A Diffeomorphic Positive Polynomial Map and its Implications in Chemistry

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Outline

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Injectivity in Dimension One vs. in Dimension Two or Higher

Injectivity in Dimension One

Let D be an interval in $\mathbb{R}$ and $f : D \to \mathbb{R}$ be a differentiable map.

$$f'(x_0) \neq 0 \Rightarrow \text{Local injectivity at } x_0 \quad \text{(Inv Fct Thm)}$$

$$\forall\, x \in D, f'(x) \neq 0 \Rightarrow \text{Global injectivity on } D \quad \text{(Mean Val Thm)}$$

Injectivity in Dimension Two or Higher

Let D be an interval in $\mathbb{R}^n$ and $f : D \to \mathbb{R}^n$ be a differentiable map.

$$\det\left(f'(x_0)\right) \neq 0 \Rightarrow \text{Local injectivity at } x_0 \quad \text{(Inv Fct Thm)}$$

$$\forall\, x \in D, \det\left(f'(x)\right) \neq 0 \not\Rightarrow \text{Global injectivity on } D$$

Non-Injective Map in Dim Two with Positive Jacobian Determinant

$$f : \mathbb{R}^2 \to \mathbb{R}^2, x = (x_1, x_2) \mapsto f(x) = (\mathrm{e}^{x_1} \cos x_2, \mathrm{e}^{x_1} \sin x_2)$$

$$f'(x) = \begin{pmatrix} \mathrm{e}^{x_1} \cos x_2 & -\mathrm{e}^{x_1} \sin x_2 \\ \mathrm{e}^{x_1} \sin x_2 & \mathrm{e}^{x_1} \cos x_2 \end{pmatrix} \qquad \det\left(f'(x)\right) = \mathrm{e}^{2x_1} > 0$$

f is constant on $\{x_1\} \times (x_2 + 2\pi\mathbb{Z})$ for every $(x_1, x_2) \in \mathbb{R}^2$.

P-matrix - Definition and Examples

Definition

A real square matrix is a P-matrix (resp. a P_0-matrix) if all its principal minors are positive (resp. nonnegative).

Examples

- A real positive-definite (resp. positive-semidefinite) matrix is a P-matrix (resp. a P_0-matrix).
- Let D and M be real $n \times n$ matrices with $D = \mathrm{diag}(d_1, \ldots, d_n)$.
  - If $d_1, \ldots, d_n \geqslant 0$ and M is a P_0-matrix, then $D + M$ is P_0-matrix.
  - If $d_1, \ldots, d_n \geqslant 0$ and M is a P-matrix, or if $d_1, \ldots, d_n > 0$ and M is a P_0-matrix, then $D + M$ is P-matrix.

P-matrix - Geometric Characterization

Sign Reversal - Definition and Example

Let A be a real square matrix, let x be a real n-vector, and $y = Ax$. The matrix A reverses the sign of x if $x_i y_i \leqslant 0$ for all $i = 1, \ldots, n$.

$$A = \begin{pmatrix} 1 & 2 \\ 3 & 4 \end{pmatrix} \qquad u = \begin{pmatrix} -5 \\ 3 \end{pmatrix} \quad v = \begin{pmatrix} 2 \\ -1 \end{pmatrix} \quad w = \begin{pmatrix} -1 \\ 1 \end{pmatrix}$$

$$Au = \begin{pmatrix} 1 \\ -3 \end{pmatrix} \quad Av = \begin{pmatrix} 0 \\ 2 \end{pmatrix} \quad Aw = \begin{pmatrix} 1 \\ 1 \end{pmatrix}$$

Matrix A reverses the sign of vectors u and v but not of vector w.

Theorem Geometric Characterization of a P-matrix

A real square matrix is a P-matrix if and only if it does not reverse the sign of any nonzero vector.

P-Matrices and Global Univalence

Global Univalence Theorem of Gale and Nikaidô

Let D be a rectangle in $\mathbb{R}^n$ and let $f : D \to \mathbb{R}^n$ be a differentiable function. If for every $x \in D$, the Jacobian matrix $\mathrm{J}(f, x)$ of f at x is a P-matrix, then f is injective.

Gale, D. and H. Nikaidô
Math. Annalen 159, 81—93 (1965)

The Jacobian Matrix and Global Univalence of Mappings*

By

David Gale and Hukukane Nikaidô in Providence and Osaka

http://dx.doi.org/10.1007/BF01360282
(Theorem 4 and Remark 4.3)

Proof exploits features of the geometric characterization of P-matrices.

Terminology: Univalence vs. Injectivity

- "Univalent" = "(Globally) Injective" = "One-to-One".
- *Speculative thoughts*:

  It appears that mathematical economists were originally more concerned with global injectivity than mainstream mathematicians. They had to address questions of uniqueness of equilibrium in various economic models. They made major contributions to the field and probably set the terminology.
- The condition "all principal minors are positive" that defines P-matrices is known in economics as the Hawkins-Simon condition after David Hawkins and Herbert A. Simon. Simon received the 1978 Nobel Prize in Economics (not for P-matrices).

A Diffeomorphic Positive Polynomial Map

Theorem

Let I be a finite subset of $\mathbb{Z}^n_{\geqslant 0}$, let $(a_\alpha)_{\alpha \in I}$ be a family over $\mathbb{R}_{\geqslant 0}$, and let the function $f = (f_1, \ldots, f_n) : \mathbb{R}^n_{\geqslant 0} \to \mathbb{R}^n_{\geqslant 0}$ be given by

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

The function f is a C^∞-diffeomorphism.

Notation: $x^\alpha = (x_1, \ldots, x_n)^{(\alpha_1, \ldots, \alpha_n)} = {x_1}^{\alpha_1} \cdots {x_n}^{\alpha_n}$.

Proof of Injectivity

- $f_i(x) = x_i + \sum_{\alpha \in I} \alpha_i \, a_\alpha \, x^\alpha$.
- $\mathrm{J}(f, x) = \mathrm{Id}_n + M(x)$ with $M(x) \cdot \mathrm{diag}(x) = \sum_{\alpha \in I} a_\alpha \, x^\alpha \, \alpha^{\mathrm{T}} \alpha$.
- Matrix $\alpha^{\mathrm{T}} \alpha = (\alpha_i \alpha_j)_{1 \leqslant i, j \leqslant n}$ is positive-semidefinite.
- $M(x) \cdot \mathrm{diag}(x)$ is positive-semidefinite.
- $M(x) \cdot \mathrm{diag}(x)$ is a P_0-matrix.
- $M(x)$ is a P_0-matrix if $x_1, \ldots, x_n > 0$.
- $M(x)$ is a P_0-matrix if $x_1, \ldots, x_n \geqslant 0$.
- $\mathrm{J}(f, x)$ is a P-matrix.
- Theorem of Gale and Nikaidô: f is injective.

Proof of Local Diffeomorphism

- $f_i(x) = x_i + \sum_{\alpha \in I} \alpha_i \, a_\alpha \, x^\alpha$.
- f is defined and infinitely differentiable on $\mathbb{R}^n$.
- $\Omega := \left\{ x \in \mathbb{R}^n : \det \left(\mathrm{J}(f, x) \right) > 0 \right\}$.
- $\Omega \supset \mathbb{R}^n_{\geqslant 0}$.
- Ω is an open set.
- Inverse Function Theorem:
  f is a local C^∞-diffeomorphism throughout Ω.

Proof of Surjectivity

- $f_i(x) = x_i + \sum_{\alpha \in I} \alpha_i \, a_\alpha \, x^\alpha$.
- $F = (F_1, \ldots, F_n) : \mathbb{R}^n_{\geqslant 0} \times \mathbb{R}^n_{\geqslant 0} \to \mathbb{R}^n_{\geqslant 0}$
  $$F_i(b, x) = \frac{b_i}{1 + \sum_{\alpha \in I, \alpha_i \geqslant 1} \alpha_i \, a_\alpha \, x^{\alpha - e_{n,i}}} .$$
- $f^{-1}(b) = \mathrm{FixPt}(F(b, -))$.
- $F\left(b, \mathbb{R}^n_{\geqslant 0}\right) \subseteq [0_n, b]$.
- Brouwer Fixed-Point Theorem: $\mathrm{FixPt}(F(b, -)) \neq \varnothing$.

Outline

Algorithm for a Particular Case

Theorem

Let $A = (a_{ij})_{1 \leqslant i,j \leqslant n}$ with $a_{ij} \in \mathbb{R}_{\geqslant 0}$, and $b = (b_1, \dots, b_n) \in \mathbb{R}^n_{\geqslant 0}$. The equation

$$x_i + \sum_{j=1}^n a_{ij}\, x_i\, x_j \;=\; b_i \;, \qquad i = 1, \dots, n$$

has a unique solution $x = (x_1, \dots, x_n) \in \mathbb{R}^n_{\geqslant 0}$.

Let $F = (F_1, \dots, F_n) : \mathbb{R}^n_{\geqslant 0} \times \mathbb{R}^n_{\geqslant 0} \to \mathbb{R}^n_{\geqslant 0}$ with

$$F_i(b, x) \;=\; \frac{b_i}{1 + \sum_{j=1}^n a_{ij}\, x_j} \;.$$

Iterations of $F(b, -)$ from b produce a sequence that encloses and linearly converges to the solution.

Partial Proof with Diffeomorphic Polynomial Map

If the matrix A is symmetric, then the existence and uniqueness of the solution is a special case of the general diffeomorphism with

$$
\begin{aligned}
I &= \left\{\alpha = (\alpha_1, \ldots, \alpha_n) \in \mathbb{Z}^n_{\geqslant 0} : \|\alpha\|_{\ell^1} = \alpha_1 + \cdots + \alpha_n = 2\right\} \\
&= \left\{2e_{n,i} : 1 \leqslant i \leqslant n\right\} \cup \left\{e_{n,ij} : 1 \leqslant i < j \leqslant n\right\}
\end{aligned}
$$

and

$$
\begin{aligned}
a_{2e_{n,i}} &= a_{ii}/2 \\
a_{e_{n,ij}} &= a_{ij} \ .
\end{aligned}
$$

Complete Proof with Banach Contraction Theorem

Theorem

With respect to the Thompson metric, the map $F(b, -)$ is a contraction with Lipschitz constant $\leqslant k = \dfrac{\|Ab\|_\infty}{1 + \|Ab\|_\infty}$.

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DISCOVER SOMETHING GREAT

Fixed points of order-reversing maps in $\mathbb{R}^n_{>0}$ and chemical equilibrium

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(Theorem 5.4)

Algorithms for General Case

Wanted: Algorithms for general case with *a priori* assurance of convergence and computational efficiency and accuracy.

Project: Consider interval methods.

Outline

Two Networks of Actual Pharmacological Relevance

$$
\begin{array}{ccccc}
R & + & L & \rightleftharpoons & RL \\
+ & & + & & \\
A & + & T & \rightleftharpoons & AT \\
\downarrow\uparrow & & \downarrow\uparrow & & \\
RA & & LT & &
\end{array}
\qquad\qquad
\begin{array}{ccccc}
R & + & A & \rightleftharpoons & RA \\
+ & & & & + \\
B & & & & B \\
\downarrow\uparrow & & & & \downarrow\uparrow \\
RB & + & A & \rightleftharpoons & RAB
\end{array}
$$

The Problem

- Questions about equilibrium state:
  - Existence
  - Uniqueness, and with respect to what
  - Whether detailed-balanced
  - Asymptotic stability
  - Computation
  - Monotonicity with respect to particular species
  - etc.
- Observations:
  - Questions are addressed on a case-by-case basis.
  - Calculations are done with approximations that even some non-mathematicians bioscientists have questioned.
- Our effort: Devise a framework to encompass networks of interest and systematically address these questions.

Complete Networks – The Idea

Structure

- Reversible binding reactions:
  (Two or more species) $\rightleftharpoons$ *(One species)*.
- Notions of elementary species and composite species.

Composite	:	Target/source of a binding/dissociation reaction.
Elementary	:	Not composite.

- Notions of composition with respect to elementary species.
- Composition identifies species.
- Reactions preserve composition.

Kinetics

- Law of Mass Action.
- Rate constants yield "consistent" cooperativity factors.

Complete Networks – Realizing the Idea

Let I finite $\subset \mathbb{Z}^n_{\geqslant 0} \setminus \{\|\cdot\|_{\ell^1} \leqslant 1\}$ and let $(J_\alpha)_{\alpha \in I}$ be a family of finite, nonempty, pairwise disjoint subsets of $\mathbb{Z}^{[1..n] \sqcup I}_{\geqslant 0} \setminus \{\|\cdot\|_{\ell^1} \leqslant 1\}$.

Complete Network of Reversible Binding Reactions

- ***Elementary species :*** $X_1, \ldots, X_n$
- ***Composite species :*** $Y_\alpha\,,\ \alpha \in I \quad (Y_\alpha = (X_1)_{\alpha_1} \cdots (X_n)_{\alpha_n})$
- ***Reactions :*** $\sum_{i=1}^n \sigma_i X_i + \sum_{\beta \in I} \sigma_\beta Y_\beta \rightleftharpoons Y_\alpha\,,\ \alpha \in I\,,\ \sigma \in J_\alpha$

Kinetic :	Law of Mass Action
$k^+_{\alpha,\sigma}\,,\ k^-_{\alpha,\sigma}$:	Association, dissociation rate constants
$a_{\alpha,\sigma} = k^+_{\alpha,\sigma} \,/\, k^-_{\alpha,\sigma}$:	Equilibrium constants

- ***Conservation of composition :***
  $\alpha = (\sigma_1, \ldots, \sigma_n) + \sum_{\beta \in I} \sigma_\beta\, \beta\,,\ \forall\, \alpha \in I,\ \forall\, \sigma \in J_\alpha$
- ***Principle of detailed balance :*** There exists a family $(a_\alpha)_{\alpha \in I}$ over $\mathbb{R}_{>0}$ such that $a_\alpha = a_{\alpha,\sigma} \prod_{\beta \in I} (a_\beta)^{\sigma_\beta}\ ,\ \forall\, \alpha \in I,\ \forall\, \sigma \in J_\alpha$.

Examples Revisited

$$
\begin{array}{ccccc}
R & + & L & \rightleftharpoons & RL \\
+ & & + & & \\
A & + & T & \rightleftharpoons & AT \\
\downharpoonleft\upharpoonright & & \downharpoonleft\upharpoonright & & \\
RA & & LT & &
\end{array}
$$

$n = 4$

$$
I : \begin{array}{cc} (1,1,0,0) & (0,1,1,0) \\ (0,0,1,1) & (1,0,0,1) \end{array}
$$

Detailed-balance condition: Void.

$$
\begin{array}{ccccc}
R & + & A & \rightleftharpoons & RA \\
+ & & & & + \\
B & & & & B \\
\downharpoonleft\upharpoonright & & & & \downharpoonleft\upharpoonright \\
RB & + & A & \rightleftharpoons & RAB
\end{array}
$$

$n = 3$

$$
I : \quad (1,1,0) \ (1,0,1) \ (1,1,1)
$$

Detailed-balance condition:

$$
a_{(R+A\rightleftharpoons RA)}\, a_{(RA+B\rightleftharpoons RAB)} = a_{(R+B\rightleftharpoons RB)}\, a_{(RB+A\rightleftharpoons RAB)} \, .
$$

Total Concentrations of Elementary Species

Definition/Theorem

The total concentration of free and bound elementary species X_i is

$$[X_i] + \sum_{\alpha \in I} \alpha_i \, [Y_\alpha]$$

and is independent of time.

Notation: $[\cdot]$ = concentration.

Equil.: Existence - Uniqueness - Characterization - Stability

Theorem

Let $b = (b_1, \ldots, b_n) \in \mathbb{R}^n_{\geqslant 0}$.

- The complete network has a unique equilibrium state at which the total concentrations of elementary species $X_1, \ldots, X_n$ are $b_1, \ldots, b_n$. Let x_i and y_α denote the concentrations of X_i and Y_α at that state.
- The vector $x = (x_1, \ldots, x_n)$ is the unique solution in $\mathbb{R}^n_{\geqslant 0}$ of the equation $x_i + \sum_{\alpha \in I} \alpha_i \, a_\alpha \, x^\alpha \;=\; b_i \;,\; i = 1, \ldots, n\,.$
- $y_\alpha = a_\alpha \, x^\alpha \;,\; \alpha \in I\,.$
- The equilibrium state is detailed-balanced.
- If a concentrations trajectory originates at a state where the total concentrations of elementary species $X_1, \ldots, X_n$ are $b_1, \ldots, b_n$, then it converges to this equilibrium state.

Outline

Potential Future Work

- Enlarge the class of networks.
  - Species not necessarily determined by composition alone.
    Allow isomers.
  - Network not necessarily reversible.
    Allow weakly reversible, i.e. strongly connected.
  - Reactions not just binding and dissociation.
    Allow multiple species at both ends of reactions.
- Algorithms to solve the polynomial equation in all cases.
- Other uses for the diffeomorphic positive polynomial map.
  Applicable models in economics or other fields?