Complexity of Solving Systems with Few Independent Monomials and Applications to Mass-action Kinetics

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Abstract. We design an algorithm for finding solutions with nonzero coordinates of systems of polynomial equations which has a better complexity bound than for known algorithms when a system contains a few linearly independent monomials. For parametric binomial systems we construct an algorithm of polynomial complexity. We discuss the applications of these algorithms in the context of chemical reaction systems.

Keywords: complexity of solving systems of polynomial equations, Smith form, toric systems, mass-action kinetics, chemical reaction networks

1 Introduction

We study systems of polynomial equations with a few linearly independent monomials. To find solutions with nonzero coordinates of such systems we design in Sect. 2 an algorithm which makes use of a combination of the multiplicative structure on the monomials with the additive structure emerging from the linear equations on monomials called Gale duality and which was used in [1] for improving Khovanskii's bound on the number of real solutions of systems of fewnomials. This combination allows one to diminish the number of variables, being crucial since the latter brings the greatest contribution into the complexity of solving systems of polynomial equations. Moreover, the designed algorithm allows one to look for positive real solutions that is important in the applications to mass-action kinetics [2–7].

Note that the designed algorithm has a better complexity bound than the one just employing the known general methods for solving systems of polynomial equations [8, 9] or inequalities [10]. So more, it has better complexity bounds than the methods relying on Gröbner bases [11] or involutive divisions [12] which have double-exponential complexity upper and lower bound [13].

In Sect. 3 we expose an algorithm finding solutions of *parametrical* binomial systems with nonzero coordinates and parameters within polynomial complexity which invokes computing the Smith canonical form of an integer matrix. Such systems also emerge in mass-action kinetics. Similar to Sect. 2 the algorithm allows one to look for positive real solutions. The polynomial complexity cannot be achieved using the general methods for solving systems of polynomial equations or, respectively, inequalities (as well as the Gröbner or involutive bases because the example of generators of an ideal from [13] with double-exponential complexity consists just of binomials).

In [14] a polynomial complexity algorithm is designed to test whether a binomial system has a finite number of affine solutions (including ones with zero coordinates). On the other hand, it is proved in [14] that the problem of counting the number of affine solutions of a binomial system is $\#P$-complete. We observe also that the problem of testing whether a system of binomial equations extended by linear equations (being customary in biochemical reactions networks) has a positive solution, is NP-hard. Indeed, adding to a system of binomials $x_i \cdot y_i = 1$, $1 \leq i \leq n$ in $2 \cdot n$ variables linear equations $x_i + y_i = 5/2$, $1 \leq i \leq n$ and a single linear equation in the variables $x_1, \ldots, x_n$, we arrive to the knapsack problem.

Potential applications of these algorithms in the context of chemical reaction networks are discussed in Sect. 4. We also expose a computational example there.

As a related work we mention also [15] where an algorithm for solving systems of *quadratic* inequalities is designed with the complexity bound being good when the number of inequalities is rather small.

2 Polynomial Systems with a Few Linearly Independent Monomials

Any system of polynomial equations can be represented in a form

$$A \cdot Y = 0 \tag{1}$$

where $A = (a_{k,j})$, $1 \leq k \leq l$, $1 \leq j \leq m$ is a matrix, and $Y = (Y_j)$, $1 \leq j \leq m$ is a vector of monomials $Y_j = X_1^{y_{j,1}} \cdots X_n^{y_{j,n}}$ in the variables $X_1, \ldots, X_n$. An algorithm designed in this Section searches for solutions of (1) with non-vanishing coordinates $x_1, \ldots, x_n \in (\overline{\mathbb{Q}})^* := \overline{\mathbb{Q}} \setminus \{0\}$. The condition of non-vanishing coordinates is not too restrictive for the purposes of mass-action kinetics since in the latter one looks usually for solutions with positive real coordinates. Assume that $y_{j,i} \leq d$, $1 \leq j \leq m$, $1 \leq i \leq n$, and that the entries $a_{k,j} \in \mathbb{Z}$ are integers, therein $|a_{k,j}| \leq M$. The assumption on $a_{k,j}$ to be integers is adopted just for the sake of simplifying complexity bounds, one could consider by the same token algebraic entries $a_{k,j} \in \overline{\mathbb{Q}}$.

The considered form of systems of polynomial equations appears, in particular, in the study of stationary solutions of the dynamical equations of the mass-action kinetics [2–4, 6, 7].

In general, the algorithm solving systems (1) (with or without imposing the condition of non-vanishing coordinates of solutions) has complexity bound polynomial in l, d^{n^2}, $\log M$ [8, 9]. In this paper we suggest an algorithm for solving systems with the complexity being better than in general when the difference $r := m - \mathrm{rk}(A)$ is small enough.

The solutions of system (1) depend on r parameters $Z_1, \ldots, Z_r$. One can thus express monomials $Y_j = \sum_{1 \le k \le r} u_{j,k} \cdot Z_k$, $1 \le j \le m$ with suitable rationals $u_{j,k} \in \mathbb{Q}$.

One can bring the matrix $y := (y_{j,i})$ to the Smith canonical form. Namely, one can find integer square matrices $B = (b_{\alpha,\beta})$ of size $m \times m$ and $C = (c_{\gamma,\delta})$ of the size $n \times n$ such that $\det(B) = \det(C) = 1$, and the matrix $V = (v_{j,i}) := ByC$, $1 \le j \le m$, $1 \le i \le n$ has the following form. The only non-vanishing entries $v_{j,i}$ are on the diagonal $v_{j,j} \ne 0$, $1 \le j \le p$ where $p := \mathrm{rk}(y)$. Moreover, $v_{1,1} | v_{2,2} | \cdots | v_{p,p}$, although we will not make use of this extra property on divisibility. The complexity of constructing matrices B, C is polynomial in n, m, $\log d$ [16]; moreover, one can make its parallel complexity poly-logarithmic [17]. In particular, $|b_{\alpha,\beta}|$, $|c_{\gamma,\delta}| \le (d \cdot \min\{n, m\})^{O(\min\{n,m\})}$.

Consider polynomials $f_s = \prod_{1 \le j \le m} Y_j^{b_{s,j}} \in \mathbb{Q}[Z_1, \ldots, Z_r]$, $1 \le s \le m$. Then $\deg(f_s) \le m \cdot (d \cdot \min\{n, m\})^{O(\min\{n,m\})}$. The input system (1) has a solution over $(\overline{\mathbb{Q}})^*$ iff system of equations $f_{p+1} = \cdots = f_m = 1$ and inequality $f_1 \cdots f_p \ne 0$ has a solution in $Z_1, \ldots, Z_r$ over $\overline{\mathbb{Q}}$. In particular, among $f_{p+1}, \ldots, f_m$ the polynomial $f_q = Y_q$, $p < q \le m$ occurs when the monomial Y_q equals 1 identically (provided that the monomial 1 is among the monomials $Y_1, \ldots, Y_m$). The latter yields an equation $(f_q =) \sum_{1 \le k \le r} u_{q,k} \cdot Z_k = 1$. One can find the irreducible components of the constructible set of solutions of the latter system using [8, 9]. Any solution $(z_1, \ldots, z_r)$ of the latter system provides a solution of the input system as follows.

Denote the monomials $W_t := \prod_{1 \le i \le n} X_i^{c_{t,i}}$, $1 \le t \le n$. Then equalities $W_t^{v_{t,t}} = f_t$, $1 \le t \le p$ impose the conditions on W_t, $1 \le t \le p$, while $W_{p+1}, \ldots, W_n$ can be chosen as arbitrary non-zeros. Finally, having $W_1, \ldots, W_n$, one can come back to $X_1, \ldots, X_n$ by means of the matrix C^{-1}.

Sometimes, in the applications to chemistry one looks for positive real solutions $X_1 > 0, \ldots, X_n > 0$ of the input system (1) [3, 4, 6, 7]. The latter is equivalent to $W_1 > 0, \ldots, W_n > 0$. This imposes the condition $f_t > 0$, $1 \le t \le p$ and one can solve the system of inequalities $f_t > 0$, $1 \le t \le p$, $f_{p+1} = \cdots = f_m = 1$ over the reals with the help of [10]. After that W_t, $1 \le t \le p$ are obtained uniquely from the equations $W_t^{v_{t,t}} = f_t$, $1 \le t \le p$, while $W_{p+1} > 0, \ldots, W_n > 0$ can be chosen in an arbitrary way. Finally, we can summarize the results.

Proposition 1. *One can design an algorithm which finds the irreducible components of the constructible set of solutions with non-vanishing coordinates $x_1, \ldots, x_n$ of a system of polynomial equations (1) within complexity polynomial in l, n, m, $(d \cdot \min\{n, m\})^{O(\min\{n,m\}) \cdot r^2}$, $\log M$. Moreover, the algorithm can find positive real solutions of (1) also within the same complexity bound.*

Note that this complexity bound is better than the bound polynomial in l, d^{n^2}, $\log M$ from [8–10] when r is significantly smaller than n. As usually, the

practical complexity bounds are apparently better than the established a priori bounds, especially when the complexity of bringing to the Smith form being small.

Remark 1. Using indeterminates $Z_1, \dots, Z_r$ in a similar way to our proposal has been done by several authors, see e.g. [2, 3] and references therein. Also using the Smith normal form has been proposed in [2] as well as [3] (in addition to using logarithms or the Hermite normal form), but for computations the Hermite normal form or Gröbner basis methods have been used in these papers. Hence although several parts of our proposed algorithms have been around for the special case of chemical reaction networks for several years, but nevertheless in addition to the complexity analysis also our proposed algorithm seems to be new in its full form.

3 Parametric Binomial Systems

Now suppose that a matrix A at each of its rows contains at most two non-vanishing entries, and moreover every entry is a monomial of the form $\beta \cdot K^E := \beta \cdot K_1^{e_1} \cdots K_q^{e_q}$. Herein $\beta \in \mathbb{Q}$ and $K_1, \dots, K_q$ play the role of parameters. Such parametric systems appear in the applications to mass-action kinetics [18, 3, 4, 6, 7]. In other words, each equation of (1) can be viewed as a binomial in the variables $X_1, \dots, X_n$, $K_1, \dots, K_q$. We pose a question, for which non-zero values of $K_1, \dots, K_q$ the system (1) has a solution in non-vanishing $x_1, \dots, x_n$? Alternatively, for which positive real values of $K_1, \dots, K_q$ the system (1) has a positive real solution?

Rewrite now the system (1) of l binomials in the form

$$X^{G_j} = \beta_j \cdot K^{H_j},\ 1 \le j \le l \tag{2}$$

where $X^{G_j} := X_1^{g_{j,1}} \cdots X_n^{g_{j,n}}$, $K^{H_j} := K_1^{h_{j,1}} \cdots K_q^{h_{j,q}}$. The algorithm brings the matrix $G := (g_{j,i})$, $1 \le j \le l$, $1 \le i \le n$ to the Smith canonical form. Thus, the algorithm yields integer unimodular matrices B', C' such that $B' \cdot G \cdot C'$ is in the Smith canonical form. Let $s := \mathrm{rk}(G)$ and the only non-vanishing entries of $B' \cdot G \cdot C'$ be its first s diagonal entries $g'_{1,1}, \dots, g'_{s,s}$. Denote $B' =: (b'_{j,\alpha})$, $1 \le j, \alpha \le l$ and $\gamma_j \cdot K^{H'_j} := \prod_{1 \le \alpha \le l} (\beta_\alpha \cdot K^{H_\alpha})^{b'_{j,\alpha}}$.

The system (2) for given non-zero $K_1, \dots, K_q$ has a solution in non-zero $X_1, \dots, X_n$ iff

$$\gamma_j \cdot K^{H'_j} = 1,\ s+1 \le j \le l \tag{3}$$

In its turn, solvability of (2) in positive real solutions $X_1, \dots, X_n$ for positive real $K_1, \dots, K_q$ imposes extra conditions $\beta_1 > 0, \dots, \beta_l > 0$.

For non-zero values of parameters $K_1, \dots, K_q$ satisfying (3) one can find monomials $\prod_{1 \le i \le n} X_i^{c'_{\mu,i}}$, $1 \le \mu \le s$, where the matrix $C' =: (c'_{\mu,i})$, $1 \le \mu, i \le n$, from the equations $(\prod_{1 \le i \le n} X_i^{c'_{\mu,i}})^{g'_{\mu,\mu}} = \gamma_\mu \cdot K^{H'_\mu}$, $1 \le \mu \le s$, while the non-zero values of the monomials $\prod_{1 \le i \le n} X_i^{c'_{\mu,i}}, s+1 \le \mu \le n$ are chosen in an

arbitrary way. Then the algorithm uniquely finds $X_1, \dots, X_n$ from the monomials $\prod_{1 \le i \le n} X_i^{c'_{\mu,i}}$, $1 \le \mu \le n$ with the help of the matrix $(C')^{-1}$. Respectively, for positive real $K_1, \dots, K_q$ to get positive real $X_1, \dots, X_n$ one chooses the positive values of the monomials $\prod_{1 \le i \le n} X_i^{c'_{\mu,i}}$, $s+1 \le \mu \le n$ in an arbitrary way.

To describe the conditions on non-zero $K_1, \dots, K_q$ satisfying (3), the algorithm brings $(l-s) \times q$ matrix $H' := (h'_{j,\alpha})$, $s+1 \le j \le l$, $1 \le \alpha \le q$, where the vector $H'_j =: (h'_{j,\alpha})$, $1 \le \alpha \le q$, to the Smith canonical form. Thus, the algorithm yields integer unimodular matrices $B'' = (b''_{j,\delta})$, $s+1 \le j, \delta \le l$, $C'' = (c''_{\mu,\alpha})$, $1 \le \mu, \alpha \le q$ such that the only non-vanishing entries of the matrix $B'' \cdot H' \cdot C''$ are its first t diagonal entries $h''_{1,1}, \dots, h''_{t,t}$, where $t = \mathrm{rk}(H')$.

Denote $\epsilon_j := \prod_{s+1 \le \delta \le l} \gamma_\delta^{-b''_{j,\delta}}$, $s+1 \le j \le l$. Then (3) has a solution in non-zero $k_1, \dots, k_q$ iff

$$\epsilon_j = 1,\ s+t+1 \le j \le l. \tag{4}$$

If (4) holds one can find the values of the monomials $\prod_{1 \le \alpha \le q} K_\alpha^{c''_{\mu,\alpha}}$, $1 \le \mu \le t$ from the equalities $(\prod_{1 \le \alpha \le q} K_\alpha^{c''_{\mu,\alpha}})^{h''_{\mu,\mu}} = \epsilon_{s+\mu}$, $1 \le \mu \le t$, while the non-zero values of the monomials $\prod_{1 \le \alpha \le q} K_\alpha^{c''_{\mu,\alpha}}$, $t+1 \le \mu \le q$ are chosen in an arbitrary way. Respectively, the latter values are taken as arbitrary positive reals when one is looking for positive reals $K_1, \dots, K_q$. After that, the algorithm finds uniquely $K_1, \dots, K_q$ from the values of the monomials $\prod_{1 \le \alpha \le q} K_\alpha^{c''_{\mu,\alpha}}$, $1 \le \mu \le q$ with the help of the matrix $(C'')^{-1}$.

Thus, the described algorithm applies twice the subroutine for constructing the Smith canonical form (and does not need to involve algorithms for solving systems of polynomial equations). Observe that solvability of (2) for non-zero $x_1, \dots, x_n$, $k_1, \dots, k_q$ is equivalent to solvability of (4). Each $\epsilon_j = \prod_{1 \le \alpha \le l} \beta_\alpha^{\lambda_{j,\alpha}}$, $s+1 \le j \le l$ for appropriate integers $\lambda_{j,\alpha} \in \mathbb{Z}$ such that

$$|\lambda_{j,\alpha}| \le (d \cdot \min\{l,n\})^{O(\min\{l,n\})} \cdot (d \cdot \min\{l,q\})^{O(\min\{l,q\})}$$

assuming that all the exponents in (2) satisfy inequalities $|g_{j,i}|, |h_{j,l}| \le d$ (due to [16, 17]).

To verify (4) the algorithm constructs a *relative factorization* of $\beta_1, \dots, \beta_l$ (for the sake of simplifying notations assume that all $\beta_1, \dots, \beta_l$ are positive integers; for rational numbers one has to consider the absolute values of their numerators and denominators). Namely, the algorithm constructs by recursion nonnegative integers $\eta_1, \dots, \eta_r$ pairwise relatively prime such that $\beta_\mu = \eta_1^{\kappa_{\mu,1}} \cdots \eta_r^{\kappa_{\mu,r}}$, $1 \le \mu \le l$ for suitable nonnegative integers $\kappa_{\mu,i}$. As a base of recursion the algorithm starts with $\beta_1, \dots, \beta_l$. Assume that at some step the algorithm has constructed $\beta'_1, \dots, \beta'_{l'}$ such that $(\beta'_1 \cdots \beta'_{l'}) | (\beta_1 \cdots \beta_l)$. Take any pair β'_i, β'_j, $1 \le i \ne j \le l'$ for which $\theta := \mathrm{GCD}(\beta'_i, \beta'_j) \ne 1$ and replace the pair β'_i, β'_j by the triple θ, β'_i/θ, β'_j/θ. If there is no such a pair the algorithm halts.

The product of the modified $(l'+1)$-tuple is a strict divisor of the product $(\beta'_1 \cdots \beta'_{l'})$ at the previous step of the algorithm. Hence after at most of

$\log_2(\beta_1 \cdots \beta_l) \leq l \cdot \log_2 M$ steps the algorithm constructs the relative factorization $\eta_1, \ldots, \eta_r$. One can easily show that the latter is unique, although we don't make use of its uniqueness. The complexity of constructing $\eta_1, \ldots, \eta_r$ is bounded by a polynomial in l, $\log M$. In particular, $\sum_{1 \leq \mu \leq l,\, 1 \leq i \leq r} \kappa_{\mu,i}$ is also bounded by a polynomial in l, $\log M$.

Now the algorithm is able to verify equalities (4) representing each $\epsilon_j = \prod_{1 \leq i \leq r} \eta_i^{\nu_{j,i}}$, $s+t+1 \leq j \leq l$ as a product of powers of $\eta_1, \ldots, \eta_r$ for appropriate integers $\nu_{j,i}$ (perhaps, nonnegative). Then $\epsilon_j = 1$ iff $\nu_{j,i} = 0$, $1 \leq i \leq r$. The complexity of computing all $\nu_{j,i}$, $s + t + 1 \leq j \leq l$, $1 \leq i \leq r$ does not exceed a polynomial in n, l, q, $\log(d \cdot M)$. Finally, we can summarize the results obtained in this section.

Proposition 2. *One can solve a parametric binomial system (2) with non-zero values of both parameters $k_1, \ldots, k_q$ and variables $x_1, \ldots, x_n$ within polynomial complexity, i.e. within a polynomial in the size n, l, q, $\log(d \cdot M)$ of the input. Within the same complexity bound one can find positive real solutions of (2).*

Remark 2. In the proof of [19, Theorem 4.1] a similar application of the Smith normal form is used for the special case of binomial systems arising for so called "deficiency zero systems" of chemical reaction networks (see [2] for a definition or Sect. 4 below; please notice that [2] as the final journal version of [19] unfortunately no longer contains the cited algorithmic application of the Smith normal form). However, for general parametric binomial systems our algorithm applying twice the subroutine for constructing the Smith canonical form seems to be new—in addition to providing a complexity analysis.

4 Applications to chemical reaction networks

There is a vast literature for chemical reaction networks with mass action kinetics. We refer to [2] and the cited literature therein for definitions relevant in our context.

In these systems the matrix A in (1) can be factored as

$$A = \tilde{Y} \cdot I_a \cdot I_k, \tag{5}$$

where $I_a = (i_{k,j})$, $1 \leq k \leq h$, $1 \leq j \leq m$ is an integer matrix with entries $0, 1, -1$, $\tilde{Y}$ is an $l \times h$-integer matrix with non-negative entries, and I_k is a matrix $k_{u,v}$ of reaction rates, which in general are seen as parameters for the system. The occurring dimensions can be interpreted as follows: n is the number of participating molecular species, l is the number of reactions, and m is the number of complexes.

Following [2] the *deficiency* of a chemical reaction network with an associated polynomial system of the form

$$\tilde{Y} \cdot I_a \cdot I_k \cdot Y$$

can be defined as

$$\operatorname{rk} I_a - \operatorname{rk} \tilde{Y} \cdot I_a.$$

Hence it is a non-negative integer.

4.1 Chemical reaction networks with toric steady states

Remarkably, many chemical reaction systems have the property that the steady state ideal of the corresponding polynomial system is a binomial ideal [18]. Using the terminology of [18] these systems are ones having toric steady states.

For a given chemical reaction network the property of having toric steady states is dependent on the parameters in general. A simple instance is given in [18, Example 2.3].

For chemical reaction networks with toric steady states for all admissible parameters Péres Millán et al. [18] establish criteria for the existence of positive equilibria, and also for so called multi-stationarity, which are basically linear algebra criteria.

However, in cases for which multi-stationarity is established, the criteria in [18] give no detailed information about the structure of the equilibria of the system, whereas our algorithm computes in polynomial time all equilibria hence allowing a detailed analysis of them.

On the other hand, in the algorithm presented in Sect. 3 we presume that already *the input system* is in the form of a parametric binomial system, whereas in [18] it is not necessary that the input system is of this form, but the main result in [18] gives sufficient conditions for a chemical reaction system to have toric steady states.

For a given chemical reaction network, which potentially has toric steady states, there are several possibilities to come up with a parametric binomial system that in turn can be solved by the algorithm presented in Sect. 3:

- Use the construction for a binomial system given in [6]. As this construction uses an enumeration of spanning trees of underlying graphs, it worst time complexity is exponential.
- As a sufficient condition one can check [18, Condition 3.1]. Then [18, Theorem 3.3] gives an easy construction for a binomial system generating the steady state ideal. A check of [18, Condition 3.1] for a given basis of $\ker A$ is easily doable. However, enumerating all possible bases of $\ker A$ yields exponential complexity. So one has to hope for suitable heuristics to come up with good test candidates among all bases of $\ker A$.
- Compute Gröbner bases (any monomial ordering would is sufficient). As already mentioned the worst time complexity is doubly-exponential, but the practical complexity could be much better for many relevant examples (as also there is freedom to use a suitable monomial ordering.

Although for all of these constructions the worst case complexity is (at least) exponential, it might nevertheless be interesting to explore their behavior for actual chemical reaction systems.

Moreover, the factorization $A = \tilde{Y} \cdot I_a \cdot I_k$—or other factorizations of the matrix A—might yield much simpler problems. For instance for deficiency zero systems the fact that $\operatorname{rk} I_a = \operatorname{rk} \tilde{Y} \cdot I_a$ implies that only $I_a \cdot I_k$ has to be considered instead of $\tilde{Y} \cdot I_a \cdot I_k$.

Although the worst-case complexity of theses methods all are worse than the one of the general algorithm given in Sect. 3, one can employ all of them and the latter algorithm using simple *coarse grained competitive parallelism*, which can be realized in many software infrastructure—e.g. the one already used a decade ago and described in [20].

Remark 3. Of course solving systems gives significantly more information than counting the number of solutions only. Also other forms of solution testing can be applied. One of these criteria is whether the projection onto one coordinate of all positive steady states of a system is unique. This property directly corresponds to the "absolute concentration robustness" [21], for which a special criterion for systems having deficiency of 1 is proven in [22].

4.2 Examples from the BioModels Database

We use examples stored in the BioModels database [23] in the following to discuss the practical relevance of the assumptions made above. Of course, for other example classes the situation might be different.

For most of the examples for which r being significantly smaller than n the deficiency of the network is 0. Hence the Deficiency-zero-theorem already gives significant information about the uniqueness [24, 2] of equilibria for these cases and also the algorithm given in the proof of [19, Theorem 4.1] could compute these unique equilibria for a fixed set of parameter, i.e. a unique solution to the polynomial system. However, we are not aware of an implementation of this method and our algorithm given in Sect. 3 is as efficient as the more restricted method of [19, Theorem 4.1].

However, there are also several example of networks having deficiency 1 or even higher deficiencies – for which no such general theorems are known, for which r being significantly smaller than n.

Example BIOMOD188 As an example we consider the model with the number 188 in the BioModels database, which was originally described in [25]. The network induces a stoichiometric matrix of size 20×20 and has a deficiency of 4. The dimension of the nullspace of the stoichiometric matrix A is 6. The rank of the exponent matrix Y is 11.

The polynomial system is as follows (with two instances of the 0-polynomial due to the automated construction of the system from the SBML description):

$$
\begin{array}{l}
k_2 \cdot x_4 - k_6 \cdot x_1 + k_8 \cdot x_3 - k_9 \cdot x_2 \cdot x_1 + k_{10} \cdot x_3 - k_{16} \cdot x_1 \cdot x_6 + k_{17} \cdot x_9, \\
k_7 \cdot x_5 - k_9 \cdot x_2 \cdot x_1 + k_{10} \cdot x_3 - k_{14} \cdot x_2 \cdot x_6 + k_{15} \cdot x_8, \\
-k_8 \cdot x_3 + k_9 \cdot x_2 \cdot x_1 - k_{10} \cdot x_3, k_3 \cdot x_2 + k_4 \cdot x_8 - k_5 \cdot x_4, k_0 \cdot x_{12} - k_1 \cdot x_5, \\
k_{13} \cdot x_{10} \cdot x_7 - k_{19} \cdot x_6, -k_{13} \cdot x_{10} \cdot x_7 + k_{19} \cdot x_6, \\
k_{14} \cdot x_2 \cdot x_6 - k_{15} \cdot x_8, k_{16} \cdot x_1 \cdot x_6 - k_{17} \cdot x_9 - k_{18} \cdot x_9, \\
k_{11} - k_{12} \cdot x_{10}, k_1 \cdot x_5 + k_5 \cdot x_4 + k_6 \cdot x_1 + k_{12} \cdot x_{10} + k_{18} \cdot x_9, \\
-k_0 \cdot x_{12}, k_8 \cdot x_3, k_7 \cdot x_5, k_6 \cdot x_1 + k_{18} \cdot x_9, k_2 \cdot x_4, k_5 \cdot x_4, k_3 \cdot x_2 + k_4 \cdot x_8, 0, 0
\end{array}
$$

Notice that the polynomial system no longer contains all of the variables in the set $\{x_1, x_2, \ldots, x_{20}\}$, but only the subset of cardinality 11 consisting of $\{x_1, x_2, x_3, x_4, x_5, x_6, x_7, x_8, x_9, x_{10}, x_{12}\}$.

Now if we consider the factorization of the polynomial system into

$$\tilde{Y} \cdot I_a \cdot I_k \cdot Y$$

with a diagonal matrix I_k one can consider the groupings according to the law of associativity:

$$(\tilde{Y} \cdot I_a \cdot I_k) \cdot Y \tag{6}$$

$$(\tilde{Y} \cdot I_a) \cdot (I_k \cdot Y) \tag{7}$$

If we consider the view expressed in (6) one has to perform the linear algebra over the field $\mathbb{Q}(k_1, \ldots, k_m)$ but having only the $x_1, \ldots, x_n$ as variables in subsequent steps. When considering the $k_1, \ldots, k_m$ as part of the monomials, i.e. taking the view expressed in (7) the linear algebra is over $\mathbb{Q}$ but the $k_1, \ldots, k_m$ are have to be counted as variables in addition to the $x_1, \ldots, x_n$. Notice that the latter view is used by Clarke [26].

Using both approaches we find that some if the F_i $(1 \leq i \leq 20)$ are zero, and hence the system does not have a solution with all non-zero entries.

When inspecting more closely which entries are zero, we find that—taking $k_1, \ldots, k_{20}$ as parameter— the $Y_3, Y_4, Y_5, Y_{10}, Y_{11}, Y_{12}, Y_{13}, Y_{16}$ are zero when expressed as linear combinations of the Z_j. When viewing the reaction constants as part of the monomials we obtain that $Y_3, Y_4, Y_5, Y_{10}, Y_{11}, Y_{13}, Y_{19}$ are zero. When resolving these condition in terms of the x_i (and k_i) we obtain in the k-as-parameter-case the logical condition

$$x_3 = 0 \wedge x_4 = 0 \wedge x_5 = 0 \wedge x_{10} = 0 \wedge x_{12} = 0 \wedge 1 = 0 \tag{8}$$

and in the k-in-monomial-case

$$k_8 \cdot x_3 = 0 \wedge k_5 \cdot x_4 = 0 \wedge k_1 \cdot x_5 = 0 \wedge k_{12} \cdot x_{10} = 0 \wedge k_0 \cdot x_{12} = 0 \wedge k_7 \cdot x_5 = 0 \wedge k_2 \cdot x_4 = 0 \wedge k_{11} = 0 \tag{9}$$

Hence there are no solutions unless $k_{11} = 0$, which is a condition leading to the inconsistency $1 = 0$ in (8)—without any further information in the k-as-parameter-case. When going back to the original description using the software infrastructure described in [27] we obtain the information that associated with constant k_{11} there is a creation of $\longrightarrow$ damDNA from "the environment"; moreover, associated with k_{12} there is a reaction denoted damDNA $\longrightarrow$ Sink. So there are some quasi-steady states involved in the SBML representation of the reaction system. Dealing rigorously with quasi-steady state approximations is an important line of research in algebraic biology (see e.g. [28]).

When considering solutions of polynomial systems we can apply the substitutions $k_{11} = 0, x_3 = 0, x_4 = 0, x_5 = 0, x_{10} = 0, x_{12} = 0$ and consider the resulting system.

Example BIOMOD053 As another example we take the model #53 from the BIOMOD database.

The chemical reaction network involves 6 species and has deficiency 2. The resulting polynomial system is as follows:

$$-k_1x_1x_2 + k_2x_3 - k_5x_1, -k_1x_1x_2 + k_2x_3 - k_7x_2x_5 + k_{10},$$
$$k_1x_1x_2 - k_2x_3 - k_3x_3 + k_4x_4 - k_9x_3 - k_{12}x_3, k_3x_3 - k_4x_4 - k_6x_4,$$
$$k_5x_1 - k_7x_2x_5 - k_8x_5 + k_{11}, k_6x_4 + k_7x_2x_5 + k_9x_3$$

Our simple prototype implementation of our algorithms using the computational infrastructure of Maple can easily determine that the system has a solution with all-non-zero entries. Our algorithm can come up with a explicit representation of the solution after some minutes of computation time. The string representation of the output is big (about 1 MB). However, the big output size is mainly due to rather lengthy polynomial expressions in the parameters occurring in the solutions. The structure of the solutions in the symbols representing a "can be chosen arbitrarily" in the methods presented above (cf. Sect. 2) is much simpler.

5 Conclusion and future work

Although several related ideas have been around in the literature on algebraic methods for chemical reaction systems the full algorithmic development given above seems to be new—in addition to providing the complexity analysis.

In contrast to the known theorems developed in the context of chemical reaction network theory—which only work in special cases but give results entirely independent of the parameters—our algorithms are universally applicable.

It will be the topic of future research to systematically apply careful implementations of the algorithms given in this paper to the networks given in databases such as BioModels database and others. For this purpose we will integrate the implementation of the algorithms described in this paper into the general infrastructure described in [27]. By these test we will not only explore the practical limits of the methods but we also might get insight into the question whether some of the properties that hold for deficiency-zero and deficiency-one systems (such as unique positive steady states for a chemical compatibility class, or the absolute concentration robustness property for a certain subclass) also hold for systems of deficiency bigger than one—at least parametrically for relevant ranges of parameters.

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