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 5: PROOF OF THE DEFICIENCY ZERO THEOREM

Although our proof of the Deficiency Zero Theorem will be fairly clean, the course we'll take is a little indirect. Readers will notice that, in a few places, we study networks of arbitrary deficiency, showing that, when special conditions prevail, the corresponding differential equations have exceptionally nice properties. Only then do we prove that those special conditions prevail automatically for networks of deficiency zero. In this way we can begin to accumulate certain results which, while especially pertinent to deficiency zero networks, have some bearing on networks of higher deficiency as well. These results will ultimately find use in subsequent lectures.

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

$$\dot{c} = \sum_{\mathcal{R}} \mathcal{K}_{y\to y'}(c)(y'-y) \quad . \tag{5.1}$$

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

$$\dot{c} = \sum_{\mathcal{R}} k_{y\to y'}\, c^y(y'-y) \quad , \tag{5.2}$$

where

$$c^y := \prod_{s\in\mathcal{S}} c_s^{\,y_s} \quad . \tag{5.3}$$

For the convenience of the reader we repeat the Deficiency Zero Theorem here:

<u>Theorem 5.1 (The Deficiency Zero Theorem). Let $\{\mathcal{S},\mathcal{C},\mathcal{R}\}$ be any reaction network of deficiency zero.</u>

(i) <u>If the network is not weakly reversible then, for arbitrary kinetics $\mathcal{K}$, the differential equations for the reaction system $\{\mathcal{S},\mathcal{C},\mathcal{R},\mathcal{K}\}$ cannot admit a positive equilibrium (i.e., an equilibrium in $\mathbb{P}^{\mathcal{S}}$).</u>

(ii) <u>If the network is not weakly reversible then, for arbitrary kinetics $\mathcal{K}$, the differential equations for the reaction system $\{\mathcal{S},\mathcal{C},\mathcal{R},\mathcal{K}\}$ cannot admit a cyclic composition trajectory containing a positive composition (i.e., a point in $\mathbb{P}^{\mathcal{S}}$).</u>

(iii) <u>If the network is weakly reversible then, for any mass action kinetics $k \in \mathbb{P}^{\mathcal{R}}$, the differential equations for the mass action system $\{\mathcal{S},\mathcal{C},\mathcal{R},k\}$ have the following properties: There exists within each positive stoichiometric compatibility class precisely one equilibrium; that equilibrium is asymptotically stable; and there cannot exist a nontrivial cyclic composition trajectory in $\mathbb{P}^{\mathcal{S}}$.</u>

<u>Remark 5.1.</u> Once we have proved Theorem 5.1 in Section 5.A and make comments on the proof in Section 5.B we shall, in Section 5.C, indicate how the statement of the theorem can be sharpened.

5.A. *Proof*

Our proof of Theorem 5.1 will be divided into three parts. First we shall prove the relatively easy parts (i) and (ii). Second, we shall prove part (iii) on the basis of the assumption that the differential equations for the mass action system $\{\mathcal{S},\mathcal{C},\mathcal{R},k\}$ admit a positive equilibrium (not necessarily one in each positive stoichiometric compatibility class). Finally, we will prove that the differential equations do indeed admit a positive equilibrium.

5.A.1 Proof of parts (i) and (ii). We begin with the following lemma (for networks of arbitrary deficiency endowed with arbitrary kinetics).

Lemma 5.2. The differential equations for a reaction system $\{\mathcal{S},\mathcal{C},\mathcal{R},\mathcal{K}\}$ admit an equilibrium in $\mathbb{P}^{\mathcal{S}}$ or a cyclic trajectory containing a point in $\mathbb{P}^{\mathcal{S}}$ only if there exists $\alpha \in \mathbb{P}^{\mathcal{R}}$ that satisfies the equation

$$\sum_{\mathcal{R}} \alpha_{y\to y'}(y'-y) = 0 \ . \tag{5.4}$$

Proof. Suppose that $c^* \in \mathbb{P}^{\mathcal{S}}$ is an equilibrium for (5.1). Then

$$\sum_{\mathcal{R}} \mathcal{K}_{y\to y'}(c^*)(y'-y) = 0 \ . \tag{5.5}$$

Since $\operatorname{supp} c^* = \mathcal{S}$ we have

$$\operatorname{supp} y \subset \operatorname{supp} c^* \ , \quad \forall\, y \in \mathcal{C} \ . \tag{5.6}$$

Thus, from our definition of a kinetics (Lecture 2) we have

$$\mathcal{K}_{y \to y'}(c^*) > 0 \quad , \quad \forall\, y \to y' \in \mathcal{R} \; . \tag{5.7}$$

Let $\alpha \in \mathbb{P}^{\mathcal{R}}$ be defined by

$$\alpha_{y \to y'} := \mathcal{K}_{y \to y'}(c^*) \quad , \quad \forall\, y \to y' \in \mathcal{R} \; . \tag{5.8}$$

From (5.5) it follows that α satisfies (5.4).

Now let $\bar{c}:[0,T] \to \bar{\mathbb{P}}$ be a solution of (5.1) such that $\bar{c}(0) = \bar{c}(T)$. Since, from the definition of a kinetics, each of the rate functions $\mathcal{K}_{y \to y'}(\cdot)$ takes non-negative values and is continuous, it follows that, for each $y \to y' \in \mathcal{R}$, the composite function $\mathcal{K}_{y \to y'}(\bar{c}(\cdot))$ takes non-negative values and is continuous. Integrating (5.1) with respect to time over the interval $[0,T]$ we obtain

$$0 = \sum_{\mathcal{R}} \left[\int_0^T \mathcal{K}_{y \to y'}(\bar{c}(t))\,dt \right](y'-y) \; . \tag{5.9}$$

Note that each of the integrals in (5.9) is non-negative. Now suppose that there exists $t_1 \in [0,T]$ such that $\bar{c}(t_1)$ is a member of $\mathbb{P}^{\mathcal{S}}$. Then, from an argument virtually identical to that given at the beginning of this proof, we have

$$\mathcal{K}_{y \to y'}(\bar{c}(t_1)) > 0 \quad , \quad \forall\, y \to y' \in \mathcal{R} . \tag{5.10}$$

This and the continuity of the $\mathcal{K}_{y \to y'}(\bar{c}(\cdot))$ ensure that each of the integrals in (5.9) is in fact positive. Letting $\alpha \in \mathbb{P}^{\mathcal{R}}$ be defined by

$$\alpha_{y \to y'} := \int_0^T \mathcal{K}_{y \to y'}(\bar{c}(t))\,dt \; , \tag{5.11}$$

we see from (5.9) that α satisfies (5.4). ///

To complete the proof of parts (i) and (ii) of Theorem 5.1 we merely combine Lemma 5.2 with Corollary 4.9, which asserts that if $\{\mathcal{S},\mathcal{C},\mathcal{R}\}$ is a deficiency zero network which is not weakly reversible then there can exist no $\alpha \in \mathbb{P}^{\mathcal{R}}$ that satisfies (5.4). ///

5.A.2. *Proof of part (iii), given the existence of an equilibrium in $\mathbb{P}^{\mathcal{S}}$.*

At the outset we will focus on a fixed mass action system $\{\mathcal{S},\mathcal{C},\mathcal{R}, k\}$ without supposing that the network $\{\mathcal{S},\mathcal{C},\mathcal{R}\}$ is of deficiency zero. Recall from Lecture 2 that the species formation rate function $f: \overline{\mathbb{P}}^{\mathcal{S}} \to \mathbb{R}^{\mathcal{S}}$ for the mass action system $\{\mathcal{S},\mathcal{C},\mathcal{R},k\}$ is given by

$$f(c) \equiv \sum_{\mathcal{R}} k_{y\to y'} c^y (y'-y) \ . \tag{5.12}$$

Thus, the differential equation (5.2) is just

$$\dot{c} = f(c) \ . \tag{5.13}$$

Recall also from Lecture 4 (Section 4.A) that the species formation rate function can be cast in the form

$$f(c) \equiv Y A_k \Psi(c) \quad , \tag{5.14}$$

where $Y:\mathbb{R}^{\mathcal{C}} \to \mathbb{R}^{\mathcal{S}}$ is the stoichiometric map for the network $\{\mathcal{S},\mathcal{C},\mathcal{R}\}$, where $A_k:\mathbb{R}^{\mathcal{C}} \to \mathbb{R}^{\mathcal{C}}$ is constructed for the mass action kinetics $k \in \mathbb{P}^{\mathcal{R}}$ as in Proposition 4.1, and where $\Psi : \overline{\mathbb{P}}^{\mathcal{S}} \to \overline{\mathbb{P}}^{\mathcal{C}}$ is given by

$$\Psi(c) \equiv \sum_{y\in\mathcal{C}} c^y \omega_y \ , \tag{5.15}$$

$\{\omega_y \in \mathbb{R}^{\mathcal{C}} : y \in \mathcal{C}\}$ denoting the standard basis for $\mathbb{R}^{\mathcal{C}}$.

If $c^* \in \bar{\mathbb{P}}^{\mathcal{S}}$ is an equilibrium of (5.13) — that is, if $f(c^*) = 0$ — then, from (5.14), we must have the inclusion

$$\Psi(c^*) \in \ker Y A_k \ .$$

It <u>may</u> happen that we have in fact the stronger inclusion

$$\Psi(c^*) \in \ker A_k \ . \tag{5.16}$$

Now if there exists a positive equilibrium, $c^* \in \mathbb{P}^{\mathcal{S}}$, satisfying the special condition (5.16) then, surprisingly enough, one can say quite a bit about the quality of solutions to (5.13). This was first observed by Horn and Jackson [HJ], but some of the arguments I give [F3] are rather different from theirs.

Throughout our discussion it will be understood that the functions f, Y, A_k and Ψ are constructed as above for the fixed mass action system $\{\mathcal{S}, \mathcal{C}, \mathcal{R}, k\}$ under consideration. Logarithms of positive vectors are taken component-wise as in Lecture 1. Many of our results will derive from the following proposition:

<u>Proposition 5.3</u>. <u>Let</u> $\{\mathcal{S}, \mathcal{C}, \mathcal{R}, k\}$ <u>be a mass action system with stoichiometric subspace</u> $S \subset \mathbb{R}^{\mathcal{S}}$ <u>and species formation rate function</u> $f: \bar{\mathbb{P}}^{\mathcal{S}} \to \mathbb{R}^{\mathcal{S}}$. <u>If there exists</u> $c^* \in \mathbb{P}^{\mathcal{S}}$ <u>such that</u>

$$A_k \Psi(c^*) = 0 \ , \tag{5.17}$$

<u>then</u>

$$f(c) \cdot (\ln c - \ln c^*) \leq 0 \ , \quad \forall c \in \mathbb{P}^{\mathcal{S}} \ . \tag{5.18}$$

<u>Moreover, for</u> $c \in \mathbb{P}^{\mathcal{S}}$ <u>the following are equivalent</u>:

(i) $f(c) \cdot (\ln c - \ln c^*) = 0$

(ii) $\ln c - \ln c^*$ <u>lies in</u> $S^{\perp}$

(iii) $A_k \Psi(c) = 0$

(iv) $f(c) = 0$.

Remark 5.2. Since c^* in Proposition 5.3 is strictly positive ($c^* \in \mathbb{P}^{\mathcal{S}}$) it follows that $\Psi(c^*)$ is strictly positive ($\Psi(c^*) \in \mathbb{P}^{\mathcal{C}}$), whereupon (5.17) requires that A_k have a strictly positive vector in its kernel. Thus, from Corollary 4.2, the hypothesis of Proposition 5.3 can be satisfied only if the network $\{\mathcal{S}, \mathcal{C}, \mathcal{R}\}$ is weakly reversible.

Proof of Proposition 5.3. Let $\mu: \mathbb{P}^{\mathcal{S}} \to \mathbb{R}^{\mathcal{S}}$ be defined by

$$\mu(c) := \ln c - \ln c^* . \tag{5.19}$$

From (5.3) it is easy to confirm that, for $c \in \mathbb{P}^{\mathcal{S}}$,

$$c^y = (c^*)^y \, e^{y \cdot \mu(c)} , \quad \forall\, y \in \mathcal{C} . \tag{5.20}$$

Therefore, from (5.12) and (5.20) we have for all $c \in \mathbb{P}^{\mathcal{S}}$

$$f(c) = \sum_{\mathcal{R}} k_{y \to y'} (c^*)^y \, e^{y \cdot \mu(c)} (y' - y) . \tag{5.21}$$

From (5.19) and (5.21) we have for all $c \in \mathbb{P}^{\mathcal{S}}$

$$f(c) \cdot (\ln c - \ln c^*) = \sum_{\mathcal{R}} k_{y \to y'} (c^*)^y \, e^{y \cdot \mu(c)} (y' \cdot \mu(c) - y \cdot \mu(c)) . \tag{5.22}$$

Now the exponential function has the following well-known property: For any α' and α in $\mathbb{R}$

$$e^{\alpha}(\alpha' - \alpha) \le e^{\alpha'} - e^{\alpha} \tag{5.23}$$

with equality holding if and only if $\alpha' = \alpha$. Using the estimate (5.23) termwise in (5.22) we obtain

$$f(c) \cdot (\ln c - \ln c^*) \leq \sum_{\mathcal{R}} k_{y \to y'} (c^*)^y (e^{y' \cdot \mu(c)} - e^{y \cdot \mu(c)}) \ , \ \forall c \in \mathbb{P}^{\mathcal{S}} \tag{5.24}$$

with equality holding if and only if

$$\mu(c) \cdot (y'-y) = 0 \quad , \quad \forall\, y \to y' \in \mathcal{R} \ . \tag{5.25}$$

Using the orthonormality of the standard basis for $\mathbb{R}^{\mathcal{C}}$, we can rewrite the right side of (5.24) as

$$[\sum_{\mathcal{R}} k_{y \to y'} (c^*)^y (\omega_{y'} - \omega_y)\ ] \cdot \sum_{y'' \in \mathcal{C}} e^{y'' \cdot \mu(c)} \omega_{y''} \tag{5.26}$$

But the term in brackets in (5.26) is just $A_k \Psi(c^*)$ which, by hypothesis, is just the zero vector of $\mathbb{R}^{\mathcal{C}}$. Thus, the right side of (5.24) vanishes for all $c \in \mathbb{P}^{\mathcal{S}}$ so that (5.24) is equivalent to (5.18).

To show that (i) and (ii) are equivalent we note that equality holds in (5.24) and, therefore, in (5.18) if and only if $c \in \mathbb{P}^{\mathcal{S}}$ satisfies (5.25). Since the stoichiometric subspace for the network is just the span of its reaction vectors, (5.25) is equivalent to the inclusion

$$\ln c - \ln c^* = \mu(c) \in S^{\perp} \ . \tag{5.27}$$

Next we show that (ii) implies (iii). From Remark 5.2 we know that the network $\{\mathcal{S}, \mathcal{C}, \mathcal{R}\}$ is weakly reversible so that its terminal strong linkage classes coincide with its linkage classes, which we denote $L^1, L^2, \ldots, L^{\ell}$. Moreover, we have from Proposition 4.1 the existence of a basis $\{x^1, x^2, \ldots, x^{\ell}\} \subset \overline{\mathbb{P}}^{\mathcal{C}}$ for $\ker A_k$ such that

$$\operatorname{supp} x^{\theta} = L^{\theta} \quad , \quad \theta = 1, 2, \ldots, \ell \ . \tag{5.28}$$

Thus, from (5.17), $\Psi(c^*) \in \mathbb{P}^{\mathcal{C}}$ has a representation of the following kind: There exist (positive) numbers $\lambda_1,\ldots,\lambda_\ell$ such that

$$\begin{aligned}\Psi(c^*) &= \sum_{y\in\mathcal{C}} (c^*)^y \omega_y \\ &= \sum_{\theta=1}^{\ell} \Big(\sum_{y\in L^\theta} (c^*)^y \omega_y \Big) \\ &= \sum_{\theta=1}^{\ell} \lambda_\theta x^\theta \quad . \end{aligned} \tag{5.29}$$

The second equation in (5.29) follows from the fact that $\mathcal{C}$ is the disjoint union of the linkage classes. From (5.28) and the third equation of (5.29) it follows easily that

$$\sum_{y\in L^\theta} (c^*)^y \omega_y = \lambda_\theta x^\theta \quad , \quad \theta = 1,2,\ldots,\ell \tag{5.30}$$

This is to say that the set

$$\{ \sum_{y\in L^\theta} (c^*)^y \omega_y \in \overline{\mathbb{P}}^{\mathcal{C}} : \theta = 1,2,\ldots,\ell \} \tag{5.31}$$

is also a basis for $\ker A_k$. Now suppose that $c \in \mathbb{P}^{\mathcal{S}}$ is such that (ii) holds or, equivalently, that

$$\mu(c) \in S^{\perp} \quad , \tag{5.32}$$

where $\mu(c)$ is as in (5.19). From (5.32) and (4.32) we have that $y'\cdot\mu(c) = y\cdot\mu(c)$ whenever y' and y are linked. That is, there exist numbers $\xi_1,\ldots,\xi_\ell$ such that

$$y \cdot \mu(c) = \xi_\theta \quad , \quad \forall\, y \in L^\theta \, . \tag{5.33}$$

From (5.15) and (5.20) we have

$$\begin{aligned}
\Psi(c) &= \sum_{y \in \mathcal{C}} c^y \omega_y \\
&= \sum_{y \in \mathcal{C}} (c^*)^y e^{y \cdot \mu(c)} \omega_y \\
&= \sum_{\theta=1}^{\ell} \Big(\sum_{y \in L^\theta} (c^*)^y e^{y \cdot \mu(c)} \omega_y \Big) \\
&= \sum_{\theta=1}^{\ell} e^{\xi_\theta} \Big(\sum_{y \in L^\theta} (c^*)^y \omega_y \Big) \, .
\end{aligned} \tag{5.34}$$

Since (5.31) is a basis for ker A_k it follows from (5.34) that $A_k \Psi(c) = 0$.

That (iii) implies (iv) follows immediately from (5.14). That (iv) implies (i) is trivial. ///

Corollary 5.4. Under the hypothesis of Proposition 5.3 the differential equations for the mass action system $\{\mathcal{S}, \mathcal{C}, \mathcal{R}, k\}$ admit precisely one equilibrium in each positive stoichiometric compatibility class.

Proof. From the equivalence of (ii) and (iv) in Proposition 5.3 the set of equilibria in $\mathbb{P}^{\mathcal{S}}$ coincides with the set

$$E = \{ c \in \mathbb{P}^{\mathcal{S}} : \ln c - \ln c^* \in S^\perp \} \, . \tag{5.35}$$

From Corollary 4.14 this set meets each positive stoichiometric compatibility class in precisely one point. ///

Remark 5.4. Under the hypothesis of Proposition 5.3 we have, from the equivalence of (iii) and (iv), that *every* equilibrium in $\mathbb{P}^{\mathcal{S}}$ satisfies (iii). Thus, *any* positive equilibrium satisfies the condition imposed on c^* in the hypothesis of Proposition 5.3, and any of them might have served as c^* in the statement of the proposition. With this in mind we can, when the hypothesis of Proposition 5.3 is satisfied, think of c^* as a fixed but *arbitrary* positive equilibrium for the mass action system $\{\mathcal{S}, \mathcal{C}, \mathcal{R}, k\}$.

Remark 5.5. Under the hypothesis of Proposition 5.3 we have from Corollary 5.4 a great deal of information about the nature of equilibrium points for the differential equations of the mass action system $\{\mathcal{S}, \mathcal{C}, \mathcal{R}, k\}$. Now we would like dynamical information as well. We shall proceed by means of Liapunov functions.

For fixed $c^* \in \mathbb{P}^{\mathcal{S}}$ let $h: \mathbb{P}^{\mathcal{S}} \to \mathbb{R}$ be defined by

$$h(c) \equiv \sum_{s \in \mathcal{S}} [c_s(\ln c_s - \ln c_s^* - 1) + c_s^*] \ . \tag{5.36}$$

Clearly,

$$h(c^*) = 0 \ . \tag{5.37}$$

Moreover, from the strict concavity of the logarithm function we have, for each $s \in \mathcal{S}$ and each $c_s > 0$,

$$\ln c_s - \ln c_s^* \geq \frac{1}{c_s} (c_s - c_s^*) \tag{5.38}$$

with equality holding if and only if $c_s = c_s^*$. From this we obtain

$$h(c) > 0 \quad , \quad c \neq c^* \ . \tag{5.39}$$

Moreover, straightforward computation gives

$$\nabla h(c) \equiv \ln c - \ln c^* . \tag{5.40}$$

From (5.40) the Hessian of h at $c \in \mathbb{P}^{\mathcal{S}}$, $G(c): \mathbb{R}^{\mathcal{S}} \to \mathbb{R}^{\mathcal{S}}$, is given by

$$G(c)\gamma = \frac{\gamma}{c} , \quad \forall\, \gamma \in \mathbb{R}^{\mathcal{S}} , \tag{5.41}$$

where $(\gamma/c)_s = \gamma_s/c_s$. Note that for all $c \in \mathbb{P}^{\mathcal{S}}$ and all non-zero $\gamma \in \mathbb{R}^{\mathcal{S}}$

$$\gamma \cdot G(c)\gamma = \sum_{s \in \mathcal{S}} \gamma_s^{\,2}/c_s > 0 . \tag{5.42}$$

Thus, the Hessian of h is positive-definite at each $c \in \mathbb{P}^{\mathcal{S}}$ so that h is strictly convex.

We are now in a position to state our next corollary of Proposition 5.3.

Corollary 5.5. *Under the hypothesis of Proposition 5.3 and with* c^* *as in that proposition, let* $h:\mathbb{P}^{\mathcal{S}} \to \mathbb{R}$ *be as in (5.36). Then, for all* $c \in \mathbb{P}^{\mathcal{S}}$,

$$\nabla h(c) \cdot f(c) \le 0 \tag{5.43}$$

with equality holding if and only if $f(c) = 0$.

Proof. This is an immediate consequence of (5.40) and Proposition 5.3. ///

Remark 5.6. Suppose that the hypothesis of Proposition 5.3 holds, that c^* is as in that proposition and that $h(\cdot)$ is as in (5.36). In rough terms Corollary 5.5 tells us that, for any positive solution $c(\cdot)$ of (5.2), the function $h(c(\cdot))$ is non-increasing along that solution and is decreasing except at equilibrium points. That is,

$$\begin{aligned}\frac{d}{dt}h(c(t)) &= \nabla h(c(t)) \cdot \dot{c}(t)\\ &= \nabla h(c(t)) \cdot f(c(t))\\ &\leq 0 \end{aligned} \tag{5.44}$$

with equality holding if and only if $\dot{c}(t) = f(c(t)) = 0$.

Corollary 5.6. Under the hypothesis of Propositon 5.3 the differential equations for the mass action system $\{\mathcal{S},\mathcal{C},\mathcal{R},k\}$ admit no nontrivial cyclic composition trajectories in $\mathbb{P}^{\mathcal{S}}$.

Proof. Suppose that $c:[0,T] \to \mathbb{P}^{\mathcal{S}}$ is a nonconstant solution of (5.2) such that $c(0) = c(T)$. With c^* as in Proposition 5.3 let $h:\mathbb{P}^{\mathcal{S}} \to \mathbb{R}$ be as in (5.36). Then

$$\begin{aligned}h(c(T)) - h(c(0)) &= \int_0^T \frac{d}{dt}h(c(t))dt\\ &= \int_0^T \nabla h(c(t)) \cdot f(c(t))dt \end{aligned} \tag{5.45}$$

From Corollary 5.5 we have that the integrand is non-positive and, since the solution is nonconstant, that the integrand is negative at some $t \in [0,T]$. This and the continuity of $\nabla h(c(\cdot)) \cdot f(c(\cdot))$ give us

$$h(c(T)) < h(c(0)). \tag{5.46}$$

But this contradicts the supposition that $c(T) = c(0)$. ///

Corollary 5.7. Under the hypothesis of Proposition 5.3 each equilibrium in $\mathbb{P}^{\mathcal{S}}$ for the differential equations of the system $\{\mathcal{S}, \mathcal{C}, \mathcal{R}, k\}$ is asymptotically stable (relative to initial conditions in the positive stoichiometric compatibility class containing that equilibrium.)

Proof. Let $c^* \in \mathbb{P}^{\mathcal{S}}$ be as in Proposition 5.3. Note that c^* is an equilibrium and is the only equilibrium in the positive stoichiometric compatibility class containing c^* (Corollary 5.4). Recall (Lecture 2) that composition trajectories having a point in the stoichiometric compatibility class containing c^* lie entirely within it. Note also that the positive stoichiometric compatibility class containing c^* is open in the relative topology on the stoichiometric compatibility class containing c^*. Now let $h: \mathbb{P}^{\mathcal{S}} \to \mathbb{R}$ be as in (5.36), and let $\bar{h}$ be the restriction of h to the positive stoichiometric compatibility class containing c^*. From (5.37), (5.39), Corollary 5.5 and Remark 5.6 it follows that $\bar{h}$ is a strict Liapunov function for c^* on the positive stoichiometric compatibility class containing it. (See, for example, Hirsch and Smale [HS].) Thus, c^* is asymptotically stable relative to initial conditions in its positive stoichiometric compatibility class. From Remark 5.4 it follows that the same argument can be made for any equilibrium in $\mathbb{P}^{\mathcal{S}}$. ///

Remark 5.7. From Corollaries 5.4, 5.6, and 5.7 we now have that any mass action system $\{\mathcal{S}, \mathcal{C}, \mathcal{R}, k\}$ which admits a positive equilibrium c^* satisfying

$$A_k \Psi(c^*) = 0 \tag{5.47}$$

will have the property that its differential equations have all the qualities described in part (iii) of the Deficiency Zero Theorem. Thus far in Section 5.~~B~~A.2 we have placed no restriction on the deficiency of the network $\{\mathcal{S}, \mathcal{C}, \mathcal{R}\}$ under discussion. The connection with deficiency zero networks comes from the following:

<u>Proposition 5.8</u>. <u>Suppose that the differential equations for a mass action system</u> $\{\mathcal{S},\mathcal{C},\mathcal{R},k\}$ <u>admit an equilibrium in</u> $\mathbb{P}^{\mathcal{S}}$. <u>If the network</u> $\{\mathcal{S},\mathcal{C},\mathcal{R}\}$ <u>has deficiency zero then the hypothesis of Proposition 5.3 is satisfied</u>.

<u>Proof</u>. Let $c^* \in \mathbb{P}^{\mathcal{S}}$ be an equilibrium. Then, from the discussion preceding Proposition 5.3, we must have

$$\Psi(c^*) \in \ker Y A_k \ . \tag{5.48}$$

Since the network has deficiency zero Corollary 4.11 gives

$$\ker Y A_k = \ker A_k \tag{5.49}$$

Thus, (5.47) holds. ///

<u>Remark 5.8</u>. Let $\{\mathcal{S},\mathcal{C},\mathcal{R}\}$ be a network of deficiency zero. For any $k \in \mathbb{P}^{\mathcal{R}}$, Remark 5.7 and Proposition 5.8 tell us that <u>the differential equations for the mass action system</u> $\{\mathcal{S},\mathcal{C},\mathcal{R},k\}$ <u>will have all the properties described in Theorem 5.1, part (iii), so long as those differential equations admit a positive equilibrium</u>. From part (i) of Theorem 5.1 (or, alternatively, from Remark 5.2 and Proposition 5.8) we know that no such equilibrium can exist if the network is <u>not</u> weakly reversible. If, however, the network <u>is</u> weakly reversible and we can show that, for <u>any</u> $k \in \mathbb{P}^{\mathcal{R}}$, the differential equations for the mass action system $\{\mathcal{S},\mathcal{C},\mathcal{R},k\}$ admit even one equilibrium in $\mathbb{P}^{\mathcal{S}}$, then part (iii) of the Deficiency Zero Theorem will have been proved. This we do in Section 5.A.3.

5.A.3. Proof of the existence of a positive equilibrium. We will follow the line of argument in [H3], which in turn draws on ideas in [F2]. Our purpose is to show that if $\{\mathcal{S}, \mathcal{C}, \mathcal{R}\}$ is a weakly reversible deficiency zero network then, for <u>any</u> $k \in \mathbb{P}^{\mathcal{R}}$, the differential equations for the mass action system $\{\mathcal{S}, \mathcal{C}, \mathcal{R}, k\}$ admit an equilibrium in $\mathbb{P}^{\mathcal{S}}$. If $Y: \mathbb{R}^{\mathcal{C}} \to \mathbb{R}^{\mathcal{S}}$ is the stoichiometric map for the network and if, for fixed but arbitrary $k \in \mathbb{P}^{\mathcal{R}}$, $A_k: \mathbb{R}^{\mathcal{C}} \to \mathbb{R}^{\mathcal{C}}$ is as in Proposition 4.1, we seek $c^* \in \mathbb{P}^{\mathcal{S}}$ such that

$$Y A_k \Psi(c^*) = 0 , \tag{5.50}$$

where $\Psi: \overline{\mathbb{P}}^{\mathcal{S}} \to \overline{\mathbb{P}}^{\mathcal{C}}$ is given by

$$\Psi(c) \equiv \sum_{y \in \mathcal{C}} c^y \omega_y \tag{5.51}$$

with

$$c^y \equiv \prod_{s \in \mathcal{S}} c_s^{y_s} . \tag{5.52}$$

Since, from Corollary 4.11, we have for zero deficiency networks

$$\ker Y A_k = \ker A_k , \tag{5.53}$$

we must in fact seek $c^* \in \mathbb{P}^{\mathcal{S}}$ such that

$$\Psi(c^*) \in \ker A_k . \tag{5.54}$$

In the spirit of Section 5.A.2 we shall find it useful to begin by considering an arbitrary weakly reversible network $\{\mathcal{S}, \mathcal{C}, \mathcal{R}\}$ (of <u>arbitrary</u> deficiency) and by finding conditions on $k \in \mathbb{P}^{\mathcal{R}}$ such that there exists $c^* \in \mathbb{P}^{\mathcal{S}}$ satisfying (5.54). (That we need only consider weakly reversible networks follows from Remark 5.2.) Then we will show that for weakly reversible <u>deficiency zero</u> networks these conditions are satisfied for <u>all</u> $k \in \mathbb{P}^{\mathcal{R}}$.

By way of preparation we let $\{\mathcal{S},\mathcal{C},\mathcal{R}\}$ be an arbitrary network (not necessarily weakly reversible) for which $Y:\mathbb{R}^{\mathcal{C}} \to \mathbb{R}^{\mathcal{S}}$ is the stoichiometric map. The <u>transpose</u> of Y is that linear transformation $Y^T:\mathbb{R}^{\mathcal{S}} \to \mathbb{R}^{\mathcal{C}}$ such that

$$(Y^T z) \cdot x = z \cdot Y x \ , \quad \forall z \in \mathbb{R}^{\mathcal{S}} \ , \forall x \in \mathbb{R}^{\mathcal{C}} \ . \tag{5.55}$$

It is easy to confirm that

$$Y^T z \equiv \sum_{y \in \mathcal{C}} (y \cdot z)\omega_y \ . \tag{5.56}$$

Let $L^1, L^2, \ldots, L^\ell$ be the linkage classes of $\{\mathcal{S},\mathcal{C},\mathcal{R}\}$. Recall that, for $\theta = 1,2,\ldots,\ell$, ω_{L^θ} is the characteristic function on L^θ ; that is,

$$\omega_{L^\theta} = \sum_{y \in L^\theta} \omega_y \ , \quad \theta = 1,2,\ldots,\ell \ . \tag{5.57}$$

We turn now to an easy but important consequence of Proposition 4.7.

<u>Lemma 5.8</u>. <u>Let</u> $\{\mathcal{S},\mathcal{C},\mathcal{R}\}$ <u>be a reaction network of deficiency</u> δ , <u>and let</u> n <u>be the number of complexes in</u> $\mathcal{C}$. <u>If</u> $Y:\mathbb{R}^{\mathcal{C}} \to \mathbb{R}^{\mathcal{S}}$ <u>is the stoichiometric map for the network and</u> $L^1, L^2, \ldots, L^\ell$ <u>are its linkage classes, then</u>

$$\dim[\operatorname{im} Y^T + \operatorname{span}(\omega_{L^1}, \omega_{L^2}, \ldots, \omega_{L^\ell})] = n - \delta \ . \tag{5.58}$$

<u>In particular</u>, <u>if</u> $\delta = 0$ <u>then</u>

$$\operatorname{im} Y^T + \operatorname{span}(\omega_{L^1}, \omega_{L^2}, \ldots, \omega_{L^\ell}) = \mathbb{R}^{\mathcal{C}} \ . \tag{5.59}$$

<u>Proof</u>. With $\Delta \subset \mathbb{R}^{\mathcal{C}}$ as in Proposition 4.7 we have from that proposition

$$\dim[\ker Y \cap \operatorname{span}(\Delta)] = \delta \quad . \tag{5.60}$$

Since $\dim \mathbb{R}^{\mathcal{C}} = n$ we have from (5.60)

$$\dim[\ker Y \cap \operatorname{span}(\Delta)]^{\perp} = n - \delta \quad . \tag{5.61}$$

However,

$$[\ker Y \cap \operatorname{span}(\Delta)]^{\perp} = (\ker Y)^{\perp} + (\operatorname{span}(\Delta))^{\perp} \quad . \tag{5.62}$$

From the well known relationship between the kernel of a linear transformation and the image of its transpose we have

$$(\ker Y)^{\perp} = \operatorname{im} Y^{T} \; . \tag{5.63}$$

Moreover, from Lemma 4.6

$$[\operatorname{span}(\Delta)]^{\perp} = \operatorname{span}(\omega_{L^1}, \omega_{L^2}, \ldots, \omega_{L^{\ell}}) \; . \tag{5.64}$$

Combining (5.61)-(5.64) we obtain (5.58). When $\delta = 0$ (5.58) tells us that the linear subspace of $\mathbb{R}^{\mathcal{C}}$ on the left of (5.59) has the same dimension as $\mathbb{R}^{\mathcal{C}}$ and therefore must coincide with it. ///

Lemma 5.8 will be used in conjunction with our next proposition, which deals with an arbitrary <u>weakly</u> <u>reversible</u> network $\{\mathcal{S}, \mathcal{C}, \mathcal{R}\}$. In its statement it will be understood that $L^1, \ldots, L^{\ell}$ are the linkage classes of the network, that Y is the stoichiometric map for the network, that $\Psi(\cdot)$ is as in (5.51) and that, for $k \in \mathbb{P}^{\mathcal{R}}$, A_k is as in Proposition 4.1. Since the network is weakly reversible its linkage classes coincide with its terminal strong linkage classes so that, from Proposition 4.1, $\ker A_k$ has a (non-negative) basis $\{x^1, x^2, \ldots, x^\ell\} \subset \bar{\mathbb{P}}^{\mathcal{C}}$ such that

$$\operatorname{supp} x^\theta = L^\theta \quad , \quad \theta = 1,2,\ldots,\ell \ . \tag{5.65}$$

Since the union of the linkage classes is $\mathcal{C}$ it follows from (5.65) that

$$\sum_{\theta=1}^{\ell} x^\theta$$

is positive — that is, a member of $\mathbb{P}^{\mathcal{C}}$. Recall that if I is a set (be it $\mathcal{S}$ or $\mathcal{C}$) and if p is a member of $\mathbb{P}^I$, then $\ln p \in \mathbb{R}^I$ is defined by

$$(\ln p)_i = \ln(p_i) \quad , \quad \forall\, i \in I \ . \tag{5.66}$$

Similarly, for $z \in \mathbb{R}^I$ the vector $e^z \in \mathbb{P}^I$ is defined by

$$(e^z)_i = e^{z_i} \ , \quad \forall\, i \in I \ . \tag{5.67}$$

<u>Proposition 5.9</u>. <u>Let</u> $\{\mathcal{S}, \mathcal{C}, \mathcal{R}\}$ <u>be a weakly reversible network (of arbitrary deficiency)</u>, <u>let</u> k <u>be an element of</u> $\mathbb{P}^{\mathcal{R}}$, <u>and let</u> $\{x^1, x^2, \ldots, x^\ell\} \subset \bar{\mathbb{P}}^{\mathcal{C}}$ <u>be a basis for</u> $\ker A_k$ <u>as in Proposition 4.1</u>. <u>The following are equivalent</u>:

(i) <u>There exists</u> $c^* \in \mathbb{P}^{\mathcal{S}}$ <u>such that</u>

$$\Psi(c^*) \in \ker A_k \ . \tag{5.68}$$

(ii) $\ln\left(\sum_{\theta=1}^{\ell} x^\theta\right)$ <u>is contained in</u> $\operatorname{im} Y^T + \operatorname{span}(\omega_{L^1}, \omega_{L^2}, \ldots, \omega_{L^\ell})$. (5.69)

Proof. Condition (ii) is obviously equivalent to:

(iii) There exist $z \in \mathbb{R}^{\mathcal{J}}$ and numbers $\{-\xi_1,-\xi_2,\ldots,-\xi_\ell\} \subset \mathbb{R}$ such that

$$\ln\left(\sum_{\theta=1}^{\ell} x^\theta\right) = Y^T z - \sum_{\theta=1}^{\ell} \xi_\theta \omega_{L\theta} . \tag{5.70}$$

With $z \in \mathbb{R}^{\mathcal{J}}$ and $\{\xi_1,\ldots,\xi_\ell\}$ as in (iii), we can take $c^* \in \mathbb{P}^{\mathcal{J}}$ and $\{\lambda_1,\ldots,\lambda_\ell\} \subset \mathbb{P}$ to be given by

$$c^* = e^z \tag{5.71}$$

and

$$\lambda_\theta = e^{\xi_\theta} \quad , \quad \theta = 1,2,\ldots,\ell \tag{5.72}$$

to see that (iii) is equivalent to:

(iv) There exist $c^* \in \mathbb{P}^{\mathcal{J}}$ and $\{\lambda_1,\ldots,\lambda_\ell\} \subset \mathbb{P}$ such that

$$\begin{aligned} Y^T \ln c^* &= \ln\left(\sum_{\theta=1}^{\ell} x^\theta\right) + \sum_{\theta=1}^{\ell} (\ln \lambda_\theta)\omega_{L\theta} \\ &= \ln\left(\sum_{\theta=1}^{\ell} \lambda_\theta x^\theta\right) . \end{aligned} \tag{5.73}$$

From (5.56) we have

$$Y^T \ln c^* = \sum_{y \in \mathcal{P}} (y \cdot \ln c^*)\, \omega_y \,, \tag{5.74}$$

and from (5.52) it follows that

$$y \cdot \ln c^* = \ln(c^*)^y \,, \quad \forall\, y \in \mathcal{P} \,. \tag{5.75}$$

Combining (5.74) and (5.75) we obtain

$$\begin{aligned} Y^T \ln c^* &= \sum_{y \in \mathcal{P}} [\ln(c^*)^y]\omega_y \\ &= \ln\Big(\sum_{y \in \mathcal{P}} (c^*)^y \omega_y\Big) \\ &= \ln \Psi(c^*) \,. \end{aligned} \tag{5.76}$$

Thus, we can combine (5.76) with (5.73) and take exponentials to assert that (iv) is equivalent to:

(v) <u>There exist</u> $c^* \in \mathbb{P}^{\delta}$ <u>and</u> $\{\lambda_1, \ldots, \lambda_\ell\} \subset \mathbb{P}$ <u>such that</u>

$$\Psi(c^*) = \sum_{\theta=1}^{\ell} \lambda_\theta \, x^\theta \,. \tag{5.77}$$

Since $\{x^1,\ldots,x^\ell\}$ is a basis for $\ker A_k$, (v) clearly implies (i). That (i) implies (v) (with <u>positive</u> λ_θ in (5.77)) follows easily from the special nature of the basis $\{x^1,\ldots,x^\ell\}$ and the fact that, for $c^* \in \mathbb{P}^{\mathcal{S}}$, $\Psi(c^*)$ is a member of $\mathbb{P}^{\mathcal{C}}$. ///

<u>Remark 5.9</u>. In Proposition 5.9 there are, of course, an infinite supply of bases for $\ker A_k$ having the special properties given in Proposition 4.1. If, however, condition (ii) is satisfied for one choice of such a basis it will be satisfied for any other choice of such a basis: It is easy to confirm that if $\{x^1,\ldots,x^\ell\}$ and $\{\bar{x}^1,\ldots,\bar{x}^\ell\}$ are two such bases, then

$$\ln\left(\sum_{\theta=1}^{\ell} x^\theta\right) \quad \text{and} \quad \ln\left(\sum_{\theta=1}^{\ell} \bar{x}^\theta\right)$$

will differ by an element of

$$\operatorname{span}(\omega_{L^1},\omega_{L^2},\ldots,\omega_{L^\ell}) .$$

<u>Remark 5.10</u>. Condition (ii) of Proposition 5.9 requires that the vector

$$\ln\left(\sum_{\theta=1}^{\ell} x^\theta\right) \in \mathbb{R}^{\mathcal{C}} \tag{5.78}$$

lie in the linear subspace

$$\operatorname{im} Y^T + \operatorname{span}(\omega_{L^1},\omega_{L^2},\ldots,\omega_{L^\ell}) \subset \mathbb{R}^{\mathcal{C}} . \tag{5.79}$$

Since $\{x^1,x^2,\ldots,x^\ell\}$ is a basis for $\ker A_k$, the values that might be taken by (5.78) will be influenced by the particular value of $k \in \mathbb{P}^{\mathcal{R}}$. On the other hand the linear subspace (5.79) <u>depends only on the network</u> $\{\mathcal{S},\mathcal{C},\mathcal{R}\}$.

We are now coming to the end of the road:

Corollary 5.10. Let $\{\mathcal{S},\mathcal{C},\mathcal{R}\}$ be any weakly reversible network of deficiency zero, and let k be any element of $\mathbb{P}^{\mathcal{R}}$. With A_k as in Proposition 4.1 and with $\Psi(\cdot)$ as in (5.51) there exists $c^* \in \mathbb{P}^{\mathcal{S}}$ such that

$$A_k \Psi(c^*) = 0 \ .$$

That is, the differential equations for the mass action system $\{\mathcal{S},\mathcal{C},\mathcal{R},k\}$ admit an equilibrium in $\mathbb{P}^{\mathcal{S}}$, and that equilibrium satisfies the hypothesis of Proposition 5.3.

Proof. For deficiency zero networks Lemma 5.8 tells us that the linear subspace (5.79) is in fact all of $\mathbb{R}^{\mathcal{C}}$. Thus, for any $k \in \mathbb{P}^{\mathcal{R}}$, condition (ii) of Proposition 5.9 is satisfied trivially. So, then, is the equivalent condition (i). ///

With Corollary 5.10 we have achieved the final objective set in Remark 5.8. This completes our proof of Theorem 5.1.