A Linear Algebra Approach for Detecting Binomiality of Steady State Ideals of Reversible Chemical Reaction Networks

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Abstract
Motivated by problems from Chemical Reaction Network Theory, we investigate whether steady state ideals of reversible reaction networks are generated by binomials. We take an algebraic approach considering, besides concentrations of species, also rate constants as indeterminates. This allows us to represent the generators of a steady state ideal as sums of binomials, which yields a corresponding coefficient matrix. On these grounds we propose an efficient algorithm for detecting binomiality. That algorithm uses exclusively elementary column and row operations on the coefficient matrix. We prove asymptotic worst case upper bounds on the time complexity of our algorithm. Furthermore, we experimentally compare its performance with other existing methods.

1 Introduction

A chemical reaction is a reaction between two sets of chemical objects called chemical complexes. The objects that form a chemical complex are chemical species. A chemical reaction network is a set of chemical reactions. For example

\[ 2A + B \xrightarrow{k_{12}} C \xrightarrow{k_{23}} A. \]

is a chemical reaction network with two reversible reactions. \( A, B \) and \( C \) are place-holders for species and \( 2A + B, B, C \) and \( A \) are the complexes. As a concrete example let us restrict ourselves to the left reaction. If we let \( A = H_2, \)
\[ B = O_2 \text{ and } C = H_2O, \text{ and replace } C \text{ with } 2C, \text{ the left reaction will be the} \]
\[ \text{reaction of hydrogen and oxygen, which forms water.} \]

A kinetics of a chemical reaction network is an assignment of a rate function
to each reaction in the network. A kinetics for a chemical reaction network is
called mass-action if for each reaction in the chemical reaction network, the rate
of the reaction is proportional to a positive real number, which is called the rate
constant. In the example above \( k_{12}, k_{21}, k_{23}, k_{32} \) are the rate constants. In this
article we generally assume mass-action kinetics. We furthermore assume that
reactions are reversible, unless explicitly specified otherwise.

The change in the concentration of each species over time in a reaction can
be described via an autonomous ordinary differential equation. For instance,
consider the chemical reaction network above and let \( x_1, x_2, x_3 \) be the inde-
terminates representing the concentrations of the species \( A, B \) and \( C \). The
corresponding differential equations are

\[
\begin{align*}
\dot{x}_1 &= p_1, & p_1 &= -2k_{12}x_1^2x_2 + k_{21}x_3 - k_{32}x_1 + k_{23}x_3, \quad (1) \\
\dot{x}_2 &= p_2, & p_2 &= -2k_{12}x_2^2x_2 + k_{21}x_3, \quad (2) \\
\dot{x}_3 &= p_3, & p_3 &= 2k_{12}x_1^2x_2 - k_{21}x_3 + k_{32}x_1 - k_{23}x_3. \quad (3)
\end{align*}
\]

Each zero of the polynomials \( p_1, p_2, p_3 \) gives a concentration of species in
which the system is stable. The zeros of \( p_1, p_2, p_3 \) are called the steady
states of the chemical reaction network. Accordingly, the ideal \( \langle p_1, p_2, p_3 \rangle \subseteq \mathbb{Q}[k_{12}, k_{21}, k_{23}, k_{32}, x_1, x_2, x_3] \) is called the steady state ideal of the chemical re-
action network.

For a thorough introduction to chemical reaction network theory, we refer
to Feinberg’s Book [15] and his lecture notes [14]. We follow the notation of
Feinberg’s book in this article.

An ideal is called binomial if it is generated by a set of binomials. In
this article we investigate whether the steady state ideal of a given chem-
ical reaction network is binomial. We are interested in efficient algorithms
for testing binomiality. Consider the steady state ideal \( I = \langle p_1, p_2, p_3 \rangle \subseteq \mathbb{Q}[k_{12}, k_{21}, k_{23}, k_{32}, x_1, x_2, x_3] \) given by Equations (1)–(3). Since \( p_3 = -p_1 \), the
steady state ideal of the above chemical reaction network is

\[
I = \langle p_1, p_2 \rangle = (-2k_{12}x_1^2x_2 + k_{21}x_3 - k_{32}x_1 + k_{23}x_3, -k_{32}x_1 + k_{23}x_3). \quad (4)
\]

Reducing \( p_1 \) with respect to \( p_2 \), we have

\[
I = \langle -2k_{12}x_1^2x_2 + k_{21}x_3, -k_{32}x_1 + k_{23}x_3 \rangle, \quad (5)
\]

which shows that the ideal \( \langle 4 \rangle \) is binomial. In this article, we work over the ring
\( \mathbb{Q}[k_{ij}, x_1, \ldots, x_n] \) and investigate binomiality over this ring.

Note that in the literature there exist also slightly different notions of bino-
miality. Eisenbud and Sturmfels in [10] call an ideal binomial if it is generated
by polynomials with at most two terms. Following this definition, some au-
thors, e.g., Dickenstein et al. in [31] have considered the steady state ideal as an
ideal in the ring $\mathbb{Q}(k_{ij})[x_1, \ldots, x_n]$ and studied the binomiality of these ideals in $\mathbb{R}[x_1, \ldots, x_n]$ after specialising $k_{ij}$ with positive real values. Although certainly an interesting problem, this is beyond the scope of this article.

Binomial ideals and toric varieties are important concepts in mathematics, both from an algebraic and a geometric point of view. They also appear in many applications, in particular in the study of biological and chemical reactions, where our motivation to study binomiality comes from. Hence, efficient tests for binomiality of a given ideal, in particular the steady state ideal of a chemical reaction network, are of great importance.

Detecting binomiality of an ideal, particularly of a steady state ideal, is a difficult problem, both from a theoretical and a practical point of view. The problem is typically solved by computing a G"{o}bner basis, which is EXPSPACE-complete [27]. Recent linear algebra approaches for solving the problem in a different setting than our problem construct large matrices which also points at the difficulty of the problem [28, 6].

There is quite comprehensive literature on chemical reaction network theory. An excellent reference to this topic is [15, 14]. As mathematical concepts, binomiality and toricity have been widely studied and their properties have been investigated by various authors, e.g., Fulton [16], Sturmfels [33], Eisenbud et al. [10]. Binomiality and toricity show up quite often in chemical reaction networks. Binomiality in the case of detailed balancing of reversible chemical reactions has been studied by Gorban et al. [18, 19] and Grigoriev and Weber [23]. The principle of detailed balancing has a historic importance, used since 1872 by Boltzmann in his H-theorem [1], by Einstein in 1916 [9], by Wegscheider [34] and by Onsager in 1968 [29].

Feinberg [13] and Horn and Jackson [24] have studied toric dynamical systems, which are tightly related to the binomiality of steady state ideals. Gatermann et al. studied deformed toricity in [17]. Crauciu et al. have considered the toricity problem over the real numbers in [7] and have presented several interesting results in this regard. Dickenstein et al. have presented sufficient linear algebra conditions for binomiality of the steady state ideals in [28]. Their idea has been developed in [30], where the concept of MESSI reactions has been introduced. Conradi and Kahle have proved in [6] that for homogenous ideals, the sufficient condition of Dickenstein et al. is necessary as well and also introduced an algorithm for testing binomiality of homogenous ideals.

The main idea of this work is based on the following observation: The steady state ideal of a reversible chemical reaction should be binomial. This can be checked from the associated differential equations. Indeed the monomials occurring in the generators of the steady state ideal originate from the complexes
and the rate constants in a given chemical reaction network and the generators of the steady state ideal are sums of those monomials.

Having said that, our main idea is to consider the generators of the steady state ideal as sums of the binomials associated to the reactions rather than the monomials associated to the complexes. This is feasible for a reversible chemical reaction network. Following the above observation and assigning a binomial to each reaction, one can write the generators of the steady state ideal as sum of those binomials with integer coefficients.

Having this representation of the generators of the steady state ideal, one can test the binomiality exclusively using elementary row and column operations on the coefficient matrix of these binomials. This can be done by computing the Hermite normal form of the coefficient matrix, which yields an efficient method for testing binomiality.

Our main contributions in this article are the following.

1. We introduce a new representation of the generators of the steady state ideal of a reversible chemical reaction as a sum of certain binomials rather than monomials.

2. Using that representation, we assign a matrix with entries in \( \mathbb{Z} \) to a reversible chemical reaction network, such that the binomiality of the steady state ideal can be tested by computing the Hermite normal form of this matrix.

3. We prove a worst-case upper bound on the time complexity of our binomiality test. We experimentally compare our test with the existing binomiality tests in the literature, which demonstrates the applicability of our method.

Our representation of the steady state ideal as a sum of certain binomials, as well as the matrices associated to them are further original ideas presented in this paper. While typically complexe-species matrices are used for testing binomiality, we use reaction-species matrices for this purpose.

The plan of the article is as follows. Section 1 gives an introduction to the necessary concepts of chemical reaction network theory, reviews the literature and presents the idea of this work. Section 2 includes the main definitions and results. In this section we show our representation of the generators of the steady state ideal of a reversible chemical reaction network and present our algorithm for testing binomiality. In Section 3 we discuss the complexity of our method. We furthermore compare our algorithm with other existing algorithms in the literature via experiments. In Section 4 we summarize our results and draw some conclusions.

2 Testing Binomiality

2.1 Sum of Binomial Representation

Consider the following reversible reaction between two complexes \( C_1 \) and \( C_2 \).
Let \( m_i, i = 1, 2, \) be the product of the concentrations of the species in \( C_i \) with the appropriate powers and integer coefficients. We call \( m_i \) the monomial associated to \( C_i \). Also let \( x_1 \) be the concentration of a species that is in \( C_1 \) and is not in \( C_2 \). The differential equation describing the kinetics of this species is

\[
\dot{x}_1 = -k_{12}m_1 + k_{21}m_2.
\]

For a species in \( C_2 \) which is not in \( C_1 \) with the concentration \( x_2 \), the differential equation will be

\[
\dot{x}_2 = k_{12}m_1 - k_{21}m_2.
\]

For a species with concentration \( x_3 \) that appears in both \( C_1 \) and \( C_2 \) the differential equation will be \( \dot{x}_3 = c(k_{12}m_1 - k_{21}m_2) \), where \( c \in \mathbb{Z} \) is the difference between the times that the species appear in \( C_2 \) and \( C_1 \). Set \( b_{12} := -k_{12}m_1 + k_{21}m_2 \) and \( b_{21} := k_{12}m_1 - k_{21}m_2 \). The steady state ideal of the above chemical reaction network is \( \langle b_{12}, b_{21} \rangle \), which is equal to \( \langle b_{12} \rangle \), since \( b_{12} = -b_{21} \).

For a reversible reaction network with more than one reaction, one can associate a binomial of the form \( b_{ij} := k_{ij}m_i - k_{ji}m_j \) to each reaction. Then the polynomials generating the steady state ideal can be written as sum of \( b_{ij} \) with integer coefficients. We make this more precise in the following definition.

**Definition 1.** Let \( C \) be a reversible chemical reaction network with the complexes \( C_1, \ldots, C_s \), let \( k_{ij}, 1 \leq i \neq j \leq s \), be the rate of the reaction from \( C_i \) to \( C_j \), and let \( x_1, \ldots, x_n \) be the concentrations of the species. We call a monomial \( m_i \) the monomial associated to \( C_i \) if \( m_i \) is the product of those concentrations that appear in \( C_i \) with the coefficients of the species as the powers. Also \( b_{ij} := -k_{ij}m_i + k_{ji}m_j \) is called the binomial associated to the reaction from \( C_i \) to \( C_j \). If there is no reaction between \( C_i \) and \( C_j \), set \( b_{ij} = 0 \).

**Example 2.** Recall the following chemical reaction network from Section 1:

\[
2A + B \xrightarrow{\frac{k_{12}}{k_{21}}} C \xrightarrow{\frac{k_{23}}{k_{32}}} A.
\]

Following the notation in Section 1 let \( x_1, x_2, x_3 \) be the indeterminates for the concentrations of \( A, B \) and \( C \), respectively. The monomials associated to the complexes \( 2A + B, C \), and \( A \) are \( 2x_1^2x_2, x_3 \), and \( x_1 \), respectively. The binomials associated to the two reactions in this network are \( b_{12} = -2k_{12}x_1^2x_2 + k_{21}x_3, b_{23} = -k_{23}x_3 + k_{32}x_1 \). As there is no reaction between the first and third complexes we have \( b_{13} = b_{31} = 0 \). Also, by definition, \( b_{21} = -b_{12} \) and \( b_{32} = -b_{23} \). Using the binomials associated to the reactions, one can write the polynomials generating the steady state ideal as

\[
p_1 = b_{12} - b_{23}, \quad p_2 = b_{12}, \quad p_3 = -b_{12} + b_{23}.
\]

Hence, the steady state ideal can be written as

\[
\langle p_1, p_2, p_3 \rangle = \langle p_1, p_2 \rangle = \langle b_{12} - b_{23}, b_{12} \rangle.
\]
As Example 2 and the definition of the binomials $b_{ij}$ in Definition 1 suggests one can write the generators of the steady state ideal of every reversible chemical reaction networks as sum of $b_{ij}$ with integer coefficients, i.e.,

$$\dot{x}_k = p_k = \sum_{j=1}^{s} c^{(k)}_{ij} b_{ij},$$

for $k = 1 \ldots n$ and $c^{(k)}_{ij} \in \mathbb{Z}$.

For clarification, we may remind the reader that in this article we assume working over $\mathbb{Q}[k_{ij}, x_1, \ldots, x_n]$. This in particular is the case for Definition 1 and the discussion afterwards. In [31], the authors specialise $k_{ij}$ with positive real values, in which case, the steady state ideal may or may not be binomial over $\mathbb{R}[x_1, \ldots, x_n]$. Similarly, specialising $k_{ij}$ in Equation (12) can result in writing $p_k$ as sum of different binomials. In other words, the representation of $p_k$ as sum of binomials in [12] is not necessarily unique. This is illustrated in the following example.

**Example 3.** [31] Example 2.3] Let $C_1 = 2A$, $C_2 = 2B$ and $C_3 = A + B$. Consider the reversible chemical reaction network given by the following reactions:

\[
\begin{align*}
2A & \xrightarrow{k_{12}} 2B \\
2A & \xrightarrow{k_{13}} A + B \\
A + B & \xrightarrow{k_{32}} 2B.
\end{align*}
\]

Assuming $x_1$ and $x_2$ to be the concentrations of $A$ and $B$, respectively, by Definition 1

$$b_{12} = -2k_{12} x_1^2 + 2k_{21} x_2^2$$

(13)

$$b_{13} = -k_{13} x_1^2 + k_{31} x_1 x_2$$

(14)

$$b_{23} = k_{23} x_2^2 - k_{32} x_1 x_2.$$  

(15)

It can be checked that the generators of the steady state ideal can be written as

$$p_1 = b_{12} + b_{13} + b_{23}$$

(16)

$$p_2 = -b_{12} - b_{13} - b_{23}.$$  

(17)

If $k_{31} = k_{32}$ then $k_{31} x_1 x_2 = k_{32} x_1 x_2$, hence $k_{31} x_1 x_2$ will occur in $b_{13}$ and $b_{23}$ with opposite signs which will be cancelled out in $b_{13} + b_{23}$, resulting in writing $p_1$ as sum of $b_{12}$ and $-k_{13} x_1^2 + k_{23} x_2^2$. This is another way of writing $p_1$ as sum of binomials.

In order to make the representation in Equation (12) as sum of binomials $b_{ij}$ unique, one solution is to consider the rates, $k_{ij}$ as indeterminates, i.e., to work over the ring $\mathbb{Q}[k_{ij}, x_1, \ldots, x_n]$. This is where our idea of working over $\mathbb{Q}[k_{ij}, x_1, \ldots, x_n]$ comes from. Assuming that $k_{ij}$, $1 \leq i, j \leq s$ are indeterminates, they will be algebraically independent over $\mathbb{Q}[x_1, \ldots, x_n]$. Therefore for
monomials \( m_t \) and \( m_{t'} \) in \( \mathbb{Q}[x_1, \ldots, x_n] \) associated to two distinct complexes and for all \( 1 \leq i, j, i', j' \leq s, k_{ij}m_t \) and \( k_{i'j'}m_{t'} \) will be distinct monomials in \( \mathbb{Q}[k_{ij}, x_1, \ldots, x_n] \). Hence binomials \( b_{ij} \) associated to the reversible reactions are not only pairwise distinct, but also their monomials are pairwise distinct in \( \mathbb{Q}[k_{ij}, x_1, \ldots, x_n] \). This implies that the generators of the steady state ideal have unique representations in \( \mathbb{Q}[k_{ij}, x_1, \ldots, x_n] \) as sum of \( b_{ij} \) with integer coefficients. Summarising, we have the following.

**Remark 4.** Given a reversible chemical reaction network with the notation of Definition 1 if \( k_{ij} \) are indeterminates then the generators of the steady state ideal can be uniquely written as sum of the binomials presented in Equation 12.

**Remark 5.** Although \( k_{ij} \) and therefore \( b_{ij} \) depend on the chemical reaction network, one can easily check that, having fixed \( n, m \in \mathbb{N} \), reversible chemical reactions with \( m \) complexes and \( n \) species are in one-to-one correspondence with the sets of linear combinations of the binomials of the form \( k_{ij}m_i - k_{ji}m_j \) with integer coefficients, where \( m_i, m_j \) are monomials in \( \mathbb{Q}[x_1, \ldots, x_n] \).

Considering the parameters \( k_{ij} \) as indeterminates, if a steady state ideal is binomial in the ring \( \mathbb{Q}[k_{ij}, x_1, \ldots, x_n] \), then its elimination ideal is binomial in the ring \( \mathbb{Q}[x_1, \ldots, x_n] \). Indeed, the elimination of a binomial ideal is a binomial ideal. This can be seen from Corollary 1.3 in [10]. We remind the reader that the definition of binomiality in this article is different from [10]. In the latter, binomial ideals have binomial and monomial generators. However, restricting the definition of binomial ideal to the ideals with only binomial generators, the result in that article still holds. Therefore, if the steady state ideal of a chemical reaction network is binomial in \( \mathbb{Q}[k_{ij}, x_1, \ldots, x_n] \), then its elimination \( I \cap \mathbb{Q}[x_1, \ldots, x_n] \) is also a binomial ideal. Geometrically, the above discussion can be explained via projection. Given a chemical reaction network, assume that reaction rates \( k_{ij} \) are indeterminates and let the number of \( k_{ij} \) be \( t \). Let \( V \) denote the steady state variety, i.e., the variety of the steady state ideal. \( V \) is a Zariski closed subset of \( \mathbb{K}^{t+n} \), where \( \mathbb{K} \) is an appropriate field (e.g., \( \mathbb{C} \)). If \( V \) is a coset of a subgroup of the multiplicative group \( (\mathbb{K}^*)^{t+n} \), the projection of \( V \) into the space generated by \( x_1 \ldots, x_n \), i.e., \( V \cap (\mathbb{K}^*)^n \) is also a coset. In particular, the projection of a group is a group. Since the variety of a binomial ideal is a coset [21] [22], the projection of the variety of a binomial ideal is the variety of a binomial ideal. As special cases, the projection of a toric variety, a shifted toric variety and a binomial variety (defined in [21] [22]) is a toric, a shifted toric and a binomial variety, respectively. For a detailed study of toricity of steady state varieties, we refer to [21].

We may mention that in [7], the authors have studied toric dynamical systems, where they have considered working over the ring \( \mathbb{Q}[k_{ij}, x_1, \ldots, x_n] \) and presented several interesting results. In particular, Theorem 7 in that article states that a chemical reaction network is toric if and only if the rates lie in the variety of a certain ideal in \( \mathbb{Q}[k_{ij}] \), called the moduli ideal.
2.2 The Algorithm

Definition 6. Let \( C \) be a reversible chemical reaction network as in Definition 1 and assume that the generators of its steady state ideal are written as the linear combination of the binomials associated to its reactions as in Equation 12, i.e.,

\[
p_k = \sum_{j=1}^{s} c_{ij}^{(k)} b_{ij} \quad \text{for} \quad k = 1, \ldots, n.
\]

We define the binomial coefficient matrix of \( C \) to be the matrix whose rows are labeled by \( p_1, \ldots, p_n \) and whose columns are labeled by non-zero \( b_{ij} \) and the entry in row \( p_k \) and column \( b_{ij} \) is \( c_{ij}^{(k)} \).

By the definition, the binomial coefficient matrix of a reversible chemical reaction network is the coefficient matrix of the binomials that occur in the representation of the generators of the steady state ideal as sum of binomials. As we consider \( k_{ij} \) indeterminates, the representation of the generators of the steady state ideal of a given complex is unique, which implies that the binomial coefficient matrix of a given complex is unique too.

Example 7. Consider the chemical reaction network in Example 2 with generators of the steady state ideal as follows.

\[
\begin{align*}
p_1 &= b_{12} - b_{23} \\
p_2 &= b_{12} \\
p_3 &= -b_{12} + b_{23}.
\end{align*}
\]

The binomial coefficient matrix of this chemical reaction network is

\[
M = \begin{pmatrix}
  b_{12} & b_{23} \\
  1 & -1 \\
  1 & 0 \\
-1 & 1
\end{pmatrix}.
\]

By definition, the entries of the binomial coefficient matrix of a reversible chemical reaction network are integers. For example, the binomial associated to the reaction

\[
4A \xrightarrow{k_{12}, k_{21}} A + B
\]

is \( b_{12} := -k_{12}x_1^4 + k_{21}x_1x_2 \), where \( x_1 \) is the concentration of \( A \) and \( x_2 \) is the concentration of \( B \). The steady state ideal is generated by \( \{3b, -b\} \), and the binomial coefficient matrix for this network is \( \begin{pmatrix} 3 \\ -1 \end{pmatrix} \).

One can test binomiality of a steady state ideal using the binomial matrix.

Theorem 8. If we assume that the rate constants \( k_{ij} \) in a reversible chemical reaction network are indeterminates, then its steady state ideal is binomial if and only if the Hermite normal form of its binomial coefficient matrix has at most one non-zero entry at each row.
Proof. Let $G = \{p_1, \ldots, p_n\} \subseteq \mathbb{Q}[k_{ij}, x_1, \ldots, x_n]$ be a generating set for the steady state ideal of a given reversible chemical reaction network $C$, and let \( \{b_{ij} \mid 1 \leq i \neq j \leq s\} \) be the ordered set of non-zero binomials associated to the reactions. Fix a term order on the monomials in $\mathbb{Q}[k_{ij}, x_1, \ldots, x_n]$.

First we prove that if the Hermite normal form of the binomial coefficient matrix has at most one non-zero entry at each row, then the steady state ideal is binomial. The proof of this side of the proposition comes from the definition of Hermite normal form. In fact, the Hermite normal form of the binomial coefficient matrix of $C$ can be computed by row reduction in that matrix, which is equivalent to the reduction of the generators of the steady state ideal with respect to each other. Therefore, computing the Hermite normal form of the binomial coefficient matrix and multiplying it with the vector of binomials $b_{ij}$, one can obtain another basis for the steady state ideal. Having this, if the Hermite normal form has at most one non-zero entry at each row, then the new basis for the steady state ideal will only include $b_{ij}$. Therefore the steady state ideal will be binomial.

Now we prove the “only if” part of the proposition, that is, if the steady state ideal of $C$ is binomial, then the Hermite normal form of the binomial coefficient matrix has at most one non-zero entry at each row. We claim that for each pair of polynomials $p_t, p_m \in G$, $p_t$ is reducible with respect to $p_m$ if and only if there exists a binomial $b_{ij}$ that occurs in both $p_t$ and $p_m$ and includes their leading terms. The “only if” part of the claim is obvious. To prove the “if” part of the claim, let $p_m$ be reducible with respect to $p_t$. Then the leading term of $p_m$ divides the leading term of $p_t$. Since the leading terms are multiples of $k_{ij}$ and these are disjoint indeterminates, this is only possible if both of the leading terms are equal. If the leading terms are equal, then $b_{ij}$ in which the leading terms occur, must itself occur in both $p_t$ and $p_m$. Therefore $p_t$ and $p_m$ share a binomial associated to a reaction, which is in contradiction with our assumption.

From the above claim and the definition of the Hermite normal form one can see that $p_1, \ldots, p_n$ are pairwise irreducible if and only if the binomial coefficient matrix of $C$ is in Hermite normal form.

Now we prove that $p_1, \ldots, p_n$ are pairwise irreducible if and only if they form a Gröbner basis in which polynomials are pairwise irreducible. Note that this does not necessarily imply that $G$ is a reduced Gröbner basis, as $p_i$ are not necessarily monic. Assume that $p_1, \ldots, p_n$ are pairwise irreducible. We prove that the greatest common divisor of each pair of the leading terms of the $p_1, \ldots, p_n$ is 1. By contradiction, assume that there exists a monomial not equal to 1 which divides the leading terms of both $p_t, p_m$, for $1 \leq t, m \leq n$. Then there exists a variable $x_l$ such that $x_l$ divides the leading terms of $p_t$ and $p_m$. Since each leading term is the monomial associated to a complex, the species with concentration $x_l$ occurs in two complexes with associated monomials as the leading terms of $p_t$ and $p_m$. Then both $p_t$ and $p_m$ have as their summand the binomials that are associated to the reactions including those complexes. As for each complex there exists at least one binomial associated, both $p_m$ and $p_t$ have as a summand one common binomial $b_{ij}$. However, we had already
Algorithm 1: Binomiality Test Over \( \mathbb{Q}[k_{ij}, x_1, \ldots, x_n] \)

Function BinomialityTest(\( C \))

\textbf{Input}: \( C = \{(m_1, \ldots, m_s) \in [X]^n, k_{ij}\} \)

\textbf{Output}: Binomial or NotBinomial

\begin{align*}
1 & b_{ij} := -k_{ij}m_i + k_{ji}m_j, 1 \leq i \neq j \leq m \\
2 & B := (b_{ij}, 1 \leq i \neq j \leq m) \\
3 & p_k := \sum c_{ij}^k b_{ij}, 1 \leq k \leq n \\
4 & M := \text{Matrix}(c_{ij}^k) \\
5 & \tilde{M} = \text{HermiteNormalForm}(M) \\
6 & G := \tilde{M}B \\
7 & \textbf{if IsBinomial}(G) \textbf{ then} \\
8 & \quad R := \text{Binomial} \\
9 & \textbf{else} \\
10 & \quad R := \text{NotBinomial} \\
11 & \textbf{return} R
\end{align*}

proved that this implies that \( p_t \) and \( p_m \) are not pairwise irreducible, which is a contradiction to the assumption that the greatest common divisor of the leading terms of \( p_t \) and \( p_m \) is not 1. Now by Buchberger’s first criterion if the greatest common divisor of the leading terms of each pair of polynomials in \( G \) is 1 then \( G \) is a Gröbner basis. The other side of this claim is obvious.

From what we have proved until now, we can conclude that the binomial coefficient matrix of \( C \) is in Hermite normal form if and only if \( G \) is a Gröbner basis with pairwise irreducible elements. On the other hand, by a result of Eisenbud and Sturmfels [10], the steady state ideal of \( C \) is binomial if and only if every Gröbner basis of it includes binomials. Therefore we conclude that the steady state ideal is binomial if and only if the Hermite normal form of the binomial coefficient matrix has at most one non-zero entry in each row.

**Example 9.** Following Example [7], one can easily see that the Hermite normal form of the binomial coefficient matrix [21] is

\[
M = \begin{pmatrix}
  b_{12} & b_{23} \\
  1 & 0 \\
  0 & 1 \\
  0 & 0
\end{pmatrix},
\]

which means that the ideal is binomial and generated by \( \{b_{12}, b_{23}\} \).

Theorem [8] yields Algorithm [1] for testing binomiality. The input of the algorithm is a reversible chemical reaction network, given by the vector of monomials associated to its complexes, \( (m_1, \ldots, m_s) \), and the rates \( k_{ij} \). It uses a function IsBinomial which takes a set of polynomials and checks if all of them are binomial.
Example 10 (Models 491 and 492, BioModels Repository[1]). These biomodels are reversible. Biomodel 491 has 52 species and 86 reactions. Our binomial coefficient matrix of this biomodel has size $52 \times 86$ and has $\pm 1$ entries. A Hermite normal form computation quickly reveals that it is binomial over $\mathbb{Q}[k_{ij}, x_1, \ldots, x_{52}]$. BioModel 492 has also 52 species, and includes 88 reactions. Our binomial coefficient matrix has entries $\pm 1$ and is of size $52 \times 88$. This biomodel is also binomial. These are consistent with the computations in [21, Table 3], which show the group structure of the steady state varieties of the models.

Generalisation to Non-Reversible Networks The binomiality test via the binomial coefficient matrix for a reversible chemical reaction network can be generalised into an arbitrary chemical reaction network. In order to do so, partition the chemical reaction network into reversible and non-reversible reactions. For each reversible reaction, assign a binomial of the form $b_{ij}$ as in Definition 1. To each irreversible reaction, assign the monomial associated to the reactant multiplied by the reaction rate. Then one can write the generators of the steady state ideal as sum of the binomials $b_{ij}$ and monomials assigned to the irreversible reactions.

Now consider the coefficient matrix of the above sum, in which the columns are labeled by those binomials and monomials associated to the reactions. Divide this matrix into two blocks, one for the reversible reactions (call it binomial block) and another one for the irreversible ones (call it monomial block). Using elementary row operations, convert the binomial block into a Hermite normal form. If all the rows of the matrix have at most one non-zero entry, then the steady state ideal is binomial. Otherwise, one can consider computing the Hermite normal form of this matrix as a preprocessing step and run another method, e.g., Gröbner bases for testing binomiality.

Notice that arguments above require that the $k_{ij}$ are indeterminates, as it is the case with our framework here. This makes rates distinct, which implies that the monomials coming from irreversible reactions do not show up in the binomials associated to the reversible reactions. So the polynomials of the steady state ideal can be uniquely represented as sum of certain binomials and monomials.

3 Complexity & Comparisons

Proposition 11. Let $r$ be the number of reactions and $n$ be the number of species of a reversible chemical reaction network $\mathcal{C}$. The asymptotic worst case time complexity of testing binomiality of the steady state ideal of $\mathcal{C}$ via Algorithm 2 can be bounded by $O(\max(r, n)^\omega)$ where $\omega \approx 2.3737$, which is also the complexity of matrix multiplication.

Proof. The operations in steps 1–4 and 7–11 are at most linear in terms of $r$ and $n$. Since $M$ is a matrix of size $n \times r$, where $r = |b_{ij}|$, and $B$ is a vector of size $r$,
computing Hermite normal form in step 5 and also the matrix multiplication in step 6 will cost at most $O(\max(r, n)^\omega)$. Therefore the total number of operations in the algorithm can be bounded by $O(\max(r, n)^\omega)$.

In [21, Section 4] it has been shown that there exists an exponential asymptotic worst case upper bound on the time complexity of testing toricity. An immediate consequence of that result is that the time complexity of testing binomiality can be bounded by the same exponential function. Following the arguments in [21], one can show that there exists an algorithm for testing binomiality over $\mathbb{Q}[k_{ij}, x_1, \ldots, x_n]$ and $\mathbb{Q}[x_1, \ldots, x_n]$ simultaneously, with an exponential upper bound for the worst case time complexity.

As mentioned earlier in Section 2, a result of Eisenbud and Sturmfels in [10], with a slightly different definition of binomial ideals, states that the reduced Gröbner basis of a binomial ideal, with respect to every term order, includes only binomials. Following this result, a typical method for testing binomiality is via computing a reduced Gröbner basis. This result can be used for computing a Gröbner basis $G$ of a steady state ideal $I$. If we consider $I \subseteq \mathbb{Q}[k_{ij}, x_1, \ldots, x_n]$ and choose an appropriate block term order, $G \cap \mathbb{Q}[x_1, \ldots, x_n]$ will be a Gröbner basis for the elimination ideal $I \cap \mathbb{Q}[x_1, \ldots, x_n]$. This argument can be useful for testing whether $I$ is binomial but the elimination ideal is not. The drawback of computing Gröbner bases is that this is EXPSPACE-complete [27]. So our algorithm is asymptotically considerably more efficient than Gröbner basis computation.

Dickenstein et al. in [28] have proposed a method for testing toricity of a chemical reaction network. The definitions and purpose of that work are slightly different from our article, hence comparisons between those two methods should be treated with caution. While we focus on binomiality of the steady state ideals of reversible reaction networks in $\mathbb{Q}[k_{ij}, x_1, \ldots, x_n]$ with the aim of efficiency of the computations, the authors of the above article are interested in algebraic dependencies between $k_{ij}$ such that the elimination ideal is binomial. Having mentioned that, our method leads to the computation of Hermite normal form of a matrix of size $n \times r$ with integer entries which is polynomial time, while Theorem 3.3. in [28] requires constructing a matrix of size $n \times s$ with entries from $\mathbb{Z}[k_{ij}]$ and finding a particular partition of its kernel.

Considering Example 2.3 in [31], our algorithm constructs the matrix $M$ and its Hermite normal form $\tilde{M}$:

$$M = \begin{pmatrix} 1 & 1 & 1 \\ -1 & -1 & -1 \end{pmatrix}, \quad \tilde{M} = \begin{pmatrix} 1 & 1 & 1 \\ 0 & 0 & 0 \end{pmatrix},$$

and we see that the steady state ideal is not binomial over $\mathbb{Q}[k_{ij}, x_1, \ldots, x_n]$. The method in [31] constructs

$$\begin{pmatrix} -2k_{12} - k_{13} & 2k_{21} + k_{23} & k_{31} - k_{32} \\ 2k_{12} + k_{13} & -2k_{21} - k_{23} & -k_{31} + k_{32} \end{pmatrix},$$

and finds an appropriate partition, which shows that the steady state ideal is binomial in $\mathbb{Q}[x_1, \ldots, x_n]$ if and only if $k_{31} = k_{32}$. As a larger example, consider...
the chemical reaction network given in Example 3.13 in [31] and assume that it is a reversible chemical reaction network. Our method constructs a matrix with entries $\pm 1$ of size $9 \times 8$ and computes its Hermite normal form (in this case reduced row echelon form, as entries are $\pm 1$). The method described in [31] leads to a $9 \times 10$ matrix with entries as linear polynomials in $\mathbb{Z}[k_{ij}]$ and computes a particular partition of the kernel of the matrix.

For homogeneous ideals, Conradi and Kahle have shown in [6] that the sufficient condition for binomiality in [31] is necessary, too. Their Algorithm 3.3 tests binomiality of a homogenous ideal, which can be generalized by homogenising. The algorithm computes a basis for the ideal degree by degree and performs reductions with respect to the computed basis elements at each degree step. Since our algorithm is intended for steady state ideals of reversible chemical reaction networks, which are not necessarily homogenous, our following comparison with the Conradi–Kahle algorithm bears a risk of being biased by homogenization. We discuss the execution of both algorithms on Example 3.15 in [31]. This chemical reaction network does not satisfy the sufficient condition presented in [31, Theorem 3.3]. Testing this condition leads to the construction of a $9 \times 13$ matrix with entries in $\mathbb{Z}[k_{ij}]$, followed by further computations, including finding a particular partition of its kernel. Theorem 3.19 in [31] is a generalisation of Theorem 3.3 there, which can test binomiality of this example by adding further rows and columns to the matrix. Conradi and Kahle also treat this example with their algorithm. This requires the construction of a coefficient matrix of size $9 \times 13$ with entries in $\mathbb{Z}[k_{ij}]$ and certain row reductions. If we add reactions so that the reaction network becomes reversible, our algorithm will construct a matrix of size $9 \times 9$ with entries $\pm 1$ and compute its Hermite normal form to test binomiality in $\mathbb{Q}[k_{ij}, x_1, \ldots, x_9]$.

4 Conclusions

Binomiality of steady state ideals is an interesting problem in chemical reaction network theory. It has a rich history and literature and is still an active research area. For instance, recently MESSI systems have been introduced [30] following the authors’ work on binomiality of a system. Finding binomiality and toricity is computationally hard from both a theoretical and a practical point of view. It typically involves computations of Gröbner bases, which is EXPSPACE-complete.

In recent work [21] we investigated toricity of steady state varieties and gave efficient algorithms. In particular, we experimentally investigated toricity of biological models systematically via quantifier elimination. Besides that, we presented exponential theoretical bounds on the toricity problem. The current article, restricting to reversible reaction networks, aims at an efficient linear algebra approach to the problem of binomiality, which can be considered as a special case of the toricity problem.

In that course, considering rates as indeterminates, we assign a unique binomial to each reaction and construct the coefficient matrix with respect to these
binomials. Our algorithm proposed here computes a Hermite normal form of this matrix in order to detect binomiality. The algorithm is quite efficient, as it constructs comparatively small matrices whose entries are integers. It is a polynomial time algorithm in terms of the number of species and reactions. While other existing methods for testing binomiality have different settings and purposes than our algorithm, for the common cases, our algorithm has advantages in terms of efficiency. One possible drawback of our work is the technical assumption of considering the rates as indeterminates. On the other hand, this allows to overcome the limitation to reversible networks.

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