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Complete set of steady states for the general stoichiometric dynamical system

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The complete set of steady states for rate constants in the range $0 \leq k_i < \infty$ and concentrations in the range $0 \leq X_i < \infty$ is given explicitly in parametric form for the general chemical reaction system. The only assumptions are that the stoichiometries are real numbers, and the reaction rates are proportional to functions of class C^k, $k > 0$; the functions are assumed to be positive in the interior of the domain. Hence, these results apply far more generally than just to chemical systems and should be valid for many ecological and economic models as well. The set of steady states in the interior of the domain is in general a simply connected differentiable manifold $\mathfrak{M}$ of dimension $n + r - d$, where n = number of species, r = number of reactions, and d = rank ν (ν = stoichiometric matrix). The full set of steady states $\mathfrak{M}^*$ consists of those in the interior ($\mathfrak{M}$) plus a frequently very complicated set of steady states lying in the boundary. $\mathfrak{M}^*$ is the union of a set of differentiable manifolds but is not itself a differentiable manifold in general. If the reaction rate laws are all monomials (i.e., products of concentrations raised to some "order of kinetics"), a working APL algorithm is given which provides enough information to construct explicitly the set of manifolds comprising $\mathfrak{M}^*$. This algorithm is used to treat an early version of the Belousov–Zhabotinski reaction mechanism. The algorithm may be used for more general rate laws with minor modifications.

I. INTRODUCTION

All chemical reaction systems and many of the models used in ecology and economics are stoichiometric dynamical systems. A general theory of these systems has recently been developed by the author.[1] Such a theory provides a general mathematical framework for investigating a chemical network's static properties, such as stability and multiple steady states, and dynamical properties, such as oscillations, explosions, evolution, or chaos.

Since Ref. 1 was written, a much more elegant approach to this body of theory has been found. This new approach will be used in this and subsequent papers to derive a number of new results.

The key idea upon which the theory of stoichiometric dynamical systems is built is that *in general* the complete set of steady states can easily be calculated. It can always be represented parametrically in a simple form. Once this is done, any static or dynamical property that can be related to the steady states is ripe for investigation. It is then possible to identify networks for which the steady states are globally attracting, or networks having no steady states, or networks where bifurcations occur from stable steady states to oscillatory or chaotic dynamics.

Since the set of steady states of network is of prime importance for all further development of the theory, the first paper in this series gives a thorough analysis of the complete set of steady states for the general stoichiometric system. The present paper develops this topic from the beginning using the new approach and can be read independently of Ref. 1. In subsequent papers which follow directly from this one, the singularities and folding of the manifold of steady states will be treated in general.

The only previous literature on this topic is the discussion in Ref. 1. This work can be related to that of Feinberg and Horn,[2] who proved that a certain set of "zero-deficiency" networks have a unique steady state. Using the explicit set of steady states found in this paper we will show in a later paper that the set of networks having a unique globally attracting steady state is very much larger than the set of zero-deficiency networks.

An outline of this paper is as follows: In Sec. II the general equations of motion for stoichiometric dynamical systems are set up. Since these equations frequently have linear combinations of the species concentrations as constants of the motion, in Sec. III we split the dynamics into two subspaces, one corresponding to a set of independent species and the other corresponding to a parameter domain containing these constants of the motion. Next (Secs. IV and V) we set up a third equivalent system of equations which has the very remarkable property that in general its complete set of steady states is a convex polyhedral cone. The flow of the second and third systems are in a one-to-one correspondence via a diffeomorphism called $\phi\psi$. Hence the map $\phi\psi$ applied to the cone of steady states of the third system gives a parametric representation of the complete set of steady states of the second system.

All the steady states mentioned so far are in the interior of the flow. The steady states on the boundary of the flow are much more complicated but they can all be generated combinatorially using a simple algorithm (Sec. VI).

Background reading on dynamical systems and convex cones may be found in Refs. 3–5.

II. GENERAL STOICHIOMETRIC CONCENTRATION DYNAMICS

The (strictly) positive orthant of real n-dimensional Euclidian space will be called $\mathbf{R}^n_+$ and its closure, the nonnegative orthant, will be called $\bar{\mathbf{R}}^n_+$.

If there are n species X_i present in a chemical system,

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their concentrations can be represented as a (strictly) positive vector $\mathbf{X} \in \mathbf{R}^n_+$, whose components are X_i.

A chemical reaction is a degree of freedom in which species are created and destroyed in fixed ratios. The general (jth) reaction can be written

$$\square - \sum_{i=1}^{n} \nu_{ij} X_i \ , \tag{2.1}$$

and this expression means that for all i and k and all $b \in \mathbf{R}_+$, whenever $b\nu_{ij}$ units of X_i are created, $b\nu_{kj}$ units of X_k are created, with negative creation ($\nu_{ij} < 0$) meaning destruction. If there are r reactions there is an $n \times r$ *stoichiometric matrix* ν whose elements are ν_{ij}. Many examples of networks and ν are given in Ref. 1. Note that since the stoichiometries of a reaction can all be multiplied by a positive number b without (for our purposes) significantly altering the meaning of Eq. (2.1), ν can be replaced by ν (diag b) for any $\mathbf{b} \in \mathbf{R}^r_+$, where the notation diag b means the diagonal matrix having b on its diagonal.

As time evolves the change in X is the consequence of changes in the underlying chemical reaction degrees of freedom. Let $v_j dt$ be the advance in the jth reaction during the infinitesimal time dt. Then during dt this degree of freedom produces $\nu_{ij} v_j dt$ units of X_i, for $i = 1, \ldots, n$. Summing these contributions over all reactions gives

$$\dot{\mathbf{X}} = \nu \mathbf{v} \ , \tag{2.2}$$

where $\dot{\mathbf{X}} \equiv d\mathbf{X}/dt$. We call v the reaction velocity vector.

This equation becomes a system of ordinary differential equations for $\mathbf{X}(t)$ when v is specified as a function of X. The general form of this function will be

$$\mathbf{v}(\mathbf{X}) = (\text{diag } \mathbf{k})\,\mathbf{u}(\mathbf{X}) \ , \tag{2.3}$$

where $\mathbf{k} \in \mathbf{R}^r_+$ is called the *effective rate constant vector* and u(X) is a vector function containing the X dependence of all the rate laws. For example, if the first reaction is

$$X_1 - X_2 \ ,$$

with Michaelis–Menton kinetics catalyzed by an enzyme X_3, we can let

$$u_1(\mathbf{X}) = \frac{X_1 X_3}{K + X_1} \ , \tag{2.4}$$

and then the first component of Eq. (2.3) is the Michaelis–Menton rate law

$$v_1 = \frac{k_1 X_1 X_3}{K + X_1} \ . \tag{2.5}$$

Note that Eq. (2.3) contains k_1 explicitly but not K. The effective rate "constant" k_1 will play a role in the theory and take various values; the constant K will play no role and will always remain fixed.

Combining the general rate law with Eq. (2.2) gives the general equations of motion

$$\dot{\mathbf{X}} = \nu\,(\text{diag } \mathbf{k})\,\mathbf{u}(\mathbf{X}) \ , \tag{2.6}$$

$$\dot{\mathbf{k}} = 0 \ . \tag{2.7}$$

Equation (2.7) is a statement that k is constant, and allows us to treat the motion as though the dynamical variables were the $(n+r)$ component column vector

$$(\mathbf{X}^t, \mathbf{k}^t)^t \equiv (X_1, \ldots, X_n, k_1, \ldots, k_r)^t \in \mathbf{R}^{n+r}_+ \ .$$

[Note: In our notation, vectors are always arrays with a single column. Hence $\mathbf{X}^t$ and $\mathbf{k}^t$ are row vectors which are concatenated (by the comma as in APL) and then transposed in the above expression to yield a column vector. Our array notation is similar to Bodewig's.[6]]

We make only the following assumptions throughout most of this paper. For any positive integers n and r, ν is any $n \times r$ real matrix, and the vector function u(X) is any k-times continuously differentiable (C^k) map u: $\mathbf{R}^n_+ \to \mathbf{R}^r_+$, for $k > 0$. Note that this assumption implies that no component of u(X) can vanish for $\mathbf{X} \in \mathbf{R}^n_+$.

Because ν (diag b) is equivalent to ν for any $\mathbf{b} \in \mathbf{R}^r_+$ and (diag a) u(X) is equivalent to u(X) for any $\mathbf{a} \in \mathbf{R}^r_+$, a *stoichiometric network* is considered to be an equivalence class of matrices and functions $[\nu, \mathbf{u}]$ satisfying the above assumptions. In the investigations which follow our results will apply to these equivalences classes; however, for simplicity, I will discuss only a particular system as specified by ν and u.

III. CONSEQUENCES OF THE STOICHIOMETRIC CONSTRAINTS

If d is the rank of the stoichiometric matrix ν, only d of the n rows of Eq. (2.6) are independent; hence, Eqs. (2.6) and (2.7) specify a *d-dimensional dynamical system*.

These equations also determine a flow $\mathfrak{F}_1$ on $\mathbf{R}^{n+r}_+$. (For an explanation of how dynamical systems are viewed as flows, see Ref. 3 or 4.) This flow consists of d-dimensional dynamical systems, each of which may be identified with a unique value of some parameter. In this section we construct the parameter set and show that it is a differentiable manifold with dimension $n + r - d$, which means it has codimension d. Thus the flow $\mathfrak{F}_1$ on $\mathbf{R}^{n+r}_+$ may be regarded as a d-codimensional manifold of d-dimensional dynamical systems.

The left null space of ν is the set of $\mathbf{y} \in \mathbf{R}^n$ such that $\mathbf{y}^t \nu = 0$. Since the rank of ν is d, the left null space has dimension $n - d$. Let γ be any $(n-d) \times n$ matrix whose $n - d$ rows span the left null space of ν. Then

$$\gamma \nu = 0 \ . \tag{3.1}$$

Multiplying Eq. (2.6) on the left by γ and integrating from time t_1 to time t_2 gives

$$\gamma \mathbf{X}(t_2) - \gamma \mathbf{X}(t_1) = 0 \ . \tag{3.2}$$

Each row of Eq. (3.2) states that a certain linear combination of concentration is an independent constant of the motion. These constants comprise the vector

$$\mathbf{C} \equiv \gamma \mathbf{X} \ , \tag{3.3}$$

and the possible values of C form the convex polyhedral cone

$$\mathcal{C}_c \equiv \{\gamma \mathbf{X} \,|\, \mathbf{X} \in \mathbf{R}^n_+\} \ . \tag{3.4}$$

Without loss of generality we may assumed the d lin-

early independent rows of ν are the first d rows. Take $X_1 \cdots X_d$ as independent variables and regard X_{d+1}, ..., X_n as dependent variables. Thus $X = (X_I^t, X_D^t)^t$, where $X_I \in \mathbf{R}_+^d$ and $X_D \in \mathbf{R}_+^{n-d}$. Similarly the first d columns of γ give the $(n-d)\times d$ matrix γ_I and the remaining $(n-d)$ columns give the $(n-d)$ matrix γ_D. Then Eq. (3.3) becomes

$$C = \gamma_I X_I + \gamma_D X_D .$$

Solving this equation for the dependent species gives

$$X_D = \gamma_D^{-1}(C - \gamma_I X_I) . \tag{3.5}$$

(The inverse of the matrix γ_D must exist, because otherwise the dependent components of X could not be calculated from the independent components.)

By writing $u(X) = u(X_I, X_D)$ and letting ν_I be the first d rows of ν, Eqs. (2.6) and (2.7) can be replaced by

$$\dot{X}_I = \nu_I \,(\text{diag } k)\, u[X_I, \gamma_D^{-1}(C - \gamma_I X_I)] , \tag{3.6}$$

$$\dot{C} = 0 , \tag{3.7}$$

$$\dot{k} = 0 . \tag{3.8}$$

Since $C \in \mathcal{C}_c$, $k \in \mathbf{R}_+^r$, and $X_I \in \mathbf{R}_+^d$, these equations specify a flow $\mathcal{F}_2$ in the dynamical variable $(X_I^t, C^t, k^t)^t$ on the open domain $\mathbf{R}_+^d \times \mathcal{C}_c \times \mathbf{R}_+^r$.

This flow $\mathcal{F}_2$ splits naturally into a dynamical part and a constant part. The dynamical part is the d-dimensional dynamical system in $X_I \in \mathbf{R}_+^d$ given by Eq. (3.6), and the constant part consists of the constants of the motion $(C^t, k^t)^t \in \mathcal{C}_c \times \mathbf{R}_+^r$. The domain of the constant part may be regarded as a differentiable manifold of dimension $n+r-d$ (since $\mathcal{C}_c$ has dimension $n-d$); hence, in the $(n+r)$-dimensional space of the flow, the parameter manifold $\mathcal{C}_c \times \mathbf{R}_+^r$ has codimension d. (Note: a manifold of dimension f embedded in a manifold of dimension $g \geq f$ is said to have codimension $g-f$.) Hence Eqs. (3.6)–(3.8) describe a d-codimensional manifold $\mathcal{C}_c \times \mathbf{R}_+^r$ of d-dimensional dynamical systems.

The flow $\mathcal{F}_2$ of Eqs. (3.6)–(3.8) maps into the flow $\mathcal{F}_1$ of Eqs. (2.6)–(2.7) under the mapping ϕ: $(X^t, k^t) \to (X_I^t, C^t, k^t)$, where C is given by Eq. (3.3). The inverse map ϕ^{-1} is given by Eq. (3.5). Since ϕ is one-to-one and both ϕ and ϕ^{-1} are continuously differentiable infinitely many times, ϕ is a C^∞ *diffeomorphism*. (Again we have considered the domains of both flows to be differentiable manifolds.) Hence the flow $\mathcal{F}_1$ of Eqs. (2.6) and (2.7) is also a d-codimensional manifold of d-dimensional dynamical systems.

IV. CONSEQUENCES OF THE GENERAL RATE LAW

The rate law for the general chemical reaction has a proportionality "constant" k_j which can take any value in $\mathbf{R}_+$. (See Ref. 1 for detailed examples.) In this section we make use of the range of k to set up a second diffeomorphism ψ^{-1} between the flow $\mathcal{F}_1$ and a flow which will be called $\mathcal{F}_0$, whose set of steady states can be calculated easily. Our purpose is to obtain the composite diffeomorphism $\phi\psi$ which maps the flow $\mathcal{F}_0$ onto the flow $\mathcal{F}_2$ of Eqs. (3.6)–(3.8) in the dynamic variable $(X_I^t, C^t, k^t)^t$. This diffeomorphism will induce a diffeomorphism from the known set of steady states of $\mathcal{F}_0$ to the set of steady states of $\mathcal{F}_2$ in the space of $(X_I^t, C^t, k^t)^t$. This diffeomorphism gives us a parametric description of the steady states of $\mathcal{F}_2$.

Let Y be the vector whose components are $Y_i = 1/X_i$. The component-by-component reciprocal of a vector (or array) will be written as

$$Y = 1/X . \tag{4.1}$$

(Note: A^{-1} means the matrix inverse while $1/A$ means the matrix of the reciprocals of each component,) Since the domain of X is $\mathbf{R}_+^n$, the domain of Y is also $\mathbf{R}_+^n$.

Equations (2.3) and (4.1) define a map ψ^{-1} which takes $(X^t, k^t)^t \in \mathbf{R}_+^{n+r}$ into $(Y^t, v^t)^t \in \mathbf{R}_+^{n+r}$. The inverse map ψ is given by

$$X = 1/Y , \tag{4.2}$$

$$k = (\text{diag } v)\,[1/u(1/Y)] . \tag{4.3}$$

Clearly, ψ is also a map from $\mathbf{R}_+^{n+r}$ to $\mathbf{R}_+^{n+r}$ and thus ψ is a one-to-one mapping. Since u(X) is continuously differentiable k times (for some $k \geq 1$), both ψ and ψ^{-1} are differentiable; hence ψ is a C^k diffeomorphism. (Again, this terminology assumes that $\mathbf{R}_+^{n+r}$ is being regarded as a differentiable manifold.)

The flow on $\mathbf{R}_+^{n+r}$ obtained by integrating Eqs. (2.6) and (2.7) is mapped by ψ^{-1} onto a flow in the dynamical variables $(Y^t, v^t)^t \in \mathbf{R}_+^{n+r}$. Is this flow in $(Y^t, v^t)^t$ the integral of some system of differential equations? Since ψ^{-1} has a first derivative and the differential Eqs. (2.6) and (2.7) do not involve derivatives higher than the first, the answer is yes. The differential equations in $(Y^t, v^t)^t$ are obtained from Eqs. (2.6) and (2.7) by changing variables using Eqs. (2.3) and (4.1).

The derivation for the $\dot{Y}$ equation is as follows. For any $i \in [1, n]$, $\dot{Y}_i = (-1/X_i^2)\dot{X}_i = -Y_i^2 \dot{X}_i$, or in vector notation

$$\dot{Y} = -(\text{diag } Y)^2 \dot{X} .$$

Substituting first Eq. (2.6) and then Eq. (2.3) in this equation gives

$$\dot{Y} = -(\text{diag } Y)^2 \nu v . \tag{4.4}$$

This is the first equation in the variable $(Y^t, v^t)^t$.

The $\dot{v}$ equation is obtained by differentiating Eq. (2.3) and using Eqs. (2.6), (2.7), (4.2), and (4.3) to express the result in terms of Y and v. We get

$$\dot{v} = (\text{diag } v)\{\text{diag}[1/u(1/Y)]\}(\nabla u)^t \nu v , \tag{4.5}$$

where $(\nabla u)^t$ is the $r \times n$ Jacobian matrix of the map u: $\mathbf{R}_+^n \to \mathbf{R}_+^r$ and is a function of Y. The dynamical system of Eqs. (4.4)–(4.5) in $(Y^t, v^t)^t$ determines a flow $\mathcal{F}_0$ on the manifold $\mathbf{R}_+^{n+r}$ which is diffeomorphic to $\mathcal{F}_1$ via the map ψ, and to $\mathcal{F}_2$ via the composite map $\phi\psi$. See Fig. 1.

V. STEADY STATES OF THE FLOW $\mathcal{F}_0$

The argument in this section proves that the steady states of the flow $\mathcal{F}_0$ in the variables Y and v comprise a convex polyhderal cone. In Fig. 1 this cone is the ray marked $\mathcal{C}$.

At steady state $\dot{Y} = 0$ and $\dot{v} = 0$; Eq. (4.4) then becomes

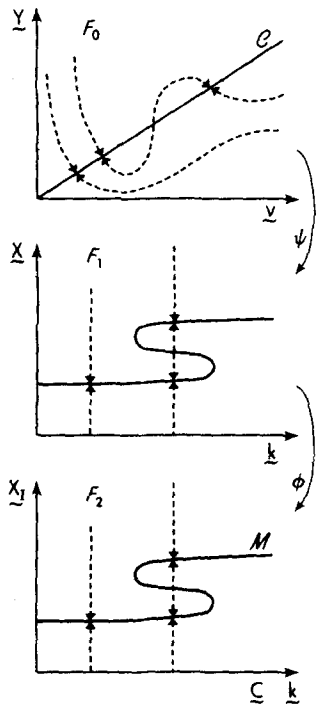

FIG. 1. The flow $\mathfrak{F}_0$ in the variables **Y** and **v** is mapped by ψ into the flow $\mathfrak{F}_1$ in the variables **X** and **k**, which is mapped by ϕ into the flow $\mathfrak{F}_2$ in the variables $\mathbf{X}_J$, **C**, and **k**. For each flow the sketch shows two trajectories and the set of steady states. The three flows and their trajectories and steady states are diffeomorphic to each other.

$$(\text{diag } \mathbf{Y})^2 \nu \mathbf{v} = 0 ,$$

however, since the $(\text{diag } \mathbf{Y})^2$ factor is a diagonal matrix with strictly positive elements, it follows that $\dot{\mathbf{Y}} = 0$ if and only if

$$\nu \mathbf{v} = 0 . \tag{5.1}$$

From Eq. (4.5), this condition implies that **v** is also zero. The set of steady states of the $(\mathbf{Y}^t, \mathbf{v}^t)^t$ dynamical system is then

$$\mathcal{C} \equiv \{(\mathbf{h}^t, \mathbf{w}^t)^t \,|\, \mathbf{h} \in \mathbf{R}^n_+,\ \mathbf{w} \in \mathbf{R}^r_+,\ \nu \mathbf{w} = 0\} . \tag{5.2}$$

Thus, $(\mathbf{Y}^t, \mathbf{v}^t)^t \in \mathbf{R}^{n+r}_+$ is at steady state if and only if $\mathbf{Y} = \mathbf{h}$ and $\mathbf{v} = \mathbf{w}$, where $(\mathbf{h}^t, \mathbf{w}^t)^t \in \mathcal{C}$.

The set of steady states can be written

$$\mathcal{C} = \mathbf{R}^n_+ \times \mathcal{C}_\nu , \tag{5.3}$$

where

$$\mathcal{C}_\nu \equiv \{\mathbf{w} \in \mathbf{R}^r_+ \,|\, \nu \mathbf{w} = 0\} . \tag{5.4}$$

$\mathcal{C}_\nu$ is the intersection of the right null space of ν with the positive orthant of $\mathbf{R}^r$. Since ν has rank d, its right null space has dimension $r - d$ and consists of those vectors in $\mathbf{R}^r$ which are orthogonal to the d linearly independent rows of ν. The intersection of the null space with the (strictly) positive orthant is either an empty set or else a set of dimension $r - d$. Hence $\mathcal{C}$ is either an empty set or else a set of dimension $n + r - d$.

The representation [Eq. (5.4)] for $\mathcal{C}_\nu$ has the disadvantage that the r components of **w** are not independent. To overcome this, we define **E** to be an $r \times f$ matrix whose columns are vectors pointing along the f edges of $\mathcal{C}_\nu$. Each edge vector is based at the apex (the origin), points in the direction of the edge, and has an arbitrary nonzero length. Any point **w** in the open cone $\mathcal{C}_\nu$ can be expressed as a positive linear combination of these edge vectors. Hence there exists $\mathbf{j} \in \mathbf{R}^f_+$ such that

$$\mathbf{w} = \mathbf{E}\mathbf{j} . \tag{5.5}$$

Conversely, for every $\mathbf{j} \in \mathbf{R}^f_+$, Eq. (5.5) gives a point $\mathbf{w} \in \mathcal{C}_\nu$. Instead of using **w** in the restricted domain $\mathcal{C}_\nu$, it is usually more convenient in practice to let **j** range over the more convenient domain $\mathbf{R}^f_+$ and then

$$\mathcal{C}_\nu = \{\mathbf{E}\mathbf{j} \,|\, \mathbf{j} \in \mathbf{R}^f_+\} . \tag{5.6}$$

Since **E** is very important to the practical application of this theory we now discuss its properties. From Eq. (5.5) and the fact that $\nu \mathbf{w} = 0$ for all **j**,

$$\nu \mathbf{E} = 0 . \tag{5.7}$$

The columns of **E** lie in the right null space of ν and any $r - d$ of them form a basis. Since any matrix ν determines a corresponding matrix **E** (up to a permutation and normalization of its columns), **E** appears to be a very important matrix and algorithms for calculating it should exist; however, there does not seem to be any publicly available computer code for this problem. To meet this need an algorithm in the language APL has been kindly provided by B. von Hohenbalken (see Fig. 2). The theory behind the algorithm appears in Ref. 7.

```
      ∇CURRENTS[□]∇
      ∇ E←CURRENTS NU;N;K;B;ER;Y;V;D;U;R;X;C
[1]   E← 0 0 ρ0
[2]   V←~∨⌿0<(∧/0≤NU)⌿NU
[3]   NU←(V←V∧~∨⌿0>(∧/0≥NU)⌿NU)/NU
[4]   →0×ι=/ρNU←NU[BASIS⌹NU;]
[5]   D←1+1↑ρNU
[6]   N←1↓ρNU
[7]   K←⌹E←(N,C←B←0)ρER←1E¯10
[8]  Δ1:→Δ4×ι0=1↑C←C COMB0 N,D
[9]   →Δ1×ι∨/(∧/K∈C,0),∧/NU[;C]=0
[10]  B←1↓X←(B∈C)/B
[11]  R←R+1↑C×0=R←1↑X
[12] Δ2:U←NU[;R[1]]⌸NU[;(ρB)ρR]-NU[;B]
[13]  →Δ3×ι∧/ER>|X←NU[;B←B,R]+.×U←U,1-+/U
[14]  R←0,X+.×NU[;C]
[15]  →((0=R←,(0,C)[Rι⌊/R]),1)/Δ1,Δ2
[16] Δ3:→Δ1×ι∨/U<-ER
[17]  U←X/U,0/B←(X←U>ER)/B
[18]  K←K,[1](R←(ιN)∈B)×ιN
[19]  →Δ1,ρE←E,R\U[⍋B]+⌊/U
[20] Δ4:E←V⌹E
      ∇
      ∇BASIS[□]∇
      ∇ B←BASIS A;S
[1]   →3,,A←A+(ρA)ρ(~S←∨⌿A≠ρB←ι0)+(+⌿A×A)*+2
[2]   S←+⌿S×S←A-A[;B]+.×(⌸A[;B←B,Sι⌈/S])+.×A
[3]   →2×ι(1E¯7<(|⌈/S)*+2)∧0≤⌈/S
      ∇
      ∇COMB0[□]∇
      ∇ C←CL COMB0 NR;K
[1]   →8×ι0=ρ,CL
[2]   →4×ι0<1↑CL
[3]   →0,C←ιNR[2]
[4]   K←NR[2]
[5]   →7×ιCL[K]≥NR[1]-NR[2]-K
[6]   →0,C←((K-1)↑CL),CL[K]+ι1+NR[2]-K
[7]   →5×ι0<K←K-1
[8]   C←0
      ∇
```

FIG. 2. An algorithm [courtesy of B. von Hohenbalken (Ref. 7)] which calculates the matrix **E** from the matrix ν (called NU). This algorithm requires a modern version of APL where the domino function calculates the pseudoinverse of nonsquare arrays. It will run under standard IBM versions of APL such as VSAPL. The algorithm CURRENTS contains no built-in restrictions on the size of ν; however, since it examines $\binom{r}{d+1}$ combinations, the running time increases rapidly with r.

VI. STEADY STATES OF THE FLOW $\mathfrak{F}_2$ IN X_I, C, AND k

The known set of steady states $\mathfrak{C}$ of the flow $\mathfrak{F}_0$ in Y and v is mapped by $\phi\psi$ into the set of steady states of the flow $\mathfrak{F}_2$ in $\mathbf{X}_I$, C, and k. Since $\phi\psi$ is a diffeomorphism, $\phi\psi\mathfrak{C}$ is the complete set of steady states of $\mathfrak{F}_2$ on the domain $\mathbf{R}_+^d \times \mathfrak{C}_c \times \mathbf{R}_+^r$.

The cone $\mathfrak{C}$ is a simply connected set of dimension $n+r-d$. Since a diffeomorphism cannot change the topological properties of a set, the set of steady states $\phi\psi\mathfrak{C}$ of $\mathfrak{F}_2$ is also a set of dimension $n+r-d$ which is a simply connected subset of $\mathbf{R}_+^{n+r}$. The codimension of the set of steady states is d. With our interpretation of $\mathbf{R}_+^{n+r}$ as a differentiable manifold, $\phi\psi\mathfrak{C}$ becomes a submanifold of codimension d. Let us call this manifold $\mathfrak{M}$, the *manifold of steady states*.

An explicit expression for $\mathfrak{M}$ is easily obtained. Given any $(\mathbf{h}^t, \mathbf{w}^t)^t \in \mathfrak{C}$, the composite map $\phi\psi$ produces the point $(\mathbf{X}_I^t, \mathbf{C}^t, \mathbf{k}^t)^t$, where $\mathbf{X}_I$ is the first d components of $1/\mathbf{h}$, and from Eqs. (3.3), (4.2), and (4.3),

$$\mathbf{C} = \gamma(1/\mathbf{h}) , \tag{6.1}$$

$$\mathbf{k} = (\text{diag } \mathbf{w})[1/\mathbf{u}(1/\mathbf{h})]. \tag{6.2}$$

The manifold of all steady states in the open set $\mathbf{R}_+^d \times \mathfrak{C}_c \times \mathbf{R}_+^r$ has now been found.

Up to this point concentrations and rate constants have been strictly positive. We now allow them to be zero and investigate the set of steady states in the closed domain $\bar{\mathbf{R}}_+^d \times \bar{\mathfrak{C}}_c \times \bar{\mathbf{R}}_+^r$. The map u must now be extended continuously to $\bar{u}$: $\bar{\mathbf{R}}_+^n \to \bar{\mathbf{R}}_+^r$. For the extended map, if $\mathbf{X} \notin \partial\mathbf{R}_+^n$ then $\bar{\mathbf{u}}(\mathbf{X}) \notin \partial\mathbf{R}_+^r$ (∂S is the notation for the boundary of any set S).

Some of the steady states in the boundary can be found by taking the closure of $\mathfrak{M}$. If $\mathfrak{M}$ approaches the boundary there must exist sequences of points $(\mathbf{X}_I^t, \mathbf{C}^t, \mathbf{k}^t)_{(i)}$, $i = 1, 2, \ldots$, in $\mathfrak{M}$ which approach the boundary. Since the right-hand sides of Eqs. (3.6)–(3.8) vanish for every point in each sequence, they also vanish in each limit by the continuity of u. Hence all points of $\bar{\mathfrak{M}}$ are steady states of the closed-domain system.

Closed-domain systems can also have steady states which are not in $\bar{\mathfrak{M}}$, as illustrated in the following example (Example 1):

$$X \xrightarrow{1} 2X \quad X \xrightarrow{2} \square \ . \tag{6.3}$$

If the rate laws are $k_1 X$ and $k_2 X$ respectively, the equation of motion is

$$\dot{X} = (k_1 - k_2)X ,$$

and

$$\bar{\mathfrak{M}} = \{(X, k_1, k_2) \,|\, X \in \bar{\mathbf{R}}_+, k_1 = k_2 \in \bar{\mathbf{R}}_+\} ; \tag{6.4}$$

however, the boundary contains the additional set of steady states

$$\bar{\mathfrak{M}}_{\text{bdy}} = \{(0, k_1, k_2) \,|\, k_1 \in \bar{\mathbf{R}}_+, k_2 \in \bar{\mathbf{R}}_+\} , \tag{6.5}$$

almost none of which are limit points of $\mathfrak{M}$ (see Fig. 3). The full set of steady states on the closed domain is $\mathfrak{M}^* \equiv \mathfrak{M} \cup \bar{\mathfrak{M}}_{\text{bdy}}$, which is not diffeomorphic to a cone.

We now find in general the complete set of steady states $\mathfrak{M}^*$ of Eqs. (3.6)–(3.8) on the closed domain $\bar{\mathbf{R}}_+^d \times \bar{\mathfrak{C}}_c \times \bar{\mathbf{R}}_+^r$. First note that Eqs. (3.3) and (3.5) have no singularities on the domain boundaries. Hence ϕ can be extended to this larger domain; the extended map $\bar{\phi}$ is also a diffeomorphism. The complete set of steady states of the flow $\mathfrak{F}_2$ on the closed domain [Eqs. (3.6)–(3.8)] is then diffeomorphic to the complete set of steady states of the flow $\mathfrak{F}_1$ [Eqs. (2.6) and (2.7)] on $\bar{\mathbf{R}}_+^n \times \bar{\mathbf{R}}_+^r$. We find the latter set and leave it to the reader to convert to the former using $\bar{\phi}$.

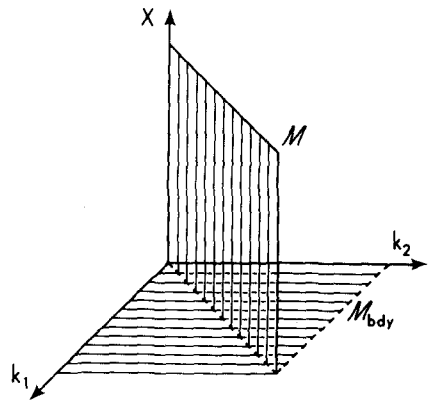

FIG. 3. Steady states on the closed orthant for flows $\mathfrak{F}_1$ and $\mathfrak{F}_2$ of Example 1.

The solution to the problem is given by an algorithm which involves operations on logical arrays (consisting of 0's and 1's). These operations can be expressed concisely in a mathematical notation devised by K. E. Iverson called APL.[8] The algorithm will be described in words and summarized in APL statements. These statements together will yield a 12 line program which should run on most computers with APL.

Each species X_i can have either $X_i = 0$ or $X_i \neq 0$. Consequently, the domain $\bar{\mathbf{R}}_+^n$ of X can be subdivided into 2^n open orthants—one for each combination of suppressed species (i.e., species with $X_i = 0$). Then $\bar{\mathbf{R}}_+^n \times \bar{\mathbf{R}}_+^r$ splits into 2^n domains. We find the steady states in each of these domains separately.

In the algorithm we first generate all 2^n domains combinatorially. A particular domain is specified by the value of an APL variable S. This is a vector whose components are the indices of the suppressed species. For example, if no species are suppressed, S is a vector with no components; or, for example, if $X_1 = X_7 = 0$, and all other species are nonzero, then $S \leftarrow 1\ 7$.

We need to know what reactions are suppressed as a consequence of a particular choice S of suppressed species. Frequently reaction rates are given by *power law kinetics* of the form

$$u_j(\mathbf{X}) = \sum_{i=1}^{n} X_i^{\kappa_{ij}} , \tag{6.6}$$

where κ is an $n \times r$ matrix giving the order of the ith species in the jth reaction (see Ref. 1). We make the reasonable assumption that $\kappa_{ij} \geq 0$ for all i, j because, if this assumption were false, a reaction rate would diverge to infinity as some $X_i \to 0$. Hence the jth reaction is sup-

pressed by S if $\kappa_{ij} > 0$ for any $i \in S$. To express this idea in APL let KAP1 be an $n \times r$ logical array indicating which elements of κ are nonzero. Then the statement

$$T \leftarrow \vee \neq \text{KAP1}[S;\ ] \tag{6.7}$$

produces an r component logical vector T with 1's corresponding to the suppressed reactions. If u(X) is not a power law another method of generating T would have to be used instead of this line in the algorithm.

The part of $\bar{\mathbf{R}}^n_+ \times \bar{\mathbf{R}}^r_+$ corresponding to S contains steady states only if no active reactions produce or consume the suppressed species. Hence all reactions that involve suppressed species must be suppressed either indirectly (because species are suppressed) or directly by setting $k_j = 0$. These suppressed reactions are given by the logical vector

$$P \leftarrow T \vee \cdot \wedge \neq \text{NU1}[S;\ ], \tag{6.8}$$

where NU1 is an $n \times r$ logical array indicating which elements of ν are nonzero.

All steady states in the domain corresponding to S must be steady states of the subnetwork of nonsuppressed reactions, which are the reactions corresponding to zero elements of P. The steady states of this subnetwork can be found by the method of this paper. It is not necessary to calculate $\mathbf{E}$ for the subnetwork because the columns of the subnetwork $\mathbf{E}$ are already columns of $\mathbf{E}$ for the full network. These columns will be indicated by the 1's in the f component logical vector B calculated as follows:

$$B \leftarrow \sim E1T \vee \cdot \wedge P, \tag{6.9}$$

where $E1T$ is an $f \times r$ logical array indicating which elements of $\mathbf{E}^t$ are nonzero. Statement (6.9) compares each column of $\mathbf{E}$ (row of $E1T$) with the suppressed reactions (P) to see if any of the elements in that column are suppressed reactions. Columns of $\mathbf{E}$ containing such elements are not in $\mathbf{E}$ for the subnetwork and all remaining ones are.

We have now found the cone of steady states corresponding to S; however, it is necessary to update the set of suppressed reactions because the cone found may lie in the orthant boundary of the subnetwork, and it may be necessary to suppress more reactions directly to obtain an orthant having this cone in its interior. The complete set of suppressed reactions consists of all reactions not used by the columns of $\mathbf{E}$ for the subnetwork. Thus

$$P \leftarrow \sim \vee \neq E1T[B \leftarrow B/\iota F;], \tag{6.10}$$

where F is f, the number of columns of $\mathbf{E}$.

Let us summarize. For each of the 2^n choices of S there is a domain of $\bar{\mathbf{R}}^n_+ \times \bar{\mathbf{R}}^r_+$. In order for there to be steady states in this domain the reactions P must all be suppressed. These suppressed reactions are of two types. First, there are reactions which are suppressed because certain species are suppressed. These reactions are given by T. Since these reactions will be suppressed whatever the effective rate constant, k_j can range over the interval $0 \le k_j < \infty$. Second, there are reactions whose suppression is essential for a steady state to exist because such reactions would cause a flow out of the domain corresponding to S due to the fact that these reactions produce or consume suppressed species. These reactions are given by $P \vee \sim T$. For these reactions it is necessary to set $k_j = 0$ to have a steady state. There are two types of domains for k_j of the suppressed reactions and they determine the domain of $\bar{\mathbf{R}}^r_+$ within which all steady states must lie when $\mathbf{X}$ lies in the domain of $\bar{\mathbf{R}}^n_+$ corresponding to S. Thus for any chosen S, we calculate T and P, which specify an orthant of $\bar{\mathbf{R}}^n_+ \times \bar{\mathbf{R}}^r_+$ having all steady states for the chosen S. The set of all steady states in the interior of this orthant can be found using the methods discussed earlier for the subnetwork of reactions and species which are not suppressed. The matrix $\mathbf{E}$ for this subnetwork consists of those columns of $\mathbf{E}$ of the full network indicated by B. This subnetwork has a cone of steady states which are mapped by ψ into the set of steady states in the interior of the orthant of $\bar{\mathbf{R}}^n_+ \times \bar{\mathbf{R}}^r_+$ determined by S, T, and P. However, we need the set of steady states on this full orthant and not just in its interior. Note that the orthant can be closed only along the part of the boundary corresponding to k. The domain of the mapping ψ can be extended to this part of the boundary and the extended map $\bar{\psi}$ remains a diffeomorphism because Eqs. (2.8) and (4.3) are linear in k and v. Hence, the solution on the full orthant of S, T, and P is the closure of the solution in its interior. We have found the complete set of steady states on the domain of $\bar{\mathbf{R}}^n_+ \times \bar{\mathbf{R}}^r_+$ for given S. After S has taken all combinations, the union of these sets is mapped via $\bar{\phi}$ onto $\bar{\mathbf{R}}^d_+ \times \bar{\mathbf{C}}_c \times \bar{\mathbf{R}}^r_+$ to yield M^*, the set of closed-domain steady states.

This algorithm should be taken literally even when the vectors have no components. For example, if B has no components, $\mathbf{E}$ for the subnetwork has no columns and this means all reactions are suppressed, either indirectly because the species S are suppressed or directly by setting $k_j = 0$. The whole orthant of $\bar{\mathbf{R}}^n_+ \times \bar{\mathbf{R}}^r_+$ corresponding to S consists of steady states because the unsuppressed species and reactions form the null network (no species, no reactions) whose steady state conditions are always satisfied.

A version of this algorithm which will run under the standard IBM product VSAPL is shown in Fig. 4. The function ALLSS takes the matrix $\mathbf{E}$ as its left argument and the concatenated matrices ν and κ as its right argument. The first four lines set up logical arrays from the input and write a heading; the next two lines generate all combinations S and control looping; the next three lines are the algorithm and the second last line formats output. The figure shows how the function is used to solve Example 1.

The operation of the algorithm for Example 1 is as follows: Since $n = 1$ and $r = 2$, $\bar{\mathbf{R}}^n_+ \times \bar{\mathbf{R}}^r_+ = \bar{\mathbf{R}}^3_+$, which is subdivided into $2^n = 2$ domains: $X = 0$ and $X \neq 0$. In the first domain $S = 1$ and Eq. (6.7) determines that both reactions are suppressed by the species. Thus $P = T = 1\ 1$. Hence, k_1 and k_2 are arbitrary so the steady states for this S all lie in the set $\{(X, k_1, k_2) \mid X = 0,\ 0 \le k_1,\ 0 \le k_2\}$. The steady states are steady states of the network of the remaining (unsuppressed) species and reactions. Since the remaining network is the null network all of its states are steady states. Thus the whole set

```
      ∇ALLSS[□]∇
      ∇ E ALLSS NK;B;D;E;E1T;F;KAP1;L;N;NU1;NS;P;R;S;T
[1]   NU1←0≠((N←NS←1↑ρNK),(R←⌈0.5×¯1↑ρNK))↑NK
[2]   KAP1←0≠(N,-R)↑NK
[3]   F←1↑ρE1T←⌽E≠S←0
[4]   ' SPEC SUPP      RX SUPP        RX ARB K       BDY CONE       DIM'
[5]   Δ1:→Δ2×ι0≠ρρS←S COMB0 N,NS
[6]   →(Δ1,0)[1+¯1=NS←NS-1]
[7]   Δ2:T←∨⌿KAP1[S;]
[8]   B←~E1T∨.∧P←T∨∨⌿NU1[S;]
[9]   P←~∨⌿E1T[B←B/ιF;]
[10]  D←(ρBASIS E[;B])+(N-ρS)++/T
[11]  (15↑ 2 0 ▼S),(15↑ 2 0 ▼(P∧~T)/ιR),(15↑ 2 0 ▼T/ιR),(15↑ 2 0 ▼B),(2 0 ▼D)
[12]  →Δ1
      ∇
      NUEX1,KAPEX1
  1 ¯1  1  1
      EEX1←CURRENTS NUEX1
      EEX1
1
1
      EEX1 ALLSS NUEX1,KAPEX1
SPEC SUPP      RX SUPP        RX ARB K       BDY CONE       DIM
1                             1 2                           2
                                             1              2
```

FIG. 4. An algorithm for finding all steady states on the closed domain and its use to solve Example 1. Lines 7–9 of the algorithm ALLSS are Eqs. (6.7)–(6.10) of this paper. Below the algorithm is a complete interactive computer session where Example 1 is solved. The arrays ν and κ are called NUEX1 and KAPEX1 and are displayed (concatenated) by the APL command "NUEX1, KAPEX1." Next the command "EEX1 ← CURRENTS NUEX1" causes the algorithm CURRENTS of Fig. 2 to calculate E for this problem and store it in the variable EEX1. The command "EEX1" displays E and we see that it is a 2×1 matrix of 1's. The final command "EEX1 ALLSS NUEX1, KAPEX1" causes ALLSS to print out the solution to Example 1 as a table. The table headings are abbreviations for "species suppressed," "reactions suppressed directly" (i.e., $k_j=0$), "reactions with arbitrary k" (i.e., $0\le k_j\le\infty$), "columns of E in the boundary cone" (i.e., column indices which give E for the subnetwork), and "dimension of the manifold of steady states for this choice of suppressed species." Note that five of the table entries are blank. A blank entry means that no species are suppressed, no reactions are suppressed, etc.

$\{(X,k_1,k_2)\,|\,X=0,\ 0\le k_1,\ 0\le k_2\}$ consists of steady states and is $\mathfrak{M}_{bdy}$ in Fig. 2. This case is covered by the first line of output from ALLSS.

In the second domain of $\bar{\mathbf{R}}^3_+$ corresponding to $X\neq 0$, S is a vector with no components. Then Eqs. (6.7) implies that no reactions are suppressed by species, and Eqs. (6.8)–(6.10) tell us that no other reactions need to be suppressed to have steady states. Thus there are steady states in the set $\{(X,k_1,k_2)\,|\,0<X,\ 0\le k_1,\ 0\le k_2\}$. To find them we look for steady states of the network of remaining species and reactions. This is the full network. The steady states in the interior of the above set are found by the earlier method to be $\mathfrak{M}$. The full set of steady states in the above set is then $\bar{\mathfrak{M}}$.

It is useful to know the dimension of a part of $\mathfrak{M}^*$ corresponding to a particular S. If the subnetwork involved has n_s species, r_s reactions, and a stoichiometric matrix of rank d_s, then $\mathfrak{M}_s$ for the subnetwork has dimension $n_s+r_s-d_s$. If there are k arbitrary rate constants, the dimension of the piece of $\mathfrak{M}^*$ corresponding to S is then

$$\dim\mathfrak{M}^*(S)=n_s+r_s-d_s+k\ , \tag{6.11}$$

because each arbitrary rate constant adds one dimension. An equivalent APL statement is

$$D=(N-\rho S)+(\rho\ \text{BASIS}\ E[;B])+(+/T)\ , \tag{6.12}$$

where the first term in parentheses gives n_s, the second term gives r_s-d_s, and the third term gives k. (Note: the second term calculates r_s-d_s using the fact that this is the dimension of $\mathcal{C}_v$ for the subnetwork. This dimension is calculated from the current matrix $E[;B]$ of the subnetwork by finding a basis for the space spanned by the columns of $E[;B]$ and counting the basis vectors. The function BASIS appears in Fig. 2.) ALLSS prints the dimension of each piece of $\mathfrak{M}^*$.

When $\bar{\mathfrak{M}}$ intersects the part of the boundary where species have been suppressed, the dimension of the intersection is at most $\dim\bar{\mathfrak{M}}$ minus the number of suppressed species. In example 1 the last line of output from ALLSS in Fig. 4 says that $\dim\bar{\mathfrak{M}}=2$. Hence $\bar{\mathfrak{M}}$ can intersect the orthant boundary where $X=0$ in a set whose maximum possible dimension is 1. Figure 3 shows this in the case; however, in an example where $\bar{\mathfrak{M}}$ were oriented differently, the intersection could have a lower dimension. Since ALLSS says that the set of steady states in the boundary $X=0$ is two-dimensional, we know that there are steady states in this part of the boundary which are not in $\bar{\mathfrak{M}}$.

VII. APPLICATION TO THE BELOUSOV–ZHABOTINSKI MECHANISM

The original mechanism of Field, Noyes, and Körös for the oscillatory Belousov-Zhabotinski reaction has been analyzed by the author.[9,10] Although this mechanism was later found to be incorrect in the way bromide ion was generated from bromomalonic acid, the mechanism will serve well to illustrate the approach of this paper. Since the mechanism has already been treated according to the approach of Ref. 1, much of the analysis has already been published and here we are concerned only with the part of the analysis that involves the new ideas

```
      NUEX2,KAPEX2
 -1   2   1   1   0   0   0  -1   1   0   0   0   0   0   0   1
  0   0   0   0  -2   6   4   0   0   0   0   0   0   1   0   0   0
  0  -1   1  -2   1   0   0   0   0   1   0   2   1   0   0   0
  0  -1  -1   0   0   0   1   1   1   1   1   0   0   0   0   0
  0   0   0   0   2  -6  -4   0   0   0   0   0   0   1   1   0
      EEX2←CURRENTS NUEX2
      EEX2
1     1.5 5     3     3     2.5 1
1     0     2     3     2     0     0
1     0     0     0     0     1     2
0     1.5 1     0     0     1.5 1
0     3     4     3     2     2     0
0     1     0     1     0     0     0
0     0     2     0     1     1     0
2     0     0     3     1     0     2
      EEX2 ALLSS NUEX2,KAPEX2
SPEC  SUPP        RX  SUPP          RX  ARB  K          BDY  CONE          DIM
1 2 3 4 5                           1 2 3 4 5 6 7                          8
1 2 3 4             6 7             1 2 3 4 5 8                            7
1 2 3 5             3               1 2 4 5 6 7 8                          8
1 2 4 5             4               1 2 3 5 6 7 8                          8
1 3 4 5                             1 2 3 4 5 6 7                          9
2 3 4 5             8               1 2 3 4 5 6 7                          8
1 2 3               3 6 7           1 2 4 5 8                              7
1 2 4               4 6 7           1 2 3 5 8                              7
1 2 5               2 3 4           1 5 6 7 8                              7
1 3 4               6 7             1 2 3 4 5 8                            8
1 3 5               3               1 2 4 5 6 7 8                          9
1 4 5               4 5             1 2 3 6 7 8                            8
2 3 4               6 7 8           1 2 3 4 5                              7
2 3 5               1 3 8           2 4 5 6 7                              7
2 4 5               4 8             1 2 3 5 6 7                            8
3 4 5               8               1 2 3 4 5 6 7                          9
1 2                 2 3 4 6 7       1 5 8                                  6
1 3                 3 6 7           1 2 4 5 8                              8
1 4                 4 5 6 7         1 2 3 8                                7
1 5                 2 3 4 5         1 6 7 8                                7
2 3                 1 3 6 7 8       2 4 5                                  6
2 4                 4 6 7 8         1 2 3 5                                7
2 5                                 5 6 7                  1 7             8
3 4                 6 7 8           1 2 3 4 5                              8
3 5                 1 3 8           2 4 5 6 7                              8
4 5                 4 5 8           1 2 3 6 7                              8
1                   2 3 4 5 6 7     1 8                                    6
2                   6 7             5                      1 7             7
3                   1 3 6 7 8       2 4 5                                  7
4                   4 5 6 7 8       1 2 3                                  7
5                   5               6 7                    1 7             8
                                                           1 2 3 4 5 6 7   9
```

FIG. 5. An analysis of the steady states of a model of the Belousov–Zhabotinski reaction mechanism. Shown is a complete interactive computer session in which the same commands are given as in the session of Fig. 4, the only difference being that the matrices ν and κ have been replaced with those for the BZ mechanism. The algorithm ALLSS in Fig. 4 will operate for any size matrices $\mathbf{E}$, ν, and κ; however, the output formatting in line 11 may truncate some printout if n, f, or r is greater than 7. This occurred in the first and fifth rows of this table, where the information that k_8 is arbitrary was truncated. For large problems the reader should change the output formatting in lines 4 and 11 of ALLSS.

in this paper.

The model has five species called T, W, X, Y, and Z, which will now be called $X_1 \cdots X_5$. The eight reactions have power law kinetics. In the analysis of the model shown in Fig. 5, the matrices ν and κ are called NUEX2 and KAPEX2 and are displayed at the top of the figure. From these matrices the reader can construct the chemical reactions, so the reactions will not be repeated here. Next the current matrix $\mathbf{E}$ (called EEX2) is calculated using CURRENTS and then $\mathbf{E}$ is displayed. The columns of this matrix were used in Ref. 9 [see Eqs. (3.12)–(3.18)] with a slightly different scaling and sequence.

The full set of steady states is then calculated from $\mathbf{E}$, ν, and κ using ALLSS. Since there are five species there are 32 ways to suppress various combinations of species, and the possibilities are listed in the left-hand column. Note that the last entry in the column is a blank entry because no species are suppressed. This case treats the full network. The third column gives the reactions which are suppressed due to the suppression of the species. These reactions have k_j in the range $0 \leq k_j \leq \infty$. The second column gives the remaining reactions which must be suppressed by setting $k_j = 0$ in order for a steady state of the nonsuppressed species to exist. Note that when no species are suppressed (the last line of the table), no reactions need be suppressed and no reactions have arbitrary k. Hence these three columns have blank entries. The fourth column gives the column indices of $\mathbf{E}$ for the cone $\mathcal{C}_v$ for each S. All columns of $\mathbf{E}$ are used when no species are suppressed. In many cases no columns of $\mathbf{E}$ are used; this means that the subnetwork has no reactions and is automatically at steady state, without any further restrictions. Otherwise the columns of $\mathbf{E}$ restrict the steady state further as illustrated later. The final column gives the dimension of the steady state manifold corresponding to each combination of suppressed species. Note that if no species are suppressed the dimension is nine. This means that $\dim \mathfrak{M} = 9$.

The fifth from the last line of the table shows that further restrictions on the steady state occur when only

species X_2 is suppressed. In this case the table says $k_6 = k_7 = 0$ and $0 \le k_5 \le \infty$. The further restrictions are given by Eqs. (6.1) and (6.2) and will be obtained explicitly for this case. The second and fifth rows of ν for this network add to zero. This means that $X_2 + X_5$ is a constant of the motion and thus if

$$\gamma = (0\ 1\ 0\ 0\ 1)\ , \tag{7.1}$$

Eq. (3.3) with this γ states the conservation of $X_2 + X_5$. Then Eq. (6.1) reads

$$C = h_2^{-1} + h_5^{-1}\ . \tag{7.2}$$

From the matrix κ in Fig. 5 and Eq. (6.6)

$$1/\mathrm{u}(1/\mathrm{h}) \equiv (h_1 h_4, h_3 h_4,\ h_4,\ h_3^2,\ h_2 h_3,\ h_5, h_5, h_1)^t. \tag{7.3}$$

Since for this network **E** in Eq. (5.5) has only two columns, which are the first and seventh columns of **E** for the whole network, we write Eq. (5.5) as

$$\mathbf{w} = \begin{pmatrix} 1 & 1 \\ 1 & 0 \\ 1 & 2 \\ 0 & 1 \\ 0 & 0 \\ 0 & 0 \\ 0 & 0 \\ 2 & 2 \end{pmatrix} \begin{pmatrix} j_1 \\ j_7 \end{pmatrix}\ . \tag{7.4}$$

Then Eq. (6.2) yields

$$k_1 = (j_1 + j_7) h_1 h_4\ , \tag{7.5}$$

$$k_2 = j_1 h_3 h_4\ , \tag{7.6}$$

$$k_3 = (j_1 + 2j_7) h_4\ , \tag{7.7}$$

$$k_4 = j_7 h_4\ , \tag{7.8}$$

$$k_8 = (2j_1 + 2j_2) h_1\ . \tag{7.9}$$

The parametric representation of $\mathfrak{M}^*(S)$ in this case has the seven parameters $(h_1, h_3, h_4, h_5) \in \bar{\mathbf{R}}_+^4$, $(j_1, j_7) \in \bar{\mathbf{R}}_+^2$ and $k_5 \in \bar{\mathbf{R}}_+$. There are seven parameters because $\mathfrak{M}^*(S)$ is seven-dimensional. The set of boundary steady states of the flow $\mathfrak{F}_1$ in this case is the set of all **X** and **k**, where $X_1 = h_1^{-1}$, $X_2 = 0$, $X_3 = h_3^{-1}$, $X_4 = h_4^{-1}$, $X_5 = h_5^{-1}$, $k_6 = k_7 = 0$, and the remaining k's are given by Eqs. (7.5)–(7.9), as the parameters take all values in their domains.

This result can be mapped using $\bar{\phi}$ to get the boundary steady states for the flow $\mathfrak{F}_2$. Let $\mathbf{X}_I = (X_1, X_2, X_3, X_4)^t$. The flow in the variables $\mathbf{X}_I$, C and k has corresponding steady states in the boundary where the components of $\mathbf{X}_I$ and k have the same expressions as previously, and C is given by Eq. (7.2), as the parameters take all values in their domains.

Each S gives a closed connected manifold $\mathfrak{M}^*(S)$ of steady states of the flow $\mathfrak{F}_2$. If a certain set S_1 of species are suppressed and then additional species are suppressed to yield S_2, it may happen that $\mathfrak{M}^*(S_2)$ is part of the boundary of $\mathfrak{M}^*(S_1)$. If so, the steady states of $\mathfrak{M}^*(S_2)$ would not need to be given explicitly as a line in the table of Fig. 5 because these steady states would already be specified by the line in the table for S_1. Thus it should be possible to delete rows from the output of ALLSS to obtain a more concise description of all the steady states.

There is a simple way to prove that certain sets $\mathfrak{M}^*(S_2)$ are not entirely contained in the boundary of a set $\mathfrak{M}^*(S_1)$. The method uses the fact that the suppression of each additional species must reduce the dimension of $\mathfrak{M}^*(S_2)$ by at least one compared with $\mathfrak{M}^*(S_1)$. For example, since $\dim \mathfrak{M} = 9$, when m species are suppressed the boundary of $\bar{\mathfrak{M}}$ cannot have a dimension greater than $9 - m$. Inspection of the table in Fig. 5 shows that in this example there are 20 manifolds $\mathfrak{M}^*(S)$ whose dimensions are too high to lie in the boundary of $\bar{\mathfrak{M}}$. The remaining manifolds are not necessarily in the boundary of $\bar{\mathfrak{M}}$, but they may be. A necessary and sufficient test has not yet been developed. This network appears to have a rich set of boundary steady states; however the minimum number of manifolds $\mathfrak{M}^*(S)$ which are needed for a full description of the steady states is not known.

VIII. DISCUSSION

A complete parametric description of all steady states on the closed domain of the general stoichiometric dynamical system has been found. It is surprising that such a general result can be obtained because the steady states are often the solutions of a system of simultaneous algebraic equations, and it is well known that these equations have closed form solutions only in a few simple cases.

The resolution of this paradox is that the difficult problem is to find $\mathbf{X}_I$ for a given C and k. We have not solved this problem. Instead, we have found a parametrized form of the manifold of all $\mathbf{X}_I$, C, and k which are steady states. Even when the parametric form of the manifold is known, it is still difficult to investigate the point(s) of the manifold having a particular C and k. Fortunately, this difficult problem need not be solved in order to answer many interesting and useful questions about stoichiometric networks.

One striking observation is the great complexity of orthant boundary steady states which seem to occur in ordinary networks. These steady states should play an important role in chemical and biological evolution. The absence of a particular form of DNA means that the state of the chemical network describing all life lies in the orthant boundary where this form of DNA is suppressed. If a mutation produces the molecule for the first time, an "explosion" of this DNA often results. The boundary steady state would then have been unstable with respect to perturbations out of the boundary. The techniques in this paper are expected to be directly applicable to the analysis of networks capable of evolution. A stability theory for perturbations out of the boundary will appear in a later paper.

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