The multistationarity problem in systems with toric steady states

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Seminario de Álgebra, Geometría algebraica y Singularidades

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Introduction

Introductory example

Consider the following digraph, $\mathfrak{N}$:

$$x_1 x_2 \underset{k_2}{\overset{k_1}{\rightleftarrows}} x_3 \xrightarrow{k_3} x_2 x_4$$

- x_1, x_2, x_3, and x_4 time dependent functions, generally nonnegative.
- k_1, k_2, k_3 are real parameters, generally strictly positive.
- We describe the graph by two vectors $\mathbf{x} := (x_1, x_2, x_3, x_4)$, $\mathbf{k} := (k_1, k_2, k_3)$ and two matrices whose columns represent the exponent vectors of the "educts" and "products" of each arrow:

$$Y_e = \begin{pmatrix} 1 & 0 & 0 \\ 1 & 0 & 0 \\ 0 & 1 & 1 \\ 0 & 0 & 0 \end{pmatrix}, \quad Y_p = \begin{pmatrix} 0 & 1 & 0 \\ 0 & 1 & 1 \\ 1 & 0 & 0 \\ 0 & 0 & 1 \end{pmatrix}.$$

Mass-action dynamics

Definition

We say that the graph $\mathfrak{N}$ has a *mass-action dynamics* if the functions x_1, x_2, x_3, x_4 are described by the following ODE system:

$$\dot{\mathbf{x}}^T = (Y_p - Y_e)\mathrm{diag}(\mathbf{k}) \left(\mathbf{x}^T\right)^{Y_e}, \mathbf{x} \geq \mathbf{0},$$

Where $\left(\mathbf{x}^T\right)^{Y_e}$ is a column vector such that

$$\left(\left(\mathbf{x}^T\right)^{Y_e}\right)_j = \prod_{i=1}^{n} x_i^{(Y_e)_{ij}}.$$

In our example:

$$\begin{pmatrix} \dot{x}_1 \\ \dot{x}_2 \\ \dot{x}_3 \\ \dot{x}_4 \end{pmatrix} = \left(\begin{pmatrix} 0 & 1 & 0 \\ 0 & 1 & 1 \\ 1 & 0 & 0 \\ 0 & 0 & 1 \end{pmatrix} - \begin{pmatrix} 1 & 0 & 0 \\ 1 & 0 & 0 \\ 0 & 1 & 1 \\ 0 & 0 & 0 \end{pmatrix} \right) \begin{pmatrix} k_1 & 0 & 0 \\ 0 & k_2 & 0 \\ 0 & 0 & k_3 \end{pmatrix} \begin{pmatrix} x_1 x_2 \\ x_3 \\ x_3 \end{pmatrix}.$$

Some history

The syntagma "mass-action" originates from the work of Guldberg and Waage back in the XIX century, which culminated with the *Law of mass-action*. This law is a rough dynamical approximation to the way molecules interact and it states that

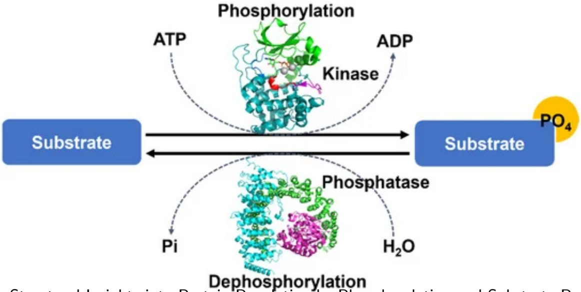
> *The rate at which a unit of a chemical species is consumed or produced by a chemical reaction is proportional to the product of the concentrations of the reactants.*

Example: the 2-site phosphorylation (to be continued)

The following network is the sequential distributive 2-site phosphorylation:

$$S+K \underset{k_2}{\overset{k_1}{\rightleftarrows}} SK \xrightarrow{k_3} S_p+K \underset{k_5}{\overset{k_4}{\rightleftarrows}} S_pK \xrightarrow{k_6} S_{pp}+K$$

$$S_{pp}+P \underset{k_8}{\overset{k_7}{\rightleftarrows}} S_{pp}P \xrightarrow{k_9} S_p+P \underset{k_{11}}{\overset{k_{10}}{\rightleftarrows}} S_pP \xrightarrow{k_{12}} S+P$$



[Source: Seok, S.-H. Structural Insights into Protein Regulation by Phosphorylation and Substrate Recognition of Protein Kinases/Phosphatases. Life 2021, 11, 957]

Steady states

Asymptotic behaviour: described by (semi)algebraic equations

$$\mathbf{0} = (Y_p - Y_e)\text{diag}(\mathbf{k})\left(\mathbf{x}^T\right)^{Y_e},$$

where now x_1, x_2, x_3, and x_4 are interpreted as real (positive) variables.

Hence, we can compute or classify the asymptotic behaviour with techniques from (computational) commutative algebra and (real) algebraic geometry:

Definition

- Each solution: *(positive/nonnegative) steady state*.
- The set of all solutions: *(positive/nonnegative) steady state variety*.
- The ideal generated by these polynomials: *steady state ideal*.

Problem:
Describe the stationary points

Problem 1

Find the **steady state variety**, that is, solve the polynomial system $\dot{x}_1 = \ldots = \dot{x}_n = 0$ for complex/real $x_1, \ldots, x_n$.

Problem 1' (informal)

Find the largest $\mathcal{K} \subset \mathbb{R}^r_{>0}$ such that, whenever $(k_1, \ldots, k_r) \in \mathcal{K}$, the polynomial system $\dot{x}_1 = \ldots = \dot{x}_n = 0$ has nonnegative solutions $x_1, \ldots, x_n$.

Problem 1"

Add to Problem 1/1' restrictions derived from conservation laws of the Polynomial ODE system.

One possible solution to Problem 1

Compute a (comprehensive) Gröbner basis for the ideal

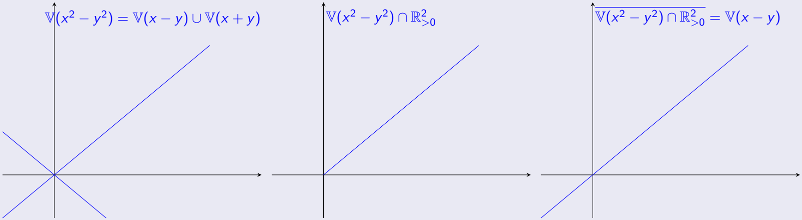
$$\langle P_1, \ldots, P_n \rangle \subset \mathbb{R}(k_1, \ldots, k_r)[x_1, \ldots, x_n].$$

Then, restrict solutions to $\mathbb{R}^n_{>0}$.

Example of Problem 1

$$\begin{aligned} \dot{x} &= x^2 - y^2 \\ \dot{y} &= -x^2 + y^2 \end{aligned}$$

Note: $I := \langle x^2 - y^2, -x^2 + y^2 \rangle = \langle x^2 - y^2 \rangle$
Then, a Gröbner basis of I is $\{x^2 - y^2\}$.



One possible solution to Problem 1'

Quantifier elimination for

$$\exists x_1, \ldots x_n \in \mathbb{R} \text{ such that}$$
$$P_1 = 0, \ldots, P_n = 0,\ k_1 > 0, \ldots, k_r > 0,\ x_1 \geq 0, \ldots, x_n \geq 0.$$

Example of Problem 1'

$$\begin{aligned} \dot{x} &= ax^2 + bx + c \\ \dot{y} &= -ax^2 - bx - c \end{aligned}$$

Then, the quantified statement

$$\begin{aligned} &\exists x, y \in \mathbb{R} \text{ such that :} \\ &ax^2 + bx + c = 0 \wedge -ax^2 - bx - c = 0 \\ &\wedge a > 0 \wedge b > 0 \wedge c > 0 \\ &\wedge x \geq 0 \wedge y \geq 0 \end{aligned}$$

is equivalent to quantifier free statement

$$a > 0 \wedge b > 0 \wedge c > 0 \wedge b^2 - 4ac \geq 0 \wedge ac \leq 0$$

which is equivalent to the easier quantifier free formula

$$a, b, c \in \emptyset.$$

One possible solution to Problem 1"

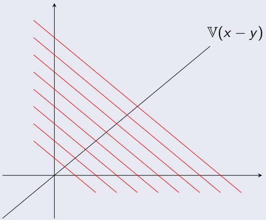
1.* Every conservation law $\phi(\mathbf{k}, \mathbf{x}) = c$ of the previous ODE system derives from a syzygy $\mathbf{g}$ of the vector $(P_1, \ldots, P_n)$, where $\nabla \times g = 0$ and $\nabla \phi = \mathbf{g}$.
2. For linear conservation laws just use linear algebra.

Example of Problem 1": Linear conservation law

$$\dot{x} = x - y$$
$$\dot{y} = -x + y$$

A Gröbner basis of I is $\{x - y\}$.

Conservation Law: $\dot{x} + \dot{y} = 0 \implies x + y = c$.



*Desoeuvres, Iosif, Lüders, Radulescu, Rahkooy, Seiß, Sturm. A Computational Approach to Polynomial Conservation Laws (2024). SIADS 23(1).

Example of Problem 1": Non-linear conservation law

Consider the following ODE system:

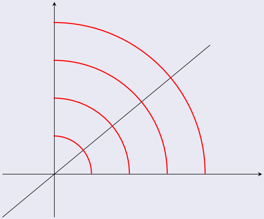
$$\begin{aligned} \dot{x} &= xy - y^2 \\ \dot{y} &= -x^2 + xy \end{aligned}$$

We have the relation $2x\dot{x} + 2y\dot{y} = 0$, obtained from the syzygy $2x(xy - y^2) + 2y(-x^2 + xy) = 0$. Since $\partial_y 2x = \partial_x 2y$, there is a ϕ such that $\nabla(x, y) = \phi$:

$$\phi = x^2 + y^2.$$

Hence, we get the conservation law

$$x^2 + y^2 = \text{constant}.$$



Problem:

Study the existence of multiple roots (multistationarity)

Problem 2

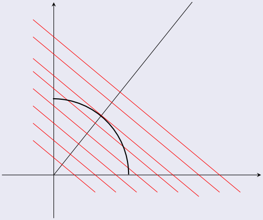
1. Classify all (or some) of the parameters $k_1, \ldots, k_r$ and the conserved quantities $c_1, \ldots, c_s$ with respect to the existence of multiple steady states.
2. Often, we are only interested in strictly positive solutions.

Example of Problem 2

Consider the following ODE system

$$\begin{aligned} \dot{x} &= (x^2 + y^2 - 2)(x - y) \\ \dot{y} &= -\dot{x} \end{aligned}$$

It has the conservation law $x + y = c$. If $c \in (\sqrt{2}, 2)$, there are three steady states. If $c \in [0, \sqrt{2}) \cup [2, \infty)$, there is only one steady state.



Relevant special case:
Dynamical systems with (positive) toric steady states

Dynamical systems with (positive) toric steady states

Consider a polynomial ODE system

$$\begin{aligned} \dot{x}_1 &= P_1(k_1, \ldots, k_r; x_1, \ldots, x_n), \\ &\vdots \\ \dot{x}_n &= P_n(k_1, \ldots, k_r; x_1, \ldots, x_n), \end{aligned}$$

where $k_1, \ldots, k_r \in \mathbb{R}_{>0}$ are parameters, $x_1 \geq 0$, ..., $x_n \geq 0$, and

$$P_1, \ldots, P_n \in \mathbb{R}(k_1, \ldots, k_r)[x_1, \ldots, x_n]$$

are polynomials in $x_1, \ldots, x_n$ and rational functions in $k_1, \ldots, k_r$.

Definition (informal, partly due to the semialgebraicity of $\mathcal{K}$)

The dynamical system defined above has:

1. toric steady states if the ideal $I := \langle P_1, \ldots, P_n \rangle$ is (generically) binomial;
2. positive toric steady states if the variety $\overline{\mathbb{V}(I) \cap \mathbb{R}^n_{>0}}$ is (generically) toric.

Example: Toric system

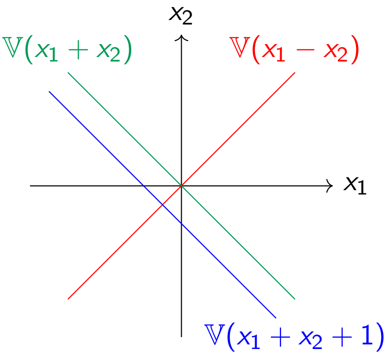
Dynamics:

$$\dot{x}_1 = x_1^3 + x_1^2 x_2 - x_1 x_2^2 - x_2^3 + x_1^2 - x_2^2$$
$$= (x_1 - x_2)(x_1 + x_2)(x_1 + x_2 + 1)$$
$$\dot{x}_2 = -\dot{x}_1$$

Positive steady states, V^+:
$\frac{x_1}{x_2} = 1$, $x_1, x_2 > 0$

Monomial parameterization of V^+:

$$\mathrm{im}\begin{pmatrix} \mathbb{R}_{>0} & \to & \mathbb{R}^2_{>0} \\ t & \mapsto & (t,t) \end{pmatrix}$$



Example: Non toric system

Dynamics:

$\dot{x}_1 = x_1^3 + x_1^2 x_2 - x_1 x_2^2 - x_2^3 + 2x_1^2 + 2x_1x_2 + x_1 + x_2 = (x_1 - x_2 + 1)(x_1 + x_2)(x_1 + x_2 + 1)$

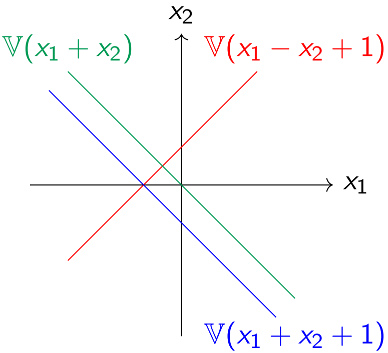
$\dot{x}_2 = -\dot{x}_1$

Positive steady states, V^+:

$x_1 = x_2 - 1$, $x_1, x_2 > 0$

NONMonomial parameterization of V^+:

$$\mathrm{im}\begin{pmatrix} [1,\infty) & \to & \mathbb{R}^2_{>0} \\ t & \mapsto & (t-1, t) \end{pmatrix}$$



Theorem (Corollary to Eisenbud, Sturmfels; 1996)

If I is a binomial ideal, then, for generic $\mathbf{k}$, $\mathbb{V}(I)$ is a finite union of cosets of the same multiplicative group.

Why binomials? (Mathematical answer)

1. Binomials are special but trinomials are not: every system of equations can be expressed as a systems of trinomials (by introducing new variables).
2. Yet, look at the following theorem (cf., Müller & Regensburger).

Theorem (Savageau, Voit; 1987)

Consider the following dynamical system

$$\dot{x}_i = f_i(x_1, \ldots, x_n), \quad x_i(0) = x_{i0}, \quad i \in [n],$$

where each f_i is a finite composition of elementary functions. Then, there is a smooth change of variables such that this system can be expressed as

$$\dot{y}_i = \alpha_i \prod_{j=1}^{m} y_j^{a_{ij}} - \beta_i \prod_{j=1}^{m} y_j^{b_{ij}}, \quad y_i \geq 0, \quad y_i(0) = y_{i0}, \quad i \in [m],$$

where $\alpha_i, \beta_i \in \mathbb{R}_{\geq 0}$, $a_{ij}, b_{ij} \in \mathbb{R}$ and there are $m - n$ relations among y_i.

MESSI biological systems (Millán, Dickenstein; 2016)

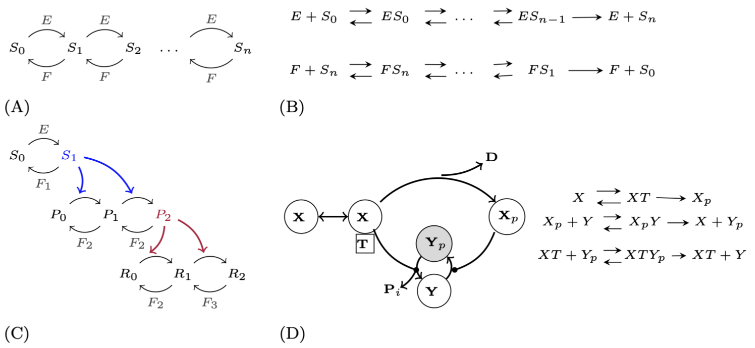


FIGURE 1. Examples of MESSI systems: Sequential n-site phosphorylation/dephosphorlation (A) distributive case [36, 51], (B) processive case [5, 31]; (C) Phosphorylation cascade; (D) Schematic diagram of an EnvZ-OmpR bacterial model [44].

(Source: Millán and Dickenstein, 2016.)

Experiment (Grigoriev, I., Rahkooy, Sturm, Weber; 2019)

For 129 models with fixed parameters, chosen from the database BioModels, the following classification arises:

Over $\mathbb{C}$

- For 22 of them, V^* is the coset of a multiplicative group[†].
- For 52 of them, $V^* = \emptyset$ and $\langle P \rangle$ has a binomial/monomial Gröbner basis.
- For 25 of them computations did not finish after 6 hours.

Over $\mathbb{R}$

- For 20 of them, V^* is the coset of a multiplicative group.
- For 53 of them, $V^* = \emptyset$.
- For 35 of them computations did not finish after 6 hours.

[†] Here, $V^* = \{x \in (\mathbb{K}^*)^n | P = 0\}$ and $\mathbb{K}^*$ is the multiplicative group of $\mathbb{K}$.

Dimension of the multistationarity problem

If n and r denote the number of variables and parameters, respectively, then, detecting multistationarity can be a $2n + r$ dimensional problem.

Lemma (Conradi, I., Kahle; 2018) (Informal)

In the toric case detecting multistationarity is an $n + q$ dimensional problem, where $q < n$ denotes the dimension of the corresponding torus.

Theorem (Conradi, I., Kahle; 2018) (Informal)

In the toric case multistationarity is a scale invariant in the space of linear conserved quantities.

Corollary (Informal)

In the toric case detecting multistationarity is an $n + q - 1$ dimensional problem. Moreover, restricting the values of the linear conserved quantities does not increase the dimension of this problem.

Monomial parameterizations of the positive steady states

Lemma (Conradi, I., Kahle; 2018)

If V^+ is toric, then, there is an *exponent matrix* $A \in \mathbb{Q}^{(n-p)\times n}$ of rank $n-p$ with $AM = 0$, a function $\psi : \mathcal{K}_\gamma^+ \to \mathbb{R}^n$, and an exponent $\eta \in \mathbb{Z}_{>0}$, such that ψ^η is a rational function and the following are equivalent:
a) $(k, x) \in V^+$,
b) $k \in \mathcal{K}_\gamma^+$ and there exist $\xi \in \mathbb{R}_{>0}^{n-p}$ such that $x = \psi(k) \star \xi^A$, where $\star$ denotes the coordinate-wise product.

Theorem (Conradi, I., Kahle; 2018)

Assume V^+ is toric with exponent matrix $A \in \mathbb{Q}^{(n-p)\times n}$, let $g_1, \dots, g_l \in \mathbb{R}[c]$, $\Box \in \{>, \geq\}^l$, and $\mathcal{F}(g(c) \Box 0)$ be any logical combination of the inequalities $g(c) \Box 0$. Then, there are $k \in \mathcal{K}_\gamma^+$ such that there is multistationarity in the region defined by $\mathcal{F}(g(c) \Box 0)$ if and only if there are $a \in \mathbb{R}_{>0}^n$ and $\xi \in \mathbb{R}_{>0}^{(n-p)} \setminus \{\mathbf{1}\}$ such that

$$Z(a\xi^A - a) = 0 \text{ and } \mathcal{F}(g(Za) \Box 0).$$

Example: the 2-site phosphorylation

Dynamics:

$$
\begin{aligned}
[\dot{S}] &= -k_1[S][K] + k_2[SK] + k_{12}[S_pP] \\
[\dot{K}] &= -k_1[S][K] + (k_2 + k_3)[SK] - k_4[K][S_p] + (k_5 + k_6)[S_pK] \\
[\dot{SK}] &= k_1[S][K] - (k_2 + k_3)[SK] \\
[\dot{S_p}] &= k_3[SK] - k_4[K][S_p] + k_5[S_pK] + k_9[S_{pp}P] - k_{10}[S_p][P] + k_{11}[S_pP] \\
[\dot{S_pK}] &= k_4[K][S_p] - (k_5 + k_6)[S_pK] \\
[\dot{S_{pp}}] &= k_6[S_pK] - k_7[S_{pp}][P] + k_8[S_{pp}P] \\
[\dot{P}] &= -k_7[S_{pp}][P] + (k_8 + k_9)[S_{pp}P] - k_{10}[S_p][P] + (k_{11} + k_{12})[S_pP] \\
[\dot{S_{pp}P}] &= k_7[S_{pp}][P] - (k_8 + k_9)[S_{pp}P] \\
[\dot{S_pP}] &= k_{10}[S_p][P] - (k_{11} + k_{12})[S_pP].
\end{aligned}
$$

Example: the 2-site phosphorylation

Conservation laws:

$$[K] + [SK] + [S_pK] = K_{\text{tot}},$$
$$[S_{pp}P] + [S_pP] + [P] = P_{\text{tot}},$$
$$[S] + [S_p] + [S_{pp}] + [SK] + [S_pK] + [S_{pp}P] + [S_pP] = S_{\text{tot}}.$$

The positive steady state variety V^+ admits a monomial parameterization:

$$[S] = \frac{(k_2 + k_3)k_4k_6(k_{11} + k_{12})k_{12}}{k_1k_3(k_5 + k_6)k_9k_{10}} \frac{\xi_1^2}{\xi_2\xi_3}$$
$$[K] = \frac{(k_5 + k_6)k_9k_{10}}{k_4k_6(k_{11} + k_{12})} \frac{\xi_2\xi_3}{\xi_1}$$
$$[SK] = \frac{k_{12}}{k_3}\xi_1$$
$$[S_p] = \frac{k_{11} + k_{12}}{k_{10}} \frac{\xi_1}{\xi_3}$$

$$[S_pK] = \frac{k_9}{k_6}\xi_2$$
$$[S_{pp}] = \frac{k_8 + k_9}{k_7} \frac{\xi_2}{\xi_3}$$
$$[P] = \xi_3$$
$$[S_{pp}P] = \xi_2$$
$$[S_pP] = \xi_1$$

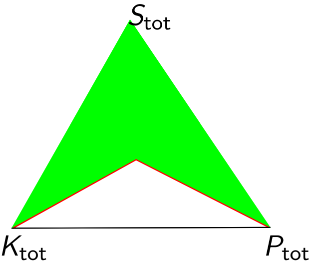
where $\xi_1, \ \xi_2, \ \xi_3 \in \mathbb{R}_{>0}$.

Example: the 2-site phosphorylation

Theorem (Bihan, Dickenstein, Giaroli; Conradi, I., Kahle; 2018)

Generically, in the space of linear conserved quantities K_{tot}, P_{tot}, and S_{tot}, multistationarity is possible if and only if

$$P_{\text{tot}} < S_{\text{tot}} \text{ or } K_{\text{tot}} < S_{\text{tot}}.$$



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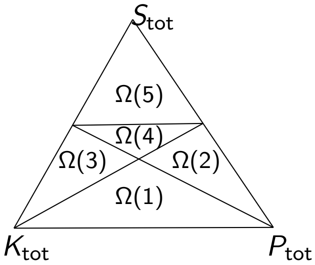

$$
\begin{aligned}
(\Omega(2),\delta_7):&\quad 0<\xi_3<\xi_1<1 \ \wedge\ \xi_2>\tfrac{\xi_1^2}{\xi_3^2},\\
(\Omega(2),\delta_5):&\quad \xi_3>1 \ \wedge\ 0<\xi_1<1 \ \wedge\ \xi_2>\xi_3^2,\\
(\Omega(4),\delta_5):&\quad \xi_3>1 \ \wedge\ 0<\xi_1<1 \ \wedge\ \xi_2>\xi_3^2,\\
(\Omega(3),\delta_3):&\quad \xi_3^2<\xi_1<\xi_3<1 \ \wedge \xi_2>1,\\
(\Omega(3),\delta_1):&\quad \xi_3>1 \ \wedge\\
&\quad \left(\left(1<\xi_1<\xi_3^{2/3} \ \wedge\ \tfrac{\xi_1}{\xi_3}<\xi_2<\tfrac{\xi_1^{3/2}}{\xi_3}\right)\vee\left(\xi_3^{2/3}<\xi_1<\xi_3 \ \wedge\ \tfrac{\xi_1}{\xi_3}<\xi_2<1\right)\right),\\
(\Omega(4),\delta_1):&\quad \xi_3>1 \ \wedge\\
&\quad \left(\left(1<\xi_1<\xi_3^{2/3} \ \wedge\ \tfrac{\xi_1}{\xi_3}<\xi_2<\tfrac{\xi_1^{3/2}}{\xi_3}\right)\vee\left(\xi_3^{2/3}<\xi_1<\xi_3 \ \wedge\ \tfrac{\xi_1}{\xi_3}<\xi_2<1\right)\right),\\
(\Omega(5),\delta_1):&\quad \xi_3>1 \ \wedge\\
&\quad \left(\left(1<\xi_1<\xi_3^{1/2} \ \wedge\ \tfrac{\xi_1}{\xi_3}<\xi_2<\tfrac{\xi_1^2}{\xi_3}\right)\vee\left(\xi_3^{1/2}<\xi_1<\xi_3 \ \wedge\ \tfrac{\xi_1}{\xi_3}<\xi_2<1\right)\right).
\end{aligned}
$$

Here, δ_i are the sign patterns of two steady states, that is, the signs of the difference between two compatible steady states.

Sufficient conditions for toricity

Proposition (Corollary to Eisenbud, Sturmfels; 1994)

Let $I \subseteq \mathbb{R}[x_1, \ldots, x_n]$ be a binomial ideal. Then, the variety $\overline{\mathbb{V}_{\mathbb{R}}(I) \cap \mathbb{R}^n_{>0}}$ is empty or toric (that is, empty or a coset of a multiplicative group).

Corollary

If $\{\dot{x}_i = P_i | i \in [n]\}$ has binomial ideal $\langle P_1, \ldots, P_n \rangle \subseteq \mathbb{R}[x_1, \ldots, x_n]$ and at least a positive steady state, then, V^+ is toric

Problem

Find other certificates for the toricity of $\overline{\mathbb{V}_{\mathbb{R}}(I) \cap \mathbb{R}^n_{>0}}$.

One possible answer (not discussed in this talk):

Theorem (Conradi, I., Kahle; 2019)/ Conjecture: generically, $\iff$

Isolation property (a technical condition on the supports of the vectors of the cone $\ker(Y_p - Y_e) \cap \mathbb{R}^r_{\geq 0}$) $\implies$ $\overline{\mathbb{V}_{\mathbb{R}}(I) \cap \mathbb{R}^n_{>0}}$ is toric.

Work in progress 1: “Sturm” Discriminants

Definition

Suppose we have a parametric system of equations in n variables such that, when we eliminate all variables, except the j^{th} one, we obtain a nonzero univariate polynomial, $p_j(x_j)$. The Sturm discriminant of this system is

$$\Delta_S(I) := \prod_{j=1}^{n} \Delta_S(p_j),$$

where $\Delta_S(p_j)$ is the product of numerators and denominators of the principal coefficients and nonzero constant terms of each element of the Sturm sequence of $p_j(x_j)$.

Theorem (Corollary to "Tarski-Seidenberg" $\in$ [1930,1948])

The Sturm discriminant separates the space of parameters in regions with equal number of positive roots.

Remark

Sturm sequences are quite inefficient for the clasification of the parameters. However, if we only seek positive solutions and we have a toric system, this method becomes much more efficient.

Macaulay2 and Maple implementations

sturmdiscriminants / **SturmDiscriminants.m2**

```
-- -*- coding: utf-8 -*-
newPackage(
    "SturmDiscriminants",
    Version => "0.1",
    Date => "October 2018",
    Authors => {{
          Name => "Alexandru Iosif",
          Email => "alexandru.iosif@ovgu.de",
          HomePage => "https://alexandru-iosif.github.io"}},
        Headline => "Computation of Sturm Discriminants",
    AuxiliaryFiles => false,
        PackageImports => {"Elimination"},
    DebuggingMode => false
)

export {
     -- 'Official' functions
     "SturmDiscriminant",
     "SturmSequence"
```

maplesturmdiscriminants / **SturmDisciminants.mpl**

```
#####
with(PolynomialIdeals):
with(Groebner):
with(Student[MultivariateCalculus]):
with(Student[LinearAlgebra]):
with(combinat):

#####
SturmDiscriminants := module()
description "Sturm Discriminants";
#Author: Alexandru Iosif
option package;


#####
export SturmSequence, SturmDiscriminant, MonomialExponent, areAlgebraicallyIndependent, GenericPolynomial;

```

I believe that this is the first time someone succeeds in computing the discriminant the dual phosphorylation system: https://bitbucket.org/alexandru-iosif/maplesturmdiscriminants/src/master/Discriminant2sites.txt

Work in progress 2:
A duality theory for mass-action networks
(Together with Lamprini Ananiadi)
(Visit our poster at Jóvenes RSME 2025, Bilbao)

Two algebro-combinatorial objects

Two objects related to the left and right kernels of $Y_p - Y_e$.

1. Siphons: Let $\mathfrak{N}$ be a mass-action network with variables $\mathcal{X}$. A *siphon* is a nonempty subset $\mathcal{S}$ of $\mathcal{X}$ such that, given an arbitrary arrow $m \to m'$ of $\mathfrak{N}$, if $\mathcal{S} \cap \mathcal{M}' \neq \emptyset$, then $\mathcal{S} \cap \mathcal{M} \neq \emptyset$ ($\mathcal{M}$ and $\mathcal{M}'$ are the variables in m and m'). They are related to the cone $\ker(A_p - A_e)^T \cap \mathbb{R}^n_{\geq 0}$.
2. (Pre)clusters[‡]: partition of the arrow set collecting relations between the coordinates of the cone $\ker(A_p - A_e) \cap \mathbb{R}^r_{\geq 0}$ (INFORMAL).

Conjecture:

Siphons and clusters are dual objects.

Theorem (Ananiadi, I.) (Evidence for the conjecture)

Maximal invariant polyhedral supports (MIPS) –objects related to siphons derived from the work of Shiu and Sturmfels– are dual to preclusters.

[‡]Clusters were introduced in 2011 by Conradi and Flockerzi in the context of the isolation property. In this talk we use the term in a slightly more general sense.

The state of art in a "non-commutative" diagram

$$
\begin{array}{ccc}
\ker(A_p - A_e) & \xleftrightarrow{\quad\text{dual}\quad} & \ker\left((A_p - A_e)^T\right) \\
\downarrow & & \downarrow \\
\text{Clustering graph} & & \text{Chamber decomposition} \\
\wr\!| & & \wr\!| \\
 & & \text{Decorations of invariant polyhedra} \\
 & & \downarrow \\
\{P \mid P \text{ is a precluster}\} & \xleftrightarrow{\quad\text{dual}\quad} & \{M \mid M \text{ is a MIPS}\} \\
\downarrow \text{Refine} & & \downarrow \text{"Refine"} \\
\{C \mid C \text{ is a cluster}\} & \xleftrightarrow{\text{¿duality relation?}} & \{S \mid S \text{ is a siphon}\}
\end{array}
$$

Question

A new case (in small codimension) of the Global Attractor Conjecture?

Some bibliography

1. Conradi, I., Kahle. *Multist. in the space of total concentrations for systems that admit a monomial parametrization* (2019).
2. Grigoriev, I., Rahkooy, Sturm, Weber. *Efficiently and effectively recognizing toricity of steady state varieties* (2021).
3. Desoeuvres, I., Lüders, Radulescu, Rahkooy, Seiß, Sturm. A Computational Approach to Polynomial Conservation Laws (2024).
4. Desoeuvres, I., Lüders, Radulescu, Rahkooy, Seiß, Sturm. Reduction of Chemical Reaction Networks with Approx. Conservation Laws (2024).
5. Franklin C McLean, Application of the law of chemical equilibrium (law of mass action) to biological problems, (1938).
6. Eberhard O Voit, Harald A Martens, and Stig W Omholt, 150 years of the mass action law, PLoS computational biology 11 (2015).

¡Muchas Gracias!
Vă Mulțumesc!