Topics in Applied Algebraic Geometry

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Homework # 2, due Tuesday March 7

Exercise 1. Let a, b, c be complex numbers such that $a + b + c = 3, a^2 + b^2 + c^2 = 5$ and $a^3 + b^3 + c^3 = 7$.

Use a Computer Algebra System to prove that $a^4 + b^4 + c^4 = 9$ and $a^5 + b^5 + c^5 \neq 11$. Find the value of $a^5 + b^5 + c^5$. Explain why we can predict beforehand that this value only depends on the given data about a, b, c.

Exercise 2. In most usual biochemical reaction networks (with positive rate constants), the intersection of the corresponding steady state variety and the linear variety L defined by the linear conservation relations (defined by polynomials of degree one of the form $\sum_i \lambda_i x_i - C = 0$), consists of finitely complex solutions (thus, in particular there are finitely many positive steady states in each stoichiometric compabitility class $L \cap \mathbb{R}^n_{\geq 0}$.)

Find a chemical reaction network with mass-action kinetics $dx_i/dt = f_i(s), i = 1, \ldots, s$ such that the ideal generated by $f_1, \ldots, f_s$ and the (linear) conservation relations (if any) does not have finitely many (complex) solutions.

Exercise 3. Consider a chemical reaction network with mass-action kinetics $dx_i/dt = f_i(s), i = 1, \ldots, s$. involving n complexes $y_1, \ldots, y_n$. Recall that a level 1 invariant is just an element of the real span of $f_1, \ldots, f_s$. How could we use Groebner bases to compute the non trivial level 1 invariants involving some subset $y_1, \ldots, y_k, k < m$ of the complexes (or decide that none exists).

Hint: Given a linear ideal (an ideal generated by polynomials of degree one), a (reduced) Groebner basis is composed again by linear polynomials obtained from the original ones by Gauss triangulation.

Exercise 4. Assume that there is a substrate S_{00} which can be phosphorylated in two sites by an enzyme E, producing the substrates S_{11} or S_{01}, which can (each of them) be then phosphorylated in the remaining site by E to produce a doubly phosphorylated substrate S_{11}, and there is another enzyme F dephosphorylating one site at a time in any order. All reactions occur under the standard enzymatic mechanism, for instance:

$$S_{10} + E \underset{k_2}{\overset{k_1}{\rightleftharpoons}} ES_{10} \xrightarrow{k_3} S_{11} + E \tag{1}$$

Denote by $[S_{ij}], [E], [F]$ the concentrations of the different species at any positive steady state. Prove that the points in 3 space of the form $(\frac{[S_{01}]^2}{[S_{00}][S_{11}]}, \frac{[S_{01}][S_{10}]}{[S_{00}][S_{11}]}, \frac{[S_{10}]^2}{[S_{00}][S_{11}]})$ lie on a plane (which depends on the rate constants). This can be used to detect a wrong modeling (in case the plotted points after some experiments don't lie approximately on a plane).

Hint: You can do the computation by hand or you can use a computer algebra system for this. How?

Exercise 5. The network in Example (S60) of the Supporting Online Material article of Shinar and Feinberg in Science (2010) is the following:

$$\begin{aligned}
XD \underset{\kappa_{21}}{\overset{\kappa_{12}}{\rightleftarrows}} X \underset{\kappa_{32}}{\overset{\kappa_{23}}{\rightleftarrows}} XT \overset{\kappa_{34}}{\to} X_p \\
X_p + Y \underset{\kappa_{65}}{\overset{\kappa_{56}}{\rightleftarrows}} X_pY \overset{\kappa_{67}}{\to} X + Y_p \\
XT + Y_p \underset{\kappa_{98}}{\overset{\kappa_{89}}{\rightleftarrows}} XTY_p \overset{\kappa_{9,10}}{\to} XT + Y \\
XD + Y_p \underset{\kappa_{12,11}}{\overset{\kappa_{11,12}}{\rightleftarrows}} XDY_p \overset{\kappa_{12,13}}{\to} XD + Y
\end{aligned} \tag{2}$$

We denote by $x_1, x_2, \ldots, x_9$ the concentrations of the species as follows:

$$x_{XD} = x_1,\ x_X = x_2,\ x_{XT} = x_3,\ x_{X_p} = x_4\ ,$$

$$x_Y = x_5,\ x_{X_pY} = x_6,\ x_{Y_p} = x_7,\ x_{XTY_p} = x_8,\ x_{XDY_p} = x_9\ .$$

Note that the numbering of the 13 complexes in the network is reflected in the names of the rate constants κ_{ij}. The corresponding differential equations $\frac{dx_k}{dt} = f_k$ under mass-action kinetics are the following:

$$\begin{aligned}
\tfrac{dx_1}{dt} &= -\kappa_{12}x_1 + \kappa_{21}x_2 - \kappa_{11,12}x_1x_7 + (\kappa_{12,11} + \kappa_{12,13})x_9 \\
\tfrac{dx_2}{dt} &= \kappa_{12}x_1 + (-\kappa_{21} - \kappa_{23})x_2 + \kappa_{32}x_3 + \kappa_{67}x_6 \\
\tfrac{dx_3}{dt} &= \kappa_{23}x_2 + (-\kappa_{32} - \kappa_{34})x_3 - \kappa_{89}x_3x_7 + (\kappa_{98} + \kappa_{9,10})x_8 \\
\tfrac{dx_4}{dt} &= \kappa_{34}x_3 - \kappa_{56}x_4x_5 + \kappa_{65}x_6 \\
\tfrac{dx_5}{dt} &= -\kappa_{56}x_4x_5 + \kappa_{65}x_6 + \kappa_{9,10}x_8 + \kappa_{12,13}x_9 \\
\tfrac{dx_6}{dt} &= \kappa_{56}x_4x_5 + (-\kappa_{65} - \kappa_{67})x_6 \\
\tfrac{dx_7}{dt} &= \kappa_{67}x_6 - \kappa_{89}x_3x_7 + \kappa_{98}x_8 - \kappa_{11,12}x_1x_7 + \kappa_{12,11}x_9 \\
\tfrac{dx_8}{dt} &= \kappa_{89}x_3x_7 + (-\kappa_{98} - \kappa_{9,10})x_8 \\
\tfrac{dx_9}{dt} &= \kappa_{11,12}x_1x_7 + (-\kappa_{12,11} - \kappa_{12,13})x_9
\end{aligned} \tag{3}$$

- Show that there are non-trivial linear conservation relations.
- Compute a reduced Gröbner basis G of the ideal $\langle f_1, \ldots, f_9 \rangle$ with respect to the lexicographical order $x_1 > x_2 > x_4 > x_5 > x_6 > x_8 > x_9 > x_3 > x_7$ and check that there is a polynomial g in G of the form

  $$g = a(\kappa)\, x_3x_7 - b(\kappa)\, x_3,$$

  with a, b polynomials in κ of degree 5 with coefficients $0, 1$. Therefore the value at any positive steady state of x_7 does not depend on the total amounts, i.e., the system shows Absolute Concentration Robustness.
- How could you check that there is no level 1 invariant only depending on x_3 and x_7? If possible, check it.

Exercise 6. Consider again the Shinar and Feinberg example in Exercise 5. How could you check if it is true that g vanishes at any steady state of the system (that is, at any common zero of $f_1, \dots, f_9$) for *any* choice of constants $k = (k_{12}, \dots, k_{12,13})$? If possible, check it (or check that this is not the case).

Prove that if $x^* \in \mathbb{R}^9_{\geq 0} \setminus \mathbb{R}^9_{>0}$ is a *boundary steady state* of the system and $x^*_7 = 0$, then $x^* = 0$. Prove that if P is a stoichiometric compatibility class that intersects the positive orthant, then $P \cap \{x_7 = 0\} = \emptyset$.

Exercise 7. Consider a chemical reaction network associated to a directed graph G, with set of species $X_1, \dots, X_n$ (and corresponding concentrations $x_1, \dots, x_n$), set of complexes $y_1, \dots, y_m$ and reaction rate constants k_{ij} for each reaction (edge) $y_i \to y_j$. Denote by $\psi(x)$ the vector $(x^{y_1}, \dots, x^{y_m})$. Endowed with mass-action kinetics, it defines the system

$$\frac{dx}{dt} = f(x) = N \cdot \psi(x) = Y \cdot A_k \cdot \psi(x).$$

Assume that $\dim(\ker(N)) = 1$.

- Prove that if $V(f) \neq \emptyset$ there exists a generator $\rho \in \mathbb{R}^m_{\geq 0}$ of $\ker(N)$ with non-negative coordinates. When this is the case, prove that

  $$V(f) = \{x \in \mathbb{R}^n_{\geq 0} : b_{ij} = \rho_j x^{y_i} - \rho_i x^{y_j} = 0,\ i, j = 1, \dots, m\,,\ i < j\}$$

  is cut out by the binomials b_{ij}. How many binomials are enough if $\rho \in \mathbb{R}^m_{>0}$?

- If $\rho \in \mathbb{R}^m_{>0}$ is positive, prove that $V_{>0}(f) \neq \emptyset$ if and only if for any vector $\lambda = (\lambda_{ij})_{i<j}$ such that $\sum_{i<j} \lambda_{ij}(y_j - y_i) = 0$ it holds that $\prod_{i<j} \left(\frac{\rho_j}{\rho_i}\right)^{\lambda_{ij}} = 1$. Is it true that it is enough to check finitely many of these conditions?