. Individual complexes are usually indicated by symbols such as y, y' or y''.

Definition 2.1. *A chemical reaction network* consists of three finite sets:

(i) a set $\mathscr{S}$, elements of which are the *species* of the network,

(ii) a set $\mathscr{C}$ of distinct vectors in $\bar{\mathbb{P}}^{\mathscr{S}}$ called the *complexes* of the network. For each $\sigma \in \mathscr{S}$ and each $y \in \mathscr{C}$, the number y_σ is the *stoichiometric coefficient of species σ in complex y.*

(iii) a relation $\mathscr{R} \subset \mathscr{C} \times \mathscr{C}$ having the following properties:

(a) $(y, y) \notin \mathscr{R}$ $\forall y \in \mathscr{C}$,

(b) For each $y \in \mathscr{C}$ there exists $y' \in \mathscr{C}$ such that $(y, y') \in \mathscr{R}$ or such that $(y', y) \in \mathscr{R}$.

Elements of $\mathscr{R}$ are called the *reactions* of the network. When (y, y') is contained in $\mathscr{R}$ we say that complex y *reacts to* complex y', and we write the more suggestive $y \to y'$ to indicate the reaction (y, y').

Example. The reaction network

$\mathscr{S} = \{A, B, C, D, E\}$,

$\mathscr{C} = \{A, 2B, A + C, D, B + E\} \subset \bar{\mathbb{P}}^{\mathscr{S}}$,

$\mathscr{R} = \{A \to 2B, 2B \to A, A + C \to D, D \to A + C, D \to B + E, B + E \to A + C\}$

is depicted in diagram (1.1).

It should be noted that *Definition 2.1 does not exclude from consideration networks containing reactions such as* $A \to 2A$ *that are apparently inconsistent with mass conservation.* Nor does the definition exclude networks containing reactions such as $0 \to y$ or $y \to 0$, where 0 is the *zero complex* (that is, the zero vector of $\mathbb{R}^{\mathscr{S}}$).

In fact, *networks containing "peculiar" reactions can be extremely useful in the description of reactors that are open to the influx and efflux of material.* Open reactors can be described in network terms by supplementing the network of "true" chemical reactions with certain "pseudoreactions" (such as $A \to 2A$, $0 \to A$ or $A \to 0$) that are incorporated to model the effect of mass transport. The appropriate differential equations then derive from the augmented network in much the same way that, for closed reactors, they derived in Section 1 from the network of true chemical reactions.* In either case, then, it makes sense to study the relationship between qualitative properties of the governing differential equations and the structure of the reaction network from which they were generated. For chemical engineers it is the dynamics of *open* reactors that are of most interest. *With this in mind, I want the working definition of a chemical reaction network to be broad enough to accommodate networks that would otherwise seem at odds with basic chemical principles.*

Chemist sometimes reserve the word *equilibrium* to describe rest points of closed reactors, while *steady-state* is used for both open and closed reactors. I make no such terminological distinction here.

Remark 2.1. It would be natural to build into the definition of a reaction network the requirement that the species set contain no more elements than actually appear in the complexes. More precisely, it would be natural to insist that

$$\bigcup_{y \in \mathscr{C}} \operatorname{supp} y = \mathscr{S}.$$

In fact, this is not done here, primarily because I will want to work with subnetworks. By a *subnetwork* of a reaction network $(\mathscr{S}, \mathscr{C}, \mathscr{R})$ I mean a reaction network $(\mathscr{S}, \mathscr{C}', \mathscr{R}')$ with $\mathscr{C}' \subset \mathscr{C}$ and $\mathscr{R}' \subset \mathscr{R}$. Note that I continue to view the complexes of the subnetwork as members of $\mathbb{R}^{\mathscr{S}}$, even when the complexes in $\mathscr{C}'$ all have support

* See [HJ], [F3] and [F4] for fuller discussions.

in a set of species that is smaller than $\mathscr{S}$. There is some convenience in this: When several subnetworks of a given parent network are under consideration simultaneously, their complexes remain members of a common vector space.**

Remark 2.2. The symbol n is reserved to denote the number of complexes in a network.

The "reacts to" relation $\mathscr{R}$ induces in the set of complexes still other relations that will assume some importance. It is understood in the following definitions that we have under consideration a fixed reaction network $(\mathscr{S}, \mathscr{C}, \mathscr{R})$.

Definition 2.2. Two complexes $y \in \mathscr{C}$ and $y' \in \mathscr{C}$ are *directly linked* (or *adjacent*) if $y \to y'$ or if $y' \to y$. If y and y' are directly linked, I write $y \leftrightarrow y'$. Two complexes $y \in \mathscr{C}$ and $y' \in \mathscr{C}$ are *linked* if any of the following conditions is satisfied:

(i) $y = y'$.
(ii) $y \leftrightarrow y'$.
(iii) There is a sequence of complexes, $y(1), y(2), \ldots, y(k)$, such that

$$y \leftrightarrow y(1) \leftrightarrow y(2) \leftrightarrow \ldots \leftrightarrow y(k) \leftrightarrow y'.$$

If y and y' are linked, I write $y \sim y'$. The equivalence relation $\sim$ induces a partition of $\mathscr{C}$ into equivalence classes called the *linkage classes* of the network.

Remark 2.3. The symbol ℓ is used to indicate the number of linkage classes in a network, and the symbol $\mathscr{C}/\sim$ is used to denote the collection of linkage classes.

Example. For network (1.1) $\ell = 2$. The linkage classes are $\{A, 2B\}$ and $\{A + C, D, B + E\}$.

Definition 2.3. A complex $y \in \mathscr{C}$ *ultimately reacts to* complex $y' \in \mathscr{C}$ if any of the following conditions is satisfied:

(i) $y = y'$.
(ii) $y \to y'$.
(iii) There is a sequence of complexes, $y(1), y(2), \ldots, y(k)$, such that

$$y \to y(1) \to y(2) \to \ldots \to y(k) \to y'.$$

If y ultimately reacts to y' I write $y \Rightarrow y'$. Two complexes y and y' are *strongly linked* if both $y \Rightarrow y'$ and $y' \Rightarrow y$. If y and y' are strongly linked, I write $y \approx y'$. The equivalence relation $\approx$ induced a partition of $\mathscr{C}$ into equivalence classes called the *strong-linkage classes* of the network.

Definition 2.4. *A terminal strong-linkage class* is a strong-linkage class containing no complex that reacts to a complex in a different strong-linkage class. (In

** Unless a subnetwork is under consideration, a reaction diagram such as (1.1) should be understood to represent a reaction network in which the species set coincides with the set of species evident in the diagram.

other words, a strong-linkage class Λ is terminal if $y \in \Lambda$ and $y \to y'$ imply that $y' \in \Lambda$.)

Remark 2.4. The symbol ℓ is reserved to indicate the number of terminal strong-linkage classes in a network.

Example. For the network

$$\begin{array}{l} \mathrm{C} \to \mathrm{D} + \mathrm{E} \rightleftarrows \mathrm{F} \\ \uparrow\downarrow \\ \mathrm{A} + \mathrm{B} \to \mathrm{G} \to \mathrm{H} \\ \qquad\quad \nwarrow \nearrow \\ \qquad\quad 2\mathrm{J} \end{array} \tag{2.1}$$

there is just one linkage class (consisting of the entire set of complexes). The strong linkage classes are $\{C, A + B\}$, $\{D + E, F\}$ and $\{G, H, 2J\}$. There are two terminal strong-linkage classes, $\{D + E, F\}$ and $\{G, H, 2J\}$. Note that for network (2.1) $\ell = 1$ and $\ell = 2$.

Example. For the network

$$\begin{array}{c} \mathrm{D} + \mathrm{E} \\ \uparrow \\ \mathrm{A} + \mathrm{B} \to \mathrm{C} \rightleftarrows 2\mathrm{F} \\ \mathrm{F} + \mathrm{A} \rightleftarrows \mathrm{G} \end{array} \tag{2.2}$$

there are two linkage classes, $\{A + B, C, 2F, D + E\}$ and $\{F + A, G\}$. The strong-linkage classes are $\{A + B\}$, $\{D + E\}$, $\{C, 2F\}$ and $\{F + A, G\}$. The terminal strong-linkage classes are $\{D + E\}$ and $\{F + A, G\}$. Here $\ell = 2$ and $\ell = 2$.

Remark 2.5. From the stipulation that the complex set be finite, it follows that, for any reaction network, each linkage class contains at least one terminal strong-linkage class. Thus, we have $\ell \geqq \ell$. As the examples indicate, equality may or may not hold.

Chemists say that a reaction network is *reversible* if its "reacts to" relation is symmetric — that is, if $y \to y'$ implies that $y' \to y$. Results that hold for reversible networks often hold also for networks that satisfy a related but far weaker condition:

Definition 2.5. A chemical reaction network is *weakly reversible* if, for the network, the "ultimately reacts to" relation is symmetric — that is, if $y \Rightarrow y'$ implies that $y' \Rightarrow y$.

It is evident that every reversible network is weakly reversible.

Examples. The network

$$\begin{array}{c} \mathrm{D}+\mathrm{E} \\ \uparrow\downarrow \\ \mathrm{A}+\mathrm{B} \rightleftarrows \mathrm{C} \rightleftarrows 2\mathrm{F} \\ \mathrm{F}+\mathrm{A} \rightleftarrows \mathrm{G} \end{array} \tag{2.3}$$

is reversible and, therefore, weakly reversible. On the other hand, network (1.1) is weakly reversible but not reversible. Neither network (2.1) nor (2.2) is weakly reversible.

Remark 2.6. The condition given for weak reversibility in Definition 2.5 is equivalent to each of the following conditions:

(i) Each reaction is contained in a directed cycle; more precisely, $y \to y'$ implies that $y' \Rightarrow y$.
(ii) Each linkage class is a strong-linkage class.
(iii) Each linkage class is a terminal strong-linkage class.

Remark 2.7. We shall see that some of the special properties of weakly reversible networks depend heavily on the coincidence of the linkage classes and the terminal strong-linkage classes. On the other hand, we shall also see that there are properties of weakly reversible networks that derive not from the actual coincidence of the linkage classes and the terminal strong-linkage classes but, rather, from the fact that the *number* of linkage classes (ℓ) is the same as the *number* of terminal strong-linkage classes (t). A network need not be weakly reversible in order that it satisfy the $t = \ell$ condition — (2.2) is an example — and it often happens that an assertion that holds true for weakly reversible networks also holds true for all networks in the far larger $t = \ell$ class. It should be kept in mind that the class of weakly reversible networks is included in the class of $t = \ell$ networks just as the class of reversible networks is included in the class of weakly reversible networks.

Our focus so far has been entirely on aspects of reaction network that derive from its character as a directed graph. That is, our concern has been exclusively with the "reacts to" relation, the precise nature of the complexes having played no role at all. In the following definitions, the algebraic structure carried by the complexes will begin to exert an influence.

When V is a vector space, a finite set $X \subset V$ is said to have *rank r* if there exists in X a linearly independent subset containing r vectors but no linearly independent subset containing $r + 1$ vectors.

Definition 2.6. The *reaction vectors* for a reaction network $\{\mathscr{S}, \mathscr{C}, \mathscr{R}\}$ are the members of the set

$$\{y' - y \in \mathbb{R}^{\mathscr{S}} \mid y \to y'\}. \tag{2.4}$$

The *rank of a reaction network* (denoted s) is the rank of its set of reaction vectors.

Examples. For network (1.1) $s = 3$. For network (2.1) $s = 6$. For networks (2.2) and (2.3) $s = 4$.

Remark 2.8. It is not difficult to show that, for any reaction network, the rank of the set (2.4) is precisely the same as the rank of the set

$$\{y' - y \in \mathbb{R}^{\mathscr{S}} \mid y \sim y'\}. \tag{2.5}$$

This implies that two networks with the same complexes and the same linkage classes have the same rank. For a network $\{\mathscr{S}, \mathscr{C}, \mathscr{R}\}$ with n complexes and ℓ linkage classes, it is easy to construct another network $\{\mathscr{S}, \mathscr{C}, \mathscr{R}'\}$ with precisely the same complexes and the same linkage classes but in which $\mathscr{R}'$ contains precisely $n - \ell$ reactions. It follows from Definition 2.6 that the rank of the network $\{\mathscr{S}, \mathscr{C}, \mathscr{R}'\}$ (and hence of $\{\mathscr{S}, \mathscr{C}, \mathscr{R}\}$) cannot exceed $n - \ell$. Thus, for a reaction network with n complexes and ℓ linkage classes, the rank s of the network must satisfy the relation

$$n - \ell - s \geqq 0. \tag{2.6}$$

Definition 2.7. The *deficiency of a reaction network* (denoted δ) is defined by the formula

$$\delta := n - \ell - s,$$

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

Examples. Networks (1.1), (2.1)–(2.3) all have deficiencies of zero. Networks (2.7)–(2.10) all have deficiencies of one. Network (2.10) was studied by EDELSTEIN [E]. Network (2.11), which was studied by HORN & JACKSON [HJ], has a deficiency of two.

$$2\mathrm{A} \rightleftarrows \mathrm{C} \rightleftarrows \mathrm{A} + \mathrm{B} \rightleftarrows \mathrm{D} \rightleftarrows 2\mathrm{B} \tag{2.7}$$

$$\mathrm{A} + \mathrm{B} \rightleftarrows \mathrm{B} + \mathrm{C},\ \mathrm{D} + \mathrm{A} \rightleftarrows \mathrm{C} + \mathrm{D} \tag{2.8}$$

$$\begin{array}{c} \mathrm{B} + \mathrm{C} \rightleftarrows \mathrm{A} \to 0 \rightleftarrows \mathrm{B} \\ \uparrow\downarrow \\ \mathrm{C} \end{array} \tag{2.9}$$

$$\begin{array}{c} \mathrm{A} \rightleftarrows 2\mathrm{A} \\ \mathrm{A} + \mathrm{B} \rightleftarrows \mathrm{C} \rightleftarrows \mathrm{B} \end{array} \tag{2.10}$$

$$\begin{array}{ccc} 3\mathrm{A} & \to & \mathrm{A} + 2\mathrm{B} \\ \uparrow & & \downarrow \\ 2\mathrm{A} + \mathrm{B} & \leftarrow & 3\mathrm{B}. \end{array} \tag{2.11}$$

Remark 2.9. From Remark 2.8 it follows that two reaction networks with the same complexes and the same linkage classes have the same deficiency. Thus, the deficiency of a network, like its rank, is affected by the "reacts to" relation only insofar as that relation induces a partition of the complexes into linkage classes. The deficiency is otherwise unaffected by the precise way in which the complexes are joined by reactions.

With each linkage class in a reaction network we can associate a subnetwork in the obvious way. For example, in network (2.3) we can associate with linkage class $\{A + B, C, D + E, 2F\}$ the subnetwork

$$\begin{array}{c} D + E \\ \uparrow\downarrow \\ A + B \rightleftarrows C \rightleftarrows 2F. \end{array}$$

A rank and a deficiency can be calculated for such a subnetwork from Definitions 2.6 and 2.7. I refer to these as the rank and deficiency *of the linkage class.* (See Remark 2.10.)

Definition 2.8. In a reaction network $\{\mathscr{S}, \mathscr{C}, \mathscr{R}\}$ the *rank of linkage class* $\mathscr{L}$ (denoted $s^{\mathscr{L}}$) is the rank of the set

$$\{y' - y \in \mathbb{R}^{\mathscr{S}} \mid y \to y',\ y \in \mathscr{L},\ y' \in \mathscr{L}\}. \tag{2.12}$$

The *deficiency of linkage class* $\mathscr{L}$ (denoted $\delta^{\mathscr{L}}$) is defined by the formula

$$\delta^{\mathscr{L}} := n^{\mathscr{L}} - 1 - s^{\mathscr{L}},$$

where $n^{\mathscr{L}}$ is the number of complexes in linkage class $\mathscr{L}$.

Remark 2.10. It is not difficult to see that the rank of the set (2.12) is the same as the rank of the set

$$\{y' - y \in \mathbb{R}^{\mathscr{S}} \mid y \in \mathscr{L},\ y' \in \mathscr{L}\}\}. \tag{2.13}$$

This implies that the rank (and deficiency) of a linkage class depend only upon the complexes that constitute the linkage class and not at all upon the fine details of the "reacts to" relation.

Remark 2.11. For a reaction network $\{\mathscr{S}, \mathscr{C}, \mathscr{R}\}$ we obviously have

$$\mathscr{R} = \bigcup_{\mathscr{L} \in \mathscr{C}/\sim} \{y \to y' \in \mathscr{R} \mid y \in \mathscr{L},\ y' \in \mathscr{L}\}. \tag{2.14}$$

(Recall that $\mathscr{C}/\sim$ denotes the collection of linkage classes for the network.) From (2.14) and elementary algebraic considerations it follows that the rank of the network and the ranks of the linkage classes must be related in the following way:

$$s \leqq \sum_{\mathscr{C}/\sim} s^{\mathscr{L}}. \tag{2.15}$$

From (2.14) and the fact that $\mathscr{C}$ is the disjoint union of the linkage classes it follows that the deficiency of the network and the deficiencies of its linkage classes must satisfy the relation

$$\delta \geqq \sum_{\mathscr{C}/\sim} \delta^{\mathscr{L}}. \tag{2.16}$$

Moreover, inequality holds in (2.16) if and only if inequality holds in (2.15).

Examples. The rank of the linkage class $\{D + E, A + B, C, 2F\}$ in network (2.3) is 3 and its deficiency is 0. In the same network the rank of linkage class $\{F + A, G\}$ is 1 and its deficiency is 0. Recall that network (2.3) has a rank of 4 and a deficiency of 0. In this case equality holds in both (2.15) and (2.16).

On the other hand, linkage classes $\{A, 2A\}$ and $\{A + B, C, B\}$ in network (2.10) have ranks of 1 and 2, respectively, while the rank of the entire network is 2. The deficiencies of the linkage classes are each 0, while the deficiency of the entire network is 1. Thus, for network (2.10) inequality holds in both (2.15) and (2.16).

3. Mass-Action Systems and their Differential Equations

By a *mass-action system* I mean a chemical reaction network taken together with a mass-action kinetics. When a reaction network $\{\mathscr{S}, \mathscr{C}, \mathscr{R}\}$ is assigned a mass-action kinetics, the rate function for reaction $y \to y'$ is given by

$$\mathscr{K}_{y \to y'}(c) = k_{y \to y'} c^y \quad \forall c \in \bar{\mathbb{P}}^{\mathscr{S}}, \tag{3.1}$$

where

$$c^y := \prod_{\sigma \in \mathscr{S}} (c_\sigma)^{y_\sigma} \tag{3.2}$$

and $k_{y \to y'}$ is the rate constant for reaction $y \to y'$. Specification of a mass-action kinetics for a network amounts to a specification of a positive rate constant for each reaction in the network.

Definition 3.1. A *mass-action system* is a reaction network $\{\mathscr{S}, \mathscr{C}, \mathscr{R}\}$ taken together with an element k in $\mathbb{P}^{\mathscr{R}}$. The number $k_{y \to y'}$ is the *rate constant* for the reaction $y \to y' \in \mathscr{R}$.

Definition 3.2. The *species-formation rate function* for a mass-action system $\{\mathscr{S}, \mathscr{C}, \mathscr{R}, k\}$ is the function $f(\cdot, k): \bar{\mathbb{P}}^{\mathscr{S}} \to \mathbb{R}^{\mathscr{S}}$ defined by

$$f(c, k) = \sum_{\mathscr{R}} k_{y \to y'} c^y (y' - y). \tag{3.3}$$

An *equilibrium* of the mass-action system is an element $c \in \bar{\mathbb{P}}^{\mathscr{S}}$ such that $f(c, k) = 0$. A *positive equilibrium* is an equilibrium in $\mathbb{P}^{\mathscr{S}}$.

Remark 3.1. The notation for the species-formation function makes explicit the dependence on the assignment of the rate constant but suppresses the obvious

dependence on the reaction network itself. The reaction network under study will generally be apparent. I shall always be interested in the *family* of species formation rate functions generated from the network by letting k take on all possible values in $\mathbb{P}^{\mathscr{R}}$.

Interpretation. For each $\sigma \in \mathscr{S}$ we have

$$f_\sigma(c, k) = \sum_{\mathscr{R}} k_{y \to y'} c^y (y'_\sigma - y_\sigma). \tag{3.4}$$

Note that y'_σ is the stoichiometric coefficient of species σ in the product complex of the reaction $y \to y'$ while y_σ is the stoichiometric coefficient of species σ in the reactant complex. With this in mind, we can interpret $y'_\sigma - y_\sigma$ as the net number of molecules of species σ produced with each occurrence of the reaction $y \to y'$. Thus, $f_\sigma(c, k)$ is the sum of all the reaction occurrence rates (per unit mixture volume) at composition c, each weighted by the net number of molecules of σ produced with each occurrence of the corresponding reaction. This is essentially the idea used in Section 1 to calculate the production rate of a species. We can therefore identify $f_\sigma(c, k)$ with the net production rate (per unit mixture volume) of species σ in a mixture of composition c. An equilibrium is then a composition at which the net production rate of every species is zero.

Remark 3.2. It is not difficult to show that if $\{\mathscr{S}, \mathscr{C}, \mathscr{R}, k\}$ is a mass-action system, then $f_\sigma(c, k) \geqq 0$ whenever $c_\sigma = 0$.

By the *differential equation corresponding to a mass-action system* $\{\mathscr{S}, \mathscr{C}, \mathscr{R}, k\}$ I mean the differential equation

$$\dot{c} = f(c, k), \tag{3.5}$$

where $f(\cdot, k)$ is the species formation rate function. An equilibrium of the mass-action system is obviously an equilibrium of the corresponding differential equation.

Example. Written for the mass-action system depicted in (1.4), equation (3.5) reduces to (1.5).

It is evident that the species-formation rate function for a mass-action system takes values entirely within the span of the reaction vectors for the underlying reaction network. This simple observation has fairly transparent geometric implications for the phase portrait of the differential equation (3.5). These can be discussed more easily once we have some additional language at our disposal.

Definition 3.3. The *stoichiometric subspace* (denoted S) for a reaction network $\{\mathscr{S}, \mathscr{C}, \mathscr{R}\}$ is the span of its reaction vectors. That is,

$$S := \operatorname{span}\{y' - y \in \mathbb{R}^{\mathscr{S}} \mid y \to y'\}.$$

Two vectors $c \in \bar{\mathbb{P}}^{\mathscr{S}}$ and $c' \in \bar{\mathbb{P}}^{\mathscr{S}}$ are *stoichiometrically compatible* if $c' - c$ lies in S. Stoichiometric compatibility is an equivalence relation that induces a partition of $\bar{\mathbb{P}}^{\mathscr{S}}$ and $\mathbb{P}^{\mathscr{S}}$ into equivalence classes respectively called the *stoichiometric compatibility classes and positive stoichiometric compatibility classes* for the network.

Remark 3.3. It is not difficult to show the stoichiometric subspace for a reaction network, like the rank of the network, is affected by the "reacts to" relation only insofar as that relation serves to partition the complexes into linkage classes. In fact, for a network $\{\mathscr{S}, \mathscr{C}, \mathscr{R}\}$,

$$S = \operatorname{span}\{y' - y \in \mathbb{R}^{\mathscr{S}} \mid y \sim y'\}.$$

Remark 3.4. Because the "velocity" given by the differential equation (3.5) invariably points along the stoichiometric subspace for the underlying reaction network, it is evident that each composition trajectory must reside entirely within a parallel of the stoichiometric subspace — that is, within a stoichiometric compatibility class. In other words, the collection of stoichiometric compatibility classes constitutes a partition of the set of all compositions ($\bar{\mathbb{P}}^{\mathscr{S}}$) into subsets that are invariant under the flow given by (3.5). It is natural, therefore, to investigate the nature of the dynamics *within* the stoichiometric compatibility classes.

Such an investigation usually begins with a study of the equilibria that the individual stoichiometric compatibility classes might contain. For a specified mass-action system, one generally is interested in questions like these: Does every positive stoichiometric compatibility class contain an equilibrium? Does there exist a positive stoichiometric compatibility class that contains more than one equilibrium? The system of differential equations (1.5) corresponding to the relatively simple mass-action system (1.4) already suggests that these are not easy questions, and the answers might of course depend on the particular values of the rate constants.

Nevertheless, in the next section I shall state theorems that permit *immediate* answers to these questions for networks that reside within a large and easily described class. As we shall see, this class includes networks of great complexity.

4. The Deficiency-Zero and Deficiency-One Theorems

The following theorem is due to HORN, JACKSON and FEINBERG.* A proof is sketched in Appendix C. The theorem provides a backdrop against which a second theorem — the main subject of this article — might be better understood.

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* The main ideas underlying the theorem are contained in [HJ, H, F1]. A survey of these articles and some additional ideas are contained in [F2]. The theorem is discussed informally in [FH1, F3, F4].

Theorem 4.1. (The Deficiency-Zero Theorem). *Let* $(\mathscr{S}, \mathscr{C}, \mathscr{R})$ *be a reaction network of deficiency zero.*

(i) *If the network is not weakly reversible, then, for arbitrary* $k \in \mathbb{P}^{\mathscr{R}}$, *the differential equation for the mass-action system* $(\mathscr{S}, \mathscr{C}, \mathscr{R}, k)$ *admits neither a positive equilibrium nor a periodic orbit in* $\mathbb{P}^{\mathscr{R}}$.

(ii) *If the network is weakly reversible, then, for arbitrary* $k \in \mathbb{P}^{\mathscr{R}}$, *the differential equation for the mass-action system* $(\mathscr{S}, \mathscr{C}, \mathscr{R}, k)$ *has the following properties: Each positive stoichiometric compatibility class contains precisely one equilibrium; this equilibrium is asymptotically stable; and there is no nontrivial periodic orbit in* $\mathbb{P}^{\mathscr{S}}$.

Remark 4.1. Asymptotic stability of an equilibrium is understood to be taken relative to initial conditions in the stoichiometric compatibility class containing that equilibrium.

Remark 4.2. The statement of the Deficiency-Zero Theorem given here is one suited to the purposes of this article; it is not intended to be the most general or the sharpest statement we might have made. For a fuller discussion of properties of deficiency-zero networks (including those endowed with kinetics that are not of mass-action type) see [F4].

Example. The reaction network depicted in (1.4) is weakly reversible and has a deficiency of zero. We can now assert that, *no matter what positive values the rate constants take, the system of differential equations given in* (1.5) *admits precisely one equilibrium in each positive stoichiometric compatibility class; this equilibrium is asymptotically stable; and there are no nontrivial cyclic composition trajectories along which all species concentrations are positive.*

I shall state and prove a theorem that extends the uniqueness and existence of equilibria given in part (ii) of Theorem 4.1 to a far wider class of networks.

To set the stage for a statement of the second theorem I want to characterize the deficiency-zero networks in a seemingly awkward way. *A reaction network has a deficiency of zero if and only if it satisfies 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.* (The "only if" part of this statement is an immediate consequence of (2.15) and the non-negativity of deficiencies.)

Thus, the results on existence and uniqueness of equilibria given in part (ii) of the Deficiency-Zero Theorem can be rephrased: *Consider a reaction network such that the deficiency of the network and the deficiencies of the linkage classes satisfy the following conditions:*

(i) $$\delta^{\mathscr{L}} = 0 \quad \forall \mathscr{L} \in \mathscr{C}/\sim, \tag{4.1}$$

(ii) $$\sum_{\mathscr{C}/\sim} \delta^{\mathscr{L}} = \delta. \tag{4.2}$$

Moreover, suppose that

(iii) *the network is weakly reversible.*

Then, no matter what (positive) rate constants are assigned to the reactions, the resulting mass-action system admits precisely one equilibrium in each positive stoichiometric compatibility class.

The next theorem I shall state — the Deficiency-One Theorem — asserts that this same result holds even when condition (i) is replaced by the far weaker requirement that the deficiency of no linkage class exceeds one. (Hence the name of the theorem.) In fact, the theorem does much more.

For a deficiency-*zero* network that is *not* weakly reversible, Theorem 4.1 tells us that there can be no assignment of (positive) rate constants such that the resulting mass-action system admits even one positive equilibrium. Thus, it is pointless to ask whether there can be multiple equilibria within a positive stoichiometric compatibility class.

On the other hand, for networks of nonzero deficiency, weak reversibility is not a precondition for the existence of positive equilibria. For example, the simple mass-action system

$$2\mathrm{A} \underset{\varepsilon}{\overset{1}{\rightleftarrows}} \mathrm{A} + \mathrm{B} \xrightarrow{1} 2\mathrm{B} \tag{4.3}$$

gives rise to the system of differential equations

$$\begin{aligned} \dot{c}_{\mathrm{A}} &= -(c_{\mathrm{A}})^2 + (\varepsilon - 1)c_{\mathrm{A}}c_{\mathrm{B}}, \\ \dot{c}_{\mathrm{B}} &= (c_{\mathrm{A}})^2 - (\varepsilon - 1)c_{\mathrm{A}}c_{\mathrm{B}}. \end{aligned} \tag{4.4}$$

There are no positive equilibria for $0 < \varepsilon \leqq 1$, but there are positive equilibria for all $\varepsilon > 1$. Note that the network shown in (4.3) is not weakly reversible and that its deficiency is 1 ($n = 3$, $\ell = 1$, $s = 1$).

For networks of nonzero deficiency, therefore, the possibility of *multiple* equilibria within a positive stoichiometric compatibility class becomes a serious one even in the absence of weak reversibility.

With respect to the uniqueness of equilibria, the Deficiency-One Theorem not only relaxes condition (4.1), *it also replaces the weak reversibility condition with the far milder condition that each linkage class contain no more than one terminal strong-linkage class.*

Theorem 4.2. (The Deficiency-One Theorem). *Let $(\mathscr{S}, \mathscr{C}, \mathscr{R})$ be a reaction network of deficiency δ, let $(\delta^{\mathscr{L}})_{\mathscr{L} \in \mathscr{C}/\sim}$ be the deficiencies of its linkage classes, and suppose that these numbers satisfy both of the following conditions:*

(i) $$\delta^{\mathscr{L}} \leqq 1 \quad \forall \mathscr{L} \in \mathscr{C}/\sim, \tag{4.5}$$

(ii) $$\sum_{\mathscr{C}/\sim} \delta^{\mathscr{L}} = \delta. \tag{4.6}$$

Moreover, suppose that

(iii) *each linkage class contains just one terminal strong-linkage class.*

If, for a particular $k \in \mathbb{P}^{\mathscr{R}}$, the mass-action system $(\mathscr{S}, \mathscr{C}, \mathscr{R}, k)$ admits a positive equilibrium, then each positive stoichiometric compatibility class contains precisely one *equilibrium. If the network is weakly reversible, then, for* every $k \in \mathbb{P}^{\mathscr{R}}$, *the mass-action system $(\mathscr{S}, \mathscr{C}, \mathscr{R}, k)$ admits a positive equilibrium.*

An improved version of Theorem 4.2 is given in Appendix A.

Remark 4.3. Suppose that the network $(\mathscr{S}, \mathscr{C}, \mathscr{R})$ satisfies conditions (i)–(iii) of Theorem 4.2 and that the mass-action system $(\mathscr{S}, \mathscr{C}, \mathscr{R}, k)$ admits the positive equilibrium c^*. I shall show in Sections 5 and 6 that the full set of positive equilibria for the system is

$$\{c \in \mathbb{P}^{\mathscr{S}} \mid \ln c - \ln c^* \in S^{\perp}\},$$

where $S^{\perp}$ is the orthogonal complement in $\mathbb{R}^{\mathscr{S}}$ of the stoichiometric subspace (relative to the standard scalar product).

Example. The simple network shown in (4.3) has one linkage class, {2A, A + B, 2B}, and that linkage class contains just one terminal strong-linkage class, {2B}. The deficiency of the network is one, so conditions (i) and (ii) are satisfied. Recall that only some assignments of rate constants give rise to positive equilibria. Theorem 4.2 tells us that, for a rate constant assignment which does give rise to a positive equilibrium, there in fact exists precisely one equilibrium in each positive stoichiometric compatibility class. (In this case, every positive stoichiometric compatibility class is characterized by an equation of the form $c_{\mathrm{A}} + c_{\mathrm{B}} = \text{constant}$.)

Example. Consider the mass-action system displayed as (4.7), in which

$$\begin{array}{ccccccc}
 & & & \overset{\alpha}{\underset{\beta}{\rightleftarrows}} & \mathrm{A} & \overset{\gamma}{\underset{\varepsilon}{\rightleftarrows}} & 2\mathrm{A} \\
\mathrm{A}+\mathrm{B} & \overset{\eta}{\underset{\iota}{\rightleftarrows}} & 2\mathrm{C} & \overset{\kappa}{\underset{\lambda}{\rightleftarrows}} & \mathrm{D} & \overset{\mu}{\underset{\nu}{\rightleftarrows}} & 2\mathrm{E} \\
 & & & \xi\downarrow\uparrow\rho & & & \\
 & & & \mathrm{C}+\mathrm{E} & & & \\
\mathrm{B}+\mathrm{C} & & & \overset{\sigma}{\underset{\tau}{\rightleftarrows}} & & \mathrm{F} & \\
 & & {\scriptstyle\chi}\searrow\nwarrow{\scriptstyle\phi} & & & {\scriptstyle\psi}\swarrow\nearrow{\scriptstyle\zeta} & \\
 & & & \mathrm{G} & & &
\end{array} \tag{4.7}$$

"0" denotes the zero complex. Note that from (3.1) a reaction of the form $0 \to y$ has a constant rate (equal to the rate constant $k_{0 \to y}$). The differential equations corresponding to (4.7) are shown in (4.8). We ask two questions: *Does the system* (4.8) *admit a positive steady state regardless of the* (*positive*) *values the rate constants take? Do there exist* (*positive*) *values for the rate constants such that some positive*

stoichiometric compatibility class contains more than one equilibrium?

$$\begin{aligned}
\dot{c}_A &= \alpha + (\gamma - \beta)c_A - \varepsilon(c_A)^2 - \eta c_A c_B + \iota(c_C)^2,\\
\dot{c}_B &= -\eta c_A c_B + \iota(c_C)^2 + \tau c_F + \phi c_G - (\chi + \tau)c_B c_C,\\
\dot{c}_C &= 2\eta c_A c_B - 2(\kappa + \iota)(c_C)^2 + (2\lambda + \xi)c_D - \rho c_C c_E,\\
\dot{c}_D &= \kappa(c_C)^2 + \rho c_C c_E + \nu(c_E)^2 - (\lambda + \mu + \xi)c_D,\\
\dot{c}_E &= (2\mu + \xi)c_D - 2\nu(c_E)^2 - \rho c_C c_E,\\
\dot{c}_F &= \sigma c_B c_C + \zeta c_G - (\tau + \psi)c_F,\\
\dot{c}_G &= \chi c_B c_C + \psi c_F - (\phi + \zeta)c_G.
\end{aligned} \tag{4.8}$$

The deficiency of the network shown in (4.7) is 2, while the deficiencies of the linkage classes (from top to bottom) are 1, 1 and 0. Thus, conditions (i) and (ii) of the Deficiency-One Theorem are satisfied. Moreover, the network is weakly reversible. We conclude, therefore, that the answers to the two question posed above are *yes* and *no*, respectively. In fact, *the system* (4.8) *admits precisely one equilibrium in each positive stoichiometric compatibility class no matter what* (*positive*) *values the rate constants take.*

Remark 4.4. With respect to the *uniqueness* of equilibria given by the Deficiency-One Theorem, we cannot drop from the hypothesis any of the conditions (i)–(iii):

It was shown by HORN & JACKSON [HJ] that there are rate constants for network (2.11) such that the resulting mass-action system admits three equilibria in a positive stoichiometric compatibility class. This network satisfies conditions (ii) and (iii) but fails to satisfy condition (i). The deficiency of the sole linkage class (and therefore of the network) is two.

The mass action equations for network (2.10) were studied by EDELSTEIN [E]*, who showed that there are rate constants that produce multiple equilibria within a positive stoichiometric compatibility class. Network (2.10) satisfies conditions (i) and (iii) but not (ii). The deficiency of the network is one, while the linkage classes both have deficiencies of zero.

To see that condition (iii) cannot be dropped, it suffices to consider the very simple mass-action system

$$2A \overset{\alpha}{\leftarrow} A + B \overset{\beta}{\rightarrow} 2B. \tag{4.9}$$

The corresponding differential equations are

$$\dot{c}_A = (\alpha - \beta)c_A c_B, \quad \dot{c}_B = (\beta - \alpha)c_A c_B. \tag{4.10}$$

When α and β are unequal, there are no positive equilibria at all. On the other hand, when α and β are equal, *every* composition is an equilibrium. Thus, when

* For a discussion of the connection between network (2.10) and the polynomial system EDELSTEIN actually studied, see [F3] or [F4].

$\alpha = \beta$, each positive stoichiometric compatibility class contains an infinite number of equilibria. The network in (4.9) has a deficiency of one and just one linkage class, and so it satisfies conditions (i) and (ii). The single-linkage class, however, contains two terminal strong-linkage classes, {2A} and {2B}, and so condition (iii) is not satisfied.

For a informal discussion of the significance of condition (iii), see Appendix IV in [F4]. This discussion, in turn, relies on ideas in [FH2].

Remark 4.5. It is not true that a mass-action system which admits positive equilibria invariably admits an equilibrium in each positive stoichiometric compatibility class. In fact, for every assignment of positive rate constants to reactions in the network

$$\begin{array}{c} \mathrm{B} \to \mathrm{A} \\ \mathrm{A} + 2\mathrm{B} \to 3\mathrm{B} \end{array} \tag{4.11}$$

there are positive stoichiometric compatibility classes that contain equilibria and others that do not. (A typical phase portrait is given in [F4].) The network has a deficiency of one, while each linkage class has a deficiency of zero, and so condition (ii) is not satisfied.

In Section 7 I shall prove that, *for a mass-action system in which the underlying network does satisfy condition* (ii), *all positive stoichiometric compatibility classes contain the same number of equilibria. This holds true even when conditions* (i) *and* (iii) *are not satisfied* (in which case the number of equilibria within a positive stoichiometric compatibility class might exceed one).

Remark 4.6. Although the uniqueness of positive equilibria guaranteed by the Deficiency-Zero Theorem extends to networks satisfying the hypothesis of the Deficiency-One Theorem, neither the stability of equilibria nor the preclusion of periodic orbits extends in the same way.

The network

$$\begin{array}{ccc} & \mathrm{A} \rightleftarrows 2\mathrm{A} & \\ & \uparrow\downarrow & \\ \mathrm{A} + \mathrm{B} \rightleftarrows \mathrm{C} & \rightleftarrows & \mathrm{B}, \end{array} \tag{4.12}$$

a perturbation of network (2.10), satisfies all the conditions of the Deficiency-One Theorem. Nevertheless, there exist rate constant values such that the corresponding mass-action differential equation admits a unique but unstable positive equilibrium and also a periodic orbit along which all species concentrations are positive.

Suppose that

$$\dot{c} = f(c, k) \tag{4.13}$$

is the differential equation for a mass-action system $\{\mathscr{S}, \mathscr{C}, \mathscr{R}, k\}$ in which the underlying network satisfies conditions (i)–(iii) of Theorem 4.2, and suppose also that the c^* is a positive equilibrium. In light of the possible instability of c^*, it is

natural to study the derivative of $f(\cdot, k)$ at c^*. The following theorem asserts that the derivative can have no eigenvector *in the stoichiometric subspace** that corresponds to an eigenvalue of *zero*. In other words, the derivative, when restricted to the stoichiometric subspace, is nonsingular.

In Theorem 4.3 $\partial_c f(c^*, k)$: $\mathbb{R}^{\mathscr{S}} \to \mathbb{R}^{\mathscr{S}}$ denotes the derivative of $f(\cdot, k)$ at c^*.

Theorem 4.3. *Suppose that $\{\mathscr{S}, \mathscr{C}, \mathscr{R}, k\}$ is a mass-action system for which the underlying reaction network satisfies conditions* (i)–(iii) *of Theorem 4.2., and suppose also that the system admits a positive equilibrium c^*. Then the stoichiometric subspace and the kernel of $\partial_c f(c^*, k)$ have only the zero vector in common.*

It might occur to some readers that Theorem 4.3, once proved, could provide the foundation for a proof of Theorem 4.2. In fact, I shall provide proofs of the theorems which are not so much sequential as they are parallel. That is, the argument in support of the uniqueness of equilibria given by Theorem 4.2 will, with only minor modification, serve also to prove Theorem 4.3.

Remark 4.7. In Definition 2.1 I required of a chemical reaction network that the complexes be elements of $\bar{\mathbb{P}}^{\mathscr{S}}$. In other words, I required that the stoichiometric coefficient of each species be non-negative (but not necessarily integer) in every complex. This restriction was, of course, motivated by the chemical considerations with which we began. In fact, there are areas of chemical reaction network theory in which non-negativity of stoichiometric coefficients plays a critical role.

On the other hand, *Theorems 4.1–4.3 remain true even when stoichiometric coefficients in the complexes are permitted to take negative values.* (In this case, the domain of the species formation rate function would be restricted to $\mathbb{P}^{\mathscr{S}}$ (Definition 3.2).) Signs of stoichiometric coefficients play no role in the arguments given here.

5. An Overview of the Proofs: Three Key Propositions

The proof of Theorem 4.2 will proceed in the following way: I begin by supposing that a network $\{\mathscr{S}, \mathscr{C}, \mathscr{R}\}$ satisfies conditions (i)–(iii) of Theorem 4.2 and that, for a fixed $k \in \mathbb{P}^{\mathscr{R}}$, the mass-action system $\{\mathscr{S}, \mathscr{C}, \mathscr{R}, k\}$ admits a positive equilibrium c^*. I shall then show that the full set of positive equilibria is identical to the set

$$\{c \in \mathbb{P}^{\mathscr{S}} \mid \ln c - \ln c^* \in S^{\perp}\}, \tag{5.1}$$

where S denotes the stoichiometric subspace for the network and $S^{\perp}$ denotes its orthogonal complement in $\mathbb{R}^{\mathscr{S}}$ (relative to the standard scalar product). This amounts to showing that the mass-action system is, in the language of HORN & JACKSON [HJ], *quasithermostatic*. The significance of the coincidence of (5.1) with the set of positive equilibria lies in the following proposition:

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* For reasons suggested by Remarks 3.4 and 4.1, eigenvectors contained in the stoichiometric subspace are the ones of real interest.

Proposition 5.1 (HORN & JACKSON). *Let $\{\mathscr{S}, \mathscr{C}, \mathscr{R}\}$ be a reaction network with stoichiometric subspace S, and let c^* be an element of $\mathbb{P}^{\mathscr{S}}$. Each positive stoichiometric compatibility class contains precisely one element of the set* (5.1).

(Appendix B contains a proof of the proposition that uses an argument somewhat different from the one given in [HJ].)

To prove the coincidence of (5.1) with the set of positive equilibria I first note that, by virtue of Definition 3.2, the postulated equilibrium c^* must satisfy the equation

$$\sum_{\mathscr{R}} k_{y \to y'}(c^*)^y(y' - y) = 0. \tag{5.2}$$

A (perhaps different) element of $\mathbb{P}^{\mathscr{S}}$, say c^{**}, is an equilibrium of the same mass-action system if and only if

$$\sum_{\mathscr{R}} k_{y \to y'}(c^{**})^y(y' - y) = 0. \tag{5.3}$$

I define $\kappa \in \mathbb{P}^{\mathscr{R}}$ by

$$\kappa_{y \to y'} = k_{y \to y'}(c^*)^y \quad \forall\, y \to y' \in \mathscr{R}. \tag{5.4}$$

It is not difficult to see that (5.2) and (5.3) are equivalent to

$$\sum_{\mathscr{R}} \kappa_{y \to y'}(y' - y) = 0, \tag{5.5}$$

$$\sum_{\mathscr{R}} \kappa_{y \to y'} \exp[y \cdot (\ln c^{**} - \ln c^*)](y' - y) = 0. \tag{5.6}$$

Thus, to prove that (5.1) coincides with the set of positive equilibria it is enough to prove:

Assertion 5.1. *Let $\{\mathscr{S}, \mathscr{C}, \mathscr{R}\}$ be a reaction network that satisfies conditions* (i)–(iii) *in Theorem 4.2, let κ be an element of $\mathbb{P}^{\mathscr{R}}$ that satisfies* (5.5), *and let $\mathbb{R}^{\mathscr{S}}$ be equipped with the standard scalar product. An element $\mu \in \mathbb{R}^{\mathscr{S}}$ satisfies the equation*

$$\sum_{\mathscr{R}} \kappa_{y \to y'} e^{y \cdot \mu}(y' - y) = 0 \tag{5.7}$$

if and only if μ is orthogonal to the stoichiometric subspace for the network.

Remark 5.1. Once coincidence of (5.1) with the set of positive equilibria is established, I shall still have to prove the last assertion in Theorem 4.2. This amounts to showing that, for a *weakly reversible* network satisfying conditions (i)–(iii), *each* assignment of rate constants actually gives rise to at least one positive equilibrium.

At this point I can explain why it is possible to construct a proof of Theorem 4.3 that is virtually identical in structure to a proof of Theorem 4.2. Suppose that $\{\mathscr{S}, \mathscr{C}, \mathscr{R}, k\}$ is a mass-action system that admits a positive equilibrium c^*. Fairly straightforward computation shows that $\partial_c f(c^*, k): \mathbb{R}^{\mathscr{S}} \to \mathbb{R}^{\mathscr{S}}$ is given by

$$\partial_c f(c^*, k)\gamma = \sum_{\mathscr{R}} \kappa_{y \to y'}(y \cdot \gamma)(y' - y), \tag{5.8}$$

where $\kappa \in \mathbb{P}^{\mathscr{R}}$ is as in (5.4) (so that κ must satisfy (5.5)) and "$\cdot$" indicates not the standard scalar product in $\mathbb{R}^{\mathscr{S}}$ *but rather the scalar product defined by*

$$x \cdot z := \sum_{\sigma \in \mathscr{S}} x_\sigma z_\sigma / c^*_\sigma. \tag{5.9}$$

To prove Theorem 4.3 it is enough to show that if the network $\{\mathscr{S}, \mathscr{C}, \mathscr{R}\}$ satisfies the conditions (i)–(iii) in Theorem 4.2, then any vector in the kernel of $\partial_c f(c^*, k)$ must be orthogonal (in the sense of scalar product (5.9)) to the stoichiometric subspace for the network. (In this case a vector in the kernel that also lies in the stoichiometric subspace can only be the zero vector.) In other words, Theorem 4.3 will be proved once I prove:

Assertion 5.2. *Let $\{\mathscr{S}, \mathscr{C}, \mathscr{R}\}$ be a reaction network that satisfies conditions* (i)–(iii) *in Theorem 4.2, let κ be an element of $\mathbb{P}^{\mathscr{R}}$ that satisfies* (5.5), *and let $\mathbb{R}^{\mathscr{S}}$ be equipped with the scalar product defined by* (5.9) (*where c^* is any fixed vector of $\mathbb{P}^{\mathscr{S}}$*). *An element $\mu \in \mathbb{R}^{\mathscr{S}}$ satisfies the equation*

$$\sum_{\mathscr{R}} \kappa_{y \to y'} (y \cdot \mu)(y' - y) = 0 \tag{5.10}$$

if and only if μ is orthogonal to the stoichiometric subspace for the network.

It is easy to see that Assertions 5.1 and 5.2 are merely special cases of

Proposition 5.2. *Let $\{\mathscr{S}, \mathscr{C}, \mathscr{R}\}$ be a reaction network of deficiency δ, let $\{\delta^{\mathscr{L}}\}_{\mathscr{L} \in \mathscr{C}/\sim}$ be the deficiencies of its linkage classes, and suppose that*

(i) $\delta^{\mathscr{L}} \leqq 1 \quad \forall \mathscr{L} \in \mathscr{C}/\sim$,

(ii) $\sum_{\mathscr{C}/\sim} \delta^{\mathscr{L}} = \delta$,

(iii) *each linkage class contains just one terminal strong-linkage class.*

Moreover, let κ be an element of $\mathbb{P}^{\mathscr{R}}$ that satisfies the condition

$$\sum_{\mathscr{R}} \kappa_{y \to y'} (y' - y) = 0, \tag{5.11}$$

let $\mathbb{R}^{\mathscr{S}}$ be equipped with a scalar product (not necessarily the standard one), and let $\phi : \mathbb{R} \to \mathbb{R}$ be continuous and strictly monotonic. An element $\mu \in \mathbb{R}^{\mathscr{S}}$ satisfies

$$\sum_{\mathscr{R}} \kappa_{y \to y'} \phi(y \cdot \mu)(y' - y) = 0 \tag{5.12}$$

if and only if μ is orthogonal to the stoichiometric subspace for the network.

It should be clear that, once Proposition 5.2 is proved, Theorem 4.3 and the first sentence in the conclusion of Theorem 4.2 will also have been proved.

Before proving Proposition 5.2, I shall state and prove Proposition 5.3, which serves to abstract some important ideas of HORN & JACKSON [HJ]. Proposition 5.3 will not only play a role in the proof of Proposition 5.2, it will also play a crucial role in Appendix C, where I sketch a proof of the Deficiency-Zero Theorem.

In order to introduce Proposition 5.3 and explain its relationship to Proposition 5.2, I want to have available a useful map. For a reaction network $\{\mathscr{S}, \mathscr{C}, \mathscr{R}\}$

the *stoichiometric map* is the linear transformation $Y: \mathbb{R}^{\mathscr{C}} \to \mathbb{R}^{\mathscr{S}}$ defined by its action on the standard basis for $\mathbb{R}^{\mathscr{C}}$ by

$$Y\omega_y = y, \quad \forall y \in \mathscr{C}. \tag{5.13}$$

Note that an element $\kappa \in \mathbb{P}^{\mathscr{R}}$ satisfies (5.11) if and only if it satisfies the equation

$$Y\left[\sum_{\mathscr{R}} \kappa_{y \to y'}(\omega_{y'} - \omega_y)\right] = 0. \tag{5.14}$$

In particular, κ might satisfy not only (5.14) but also the special condition

$$\sum_{\mathscr{R}} \kappa_{y \to y'}(\omega_{y'} - \omega_y) = 0.$$

When κ does satisfy this special condition, then, *even in the absence of deficiency restrictions*, the conclusions of Proposition 5.2 remain true. In fact, we can say even more:

Proposition 5.3. *For the reaction network* $\{\mathscr{S}, \mathscr{C}, \mathscr{R}\}$, *let* κ *be an element of* $\mathbb{P}^{\mathscr{R}}$ *that satisfies the condition*

$$\sum_{\mathscr{R}} \kappa_{y \to y'}(\omega_{y'} - \omega_y) = 0, \tag{5.15}$$

let $\mathbb{R}^{\mathscr{S}}$ *be equipped with a scalar product (not necessarily the standard one), and let* $\phi: \mathbb{R} \to \mathbb{R}$ *be continuous and strictly monotonic. If* $\phi(\cdot)$ *is increasing [decreasing], then*

$$\sum_{\mathscr{R}} \kappa_{y \to y'} \phi(y \cdot \mu)(y' - y) \cdot \mu \leqq [\geqq] \, 0 \quad \forall \mu \in \mathbb{R}^{\mathscr{S}}. \tag{5.16}$$

Moreover, the following are equivalent:

(i) $\sum_{\mathscr{R}} \kappa_{y \to y'} \phi(y \cdot \mu)(y' - y) \cdot \mu = 0$,

(ii) μ *is orthogonal to the stoichiometric subspace for the network,*

(iii) $\sum_{\mathscr{R}} \kappa_{y \to y'} \phi(y \cdot \mu)(y' - y) = 0$.

Proof. I suppose that $\phi(\cdot)$ is increasing. There is no difficulty in extending the argument to decreasing $\phi(\cdot)$.

Let $\Phi: \mathbb{R} \to \mathbb{R}$ have derivative $\phi(\cdot)$. From the mean value theorem and the supposition that $\phi(\cdot)$ is strictly increasing it follows that

$$\phi(a)(b - a) \leqq \Phi(b) - \Phi(a) \quad \text{for all } a, b \in \mathbb{R}, \tag{5.17}$$

with equality holding if and only if $a = b$. From this and the positivity of κ I obtain the estimate

$$\sum_{\mathscr{R}} \kappa_{y \to y'} \phi(y \cdot \mu)(y' - y) \cdot \mu \leqq \sum_{\mathscr{R}} \kappa_{y \to y'} [\Phi(y' \cdot \mu) - \Phi(y \cdot \mu)], \tag{5.18}$$

with equality holding if and only if $(y' - y) \cdot \mu = 0$ for all $y \to y' \in \mathbb{R}$ — that is, if and only if μ is orthogonal to the stoichiometric subspace. Note, however, that the right side of (5.18) can be written

$$\left\{\sum_{\mathscr{R}} \kappa_{y \to y'}(\omega_{y'} - \omega_y)\right\} * \left\{\sum_{y'' \in \mathscr{C}} \Phi(y'' \cdot \mu)\omega_{y''}\right\}, \tag{5.19}$$

where " $*$ " indicates the standard scalar product in $\mathbb{R}^{\mathscr{C}}$. Thus, when (5.15) holds, the right side of (5.18) reduces to 0 for all $\mu \in \mathbb{R}^{\mathscr{S}}$. This gives the result in (5.16) and the equivalence of (i) and (ii).

It is obvious that (iii) implies (i).

The proof will be complete once I show that (ii) implies (iii). For each linkage class $\mathscr{L} \in \mathscr{C}/\sim$, I denote by $\mathscr{L} \to \mathscr{L}$ the set of reactions in the network of the form $y \to y'$ with y in $\mathscr{L}$ (in which case y' must also belong to $\mathscr{L}$). From the independence of the standard basis for $\mathbb{R}^{\mathscr{C}}$ it is easy to see that (5.15) actually implies (5.20):

$$\sum_{\mathscr{L} \to \mathscr{L}} \kappa_{y \to y'}(\omega_{y'} - \omega_y) = 0 \quad \forall\, \mathscr{L} \in \mathscr{C}/\sim . \tag{5.20}$$

Acting with the stoichiometric map on both sides of each of the equations in (5.20), we can see that κ satisfies

$$\sum_{\mathscr{L} \to \mathscr{L}} \kappa_{y \to y'}(y' - y) = 0 \quad \forall\, \mathscr{L} \in \mathscr{C}/\sim . \tag{5.21}$$

This observation and the following lemma will establish that (ii) implies (iii):

Lemma 5.1. *Let $\{\mathscr{S}, \mathscr{C}, \mathscr{R}\}$ be a reaction network, and let κ be an element of $\mathbb{R}^{\mathscr{R}}$ that satisfies the condition given in* (5.21). *Moreover, let $\mathbb{R}^{\mathscr{S}}$ be equipped with a scalar product (not necessarily the standard one). If $\mu \in \mathbb{R}^{\mathscr{S}}$ is orthogonal to the stoichiometric subspace, then for any function $\phi : \mathbb{R} \to \mathbb{R}$,*

$$\sum_{\mathscr{R}} \kappa_{y \to y'} \phi(y \cdot \mu)(y' - y) = 0. \tag{5.22}$$

Proof. For μ orthogonal to the stoichiometric subspace, it follows from Remark 3.3 that $y \cdot \mu = y' \cdot \mu$ whenever y and y' are complexes in the same linkage class. In other words, there is a set of numbers $\{z_{\mathscr{L}} \mid \mathscr{L} \in \mathscr{C}/\sim\}$ such that $y \cdot \mu = z_{\mathscr{L}}$ for all $y \in \mathscr{L}$. Thus, the left side of (5.22) takes the form

$$\sum_{\mathscr{C}/\sim} \phi(z_{\mathscr{L}}) \sum_{\mathscr{L} \to \mathscr{L}} \kappa_{y \to y'}(y' - y).$$

From this and (5.21) it is clear that (5.22) holds. □

This completes the proof of Proposition 5.3.

Remark 5.2. It is not difficult to see how the proof of Proposition 5.3 can be extended to show that (i), (ii) and (iii) are equivalent to each of the following:

(iv) $\sum_{\mathscr{R}} \kappa_{y \to y'} \phi(y \cdot \mu)(\omega_{y'} - \omega_y) = 0$,

(v) $\sum_{\mathscr{L} \to \mathscr{L}} \kappa_{y \to y'} \phi(y \cdot \mu)(\omega_{y'} - \omega_y) = 0 \quad \forall\, \mathscr{L} \in \mathscr{C}/\sim$,

(vi) $\sum_{\mathscr{L} \to \mathscr{L}} \kappa_{y \to y'} \phi(y \cdot \mu)(y' - y) = 0 \quad \forall\, \mathscr{L} \in \mathscr{C}/\sim$.

Remark 5.3. Proposition 5.3 asserts that, when κ satisfies not only condition (5.11) but also the stronger condition (5.15), the conclusion of Proposition 5.2 holds even for networks that fail to obey the deficiency restrictions imposed there. It should be

noted, however, that *condition* (5.15) *itself carries a hidden implication for network structure*: It will be a consequence of Lemma 6.1.1 that no $\kappa \in \mathbb{P}^{\mathscr{R}}$ can satisfy condition (5.15) unless the underlying network is *weakly reversible*. (See Remark 6.1.1.)

Remark 5.4. Proposition 5.3 is essentialy abstracted from results already contained in [HJ]. The proof given here, however, is substantially different from the one given by HORN & JACKSON. Their argument, which is more graph-theoretical in spirit, relies upon a decomposition of the (weakly reversible) network under study into simple cycles.

For readers who wish to pursue the connection between Proposition 5.3 and the work of HORN & JACKSON, an interpretation of condition (5.15) might be helpful: If, for each reaction $y \to y' \in \mathscr{R}$, we think of the number $\kappa_{y \to y'}$ as a current flowing from complex y to complex y', then condition (5.15) amounts to a requirement that, at each complex, the current inflow be exactly balanced by the current outflow. (To see this, it is helpful to study the scalar component equations encoded by the vector equation (5.15).) In the language of HORN & JACKSON we would say that (5.15) imposes upon κ a condition of *complex balancing*.

Lemma 5.1 served to complete the proof of Proposition 5.3. It is perhaps already evident that Lemma 5.1 also takes us just a step away from a proof of the (relatively easy) "if" part of Proposition 5.2. In fact, the "if" part of Proposition 5.2 holds for reaction networks that satisfy condition (ii) of Proposition 5.2, even when conditions (i) and (iii) are not satisfied. This is the content of the following lemma.

Lemma 5.2. *Let* $\{\mathscr{S}, \mathscr{C}, \mathscr{R}\}$ *be a reaction network that satisfies condition* (ii) *in Proposition 5.2, and let* κ *be an element of* $\mathbb{R}^{\mathscr{R}}$ *that satisfies the condition*

$$\sum_{\mathscr{R}} \kappa_{y \to y'}(y' - y) = 0. \tag{5.23}$$

Moreover, let $\mathbb{R}^{\mathscr{S}}$ *be equipped with a scalar product (not necessarily the standard one). If* $\mu \in \mathbb{R}^{\mathscr{S}}$ *is orthogonal to the stoichiometric subspace, then for any function* $\phi : \mathbb{R} \to \mathbb{R}$,

$$\sum_{\mathscr{R}} \kappa_{y \to y'} \phi(y \cdot \mu)(y' - y) = 0. \tag{5.24}$$

Proof. It is easy to see that (5.23) can be written in the form

$$\sum_{\mathscr{L} \in \mathscr{C}/\sim} \sum_{\mathscr{L} \to \mathscr{L}} \kappa_{y \to y'}(y' - y) = 0. \tag{5.25}$$

Note that in (5.25) the sum over $\mathscr{L} \to \mathscr{L}$ lies in the linear subspace

$$S^{\mathscr{L}} := \operatorname{span}\{y' - y \in \mathbb{R}^{\mathscr{S}} \mid y \to y',\ y \in \mathscr{L},\ y' \in \mathscr{L}\}, \tag{5.26}$$

the dimension of which is the rank, $s^{\mathscr{L}}$, of linkage class $\mathscr{L}$ (Definition 2.8). Note also that the stoichiometric subspace for the network is the sum of subspaces of the kind given in (5.26):

$$S = \sum_{\mathscr{C}/\sim} S^{\mathscr{L}}. \tag{5.27}$$

Moreover, the sum in (5.27) is *direct* precisely when the rank of the network and the ranks of the individual linkage classes satisfy the equation

$$s = \sum_{\mathscr{C}/\sim} s^{\mathscr{L}}. \tag{5.28}$$

But, from Remark 2.11, (5.28) is equivalent to condition (ii) in Proposition 5.2, which we have presumed to hold for the network under study. For the network, then, (5.23) is equivalent to

$$\sum_{\mathscr{L} \to \mathscr{L}} \kappa_{y \to y'}(y' - y) = 0 \quad \forall\, \mathscr{L} \in \mathscr{C}/\sim . \tag{5.29}$$

This and Lemma 5.1 ensure that (5.24) holds. □

The "only if" part of Proposition 5.2 remains to be proved. This will be done in Section 6.

6. Proof of Proposition 5.2

The proof of the "only if" assertion in Proposition 5.2 will be divided into three parts. The first part contains some preliminaries. In the second part the proposition is proved for a network containing just one linkage class. In the third part, the result for the single linkage class is extended to networks having an arbitrary number of linkage classes. It should be kept in mind that the "if" assertion in Proposition 5.2 is already a consequence of Lemma 5.2.

6.1. Preliminaries

Here I consider a reaction network $\{\mathscr{S}, \mathscr{C}, \mathscr{R}\}$. Recall from Section 1 that $(\omega_y \in \mathbb{R}^{\mathscr{C}} \mid y \in \mathscr{C})$ denotes the standard basis for $\mathbb{R}^{\mathscr{C}}$. Recall also that the *stoichiometric map* for the network is the linear transformation $Y : \mathbb{R}^{\mathscr{C}} \to \mathbb{R}^{\mathscr{S}}$ that acts on this basis as in (6.1.1):

$$Y\omega_y = y, \quad \forall\, y \in \mathscr{C}. \tag{6.1.1}$$

For each $\alpha \in \mathbb{R}^{\mathscr{R}}$ I define the linear transformation $A_\alpha : \mathbb{R}^{\mathscr{C}} \to \mathbb{R}^{\mathscr{C}}$ by

$$A_\alpha x \equiv \sum_{\mathscr{R}} \alpha_{y \to y'} x_y (\omega_{y'} - \omega_y). \tag{6.1.2}$$

(Here x_y is the "y^{th} component" of $x \in \mathbb{R}^{\mathscr{C}}$ relative to the standard basis.) Note that the composite map $YA_\alpha : \mathbb{R}^{\mathscr{C}} \to \mathbb{R}^{\mathscr{S}}$ is given by

$$YA_\alpha x \equiv \sum_{\mathscr{R}} \alpha_{y \to y'} x_y (y' - y). \tag{6.1.3}$$

I want to reformulate Proposition 5.2 in terms of the kernel of such a map. In preparation for the reformulation I recall from Section 1 that $\omega_{\mathscr{C}} \in \mathbb{R}^{\mathscr{C}}$ is the

characteristic function on $\mathscr{C}$. That is, every component of $\omega_{\mathscr{C}}$ (relative to the standard basis for $\mathbb{R}^{\mathscr{C}}$) is 1:

$$\omega_{\mathscr{C}} := \sum_{y \in \mathscr{C}} \omega_y. \tag{6.1.4}$$

Thus, we have

$$YA_\alpha \omega_{\mathscr{C}} \equiv \sum_{\mathscr{R}} \alpha_{y \to y'}(y' - y). \tag{6.1.5}$$

For the network under consideration, an element $\kappa \in \mathbb{P}^{\mathscr{R}}$ satisfies condition (5.11) precisely when $\omega_{\mathscr{C}}$ is contained in $\ker YA_\kappa$. (I note for future reference that κ satisfies the stronger condition (5.15) precisely when $\omega_{\mathscr{C}}$ is contained in $\ker A_\kappa$.)

Proposition 5.2 (Reformulated). *Let $\{\mathscr{S}, \mathscr{C}, \mathscr{R}\}$ be a reaction network of deficiency δ, let $(\delta^{\mathscr{L}})_{\mathscr{L} \in \mathscr{C}/\sim}$ be the deficiencies of its linkage classes, and suppose that*

(i) $\delta^{\mathscr{L}} \leqq 1$ *for all* $\mathscr{L} \in \mathscr{C}/\sim$,
(ii) $\sum_{\mathscr{C}/\sim} \delta^{\mathscr{L}} = \delta$,
(iii) *each linkage class contains just one terminal strong-linkage class.*

Moreover, let κ be an element of $\mathbb{P}^{\mathscr{R}}$ that satisfies the condition

$$\omega_{\mathscr{C}} \in \ker YA_\kappa, \tag{6.1.6}$$

let $\mathbb{R}^{\mathscr{S}}$ be equipped with a scalar product (not necessarily the standard one), and let $\phi: \mathbb{R} \to \mathbb{R}$ be continuous and strictly monotonic. An element $\mu \in \mathscr{R}^{\mathscr{S}}$ satisfies the condition

$$\sum_{y \in \mathscr{C}} \phi(y \cdot \mu)\omega_y \in \ker YA_\kappa \tag{6.1.7}$$

(if and) only if μ is orthogonal to the stoichiometric subspace for the network.

This reformulated version of Proposition 5.2 will be proved after I gather information about the influence of reaction-network structure on the nature of $\ker YA_\alpha$ (for arbitrary $\alpha \in \mathbb{P}^{\mathscr{R}}$). I begin by studying the kernel of A_α, which is obviously contained in the kernel of YA_α. Unless a statement to the contrary is given, I do not assume in what follows that the network under study satisfies the conditions of Proposition 5.2.

The following lemma is proved in the Appendix of [FH2].

Lemma 6.1.1. *Let $\{\mathscr{S}, \mathscr{C}, \mathscr{R}\}$ be a reaction network with terminal strong-linkage classes $\{\Lambda^1, \Lambda^2, \ldots, \Lambda^\ell\}$, let α be an element of $\mathbb{P}^{\mathscr{R}}$, and let $A_\alpha: \mathbb{R}^{\mathscr{C}} \to \mathbb{R}^{\mathscr{C}}$ be as in* (6.1.2). *The kernel of A_α contains a basis*

$$\{b^1, b^2, \ldots, b^\ell\} \subset \bar{\mathbb{P}}^{\mathscr{C}}$$

having the property that

$$\operatorname{supp} b^\theta = \Lambda^\theta, \quad \theta = 1, 2, \ldots, \ell. \tag{6.1.8}$$

Remark 6.1.1. It is important to note that the basis described in Lemma 6.1.1 lies entirely in $\overline{\mathbb{P}}^{\mathscr{C}}$. That is, b_y^θ is *positive* for each $y \in \Lambda^\theta$ and is *zero* for each $y \notin \Lambda^\theta$.

It is an immediate consequence of Lemma 6.1.1 that, for arbitrary $\alpha \in \mathbb{P}^{\mathscr{R}}$, every $x \in \ker A_\alpha$ has the property that $x_y = 0$ for each $y \in \mathscr{C}$ that does not lie in a terminal strong-linkage class. If the underlying network is not weakly reversible, it has at least one complex that is "nonterminal", and so $\ker A_\alpha$ can contain no element that is strictly positive (i.e., that lies in $\mathbb{P}^{\mathscr{C}}$). In particular $\ker A_\alpha$ cannot contain $\omega_{\mathscr{C}}$. Viewed from a slightly different perspective, this last observation has the following implication: *If a network $\{\mathscr{S}, \mathscr{C}, \mathscr{R}\}$ is not weakly reversible, there can exist no $\alpha \in \mathbb{P}^{\mathscr{R}}$ that satisfies the equation*

$$\sum_{\mathscr{R}} \alpha_{y \to y'}(\omega_{y'} - \omega_y) = 0.$$

Remark 6.1.2. Lemma 6.1.1 asserts, among other things, that for each $\alpha \in \mathbb{P}^{\mathscr{R}}$, the dimension of $\ker A_\alpha$ is identical to the number of terminal strong-linkage classes in the network. Thus, we can calculate the dimension of the range of A_α from the standard result that relates the dimensions of the domain, range and kernel of a linear mapping:

$$\dim(\operatorname{rng} A_\alpha) = \dim \mathbb{R}^{\mathscr{C}} - \dim(\ker A_\alpha) = n - \ell, \tag{6.1.9}$$

where n is the number of complexes in the network and ℓ is the number of terminal strong-linkage classes.

Remark 6.1.3. From (6.1.2) it is apparent that, for each $\alpha \in \mathbb{R}^{\mathscr{R}}$, the range of A_α is contained in the span of the set

$$\Delta^{\rightarrow} := \{\omega_{y'} - \omega_y \in \mathbb{R}^{\mathscr{C}} \mid y \to y'\}. \tag{6.1.10}$$

On the other hand, it is not difficult to prove that span $(\Delta^{\rightarrow})$ coincides with the span of the set

$$\Delta^{\sim} := \{\omega_{y'} - \omega_y \in \mathbb{R}^{\mathscr{C}} \mid y \sim y'\}. \tag{6.1.11}$$

(Recall that $y \sim y'$ indicates that the complexes y and y' are linked.) Thus, the "reacts to" relation influences the nature of span $(\Delta^{\rightarrow})$ only insofar as it serves to partition the complexes into linkage classes. In particular, the dimension of span $(\Delta^{\sim})$ and therefore of span $(\Delta^{\rightarrow})$ is readily shown to be $n - \ell$, where n is the number of complexes and ℓ is the number of linkage classes.* In summary, we always have

$$\operatorname{rng} A_\alpha \subset \operatorname{span}(\Delta^{\rightarrow}), \tag{6.1.12}$$

$$\dim \operatorname{span}(\Delta^{\rightarrow}) = n - \ell, \tag{6.1.13}$$

where n is the number of complexes and ℓ is the number of linkage classes in the network. From (6.1.12), (6.1.13) and Remark 6.1.2 we obtain

* See [F1] for a proof in a slightly different context.

Lemma 6.1.2. *Let $\{\mathscr{S}, \mathscr{C}, \mathscr{R}\}$ be a reaction network in which each linkage class contains just one terminal strong-linkage class (i.e., in which $t = \ell$). For every $\alpha \in \mathbb{P}^{\mathscr{R}}$,*

$$\operatorname{rng} A_\alpha = \operatorname{span}(\Delta^{\rightarrow}). \tag{6.1.14}$$

We are now in a position to calculate $\dim \ker Y A_\alpha$ (for arbitrary $\alpha \in \mathbb{P}^{\mathscr{R}}$) when the underlying network satisfies the $t = \ell$ condition.

Lemma 6.1.3. *Let $\{\mathscr{S}, \mathscr{C}, \mathscr{R}\}$ be a reaction network in which each linkage class contains just one terminal strong-linkage class. For each $\alpha \in \mathbb{P}^{\mathscr{R}}$*

$$\dim(\ker Y A_\alpha) = \delta + \ell, \tag{6.1.15}$$

where δ is the deficiency of the network and ℓ is the number of linkage classes.

Proof. From the standard result relating the dimensions of the domain, range and kernel of a linear mapping we have

$$\dim(\ker Y A_\alpha) = \dim \mathbb{R}^{\mathscr{C}} - \dim(\operatorname{rng} Y A_\alpha). \tag{6.1.16}$$

Since each linkage class contains just one terminal strong-linkage class, Lemma 6.1.2 ensures that $\operatorname{rng} A_\alpha = \operatorname{span}(\Delta^{\rightarrow})$. Thus, we have

$$\begin{aligned} \operatorname{rng} Y A_\alpha &= Y(\operatorname{rng} A_\alpha) \\ &= Y(\operatorname{span}\{\omega_{y'} - \omega_y \in \mathbb{R}^{\mathscr{C}} \mid y \to y'\}) \\ &= \operatorname{span}\{y' - y \in \mathbb{R}^{\mathscr{S}} \mid y \to y'\}. \end{aligned} \tag{6.1.17}$$

In other words, the range of $Y A_\alpha$ coincides with the stoichiometric subspace for the network, and so its dimension is the rank s of the network. Since the dimension of $\mathbb{R}^{\mathscr{C}}$ is just the number of complexes in the network, (6.1.16) reduces to

$$\dim(\ker Y A_\alpha) = n - s. \tag{6.1.18}$$

The desired result (6.1.15) then follows from (6.1.18) and the definition of the deficiency: $\delta := n - \ell - s$. □

Remark 6.1.4. Here I consider an arbitrary network $\{\mathscr{S}, \mathscr{C}, \mathscr{R}\}$, not necessarily one that satisfies the $t = \ell$ condition. Suppose that, for a specified $\alpha \in \mathbb{R}^{\mathscr{R}}$, the vector $x \in \mathbb{R}^{\mathscr{C}}$ lies in $\ker Y A_\alpha$. Since the map A_α takes values in $\operatorname{span}(\Delta^{\rightarrow})$, it is evident that $A_\alpha x$ lies in

$$(\ker Y) \cap \operatorname{span}(\Delta^{\rightarrow}) \subset \mathbb{R}^{\mathscr{C}}. \tag{6.1.19}$$

Because the linear subspace (6.1.19) has some importance, I want to characterize the vectors it contains. Let g be an element of $\mathbb{R}^{\mathscr{C}}$. I represent g in terms of the standard basis for $\mathbb{R}^{\mathscr{C}}$ by

$$g = \sum_{y \in \mathscr{C}} g_y \omega_y. \tag{6.1.20}$$

After applying Y to both sides of (6.1.20), we can see that g lies in $\ker Y$ if and only if

$$\sum_{y \in \mathscr{C}} g_y y = 0. \tag{6.1.21}$$

Moreover, it is not difficult to show that g lies in $\operatorname{span}(\Delta^{\rightarrow})$ (or, equivalently, $\operatorname{span}(\Delta^{\sim})$) if and only if

$$\sum_{y \in \mathscr{L}} g_y = 0 \quad \forall \mathscr{L} \in \mathscr{C}/\sim . \tag{6.1.22}$$

Thus, g is contained in $(\ker Y) \cap \operatorname{span}(\Delta^{\rightarrow})$ if and only if both (6.1.21) and (6.1.22) hold.

In the next lemma I relate the dimension of $(\ker Y) \cap \operatorname{span}(\Delta^{\rightarrow})$ to the deficiency:

Lemma 6.1.4. *If, for a reaction network* $\{\mathscr{S}, \mathscr{C}, \mathscr{R}\}$, $Y: \mathbb{R}^{\mathscr{C}} \to \mathbb{R}^{\mathscr{S}}$ *is the stoichiometric map,* $\Delta^{\rightarrow}$ *is as in* (6.1.10) *and* δ *is the deficiency, then*

$$\delta = \dim [(\ker Y) \cap \operatorname{span}(\Delta^{\rightarrow})]. \tag{6.1.23}$$

In particular, if the deficiency is zero then

$$(\ker Y) \cap \operatorname{span}(\Delta^{\rightarrow}) = \{0\}. \tag{6.1.24}$$

Proof. Let $Y': \operatorname{span}(\Delta^{\rightarrow}) \to \mathbb{R}^{\mathscr{S}}$ be the restriction of Y to $\operatorname{span}(\Delta^{\rightarrow})$. From the standard result relating the dimensions of the domain, range and kernel of a linear transformation we have

$$\dim \ker Y' = \dim \operatorname{span}(\Delta^{\rightarrow}) - \dim \operatorname{rng} Y'. \tag{6.1.25}$$

Note that

$$\operatorname{rng} Y' = Y[\operatorname{span}(\Delta^{\rightarrow})] = \operatorname{span}\{y' - y \in \mathbb{R}^{\mathscr{S}} \mid y \to y\}. \tag{6.1.26}$$

Thus, the range of Y' coincides with the stoichiometric subspace, and so its dimension is the rank s of the network. From this, (6.1.13) and (6.1.25) we obtain

$$\dim [(\ker Y) \cap \operatorname{span}(\Delta^{\rightarrow})] = \dim \ker Y' = n - \ell - s = \delta. \tag{6.1.27}$$

The last sentence of the lemma is a trivial consequence of (6.1.23). □

Remark 6.1.5. Let $\{\mathscr{S}, \mathscr{C}, \mathscr{R}\}$ be a reaction network *of deficiency zero*, and let α be an arbitrary element of $\mathbb{R}^{\mathscr{R}}$. From Lemma 6.1.4 and the discussion at the beginning of Remark 6.1.4 it is evident that a vector $x \in \mathbb{R}^{\mathscr{C}}$ satisfies the equation $YA_\alpha x = 0$ if and only if x satisfies the equation $A_\alpha x = 0$. In other words, for a deficiency-zero network the kernel of A_α is not only contained in but actually coincides with the kernel of YA_α.

There is one more feature of the map A_α that will be useful to have on record. Suppose that, for a reaction network $\{\mathscr{S}, \mathscr{C}, \mathscr{R}\}$, P and Q are subsets of $\mathscr{C}$. The symbol $P \to Q$ is used to denote the set of reactions defined as follows:

$$P \to Q := \{y \to y' \in \mathscr{R} \mid y \in P, y' \in Q\}. \tag{6.1.28}$$

In particular, $\mathscr{C} \to \{y\}$ is the set of all reactions having y as the product complex, and $\{y\} \to \mathscr{C}$ is the set of all reactions having y as the reactant complex. When P is a subset of $\mathscr{C}$, the symbol P' denotes the complement of P in $\mathscr{C}$.

Lemma 6.1.5. *Let $\{\mathscr{S}, \mathscr{C}, \mathscr{R}\}$ be a reaction network, let α be an element of $\mathbb{R}^{\mathscr{R}}$, and let $A_\alpha: \mathbb{R}^{\mathscr{C}} \to \mathbb{R}^{\mathscr{C}}$ be as in* (6.1.2). *If x and z are elements of $\mathbb{R}^{\mathscr{C}}$ related by*

$$z = A_\alpha x, \tag{6.1.29}$$

then, for each $P \subset \mathscr{C}$,

$$\sum_{y \in P} z_y = \sum_{P' \to P} \alpha_{y' \to y} x_{y'} - \sum_{P \to P'} \alpha_{y \to y'} x_y. \tag{6.1.30}$$

Proof. From (6.1.2) it is not difficult to see that, for each $y \in \mathscr{C}$,

$$z_y = \sum_{\mathscr{C} \to \{y\}} \alpha_{y' \to y} x_{y'} - \sum_{\{y\} \to \mathscr{C}} \alpha_{y \to y'} x_y. \tag{6.1.31}$$

If P is a subset of $\mathscr{C}$, it follows from (6.1.31) that

$$\sum_{y \in P} z_y = \sum_{\mathscr{C} \to P} \alpha_{y' \to y} x_{y'} - \sum_{P \to \mathscr{C}} \alpha_{y \to y'} x_y. \tag{6.1.32}$$

Note that

$$\mathscr{C} \to P = (P \to P) \cup (P' \to P),$$

$$P \to \mathscr{C} = (P \to P) \cup (P \to P').$$

From this and (6.1.32) the desired result follows.

6.2. *Proof of Proposition 5.2 when $\ell = t = 1$*

Here I prove the "only if" part of Proposition 5.2 (reformulated as in § 6.1) for reaction networks that have just one linkage class. In this case, condition (ii) of Theorem 4.2 is satisfied trivially, and so only conditions (i) and (iii) assume importance. For a network having just one linkage class, condition (i) amounts to a requirement that the deficiency of the network be either zero or one. Condition (iii) amounts to a requirement that the network have just one terminal strong-linkage class.

Thus, *I consider a reaction network $\{\mathscr{S}, \mathscr{C}, \mathscr{R}\}$ of deficiency zero or one, and I suppose that $\Lambda \subset \mathscr{C}$ is the only terminal strong-linkage class.* (The sole linkage class coincides with the set of complexes.) The vector space $\mathbb{R}^{\mathscr{S}}$ is presumed to be equipped with a scalar product, "$\cdot$" (not necessarily the standard one), and $\phi \in \mathbb{R} \to \mathbb{R}$ is understood to be strictly monotonic. *For the sake of definiteness, I take $\phi(\cdot)$ to be increasing.* (The proof of Proposition 5.2 for decreasing $\phi(\cdot)$ is

virtually identical.) In what follows, Y is again the stoichiometric map for the network, and $\omega_{\mathscr{C}}$ is as in (6.1.4).

Let $\kappa \in \mathbb{P}^{\mathscr{R}}$ satisfy the condition

$$\omega_{\mathscr{C}} \in \ker Y A_\kappa, \tag{6.2.1}$$

where A_κ is as in (6.1.2). My objective is to show that $\mu \in \mathbb{R}^{\mathscr{S}}$ satisfies the condition

$$\sum_{y \in \mathscr{C}} \phi(y \cdot \mu)\omega_y \in \ker Y A_\kappa \tag{6.2.2}$$

only if μ is orthogonal to the stoichiometric subspace for the network.

Remark 6.2.1. To say that μ is orthogonal to the stoichiometric subspace is to say that μ is orthogonal to every reaction vector. (That is, $(y' - y)\cdot\mu = 0$ whenever $y \to y'$.) For a reaction network having just one linkage class this is equivalent to a requirement that $y \cdot \mu = y' \cdot \mu$ for all y and y' in $\mathscr{C}$ (Remark 3.3).

I begin by noting that when $\omega_{\mathscr{C}}$ lies not only in $\ker Y A_\kappa$ but also in $\ker A_\kappa$ we have

$$A_\kappa \omega_{\mathscr{C}} = \sum_{\mathscr{R}} \kappa_{y \to y'}(\omega_{y'} - \omega_y) = 0, \tag{6.2.3}$$

and so condition (5.15) in Proposition 5.3 is satisfied. In this case, the conclusion of Proposition 5.2 already obtains.

Thus, *I suppose that $\omega_{\mathscr{C}}$ is not contained in* $\ker A_\kappa$. Recall that the network under study is presumed to have a deficiency of either zero or one. Since $\omega_{\mathscr{C}}$ is not contained in $\ker A_\kappa$, it is evident from (6.2.1) that the kernels of A_κ and $Y A_\kappa$ do not coincide. In this case, the network can *only* have a deficiency of one (Remark 6.1.5). From Lemma 6.1.3 it follows that

$$\dim \ker Y A_\kappa = 2.$$

I want to use a basis for $\ker Y A_\kappa$ that has especially attractive properties. Recall that Λ is the terminal strong-linkage class in the network under study. Let b be an element of $\mathbb{R}^{\mathscr{C}}$ such that

$$b \in \ker A_\kappa, \tag{6.2.4a}$$

$$b_y > 0 \quad \forall y \in \Lambda, \tag{6.2.4b}$$

$$b_y = 0 \quad \forall y \notin \Lambda. \tag{6.2.4c}$$

(Lemma 6.1.1 ensures that there is such a vector and that all such vectors are identical up to multiplication by a positive constant.) By supposition, $\omega_{\mathscr{C}}$ does not lie in $\ker A_\kappa$, and so $\omega_{\mathscr{C}}$ and b cannot be colinear. On the other hand, both vectors lie in $\ker Y A_\kappa$, whereupon $\{\omega_{\mathscr{C}}, b\}$ is a basis for $\ker Y A_\kappa$.

Now suppose that $\mu \in \mathbb{R}^{\mathscr{S}}$ satisfies condition (6.2.2). In this case there is precisely one pair of numbers, ξ and η, such that

$$\sum_{y \in \mathscr{C}} \phi(y \cdot \mu)\omega_y = \xi \omega_{\mathscr{C}} + \eta b. \tag{6.2.5a}$$

This is equivalent to

$$\phi(y \cdot \mu) = \xi + \eta b_y \quad \forall y \in \mathscr{C}. \tag{6.2.5b}$$

Remark 6.2.2. From (6.2.5b), (6.2.4c) and the strict monotonicity of $\phi(\cdot)$ it follows that $y \cdot \mu = y' \cdot \mu$ when neither y nor y' lies in the terminal strong-linkage class Λ.

I want to show that μ is orthogonal to the stoichiometric subspace for the network or, what amounts to the same thing, that $y \cdot \mu = y' \cdot \mu$ for all y and y' in $\mathscr{C}$. Since $\phi(\cdot)$ is strictly monotonic (and therefore injective), *this will be achieved if I can show that* η *in* (6.2.5) *can only be zero.* In fact, I shall show that η can be neither positive nor negative.

To begin, I arrange the complexes in a sequence $y(1), y(2), \ldots, y(n)$ having the property that

$$b_{y(1)} \geqq b_{y(2)} \geqq b_{y(3)} \geqq \cdots \geqq b_{y(n)}. \tag{6.2.6}$$

Remark 6.2.3. The number of complexes in the terminal strong-linkage class Λ is denoted by m. From (6.2.4) and (6.2.6) it is evident that the set $\{y(1), y(2), \ldots, y(m)\}$ coincides with Λ.

Remark 6.2.4. It is important to note that *inequality must hold somewhere in the string* (*6.2.6*), for otherwise $\omega_{\mathscr{C}}$ and b would be colinear (in contradiction to the supposition that $\omega_{\mathscr{C}} \notin \ker A_\kappa$). In particular, an inequality must be present in the string whether or not $\Lambda = \mathscr{C}$. When $\Lambda \neq \mathscr{C}$ (i.e., when $m \neq n$) the presence of an inequality is already ensured by (6.2.4).

Note that if η in (6.2.5) is positive, the relations shown in (6.2.7)

$$y(1) \cdot \mu \geqq y(2) \cdot \mu \geqq y(3) \cdot \mu \geqq \cdots \geqq y(n) \cdot \mu \tag{6.2.7}$$

are immediate consequences of (6.2.5b), (6.2.6) and the supposition that $\phi(\cdot)$ is (strictly) increasing. Note also that *strict inequality holds in* (6.2.7) *precisely where strict inequality holds in* (6.2.6). On the other hand, if η is negative, we have the relations

$$y(1) \cdot \mu \leqq y(2) \cdot \mu \leqq y(3) \cdot \mu \leqq \cdots \leqq y(n) \cdot \mu, \tag{6.2.8}$$

with strict inequality holding in (6.2.8) *precisely where strict inequality holds in* (6.2.6). I will show that neither of these situations can obtain.

Since $\omega_{\mathscr{C}}$ is not contained in $\ker A_\kappa$, the vector

$$g := A_\kappa \omega_{\mathscr{C}} \tag{6.2.9}$$

is *nonzero.* Since $\omega_{\mathscr{C}}$ is contained in $\ker Y A_\kappa$, it follows from Remark 6.1.4 that g lies in

$$(\ker Y) \cap \operatorname{span}(\Delta^{\rightarrow}).$$

From the same remark it also follows that g must satisfy both of the following equations:

$$\sum_{y \in \mathscr{C}} g_y y = 0, \tag{6.2.10}$$

$$\sum_{y \in \mathscr{C}} g_y = 0. \tag{6.2.11}$$

Some manipulation of (6.2.10), (6.2.11) gives

$$\begin{aligned} & g_{y(1)}(y(1) - y(2)) + (g_{y(1)} + g_{y(2)})(y(2) - y(3)) \\ & \quad + (g_{y(1)} + g_{y(2)} + g_{y(3)})(y(3) - y(4)) \\ & \quad + \cdots + \left(\sum_{j=1}^{n-1} g_{y(j)} \right)(y(n-1) - y(n)) = 0. \end{aligned} \tag{6.2.12}$$

Taking the scalar product of both sides of (6.2.12) with μ, I obtain

$$\sum_{i=1}^{n-1} \left(\sum_{j=1}^{i} g_{y(j)} \right)(y(i) \cdot \mu - y(i+1) \cdot \mu) = 0. \tag{6.2.13}$$

To show that η in (6.2.5) must be zero, I shall argue that should η be positive, each term in the outer sum on the left side of (6.2.13) would be non-negative and at least one would be positive. On the other hand, should η be negative, each term in the sum would be nonpositive and at least one would be negative. In either case (6.2.13) would be contradicted.

I shall need the following lemma, which is written for an arbitrary network (not necessarily the special one under study in this section):

Lemma 6.2.1. *For a reaction network* $\{\mathscr{S}, \mathscr{C}, \mathscr{R}\}$, *let* κ *be an element of* $\mathbb{P}^{\mathscr{R}}$, *let* $A_\kappa : \mathbb{R}^{\mathscr{C}} \to \mathbb{R}^{\mathscr{C}}$ *be as in* (6.1.2), *and let*

$$g := A_\kappa \omega_{\mathscr{C}}. \tag{6.2.14}$$

Moreover, let $\Lambda \subset \mathscr{C}$ *be a terminal strong-linkage class, and let* $b \in \bar{\mathbb{P}}^{\mathscr{C}}$ *be an element of* $\ker A_\kappa$ *with* $\operatorname{supp} b = \Lambda$. *If the complexes of* Λ *are arranged in a sequence* $y(1), y(2), \ldots, y(m)$ *in such a way that*

$$b_{y(1)} \geqq b_{y(2)} \geqq b_{y(3)} \geqq \cdots \geqslant b_{y(m)}, \tag{6.2.15}$$

then, for $i = 1, 2, \ldots, m$,

$$\sum_{j=1}^{i} g_{y(j)} \geqq 0. \tag{6.2.16}$$

In fact, for each $1 \leqq i < m$, *inequality holds in* (6.2.16) *if* $b_{y(i)}$ *is greater than* $b_{y(i+1)}$. *When* $i = m$, *inequality holds in* (6.2.16) *if and only if* Λ *is smaller than the linkage class containing it.*

Remark 6.2.5. The conclusion of the lemma depends only upon the stipulation that $\kappa_{y \to y'}$ be positive for each $y \to y' \in \mathscr{R}$. Condition (6.2.1) plays no role.

Proof of Lemma 6.2.1. Let P be an arbitrary subset of $\mathscr{C}$, and let P' be its complement. Since $A_\kappa \omega_{\mathscr{C}} = g$ and $A_\kappa b = 0$, Lemma 6.1.5 implies that

$$\sum_{P' \to P} \kappa_{y' \to y} - \sum_{P \to P'} \kappa_{y \to y'} = \sum_{y \in P} g_y, \tag{6.2.17}$$

$$\sum_{P' \to P} \kappa_{y' \to y} b_{y'} - \sum_{P \to P'} \kappa_{y \to y'} b_y = 0. \tag{6.2.18}$$

By identifying P with the set $\Lambda = \{y(1), y(2), \ldots, y(m)\}$, I first prove (6.2.16) for the case $i = m$. (The last sentence of the lemma is a by-product of the argument.) Since Λ is a terminal strong-linkage class, there are no reactions in the set $\Lambda \to \Lambda'$. In this case, (6.2.17) reduces to

$$\sum_{\Lambda' \to \Lambda} \kappa_{y' \to y} = \sum_{j=1}^{m} g_{y(j)}. \tag{6.2.19}$$

Note that $\kappa_{y' \to y}$ is positive for each $y \to y' \in \mathscr{R}$. If Λ is smaller than the linkage class containing it, the set $\Lambda' \to \Lambda$ is not empty, in which case both sides of (6.2.19) are positive. On the other hand, if Λ coincides with the linkage class containing it, the set $\Lambda' \to \Lambda$ is empty. In this case, both sides of (6.2.19) are zero.

To prove the rest of the lemma, I identify P in (6.2.17) and (6.2.18) with the set $I := \{y(1), y(2), \ldots, y(i)\}$, where i is a fixed positive integer less than m. In this case, (6.2.15) and (6.2.18) imply that

$$b_{y(i+1)} \left(\sum_{I' \to I} \kappa_{y' \to y} \right) - b_{y(i)} \left(\sum_{I \to I'} \kappa_{y \to y'} \right) \geqq 0. \tag{6.2.20}$$

Since

$$b_{y(i)} \geqq b_{y(i+1)}, \tag{6.2.21}$$

it follows from (6.2.20) that

$$\sum_{I' \to I} \kappa_{y' \to y} - \sum_{I \to I'} \kappa_{y \to y'} \geqq 0 \tag{6.2.22}$$

and, moreover, that inequality in (6.2.21) implies inequality in (6.2.22). This and (6.2.17) give (6.2.16) with inequality holding in (6.2.16) when inequality holds in (6.2.21). □

For the special network under study in this section, I can now argue that η in (6.2.5) can only be zero. Were η positive, the relations in (6.2.7) would obtain with strict inequality holding in (6.2.7) precisely where strict inequality holds in (6.2.6). From Remark 6.2.2 and Lemma 6.2.1, it would then follow that each of the terms in the outer sum on the left side of (6.2.13) is non-negative. Moreover, it would follow from Remark 6.2.4 and the same lemma that at least one term is positive. Thus, equation (6.2.13) would be contradicted. Were η negative, the relations in (6.2.8) would obtain, and we would be led to a similar contradiction of (6.2.13).

Since η must be zero, it follows from (6.2.5b) and the strict monotonicity of $\phi(\cdot)$ that $y \cdot \mu = y' \cdot \mu$ for all y and y' in $\mathscr{C}$. This is to say that μ is orthogonal to the stoichiometric subspace, which is what we set out to prove.

6.3. Proof of Proposition 5.2 for an Arbitrary Number of Linkage Classes

I can now complete the proof of Proposition 5.2. In fact, I shall state and prove a slightly broader version of the proposition. This will prepare the way for the improved versions of Theorems 4.2 and 4.3 given in Appendix A.

I need a small amount of new vocabulary. A *partition of a reaction network* $\{\mathscr{S}, \mathscr{C}, \mathscr{R}\}$ is specified by a family of subnetworks, $\{\mathscr{S}, \mathscr{C}^i, \mathscr{R}^i\}_{i \in I}$, such that $\{\mathscr{R}^i\}_{i \in I}$ is a partition of $\mathscr{R}$. The partition is *direct* if

$$s = \sum_{i \in I} s^i, \tag{6.3.1}$$

where s is the rank of the parent network and s^i is the rank of subnetwork $\{\mathscr{S}, \mathscr{C}^i, \mathscr{R}^i\}$. If S is the stoichiometric subspace of the parent network and if $\{S^i\}_{i \in I}$ is the collection of stoichiometric subspaces associated with the subnetworks, we have

$$S = \sum_{i \in I} S^i. \tag{6.3.2}$$

Moreover, the subspace sum is direct precisely when the network partition is direct.

The following lemma improves Lemma 5.2.

Lemma 6.3.1. *Suppose that the reaction network $\{\mathscr{S}, \mathscr{C}, \mathscr{R}\}$ admits a direct partition into subnetworks such that each subnetwork has just one linkage class. Let κ be an element of $\mathbb{P}^{\mathscr{R}}$ that satisfies the condition*

$$\sum_{\mathscr{R}} \kappa_{y \to y'}(y' - y) = 0, \tag{6.3.3}$$

and let $\mathbb{R}^{\mathscr{S}}$ be equipped with a scalar product (not necessarily the standard one). For any function $\phi : \mathbb{R} \to \mathbb{R}$, an element $\mu \in \mathbb{R}^{\mathscr{S}}$ satisfies the equation

$$\sum_{\mathscr{R}} \kappa_{y \to y'} \phi(y \cdot \mu)(y' - y) = 0 \tag{6.3.4}$$

if μ is orthogonal to the stoichiometric subspace of the network.

Proof. Suppose that the partition $\{\mathscr{S}, \mathscr{C}^i, \mathscr{R}^i\}_{i \in I}$ has the stated properties. As before, I denote by S the stoichiometric subspace for the network $\{\mathscr{S}, \mathscr{C}, \mathscr{R}\}$ and by S^i the stoichiometric subspace for the subnetwork $\{\mathscr{S}, \mathscr{C}^i, \mathscr{R}^i\}$.

Note that (6.3.3) and (6.3.4) are, respectively, equivalent to

$$\sum_{i\in I}\left[\sum_{\mathscr{R}^i} \kappa_{y\to y'}(y'-y)\right]=0,$$

$$\sum_{i\in I}\left[\sum_{\mathscr{R}^i} \kappa_{y\to y'}\phi(y\cdot\mu)(y'-y)\right]=0.$$

In each of these equations the sum over $\mathscr{R}^i$ takes values in S^i. Because the partition is direct, (6.3.3) and (6.3.4) are, respectively, equivalent to

$$\sum_{\mathscr{R}^i} \kappa_{y\to y'}(y'-y)=0 \quad \forall\, i\in I, \tag{6.3.3}'$$

$$\sum_{\mathscr{R}^i} \kappa_{y\to y'}\phi(y\cdot\mu)(y'-y)=0 \quad \forall\, i\in I. \tag{6.3.4}'$$

Suppose that $\mu\in\mathbb{R}^{\mathscr{S}}$ is orthogonal to the stoichiometric subspace for the network. Then $y\cdot\mu=y'\cdot\mu$ whenever y and y' are linked (Remark 3.3). Since each subnetwork has just one linkage class, it follows that, for each $i\in I$, $y\cdot\mu=y'\cdot\mu$ whenever y and y' are both members of $\mathscr{C}^i$. This and (6.3.3)′ imply (6.3.4)′. □

I shall prove the following proposition, of which Proposition 5.2 is an immediate consequence.

Proposition 6.3.1. *Suppose that the reaction network $(\mathscr{S},\mathscr{C},\mathscr{R})$ admits a partition into subnetworks such that*

(i) *the deficiency of each subnetwork is either zero or one,*

(ii) *the partition is direct,*

(iii) *each subnetwork has just one terminal strong-linkage class (and, therefore, just one linkage class).*

Let κ be an element of $\mathbb{P}^{\mathscr{R}}$ that satisfies the condition

$$\sum_{\mathscr{R}} \kappa_{y\to y'}(y'-y)=0, \tag{6.3.3}$$

let $\mathbb{R}^{\mathscr{S}}$ be equipped with a scalar product (not necessarily the standard one), and let $\phi:\mathbb{R}\to\mathbb{R}$ be continuous and strictly monotonic. An element $\mu\in\mathbb{R}^{\mathscr{S}}$ satisfies the equation

$$\sum_{\mathscr{R}} \kappa_{y\to y'}\phi(y\cdot\mu)(y'-y)=0 \tag{6.3.4}$$

if and only if μ is orthogonal to the stoichiometric subspace for the network.

Proof. The "if" assertion already follows from Lemma 6.3.1.

To prove the "only if" part, I suppose that the partition $(\mathscr{S},\mathscr{C}^i,\mathscr{R}^i)_{i\in I}$ has the properties given in the proposition statement. Again I denote by S the stoichiometric subspace for the network $(\mathscr{S},\mathscr{C},\mathscr{R})$ and by S^i the stoichiometric subspace for the subnetwork $(\mathscr{S},\mathscr{C}^i,\mathscr{R}^i)$. As in the proof of Lemma 6.3.1, it is worth noting that

(6.3.3) and (6.3.4) are equivalent to

$$\sum_{\mathscr{R}^i} \kappa_{y \to y'}(y' - y) = 0 \quad \forall i \in I, \tag{6.3.3}'$$

$$\sum_{\mathscr{R}^i} \kappa_{y \to y'} \phi(y \cdot \mu)(y' - y) = 0 \quad \forall i \in I. \tag{6.3.4}'$$

Suppose that μ satisfies (6.3.4)′ but is not orthogonal to S. In this case, it follows from (6.3.2) that, for some $j \in I$,

$$\mu \notin (S^j)^{\perp}. \tag{6.3.5}$$

By supposition, we have

$$\sum_{\mathscr{R}^j} \kappa_{y \to y'}(y' - y) = 0, \tag{6.3.6}$$

$$\sum_{\mathscr{R}^j} \kappa_{y \to y'} \phi(y \cdot \mu)(y' - y) = 0. \tag{6.3.7}$$

By virtue of (i) and (iii) above, the reaction network $(\mathscr{S}, \mathscr{C}^j, \mathscr{R}^j)$ has just one linkage class and satisfies conditions (i) and (iii) of Proposition 5.2. In Section 6.2 it was established that, for such a network, the conclusion of Proposition 5.2 obtains. In particular, (6.3.5)–(6.3.7) cannot hold simultaneously. We have a contradiction. □

It remains to be argued that Proposition 5.2 emerges as a corollary of Proposition 6.3.1. The following lemma is simple, but it is worth having on record.

Lemma 6.3.2. *A reaction network that satisfies condition* (ii) *of Proposition 5.2 admits a direct partition into subnetworks such that each subnetwork has just one linkage class. Moreover, if the reaction network also satisfies conditions* (i) *and* (iii) *of Proposition 5.2, then it admits a partition meeting all the requirements of Proposition 6.3.1.*

Proof. Let $(\mathscr{S}, \mathscr{C}, \mathscr{R})$ be a reaction network, and consider the partition $(\mathscr{S}, \mathscr{C}^{\mathscr{L}}, \mathscr{R}^{\mathscr{L}})_{\mathscr{L} \in \mathscr{C}/\sim}$, where $\mathscr{C}^{\mathscr{L}} := \mathscr{L}$ and

$$\mathscr{R}^{\mathscr{L}} := \{y \to y' \in \mathscr{R} \mid y \in \mathscr{L}, y' \in \mathscr{L}\}.$$

(In other words, with each linkage class we associate a subnetwork in the obvious way.) If the network $(\mathscr{S}, \mathscr{C}, \mathscr{R})$ satisfies condition (ii) of Proposition 5.2, then the partition is direct (Remark 2.11). Moreover, each subnetwork has just one linkage class. If the network satisfies conditions (i) and (iii) of Proposition 5.2, it is evident that the partition given here satisfies all the requirements stated in Proposition 6.3.1. □

Having completed the proof of Proposition 5.2, I have, in effect, proved all of Theorem 4.3 and most of Theorem 4.2. What remains to be shown is the existence

of a positive equilibrium when the network described in Theorem 4.2 is weakly reversible. This is the subject of Section 8.

Section 7 amounts to a digression. Recall that the "if" part of Proposition 5.2 derived in Section 5 solely from a stipulation that the deficiency of the network be the sum of the deficiencies of its individual linkage classes. I want to show that, for networks which satisfy this condition (or, in fact, the weaker condition stated in Lemma 6.3.1), there is a certain unformity in the way equilibria are distributed among the positive stoichiometric compatibility classes.

7. Digression: The Distribution of Equilibria for Mass-Action Systems

For a mass-action system it need not be true that all positive stoichiometric compatiblity classes contain the same number of equilibria. For example, it is possible to assign fixed rate constants to network (2.10) in such a way that there are positive stoichiometric compatibility classes containing one, two and three equilibria. Moreover, for any assignment of rate constants to network (4.11), there are positive stoichiometric compatibility classes containing no equilibrium, one equilibrium and two equilibria.

On the other hand, Theorem 4.2 describes a class of networks for which the distribution among the positive stoichiometric compatibility classes is invariably uniform. When a network satisfies conditions (i), (ii) and (iii) in the theorem statement, we can be sure each positive stoichiometric compatibility class contains precisely one equilibrium or else that no positive stoichiometric compatibility class contains an equilibrium.

I want to argue here that condition (ii) *by itself* (in fact, a somewhat weaker condition) ensures that, for a mass-action system, *all positive stoichiometric compatibility classes contain the same number of equilibria.* Taken with condition (ii), conditions (i) and (iii) serve to place a bound on that number.

For example, the (deficiency-two) network (2.11) fails to satisfy condition (i). There are, in fact, assignments of rate constants for which three equilibria are admitted within a positive stoichiometric compatibility class [HJ]. For any such assignment it happens that *every* positive stoichiometric compatibility class contains three equilibria. Note that network (2.11) satisfies condition (ii) trivially, as does any reaction network having just one linkage class.

The uniform distribution of equilibria among the positive stoichiometric compatibility classes is ensured by Proposition 7.1, in which $\mathbb{R}^{\mathscr{S}}$ carries the standard scalar product. (Recall from §6.3 that networks that satisfy condition (ii) of Theorem 4.2 also satisfy the condition given in the first sentence of the proposition statement.)

Proposition 7.1. *Suppose that the reaction network* $(\mathscr{S}, \mathscr{C}, \mathscr{R})$ *admits a direct partition such that each subnetwork in the partition has just one linkage class. Suppose also that, for* $k \in \mathbb{P}^{\mathscr{R}}$, *the mass-action system* $(\mathscr{S}, \mathscr{C}, \mathscr{R}, k)$ *admits a positive equilibrium,* c^*. *If* $S \subset \mathbb{R}^{\mathscr{S}}$ *is the stoichiometric subspace for the network, then every element of the set*

$$(c \in \mathbb{P}^{\mathscr{S}} \mid \ln c - \ln c^* \in S^{\perp})$$

is also an equilibrium. Moreover, there is a bijective correspondence between the set of equilibria in one positive stoichiometric compatibility class and the set of equilibria in any other positive stoichiometric compatibility class.

Proof. For each $a \in \mathbb{P}^{\mathscr{S}}$ let

$$Q(a) := \{c \in \mathbb{P}^{\mathscr{S}} \mid \ln c - \ln a \in S^{\perp}\}. \tag{7.1}$$

Recall that, for arbitrary $a \in \mathbb{P}^{\mathscr{S}}$, Proposition 5.1 asserts the existence of precisely one element of the set $Q(a)$ in each positive stoichiometric compatibility class. It is easy to see that

$$b \in Q(a) \text{ implies that } a \in Q(b). \tag{7.2}$$

By supposition, $c^* \in \mathbb{P}^{\mathscr{S}}$ is an equilibrium of the mass action system $(\mathscr{S}, \mathscr{C}, \mathscr{R}, k)$. Thus, we have

$$\sum_{\mathscr{R}} k_{y \to y'} (c^*)^y (y' - y) = 0. \tag{7.3}$$

When $\kappa_{y \to y'}$ in Lemma 6.3.1 is identified with $\kappa_{y \to y'} (c^*)^y$ and $\phi(\cdot)$ is taken to be the exponential function, the lemma asserts that $c \in \mathbb{P}^{\mathscr{S}}$ satisfies the equation

$$\sum_{\mathscr{R}} k_{y \to y'} (c^*)^y (\exp[y \cdot (\ln c - \ln c^*)]) (y' - y) = 0 \tag{7.4}$$

when $(\ln c - \ln c^*)$ lies in $S^{\perp}$. On the other hand, (7.4) is equivalent to

$$\sum_{\mathscr{R}} k_{y \to y'} (c)^y (y' - y) = 0, \tag{7.5}$$

which is to say that c is an equilibrium. Thus, I have shown that, *when $c^* \in \mathbb{P}^{\mathscr{S}}$ is an equilibrium, every element of the set $Q(c^*)$ is an equilibrium.*

By virtue of Proposition 5.1, each positive stoichiometric compatibility class contains precisely one member of $Q(c^*)$. (A positive stoichiometric compatibility class might contain other equilibria as well, those that are not members of $Q(c^*)$.)

Now suppose that E° and $E^{\dagger}$ are the sets of equilibria in two distinct positive stoichiometric compatibility classes. Let $q: E^{\circ} \to E^{\dagger}$ be the map that assigns to each $c^{\circ} \in E^{\circ}$ the (unique) element of $E^{\dagger}$ contained in $Q(c^{\circ})$. I want to show that $q(\cdot)$ is bijective.

To see that $q(\cdot)$ is injective, suppose that, on the contrary, c_1° and c_2° are distinct elements of E° with $q(c_1^{\circ}) = q(c_2^{\circ})$. From (7.2) both c_1° and c_2° are members of $Q(q(c_1^{\circ}))$. From Proposition 5.1, however, $Q(q(c_1^{\circ}))$ meets the positive stoichiometric compatibility class containing both c_1° and c_2° in precisely one point. We have a contradiction.

To see that $q(\cdot)$ is surjective, suppose that $c^{\dagger}$ is a member of $E^{\dagger}$. Note that $Q(c^{\dagger})$ consists entirely of equilibria and meets the positive stoichiometric compatibility class containing E° in precisely one point. In other words, E° contains precisely one point of $Q(c^{\dagger})$. From (7.2) it is easy to see that this point is mapped by $q(\cdot)$ into $c^{\dagger}$.

Thus, $q(\cdot)$ gives a bijective correspondence between elements of E° and elements of $E^\dagger$. □

8. Weak Reversibility and the Existence of a Positive Equilibrium

The last sentence of Theorem 4.2 remains to be proved. I want to show that, for a *weakly reversible* reaction network that satisfies conditions (i) and (ii) in the theorem statement, each assignment of rate constants gives rise to a (strictly) positive equilibrium for the corresponding mass-action differential equations. (Recall that a weakly reversible network satisfies condition (iii) trivially.)

The proof is given in two parts. In the first part I demonstrate the existence of a positive equilibrium for weakly reversible networks that satisfy condition (i) and have just one linkage class. (For networks having just one linkage-class, condition (ii) is satisfied trivially.) Then, in the second part, I extend the result for a single linkage class to networks having more than one linkage class.

8.1. Networks Having Just One Linkage Class

Here I suppose that $(\mathscr{S}, \mathscr{C}, \mathscr{R})$ is a *weakly reversible* reaction network that has just one linkage class. I also suppose that condition (i) of Theorem 4.2 is satisfied, which is to say that *the network has a deficiency of zero or one.* Moreover, I take k to be an arbitrary element of $\mathbb{P}^{\mathscr{R}}$. I want to show that the mass-action system $\{\mathscr{S}, \mathscr{C}, \mathscr{R}, k\}$ admits a (strictly) positive equilibrium. That is, I want to prove the existence of a composition $c \in \mathbb{P}^{\mathscr{S}}$ which satisfies the equation

$$\sum_{\mathscr{R}} k_{y \to y'} (c)^y (y' - y) = 0, \tag{8.1.1}$$

where

$$(c)^y := \prod_{\sigma \in \mathscr{S}} (c_\sigma)^{y_\sigma}. \tag{8.1.2}$$

It is not difficult to see that (8.1.1) is equivalent to the inclusion

$$\sum_{y \in \mathscr{C}} (e^{y \cdot \ln c})\, \omega_y \in \ker Y A_k \cap \mathbb{P}^{\mathscr{C}}. \tag{8.1.3}$$

Here $Y : \mathbb{R}^{\mathscr{C}} \to \mathbb{R}^{\mathscr{S}}$ is the stoichiometric map for the network, $A_k : \mathbb{R}^{\mathscr{C}} \to \mathbb{R}^{\mathscr{C}}$ is the linear map defined in (6.1.2), $\{\omega_y \mid y \in \mathscr{C}\}$ is the standard basis for $\mathbb{R}^{\mathscr{C}}$, and "$\cdot$" indicates the standard scalar product in $\mathbb{R}^{\mathscr{S}}$. (Throughout this section, both $\mathbb{R}^{\mathscr{S}}$ and $\mathbb{R}^{\mathscr{C}}$ are understood to carry their standard scalar products.)

The weakly reversible network under study has just one terminal strong-linkage class; it consists of the entire set of complexes. *From Lemma 6.1.1 it follows that* $(\ker A_k) \cap \mathbb{P}^{\mathscr{C}}$ *(and, therefore,* $(\ker Y A_k) \cap \mathbb{P}^{\mathscr{C}}$*) is not empty.*

By $Y^T : \mathbb{R}^{\mathscr{S}} \to \mathbb{R}^{\mathscr{C}}$ I mean the linear map defined by

$$Y^T z \equiv \sum_{y \in \mathscr{C}} (y \cdot z)\, \omega_y. \tag{8.1.4}$$

It is easy to see that Y^T, in fact, the transpose of Y. That is,

$$x \cdot Y^T z = (Yx) \cdot z \quad \forall x \in \mathbb{R}^{\mathscr{C}}, z \in \mathbb{R}^{\mathscr{S}}. \tag{8.1.5}$$

Lemma 8.1.1. *The following are equivalent:*
(i) *There is a* $c \in \mathbb{P}^{\mathscr{S}}$ *that satisfies* (8.1.3) (*and, therefore,* (8.1.1)).
(ii) *There are* $z \in \mathbb{R}^{\mathscr{S}}$, $\xi \in \mathbb{R}$, *and* $a \in (\ker YA_k) \cap \mathbb{P}^{\mathscr{C}}$ *such that*

$$Y^T z + \xi \omega_{\mathscr{C}} = \ln a. \tag{8.1.6}$$

Proof. (ii) $\Rightarrow$ (i): Let z, ξ and a be as in (ii), take $c \in \mathbb{P}^{\mathscr{S}}$ to satisfy $z = \ln c$, and take $\lambda \in \mathbb{P}$ to satisfy $\xi = -\ln \lambda$. Then

$$Y^T \ln c = \ln a + (\ln \lambda)\omega_{\mathscr{C}} = \ln(\lambda a). \tag{8.1.7}$$

Note that λa lies in $\ker YA_k$ and that

$$Y^T \ln c = \sum_{y \in \mathscr{C}} (y \cdot \ln c)\omega_y. \tag{8.1.8}$$

It follows easily that (8.1.7) implies (8.1.3).

The proof that (i) implies (ii) is similar. □

Lemma 8.1.1 reduces the problem to this: *Show that the set*

$$\Gamma := (\ln a \in \mathbb{R}^{\mathscr{C}} \mid a \in (\ker YA_k) \cap \mathbb{P}^{\mathscr{C}}) \tag{8.1.9}$$

meets the linear subspace

$$U := \operatorname{rng} Y^T + \operatorname{span}(\omega_{\mathscr{C}}) \subset \mathbb{R}^{\mathscr{C}}. \tag{8.1.10}$$

It is not difficult to establish that

$$U = [(\ker Y) \cap \operatorname{span}(\Delta)]^{\perp}, \tag{8.1.11}$$

where

$$\Delta := \{\omega_y - \omega_{y'} \mid y, y' \in \mathscr{C}\}. \tag{8.1.12}$$

For the (single linkage class) network under study, it follows from Lemma 6.1.4 that

$$\delta = \dim[(\ker Y) \cap \operatorname{span}(\Delta)], \tag{8.1.13}$$

where δ is the deficiency of the network. If the deficiency is zero, then, from (8.1.11), U coincides with $\mathbb{R}^{\mathscr{C}}$. In this case, the set Γ certainly meets U, and the existence of a positive equilibrium is established.

Hereafter, then, *I suppose that the deficiency of the network is one.* From (8.1.11) and (8.1.13) it follows that the linear subspace U is a hyperplane in $\mathbb{R}^{\mathscr{C}}$. To show that the (connected) set Γ meets U, I show that there are elements of Γ on both sides of U.

In fact, let g be some fixed nonzero member of the (one-dimensional) linear subspace

$$(\ker Y) \cap \operatorname{span}(\Delta). \tag{8.1.14}$$

I shall show that there are elements of Γ, say γ^+ and γ^-, such that

$$g \cdot \gamma^+ > 0, \quad g \cdot \gamma^- < 0. \tag{8.1.15}$$

From this the existence of a positive equilibrium follows: condition (8.1.15) requires that the connected set Γ contain an element γ° for which

$$g \cdot \gamma^\circ = 0.$$

On the other hand, (8.1.11) and (8.1.13) imply that γ° lies in U. Thus, Γ meets U at least in the point γ°.

I shall begin to study the set Γ by first studying the convex cone $(\ker YA_k) \cap \mathbb{P}^{\mathscr{C}}$. From Lemma 6.1.3 it follows that

$$\dim(\ker YA_k) = 2. \tag{8.1.16}$$

It is not difficult to see that I can choose for $\ker YA_k$ a basis $\{p^1, p^2\} \subset \bar{\mathbb{P}}^{\mathscr{C}}$ such that

$$(\ker YA_k) \cap \mathbb{P}^{\mathscr{C}} = \{\lambda_1 p^1 + \lambda_2 p^2 \mid \lambda_1 > 0,\ \lambda_2 > 0\}. \tag{8.1.17}$$

In fact, p^1 and p^2 lie along the two extreme rays of the closed convex cone $(\ker YA_k) \cap \bar{\mathbb{P}}^{\mathscr{C}}$. Both vectors reside in the boundary of $\bar{\mathbb{P}}^{\mathscr{C}}$. (That is, there are complexes y and y' such that $p^1_y = 0$ and $p^2_{y'} = 0$.)

Since A_k takes values in $\operatorname{span}(\Delta)$ and both p^1 and p^2 lie in $\ker YA_k$, it must be the case that $A_k p^1$ and $A_k p^2$ lie in the (one-dimensional) linear subspace $(\ker Y) \cap \operatorname{span}(\Delta)$. Consequently, there are numbers ξ^1 and ξ^2 such that

$$A_k p^1 = \xi^1 g,\ A_k p^2 = \xi^2 g. \tag{8.1.18}$$

Lemma 8.1.2. *The numbers ξ^1 and ξ^2 are nonzero and of opposite sign.*

Proof. Let x be an element of $\ker A_k \cap \mathbb{P}^{\mathscr{C}}$. Since $\ker A_k$ is contained in $\ker YA_k$, special properties of the basis $\{p^1, p^2\}$ ensure the existence of numbers $\lambda_1 > 0$, $\lambda_2 > 0$ such that

$$x = \lambda_1 p^1 + \lambda_2 p^2. \tag{8.1.19}$$

After first acting on both sides of (8.1.19) with A_k and then invoking (8.1.18), we obtain the relation

$$(\lambda_1 \xi^1 + \lambda_2 \xi^2) g = 0. \tag{8.1.20}$$

Since g is not the zero vector and both λ_1 and λ_2 are positive, either ξ^1 and ξ^2 are nonzero and of opposite sign or else ξ^1 and ξ^2 are both zero.

This second possibility leads to a contradiction: For the weakly reversible single-linkage-class network under study, Lemma 6.1.1 indicates that $\ker A_k$ is one-dimensional. Should both ξ^1 and ξ^2 be zero, it would follow from (8.1.18) that p^1 and p^2 are (colinear) members of $\ker A_k$. But then $\{p^1, p^2\}$ could not be a basis for $\ker YA_k$. □

In preparation for the next lemma, recall that if χ is a subset of $\mathscr{C}$, then $\omega_\chi \in \mathbb{R}^{\mathscr{C}}$ is the characteristic function on χ. Stated differently,

$$\omega_\chi = \sum_{y \in \chi} \omega_y.$$

Recall also that, for $x \in \mathbb{R}^{\mathscr{C}}$, $\operatorname{supp} x := \{y \in \mathscr{C} \mid x_y \neq 0\}$.

Lemma 8.1.3. *Suppose that p is a nonzero element of $\bar{\mathbb{P}}^{\mathscr{C}}$ such that $\operatorname{supp} p \neq \mathscr{C}$. Then*

$$\omega_{\operatorname{supp} p} \cdot A_k p < 0. \tag{8.1.21}$$

Proof. I denote by $(\operatorname{supp} p)'$ the complement of $\operatorname{supp} p$ in $\mathscr{C}$. A straightforward calculation (using the definition of A_k given in (6.1.2) and the orthonormality of the standard basis for $\mathbb{R}^{\mathscr{C}}$) gives the equation

$$\omega_{\operatorname{supp} p} \cdot A_k p = -\sum_{\operatorname{supp} p \to (\operatorname{supp} p)'} k_{y \to y'} p_y. \tag{8.1.22}$$

Here $\operatorname{supp} p \to (\operatorname{supp} p)'$ is the set of reactions of the form $y \to y'$ with $y \in \operatorname{supp} p$ and $y' \in (\operatorname{supp} p)'$. Note that neither $\operatorname{supp} p$ nor $(\operatorname{supp} p)'$ is empty. Since the network under study is weakly reversible and has just one linkage class, the set $\operatorname{supp} p \to (\operatorname{supp} p)'$ is not empty. The conclusion of the lemma follows from the fact that each term in the sum on the right of (8.1.22) is positive. □

Lemma 8.1.4. *With p^1, p^2 and g as before, $\omega_{\operatorname{supp} p^1} \cdot g$ and $\omega_{\operatorname{supp} p^2} \cdot g$ are nonzero and of opposite sign.*

Proof. From (8.1.18) and Lemma 8.1.3

$$\omega_{\operatorname{supp} p^1} \cdot A_k p^1 = \xi^1(\omega_{\operatorname{supp} p^1} \cdot g) < 0, \tag{8.1.23a}$$

$$\omega_{\operatorname{supp} p^2} \cdot A_k p^2 = \xi^2(\omega_{\operatorname{supp} p^2} \cdot g) < 0. \tag{8.1.23b}$$

From Lemma 8.1.2 ξ^1 and ξ^2 are of opposite sign. This and (8.1.23) give the desired result. □

We are now in a position to study the set Γ. Note that

$$\Gamma = \{\ln(\lambda_1 p^1 + \lambda_2 p^2) \in \mathbb{R}^{\mathscr{C}} \mid \lambda_1 > 0, \lambda_2 > 0\}. \tag{8.1.24}$$

I want to examine the sign of

$$g \cdot \ln(\lambda_1 p^1 + \lambda_2 p^2)$$

as λ_1 and λ_2 range over positive values. To begin, I set $\lambda_2 = 1$ and let λ_1 get large. It is not difficult to see that

$$\ln(\lambda_1 p^1 + p^2) = (\ln \lambda_1)\omega_{\operatorname{supp} p^1} + \sum_{y \in \operatorname{supp} p^1} \ln(p_y^1 + (p_y^2/\lambda_1))\omega_y$$

$$+ \sum_{y \in (\operatorname{supp} p^1)'} \ln(p_y^2)\omega_y.$$

From this it is clear that, as λ_1 gets large, $g \cdot \ln(\lambda_1 p^1 + p^2)$ takes the sign of $g \cdot \omega_{\text{supp } p^1}$. In a similar way, I can take $\lambda_1 = 1$ and let λ_2 get large to argue that $g \cdot \ln(p^1 + \lambda_2 p^2)$ eventually takes the sign of $g \cdot \omega_{\text{supp } p^2}$. By virtue of Lemma 8.1.4 we now have

Lemma 8.1.5. *The set Γ contains elements γ^+ and γ^- such that*

$$g \cdot \gamma^+ > 0, \quad g \cdot \gamma^- < 0.$$

Taken together with arguments given earlier in this section, Lemma 8.1.5 ensures the existence of a positive equilibrium.

8.2. Networks Having More than One Linkage Class

In §8.1 I proved the existence of a positive equilibrium for any mass-action system in which the underlying reaction network is weakly reversible, has a deficiency of zero or one and contains just a single linkage class. Here I extend that result to a wider class of weakly reversible networks, a class which contains (but is not limited to) all weakly reversible networks that satisfy the conditions of Theorem 4.2.

To state the extension, I draw on language introduced at the beginning of §6.3:

Proposition 8.2.1. *Suppose that a weakly reversible reaction network $(\mathscr{S}, \mathscr{C}, \mathscr{R})$ admits a partition into subnetworks such that*
(i) *the deficiency of each subnetwork is either zero or one,*
(ii) *the partition is direct,*
(iii) *each subnetwork has just one linkage class.*
Then, for any $k \in \mathbb{P}^{\mathscr{R}}$, the mass-action system $(\mathscr{S}, \mathscr{C}, \mathscr{R}, k)$ admits a positive equilibrium.

Remark 8.2.1. A weakly reversible reaction network that satisfies the conditions of Theorem 4.2 also admits a partition of the kind described in Proposition 8.2.1 (Recall the proof of Lemma 6.3.2.) Thus, proof of the last sentence in Theorem 4.2 will be completed once Proposition 8.2.1 is proved.

For the proof of Proposition 8.2.1 I shall need a little more terminology: If $k \in \mathbb{P}^{\mathscr{R}}$ is a mass-action kinetics for a reaction network $\{\mathscr{S}, \mathscr{C}, \mathscr{R}\}$, then by the *mass-action subsystem corresponding to subnetwork* $\{\mathscr{S}, \mathscr{C}', \mathscr{R}'\}$ I mean the mass-action system $\{\mathscr{S}, \mathscr{C}', \mathscr{R}', k'\}$, where k' is the restriction of k to $\mathscr{R}'$.

When the network in Proposition 8.2.1 is assigned a fixed mass-action kinetics, the results of §8.1 ensure that each of the mass-action subsystems induced by the indicated partition admits a positive equilibrium. To show that the parent mass-action system itself admits a positive equilibrium, I will show that the various mass-action subsystems have a positive equilibrium in common.

Lemma 8.2.1. *Suppose that $\{\mathscr{S}, \mathscr{C}, \mathscr{R}, k\}$ is a mass-action system and that the network $\{\mathscr{S}, \mathscr{C}, \mathscr{R}\}$ admits a direct partition into subnetworks $\{\mathscr{S}, \mathscr{C}', \mathscr{R}'\}$ and*

$\{\mathscr{S}, \mathscr{C}'', \mathscr{R}''\}$. *Suppose further that there are compositions* $c' \in \mathbb{P}^{\mathscr{S}}$ *and* $c'' \in \mathbb{P}^{\mathscr{S}}$ *such that the sets*

$$\{c \in \mathbb{P}^{\mathscr{S}} \mid \ln c - \ln c' \in (S')^{\perp}\}, \tag{8.2.1}'$$

$$\{c \in \mathbb{P}^{\mathscr{S}} \mid \ln c - \ln c'' \in (S'')^{\perp}\} \tag{8.2.1}''$$

consist entirely of equilibria for, respectively, the mass-action subsystems $\{\mathscr{S}, \mathscr{C}', \mathscr{R}', k'\}$ *and* $\{\mathscr{S}, \mathscr{C}'', \mathscr{R}'', k''\}$. *Then the mass-action system* $\{\mathscr{S}, \mathscr{C}, \mathscr{R}, k\}$ admits a positive equilibrium. In fact, there is a composition $c^* \in \mathbb{P}^{\mathscr{S}}$ *such that the set*

$$\{c \in \mathbb{P}^{\mathscr{S}} \mid \ln c - \ln c^* \in S^{\perp}\} \tag{8.2.2}$$

consists entirely of equilibria for $\{\mathscr{S}, \mathscr{C}, \mathscr{R}, k\}$. (*Here S is the stoichiometric subspace for the network* $\{\mathscr{S}, \mathscr{C}, \mathscr{R}\}$, *while S′ and S″ are the stoichiometric subspaces for the subnetworks* $\{\mathscr{S}, \mathscr{C}', \mathscr{R}'\}$ *and* $\{\mathscr{S}, \mathscr{C}'', \mathscr{R}''\}$.)

Proof. It is not difficult to see that any composition which is an equilibrium for both of the mass-action subsystems $\{\mathscr{S}, \mathscr{C}', \mathscr{R}', k'\}$ and $\{\mathscr{S}, \mathscr{C}'', \mathscr{R}'', k''\}$ is, in fact, an equilibrium of the parent system $\{\mathscr{S}, \mathscr{C}, \mathscr{R}, k\}$. Thus, to show that the parent system admits a positive equilibrium, it is enough to show that the sets in (8.2.1) intersect.

It is an easy exercise to show that the affine subspaces

$$\ln c' + (S')^{\perp}, \quad \ln c'' + (S'')^{\perp} \tag{8.2.3}$$

meet if and only if

$$\ln c' - \ln c'' \in (S')^{\perp} + (S'')^{\perp}. \tag{8.2.4}$$

Note that

$$(S')^{\perp} + (S'')^{\perp} = (S' \cap S'')^{\perp}. \tag{8.2.5}$$

Since the network partition is direct, we have $S' \cap S'' = \{0\}$. This and (8.2.5) ensure that

$$(S')^{\perp} + (S'')^{\perp} = \mathbb{R}^{\mathscr{S}}, \tag{8.2.6}$$

so condition (8.2.4) is clearly satisfied. Let $z \in \mathbb{R}^{\mathscr{S}}$ lie in the intersection of the sets in (8.2.3), and let

$$c^* := e^z. \tag{8.2.7}$$

By virtue of (8.2.7) c^* lies in both sets of (8.2.1) and so is an equilibrium of the mass-action system $\{\mathscr{S}, \mathscr{C}, \mathscr{R}, k\}$.

Note that the intersection of the affine subspaces in (8.2.3) is the affine subspace

$$\ln c^* + [(S')^{\perp} \cap (S'')^{\perp}]. \tag{8.2.8}$$

Thus, each member of the set

$$\{c \in \mathbb{P}^{\mathscr{S}} \mid \ln c - \ln c^* \in (S')^{\perp} \cap (S'')^{\perp}\} \tag{8.2.9}$$

is common to both sets of (8.2.1) and so is an equilibrium of the mass action system $\{\mathscr{S}, \mathscr{C}, \mathscr{R}, k\}$. On the other hand,

$$(S')^{\perp} \cap (S'')^{\perp} = (S' + S'')^{\perp} = S^{\perp} \tag{8.2.10}$$

so that (8.2.9) coincides with (8.2.2). □

Lemma 8.2.1 and an inductive argument give:

Lemma 8.2.2. *Suppose that $\{\mathscr{S}, \mathscr{C}, \mathscr{R}, k\}$ is a mass-action system and that the network $\{\mathscr{S}, \mathscr{C}, \mathscr{R}\}$ admits a direct partition into the family of subnetworks $\{\mathscr{S}, \mathscr{C}^i, \mathscr{R}^i\}_{i \in I}$. Suppose further that, for each $i \in I$, there is a composition $c^i \in \mathbb{P}^{\mathscr{S}}$ such that the set*

$$\{c \in \mathbb{P}^{\mathscr{S}} \mid \ln c - \ln c^i \in (S^i)^{\perp}\} \tag{8.2.11}$$

consists entirely of equilibria for the mass-action subsystem $\{\mathscr{S}, \mathscr{C}^i, \mathscr{R}^i, k^i\}$. Then the mass-action system $\{\mathscr{S}, \mathscr{C}, \mathscr{R}, k\}$ admits a positive equilibrium.

I shall also need

Lemma 8.2.3. *Suppose that $\{\mathscr{S}, \mathscr{C}, \mathscr{R}, k\}$ is a mass-action system such that the network $\{\mathscr{S}, \mathscr{C}, \mathscr{R}\}$ admits a direct partition into a family of subnetworks $\{\mathscr{S}, \mathscr{C}^i, \mathscr{R}^i\}_{i \in I}$, each subnetwork having just one linkage class. Suppose further that, for each $i \in I$, the mass-action subsystem $\{\mathscr{S}, \mathscr{C}^i, \mathscr{R}^i, k^i\}$ admits a positive equilibrium (i.e., an equilibrium in $\mathbb{P}^{\mathscr{S}}$). Then the mass-action system $\{\mathscr{S}, \mathscr{C}, \mathscr{R}, k\}$ admits a positive equilibrium.*

Proof. Suppose that $c^i \in \mathbb{P}^{\mathscr{S}}$ is an equilibrium for the mass-action system $\{\mathscr{S}, \mathscr{C}^i, \mathscr{R}^i, k^i\}$. The subnetwork $\{\mathscr{S}, \mathscr{C}^i, \mathscr{R}^i\}$, viewed as a solitary reaction network having just one linkage class, satisfies the condition of Proposition 7.1 trivially. It follows, then, that members of the set

$$\{c \in \mathbb{P}^{\mathscr{S}} \mid \ln c - \ln c^i \in (S^i)^{\perp}\}$$

are all equilibria for $\{\mathscr{S}, \mathscr{C}^i, \mathscr{R}^i, k^i\}$. The existence of a positive equilibrium for the mass-action system $\{\mathscr{S}, \mathscr{C}, \mathscr{R}, k\}$ follows from Lemma 8.2.2. □

Lemma 8.2.4. *In a direct partition of a weakly reversible reaction network each subnetwork is weakly reversible.*

Proof. Consider a direct partition of a weakly reversible network $\{\mathscr{S}, \mathscr{C}, \mathscr{R}\}$, and suppose that $y \to y'$ is a reaction in a particular subnetwork of the partition. I want to show that, in the subnetwork, y' ultimately reacts to y.

Weak reversiblity of the parent network ensures that y' ultimately reacts to y in $\{\mathscr{S}, \mathscr{C}, \mathscr{R}\}$. That is, there is a sequence of complexes in $\mathscr{C}$, say $y(1), \ldots, y(k)$, such that $y(1) = y'$, $y(k) = y$ and such that $\mathscr{R}$ contains the chain

$$y(1) \to y(2) \to \cdots \to y(k). \tag{8.2.12}$$

Note that the reaction vectors corresponding to members of the cycle

$$y(k) \to y(1) \to y(2) \to \cdots \to y(k) \tag{8.2.13}$$

constitute a linearly dependent set in $\mathbb{R}^{\mathscr{S}}$ and, in fact, satisfy the equation

$$(y(k) - y(k-1)) + \cdots + (y(2) - y(1)) + (y' - y) = 0.$$

From this and the fact that the partition is *direct* it follows that the subnetwork containing $y \to y'$ must also contain the reactions shown in (8.2.12). This is to say that, in the subnetwork, y' ultimately reacts to y. □

Proof of Proposition 8.2.1. Suppose that the weakly reversible reaction network $\{\mathscr{S}, \mathscr{C}, \mathscr{R}\}$ admits a partition $\{\mathscr{S}, \mathscr{C}^i, \mathscr{R}^i\}_{i \in I}$ of the kind described in the proposition statement, and let $k \in \mathbb{P}^{\mathscr{R}}$ be a mass-action kinetics for the network. Since each subnetwork in the partition is weakly reversible and has a deficiency of zero or one, the results of §8.1 ensure that, for each $i \in I$, the mass-action subsystem $\{\mathscr{S}, \mathscr{C}^i, \mathscr{R}^i, k^i\}$ admits a positive equilibrium. From Lemma 8.2.3 it follows that there is a positive equilibrium for the mass-action system $\{\mathscr{S}, \mathscr{C}, \mathscr{R}, k\}$. □

9. A Remark about Networks of Deficiency One

It should be clear that the Deficiency-One Theorem can sometimes give information about networks with deficiencies of two or more. (Recall the discussion of network (4.7).) The name of the theorem refers not to the deficiency of an entire network but, rather, to the deficiencies of its linkage classes.

On the other hand, there are networks of deficiency 1 for which the theorem gives no information at all. Deficiency-one networks always satisfy condition (i) of the theorem statement, but they might fail to satisfy conditions (ii) or (iii).

With respect to the their capacity to admit multiple positive equilibria, deficiency-one networks that fail to satisfy condition (iii) are, in some ways, not worth studying: Consider a mass-action system for which the underlying network violates condition (iii) and has a deficiency of one, and suppose that the system admits at least one positive equilibrium. For reasons discussed in Appendix IV of [F4], there generally is a stoichiometric compatibility class that contains an *uncountable* set of positive equilibria. On the other hand, "nearby" mass-action systems for which condition (iii) *is* satisfied behave in a very different way. In particular, the pathology described can normally be perturbed away by adding sufficiently many reactions to make the original network reversible, even when rate constants for the reactions added are taken to be vanishingly small. In this sense, the original system carries with it a kind of structural instability that makes it unsuited to the description of real reactors.

Among the deficiency-one networks that *do* satisfy condition (iii), *those that fail to satisfy the conditions of the Deficiency-One Theorem are precisely those in which each linkage class has a deficiency of zero.* (Condition (ii) is violated.) It turns out that networks of this kind are rather important in applications (especially in the

description of certain catalytic reactors). Some have the capacity to admit multiple equilibria while others do not, and so we are led to the following problem:

Given a deficiency-one network that satisfies condition (iii) *and in which each linkage class has a deficiency of zero, determine whether there is as assignment of rate constants such that the resulting mass-action differential equations admit more than one equilibrium in a positive stoichiometric compatibility class.*

Even in the circumscribed class of networks for which the problem is posed, there is already a great deal of delicacy in the relationship between network structure and the capacity for multiple equilibria. In [F5] I described a procedure for making the required determination, at least when the network in question satisfies certain weak structural conditions. The theory behind that procedure is given in [F6].

Appendix A. An Improvement of the Deficiency One-Theorem

In the proofs of Theorems 4.2 and 4.3 I considered first networks having just one linkage class, and then, in §§ 6.3 and 8.2, I extended the results obtained to networks having several linkage classes. In making the extension, I showed that the conclusions of Theorems 4.1 and 4.2 actually obtain under conditions slightly weaker than those given in the statements of the theorems.

My purpose here is to summarize the more general results. I use language introduced at the beginning of §6.3.

Theorem A.1. *Suppose that the reaction network* $\{\mathscr{S}, \mathscr{C}, \mathscr{R}\}$ *admits a partition into subnetworks such that*

(i) *the deficiency of each subnetwork is either zero or one,*

(ii) *the partition is direct,*

(iii) *each subnetwork has just one terminal strong-linkage class (and, therefore, just one linkage class).*

If, for a particular $k \in \mathbb{P}^{\mathscr{R}}$, *the mass-action system* $\{\mathscr{S}, \mathscr{C}, \mathscr{R}, k\}$ *admits a positive equilibrium, then each positive stoichiometric compatibility class contains* precisely one *equilibrium. Moreover, for each positive equilibrium* c^*, *the stoichiometric subspace and the kernel of* $\partial_c f(c^*, k)$ *have only the zero vector in common. If the network is weakly reversible, then, for* every $k \in \mathbb{P}^{\mathscr{R}}$, *the mass-action system* $\{\mathscr{S}, \mathscr{C}, \mathscr{R}, k\}$ *admits a positive equilibrium.*

By means of a simple example, I want to show that Theorem A.1 really does improve Theorems 4.2 and 4.3 (if only in a modest way). Consider the network

$$2A \leftrightarrows A + B \leftrightarrows 2B \leftrightarrows B + C \leftrightarrows 2C. \tag{A.1}$$

The deficiency of (A.1) is easily calculated to be 2 ($n = 5$, $l = 1$, $s = 2$), and so condition (i) of Theorem 4.2 is not satisfied. Note, however, that (A.1) admits a *direct* partition into a pair of subnetworks

$$2A \leftrightarrows A + B \leftrightarrows 2B,$$
$$2B \leftrightarrows B + C \leftrightarrows 2C,$$

each of which has a deficiency of one. The partition clearly satisfies the requirements of Theorem A.1; and so we can conclude (among other things) that, for any assignment of rate constants to the reactions in network (A.1), the corresponding mass-action differential equations admit precisely one equilibrium in each positive stoichiometric compatibility class.

Appendix B. Proof of Proposition 5.1.

Proposition 5.1 emerges as a corollary of the following proposition. (Recall the notation scheme introduced in Section 1.)

Proposition B.1. *Let I be a finite set, let U be a linear subspace of $\mathbb{R}^I$, and let a and b be elements of $\mathbb{P}^I$. There is a (unique) element $\mu \in U^\perp$ such that*

$$ae^\mu - b$$

is an element of U. (Here $\mathbb{R}^I$ is understood to carry the standard scalar product.)

Proof. By $\varphi : \mathbb{R}^I \to \mathbb{R}$ I mean the function

$$\varphi(x) := \sum_{i \in I} (a_i \exp(x_i) - b_i x_i). \tag{B.1}$$

Straightforward computation shows that the gradient of φ at $x \in \mathbb{R}^I$ is given by

$$\nabla\varphi(x) = ae^x - b \tag{B.2}$$

and that the Hessian of φ at x, $H(x) : \mathbb{R}^I \to \mathbb{R}^I$, is given by

$$H(x)\gamma \equiv (ae^x)\gamma. \tag{B.3}$$

Note that, for each $x \in \mathbb{R}^I$, $H(x)$ is positive-definite: For all nonzero $\gamma \in \mathbb{R}^I$

$$\gamma \cdot H(x)\gamma = \gamma \cdot (\mathrm{ae}^x)\gamma = \sum_{i \in I} a_i \exp(x_i)(\gamma_i)^2 > 0. \tag{B.4}$$

Thus, the function φ is strictly convex.

Next I show that, for any nonzero $x \in \mathbb{R}^I$,

$$\lim_{\alpha \to \infty} \varphi(\alpha x) = \infty. \tag{B.5}$$

Note that

$$\varphi(\alpha x) := \sum_{i \in I} (a_i \exp(\alpha x_i) - \alpha b_i x_i). \tag{B.6}$$

For $x_i \neq 0$, the positivity of a_i and b_i gives

$$\lim_{\alpha \to \infty} (a_i \exp(\alpha x_i) - \alpha b_i x_i) = \infty, \tag{B.7}$$

while for $x_i = 0$ we have

$$a_i \exp(\alpha x_i) - \alpha b_i x_i = a_i \quad \forall \alpha . \tag{B.8}$$

Thus, for $x \neq 0$, (B.6)–(B.8) imply (B.5).

Now let φ° be the restriction of φ to $U^\perp$. Since φ is continuous and convex, so is φ°. The continuity of φ° and a standard result for convex functions ensure that the set

$$C := \{x \in U^\perp \mid \varphi^\circ(x) \leqq \varphi^\circ(0)\} \tag{B.9}$$

is closed and convex (and obviously contains the zero vector). Moreover, it follows from (B.5) that C contains no half-line with endpoint 0. Since, in a finite-dimensional vector space, every unbounded closed convex set containing 0 must contain a half-line with endpoint 0 ([SW, p. 105]), it follows that C is bounded and, therefore, compact.

Thus, there is a vector $\mu \in C$ such that

$$\varphi^\circ(\mu) \leqq \varphi^\circ(x) \quad \forall x \in C. \tag{B.10}$$

In fact, from the definition of C it follows that

$$\varphi^\circ(\mu) \leqq \varphi^\circ(x) \quad \forall x \in U^\perp . \tag{B.11}$$

For all $\gamma \in U^\perp$, therefore,

$$\begin{aligned} 0 &= \frac{\mathrm{d}}{\mathrm{d}\theta} \varphi^\circ(\mu + \theta\gamma)|_{\theta=0} \\ &= \frac{\mathrm{d}}{\mathrm{d}\theta} \varphi(\mu + \theta\gamma)|_{\theta=0} \\ &= \nabla\varphi(\mu)\cdot\gamma . \end{aligned}$$

It follows that $\nabla\varphi(\mu)$ must lie in U. From (B.2) we have the inclusion

$$ae^\mu - b \in U. \tag{B.12}$$

Thus, $\mu \in U^\perp$ has the required property.

To prove that there is only one such element in $U^\perp$, I suppose that $\mu' \in U^\perp$ satisfies the inclusion

$$\mathrm{a}e^{\mu'} - b \in U. \tag{B.13}$$

From (B.12) and (B.13) it follows that

$$a(e^{\mu'} - e^\mu) \in U.$$

Since $\mu' - \mu$ lies in $U^\perp$, we must have

$$\begin{aligned} 0 &= (\mu' - \mu)\cdot[a(e^{\mu'} - e^\mu)] \\ &= \sum_{i \in I} a_i(\mu_i' - \mu_i)[\exp(\mu_i') - \exp(\mu_i)]. \end{aligned} \tag{B.14}$$

Because each a_i is positive and the exponential function is strictly increasing, (B.14) can hold only if $\mu_i' = \mu_i$ for each $i \in I$, that is, only if $\mu' = \mu$. □

I am now in a position to prove

Proposition 5.1. (HORN & JACKSON) *Let $\{\mathscr{S}, \mathscr{C}, \mathscr{R}\}$ be a reaction network with stoichiometric subspace S, and let c^* be an element of $\mathbb{P}^{\mathscr{S}}$. Each positive stoichiometric compatibility class contains precisely one element of the set*

$$E := \{c \in \mathbb{P}^{\mathscr{S}} \mid \ln c - \ln c^* \in S^{\perp}\}. \tag{B.15}$$

Proof. Let p be an arbitrary element of $\mathbb{P}^{\mathscr{S}}$. I begin by showing that E meets the positive stoichiometric compatibility class containing p. Proposition B.1 ensures the existence of $\mu \in S^{\perp}$ such that

$$c^* e^{\mu} - p \in S. \tag{B.16}$$

Now I define $c \in \mathbb{P}^{\mathscr{S}}$ by

$$c := c^* e^{\mu}. \tag{B.17}$$

From (B.16) it is clear that c lies in the positive stoichiometric compatibility class containing p. Taking logarithms in (B.17) I obtain

$$\ln c - \ln c^* = \mu \in S^{\perp}. \tag{B.18}$$

Thus, c lies in E as well.

Now I show that c is the only member of E that lies in the positive stoichiometric compatibility class containing p. Suppose, on the contrary, that c' is another such element of E. Since c' lies in E, the vector

$$\mu' := \ln c' - \ln c^* \tag{B.19}$$

lies in $S^{\perp}$. Note that

$$c' = c^* e^{\mu'}. \tag{B.20}$$

By supposition c' lies in the positive stoichiometric compatibility class containing p. This and (B.20) lead to the inclusion

$$c^* e^{\mu'} - p \in S. \tag{B.21}$$

From (B.16), (B.21) and Proposition B.1 it follows that $\mu' = \mu$, which, in turn, implies that $c' = c$. □

Appendix C. The Deficiency-Zero Theorem: A Sketch of a Proof

Material accumulated in Sections 5 and 6 already takes us well along the way toward a proof of the Deficiency-Zero Theorem. In fact, I can sketch a proof of a somewhat better version with no real increase in difficulty. In the improvement I extend results in the (relatively easy) part (i) to networks endowed with kinetics other than mass-action.

Recall from Section 1 that a *kinetics* for a reaction network $\{\mathscr{S}, \mathscr{C}, \mathscr{R}\}$ is an assignment to each $y \to y' \in \mathscr{R}$ of a *rate function* $\mathscr{K}_{y \to y'}$: $\overline{\mathbb{P}}^{\mathscr{S}} \to \overline{\mathbb{P}}$. Hereafter, *I require of a kinetics that each such function be continuous and that each take strictly positive values on* $\mathbb{P}^{\mathscr{S}}$. (For the purposes of this appendix, even weaker restrictions would do.) The second requirement reflects the idea that each reaction should proceed at a nonzero rate, however slowly, whenever all species in the network have nonzero molar concentrations. When a reaction network $\{\mathscr{S}, \mathscr{C}, \mathscr{R}\}$ is endowed with a kinetics $\{\mathscr{K}_{y \to y'}(\cdot)\}_{y \to y' \in \mathscr{R}}$, the corresponding differential equation is

$$\dot{c} = \sum_{\mathscr{R}} \mathscr{K}_{y \to y'}(c)(y' - y). \tag{C.1}$$

With this as background, I can state the improvement of Theorem 4.1.

Theorem C.1 (The Deficiency-Zero Theorem). *Let* $\{\mathscr{S}, \mathscr{C}, \mathscr{R}\}$ *be a reaction network of deficiency zero.*

(i) *If the network is not weakly reversible, then, for arbitrary kinetics (not necessarily mass-action), the corresponding differential equation admits neither a positive equilibrium nor a periodic orbit in* $\mathbb{P}^{\mathscr{S}}$.

(ii) *If the network is weakly reversible, then, for arbitrary* $k \in \mathbb{P}^{\mathscr{R}}$, *the differential equation for the mass-action system* $\{\mathscr{S}, \mathscr{C}, \mathscr{R}, k\}$ *has the following properties: Each positive stoichiometric compatibility class contains* precisely one *equilibrium; this equilibrium is asymptotically stable; and there is no nontrivial periodic orbit in* $\mathbb{P}^{\mathscr{S}}$.

For our purposes, the central fact about deficiency-zero networks is given in the following lemma:

Lemma C.1. *Suppose that the deficiency of reaction network* $\{\mathscr{S}, \mathscr{C}, \mathscr{R}\}$ *is zero. Then* $\alpha \in \mathbb{R}^{\mathscr{R}}$ *satisfies the equation*

$$\sum_{\mathscr{R}} \alpha_{y \to y'}(y' - y) = 0 \tag{C.2}$$

only if α *also satisfies the equation*

$$\sum_{\mathscr{R}} \alpha_{y \to y'}(\omega_{y'} - \omega_y) = 0. \tag{C.3}$$

(*Here* $\{\omega_y \in \mathbb{R}^{\mathscr{C}} \mid y \in \mathscr{C}\}$ *is the standard basis for* $\mathbb{R}^{\mathscr{C}}$.)

Proof. Suppose that $\alpha \in \mathbb{R}^{\mathscr{R}}$ satisfies (C.2). Letting $Y: \mathbb{R}^{\mathscr{C}} \to \mathbb{R}^{\mathscr{S}}$ be the stoichiometric map for the network, I can rewrite (C.2) as

$$Y\left[\sum_{\mathscr{R}} \alpha_{y \to y'}(\omega_{y'} - \omega_y)\right] = 0. \tag{C.4}$$

Note that the vector in the bracket is a member of span$(\Delta^{\rightarrow})$, where

$$\Delta^{\rightarrow} := \{\omega_{y'} - \omega_y \in \mathbb{R}^{\mathscr{C}} \mid y \to y'\}. \tag{C.5}$$

For a deficiency-zero network, span$(\Delta^{\rightarrow})$ meets the kernel of Y only in the zero vector (Lemma 6.1.4). From this it follows that (C.3) holds. □

The following lemma asserts that, for a network of arbitrary deficiency, there can be a *positive* solution to (C.3) only if the network is weakly reversible.

Lemma C.2. *If, for a reaction network* $\{\mathscr{S}, \mathscr{C}, \mathscr{R}\}$, *there is an element* $\alpha \in \mathbb{P}^{\mathscr{R}}$ *that satisfies the equation*

$$\sum_{\mathscr{R}} \alpha_{y \to y'} (\omega_{y'} - \omega_y) = 0, \tag{C.3}$$

then the network is weakly reversible.

Proof. A proof in a slightly different context is given in [H]. Here I give a different proof based on Lemma 6.1.1. Suppose that $\alpha \in \mathbb{P}^{\mathscr{R}}$ satisfies (C.3), and let $A_\alpha : \mathbb{R}^{\mathscr{C}} \to \mathbb{R}^{\mathscr{C}}$ be as in (6.1.2). Note that (C.3) is equivalent to

$$A_\alpha \omega_{\mathscr{C}} = 0,$$

where $\omega_{\mathscr{C}} \in \mathbb{P}^{\mathscr{C}}$ is the characteristic function on $\mathscr{C}$. (See (6.1.4).) It follows from Lemma 6.1.1 (Remark 6.1.1) that A_α can have an element of $\mathbb{P}^{\mathscr{C}}$ in its kernel only if the network is weakly reversible. □

Taken together, Lemmas C.1 and C.2 give

Lemma C.3. *If, for a deficiency-zero reaction network* $\{\mathscr{S}, \mathscr{C}, \mathscr{R}\}$, *there is an element* $\alpha \in \mathbb{P}^{\mathscr{R}}$ *that satisfies the equation*

$$\sum_{\mathscr{R}} \alpha_{y \to y'} (y' - y) = 0,$$

then the network is weakly reversible.

I am now in a position to prove part (i) of Theorem C.1.

Proof of part (i) of Theorem C.1. Suppose that the deficiency-zero network $\{\mathscr{S}, \mathscr{C}, \mathscr{R}\}$ is endowed with a kinetics $\{\mathscr{K}_{y \to y'}(\cdot)\}_{y \to y' \in \mathscr{R}}$.

If (C.1) admits the equilibrium c^*, we have

$$\sum_{\mathscr{R}} \mathscr{K}_{y \to y'}(c^*)(y' - y) = 0.$$

Recall that the reaction-rate functions take (strictly) positive values on $\mathbb{P}^{\mathscr{S}}$. Thus if c^* lies in $\mathbb{P}^{\mathscr{S}}$, I can make the identification

$$\alpha_{y \to y'} = \mathscr{K}_{y \to y'}(c^*), \quad \forall\, y \to y' \in \mathscr{R}$$

in Lemma C.3 to conclude that the network is weakly reversible.

Now suppose that the differential equation (C.1) admits a periodic solution $\bar{c}(\cdot): I \to \mathbb{P}^{\mathscr{S}}$ (where I is an open interval of the real line). Let T' and T be elements in I such that $T' > T$ and $\bar{c}(T') = \bar{c}(T)$. Integrating both sides of (C.1) over the interval $[T, T']$, I obtain

$$\sum_{\mathscr{R}} \left[\int_T^{T'} \mathscr{K}_{y \to y'}(\bar{c}(\tau))\, d\tau \right](y' - y) = 0.$$

Note that each of the integrals is positive; and so, after making the identification

$$\alpha_{y \to y'} = \int_T^{T'} \mathscr{K}_{y \to y'}(\bar{c}(\tau))\, d\tau, \quad \forall\, y \to y' \in \mathscr{R},$$

I can invoke Lemma C.3 again to conclude that the network is weakly reversible. □

Part (ii) of Theorem C.1 remains to be proved. Hereafter I suppose that $\{\mathscr{S}, \mathscr{C}, \mathscr{R}\}$ is a weakly reversible deficiency-zero reaction network and that k is an element of $\mathbb{P}^{\mathscr{R}}$.

The Deficiency-One Theorem, proved in Sections 5–8, already ensures that the mass-action system $\{\mathscr{S}, \mathscr{C}, \mathscr{R}, k\}$ admits precisely one equilibrium in each positive stoichiometric compatibility class. (Recall that every weakly reversible deficiency zero network satisfies conditions (i)–(iii) of the Deficiency-One Theorem.) Thus, I need only show that each positive equilibrium is asymptotically stable (relative to initial conditions in the same stoichiometric compatibility class) and that there are no periodic orbits in $\mathbb{P}^{\mathscr{S}}$.

Proof of part (ii) of Theorem C.1. I shall use a Liapunov function. During the course of the proof, $\mathbb{R}^{\mathscr{S}}$ carries the standard scalar product, and, as in Definition 3.2, $f(\cdot, k)$ denotes the species-formation-rate function for the mass-action system $\{\mathscr{S}, \mathscr{C}, \mathscr{R}, k\}$.

Suppose that $c^* \in \mathbb{P}^{\mathscr{S}}$ is an equilibrium. Then

$$\sum_{\mathscr{R}} k_{y \to y'}(c^*)^y (y' - y) = 0. \tag{C.6}$$

From (C.6) and Lemma C.1 it follows that

$$\sum_{\mathscr{R}} k_{y \to y'}(c^*)^y (\omega_{y'} - \omega_y) = 0. \tag{C.7}$$

In the statement of Proposition 5.3 I take

$$\kappa_{y \to y'} = k_{y \to y'}(c^*)^y \quad \forall\, y \to y' \in \mathscr{R}, \tag{C.8}$$

$$\phi(\cdot) = \exp(\cdot). \tag{C.9}$$

Moreover, for each $c \in \mathbb{P}^{\mathscr{S}}$ I let

$$\mu(c) := \ln c - \ln c^*. \tag{C.10}$$

Then, from (C.7) and Proposition 5.3, it follows that

$$f(c, k) \cdot (\ln c - \ln c^*) \leqq 0 \quad \forall c \in \mathbb{P}^{\mathscr{S}} \tag{C.11a}$$

with

$$f(c, k) \cdot (\ln c - \ln c^*) = 0 \text{ if and only if } f(c, k) = 0. \tag{C.11b}$$

By $h: \mathbb{P}^{\mathscr{S}} \to \mathbb{R}$ I mean the function

$$h(c) = \sum_{\sigma \in \mathscr{S}} [c_\sigma(\ln c_\sigma - \ln c_\sigma^* - 1) + c_\sigma^*]. \tag{C.12}$$

Note that

$$\nabla h(c) = \ln c - \ln c^*. \tag{C.13}$$

Thus, from (C.11) we have

$$\nabla h(c) \cdot f(c, k) \leqq 0 \quad \forall c \in \mathbb{P}^{\mathscr{S}} \tag{C.14a}$$

with

$$\nabla h(c) \cdot f(c, k) = 0 \text{ if and only if } f(c, k) = 0. \tag{C.14b}$$

Now I want to show that $h(\cdot)$ has a strict minimum at c^*. Clearly,

$$h(c^*) = 0. \tag{C.15}$$

Moreover, from the strict concavity of the logarithm function it follows that, for every positive value of c_σ,

$$\ln c_\sigma - \ln c_\sigma^* \geqq \frac{1}{c_\sigma}(c_\sigma - c_\sigma^*)$$

with equality holding if and only if $c_\sigma = c_\sigma^*$. From this it is easy to see that

$$h(c) > 0 \quad \forall c \neq c^*. \tag{C.16}$$

Now suppose that $\bar{c}(\cdot): I \to \mathbb{P}^{\mathscr{S}}$ is a solution of the differential equation

$$\dot{c} = f(c, k), \tag{C.17}$$

where I is an open interval of the real line. Suppose also that T and T' are members of I with $T' > T$. Then

$$h(\bar{c}(T')) - h(\bar{c}(T)) = \int_T^{T'} \nabla h(\bar{c}(t)) \cdot f(\bar{c}(t), k)\, \mathrm{d}t. \tag{C.18}$$

If $\bar{c}(\cdot)$ is not constant on $[T, T']$, it follows from (C.14) and (C.18) that

$$h(\bar{c}(T') < h(\bar{c}(T)). \tag{C.19}$$

In particular, it cannot be the case that $\bar{c}(T) = \bar{c}(T')$. From this it follows that there can be no nontrivial periodic orbit in $\mathbb{P}^{\mathscr{S}}$.

From (C.14)–(C.16) it already follows that $h(\cdot)$ is a Liapunov function [HS] for the equilibrium c^*. In fact, it is easy to see that, if we study the restriction of the flow given by (C.17) to the stoichiometric compatibility class containing c^*, then the

restriction of $h(\cdot)$ to the positive stoichiometric compatibility class containing c^* becomes a *strict* Liapunov function for c^*. (Recall (C.14b) and the fact that c^* is the only equilibrium in the positive stoichiometric compatibility class containing it.) From this it follows that c^* is asymptotically stable (relative to initial conditions in its stoichiometric compatibility class). □

Remark C.1. In the proof of part (ii) we relied on the (relatively difficult) Deficiency-One Theorem to ensure the existence and uniqueness of an equilibrium within each positive stoichiometric compatibility class. In fact, for a mass-action system in which the underlying network is weakly reversible and has a deficiency of zero, the *uniqueness* of equilibria derives directly from Propositions 5.1 and 5.3:

As in the proof of part (ii), let c^* be a positive equilibrium for the mass-action system $\{\mathscr{S}, \mathscr{C}, \mathscr{R}, k\}$. Following the line of argument given there, we can obtain from Proposition 5.3 not only (C.11b) but also, for $c \in \mathbb{P}^{\mathscr{S}}$,

$$f(c, k) = 0 \text{ if and only if } (\ln c - \ln c^*) \in S^{\perp}. \tag{C.20}$$

(As usual, $S^{\perp}$ is the orthogonal complement of the stoichiometric subspace.) From Proposition 5.1 it follows that c^* is the only equilibrium in the positive stoichiometric compatibility class containing it.

It is perhaps also worth noting that the argument given in Section 8 for the *existence* of a positive equilibrium becomes substantially simpler if attention is restricted to weakly reversible deficiency-zero networks.

Remark C.2. Let $\{\mathscr{S}, \mathscr{C}, \mathscr{R}\}$ be a weakly reversible deficiency-zero network, let k be an element of $\mathbb{P}^{\mathscr{R}}$, and let $c^* \in \mathbb{P}^{\mathscr{S}}$ be an equilibrium of the mass-action system $\{\mathscr{S}, \mathscr{C}, \mathscr{R}, k\}$. I want to show that the restriction of $\partial_c f(c^*, k)$ to the stoichiometric subspace is negative-definite (relative to a certain scalar product). This implies that all eigenvalues of the restriction (more precisely, of its complexification) have negative real part. In this sense, the equilibrium c^* is not only asymptotically stable *but also hyperbolic.* (Recall from Remark 3.4 that we generally study the flow *within* a stoichiometric compatibility class. The governing vector field invariably points along the stoichiometric subspace.)

As in the proof of Theorem C.1, part (ii), we have

$$\sum_{\mathscr{R}} k_{y \to y'} (c^*)^y (\omega_{y'} - \omega_y) = 0. \tag{C.21}$$

The derivative $\partial_c f(c^*, k): \mathbb{R}^{\mathscr{S}} \to \mathbb{R}^{\mathscr{S}}$ is given by

$$\partial_c f(c^*, k)\gamma \equiv \sum_{\mathscr{R}} k_{y \to y'} (c^*)^y (y \cdot \gamma)(y' - y), \tag{C.22}$$

where "$\cdot$" indicates not the standard scalar product in $\mathbb{R}^{\mathscr{S}}$ *but rather the scalar product defined by*

$$x \cdot z := \sum_{\sigma \in \mathscr{S}} \frac{x_\sigma z_\sigma}{c^*_\sigma}. \tag{C.23}$$

In Proposition 5.3 we can take

$$\kappa_{y \to y'} = k_{y \to y'}(c^*)^y \quad \forall y \to y' \in \mathscr{R},$$
$$\phi(x) \equiv x$$

to conclude that

$$\gamma \cdot \partial_c f(c^*, k)\gamma \leqq 0, \quad \forall \gamma \in \mathscr{R}^{\mathscr{S}} \tag{C.24}$$

with equality holding if and only if $\gamma \in S^{\perp}$. (Here S is again the stoichiometric subspace, but now orthogonality is measured with respect to the scalar product given in (C.23).) In particular, we have

$$\gamma \cdot \partial_c f(c^*, k)\gamma < 0 \quad \forall \gamma \in S, \gamma \neq 0. \tag{C.25}$$

In other words, the restriction of $\partial_c f(c^*, k)$ to the stoichiometric subspace is negative-definite.

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* In [FH2] the formal definition of a linkage class is constructed incorrectly. It should read as Definition 2.2 does here.

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Department of Chemical Engineering
University of Rochester
Rochester, New York 14627

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