Taken from a scanned copy of "Lectures on Chemical Reaction Networks," given by Martin Feinberg at the Mathematics Research Center, University of Wisconsin-Madison in the autumn of 1979.

LECTURE 4: SOME DEFINITIONS AND PROPOSITIONS

My purpose in this lecture is to accumulate some technical material that will eventually play a role in proofs of both the Deficiency Zero Theorem and the Deficiency One Theorem. Because some of the material will find no use for quite a while, this lecture will require a small amount of patience from the reader. Although I could have developed certain results at the point of first use in later lectures, there are two reasons for not proceeding in this way. First, many of the definitions, propositions and corollaries in this lecture are so strongly interrelated that there are clear advantages in having them all recorded in one place to be drawn upon as the need arises. Second, I think the price paid here for the resulting stockpile of technical material will be more than offset by a smoother, uninterrupted flow of ideas in subsequent lectures.

In Section 4.A I provide some background for the balance of this lecture. In particular, I try to supply some movitation for the questions we shall ask. In Section 4.B I discuss some properties of a reaction network that derive solely from its structure as a directed graph. Thus, in Section 4.B the nature of the reaction arrows plays the dominant role, while the precise character of the complexes sitting at the heads and tails of the reaction arrows plays virtually no role at all. In Section 4.C I begin to investigate some interplay of "stoichiometry" — that is, of the algebraic nature of the complexes — with a network's graphical structure. Finally, in Section 4.D I present a proposition which is somewhat disconnected from everything else in this lecture but which will play an important role in our study of the existence and uniqueness of positive equilibria.

Some of the definitions given in this lecture are new. Others merely serve to make formal certain ideas we have introduced in an informal way in previous lectures. Still others were actually recorded before but are repeated here for the reader's convenience.

4.A. Some Motivation

Before proceeding to the substantive part of this lecture I want to supply some motivation for the results we shall accumulate. In particular, I want to provide an indication of how the various objects discussed in some of the propositions (and their corollaries) will ultimately play a role in subsequent lectures.

Recall that the (vector) differential equation for a reaction system $\{\mathcal{S},\mathcal{C},\mathcal{R},\mathcal{K}\}$ is given by

$$\dot{c} = \sum_{\mathcal{R}} \mathcal{K}_{y\to y'}\,(c)\,(y'-y) \quad . \tag{4.1}$$

In particular, the differential equation for a mass action system $\{\mathcal{S},\mathcal{C},\mathcal{R},k\}$ is given by

$$\dot{c} = \sum_{\mathcal{R}} k_{y\to y'}\,c^{y}(y'-y) \quad , \tag{4.2}$$

where, for each $y \in \mathcal{C}$,

$$c^{y} := \prod_{s\in\mathcal{S}} c_{s}^{\,y_s} \quad . \tag{4.3}$$

From the discussion of notation in Lecture 1 it should also be recalled that

$$\{\omega_y \in \mathbb{R}^{\mathcal{C}} : y \in \mathcal{C}\} \tag{4.4}$$

is the standard basis for $\mathbb{R}^{\mathcal{C}}$.

I am now going to reformulate equations (4.1) and (4.2). To do this I shall require three mappings. For a network $\{\mathcal{S},\mathcal{C},\mathcal{R}\}$ let $Y:\mathbb{R}^{\mathcal{C}} \to \mathbb{R}^{\mathcal{S}}$ be the linear transformation defined by its action on the standard basis for $\mathbb{R}^{\mathcal{C}}$ as follows:

$$Y\omega_y = y \quad , \quad \forall\, y \in \mathcal{C} \quad . \tag{4.5}$$

Moreover, let $\Psi: \overline{\mathbb{P}}^{\mathcal{S}} \to \overline{\mathbb{P}}^{\mathcal{C}}$ be defined by

$$\Psi(c) \equiv \sum_{y \in \mathcal{C}} c^y \omega_y \; ; \tag{4.6}$$

that is, the "y^{th} component" of $\Psi(c)$ is given by

$$\Psi_y(c) = c^y \; .$$

Finally, for each $k \in \mathbb{P}^{\mathcal{R}}$ let $A_k: \mathbb{R}^{\mathcal{C}} \to \mathbb{R}^{\mathcal{C}}$ be the linear transformation defined by

$$A_k(x) \equiv \sum_{\mathcal{R}} k_{y \to y'} \, x_y \, (\omega_{y'} - \omega_y) \; . \tag{4.7}$$

With very little effort one can see that the differential equation (4.1) for a reaction system $\{\mathcal{S}, \mathcal{C}, \mathcal{R}, \mathcal{K}\}$ can be written

$$\dot{c} = Y[\sum_{\mathcal{R}} \mathcal{K}_{y \to y'}(c)(\omega_{y'} - \omega_y)] \tag{4.8}$$

and that the differential equation (4.2) for a mass action system $\{\mathcal{S}, \mathcal{C}, \mathcal{R}, k\}$ can be written

$$\dot{c} = Y \, A_k \, \Psi(c) \; . \tag{4.9}$$

Now if we want to study the equilibrium points of the differential equation (4.8) we must ask when $c \in \overline{\mathbb{P}}^{\mathcal{S}}$ is such that the bracketed vector in (4.8) lies in the kernel of Y. Thus, it is clear that we should know something about $\ker Y$. In fact, we can go a little further: Since, for every $c \in \overline{\mathbb{P}}^{\mathcal{S}}$, the vector

$$\sum_{\mathcal{R}} \mathcal{K}_{y \to y'}(c)(\omega_{y'} - \omega_y)$$

lies in the linear subspace of $\mathbb{R}^{\mathcal{C}}$ spanned by the set

$$\{\omega_y, -\omega_y \in \mathbb{R}^{\mathcal{C}} : y \to y'\} , \tag{4.10}$$

we should pay particular attention to that part of $\ker Y$ that meets the span of (4.10). (The dimension of the intersection will turn out to be the deficiency of the network.) There is still something more that we can say: Recall that each of the rate functions in (4.8) take non-negative values and that they all take positive values on $\mathbb{P}^{\mathcal{A}}$ (Remark 2.4). Thus, we should be especially interested in that part of $\ker Y$ that contains elements of the form

$$\sum_{\mathcal{R}} \alpha_{y\to y'}(\omega_y, -\omega_y) ,$$

where the $\alpha_{y\to y'}$ are non-negative or, when we study strictly positive equilibria, where each $\alpha_{y\to y'}$ is positive.

Similarly, if we want to study the equilibrium points of the differential equation (4.9) we must ask when $c \in \overline{\mathbb{P}}^{\mathcal{A}}$ is such that $\Psi(c)$ lies in the kernel of $Y A_k$. Note that since $\Psi(\cdot)$ takes values in $\overline{\mathbb{P}}^{\mathcal{C}}$ we shall be especially interested in

$$\ker Y A_k \cap \overline{\mathbb{P}}^{\mathcal{C}} .$$

Note also that, when c is positive (i.e., when c lies in $\mathbb{P}^{\mathcal{A}}$), $\Psi(c)$ is also positive (i.e., $\Psi(c)$ lies in $\mathbb{P}^{\mathcal{C}}$). Thus, when we study strictly positive equilibria of (4.9) we shall want to know something about the nature of

$$\ker Y A_k \cap \mathbb{P}^{\mathcal{C}} .$$

Since we have the obvious inclusion

$$\ker A_k \subset \ker Y A_k ,$$

we can begin to study the structure of $\ker Y A_k$ by first studying $\ker A_k$.

With these considerations kept in mind, the reader should have some sense of how the results we shall compile in this lecture will ultimately find use.

There is one final observation we might make. The mappings Y and Ψ for a reaction network $\{\mathcal{S}, \mathcal{C}, \mathcal{R}\}$ are heavily influenced by stoichiometry — that is, by the nature of the complexes contained in $\mathcal{C}$ — but not at all by the "reacts to" relation $\mathcal{R}$. Just the reverse is true of the mapping A_k and the set (4.10), for while $\mathcal{R}$ enters their construction in a very direct way, $\mathcal{C}$ merely plays the role of an index set. In this sense, A_k and the set (4.10) are objects that relate to the structure of a network essentially through its graphical character, and we can study these objects without paying much attention to the stoichiometrical information carried by the set $\mathcal{C}$. In fact, we shall begin by investigating how a network's graphical structure influences the nature of the set (4.10) and properties of the mapping A_k.

4.B. Some Graphical Aspects of Reaction Networks

The "reacts to" relation $\mathcal{R}$ gives a reaction network its character as a directed graph. The complexes play the role of the "vertices" while the reactions play the role of the (directed) "arcs." The "reacts to" relation in turn induces other relations in the set of complexes. As we explore these it will be understood that we are considering a fixed reaction network $\{\mathcal{S}, \mathcal{C}, \mathcal{R}\}$.

Definition 4.1. Two complexes $y \in \zeta$ and $y' \in \zeta$ are directly linked if $y \to y'$ or if $y' \to y$. If y and y' are directly linked we write $y \leftrightarrow y'$. Two complexes $y \in \zeta$ and $y' \in \zeta$ are linked if any of the following conditions are satisfied:

(i) $y = y'$

(ii) $y \leftrightarrow y'$

(iii) ζ contains a sequence $\{y_1, y_2, \ldots, y_k\}$ such that

$$y \leftrightarrow y_1 \leftrightarrow y_2 \leftrightarrow \ldots \leftrightarrow y_k \leftrightarrow y' .$$

If y and y' are linked we write $y \sim y'$. The equivalence relation $\sim$ induces a partition of ζ into a family of equivalence classes $\{L^\theta\}$ called the linkage classes of the network. We reserve the symbol ℓ for the number of linkage classes in a network.

Definition 4.2. A complex $y \in \zeta$ ultimately reacts to a complex $y' \in \zeta$ if any of the following conditions are satisfied:

(i) $y = y'$

(ii) $y \to y'$

(iii) ζ contains a sequence $\{y_1, y_2, \ldots, y_k\}$ such that

$$y \to y_1 \to y_2 \to \ldots \to y_k \to y' .$$

If y ultimately reacts to y' we write $y \Rightarrow y'$. Two complexes $y \in \zeta$ and $y' \in \zeta$ are strongly linked if both $y \Rightarrow y'$ and $y' \Rightarrow y$. If y and y' are strongly linked we write $y \approx y'$. The equivalence relation $\approx$ induces a partition of ζ into a family of equivalence classes $\{\Lambda^\rho\}$ called the strong linkage classes of the network.

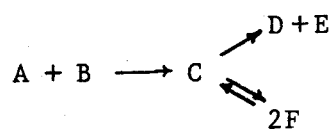
Remark 4.1. Clearly $y \approx y'$ implies that $y \sim y'$. Thus, every strong linkage class lies within a linkage class. In fact, every linkage class is the disjoint union of strong linkage classes.

The linkage classes of a reaction network correspond to what, in graph theoretical terminology, are sometimes called the weak components of a directed graph, and the strong linkage classes correspond to what are sometimes called the strong components. (See, for example, Harary [H1].) Unfortunately, in chemical terminology the word "component" is sometimes used as a synonym for "species."

Definition 4.3. A terminal strong linkage class is a strong linkage class Λ with the property that no complex in Λ reacts to a complex not in Λ; that is, $y \in \Lambda$ and $y \to y'$ imply that y' is in Λ. We reserve the symbol t for the number of terminal strong linkage classes in a network.

An example or two might help clarify the intent of the definitions listed thus far.

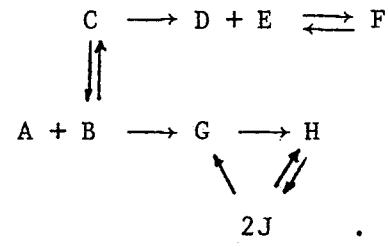
Example 4.1. Consider the network



$$F + A \rightleftharpoons G \quad .$$

The linkage classes are: {A+B, C, D+E, 2F} and {F+A,G}; thus, $\ell = 2$. The strong linkage classes are: {A+B},{C,2F}, {D+E} and {F+A,G}. The terminal strong linkage classes are: {D+E} and {F+A,G}; thus, $t = 2$

Example 4.2. Consider the network



There is but one linkage class: {C,A+B,D+E,F,G,H,2J} ; thus, $\ell = 1$. The strong linkage classes are: {C,A+B}, {D+E,F}, {G,H,2J} . The terminal strong linkage classes are: {D+E,F} and {G,H,2J}; thus, $t = 2$.

Remark 4.2. It should be clear that for any network each linkage class contains at least one terminal strong linkage class. Thus, $t - \ell \geq 0$; and, as Examples 4.1 and 4.2 indicate, equality may or may not obtain.

Definition 4.4. A reaction network is reversible if, for that network, the "reacts to" relation ($\rightarrow$) is symmetric — that is, if $y' \rightarrow y$ then $y \rightarrow y'$.

Neither of the networks displayed in Examples 4.1 and 4.2 is reversible. However, the network

$$A + B \rightleftarrows C \rightleftarrows D$$

$$D + C \rightleftarrows E$$

is reversible.

Definition 4.5. A reaction network is weakly reversible if, for that network, any of the following (equivalent) conditions is satisfied:

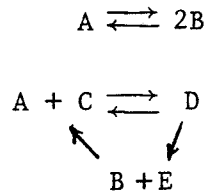
(i) The "ultimately reacts to" relation ($\Rightarrow$) is symmetric; that is, whenever $y \Rightarrow y'$ we also have $y' \Rightarrow y$.

(ii) Each reaction is contained in a directed cycle; that is, whenever $y \to y'$ we also have $y' \Rightarrow y$.

(iii) Each linkage class is a strong linkage class.

(iv) Each linkage class is a terminal strong linkage class.

It is an easy exercise to check the equivalence of (i)-(iv). Neither of the networks shown in Examples 4.1 or 4.2 is weakly reversible. Recall, however, that the network



is weakly reversible. Clearly, every reversible network is also weakly reversible, but, of course, the converse is not true.

Remark 4.3. As we shall see, the coincidence of the linkage classes and terminal strong linkage classes makes for a certain pleasantness in dealing with weakly reversible networks. Some, but not all, of the nice features a weakly reversible network enjoys derive simply from the fact that the number of its linkage classes is identical to the number of its terminal strong linkage classes (i.e., $t = \ell$). A network need not be weakly reversible for it to have this property — recall Example 4.1 — and it often happens that certain assertions that hold true for weakly reversible networks carry over (perhaps with minor modifications) to networks for which $t = \ell$.

We are now in a position to state the first of three propositions in this lecture. It will give important qualitative information about the structure of the kernel of the linear transformation A_k discussed in Section 4.A. Although I introduced A_k in consideration of a mass action system (with k the vector of rate constants), I prefer to regard Proposition 4.1 merely as a technical result about a family of linear transformations induced by a network's graphical structure. That is, in Proposition 4.1 I attribute no particular "chemical" interpretation to k. As we shall see, Proposition 4.1 acts as a "master proposition" from which several results follow, some (e.g., Corollary 4.3) having implications for reaction systems which are not necessarily mass action.

Recall from Lecture 1 that if x is an element of $\mathbb{R}^{\mathcal{C}}$ then the support of x is defined by

$$\text{supp } x: = \{y \in \mathcal{C} : x_y \neq 0\}.$$

Proposition 4.1. Let $\{\mathcal{S},\mathcal{C},\mathcal{R}\}$ be a reaction network with terminal strong linkage classes $\{\Lambda^1, \Lambda^2,\ldots,\Lambda^t\}$, let k be any vector in $\mathbb{P}^{\mathcal{R}}$, and let $A_k: \mathbb{R}^{\mathcal{C}} \to \mathbb{R}^{\mathcal{C}}$ be the linear transformation defined by

$$A_k(x) = \sum_{\mathcal{R}} k_{y\to y'} x_y(\omega_y,-\omega_y) .$$

Then the kernel of A_k has a basis $\{x^1, x^2,\ldots,x^t\} \subset \overline{\mathbb{P}}^{\mathcal{C}}$ such that

$$\text{supp } x^i = \Lambda^i , \quad i = 1,2,\ldots,t .$$

Remark 4.4. Proposition 4.1, which is crucial to a lot that we shall do tells us that no matter how $k \in \mathbb{P}^{\mathcal{R}}$ is chosen the kernel of A_k maintains a definite relationship to the graphical structure of the network $\{\mathcal{S}, \mathcal{C}, \mathcal{R}\}$ from which A_k derives. In particular, $\ker A_k$ will always have dimension t, where t is the number of terminal strong linkage classes in the network. Moreover, $\ker A_k$ will have a nice basis: In that basis there will be a vector x^i corresponding to terminal strong linkage class Λ^i such that $x^i_y > 0$ for all $y \in \Lambda^i$ and $x^i_y = 0$ for all $y \notin \Lambda^i$.

Readers familiar with theorems of the Perron-Frobenius type will realize that these might provide the basis for a proof of Proposition 4.1. However, one then has the job of drawing connections between the matrix language employed, for example, in Gantmacher's book [G] and the essentially graphical language introduced thus far. Things get a little awkward. With this in mind Horn and I gave what amounts to a "from scratch" proof of Proposition 4.1 in the appendix of reference [FH2].* That proof, which is essentially graph-theoretical in spirit and which makes no use of Perron-Frobenius theorems, is a little too long to include here. Instead I refer interested readers to [FH2]. For a Perron-Frobenius argument in the narrower context of weakly reversible networks readers should see the appendix of an earlier article by Horn [H3].

In the following corollary to Proposition 4.1 we address the question of when $\ker A_k$ contains a strictly positive vector — that is, an element of $\mathbb{P}^{\mathcal{C}}$.

*Definition 8 in [FH2] is incorrectly constructed and should read as Definition 4.2 here. However, Definition 8 plays no role either in the statement or proof of the proposition in the appendix of [FH2], which is the same as Proposition 4.1 here apart from trivial differences in terminology and notation.

Corollary 4.2. Let $\{\mathcal{S},\mathcal{C},\mathcal{R}\}$ be a reaction network, let k be any vector of $\mathbb{P}^{\mathcal{R}}$, and let A_k be as in Proposition 4.1. Then

$$\ker A_k \cap \mathbb{P}^{\mathcal{C}}$$

is non-empty if and only if the network is weakly reversible.

Proof. Suppose the network is not weakly reversible. Then there exists a complex $\hat{y} \in \mathcal{C}$ that does not reside in any terminal strong linkage class; otherwise the linkage classes would coincide with the terminal strong linkage classes, thereby ensuring weak reversibility. Since, by virtue of Proposition 4.1, every vector in $\ker A_k$ is a linear combination of vectors with support in the terminal strong linkage classes it must be the case that $x_{\hat{y}} = 0$ for every $x \in \ker A_k$. Thus, $\ker A_k \cap \mathbb{P}^{\mathcal{C}}$ is empty.

On the other hand if the network is weakly reversible then every complex is a member of some terminal strong linkage class. In this case the sum of the basis vectors described in Proposition 4.1 is a member of $\ker A_k \cap \mathbb{P}^{\mathcal{C}}$. ///

Corollary 4.3. Let $\{\mathcal{S},\mathcal{C},\mathcal{R}\}$ be a reaction network. There exists $\alpha \in \mathbb{P}^{\mathcal{R}}$ such that

$$\sum_{\mathcal{R}} \alpha_{y \to y'} (\omega_{y'} - \omega_y) = 0 \tag{4.12}$$

if and only if the network is weakly reversible.

Proof. First we shall prove the existence of the required α when the network is weakly reversible. Let k be any vector of $\mathbb{P}^{\mathcal{R}}$, and let A_k be as in Proposition 4.1. From the weak reversibility of the network and Corollary 4.2 we have the existence of $\hat{x} \in \ker A_k \cap \mathbb{P}^{\mathcal{C}}$. Thus,

$$\sum_{\mathcal{R}} k_{y \to y'} \hat{x}_y(\omega_y, -\omega_y) = 0 \quad .$$

To obtain the desired $\alpha \in \mathbb{P}^{\mathcal{R}}$ we let

$$\alpha_{y \to y'} = k_{y \to y'} \hat{x}_y \quad , \quad \forall\, y \to y' \in \mathcal{R} \quad .$$

Next, we shall suppose that the network is not weakly reversible, and we shall show that there can exist no $\alpha \in \mathbb{P}^{\mathcal{R}}$ that solves (4.12). Suppose that such an α exists. Let $A_\alpha: \mathbb{R}^{\mathcal{C}} \to \mathbb{R}^{\mathcal{C}}$ be as in Proposition 4.1:

$$A_\alpha(x) \equiv \sum_{\mathcal{R}} \alpha_{y \to y'} x_y(\omega_y, -\omega_y) \quad . \tag{4.13}$$

Moreover, let $\bar{x} \in \mathbb{R}^{\mathcal{C}}$ be that vector such that $\bar{x}_y = 1$ for all $y \in \mathcal{C}$. Since α satisfies (4.12) we have from (4.13) that $A_\alpha(\bar{x}) = 0$. Thus, $\bar{x}$ lies in $\ker A_\alpha \cap \mathbb{P}^{\mathcal{C}}$, which contradicts the conclusion of Corollary 4.2. ///

Remark 4.4. In Lecture 6 we shall discuss the notion of complex balancing. This simple idea, introduced into chemical reactor theory by Horn and Jackson [HJ], has surprising and profound uses in the study of the differential equations for reactors with intricate chemistry. It happens that equation (4.12) and Corollary 4.3 have such a natural interpretation in terms of complex balancing that we would do well to give that interpretation here, at least in an informal way.

Consider a reaction network $\{\mathcal{L}, \mathcal{C}, \mathcal{R}\}$. For each $y \in \mathcal{C}$ let

$$\mathcal{R}_{y\to} := \{y \to y' \in \mathcal{R} : y' \in \mathcal{C}\}$$

and (4.14)

$$\mathcal{R}_{\to y} := \{y' \to y \in \mathcal{R} : y' \in \mathcal{C}\} .$$

That is, $\mathcal{R}_{y\to}$ [resp., $\mathcal{R}_{\to y}$] is the set of all reactions that have y as the reactant [product] complex. Now let α be an element of $\overline{\mathbb{P}}^{\mathcal{R}}$ (not necessarily strictly positive). The left side of (4.12) can be rearranged to give*

$$\sum_{y \in \mathcal{C}} \Big(\sum_{\mathcal{R}_{\to y}} \alpha_{y' \to y} - \sum_{\mathcal{R}_{y\to}} \alpha_{y \to y'} \Big) \omega_y . \tag{4.15}$$

Thus, α satisfies (4.12) if and only if

$$\sum_{\mathcal{R}_{\to y}} \alpha_{y' \to y} - \sum_{\mathcal{R}_{y\to}} \alpha_{y \to y'} = 0 \ , \ \forall\, y \in \mathcal{C} . \tag{4.16}$$

*If either $\mathcal{R}_{\to y}$ or $\mathcal{R}_{y\to}$ is empty the corresponding sum in (4.15) will be understood to be zero.

Now if, for each $y \to y' \in \mathcal{R}$, we think of $\alpha_{y \to y'}$ as a "current" flowing from complex y to complex y' then, for each $y \in \mathcal{C}$, we can think of the y^{th} component of the vector (4.15) as the net current flowing to complex y from all other complexes. Thus, (4.16) describes a condition wherein, for each complex, the total current flowing to that complex is exactly balanced by the total current flowing away from that complex. In this sense we would say that $\alpha \in \overline{\mathbb{P}}^{\mathcal{R}}$ satisfying (4.16) or, equivalently, (4.12) is complex balanced.

What Corollary (4.3) asserts is that there exists a strictly positive complex balanced α — that is, a complex balanced α in $\mathbb{P}^{\mathcal{R}}$ — if and only if the network $\{\mathcal{A}, \mathcal{C}, \mathcal{R}\}$ is weakly reversible. For what amounts to a more direct proof of the "only if" part (without recourse to Proposition 4.1) see Horn's proof of Theorem 2B in [H3]; his Theorem 4B in the same article gives the "if" part as well.

In Section 4.A. I indicated why the set (4.10) will have some importance for us. Here I denote that set by the symbol Δ' : For a reaction network $\{\mathcal{A}, \mathcal{C}, \mathcal{R}\}$ let

$$\Delta' := \{\omega_{y'} - \omega_y \in \mathbb{R}^{\mathcal{C}} : y \to y'\} \quad . \tag{4.17}$$

Since $y \to y'$ implies that y and y' are linked ($y \sim y'$) it follows that Δ' is contained in the set

$$\Delta := \{\omega_{y'} - \omega_y \in \mathbb{R}^{\mathcal{C}} : y \sim y'\} \tag{4.18}$$

and that

$$\text{span}(\Delta') \subset \text{span}(\Delta) \tag{4.19}$$

In fact, we have the following:

Lemma 4.4. For a reaction network $\{\mathcal{S},\mathcal{C},\mathcal{R}\}$ let Δ' and Δ be as in (4.17) and (4.18). Then

$$\text{span}(\Delta') = \text{span}(\Delta) \ . \tag{4.20}$$

Proof. In light of (4.19) it is enough to show that span(Δ) is contained in span(Δ') or, equivalently, that Δ is contained in span(Δ'). Suppose that $\omega_{y'}-\omega_y$ is a member of Δ. Then y' and y are linked, and one of the three possibilities listed in Definition 4.1 must obtain. If $y = y'$, then $\omega_{y'}-\omega_y = 0$, and $\omega_{y'}-\omega_y$ lies in span (Δ'). If y and y' are directly linked ($y \leftrightarrow y'$) then either $y \to y'$ or $y' \to y$ so that either $\omega_{y'}-\omega_y$, or $\omega_{y'}-\omega_y$ is a member of Δ'; in either case $\omega_{y'}-\omega_y$ is a member of span(Δ'). If $\mathcal{C}$ contains a sequence $\{y_1,y_2,\ldots,y_k\}$ such that

$$y \leftrightarrow y_1 \leftrightarrow y_2 \leftrightarrow \ldots \leftrightarrow y_k \leftrightarrow y'$$

then, by the argument immediately preceding, the vectors

$$\{\omega_{y'}-\omega_{y_k},\ \omega_{y_k}-\omega_{y_{k-1}},\ \ldots,\omega_{y_2}-\omega_{y_1},\ \omega_{y_1}-\omega_y\}$$

are all members of span(Δ'). So then is their sum, $\omega_{y'}-\omega_y$. ///

Lemma 4.5. Let $\{\mathcal{S},\mathcal{C},\mathcal{R}\}$ be a reaction network with n complexes and ℓ linkage classes, and let Δ' and Δ be defined as in (4.17) and (4.18). Then

$$\dim[\text{span}(\Delta')] = \dim[\text{span}(\Delta)] = n-\ell \ . \tag{4.21}$$

Proof. By virtue of Lemma 4.5 we need only prove the last equality in (4.21). Let $\{L^1, L^2, \ldots, L^\ell\}$ be the linkage classes of the network, and, for $\theta = 1,2,\ldots,\ell$, let

$$\Delta^\theta := \{\omega_y - \omega_{y'} \in \mathbb{R}^{\mathcal{C}} : y \in L^\theta,\ y' \in L^\theta\} . \tag{4.22}$$

Then

$$\Delta = \bigcup_{\theta=1}^{\ell} \Delta^\theta$$

and

$$\text{span}(\Delta) = \text{span}(\Delta^1) \oplus \text{span}(\Delta^2) \oplus \ldots \oplus \text{span}(\Delta^\ell). \tag{4.23}$$

Now let n_θ denote the number of complexes in L^θ, and let those complexes be denoted $y_1, y_2, \ldots, y_{n_\theta}$. Then any element of Δ^θ can be written as a linear combination of the linearly independent set

$$\{\omega_{y_2} - \omega_{y_1},\ \omega_{y_3} - \omega_{y_1},\ \ldots,\ \omega_{y_{n_\theta}} - \omega_{y_1}\}.$$

Thus, $\dim \text{span}(\Delta^\theta) = n_\theta - 1$. From (4.23) it follows that

$$\dim[\text{span}(\Delta)] = \sum_{\theta=1}^{\ell} (n_\theta - 1) = n - \ell . \qquad ///$$

In preparation for our next lemma we recall from Lecture 1 some matters of notation. Let $\{\mathcal{A}, \mathcal{C}, \mathcal{R}\}$ be a reaction network with linkage classes $\{L^1, L^2, \ldots, L^\ell\}$. Recall that $\omega_{L^\theta} \in \mathbb{R}^{\mathcal{C}}$ is the characteristic function for the set $L^\theta \subset \mathcal{C}$. That is, ω_{L^θ} is the vector of $\mathbb{R}^{\mathcal{C}}$ whose y^{th} component is unity for each $y \in L^\theta$ and is zero for each $y \notin L^\theta$. Recall also that $\mathbb{R}^{\mathcal{C}}$ is endowed with the standard scalar product.

Lemma 4.6. Let $\{\mathcal{S},\mathcal{C},\mathcal{R}\}$ be a reaction network with linkage classes $\{L^\theta\}_{\theta=1,2,..,\ell}$, and let Δ be defined as in (4.18). Then the set

$$\{\omega_{L^\theta}\}_{\theta=1,2,\ldots,\ell} \subset \mathbb{R}^{\mathcal{C}} \tag{4.24}$$

is a basis for $[\text{span}(\Delta)]^\perp$.

Proof. It is obvious that each element of (4.24) is orthogonal to each element of Δ and, therefore, to each vector of span(Δ). Moreover, the set (4.24) is clearly linearly independent. Since $\dim(\mathbb{R}^{\mathcal{C}}) = n$, where n is the number of complexes in $\mathcal{C}$, it follows from Lemma 4.5 that the dimension of the orthogonal complement of span (Δ) is $n - (n-\ell) = \ell$. Thus, (4.24) is a basis for $[\text{span}(\Delta)]^\perp$. ///

Remark 4.5. Let $\{\mathcal{S},\mathcal{C},\mathcal{R}\}$ be a reaction network. From Lemma 4.6 we have that a vector $g \in \mathbb{R}^{\mathcal{C}}$ lies in span(Δ) if and only if

$$g \cdot \omega_{L^\theta} = 0 \ , \ \theta = 1,2,\ldots,\ell \ .$$

That is, g lies in span (Δ) or, equivalently, in span(Δ') if and only if

$$\sum_{y \in L^\theta} g_y = 0 \ , \ \theta = 1,2,\ldots,\ell \ .$$

We are now in a position to state our next corollary of Proposition 4.1. For a network $\{\mathcal{S},\mathcal{C},\mathcal{R}\}$ it is clear that, for any $k \in \mathbb{R}^{\mathcal{R}}$, the linear transformation A_k takes values in span(Δ) — that is, the image of A_k lies in span(Δ). We shall be interested to know when $\text{im}\, A_k$ is identical to span(Δ).

Corollary 4.6. Let $\{\mathcal{S},\mathcal{C},\mathcal{R}\}$ be a reaction network, let k be any element of $\mathbb{R}^{\mathcal{R}}$, and let $A_k:\mathbb{R}^{\mathcal{C}} \to \mathbb{R}^{\mathcal{C}}$ be as in Proposition 4.1. Then

$$\text{im}\, A_k = \text{span}(\Delta) \tag{4.25}$$

if and only if each linkage class of the network contains precisely one terminal strong linkage class. In particular, (4.25) holds if the network is weakly reversible.

Proof. Since $\text{im}\, A_k$ is contained in span(Δ) we need only examine circumstances under which the dimensions of these linear subspaces of $\mathbb{R}^{\mathcal{C}}$ are identical. From Lemma 4.5 we have that dim span(Δ) = $n-\ell$, where n is the number of elements in $\mathcal{C}$ and ℓ is the number of linkage classes in the network. Since dim ($\mathbb{R}^{\mathcal{C}}$) = n, it follows from Proposition 4.1 and the standard theorem relating the dimensions of the domain, kernel and image of a linear transformation that

$$\dim\, (\text{im}\, A_k) = n-t\,, \tag{4.26}$$

where t is the number of terminal strong linkage classes in the network. Thus,

$$\dim \text{span}(\Delta) - \dim \text{im}\, A_k = t-\ell\,, \tag{4.27}$$

so (4.25) holds if and only if $t = \ell$ — that is, if and only if each linkage class contains precisley one terminal strong linkage class. This condition holds trivially for weakly reversible networks. ///

Remark 4.6. Note that when the graphical condition in Corollary 4.6 is satisfied, the image of A_k is in fact independent of any particular choice of $k \in \mathbb{P}^{\mathcal{R}}$; rather, $\operatorname{im} A_k$ depends only on the nature of the linkage classes of the network. To some extent it is this fact that makes networks for which $t = \ell$ (and weakly reversible networks in particular) relatively easy to study. When t exceeds ℓ the location of $\operatorname{im} A_k$ in $\mathbb{R}^{\mathcal{C}}$ will generally be influenced by k .

4.C. *Some Interplay of Stoichiometry and Graphical Structure*

The definitions and results recorded in Section 4.B pertained entirely to the graphical structure of a network $\{\mathcal{S},\mathcal{C},\mathcal{R}\}$. Our focus was exclusively on the "reacts to" relation $\mathcal{R}$, and "stoichiometry" — that is, the precise nature of the complexes in $\mathcal{C}$ — played a role only insofar as the elements of $\mathcal{C}$ provided names for the vertices of a directed graph. In what follows, however, the complexes of a network will enter our analysis in a more forceful way as we examine some interplay between the network's stoichiometry and its graphical character.

We begin by recalling some definitions from Lecture 2.

Definition 4.6. The reaction vectors for a network $\{\mathcal{S},\mathcal{C},\mathcal{R}\}$ are the members of the set

$$\{y'-y \in \mathbb{R}^{\mathcal{S}} : y \to y'\}. \tag{4.28}$$

The rank of the network is the rank of its set of reaction vectors. We reserve the symbol s to denote the rank of a network. The stoichiometric subspace for the network is the span of its reaction vectors. We reserve the symbol S to denote the stoichiometric subspace of a network. (Note that $\dim S = s$.)

In the next definition we give official status to the linear transformation Y introduced in Section 4.A.

Definition 4.7. For a reaction network $\{\mathcal{S},\mathcal{C},\mathcal{R}\}$ the stoichiometric map $Y:\mathbb{R}^{\mathcal{C}} \to \mathbb{R}^{\mathcal{S}}$ is that linear transformation defined by its action on the standard basis for $\mathbb{R}^{\mathcal{C}}$ as follows:

$$Y\omega_y = y \ , \ \forall\, y \in \mathcal{C} \ . \tag{4.29}$$

Remark 4.7. Let $\{\mathcal{S},\mathcal{C},\mathcal{R}\}$ be a reaction network. Since, for any pair $y, y' \in \mathcal{C}$, we have

$$y'-y = Y(\omega_{y'},-\omega_y) \ ,$$

it is clear that the set of reaction vectors for the network is given by the image of the set Δ' (defined in (4.17)) under the map Y. Thus, the stoichiometric subspace for the network is given by the image of span (Δ') under Y. In fact, we have from Lemma 4.4

$$S = Y[\text{span}(\Delta')] = Y[\text{span}(\Delta)] \ . \tag{4.30}$$

Moreover, from Corollary 4.6 and (4.30) we have the following: Let k be any element of $\mathbb{P}^{\mathcal{R}}$, and let $A_k:\mathbb{R}^{\mathcal{C}} \to \mathbb{R}^{\mathcal{C}}$ be constructed as in Proposition 4.1. Then, if each linkage class of the network contains precisely one terminal strong linkage class, the stoichiometric subspace is given by

$$S = Y[\text{im } A_k] = \text{im } YA_k \tag{4.31}$$

In particular, (4.31) holds if the network is weakly reversible.*

For future reference we also record the following easy consequence of (4.30): For any reaction network $\{\mathcal{S},\mathcal{C},\mathcal{R}\}$

$$S = \text{span}\{y'-y \in \mathbb{R}^{\mathcal{S}} \ : \ y \sim y'\} \ . \tag{4.32}$$

*For a more extensive discussion of conditions under which (4.31) holds see [FH2].

Now we recall our definition of deficiency:

Definition 4.8. The deficiency (denoted δ) of a reaction network is defined by

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

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

In Section 4.A I indicated why, for a given network, it is worth knowing something about the intersection of the kernel of Y with span (Δ') (or, equivalently, with span(Δ)). Our next proposition ties the deficiency of the network to the dimension of that intersection [F2].

Proposition 4.7. Let $\{\mathcal{S}, \mathcal{C}, \mathcal{R}\}$ be a reaction network. If $Y:\mathbb{R}^{\mathcal{C}} \to \mathbb{R}^{\mathcal{S}}$ is the stoichiometric map for the network, if

$$\Delta := \{\omega_y, -\omega_y \in \mathbb{R}^{\mathcal{C}} : y \sim y'\} \ ,$$

and if δ is the deficiency of the network, then

$$\delta = \dim[\ker Y \cap \text{span}(\Delta)] \ .$$

In particular, if the deficiency of the network is zero then

$$\ker Y \cap \text{span}(\Delta) = \{0\} \ .$$

Proof. Let $\bar{Y}$: span(Δ) $\rightarrow \mathbb{R}^{\ell}$ be the restriction of Y to span(Δ). Then, from the standard theorem relating the dimensions of the domain, kernel, and image of a linear transformation, we have

$$\dim \text{span}(\Delta) = \dim \ker \bar{Y} + \dim \text{im } \bar{Y} \ . \tag{4.36}$$

From Lemma 4.5 we have dim span(Δ) = $n - \ell$. Moreover,

$$\text{im } \bar{Y} = Y[\text{span}(\Delta)] \ ,$$

which, from Remark 4.6, is just S, the stoichiometric subspace of the network. But dim S = s, where s is the rank of the network. Finally,

$$\ker \bar{Y} = \ker Y \bigcap \text{span}(\Delta) \ .$$

Thus, rearrangement of (4.36) gives

$$\dim[\ker Y \bigcap \text{span}(\Delta)] = n - \ell - s = \delta. \qquad ///$$

Remark 4.8. We note in passing that Proposition 4.7 ensures that the deficiency of any reaction network is non-negative.

Remark 4.9. Let $\{\mathcal{S},\mathcal{C},\mathcal{R}\}$ be a reaction network, and let

$$g = \sum_{y \in \mathcal{C}} g_y \omega_y \tag{4.33}$$

be an element of $\mathbb{R}^{\mathcal{C}}$. In Remark 4.5 we observed that g lies in span(Δ) if and only if

$$\sum_{y \in L^\theta} g_y = 0 , \quad \theta = 1,2,\ldots,\ell , \tag{4.34}$$

where $\{L^1,L^2,\ldots,L^\ell\}$ are the linkage classes of the network. If Y is the stoichiometric map for the network then we can operate on both sides of (4.33) to see that g lies in ker Y if and only if

$$\sum_{y \in \mathcal{C}} g_y y = 0 . \tag{4.35}$$

Thus, g lies in ker $Y \cap$ span(Δ) if and only if it satisfies both (4.34) and (4.35). If the deficiency of the network is zero we have from Proposition 4.7 that the only solution to (4.34) and (4.35) is the trivial $g = 0$. If the deficiency of the network is one we have the existence of a non-zero g that solves (4.34) and (4.35), and the only other solutions are scalar multiples of g.

At the beginning of the next lecture we shall want to know when the reaction vectors of a network are such that <u>strictly</u> positive linear combination of them can give the zero vector. That is, we shall want to know when, for a reaction network $\{\mathcal{S},\mathcal{C},\mathcal{R}\}$, there exists $\alpha \in \mathbb{P}^{\mathcal{R}}$ such that

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

We begin to address this question in our first corollary of Proposition 4.7.

Corollary 4.8. Let $\{\mathcal{S}, \mathcal{C}, \mathcal{R}\}$ be a reaction network. Then $\alpha \in \mathbb{R}^{\mathcal{R}}$ satisfies the equation

$$\sum_{\mathcal{R}} \alpha_{y \to y'}(y'-y) = 0 \tag{4.37}$$

if it satisfies the equation

$$\sum_{\mathcal{R}} \alpha_{y \to y'}(\omega_y, -\omega_y) = 0 \ . \tag{4.38}$$

Moreover, if the deficiency of the network is zero then α satisfies (4.37) *only* if it also satisfies (4.38).

Proof. Drawing upon the stoichiometric map for the network, we can rewrite equation (4.37) as follows:

$$Y\left[\sum_{\mathcal{R}} \alpha_{y \to y'}(\omega_y, -\omega_y)\right] = 0 \ . \tag{4.39}$$

Thus, if $\alpha \in \mathbb{R}^{\mathcal{R}}$ solves (4.38) it also solves (4.37). To prove the last part of the corollary we suppose that α solves (4.37) and, therefore, (4.39). Since the quantity in brackets on the left side of (4.39) is clearly a member of span (Δ) we must have the inclusion

$$\sum_{\mathcal{R}} \alpha_{y \to y'}(\omega_y, -\omega_y) \in \ker Y \bigcap \text{span}(\Delta) \tag{4.40}$$

If the deficiency of the network is zero then Proposition 4.7 ensures that the set on the right side of (4.40) contains only the zero vector of $\mathbb{R}^{\mathcal{C}}$. Thus, α satisfies (4.38). ///

Corollary 4.8 is stated in terms of α in $\mathbb{R}^{\mathcal{R}}$, not necessarily in $\mathbb{P}^{\mathcal{R}}$ or even $\overline{\mathbb{P}}^{\mathcal{R}}$. Next we focus on strictly positive solutions of (4.37).

Corollary 4.9. Let $\{\mathcal{S}, \mathcal{C}, \mathcal{R}\}$ be a reaction network of deficiency zero. Then there exists $\alpha \in \mathbb{P}^{\mathcal{R}}$ that satisfies

$$\sum_{\mathcal{R}} \alpha_{y \to y'}(y'-y) = 0 \tag{4.37}$$

if and only if the network is weakly reversible.

Proof. This is an immediate consequence of Corollaries 4.3 and 4.8. ///

Remark 4.10. A network which has a non-zero deficiency may admit a strictly positive solution to (4.37) even if the network is not weakly reversible. For example, the network

$$2A \longrightarrow A + B \longleftarrow 2B$$

is not weakly reversible and has a deficiency of one ($n = 3$, $\ell = 1$, $s = 1$). Equation (4.37) takes the form

$$\alpha_{2A \to A+B}(A+B - 2A) + \alpha_{2B \to A+B}(A+B - 2B) = 0 .$$

A strictly positive solution is given by $\alpha_{2A \to A+B} = 1$, $\alpha_{2B \to A+B} = 1$.

Taken together, Corollaries 4.8 and 4.9 tell us that for all weakly reversible networks of deficiency zero there will exist strictly positive solutions to (4.37) and that all such solutions will also satisfy (4.38). In our next corollary we address the situation for weakly reversible networks of non-zero deficiency.

Corollary 4.10. Let $\{\mathcal{S},\mathcal{C},\mathcal{R}\}$ be a weakly reversible network of non-zero deficiency. Then there exists $\alpha \in \mathbb{P}^{\mathcal{R}}$ that satisfies (4.38) and, therefore, (4.37). Moreover, there exists $\bar{\alpha} \in \mathbb{P}^{\mathcal{R}}$ that satisfies (4.37) but not (4.38).

Proof. The existence of $\alpha \in \mathbb{P}^{\mathcal{R}}$ satisfying (4.38) is given by Corollary 4.3. Since the deficiency of the network is non-zero it follows from Proposition 4.7 that there exists a non-zero vector g in

$$\ker Y \bigcap \text{span}(\Delta) \ .$$

From Lemma 4.4 we have that $\text{span}(\Delta) = \text{span}(\Delta')$. Consequently, g lies in $\text{span}(\Delta')$ so that there exists $\beta \in \mathbb{R}^{\mathcal{R}}$ satisfying

$$g = \sum_{\mathcal{R}} \beta_{y \to y'}(\omega_{y'} - \omega_y) \ . \tag{4.41}$$

Now let $\alpha \in \mathbb{P}^{\mathcal{R}}$ solve (4.38) and choose $\lambda \in \mathbb{P}$ to be sufficiently large so that

$$\bar{\alpha} := \beta + \lambda \alpha \tag{4.42}$$

is a member of $\mathbb{P}^{\mathcal{R}}$. From (4.41) and (4.38) it follows that

$$g = \sum_{\mathcal{R}} \bar{\alpha}_{y \to y'}(\omega_{y'} - \omega_y) \ . \tag{4.43}$$

Since g is non-zero, (4.43) ensures that $\bar{\alpha}$ does not satisfy (4.38). To see that $\bar{\alpha}$ satisfies (4.37) we need only recall that g lies in $\ker Y$; acting with Y on both sides of (4.43) we obtain

$$0 = \sum_{\mathcal{R}} \bar{\alpha}_{y \to y'}(y' - y) \ . \qquad ///$$

Remark 4.11. Corollaries (4.8)-(4.10) lend themselves to interpretation in terms of complex balancing (Remark 4.4). Recall that for a network $\{\mathcal{S},\mathcal{C},\mathcal{R}\}$ we said that an element $\alpha \in \overline{\mathbb{P}}^{\mathcal{R}}$ is complex balanced if it satisfies (4.38). Our focus on non-negative α in Remark 4.4 was merely intended to facilitate a "physical" interpretation of the complex balancing condition. Henceforth we shall say that any element $\alpha \in \mathbb{R}^{\mathcal{R}}$ (not necessarily non-negative) that satisfies (4.38) is complex balanced. With this in mind, we can then state the following: For a network $\{\mathcal{S},\mathcal{C},\mathcal{R}\}$:

(i) All complex balanced $\alpha \in \mathbb{R}^{\mathcal{R}}$ are solutions of (4.37). [Corollary 4.8]

(ii) If the deficiency of the network is zero then all $\alpha \in \mathbb{R}^{\mathcal{R}}$ that solve (4.37) are complex balanced. [Corollary 4.8]

(iii) If the network is not weakly reversible then, regardless of its deficiency, there exists no complex balanced $\alpha \in \mathbb{P}^{\mathcal{R}}$. [Corollary 4.3]

(iv) If the network is not weakly reversible and its deficiency is zero then there exists no $\alpha \in \mathbb{P}^{\mathcal{R}}$ that solves (4.37). [Corollary 4.9]

(v) If the network is weakly reversible then, regardless of its deficiency, there exists a complex balanced $\alpha \in \mathbb{P}^{\mathcal{R}}$ that solves (4.37). [Corollaries 4.8-4.10]

(vi) If the network is weakly reversible and its deficiency is non-zero then there exists $\alpha \in \mathbb{P}^{\mathcal{R}}$ that solves (4.37) and is not complex balanced. [Corollary 4.10]

Ideas like these, which turn out to be surprisingly important, were studied in [F2] and [H3].

In Section 4.A I attempted to provide a small amount of motivation for the collection of results we have assembled thus far. There I indicated why for a mass action system $\{\mathcal{S},\mathcal{C},\mathcal{R},k\}$, it would be helpful to know something, about the nature of $\ker Y A_k$, where Y is the stoichiometric map for the network and A_k is the linear transformation constructed as in Proposition 4.1. In fact, Proposition 4.1 was motivated by the idea that $\ker A_k$ is <u>part</u> of $\ker Y A_k$. In our next corollary we show that for networks of deficiency zero, $\ker A_k$ is <u>all</u> of $\ker Y A_k$.

Corollary 4.11. Let $\{\mathcal{S}, \mathcal{C}, \mathcal{R}\}$ be a reaction network of deficiency zero, and let k be any element of $\mathbb{P}^{\mathcal{R}}$. If $Y: \mathbb{R}^{\mathcal{C}} \to \mathbb{R}^{\mathcal{S}}$ is the stoichiometric map for the network and $A_k: \mathbb{R}^{\mathcal{C}} \to \mathbb{R}^{\mathcal{C}}$ is as in Proposition 4.1 then

$$\ker Y A_k = \ker A_k .$$

Proof. Since $\ker A_k$ is obviously contained in $\ker Y A_k$ we need only show that $\ker Y A_k$ is contained in $\ker A_k$. For $x \in \ker Y A_k$ we have

$$A_k x \in \ker Y .$$

Since A_k takes values in $\text{span}(\Delta)$, where Δ is defined for the network by (4.18), we have in fact the inclusion

$$A_k x \in \ker Y \cap \text{span}(\Delta) .$$

Thus, from Proposition 4.7, $A_k x = 0$ so that x is contained in $\ker A_k$, and we have $\ker Y A_k = \ker A_k$. ///

Remark 4.12. Corollary 4.11 tells us that, for a zero deficiency network $\{\mathcal{S}, \mathcal{C}, \mathcal{R}\}$, the structure of $\ker Y A_k$ is precisely that given by Proposition 4.1, regardless of the value that $k \in \mathbb{P}^{\mathcal{R}}$ takes. In particular, $\dim \ker Y A_k$ is equal to the number of terminal strong linkage classes in the network. If each linkage class contains precisely one terminal strong linkage class then, obviously, $\dim \ker Y A_k$ is equal to the number of linkage classes. This last statement admits a generalization for networks of arbitrary deficiency:

Corollary 4.12. Let $\{\mathcal{S},\mathcal{C},\mathcal{R}\}$ be a reaction network for which each linkage class contains precisely one terminal strong linkage class, and let k be any element of $\mathbb{R}^{\mathcal{R}}$. If Y is the stoichiometric map for the network, if A_k is as in Proposition 4.1, if δ is the deficiency of the network and if ℓ is the number of its linkage classes then

$$\dim(\ker Y A_k) = \ell + \delta. \tag{4.44}$$

In particular, (4.44) holds if the network is weakly reversible.

Proof. For the linear transformation $Y A_k: \mathbb{R}^{\mathcal{C}} \to \mathbb{R}^{\mathcal{S}}$ we have the standard relationship between the dimensions of the domain, kernel and image. Since $\dim \mathbb{R}^{\mathcal{C}} = n$ (the number of complexes) we have

$$\dim \ker Y A_k = n - \dim \operatorname{im} Y A_k . \tag{4.45}$$

Because each linkage class contains precisely one terminal strong linkage class we know (Remark 4.7) that $\operatorname{im} Y A_k = S$, where S is the stoichiometric subspace of the network. Moreover, $\dim S = s$, where s is the rank of the network. Thus, from (4.45),

$$\begin{aligned} \dim \ker Y A_k &= n - s \\ &= \ell + (n - \ell - s) \\ &= \ell + \delta. \end{aligned}$$

///

Remark 4.13. For networks having more terminal strong linkage classes than linkage classes equation (4.44) need not hold. In fact, it need not hold even when the number of linkage classes in (4.44) is replaced by the number of strong terminal linkage classes. For such networks $\dim \ker Y A_k$ may depend on the particular $k \in \mathbb{P}^{\mathcal{R}}$ with which A_k is constructed. Consider, for example, the network

$$2A \longleftarrow A+B \longrightarrow 2B \ , \tag{4.46}$$

for which there are two terminal strong linkage classes — $\{2A\}$ and $\{2B\}$ — and one linkage class, $\{2A, A+B, 2B\}$. It is not difficult to show that, for $k_{A+B \to 2A} = k_{A+B \to 2B}$, $\dim \ker Y A_k = 3$ while, for $k_{A+B \to 2A} \neq k_{A+B \to 2B}$, $\dim \ker Y A_k = 2$.

The problem with network (4.46) is that, for at least certain values of k, $\operatorname{im} Y A_k$ need not coincide with S, the stoichiometric subspace of the network. (Recall that this coincidence played a role in the proof of Corollary 4.12.) An extensive discussion of the relationship between $\operatorname{im} Y A_k$ and S for networks in general is given in [FH2]. From results contained there it is not difficult to show that, for any network $\{\mathcal{C}, \mathcal{G}, \mathcal{R}\}$ and for all $k \in \mathbb{P}^{\mathcal{R}}$, one has

$$\ell + \delta \leq \dim \ker Y A_k \leq t + \delta \ , \tag{4.47}$$

where δ is the deficiency, ℓ is the number of linkage classes, and t is the number of terminal strong linkage classes. Moreover, for <u>all</u> $k \in \mathbb{P}^{\mathcal{R}}$ strict inequality holds in the lower estimate of (4.47) provided that $t - \ell > \delta$ (or, equivalently, $n - t - s < 0$, where n is the number of complexes). Note that for (4.46) $\delta = 1$, $\ell = 1$ and $t = 2$ so that this condition is not satisfied.

4.D. A Proposition Concerning the Nature of Equilibria

Before closing this lecture I shall need one more proposition. Because it is somewhat disconnected from those results we have accumulated so far I should provide some additional motivation for what we are about to do. I begin by recalling some definitions stated in Lecture 2.

Definition 4.9. Let $\{\mathcal{S}, \mathcal{C}, \mathcal{R}\}$ be a reaction network, and let $S \subset \mathbb{R}^{\mathcal{S}}$ be its stoichiometric subspace. Two vectors $c \in \overline{\mathbb{P}}^{\mathcal{S}}$ and $c' \in \overline{\mathbb{P}}^{\mathcal{S}}$ are stoichiometrically compatible if $c'-c$ lies in S. Stoichiometric compatibility is an equivalence relation that induces a partition of $\overline{\mathbb{P}}^{\mathcal{S}}$ [resp., $\mathbb{P}^{\mathcal{S}}$] into equivalence classes called the stoichiometric compatibility classes [resp., positive stoichiometric compatibility classes] for the network. In particular, the stoichiometric compatibility class containing $c \in \overline{\mathbb{P}}^{\mathcal{S}}$ is the set $(c+S) \cap \overline{\mathbb{P}}^{\mathcal{S}}$, and the positive stoichiometric compatibility class containing $c \in \mathbb{P}^{\mathcal{S}}$ is the set $(c+S) \cap \mathbb{P}^{\mathcal{S}}$.

In proving parts of both theorems stated in Lecture 3 I shall have to show that, under certain circumstances, the differential equations for a mass action system $\{\mathcal{S}, \mathcal{C}, \mathcal{R}, k\}$ admit precisely one equilibrium point in each positive stoichiometric compatibility class. To do this I will show that, under the given circumstances, the set of all positive equilibrium points is identical to the set

$$E := \{c \in \mathbb{P}^{\mathcal{S}} : \ln c - \ln c^* \in S^{\perp}\}, \tag{4.48}$$

where c^* is a fixed element of $\mathbb{P}^{\mathcal{S}}$, where $S^{\perp}$ is the orthogonal complement (relative to the standard scalar product in $\mathbb{R}^{\mathcal{S}}$) of the

stoichiometric subspace for the network, and where $\ln c$ is that vector of $\mathbb{R}^{\mathcal{S}}$ defined by

$$(\ln c)_s = \ln c_s \quad , \quad \forall s \in \mathcal{S} . \tag{4.49}$$

Thus, to show that each positive stoichiometric compatibility class contains precisely one equilibrium it will be useful to know that the set E meets each positive stoichiometric compatibility class in precisely one point.

Uniqueness is easy: Suppose that c' and c are stoichiometrically compatible and are members of E. From stoichiometric compatibility we have that

$$c' - c \in S , \tag{4.50}$$

and, from (4.48), it follows easily that

$$\ln c' - \ln c \in S^{\perp} . \tag{4.51}$$

Thus, from (4.50) and (4.51) we have

$$0 = (c'-c) \cdot (\ln c' - \ln c) = \sum_{s \in \mathcal{S}} (c'_s - c_s)(\ln c'_s - \ln c_s) . \tag{4.52}$$

Since the function $\ln: \mathbb{P} \to \mathbb{R}$ is strictly monotonically increasing, (4.52) can hold only if, for all $s \in \mathcal{S}$, $c'_s = c_s$ — that is, only if $c' = c$.

It is somewhat more difficult to show that each positive stoichiometric compatibility class in fact meets E. The argument I shall give is essentially a variation of that given by Horn and Jackson [HJ, Section 4]. The result we seek will emerge as a consequence of our next proposition. In preparation for its statement we review some matters of notation. If x is a member of $\mathbb{R}^{\mathcal{S}}$, then $e^x \in \mathbb{P}^{\mathcal{S}}$ is defined by

$$(e^x)_s = e^{x_s} , \quad \forall s \in \mathcal{S} .$$

If x and y are members of $\mathbb{R}^{\mathcal{S}}$, then $xy \in \mathbb{R}^{\mathcal{S}}$ is defined by

$$(xy)_\delta = x_\delta y_\delta , \quad \forall\, \delta \in \mathcal{S} .$$

In particular, for $a \in \mathbb{R}^{\mathcal{S}}$ and $x \in \mathbb{R}^{\mathcal{S}}$ we have

$$(a\, e^x)_\delta = a_\delta e^{x_\delta} , \quad \forall\, \delta \in \mathcal{S} .$$

In Proposition 4.13 $\mathbb{R}^{\mathcal{S}}$ is endowed with the standard scalar product.

Proposition 4.13. Let $\mathcal{S}$ be any finite set, let $\mathbb{R}^{\mathcal{S}}$ be the vector space generated by $\mathcal{S}$, let S be a linear subspace of $\mathbb{R}^{\mathcal{S}}$, and let a and b be elements of $\mathbb{P}^{\mathcal{S}}$. There exists a (unique) vector $\mu \in S^{\perp}$ such that

$$a\, e^{\mu} - b$$

is an element of S.

Proof. Let $\phi: \mathbb{R}^{\mathcal{S}} \to \mathbb{R}$ be defined by

$$\phi(x) := \sum_{\delta \in \mathcal{S}} (a_\delta\, e^{x_\delta} - b_\delta x_\delta) . \tag{4.53}$$

Straightforward computation shows that the gradient of ϕ at x is given

$$\nabla\phi(x) = a\, e^x - b \tag{4.54}$$

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

$$H(x)\gamma \equiv (a\, e^x)\gamma . \tag{4.55}$$

Moreover, for each $x \in \mathbb{R}^{\mathcal{J}}$, $H(x)$ is positive-definite: For all non-zero $\gamma \in \mathbb{R}^{\mathcal{J}}$

$$\gamma \cdot H(x)\gamma = \gamma \cdot a e^{x}\gamma = \sum_{\delta \in \mathcal{J}} a_\delta e^{x_\delta}(\gamma_\delta)^2 > 0 \ . \tag{4.56}$$

Thus, the function ϕ is strictly convex.

Next we wish to show that, for any non-zero $x \in \mathbb{R}^{\mathcal{J}}$,

$$\lim_{\alpha \to \infty} \phi(\alpha x) = \infty \ . \tag{4.57}$$

Note that

$$\phi(\alpha x) = \sum_{\delta \in \mathcal{J}} (a_\delta e^{\alpha x_\delta} - \alpha\, b_\delta x_\delta) \tag{4.58}$$

Note also that, for $x_\delta \neq 0$, the positivity of a_δ and b_δ give

$$\lim_{\alpha \to \infty} (a_\delta\, e^{\alpha x_\delta} - \alpha\, b_\delta x_\delta) = \infty \ , \tag{4.59}$$

while for $x_\delta = 0$ we have

$$(a_\delta\, e^{\alpha x_\delta} - \alpha\, b_\delta x_\delta) = a_\delta \ , \ \forall\, \alpha \in \mathbb{R} \ . \tag{4.60}$$

Thus, for $x \neq 0$, (4.58)-(4.60) imply (4.57).

Now let $\bar{\phi}: S^{\perp} \to \mathbb{R}$ be the restriction of ϕ to $S^{\perp}$. Since ϕ is continuous and convex so is $\bar{\phi}$. Thus, the continuity of $\bar{\phi}$ and a standard result for convex functions give that the set

$$C := \{x \in S^{\perp} : \bar{\phi}(x) \leq \bar{\phi}(0)\} \tag{4.61}$$

is closed, convex (and obviously contains the zero vector). Moreover, it follows from (4.57) that C contains no half-line with end-point 0. Since, in a finite-dimensional vector space, every unbounded closed convex set containing 0 must contain a half-line with end-point 0 — see [SW], p.105 — it follows that C is bounded and therefore compact.

Thus, there exists $\mu \in C$ such that

$$\bar{\phi}(\mu) \leq \bar{\phi}(x) \ , \ \forall\, x \in C \ . \tag{4.62}$$

In fact, from the definition of C we have

$$\bar{\phi}(\mu) \leq \bar{\phi}(x) \ , \ \forall\, x \in S^{\perp} \ . \tag{4.63}$$

Thus, for all $\gamma \in S^{\perp}$,

$$0 = \frac{d}{d\theta}\, \bar{\phi}(\mu + \theta\gamma)\Big|_{\theta=0}$$

$$= \frac{d}{d\theta}\, \phi(\mu + \theta\gamma)\Big|_{\theta=0}$$

$$= \nabla\phi(\mu) \cdot \gamma$$

It follows that $\nabla\phi(\mu)$ must lie in S so that, from (4.54), we have the inclusion

$$a\, e^{\mu} - b \in S \ . \tag{4.64}$$

Thus, $\mu \in S^{\perp}$ satisfies the requirement of the proposition.

To prove uniqueness we presume that $\mu' \in S^{\perp}$ also satisfies the inclusion

$$a\, e^{\mu'} - b \in S \ . \tag{4.65}$$

From (4.64) and (4.65) we have

$$a(e^{\mu'} - e^{\mu}) \in S ,$$

and, since $\mu'-\mu$ lies in $S^{\perp}$, we must have

$$0 = (\mu'-\mu) \cdot [a(e^{\mu'}-e^{\mu})] = \sum_{\delta \in \mathcal{S}} a_{\delta}(\mu'_{\delta}-\mu_{\delta})(e^{\mu'_{\delta}}-e^{\mu_{\delta}}). \tag{4.66}$$

Since each a_{δ} is positive and since the exponential function is strictly monotonically increasing, (4.66) can hold only if, for all $\delta \in \mathcal{S}$, $\mu'_{\delta} = \mu_{\delta}$ — that is, only if $\mu' = \mu$. ///

Remark 4.14. There is an interesting observation that can be made here. With $\mathbb{R}^{\mathcal{S}}$ and S as in Proposition 4.13 it is a standard result in linear algebra that any $b \in \mathbb{R}^{\mathcal{S}}$ has a unique representation

$$b = x_1 + x_2 , \quad x_1 \in S^{\perp} , \quad x_2 \in S .$$

Taking $a_{\delta} = 1$ for all $\delta \in \mathcal{S}$ in Proposition 4.13, we obtain a similar (but deeper) result: Any positive $b \in \mathbb{R}^{\mathcal{S}}$ — that is, any $b \in \mathbb{P}^{\mathcal{S}}$ — admits a unique representation

$$b = e^{\mu_1} + \mu_2 , \quad \mu_1 \in S^{\perp}, \mu_2 \in S .$$

Corollary 4.14. Let $\{\mathcal{S}, \mathcal{C}, \mathcal{R}\}$ be a reaction network with stoichiometric subspace $S \subset \mathbb{R}^{\mathcal{S}}$. For any $c^* \in \mathbb{P}^{\mathcal{S}}$ the set

$$E := \{c \in \mathbb{P}^{\mathcal{S}} : \ln c - \ln c^* \in S^{\perp}\}$$

meets each positive stoichiometric compatibility class in precisely one point.

Proof. Let p be an arbitrary element of $\mathbb{P}^{\mathcal{S}}$. We shall show that E meets the positive stoichiometric compatibility class containing p in precisely one point. That there can be at most one such point was proved in the discussion prior to the statement of Proposition 4.13. To prove the existence of such a point we note that Proposition 4.13 ensures the existence of $\mu \in S^{\perp}$ such that

$$c^* e^{\mu} - p \in S . \tag{4.67}$$

Now let $c \in \mathbb{P}^{\mathcal{S}}$ be defined by

$$c := c^* e^{\mu} . \tag{4.68}$$

From (4.67), (4.68), and Definition 4.9 it is clear that c lies in the positive stoichiometric compatibility class containing p. Taking logarithms of both sides of (4.68) we obtain

$$\ln c - \ln c^* = \mu \in S^{\perp} \tag{4.69}$$

Thus, c lies in E as well. ///

Having assembled a reasonable "bag of tools", we turn now to proof of the Deficiency Zero Theorem.