

THE S-C-L GRAPH IN CHEMICAL KINETICS

D. SIEGEL AND Y.F. CHEN

ABSTRACT. We present two results that provide sufficient conditions for the applicability of the Deficiency Zero Theorem of Horn, Jackson and Feinberg and a theorem due to Vol'pert. In both cases the Species-Complex-Linkage class (S-C-L) graph is assumed to be acyclic.

1. Introduction. The structure of certain graphs induced by chemical reaction networks plays a vital role in the study of chemical kinetics. In this paper the Species-Complex-Linkage (S-C-L) graph which was first introduced by Schlosser and Feinberg will be related to two other graphs, namely, the HJF-graph (standard reaction diagram) studied by Horn-Jackson-Feinberg and the V -graph introduced by Vol'pert. The Deficiency Zero Theorem by Horn, Jackson and Feinberg and a theorem due to Vol'pert give significant information about the qualitative behavior of certain chemical kinetics systems of mass action type based upon their graphical structure. Our results here provide sufficient conditions for the applicability of the two theorems.

2. Definitions and terminology. We will consider a general closed chemical network with n species. An introduction of definitions and terminology is necessary. Our notations are based on [2, 6, 8] and [4]. It should be understood that we use the standard terminology of graph theory (see, for example, [5] and [1]).

Definition 1. A *complex* Y^c is a formal linear combination of species, $Y^c = \sum_{i=1}^n \alpha_i A_i$, where A_i s denote species. Each stoichiometric coefficient, α_i , is a nonnegative integer and $\alpha_i \neq 0$ for some i . $\tilde{Y} = \sum_{i=1}^n \alpha_i \mathbf{e}_i$ is the vector corresponding to Y^c , where $\{\mathbf{e}_i\}$ is the standard basis in \mathbf{R}^n .

Received by the editors on September 9, 1992, and in revised form on November 17, 1992.

Research of the first author partially supported by Natural Sciences and Engineering Research Council of Canada Grant OGP0009345.

Research of the second author partially supported by a Natural Sciences and Research Council of Canada Post-Graduate Scholarship.

Definition 2. A *critical species* is a species that appears in two or more distinct complexes.

Definition 3. The standard reaction diagram (HJF-graph) of a chemical network is a digraph whose vertices are distinct complexes of the network and whose arcs are drawn to indicate the “reacts to” relation in the set of complexes.

Definition 4. The linkage classes of a chemical network are the connected components of the standard reaction diagram. The symbol l will be used to denote the number of *linkage classes* in a network.

Definition 5. If \tilde{x} is a vector in \mathbf{R}^n , then the support of \tilde{x} , $\text{supp } \tilde{x} := \{i : x_i \neq 0, 1 \leq i \leq n\}$ where x_i is the i th component in \tilde{x} .

Definition 6. The *stoichiometric subspace*, S , of a chemical network is the span of its reaction vectors. That is,

$$S := \text{span} \{ \tilde{Y}_j - \tilde{Y}_i : Y_i^c \rightarrow Y_j^c \in \mathcal{R} \}$$

where \tilde{Y}_i and \tilde{Y}_j are the corresponding vectors of complexes Y_i^c and Y_j^c in \mathbf{R}^n , respectively.

Definition 7. The *deficiency of a chemical network*, δ , is defined as follows

$$\delta := m - l - s$$

where m is the number of complexes in the network, l is the number of linkage classes and s is the dimension of the stoichiometric subspace. It can be shown that $\delta \geq 0$ (see [4]).

Definition 8. The *deficiency of the h th linkage class* is defined as follows

$$\delta_h = m_h - 1 - s_h$$

where m_h is the number of complexes in that linkage class and s_h is defined as

$$s_h := \dim (\text{span} \{ \tilde{Y}_j - \tilde{Y}_i \in \mathbf{R}^n : Y_i^c \rightarrow Y_j^c \in \mathcal{R}, Y_i^c, Y_j^c \in V(L_h) \})$$

where $V(L_h)$ denotes the vertex set of the linkage class L_h .

Definition 9. A network is *weakly reversible* if for any two complexes \mathcal{C}_1 and \mathcal{C}_2 in the same linkage class there exists a directed arrow pathway (consisting of one or more reaction arrows) joining \mathcal{C}_1 to \mathcal{C}_2 in the standard reaction diagram.

Definition 10. The V -graph of a chemical network is a *bipartite digraph* whose vertex set is partitioned into the species set $\mathcal{S} = \{A_1, A_2, \dots, A_n\}$ of the network and the reaction set $\mathcal{R} = \{r_1, r_2, \dots, r_r\}$ and whose arcs are drawn from A_i to r_j if A_i enters the reaction r_j , and from r_j to A_i if A_i is in the product of the reaction r_j . Also, the coefficient of every species is attached to the corresponding arc as its label.

Definition 11. The S-C-L graph (first given in [7]) of a chemical network is a bipartite graph whose vertex set is partitioned into the species set $\mathcal{S} = \{A_1, A_2, \dots, A_n\}$ of the network and the linkage class set $\mathcal{L} = \{L_1, L_2, \dots, L_l\}$ and whose edges are drawn as follows. For each complex, $Y^c \in \mathcal{C}$, in which a species appears, draw an edge connecting that species vertex to the linkage class vertex for the linkage class containing Y^c . In addition, label each edge by writing the complex for which it was drawn.

3. The Deficiency Zero Theorem and Vol'pert's Theorem.

We continue to use the notations introduced in the previous section. Let $\mathcal{S}, \mathcal{C}, \mathcal{R}$ denote a set of species, a set of complexes, and a set of reactions in a chemical network, respectively. Let \mathcal{K} denote an arbitrary kinetics and A_i each species for $1 \leq i \leq n$. Also, let $\tilde{C} = (C_{A_1}, C_{A_2}, \dots, C_{A_n})$ be the composition vector in $\bar{\mathbf{P}}^n$, where $\bar{\mathbf{P}}^n = \{\tilde{x} \in \mathbf{R}^n : x_i \geq 0, \forall i\}$. Also, let $\mathbf{P}^n = \{\tilde{x} \in \mathbf{R}^n : x_i > 0, \forall i\}$. Then for a reaction system $\{\mathcal{S}, \mathcal{C}, \mathcal{R}, \mathcal{K}\}$, the species formation function $\tilde{f} : \bar{\mathbf{P}}^n \mapsto \mathbf{R}^n$ is defined as follows:

$$(1) \quad \tilde{f}(\tilde{C}) \equiv \sum_{\mathcal{R}} \mathcal{K}_{Y_i^c \rightarrow Y_j^c}(\tilde{C})(\tilde{Y}_j - \tilde{Y}_i), \quad \tilde{C} \in \bar{\mathbf{P}}^n$$

where \mathcal{R} is an abbreviation for " $Y_i^c \rightarrow Y_j^c \in \mathcal{R}$," and $K_{Y_i^c \rightarrow Y_j^c}(\tilde{C})$ is an assignment to a reaction $Y_i^c \rightarrow Y_j^c$, $Y_i^c \neq Y_j^c$, of a continuous rate

function $\mathcal{K}_{Y_i^c \rightarrow Y_j^c} : \bar{\mathbf{P}}^n \rightarrow \bar{\mathbf{P}}$ such that $\mathcal{K}_{Y_i^c \rightarrow Y_j^c}(\tilde{C}) > 0$ if and only if $\text{supp } \tilde{Y}_i \subset \text{supp } \tilde{C}$. Let $\tilde{Y}_i = (d_{i1}, \dots, d_{in})$. The species formation rate function for a mass action system takes the form

$$(2) \quad \tilde{f}(\tilde{C}) = \sum_{\mathcal{R}} k_{Y_i^c \rightarrow Y_j^c} \left(\prod_{p=1}^n C_{A_p}^{d_{ip}} \right) (\tilde{Y}_j - \tilde{Y}_i)$$

where $k_{Y_i^c \rightarrow Y_j^c}$ is called the rate constant for the reaction $Y_i^c \rightarrow Y_j^c$ and is a positive real number. By the differential equations for a reaction system, we mean

$$(3) \quad \dot{\tilde{C}} = \tilde{f}(\tilde{C})$$

where the overdot indicates differentiation with respect to time. This is a vector differential equation which encodes a system of n scalar equations, one for each species in the network. The n component equations of (3) with an arbitrary kinetics are as follows

$$(4) \quad \dot{C}_{A_p} = \sum_{\mathcal{R}} \mathcal{K}_{Y_i^c \rightarrow Y_j^c}(\tilde{C})(d_{jp} - d_{ip}), \quad \forall A_p \in \mathcal{S}, \tilde{C} \in \bar{\mathbf{P}}^n.$$

For a mass action system, (3) takes the form

$$(5) \quad \dot{C}_{A_p} = \sum_{\mathcal{R}} k_{Y_i^c \rightarrow Y_j^c} \left(\prod_{p=1}^n C_{A_p}^{d_{ip}} \right) (\tilde{Y}_j - \tilde{Y}_i).$$

This is a polynomial system provided the d_{ip} s are nonnegative integers. We will always assume that this is true although many results hold without this restriction. It follows that a steady state of a reaction system is a composition \tilde{C}^* such that

$$\tilde{0} = \sum_{\mathcal{R}} \mathcal{K}_{Y_i^c \rightarrow Y_j^c}(\tilde{C}^*)(\tilde{Y}_j - \tilde{Y}_i).$$

Now we introduce the deficiency zero theorem and Vol'pert's theorem. For a general discussion, see [2, p. 42–46].

Theorem 1 (The Deficiency Zero Theorem, [4, p. 20, Lecture 3] or [6, 3]). *For any reaction network of deficiency zero, the following statements hold true:*

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

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

Remark. Theorem 1(i) implies that for a deficiency zero system that is not weakly reversible, an equilibrium concentration cannot be positive; i.e., if it exists then at least one of its coordinates is zero.

Theorem 2 (Vol'pert's Theorem, [8, p. 632–633]). *Suppose that (5) is a polynomial system of equations with an acyclic V-graph. Then:*

- (i) *The solution of (5) is defined for $t > 0$.*
- (ii) *There does not exist a nonnegative periodic solution of (5).*
- (iii) *Each solution of (5) has a limit as $t \rightarrow \infty$, and this limit is an equilibrium point of (5).*
- (iv) *Any nonnegative equilibrium point of (5) is a solution of the following system of equations:*

$$k_{Y_i^c \rightarrow Y_j^c} \left(\prod_{p=1}^n C_{A_p}^{d_{ip}} \right) = 0, \quad \forall Y_i^c \rightarrow Y_j^c \in \mathcal{R}.$$

- (v) *For each solution to (5) there exists a constant K , $K > 0$, so that the following inequalities hold:*

$$\int_0^\infty |\dot{C}_{A_p}(s)| ds < K, \quad \forall p, p = 1, \dots, n.$$

4. Some results connecting the two theorems. In this section some connections are given between HJF-graphs and V-graphs based

upon consideration of S-C-L graphs which were first introduced by Schlosser and Feinberg [7]. We will be using a significant amount of graph theory as a bridge to our final results. We begin with some propositions.

Proposition 1 ([1, p. 26]). *Every nontrivial tree has at least two vertices of degree one.*

Proposition 2. *The S-C-L graph is cyclic if and only if one of the following conditions holds*

(i) *Some species appear more than once within the same linkage class.*

(ii) *There exists at least one pair of species sets corresponding to different linkage classes such that their intersection contains at least two distinct species.*

(iii) *There exists at least one group of species sets corresponding to different linkage classes, $\mathcal{S}^1, \mathcal{S}^2, \dots, \mathcal{S}^p$, such that $\mathcal{S}^1 \cap \mathcal{S}^2 = \{A_{12}\}$, $\mathcal{S}^2 \cap \mathcal{S}^3 = \{A_{23}\}, \dots, \mathcal{S}^p \cap \mathcal{S}^1 = \{A_{p1}\}$ for some distinct species $A_{i(i+1)}$, $1 \leq i \leq p-1$, A_{p1} .*

Proof. If the S-C-L graph is cyclic, there exists a cycle \bar{p} such that $\bar{p} = L_1 A_1 L_2 A_2 \dots L_k A_k L_1$. If $k = 1$, then $\bar{p} = L_1 A_1 L_1$. By Definitions 2 and 11, A_1 is a critical species in the linkage class L_1 . Thus (i) is true. If $k = 2$, then $\bar{p} = L_1 A_2 L_2 A_2 L_1$. It follows that $\{A_1, A_2\} \subset \mathcal{S}(L_1) \cap \mathcal{S}(L_2)$ by Definition 11. So (ii) is true. If $k \geq 3$ and (ii) does not hold, then $\{A_1\} = \mathcal{S}^1 \cap \mathcal{S}^2$, $\{A_2\} = \mathcal{S}^2 \cap \mathcal{S}^3, \dots, \{A_k\} = \mathcal{S}^k \cap \mathcal{S}^1$ by Definition 11. Thus, (iii) is true.

Suppose either (i), (ii) or (iii) holds. Then, if (i) holds, there exists at least a cycle \bar{p} such that $\bar{p} = L_i A_i L_i$ by Definition 11. It follows that the S-C-L graph is cyclic. If (ii) holds, there exists at least two species sets \mathcal{S}_i and \mathcal{S}_j corresponding to linkage classes L_i and L_j , $i \neq j$, such that there exists at least two distinct species A_i and A_j , where $\{A_i, A_j\} \subset (\mathcal{S}_i \cap \mathcal{S}_j)$. It follows that there exists a cycle \bar{p} such that $\bar{p} = L_i A_i L_j A_j L_i$. Thus, the S-C-L graph is cyclic. Finally, if (iii) holds, there exists a cycle \bar{p} such that $\bar{p} = L_1 A_{12} L_2 A_{33} L_3 \dots L_p A_{p1} L_1$. Thus, the S-C-L graph is again cyclic. \square

Lemma 1. *A connected graph G in which every vertex is contained in at least two edges must have a closed path.*

Proof. Suppose that G has no closed paths. It follows that G is a tree since G is connected. By Proposition 1, G has at least two vertices of degree one. But every vertex of G is said to be contained in at least two edges. This is a contradiction. \square

Lemma 2. *If each vertex of a connected, nontrivial and acyclic graph G is on some edge, then there must exist at least two vertices of degree one in G .*

Proof. Obviously, G is a nontrivial tree. Thus, the result follows from Proposition 1. \square

Lemma 3. *If some reaction vectors from a single linkage class in a chemical network are linearly independent, then the corresponding graph G whose vertices are complexes and whose edges are reactions corresponding to the reaction vectors is acyclic.*

Proof. In constructing G , an edge is drawn to connect two vertices when a reaction occurs among them. Suppose that G is cyclic so that there exists a closed path \bar{p} and $\bar{p} = Y_1^c e_1 Y_2^c \dots Y_N^c e_N Y_1^c$, where N is the number of reactions in \bar{p} . Let $\tilde{y}_i = \tilde{Y}_{i+1} - \tilde{Y}_i$, $1 \leq i \leq N$, with $Y_{N+1}^c = Y_1^c$. Then \tilde{y}_i or $-\tilde{y}_i$ is a reaction vector and $\sum_{i=1}^N \tilde{y}_i = 0$. This implies that the reaction vectors are not linearly independent, which is a contradiction. \square

Lemma 4. *A linear combination \tilde{y}^* with nonzero coefficients of one or more linearly independent reaction vectors in a linkage class of a chemical network satisfies $|\text{supp } \tilde{y}^*| \geq 2$, where $|\text{supp } \tilde{y}^*|$ is the number of elements in $\text{supp } \tilde{y}^*$, provided that there exists no critical species within this linkage class.*

Proof. Let \tilde{y}^* be a linear combination of some linearly independent reaction vectors $\tilde{y}_1, \tilde{y}_2, \dots, \tilde{y}_h$ in a linkage class. Without loss of

generality, assume the following

$$(6) \quad \tilde{y}^* = \sum_{i=1}^h d_i \tilde{y}_i, \quad \text{where } d_i \neq 0, \forall i.$$

By the definition of a linkage class all complexes belonging to the same linkage class are connected by some reactions. Additionally, each reaction contains exactly two complexes.

Now construct a graph G whose vertices and edges are complexes and reactions, respectively, occurring in \tilde{y}_i , for all i . In other words, each vertex represents a complex and each edge is drawn corresponding to the occurrence of a reaction between its connected vertices. By Lemma 3, G has no closed path. It then follows that there exist at least two vertices of degree one by Lemma 2. Thus, there exist at least two distinct complexes among the \tilde{y}_i 's which occur only once. Since one complex comprises at least one species and it is assumed that there exists no critical species within the linkage class, \tilde{y}^* must contain at least two distinct species. \square

Lemma 5. *If there exist no critical species within the linkage class L_i , then $\delta_i = 0$.*

Proof. Let m_i be the number of complexes in the linkage class L_i , and let those complexes be denoted $Y_1^c, Y_2^c, \dots, Y_{m_i}^c$. Since there exists no critical species in L_i , any reaction vector $\tilde{Y}_q - \tilde{Y}_p \in \mathbf{R}^n$ corresponding to the reaction $Y_p^c \rightarrow Y_q^c \in \mathcal{R}_i$, where \mathcal{R}_i is the set of reactions in L_i can be written as a linear combination of the linearly independent set

$$\{\tilde{Y}_2 - \tilde{Y}_1, \tilde{Y}_3 - \tilde{Y}_1, \tilde{Y}_4 - \tilde{Y}_1, \dots, \tilde{Y}_{m_i} - \tilde{Y}_1\}.$$

Further if we construct the same graph G as in Lemma 3, then we observe that each $\tilde{Y}_k - \tilde{Y}_1$ is in the stoichiometric subspace S . This follows from the fact that there is a path p in G connecting Y_1^c and Y_k^c since L_i is connected. Let $p = Y_1^c e_1 Y_{r_2}^c e_2 \cdots Y_{r_{k-1}}^c e_{k-1} Y_k^c$. The vectors $\tilde{Y}_{r_{i+1}} - \tilde{Y}_{r_i}$, $1 \leq i \leq k-1$, with $r_1 = 1$, $r_k = k$ are in S . Thus, $\tilde{Y}_k - \tilde{Y}_1 = \sum_{i=1}^{k-1} (\tilde{Y}_{r_{i+1}} - \tilde{Y}_{r_i})$ is in S . It follows that

$$s_i = m_i - 1 \quad \text{and} \quad \delta_i = m_i - 1 - s_i = 0. \quad \square$$

Now we are ready to introduce one of the connections between the different graphs.

Theorem 3. *If the S-C-L graph of a chemical network is acyclic, then the deficiency δ of the chemical network is zero.*

Proof. Since the S-C-L graph is acyclic, there exists no critical species within any single linkage class. Now suppose $\delta \neq 0$, that is, $\delta > 0$. By the definition of δ and Lemma 5, the following holds:

$$\delta = \sum_{i=1}^l m_i - l - s = \sum_{i=1}^l (m_i - 1) - s = \sum_{i=1}^l s_i - s$$

where m_i denotes the number of complexes in each linkage class, l is the total number of linkage classes in the network, s_i is the rank of the linkage class L_i , and s is the dimension of the stoichiometric subspace of the network. It follows that $\sum_{i=1}^l s_i > s$ by our previous assumption that $\delta > 0$.

Without loss of generality, assume that there exists a reaction vector \tilde{v}_p in a linkage class L_p such that \tilde{v}_p is a linear combination of other reaction vectors \tilde{y}_i^k from other linkage classes, in which i indicates the linkage class, for $1 \leq k \leq m_i - 1$ and $1 \leq i \leq p - 1$, and $\tilde{y}_i^1, \dots, \tilde{y}_i^{m_i-1}$ are linearly independent for all i . That is,

$$(7) \quad \begin{aligned} \tilde{v}_p = & a_1^1 \tilde{y}_1^1 + a_1^2 \tilde{y}_1^2 + \dots + a_1^{m_1-1} \tilde{y}_1^{m_1-1} \\ & + \dots + a_{p-1}^1 \tilde{y}_{p-1}^1 + \dots + a_{p-1}^{m_{p-1}-1} \tilde{y}_{p-1}^{m_{p-1}-1} \end{aligned}$$

where for each i , at least one a_i^k is nonzero. Now, combining all linearly independent vectors in each linkage class, we obtain

$$(8) \quad \tilde{v}_p = d_1 \tilde{v}_1 + d_2 \tilde{v}_2 + \dots + d_{p-1} \tilde{v}_{p-1}$$

where d_i is nonzero for all i . By Lemma 4, \tilde{v}_i has at least two nonzero components for $1 \leq i \leq p - 1$.

Let L_i be the linkage class corresponding to \tilde{v}_i , \mathcal{S}_i the species set of \tilde{v}_i and $|\mathcal{S}_i \cap \mathcal{S}_j|$ the number of elements in the intersection of \mathcal{S}_i and \mathcal{S}_j where $i \neq j$, $1 \leq i, j \leq p$. Let G be the graph with vertices L_i

and with edge e_{ij} connecting vertices L_i and L_j when $|\mathcal{S}_i \cap \mathcal{S}_j| \geq 1$. Further, $|\mathcal{S}_i \cap \mathcal{S}_j| \leq 1$ by Proposition 2(ii). Thus, for any two distinct linkage classes L_i and L_j , either $|\mathcal{S}_i \cap \mathcal{S}_j| = 1$ or $|\mathcal{S}_i \cap \mathcal{S}_j| = 0$. It follows from (8) and the previous result that $|\text{supp } \tilde{v}_i| \geq 2$ for all i that for any \mathcal{S}_i , there exists $i_1, i_2, i_1 \neq i, i_2 \neq i, i_1 \neq i_2$, such that $|\mathcal{S}_i \cap \mathcal{S}_{i_1}| = |\mathcal{S}_i \cap \mathcal{S}_{i_2}| = 1$. Thus, each vertex L_i in G is connected to two other linkage classes. By Lemma 1 there exists a closed path in G . By Proposition 2(iii), the S-C-L graph is cyclic. \square

Corollary 1. *If a chemical network has either a periodic solution or multiple steady states in \mathbf{P}^n , then its S-C-L graph is cyclic.*

Proof. Suppose the S-C-L graph is acyclic. Then $\delta = 0$ by Theorem 3. Theorem 1 has precluded the possibility of having either a periodic solution or multiple steady states in \mathbf{P}^n for a chemical network of deficiency zero. Thus, the result follows. \square

Here is a second connection between the different graphs.

Theorem 4. *If the S-C-L graph and the HJF-graph of a chemical network are both acyclic, then the V-graph of the chemical network is acyclic.*

Proof. Suppose that the V-graph is cyclic. Then there must exist at least one cycle in the V-graph. Denote this cycle by \bar{p} . Here an introduction of two graphs \bar{p}_{m1} and \bar{p}_{m2} which are both modified versions of \bar{p} is necessary, where \bar{p}_{m1} is defined when the vertices in \bar{p} come from the same linkage class, and \bar{p}_{m2} is defined when the vertices in \bar{p} come from at least two different linkage classes.

a. The \bar{p}_{m1} graph is formed by removing each reaction vertex in \bar{p} , merging both adjacent arcs of the removed reaction vertex together, returning each removed reaction vertex as a label along the corresponding merged-arc, and replacing each species vertex by its corresponding complex.

b. The \bar{p}_{m2} graph is formed by replacing all the reaction vertices by their corresponding linkage classes, discarding everything between any

two identical linkage class vertices by merging the two identical ones together, and changing all arcs into edges.

Now consider the following cases for \bar{p} .

Case (i). All species in \bar{p} belong to just one linkage class which contains no critical species. In this case p_{m1} is a subgraph of the HJF-graph of the network. Since it is cyclic, the HJF-graph is cyclic.

Case (ii). All species in \bar{p} belong to just one linkage class which contains critical species. By Proposition 2(i), the S-C-L graph of the network must be cyclic.

Case (iii). The species in \bar{p} do not belong to a single linkage class.

There exist at least two distinct linkage class vertices in \bar{p}_{m2} by our assumptions in this case. The \bar{p}_{m2} graph induced by \bar{p} is obviously a bipartite graph which is cyclic itself. All distinct critical species in \bar{p} will be vertices in \bar{p}_{m2} and \bar{p}_{m2} is a subgraph of the S-C-L graph. The S-C-L graph is therefore cyclic. \square

REFERENCES

1. J.A. Bondy and U.S.R. Murty, *Graph theory with applications*, The Macmillan Press, London, 1976.
2. P. Erdi and J. Toth, *Mathematical models of chemical reactions*, Princeton University Press, New Jersey, 1989.
3. M. Feinberg, *Complex balancing in general kinetic systems*, Arch. Rational Mech. Anal. **49** (1972), 187–194.
4. ———, *Lectures on chemical reaction networks*, Unpublished lectures given at the Mathematics Research Center, University of Wisconsin, 1979.
5. F. Harary, *Graph theory*, Addison-Wesley Publishing, Massachusetts, 1969.
6. F. Horn and R. Jackson, *General mass action kinetics*, Arch. Rational Mech. Anal. **47** (1972), 81–116.
7. P.M. Schlosser and M. Feinberg, *A graphical determination of the possibility of multiple steady states in complex isothermal CFSTRs*, in *Complex chemical reaction systems* (J. Warnatz and W. Jager, eds.), Springer-Verlag, Berlin, 1987.
8. A.I. Vol'pert and S.I. Hudjaev, *Analysis in classes of discontinuous functions and equations of mathematical physics*, Chapter 12, Marinus Nijhoff Publishers, Dordrecht, Netherlands, 1985.

DEPARTMENT OF APPLIED MATHEMATICS, UNIVERSITY OF WATERLOO, WATERLOO, ONTARIO, CANADA N2L 3G1