

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 .

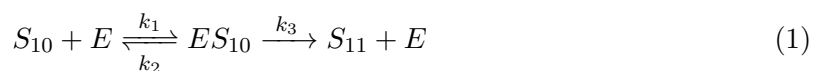
Exercise 2. In most usual biochemical reaction networks (with positive rate constants), the intersection of the corresponding steady state variety and the linear variety L defined by the linear conservation relations (defined by polynomials of degree one of the form $\sum_i \lambda_i x_i - C = 0$), consists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

Find a chemical reaction network with mass-action kinetics $dx_i/dt = f_i(s)$, $i = 1, \dots, s$ such that the ideal generated by f_1, \dots, 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 $dx_i/dt = f_i(s)$, $i = 1, \dots, s$, involving n complexes y_1, \dots, y_n . Recall that a level 1 invariant is just an element of the real span of f_1, \dots, f_s . How could we use Groebner bases to compute the non trivial level 1 invariants involving some subset y_1, \dots, 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.

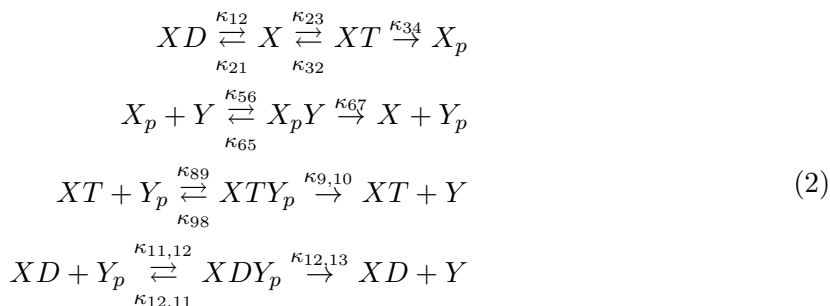
Exercise 4. Assume that there is a substrate S_{00} which can be phosphorylated in two sites by an enzyme E , producing the substrates S_{11} or S_{01} , which can (each of them) be then phosphorylated in the remaining site by E to produce a doubly phosphorylated substrate S_{11} , and there is another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



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:



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

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

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

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:

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

- Show that there are non-trivial linear conservation relations.
- Compute a reduced Gröbner basis G of the ideal $\langle f_1, \dots, f_9 \rangle$ 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

$$g = a(\kappa) x_3 x_7 - b(\kappa) x_3,$$

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 $x^* \in \mathbb{R}_{\geq 0}^9 \setminus \mathbb{R}_{> 0}^9$ 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) $y_i \rightarrow y_j$. 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 $\rho \in \mathbb{R}_{\geq 0}^m$ of $\ker(N)$ with non-negative coordinates. When this is the case, prove that

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

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

- If $\rho \in \mathbb{R}_{> 0}^m$ 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?