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On The Geometry of Equilibrium Solutions of Kinetic Systems Obeying the Mass Action Law ⋆

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Abstract: In this contribution the problem relating dynamic behavior and parameter values for weakly reversible chemical reaction networks (CRNs) that obey the mass action law is revisited. The approach is founded on previous methods and results discussed in [15, 16] for weakly reversible CRNs. Two new research directions are however undertaken in this study, one of them exploits an alternative factorization of the Kernel of the Kirchhoff matrix A_k which in a natural way links complex balance with zero deficiency. The other one intends to use the convex structure of the so-called family of solutions described in [15] on the space of reaction channels.

1. INTRODUCTION

Deterministic reaction kinetic models obeying the mass action law (MAL) form an important subclass within nonnegative systems, since they have good dynamical description properties in spite of their simple algebraic structure. Such models are capable of producing all the important qualitative features (such as stable and unstable equilibria, multiple equilibria, bifurcation phenomena, oscillatory and even chaotic behaviour) that support the better understanding of complex processes in artificial or natural systems [9, 3].

Chemical reaction network theory (CRNT) is originated in the 1970's by the pioneering works of Horn, Jackson and Feinberg [14, 11]. The deficiency of a CRN is a nonnegative integer number that only depends on the stoichiometry and the graph structure of a CRN but not on the reaction rate coefficients [11]. Also in [11], the stability of CRNs with zero deficiency is proved with a given Lyapunov function that is independent of the system parameters and therefore suggests a robust stability property with respect to parameter changes.

Weakly reversible networks (characterized by the property that each node in their reaction graphs lies on at least one directed cycle) form a particularly important class of reaction networks because strong properties are known about their dynamics. A still unpublished but significant result claims the existence of at least one positive equilibrium point within each stoichiometric compatibility class for weakly reversible CRNs [8]. An important subclass within weakly reversible networks is the set of CRNs with complex balanced equilibrium points. The geometrical structure of complex balanced equilibrium points is explored in [7] and is shown to be a toric variety. Here we have to mention three important conjectures that emphasize the significance of weakly reversible and complex balanced CRNs. The *Global Attractor Conjecture* says that for any complex balanced CRN and any initial condition $x(0) \in \mathbb{R}^n_+$, the equilibrium point x^* is a global attractor in the corresponding positive stoichiometric compatibility class. According to the *Persistency Conjecture*, the dynamics of any weakly reversible mass-action system is persistent. The *Boundedness Conjecture* says that any weakly reversible reaction network with mass-action kinetics has bounded trajectories. Recently, both the Global Attractor Conjecture and the Boundedness conjecture have been successfully proved for one linkage class reaction networks by the same author [2, 1].

The relationship between the chemical network structure and the possibility of multiple equilibria is investigated in [5] from and algebraic and in [6] from a structural point of view. The possibility of multistationarity of CRNs with mass action dynamics was investigated in [12] through subnetwork analysis and recently in [4] by setting up an appropriate set of linear inequalities

The characterization of equilibrium points of weakly reversible CRNs using the so-called 'family of solutions' was introduced in [15] and with additonal geometric constraints it was effectively used for establishing conditions on the possibility of having multiple equilibrium points within a stoichiometric compatibility class [16]. The purpose of this paper is to extend the results published in [15, 16] by presenting an improved parametrization of the family of solutions. Using the developed description of CRN structure and dynamics, we relate known results in CRNT with it, such as the structure and the local stability of complex balanced equilibrium points.

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2. FORMAL DESCRIPTION OF REACTION NETWORKS

Let m be the number of molecular species participating on a given set of r irreversible chemical reaction steps and $\mathbf{c} \in \mathbb{R}^m$ the corresponding vector of species concentrations (defined as number of molecules, e.g. mole numbers per unit of volume). Each reaction step transforms a set of chemical species (reactants) into another (products). In CRNT, the sets of chemical species participating on reaction steps are called *complexes*. Complexes and reaction steps conform a reaction network, accepting a graph description where the former correspond with the nodes and the latter with the (directed) edges of the network.

Let $\mathcal{C} = \{\mathcal{C}_1, \ldots, \mathcal{C}_n\}$ be the set of complexes present in a given reaction network. In order to construct the graph, we follow the description in [15], and associate to each complex $\mathcal{C}_i$ a set $\mathcal{I}_i$ of integer elements with ordinality in n, and a pair of vectors $\{\boldsymbol{y}_i, \boldsymbol{\varepsilon}_i\}$. The set $\mathcal{I}_i$ collects those complexes reached from $\mathcal{C}_i$. Vector $\boldsymbol{y}_i \in \mathbb{R}^m$ has as entries the (positive) stoichiometric coefficients of the molecular species that participate in complex i. Finally, vector $\boldsymbol{\varepsilon}_i \in \mathbb{N}^n$ denotes the ith standard unit vector in the Euclidean space (where the ith element is 1, while all the other elements are zero).

The reaction rates R_{ij} at which any complex i transforms into j are assumed to obey the mass action law so that:

$$R_{ij} = k_{ij}\psi_i(\mathbf{c}), \tag{1}$$

with $k_{ij} > 0$ being the reaction rate constants and $\psi_i(c) : \mathbb{R}^m \to \mathbb{R}$ functions of the form:

$$\psi_i(\mathbf{c}) = \prod_{j=1}^{m} c_j^{y_{ji}} \equiv \mathbf{c}^{\boldsymbol{y}_i} \tag{2}$$

Whenever $\mathbf{c}$ is a strictly positive vector (meaning all components strictly positive), the following alternative representation may be more convenient:

$$\ln \psi_i(c) = y_i^{\mathrm{T}} \ln c \tag{3}$$

where the natural logarithm $\ln(\cdot)$ operates on any vector element-wise. The stoichiometric vectors y_i associated to the complexes of the network will be collected in the so-called *molecularity matrix* $Y \in \mathbb{R}^{m\times n}$.

2.1 Graph structure of reaction networks

The graph for a chemical reaction network is built by linking complexes $\mathcal{C}_i \to \mathcal{C}_j$ for every i and $j \in \mathcal{I}_i$. The resulting graph structure is composed of a number ℓ of "isolated" sub-graphs known in CRNT as *linkage classes* (they are also called connected components).

For each linkage class $\lambda = 1, ..., \ell$, we define the set $\mathcal{L}_\lambda$ as the one which contains as elements the indices of the complexes that belong to that linkage class [1].

For each λ we also select a complex (we refer to as *the reference*) j_λ and define a n-dimensional vector $\boldsymbol{\omega}_\lambda$ associated to the linkage class as follows: [2]

$$\omega_{\lambda i} = \begin{cases} 1 & \text{if } \ i \in \mathcal{L}_\lambda \\ 0 & \text{otherwise} \end{cases} \tag{4}$$

Vectors $\boldsymbol{\omega}_\lambda$ $(\lambda : 1, ..., \ell)$ are orthogonal to each other since by construction, sets $\mathcal{L}_\lambda$ for $\lambda = 1, ..., \ell$ are disjoint.

Complexes within a linkage class are connected by sequences of irreversible reaction steps defining *directed paths*. Two complexes are strongly linked if they can be reached from each other by directed paths (trivially every complex is strongly linked to itself). The largest set of strongly linked complexes defines a *strong terminal linkage class* if no other complex can be reached from its elements (such set in graph theory it is known as strongly connected component or strong component). A linkage class $\mathcal{L}_\lambda$ is said to be *weakly reversible* if all its complexes are strongly linked. Weakly reversible networks are those composed by weakly reversible linkage classes.

2.2 The dynamics of reaction networks

The net change in time of species concentrations follows the set of ordinary differential equations [3] [11]:

$$\dot{\mathbf{c}} = Y \cdot A_k(\boldsymbol{\psi}) \equiv Y \cdot \sum_{\lambda=1}^{\ell} A_k^\lambda(\boldsymbol{\psi}), \tag{5}$$

where $\boldsymbol{\psi}(\mathbf{c}) \in \mathbb{R}^n$ is a vector containing as entries the scalar function monomials (2) and $A_k^\lambda(\boldsymbol{\psi})$ a linear operator that accepts the following factorizations:

$$A_k^\lambda(\boldsymbol{\psi}) = \sum_{i\in\mathcal{L}_\lambda} \psi_i(\mathbf{c}) \sum_{j\in\mathcal{I}_i} k_{ij} \cdot (\boldsymbol{\varepsilon}_j - \boldsymbol{\varepsilon}_i). \tag{6a}$$

$$A_k^\lambda(\boldsymbol{\psi}) = \sum_{i\in\mathcal{L}_\lambda\setminus j_\lambda} \phi_i(\boldsymbol{\psi})(\boldsymbol{\varepsilon}_i - \boldsymbol{\varepsilon}_{j_\lambda}), \tag{6b}$$

ϕ_i in (6b) correspond with the net reaction rate flux around complex i, so that $\phi_i(\boldsymbol{\psi}) = \sum_{j\in\mathcal{L}_\lambda\setminus i}(R_{ji} - R_{ij})$. From orthogonality of vectors $\boldsymbol{\varepsilon}_i$, each *net kinetic flux* ϕ_i can also be expressed as:

$$\phi_i(\boldsymbol{\psi}) = \boldsymbol{\varepsilon}_i^{\mathrm{T}} A_k^\lambda(\boldsymbol{\psi}) \ \text{ for } \quad \text{every } i \in \mathcal{L}_\lambda \setminus j_\lambda \tag{7}$$

$$\phi_{j_\lambda} \equiv \boldsymbol{\varepsilon}_{j_\lambda}^{\mathrm{T}} A_k^\lambda(\boldsymbol{\psi}) = -\sum_{i\in\mathcal{L}_\lambda\setminus j_\lambda} \phi_i. \tag{8}$$

Network fluxes can be written in vector form as:

$$\boldsymbol{\phi}(\boldsymbol{\psi}) = M(k)\boldsymbol{\psi} \tag{9}$$

where $M(k)$ is the $n \times n$ matrix with rows $\boldsymbol{m}_i(k) \in \mathbb{R}^n$, so that $\phi_i(\boldsymbol{\psi}) = \boldsymbol{m}_i^T(k)\boldsymbol{\psi}$. For every $i \in \mathcal{L}_\lambda$ the rows have the following structure:

$$m_{ij} = \begin{cases} k_{ji} \geq 0 & \text{for } \ j \in \mathcal{L}_\lambda \setminus i \\ -\sum_{j\in\mathcal{L}_\lambda} k_{ij} > 0 & \text{for } \ j = i \\ 0 & \text{for } \ j \notin \mathcal{L}_\lambda \end{cases} \tag{10}$$

Note that since the closure relation (8) is valid for any $\boldsymbol{\psi}$, vectors $\boldsymbol{m}_i$ must satisfy that:

$$\sum_{i\in\mathcal{L}_\lambda} \boldsymbol{m}_i(k) = 0 \ \text{ for } \ \lambda = 1, ..., \ell \tag{11}$$

[1] To be precise, the set $\mathcal{L}_\lambda$ will be that containing as elements $\mathcal{L}_\lambda = \{i_1, i_2, ..., i_{N_\lambda}\}$, with $N_\lambda = \mathcal{N}(\mathcal{L}_\lambda)$, being i_j the cardinality associated to complex $\mathcal{C}_{i_j}$, and $\mathcal{N}(\cdot)$ the operator which indicates the number of elements in the set.

[2] Vector $\boldsymbol{\omega}_\lambda$ is referred in classical CRNT as the *characteristic function* of linkage class λ.

[3] Such description entails a number of chemical reactions taking place on a well mixed closed domain or vessel at constant temperature.

2.3 Kernel and Image of the operator $A_k(\psi)$

The image of $A_k(\boldsymbol{\psi})$ lies within the subspace:

$$\Delta_\lambda = \text{span}\{\boldsymbol{\varepsilon}_i - \boldsymbol{\varepsilon}_{j_\lambda} \mid i \in \mathcal{L}_\lambda \setminus j_\lambda\}, \text{ and } \Delta = \bigcup_{\lambda=1}^{\ell} \Delta_\lambda \tag{12}$$

This can be concluded by inspection of (6). Since vectors in Δ_λ are linearly independent, they form a basis for the subspace, being its dimension $N_\lambda - 1$. Hence, $dim(\Delta) = \ell \cdot (N_\lambda - 1) = n - \ell$.

Because the elements of the set Δ are linearly independent, the null space of $A_k(\boldsymbol{\psi})$ requires $\boldsymbol{\phi} = 0$ and therefore coincides with the null space associated to the matrix $M(k)$. The zero flux condition on each complex is known as *complex balance* [13].

The dimension of the null space of $M(k)$ equals the number of linkage classes. Each element of its basis $\boldsymbol{\mu}_j(k)$ is a vector with nonnegative elements, positive if the complexes are in a terminal linkage class and zero otherwise (Proposition 4.1 in [11]).

As a direct consequence, all elements are positive if the linkage class is weakly reversible. The dimension of the null space being ℓ is a consequence of (11) and the structure of vectors (10) extended to every linkage class. This in turn is equivalent to assert that $M(k)$ is a column conservation matrix.

In addition, each vector $\boldsymbol{\varepsilon}_i - \boldsymbol{\varepsilon}_{j_\lambda}$ can be expressed in terms of $N_\lambda - 1$ linearly independent column vectors of $M(k)$ with column numbers in $\mathcal{L}_\lambda$. Let $\boldsymbol{\varphi}_i$ be a vector satisfying that:

$$\boldsymbol{\varepsilon}_i - \boldsymbol{\varepsilon}_{j_\lambda} = M(k)\boldsymbol{\varphi}_i$$

Without loss of generality it can be set up so that $\boldsymbol{\varepsilon}_{j_\lambda}^T \boldsymbol{\varphi}_i = 0$ for every $i \in \mathcal{L}_\lambda$ and $\lambda = 1, ..., \ell$, namely having zero values at the location of the references j_λ.

In summary, vectors $\boldsymbol{\mu}_j(k)$ and $\boldsymbol{\varphi}_i(k)$ are solutions of the following set of equations:

$$\begin{array}{ll} M(k)\boldsymbol{\mu}_j = 0 & \text{for } j \in \mathcal{R} \\ M(k)\boldsymbol{\varphi}_i = \boldsymbol{\varepsilon}_i - \boldsymbol{\varepsilon}_{j_\lambda} & \text{for } i \in \mathcal{L}_\lambda \setminus j_\lambda \text{ and } \lambda = 1, ..., \ell \end{array} \tag{13}$$

where the set $\mathcal{R}$ is that which collects the indexes of the reference complexes j_λ (one per linkage class).

2.4 The stoichiometric subspace and reaction simplex

The so-called stoichiometric subspace Σ is defined as that spanned by the union over all linkage classes λ of the vector sets:

$$\Sigma_\lambda = \text{span}\{\boldsymbol{y}_i - \boldsymbol{y}_{j_\lambda} \mid i \in \mathcal{L}_\lambda \setminus j_\lambda\} \text{ and } \Sigma = \bigcup_{\lambda=1}^{\ell} \Sigma_\lambda \tag{14}$$

Alternatively, by denoting each vector in Σ as $\Delta y_i = \boldsymbol{y}_i - \boldsymbol{y}_{j_\lambda}$, the stoichiometric subspace can be re-defined as:

$$\Sigma = \text{span}\{\Delta \boldsymbol{y}_i \mid i \in \mathcal{L}_R \equiv \mathcal{L} \setminus \mathcal{R}\} \text{ with } \mathcal{L} = \cup_\lambda \mathcal{L}_\lambda \tag{15}$$

Note that the number of elements in set (15) coincides with $n - \ell$, the dimension of Δ. Thus if $s = \dim(\Sigma)$, the number of dependent vectors in Σ will be:

$$\delta = n - \ell - s \tag{16}$$

Vectors in the set Σ are related by δ linear combinations:

$$\sum_{i \in \mathcal{L}_R} \gamma_{ik} \Delta \boldsymbol{y}_i = 0 \qquad \text{for all} \qquad k = 1, ..., \delta \tag{17}$$

where parameters γ_{ik} are the entries of vectors $\boldsymbol{\gamma_k}$ which conform a basis for the null space of the stoichiometric subspace.

In the sequel we will be particularly interested in motions of system (5) restricted to the convex region resulting from the intersection of the positive orthant in the concentration space and a linear variety associated to the stoichiometric subspace Σ (also known in CRNT as *compatibility class*). Such region, known either as *reaction simplex* or *reaction polyhedron*, is formally defined with respect to a reference concentration vector $\mathbf{c}_0$ as:

$$\Omega(\mathbf{c}_0) = \{\mathbf{c} \in \mathbb{R}^m | \mathbf{c} \geq 0, B^{\mathrm{T}}(\mathbf{c} - \mathbf{c}_0) = 0\} \tag{18}$$

where $B \in \mathbb{R}^{(m \times m-s)}$ is a full rank matrix that spans column-wise the orthogonal complement $\Sigma^\perp$, i.e. $B \equiv \Sigma^\perp$.

3. THE STRUCTURE OF EQUILIBRIUM SOLUTIONS IN CHEMICAL REACTION NETWORKS

3.1 The family of solutions

Equilibrium solutions can be expressed in terms of vectors $\boldsymbol{\mu}_j(k)$ and $\boldsymbol{\varphi}_i(k)$ defined in (13) as follows:

$$\boldsymbol{\psi}(\psi_j, \phi_i) = \sum_{j \in \mathcal{R}} \psi_j \boldsymbol{\mu}_j + \sum_{i \in \mathcal{L}_\mathcal{R}} \phi_i \boldsymbol{\varphi}_i \tag{19}$$

what takes us to the following result which suggest a general structure for the equilibrium solutions of (5).

Lemma 1
Every feasible equilibrium solution of (5) can be written in the form:

$$\boldsymbol{F}(\psi_j; \alpha_k) = \sum_{j \in \mathcal{R}} \psi_j \boldsymbol{\mu}_j + \sum_{k=1}^{\delta} \alpha_k \sum_{i \in \mathcal{L}_\mathcal{R}} \gamma_{ik} \boldsymbol{\varphi}_i \tag{20}$$

where $\boldsymbol{\mu}_j$ and $\boldsymbol{\varphi}_k$ are solutions of (13), γ_{ik} are parameters that solve (17) and α_k for $k = 1, \ldots, \delta$ are arbitrary parameters.

Proof: That for any $\alpha_k \in \mathbb{R}$ with $k = 1, \ldots, \delta$, relation (20) is an equilibrium solution can be shown by substituting the expression into equation (5), and making use of (13) so that:

$$A_k(\boldsymbol{F}) = \sum_{k=1}^{\delta} \alpha_k \sum_{\lambda=1}^{\ell} \sum_{i \in \mathcal{L}_\lambda \setminus j_\lambda} \gamma_{ik} \left(\boldsymbol{\varepsilon}_i - \boldsymbol{\varepsilon}_{j_\lambda}\right) \tag{21}$$

and

$$Y \cdot A_k(\boldsymbol{F}) = \sum_{k=1}^{\delta} \alpha_k \sum_{i \in \mathcal{L}_R} \gamma_{ik} \Delta \boldsymbol{y}_i \tag{22}$$

where according to (17), the term $Y \cdot A_k(\boldsymbol{F}) = 0$. To prove that every equilibrium solution can be written in the form (20), we make use of (19), (13) and (17) to recover (20) with $\alpha_k \equiv \phi_k$ for $k = 1, ..., \delta$. □

From now on we will refer to equation (20) as *the family of equilibrium solutions*. Among all possible elements satisfying (20) we will concentrate on those being strictly positive. To that purpose we will define the set:

$$\mathcal{F}(\boldsymbol{\alpha}) = \{\boldsymbol{F} > 0 \mid \psi_j > 0;\ \alpha_k \in \mathbb{R} \text{ for } j \in \mathcal{R}, k = 1, \ldots, \delta\} \tag{23}$$

Example Let us consider the reaction network shown in Fig. 1. The CRN structure can be described by the

following connection rules: $\mathcal{I}_1 = \{3\}$, $\mathcal{I}_2 = \{5\}$, $\mathcal{I}_3 = \{1\}$, $\mathcal{I}_4 = \{5\}$, $\mathcal{I}_5 = \{2, 4\}$ and a molecularity matrix:

$$Y = \begin{pmatrix} 1 & 2 & 1 & 2 & 2 \\ 0 & 1 & 1 & 1 & 1 \\ 0 & 0 & 1 & 3 & 2 \end{pmatrix}$$

For this case sets $\mathcal{L}_\lambda$ are:

$\mathcal{L}_1 = \{1, 3\}$, $\mathcal{L}_2 = \{2, 5, 4\}$.

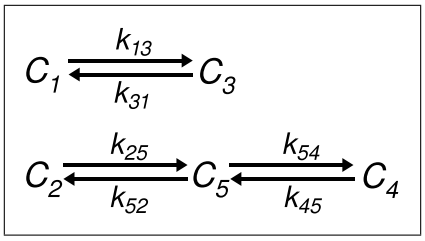

Fig. 1. Reaction network in Example 1. Complexes are denoted by $C_1, \ldots, C_5$

We choose complexes 3 and 4 as references so that $\mathcal{R} = \{3, 4\}$, and the set $\mathcal{L}_R$ defined in (15) becomes $\mathcal{L}_R = \{1, 2, 5\}$. The stoichiometric subspace is that spanned by the following column vectors:

$$\Sigma = \begin{pmatrix} 0 & 0 & 0 \\ -1 & 0 & 0 \\ -1 & -3 & -1 \end{pmatrix} \tag{24}$$

As $s = 2$, $\delta = 1$ and $\boldsymbol{\gamma_1} = [\,0\ 1\ -3\,]^T$. The non-zero off-diagonal elements of $M(k)$ are the following: $M(k)_{i,j} = k_{ji}$ for $(i, j) = (1, 3)$, $(2, 5)$, $(3, 1)$, $(4, 5)$, $(5, 2)$ and $(5, 4)$.

The expression for the set of equilibrium solutions (20) takes the form:

$$\boldsymbol{F}(\psi_3, \psi_4; \alpha_2) = \sum_{j\in\{3,4\}} \psi_j \boldsymbol{\mu}_j + \alpha_1 \sum_{i\in\{1,2,5\}} \gamma_{i1} \boldsymbol{\varphi}_i \tag{25}$$

In (25) the $\boldsymbol{\mu}$ vectors are:

$$\boldsymbol{\mu}_3 = [k_{31}/k_{13}\ 0\ 1\ 0\ 0]^T,$$
$$\boldsymbol{\mu}_4 = [0\ k_{52}k_{45}/(k_{25}k_{54})\ 0\ 1\ k_{45}/k_{54}]^T$$

Using (13), we obtain the following φ vectors:

$$\varphi_1 = \begin{pmatrix} \frac{-1}{k_{13}} & 0 & 0 & 0 & 0 \end{pmatrix}^T,$$
$$\varphi_2 = \begin{pmatrix} \frac{k_{31}}{k_{13}} & -\frac{k_{54}+k_{52}}{k_{25}k_{54}} & 1 & 0 & -\frac{1}{k_{54}} \end{pmatrix}^T,$$
$$\varphi_5 = \begin{pmatrix} \frac{k_{31}k_{52}}{k_{13}k_{25}k_{54}} & \frac{-k_{52}}{k_{25}k_{54}} & \frac{-k_{52}}{k_{25}k_{54}} & 0 & \frac{-1}{k_{54}} \end{pmatrix}^T.$$

For determining the γ parameters, we obtain the following set of equations:

$$\gamma_{11}\Delta\boldsymbol{y}_1 + \gamma_{21}\Delta\boldsymbol{y}_2 + \gamma_{51}\Delta\boldsymbol{y}_5 = 0, \tag{26}$$

where the $\Delta\boldsymbol{y}$-s are computed according to (15) as

$$\Delta\boldsymbol{y}_1 = \boldsymbol{y}_1 - \boldsymbol{y}_3 = (\,0\ -1\ -1\,)^T,$$
$$\Delta\boldsymbol{y}_2 = \boldsymbol{y}_2 - \boldsymbol{y}_4 = (\,0\ 0\ -3\,)^T,$$
$$\Delta\boldsymbol{y}_5 = \boldsymbol{y}_5 - \boldsymbol{y}_4 = (\,0\ 0\ -1\,)^T.$$

Finally, for the solution of (26), we obtain

$$\gamma_{11} = 0, \quad \gamma_{51} = -3\gamma_{21}.$$

3.2 Additional solvability constraints

Every feasible equilibrium solution must belong to the family of solutions (23), but in addition its elements must also satisfy (3), which in vectorial form becomes:

$$\ln \boldsymbol{\psi} = Y^{\mathrm{T}} \ln \mathbf{c} \tag{27}$$

We then say that a feasible equilibrium solution exists for a given set of parameters α_k, with $k = 1, ..., \delta$, if there is some $\mathbf{c} > 0$ solving the following set of equations:

$$\boldsymbol{F}(\psi_j(\mathbf{c}); \alpha_k) = \exp\left(Y^{\mathrm{T}} \ln \mathbf{c}\right) \tag{28}$$

A complex balanced equilibrium solution exists if there is some $\mathbf{c} > 0$ which satisfies (28) for $\alpha_k = 0$ with $k = 1, \cdots, \delta$. Substituting (20) into (28), re-ordering terms and using the logarithm we also get:

$$\ln \sum_{j\in\mathcal{R}} \boldsymbol{\mu}_j + \sum_{\lambda=1}^{\ell} \boldsymbol{\omega}_j \boldsymbol{y}_{j_\lambda}^T \ln \mathbf{c} \tag{29}$$
$$= \ln\left(\exp\left(Y^{\mathrm{T}} \ln \mathbf{c}\right) - \sum_{k=1}^{\delta} \alpha_k \sum_{i\in\mathcal{L}_\mathcal{R}} \gamma_{ik} \boldsymbol{\varphi}_i\right)$$

where the following equivalence has been used:

$$\ln\left(\sum_{j\in\mathcal{R}} \psi_j \boldsymbol{\mu}_j\right) = \ln \sum_{j\in\mathcal{R}} \boldsymbol{\mu}_j + \sum_{\lambda=1}^{\ell} \boldsymbol{\omega}_j \boldsymbol{y}_{j_\lambda}^T \ln \mathbf{c} \tag{30}$$

The representation of the family of feasible equilibrium solutions we just discussed is complementary to the one described by [15] based on the intersection of the so-called family and manifold of solutions, and employed to find conditions in the parameter space for the existence of complex dynamic behavior.

4. STABLE EQUILIBRIUM IN CHEMICAL REACTION NETWORKS: THE HORN SET

In this section we characterize a particular set of reaction rate parameters (reaction rate constants) that will lead to stable equilibria. The set will be referred to in the sequel as the "Horn set" after the name of one of the founders of CRNT who described the properties of complex balance solutions [13]. The discussion we provide here revisits his findings on a geometric context. The Horn set is defined as follows:

$$\mathcal{H}(K) = \left\{ k_{ij} > 0 \mid \ln \sum_{j\in\mathcal{R}} \boldsymbol{\mu}_j(k_{ij}) \in \mathrm{Im}\left(Y^T - \sum_{\lambda=1}^{\ell} \boldsymbol{\omega}_\lambda \boldsymbol{y}_{j_\lambda}^T\right) \right\} \tag{31}$$

In the following three propositions, we will show how the previously developed description can be used for revisiting and analyzing known results in CRNT.

Proposition 1

Chemical reaction networks with any set of parameters $K \in \mathcal{H}$ will only accept complex balance equilibrium solutions

Proof: That any set of parameters $K \in \mathcal{H}$ is compatible with a complex balance solution follows directly from the definition of the set. That is to say, for any element $K \in \mathcal{H}$ there exists some constant parameter vector γ - equivalently a parameter vector $\xi^* = \exp(\gamma)$- such that:

$$\ln \sum_{j\in\mathcal{R}} \boldsymbol{\mu}_j(k_{ij}) = \left(Y^T - \sum_{\lambda=1}^{\ell} \boldsymbol{\omega}_\lambda \boldsymbol{y}_{j_\lambda}^T\right) \ln \xi^* \tag{32}$$

Reordering terms in the previous expression we get that:

$$\ln \sum_{j\in\mathcal{R}} \boldsymbol{\mu}_j(k_{ij}) + \sum_{\lambda=1}^{\ell} \boldsymbol{\omega}_j \boldsymbol{y}_{j_\lambda}^T \ln \xi^* = Y^T \ln \xi^* \tag{33}$$

Using $\ln \psi_{j_\lambda}^* = \boldsymbol{y}_{j_\lambda}^T \ln \xi^*$, with $\lambda = 1, ..., \ell$, we obtain the equivalent relation:

$$\ln \sum_{j\in\mathcal{R}} \boldsymbol{\mu}_j(k_{ij})\psi_j = Y^T \ln \xi^* \tag{34}$$

which coincides with equation (28) -equivalently eqn (29)- with $\alpha_k = 0$ for all k, that is to say, a complex balance equilibrium solution.

To prove that solutions other than complex balance ones are not possible with the same reaction rate coefficients, we assume that one such solution exists for the same parameter set which produces (34). Let us first note that parameters must obey the following relations:

$$\varepsilon_i^T \sum_{j\in\mathcal{R}} \boldsymbol{\mu}_j = \exp\left[(\boldsymbol{y}_i - \boldsymbol{y}_{j_\lambda})^T \ln \xi^*\right] \quad \text{for} \quad i \in \mathcal{L}_\lambda, \tag{35}$$

and $\lambda = 1, ..., \ell$. Substituting this expression into (29) (with ξ replacing $\mathbf{c}$) we get (element-wise):

$$(\boldsymbol{y}_i - \boldsymbol{y}_{j_\lambda})^T \ln \xi^* + \boldsymbol{y}_{j_\lambda}^T \ln \xi = \tag{36}$$
$$\ln\left(\exp\left(\boldsymbol{y}_i^{\mathrm{T}} \ln \xi\right) - \sum_{k=1}^{\delta} \alpha_k \sum_{i\in\mathcal{L}_\mathcal{R}} \gamma_{jk}(\boldsymbol{\varphi}_j)_i\right)$$

Adding and subtracting $y_i^T \ln \xi$ on the left hand side, and re-ordering the terms we obtain the equivalent expressions:

$$x_i = a_i(\xi;\xi^*)x_i + \sum_{k=1}^{\delta} \alpha_k \sum_{j\in\mathcal{L}\setminus\mathcal{R}} \gamma_{jk}(\boldsymbol{\varphi}_j)_i \tag{37}$$
$$a_i(\xi;\xi^*) = \exp\left[(\boldsymbol{y}_i - \boldsymbol{y}_{j_\lambda})^T (\ln \xi^* - \ln \xi)\right]$$

with $x_i = \exp(\boldsymbol{y}_i^T \ln \xi)$. The existence of solutions other than complex balance relates directly to the solvability of (37), namely finding a ξ vector for parameters α_k others than zero satisfying the equation for every $i \in \mathcal{L}_\lambda$ and $\lambda = 1, ..., \ell$.

Equality holds only for $a(\xi;\xi^*) = 1$ and $\alpha_k = 0$ for every $k \in \mathcal{L}_\lambda \setminus j_\lambda$, i.e. complex balance solutions. □

Proposition 2

Complex balanced solutions are unique in the sense that there is only one complex balance solutions per compatibility class

Proof: To show this we make use of equation (29) and suppose there are two solutions $\ln \xi$ and $\ln \xi'$ associated to the same parameter set $K \in \mathcal{H}$, with ξ and ξ' in the same compatibility class. Then we have for every $i \in \mathcal{L}_\lambda$ and $\lambda = 1, ..., \ell$ that:

$$\varepsilon_i^T \ln \sum_{j\in\mathcal{R}} \boldsymbol{\mu}_j + \boldsymbol{y}_{j_\lambda}^T \ln \xi = \boldsymbol{y}_i^T \ln \xi \tag{38}$$

$$\varepsilon_i^T \ln \sum_{j\in\mathcal{R}} \boldsymbol{\mu}_j + \boldsymbol{y}_{j_\lambda}^T \ln \xi' = \boldsymbol{y}_i^T \ln \xi' \tag{39}$$

Subtracting one expression from the other we get:

$$(\boldsymbol{y}_i - \boldsymbol{y}_{j_\lambda})^T (\ln \xi - \ln \xi') = 0 \text{ for } i \in \mathcal{L}_\lambda \setminus j_\lambda \quad \text{and,} \ \lambda = 1, ..., \ell \tag{40}$$

In other words $(\ln \xi - \ln \xi') \in \Sigma^{\perp}$. Since by assumption, ξ and ξ' are in the same compatibility class we must also have that:

$$(\ln \xi - \ln \xi')^T (\xi - \xi') = 0 \tag{41}$$

But according to Lemma 2 with a convex function candidate:

$$V(\xi) = \sum_{i=1}^{m} \xi_i(\ln \xi_i - 1) \tag{42}$$

$[\ln(\xi) - \ln(\xi')]^T (\xi - \xi') \geq 0$ for any $\xi, \xi' \in \mathbb{X}$, with strict inequality. This implies that in order for equation (41) to hold $\xi \equiv \xi'$. In other words, there is just one equilibrium solution per compatibility class. □

Proposition 3

The positive equilibrium points of any complex balanced network are locally asymptotically stable within the corresponding stoichiometric compatibility class.

Proof: First of all, let us make use of (6a) to write the right hand side of (5) as a summation over λ of functions:

$$\mathbf{f}^\lambda(\xi) = \sum_{i\in\mathcal{L}_\lambda} \psi_i(\xi) \sum_{j\in\mathcal{I}_i} k_{ij} \cdot (\boldsymbol{y}_j - \boldsymbol{y}_i) \tag{43}$$

Select some positive reference $\xi^* > 0$ (its associated vector $\boldsymbol{\psi}^*$ is strictly positive) and re-write the previous expression in the equivalent form:

$$\mathbf{f}^\lambda(\xi) = \sum_{i\in\mathcal{L}_\lambda} \mathrm{e}^{\boldsymbol{y}_i^T \overline{\nu}} \sum_{j\in\mathcal{I}_i} \psi_i^* k_{ij} \cdot (\boldsymbol{y}_j - \boldsymbol{y}_i) \tag{44}$$

where $\overline{\nu} = \ln \xi - \ln \xi^*$. Consider also the following scalar function:

$$g^\lambda(\xi;\xi^*) \equiv \overline{\nu}^T \mathbf{f}^\lambda(\xi) = \sum_{i\in\mathcal{L}_\lambda} \mathrm{e}^{x_i} \sum_{j\in\mathcal{I}_i} \psi_i^* k_{ij} \cdot (x_j - x_i) \tag{45}$$

where $x_i = \boldsymbol{y}_i^T \overline{\nu}$. An upper bound for $g^\lambda(\xi;\xi^*)$ can be established from Lemma 2 in the Appendix with $V(x) = \mathrm{e}^x : \mathbb{R} \to \mathbb{R}$ so that:

$$\mathrm{e}^{x_i}(x_j - x_i) \leq \mathrm{e}^{x_j} - \mathrm{e}^{x_i} \tag{46}$$

For any scalars x_i and x_j. Strict convexity of $V(x)$ ensures that the equality holds only if $x_i = x_j$. We also have that

$$\mathrm{e}^{x_j} - \mathrm{e}^{x_i} = (\boldsymbol{\varepsilon}_j - \boldsymbol{\varepsilon}_i)^T \sum_{k=1}^{n} \boldsymbol{\varepsilon}_k \mathrm{e}^{x_k} \tag{47}$$

Combining (47) with (46) and substituting the resulting expression in (45) we get:

$$g^\lambda(\xi;\xi^*) \leq \left(\sum_{i=1}^{n} \mathrm{e}^{x_i} \boldsymbol{\varepsilon}_i^T\right) \left[\sum_{i\in\mathcal{L}_\lambda} \psi_i^* \sum_{j\in\mathcal{I}_i} k_{ij} \cdot (\boldsymbol{\varepsilon}_j - \boldsymbol{\varepsilon}_i)\right] \equiv \tag{48}$$
$$\left(\sum_{i=1}^{n} \mathrm{e}^{x_i} \boldsymbol{\varepsilon}_i^T\right) A_k^\lambda(\boldsymbol{\psi}^*)$$

Where we recall once again that the equality holds if and only if $x_i = x_j$ for every $i, j \in \mathcal{L}_\lambda$. The result then follows using B_1 in the proof of Lemma 2 (in the Appendix) as a Lyapunov function candidate, since we have:

$$\dot{B}_1 = \sum_{\lambda=1}^{\ell} g^\lambda(\xi;\xi^*) \leq \left(\sum_{i=1}^{n} \mathrm{e}^{x_i} \boldsymbol{\varepsilon}_i^T\right) \sum_{\lambda=1}^{\ell} A_k^\lambda(\boldsymbol{\psi}^*) = 0 \tag{49}$$

Therefore $B_1(\xi;\xi^*) \geq 0$ and $\dot{B}_1(\xi;\xi^*) \leq 0$ □

Then, an estimate on the stability neighborhood can be given by computing an appropriate level-set of B_1 around the selected equilibrium point in the positive orthant. We also remark that as the *Global Attractor Conjecture* has recently been proved for CRNs containing one linkage class

[1] (see also the Introduction), therefore computing the domain of attraction now can have significance only in the multiple linkage class case.

5. CONCLUSION

The geometry of equilibrium solutions in weakly reversible CRNs with mass action dynamics was examined in this paper. For this, the so-called 'family of solutions' structure introduced originally in [15] was used and extended. Using the reported improved parametrization, future work will be focused on making the rank conditions published in [16] computationally more treatable to explore parametric regions leading to multiple equilibrium points within a stoichiometric compatibility class.

Appendix A. A LEMMA FOR CONVEX FUNCTIONS

Lemma 2
Let $V(x) : \mathbb{X} \to \mathbb{R}$, with $\mathbb{X} \subseteq \mathbb{R}^n$ its domain, a convex function with continuous derivatives on $\mathbb{X}$, and $\nu(x) : \mathbb{X} \to \mathbb{R}^n$ be the gradient of $V(x)$. Then the following inequalities hold for every $x \in \mathbb{X}$:

(i) *$\nu^T(x_1)(x - x_1) \leq V(x) - V(x_1)$ for any $x_1 \in \mathbb{X}$.*
(ii) *$[\nu(x_2) - \nu(x_1)]^T (x_2 - x_1) \geq 0$ for any $x_1, x_2 \in \mathbb{X}$.*

inequalities are strict whenever $x \neq x_1$ or $x_1 \neq x_2$ in (i) and (ii), respectively.

Proof: In order to prove the first part choose any $x_1 \in \mathbb{X}$ and construct a function $B_1(x; x_1)$ as the difference between $V(x)$ and its supporting hyperplane at x_1. The supporting hyperplane is of the form:

$H(x; x_1) = V(x_1) + \nu^T(x_1)(x - x_1)$, and $B_1(x; x_1) = V(x) - H(x; x_1)$

By construction the function is strictly positive, i.e. it is positive for all $x \in \mathbb{X}$ other than x_1, so the result (i) follows in a straightforward manner since:

$B_1(x; x_1) \equiv V(x) - V(x_1) - \nu^T(x_1)(x - x_1) \geq 0$, so that $V(x) - V(x_1) \geq \nu^T(x_1)(x - x_1)$

To prove the second part, we note that $B_1(x; x_1)$ is itself a convex function since $\nabla_x B_1 = \nu(x) - \nu(x_1)$ so its hessian coincides with that of the convex function $V(x)$. By using the same supporting hyperplane argument we construct the following strictly positive definite function around some $x_2 \in \mathbb{X}$:

$B_2(x; x_1, x_2) \equiv B_1(x; x_1) - B_1(x_2; x_1) - [\nu(x_2) - \nu(x_1)]^T (x - x_2) \geq 0$

where the inequality holds for any $x \in \mathbb{X}$. In particular it holds for $x = x_1$, thus:

$B_1(x_2; x_1) + [\nu(x_2) - \nu(x_1)]^T (x_1 - x_2) \leq 0$

which implies that $B_1(x_2; x_1) \leq [\nu(x_2) - \nu(x_1)]^T (x_2 - x_1)$, and the assertion is in this way proved. □

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