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Univalent positive polynomial maps and the equilibrium state of chemical networks of reversible binding reactions

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Dedicated to the memory of Patrice C. Gnacadja, beloved father and inspiring mentor

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ABSTRACT

We consider a map $f = (f_1, \ldots, f_n) : \mathbb{R}^n_{\geqslant 0} \to \mathbb{R}^n_{\geqslant 0}$ given for $x = (x_1, \ldots, x_n)$ by

$$f_i(x) = x_i \psi_i(x_i) + \sum_{\alpha \in I} \alpha_i a_\alpha x^\alpha$$

where I is a finite subset of $\mathbb{Z}^n_{\geqslant 0}$, a_α is a constant in $\mathbb{R}_{\geqslant 0}$ for each $\alpha \in I$, and $\psi_1, \ldots, \psi_n$ are differentiable order-preserving functions $\mathbb{R}_{\geqslant 0} \to \mathbb{R}_{>0}$. We prove that f is a bijection. Surjectivity arises as a consequence of the Brouwer Fixed-Point Theorem. For injectivity, we show that the Jacobian matrix of f is everywhere a P-matrix and we then apply the Gale–Nikaidô Global Univalence Theorem. With $\psi_1 = \cdots = \psi_n = 1$, f is a positive polynomial map of interest in the study of chemical networks of reversible binding reactions. For these, we propose notions of elementary and composite species and of normal and complete networks. Many networks in pharmacology and other fields fall in these classes. We prove that their equilibrium states and detailed-balanced states coincide and are unique with respect to total concentrations of elementary species. The map f gives rise to an equation that has a unique solution which gives the equilibrium state. We also prove that concentrations always converge to the equilibrium state, thereby settling for complete networks the Global Attractor Conjecture, which affirms this property for the larger class of complex-balancing networks.

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1. Introduction

We discuss in this article the equilibrium states of certain chemical reaction networks of interest in biosciences. We use new results on global univalence that are of interest in their own right. These and related topics are presented in Sections 2–4. We begin by recording the notion of P-matrix and its use to obtain injectivity. We then prove global injectivity and bijectivity for certain classes of maps and we note relations with aspects of the theory of fixed points. Some of the maps considered appear naturally when studying the detailed-balanced states of the reaction networks we focus on. Interestingly, P-matrices and global univalence have recently found a number of applications in the study of chemical reaction networks; see for instance Soulé [33], Craciun and Feinberg [10], and Banaji, Donnell and Baigent [2]. Sections 5–8 cover the reaction network theoretic topics. We define notions of elementary and composite species. These attributes are relative to a given network and are consistent with chemical intuition. We then propose the class of normal networks and the larger class of complete networks, both within networks of reversible binding reactions. Many networks of interest in biosciences, e.g. pharmacology, fall in these classes. We apply results from the first part to prove the existence and uniqueness of the detailed-balanced state of normal networks with respect to total concentrations of elementary species. We also prove that detailed-balanced state and equilibrium state coincide. We then extend these results to complete networks. We proceed by induction on the new notion of height of a species; a complete network has a canonically associated normal network and normal networks are simply complete networks of height one. Finally we address the issue of convergence to equilibrium state. This property, which is conjectured in Horn [22] and in Craciun, Dickenstein, Shiu and Sturmfels [9] to hold for complex-balancing networks, is shown to hold for complete networks.

The following notations will be used throughout the paper. For $m, n \in \mathbb{Z}$, $[m..n] = \{k \in \mathbb{Z}\colon\ m \leqslant k \leqslant n\}$. If M is an $n \times n$ matrix and $K \subseteq [1..n]$, $M_{|K}$ is the principal submatrix of M supported on K. We denote $e_{n,i}$ the n-tuple having 1 in position i and 0 elsewhere. We denote 0_n and 1_n the n-tuples whose components all equal 0 and 1 respectively. For $x = (x_1, \ldots, x_n) \in \mathbb{R}^n$ and $\alpha = (\alpha_1, \ldots, \alpha_n) \in \mathbb{R}^n$, if ${x_i}^{\alpha_i}$ is defined for all $i \in [1..n]$, then $x^\alpha = {x_1}^{\alpha_1} \cdots {x_n}^{\alpha_n}$. The length of α is $|\alpha| = |\alpha_1| + \cdots + |\alpha_n|$, its ℓ^1-norm.

2. P-matrices

A real square matrix is said to be a P-matrix (resp. a P_0-matrix) if all its principal minors are positive (resp. non-negative). Berman and Plemmons [3] have several characterizations and properties of P-matrices and of P_0-matrices in Chapter 6, Sections 2 and 4 respectively. Also, any real positive-definite (resp. real positive-semidefinite) matrix is a P-matrix (resp. a P_0-matrix); see for instance Horn and Johnson [24, Section 7.1.5] or Bhatia [4, Section 1.1, Condition (ii)].

The following lemma will lead to another means of obtaining P- and P_0-matrices. It can be derived from the n-linearity of the determinant, and is found in Garcia and Zangwill [17, Lemma 1].

Lemma 2.1. *Let D and M be $n \times n$ matrices over some commutative ring with identity, with $D = \operatorname{diag}(d_1, \ldots, d_n)$. We have*

$$\begin{aligned}\det(D + M) &= \sum_{K \subseteq [1..n]} \left(\prod_{i \in [1..n] \setminus K} d_i \right) \det(M_{|K}) \\ &= d_1 \cdots d_n + \det M + \sum_{\emptyset \neq K \subsetneq [1..n]} \left(\prod_{i \in [1..n] \setminus K} d_i \right) \det(M_{|K}).\end{aligned}$$

Lemma 2.1 immediately implies the next result.