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Solving polynomial equations for chemical problems using Gröbner bases

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We explain the Gröbner basis method for solving simultaneous polynomial equations in several variables and describe some applications to chemical kinetics, stereochemistry, compartmental analysis and other chemical topics.

1. Introduction

Chemists solve millions of sets of simultaneous linear equations each year, using powerful software resources that have been developed with the support of the extensive literature of linear algebra. Solving a set of polynomial equations in several variables with integer exponents is a more difficult problem that has been tackled by iterative numerical methods most often in the past. The analytical and mixed numerical/analytical solution of polynomial systems using Gröbner basis methods and other classical and modern elimination methods supported by software systems such as MAPLE and MATHEMATICA has started to find use in several fields. Work that has been reported in chemistry, chemical physics and chemical biology includes

(1) stereochemistry, conformational analysis and protein folding [1–7],
(2) enzyme kinetics [8–14],
(3) compartmental analysis and global identifiability in metabolic systems [15–20],
(4) identifiability in molecular spectroscopy [21],
(5) small molecule and polymerization kinetics [22, 23],
(6) electronic structure [24],
(7) thermodynamics [25],
(8) visualization of crystal structures [26, 27],
(9) nonlinear optics, electronic properties of nanosystems and other chemical problems that involve systems of nonlinear differential equations [28–30],
(10) statistical studies of biological sequence analysis and evolutionary trees [31–33].

The method of 'Gröbner bases' based on a theory developed by Buchberger to handle a much larger class of problems, in his 1965 PhD thesis published in [34], lets users determine

(1) whether solutions of a polynomial system exist,
(2) their multiplicity, when they do exist, and
(3) a set of polynomials with the same roots that are easier to solve.

The literature of Gröbner bases is considerable. A recent major overview [35] discusses both theory and applications. It provides an extensive bibliography and includes the English translation of [34].

For a simple example of a Gröbner basis calculation, suppose that a piece of equipment must be installed in a rectangular box that has a capacity of 6 cm^3, a surface area of 22 cm^2 and a total edge length of 24 cm, because of some scenario involving the radiation or absorption or catalytic properties of the surfaces and edges. How long are the edges? Call the edge lengths x, y, z. The geometrical conditions are expressed directly by

$$xyz = 6, \quad 2xy + 2yz + 2zx = 22\,, \quad 4x + 4y + 4z = 24. \tag{1}$$

We work with the polynomials that are formed by the transpositions which make each right-hand side zero.

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$$xyz - 6 = 0, \quad 2xy + 2yz + 2zx - 22 = 0, \\ 4x + 4y + 4z - 24 = 0. \tag{2}$$

The Gröbner basis for the problem in hand is just the triangular system

$$x + y + z - 6, \quad y^2 + yz - 6y + z^2 - 6z + 11, \\ z^3 - 6z^2 + 11z - 6, \tag{3}$$

when some simple conventions are applied to select a unique set from the infinite number of sets that are possible. These conventions are explained in section 5. They are needed, for example, because scaling all the polynomials uniformly leaves the roots unchanged. The implicit use of these rules lets us say 'the' instead of 'a' Gröbner base in the discussion of the examples throughout the paper.

The third of the polynomials in equation (3) factors to $(z-1)(z-2)(z-3)$. Substituting the root $z = 1$ in the second polynomial gives $y^2 - 5y + 6$. This factors to $(y-2)(y-3)$. Substituting the roots $z = 1$, $y = 2$, in the first polynomial gives $(y - 3)$. So $x = 1$, $y = 2$, $z = 3$ is a solution of the original equations and, by symmetry, so are (x, y, z) set to all permutations of 1, 2, 3.

Several computer algebra systems include commands that implement Buchberger's algorithm and subsequent refinements to perform the conversion. For example,

$$\texttt{GroebnerBasis}[\{\texttt{xyz} - 6, 2\texttt{xy} + 2\texttt{yz} + 2\texttt{zx} - 22, \\ 4\texttt{x} + 4\texttt{y} + 4\texttt{z} - 24\}, \texttt{x}, \texttt{y}, \texttt{z}\}]. \tag{4}$$

in MATHEMATICA. The list $\{\texttt{x}, \texttt{y}, \texttt{x}\}$ that comprises the second argument of the GroebnerBasis expression identifies the variables and the priority with which these are eliminated. Using $\{\texttt{z}, \texttt{y}, \texttt{x}\}$ gives a Gröbner basis with z and x interchanged, relative to equation (3).

> *Throughout this paper, the priority x, y, z is tacitly assumed.*

To some extent, the construction of Gröbner bases can be taken for granted as the algorithmic basis of 'black box' software. Chemists do need the empowerment of understanding the underlying principles and terminology, however, for several reasons besides intellectual curiosity.

(1) At times, an algorithm that has practical value can be based on the details of a problem that are known to the applications experts, where algorithms for the general problem are impractical. For example, Canny's work on the complexity of robot motion planning [36, 37] particularized Macaulay's classical treatment of resultants [38]. Recently, Coutsias *et al.* developed a very powerful algorithm for a linkage problem that is particularized to certain details of protein folding [1].
(2) Some applications of algebraic methods to chemical and biological problems are being reported in language that is unfamiliar to the overwhelming majority of natural scientists. Chemists need to be able to assess the benefits and transferability of this work and to use it when applicable.
(3) The methods of Gröbner bases have been extended via differential algebra to serve as powerful tools for the solution of systems of partial differential equations (PDEs) that occur in many areas of chemistry, chemical physics and chemical biology,
(4) The infrastructure of the methods reported here supports a growing body of work on algebraic and computational geometry and further mathematical topics that have potential application to the natural sciences.

The geometrical problems of chemistry, besides visualization, include

(1) linkage analysis in relation to the conformations of small molecules, proteins and transition states, and to biomolecular motors and tensegrity structures,
(2) shape matching in relation to the passage of molecules and particles through a variety of continuous media, channels and entrances, e.g. in diffusion, drug delivery and protein–ligand interaction, and to molecular aggregation,
(3) further visibility issues, i.e. whether the linear path between two points is obstructed in equipment design (e.g. baffles to reduce Rayleigh scattering in laser spectroscopy, discussed in the early and recent publications [39] and [40], respectively, and numerous papers between them), imaging and, perhaps, intramolecular obstruction of emission/reabsorbtion processes.

Multivariate polynomial equations thus merit increased attention in chemical research and education. Gröbner bases provide a powerful tool for dealing with these equations. Unfortunately, the explanations in many texts on computer algebra bring to mind the opening sentences of Lipkin's 1965 book *Lie Groups for Pedestrians* [41]:

> 'As a graduate student in experimental physics ... all attempts to follow a lecture course [on certain algebraic topics] resulted in a losing battle with characters, cosets, classes, invariant subgroups, normal divisors and assorted lemmas. It was impossible to learn all the definitions of new terms defined in one lecture and remember them until the next. The result was complete chaos. It was a great surprise to learn later on that (1) [the] techniques can be useful, (2) they can be learned without memorizing the large number of definitions and lemmas which frighten the uninitiated.'

In a recent talk to a group of algebraists, MPB pointed out that 'ring', 'field' and 'ideal' are part of the daily vocabulary of chemists for whom these words evoke images that are utterly disjoint from their algebraic usage. And whilst these terms are staples of most of the traditional explanations of Gröbner bases, they can be bypassed completely at the outset. Buchberger customized an account for practitioners of systems theory (see, e.g. [42, 43]). Here, we defer the precise definition that is needed in a rigorous development, and describe features which, whilst sufficient for present purposes, comprise only part of the sophisticated, wide ranging and difficult mathematical content and implications of Gröbner basis theory. We proceed via

(1) an explanation of the division of polynomials in several variables,
(2) the definition and calculation of certain 'S-polynomials'that simply generalize the expressions that are formed in the course of Gaussian elimination,
(3) the basic algorithm that Buchberger invented along with the S-polynomials,
(4) some simple operations to convert the output of this algorithm to canonical form,
(5) a summary of a few special cases and caveats,
(6) references to more rigorous accounts.

The Gröbner basis for the rectangular box example (and for many others) is simply a 'triangularized' set of polynomials that have the same set of roots as the input polynomials. A more spectacular example, reported by Levelt [44], begins with the polynomials

$$\begin{gathered} yz^3 + xy^2 - xz^2 - 3yz^2 + x^2 - xy + 2yz, \\ xy^3z + x^2y^2 - x^2z^2 - 3xyz^2 + z^4 + x^3 - x^2y \\ +2xyz - 3z^3 + y^2 + z^2, \\ y^2z^3 + z^5 + xy^3 - xyz^2 - 3y^2z^2 - 3z^4 + x^2y - xy^2 \\ +3y^2z + 2z^3 - 3z^2 + 2z. \end{gathered} \tag{5}$$

The Gröbner basis of these three polynomials consists of the very short triangular system

$$x^2 - xy, \quad y^2 - z^2, \quad z^3 - 3z^2 + 2z. \tag{6}$$

Hence (x, y, z) can take values:

$$\begin{gathered} (0,0,0),(0,1,1),(1,1,1),(0,\ -1,1),(-1,\ -1,1), \\ (0,2,2),(2,2,2),(0,\ -2,2),(-2,\ -2,2). \end{gathered} \tag{7}$$

Very few problems in the real world show such remarkable simplification and even when the Gröbner basis is triangular, its elements may be very long. Informally, the Gröbner basis of a set of polynomials P is another set of polynomials G that

(1) have the same set of common roots as the polynomials comprising P,
(2) satisfy a certain property involving the 'S-polynomials' mentioned above.

In the happiest of circumstances,

(1) G is triangular,
(2) the member that contains a single variable can be factored,
(3) so can the polynomials that result from the successive back substitutions.

Often, G is triangular, but some (or all) of the polynomials cannot be factored. Then, the roots must be approximated numerically. And if there are not enough equations, the Gröbner basis can be 'incompletely triangular' for example, giving a polynomial containing (u, v), a polynomial containing (u, v, w) and a polynomial containing (u, v, w, x) for a system containing variables (u, v, w, x). The Gröbner basis then leads to

(1) analytic expressions for (v, w, x) in terms of u, if the equations obtained by setting the constituent polynomials to zero are sufficiently simple, and
(2) to numerical approximation of the roots at points on a grid of (v, w, x) values that just requires the solution of polynomials in a single variable, otherwise.

The starting polynomials may contain symbolic constants and or coefficients. For example, the Gröbner basis with respect to variables $\{x, y, z\}$ of

$$xyz - a, \quad 2xy + 2yz + 2zx - b, \quad 4x + 4y + z - c \quad (8)$$

is

$$z^3 - az^2 + bz - c, \quad y^2 - ay + z^2 + yz - az + b, \quad x + y + z - a. \quad (9)$$

Software to compute Gröbner bases distinguishes the variables from the other symbols by reference to the list of variables that is included in the arguments.

It must be noted that whilst a Gröbner basis may be triangular, the converse is not necessarily true. Conversely, some mathematicians are interested in applications of Gröbner bases that are not motivated by a need to solve simultaneous polynomial equations. In these circumstances, the Gröbner basis need not be triangular, even though it satisfies Buchberger's criterion involving the 'S-polynomials' that we describe later. Using the Gröbner basis methodology to solve polynomial equations has the advantage that Buchberger's algorithm and its refinements generate the Gröbner basis without fail, given enough computer time. Consequently, the method can get as close as possible to triangularization. Also, a triangular system that is not Gröbner basis can always be converted to one that is. Additionally a non-triangular Gröbner basis can always be triangularized. Natural scientists who deal with matrix problems should note that in the branch of algebra that gave rise to Gröbner basis theory, 'basis' does *not* mean what it does in linear algebra and eigenfunction theory.

2. Polynomial division

As a preliminary to the main discussion, which is quite novel to the Gröbner basis literature, and possibly shocking to some algebraists, we describe a non-standard way of handling a very commonplace problem—reducing

$$20x^3 + 21x^2 - 8x + 3$$

to a sum of Legendre polynomials. We do this to introduce the process of 'polynomial reduction'. Instead of using the orthogonality of the Legendre polynomials and integration, we proceed as follows.

(1) Divide the expression by $P_3(x) = 5x^3/2 - 3x/2$. The quotient is given by dividing the highest term in the dividend by the highest term in the divisor, that is dividing $20x^3$ by $5x^3/2$. This gives 8 and, because $8P_3(x) = 20x^3 - 12x$, the remainder is $21x^2 + 4x + 3$.
(2) Divide this remainder by $P_2(x) = 3x^2/2 - 1/2$. The new quotient is given by dividing $21x^2$ by $3x^2/2$. This gives 14 and, because $14P_2(x) = 21x^2 - 7$, the new remainder is $4x + 10$.
(3) Divide this remainder by $P_1(x) = x$. This gives a quotient of 4 and remainder 10.
(4) Divide this remainder by $P_0(x) = 1$. This gives a quotient of 10 and final remainder 0.

Hence

$$20x^3 + 21x^2 - 8x + 3 = 8P_3(x) + 14P_2(x) + 4P_1(x) + 10P_0(x). \quad (10)$$

Here, we regard ax^m to be divisible by bx^n when dealing with polynomials in x if $m \geq n$. Then, when dealing with multivariate polynomials in $x_1, x_2, \ldots$, we regard $ax_1^{m_1}x_2^{m_2} \ldots$ to be divisible by $bx_1^{n_1}x_2^{n_2} \ldots$ if the concatenation $(m_1, m_2, \ldots)$ follows $(n_1, n_2, \ldots)$ in odometer order, i.e. $m_1 > n_1$ or $m_1 = n_1$ and $m_2 > n_2$ or $\ldots$. The coefficient a/b in the quotient need not be cancellable.

Now consider the polynomials

$$\begin{aligned} f_1 &= 20xz^2 - 20xz + 5x + 4z^2 - 4z + 1, \\ f_2 &= 6yz - 15y - 2z + 5, \\ f_3 &= 840xyz - 420xy - 120xz + 60x - 840yz \\ &\quad + 420y + 120z - 60. \end{aligned} \quad (11)$$

These have been handpicked to produce a Gröbner basis that is concise and triangular. Also, the set of polynomials comprising equation (11) allows a concise demonstration that their input to a Gröbner basis computation produces a result with the requisite properties. This result can be computed by hand or using built-in functions of MAPLE, MATHEMATICA and other symbolic calculation software, that implement Buchberger's algorithm. Usually, these functions have names like `GroebnerBasis[]` with `{x, y, z}` as the list of variables. In the canonical form that we use, the basis consists of the three polynomials

$$\begin{aligned} g_1 &= -8z^3 + 28z^2 - 22z + 5, \\ g_2 &= -84y - 4z^2 + 4z + 27, \\ g_3 &= -20xz + 10x - 12z^2 + 32z - 13. \end{aligned} \quad (12)$$

Because we use `{x, y, z}` as the list of variables, each f_ℓ and g_ℓ is arranged so that concatenating the powers of x, y and z in successive terms gives a sequence of numbers that decrease from left to right, that is, 102, 101, 100, 002, 001, 000 for f_1, 011, 010, 001, 000 for $f_2, \ldots$,101, 100, 002, 001, 000 for g_3.

To show that the common roots of $\{f_1, f_2, f_3\}$ are the same as the common roots of $\{g_1, g_2, g_3\}$, we show that the f's are linear combinations of the g's. To write f_1 in terms of the g's, we follow the method described in [45] (see Algorithm 21.11) and in many other sources.

(1) Test if the leading term in f_1 is divisible by the leading term in g_1. These terms are $20xz^2$ and $-8x^2$, so the test fails.
(2) Test if the leading term in f_1 is divisible by the leading term in g_2. These terms are $20xz^2$ and $-84y$, so the test fails.
(3) Test if the leading term in f_1 is divisible by the leading term in g_3. These terms are $20xz^2$ and $-20xz$, so the test succeeds. The quotient of the terms is $-z$.
(4) Compute the remainder $r_1 = f_1 - (-z \times g_3)$. This is $-10xz + 5x - 12z^2 + 36z^2 - 17z + 1$.
(5) The leading term in this remainder is $-10xz$. It is not divisible by the leading term of g_1 or g_2, but it is divisible by the leading term of g_3. Hence the quotient 1/2 and the remainder $r_2 = r_1 - (1/2 \times g_3) = -12z^3 + 42z^2 - 33z + 15/2$.
(6) The leading term in this remainder r_2 is $-12z^3$. Division by the leading term of g_1 gives 3/2. The remainder $r_3 = r_2 - (3/2 \times g_1)$ is zero.

Hence, $f_1 = 3/2g_1 - (z + 1/2)g_3$. To summarize this process in tabular form, as shown in table 1, we use the names $d_1, d_2, \ldots$ for the successive dividends f_1, r_1, $r_2, \ldots$. If row k contains an entry v in the column headed g_ℓ, then $d_k = v \times g_\ell + d_{k+1}$. The reduction of f_2 is represented correspondingly as shown in table 2. Thus, $f_2 = 1/28g_1 + (-z/14 + 5/28)g_2$. The reduction of f_3 is represented correspondingly as shown in table 3. Thus, $f_3 = (5x - 11)g_1 + (-10xz + 5x + 10z - 5)g_2 + (4z - 10)g_3$. The reduction process summarized by the tables in this section is defined as follows. The relationship $d_k = v \times g_\ell + d_{k+1}$ is verbalized, d_k reduces to d_{k+1} modulo g_ℓ, and it is formalized $d_k \rightarrow_{g_\ell} d_{k+1}$. By extension, a polynomial f is said to reduce to h modulo $G = \{g_1, g_2, \ldots\}$ if f reduces to h via a succession of reductions modulo $g_\ell \in G$. Some further details are discussed in section 5.

Table 1.

		divisor		
k	d_k	g_1	g_2	g_3
1	$20xz^2 - 20xz + 5x + 4z^2 - 4z + 1$			$-z$
2	$-10xz + 5x - 12z^2 + 36z^2 - 17z + 1$			1/2
3	$-12z^3 + 42z^2 - 33z + 15/2$	3/2		
4	0			

Table 2.

		divisor		
k	d_k	g_1	g_2	g_3
1	$6yz - 15y - 2z + 5$		$-z/14$	
2	$-15y - 2z^3/7 + 2z^2/7 - z/14 + 5$		5/28	
3	$-2z^3/7 + z^2 + 11z/14 + 5/28$	1/28		
4	0			

3. S-polynomials

In using Gaussian elimination to solve the equations

$$f_1 = 2x + 3y - 5 = 0, \quad f_2 = x + y - 3 = 0\,, \qquad (13)$$

the combination $f_2 - 1/2 \times f_1 = -(y + 1)/2$ is a very simple example of an S-polynomial, which is written as $S(f_2, f_1)$. Correspondingly, in using elementary methods to solve

Table 3.

		divisor		
k	d_k	g_1	g_2	g_3
1	$840xyz - 420xy - 120xz + 60x - 840yz + 420y + 120z - 60$		$-10xz$	
2	$-420xy - 40xz^3 + 40xz^2 + 150xz + 60x + 840yz + 420y + 120z - 60$		$5x$	
3	$-40xz^3 + 60xz^2 + 130xz - 75x + 840yz + 420y + 120z - 60$	$5x$		
4	$-80xz^2 + 240xz + 100x - 840yz + 420y + 120z - 60$			$4z$
5	$200xz - 100x - 840yz - 420y + 48z^3 + 128z^2 + 172z - 60$			-10
6	$-840yz + 48z^3 - 248z^2 + 492z + 420y - 190$		$10z$	
7	$420y + 88z^3 - 288z^2 + 222z - 190$		-5	
8	$88z^3 - 308z^2 + 242z - 55$	-11		
9	0			

$$f_3 = x - 1 = 0, \quad f_4 = xy - 2 = 0, \tag{14}$$

the combination $y \times f_3 - f_4 = 2 - y$ is the S-polynomial $S(f_3, f_4)$. The S-polynomials $S_{i,j} = S(g_i, g_j)$ constructed from the (g_1, g_2, g_3) that comprise equation (12) illustrate the general form more strongly.

$$S_{12} = \frac{yz^3}{-8z^3} g_1 - \frac{yz^3}{-84y} g_2,$$

$$S_{23} = \frac{xyz}{-84y} g_2 - \frac{xyz}{-20xz} g_3,$$

$$S_{31} = \frac{xz^3}{-20xz} g_3 - \frac{xz^3}{-8z^3} g_1. \tag{15}$$

The numerator of each term in S_{12} is formed from the least common multiple (LCM) of the leading terms in g_1 and g_2 (i.e. $-8z^3$ and $-84y$) by dropping the coefficient, i.e. the factors that are free of x, y and z. The numerators in S_{23} are formed correspondingly from $-84y$ and $-20xz$, and in S_{31} from $-20xz$ and $-8z^3$. In general, given two polynomials (g_i, g_j), their S-polynomial is

$$\frac{M}{v_i} g_i - \frac{M}{v_j} g_j, \tag{16}$$

where v_ℓ is the leading term of g_ℓ and M is formed from the LCM of v_i and v_j by dropping the coefficient. As a result, the leading terms in the two parts of this expression are equal. The explicit S-polynomials for the problem in hand are

$$S_{12} = -\frac{7yz^2}{2} + \frac{11yz}{4} - \frac{5y}{8} - \frac{z^5}{21} + \frac{z^4}{21} + \frac{9z^3}{28},$$

$$S_{23} = \frac{xy}{2} + \frac{xz^3}{21} - \frac{xz^2}{21} - \frac{9xz}{28} - \frac{3yz^2}{5} + \frac{8yz}{5} - \frac{13y}{20},$$

$$S_{31} = xz^3 - \frac{xz^2}{2} - z^5 + \frac{41z^4}{10} - \frac{87z^3}{20} + \frac{51z^2}{40}. \tag{17}$$

> *The S-polynomials are of vital importance here because, for every pair of members of a Gröbner basis, their S-polynomial can be written as the sum of some or all the members of the basis, weighted by polynomials with rational coefficients.*

In other words, each S-polynomial can be reduced to zero by a succession of polynomial divisions by members of the basis, in the style of the preceding section. For example, the reduction of S_{12} corresponding to the basis equation (12) takes 7 steps: this is illustrated in table 4. Hence

Table 4.

k	d_k	divisor g_1	divisor g_2	divisor g_3
1	$-\frac{7yz^2}{2} + \frac{11yz}{4} - \frac{5y}{8} - \frac{z^5}{21} + \frac{z^4}{21} + \frac{9z^3}{28}$		$\frac{-z^2}{24}$	
2	$\frac{11yz}{4} - \frac{5y}{8} - \frac{z^5}{21} + \frac{3z^4}{14} + \frac{13z^3}{84} - \frac{9z^2}{8}$		$\frac{-11z}{336}$	
3	$-\frac{5y}{8} + \frac{z^5}{21} + \frac{3z^4}{14} + \frac{z^3}{42} - \frac{167z^2}{168} + \frac{99z}{112}$		$\frac{5}{672}$	
4	$-\frac{z^5}{21} + \frac{3z^4}{14} + \frac{z^3}{42} - \frac{27z^2}{28} + \frac{41z}{48} - \frac{45}{224}$	$\frac{z^2}{168}$		
5	$\frac{z^4}{21} + \frac{13z^3}{84} - \frac{167z^2}{168} + \frac{41z}{48} - \frac{45}{224}$	$\frac{-z}{168}$		
6	$\frac{9z^3}{28} - \frac{9z^3}{8} + \frac{99z}{112} - \frac{45}{224}$	$\frac{-9}{224}$		
7	0			

$$S_{12} = \left(\frac{z^2}{168} - \frac{z}{168} - \frac{9}{224}\right) g_1 + \left(\frac{z^2}{24} - \frac{11z}{336} + \frac{5}{672}\right) g_2. \tag{18}$$

The reduction of S_{23} takes 8 steps and gives

$$S_{23} = \left(-\frac{x}{168} + \frac{3z^2}{420} - \frac{2z}{105} + \frac{13}{1680}\right) g_2 + \left(-\frac{z^2}{420} + \frac{z}{420} + \frac{9}{560}\right) g_3. \tag{19}$$

The reduction of S_{31} takes 7 steps and gives

$$S_{31} = \left(-\frac{x}{8} + \frac{z^2}{8} - \frac{3z}{40} + \frac{13}{80}\right) g_1 + \left(-\frac{3z}{20} + \frac{1}{16}\right) g_3. \tag{20}$$

The details are given in Supplementary Material (BLDSC Supplementary Material no. 16161).

Another way of describing the property of the S-polynomials of a Gröbner basis is that they belong to the 'ideal' which the basis 'generates'. The Buchberger algorithm uses S-polynomials to extend the set of polynomials that needs solution into a kind of self-consistency in this respect. For present purposes, it is sufficient to describe the ideal generated by a set of multivariate polynomials $p_1, \ldots, p_n$ as the (much larger) set $q_1 p_1 + \cdots q_n p_n$, where $q_1, \ldots, q_n$ are polynomials in the same set of variables.

4. Finding the edge lengths of the box

By aiming for a basis that satisfies the S-polynomial condition defined earlier, Buchberger was able to construct an algorithm that leads inexorably to a triangular basis when this exists. The rectangular box example of section 1 provides a simple illustration.

4.1. *S-polynomials, round 1*

Begin with the three polynomials that need to be solved, i.e. the left-hand sides of the three items that comprise equation (2). Call these f_1, f_2, f_3. Compute the S-polynomials of f_1 with f_2, f_1 with f_3 and f_2 with f_3. Call these S_{12}, S_{13} and S_{23}. From the definition equation (16),

$$\begin{aligned} S_{12} &= \frac{xyz}{xyz}f_1 - \frac{xyz}{2xy}f_2 = -xz^2 - yz^2 + 11z - 6,\\ S_{13} &= \frac{xyz}{xyz}f_1 - \frac{xyz}{4x}f_3 = -y^2z - yz^2 + 6yz - 6,\\ S_{23} &= \frac{xy}{2xy}f_2 - \frac{xy}{4x}f_3 = xz - y^2 + 6y - 11. \end{aligned} \tag{21}$$

Next, compute the remainders that are left after reduction of S_{12}, S_{13} and S_{23} by $\{f_1, f_2, f_3\}$ as explained in section 2. Call the results f_4, f_5 and f_6. For the first of these reductions, the leading terms of S_{12}, f_1, f_2 and f_3 are $-xz^2$, xyz, $2xy$ and $4x$, respectively. Consequently, the leading term of S_{12} is not divisible by the leading term of f_1 or f_2, but it is divisible by the leading term of f_3. The quotient is $z^2/4$, leaving the remainder $z^3 - 6z^2 + 11z - 6$. This has the leading term z^3, which is not divisible by the leading terms of f_1, f_2 or f_3. Now test if *any* term of the remainder is divisible by the leading terms of f_1, f_2 or f_3. None is, so we call this remainder f_4 and retain it for the use described below.

Correspondingly, the leading term of S_{13} is $-y^2z$. This is not divisible by xyz or $2xy$ or $4x$. Neither is any later term of S_{13}, so the quotient is 0 and the remainder is the entirety of S_{13}. Give this the systematic name f_5 and retain it for later use.

Finally, for the present round, the leading term of S_{23} is xz. This is not divisible by the leading terms of f_1 or f_2 but division by the leading term of f_3 gives the quotient $z/4$. Hence the remainder is $-y^2 - yz + 6y - z^2 + 6z - 11$. The leading term $-y^2$ is not divisible by the leading terms of f_1, f_2 or f_3. Neither is any later term in this remainder of the division of S_{23} by f_3. Accordingly, call this remainder f_6.

4.2. *S-polynomials, round 2*

Construct the S-polynomials between all pairs of members of the list $\{f_1, \ldots, f_6\}$ which have not been formed already. Hence:

$$\begin{aligned} S_{14} &= 6xyz^2 - 11xyz + 6xy - 6z^2,\\ S_{15} &= -xyz^2 + 6xyz - 6x - 6y,\\ S_{16} &= -xyz^2 + 6xyz - xz^3 + 6xz^2 - 11xz - 6y,\\ S_{24} &= 6xyz^2 - 11xyz + 6xy + xz^4 + yz^4 - 11z^3,\\ S_{25} &= 6xyz - 6x + y^2z^2 - 11yz,\\ S_{26} &= 6xy - xz^2 + 6xz - 11x + y^2z - 11y,\\ S_{34} &= 6xz^2 - 11xz + 6x + yz^3 + z^4 - 6z^3,\\ S_{35} &= -xyz^2 + 6xyz - 6x + y^3z + y^2z^2 - 6y^2z,\\ S_{36} &= -xyz + 6xy - xz^2 + 6xz - 11x + y^3 + y^2z - 6y^2,\\ S_{45} &= -6y^2z^2 + 11y^2z - 6y^2 - yz^4 + 6yz^3 - 6z^2,\\ S_{46} &= -6y^2z^2 + 11y^2z - 6y^2 - yz^4 + 6yz^3\\ &\quad - z^5 + 6z^4 - 11z^3,\\ S_{56} &= -z^3 + 6z^2 - 11z + 6. \end{aligned} \tag{22}$$

Reduce all of these modulo $\{f_1, \ldots, f_6\}$. Each gives a zero remainder. For readers who would like to check, the 12 reductions show that

$$\begin{aligned} S_{14} &= (6z - 11)f_1 + 3f_2 - 3zf_3,\\ S_{15} &= (-z + 6)f_1 - 3/2f_3,\\ S_{16} &= (-z + 6)f_1 + (-z^3/4 + 3z^2/2 - 11z/4)f_3\\ &\quad + (y + z - 6)f_4,\\ S_{24} &= (6z - 11)f_1 + 3f_2 + (z^4/4 - 3z/2)f_3 - z^2f_4,\\ S_{25} &= 6f_1 - 3/2f_2 - yf_4 - zf_5,\\ S_{26} &= 3f_2 + (-z^2/2 - 11/4)f_3 + f_4 - f_5,\\ S_{34} &= (3/2 - 11z/4 + 3z^2/2)f_3 + (-6 + y + z)f_4,\\ S_{35} &= (6 - z)f_1 - 3/2f_3 - yf_5,\\ S_{36} &= -f_1 + 3f_2 + (-11/4 - z^2/4)f_3 + f_4 - yf_6,\\ S_{45} &= (6y - yz)f_4 + (-11 + 6z)f_5 + 6f_6,\\ S_{46} &= (6y - yz - z^2)f_4 + (-11 + 6z)f_5 + 6f_6,\\ S_{56} &= f_4. \end{aligned} \tag{23}$$

For readers who would like to follow the actual divisions, the successive divisors in the reduction of S_{14} are f_1, f_2, f_3. The same is true of S_{15}, S_{16} and S_{24}. In particular, the successive divisors and quotients in the reduction of S_{14} are (f_1, $6z$), (f_1, -11), (f_2, 3) and (f_3, $-3z$). For S_{25}, however, the succession is (f_5, $6z$), (f_5, -11), (f_6, 6), (f_4, $-yz$), (f_4, $6y$). Further details are given in the Supplementary Material.

Because the remainders of this second round are zero, the set of polynomials $\{f_1, \ldots, f_6\}$ constitute a Gröbner basis, albeit in a form that can be reduced still further, to obtain a uniquely defined 'reduced Gröbner basis' useful for some applications.

4.3. *Redundancy removal*

The set of polynomials $\{f_1, \ldots, f_6\}$

(1) has the same common roots as $f_1, \ldots, f_3$,
(2) includes redundant elements, which can be removed to leave a smaller set that has the same common roots and allows a complete construction of these with greater ease than from the polynomials with which we started.

The redundant members are characterized by a leading term that is divisible by the leading term of a non-redundant member. This redundancy criterion was part of Buchberger's original derivation. Specifically, f_3 is dropped because its leading term is xyz and the leading term of f_1 is $4x$. The polynomial f_2 is dropped because its leading term is $2xy$. This, too, is divisible by the leading term of f_1. The polynomial f_5 is dropped because its leading term is $-y^2z$ and the leading term of f_6 is $-y^2$. Hence the selection of $\{f_1, f_4, f_6\}$.

4.4. *Normalization*

After redundancies have been removed, each polynomial in the Gröbner basis which results is normalized by division by the coefficient in the leading term. Accordingly, for the rectangular box problem, f_1, f_4 and f_6 are divided by 4, 1 and -1. Hence the basis given earlier as equation (3).

5. Some further details and definitions

The rectangular box problem terminates after the second set of S-polynomials has been computed. A slightly longer example consists of the reduction of

$$f_1 = x^3 - 3x^2 - 2xy + 7x + 2y - 5,$$
$$f_2 = x^2y - 2x^2 - 2xy - 2y^2 + 5x + 9y - 11. \quad (24)$$

to the triangular form

$$g_5 = x - 2y^2 + 8y - 9,$$
$$g_6 = y^3 - 6y^2 + 12y - 8. \quad (25)$$

This takes 3 cycles and the number of polynomials in the basis swells from 2 to 7 before redundancies are removed. Details are given in the Supplementary Material. For both of these examples, we have followed the original algorithm designed by Buchberger. The process of computing S-polynomials and reducing these in alternation, which leads from an initial set of polynomials $\{f_1, \ldots, f_{n_1}\}$ to a final set $\{f_1, \ldots, f_{n_K}\}$ that allows no further reduction is stated formally in the Supplementary Material, too. It can be shown that

(1) the process terminates for some $k = K$,
(2) if the equations are consistent, then all the remainders in the final cycle are 0, and the initial set $\{f_1, \ldots, f_{n_1}\}$ and the final set $\{f_1, \ldots, f_{n_K}\}$ have the same set of the common roots,
(3) if the equations are inconsistent, i.e. there are no common roots, then one or more of the remainders in the final cycle is a number when the polynomials consist entirely of variables and numerical coefficients. If the initial polynomials contain symbolic coefficients then the inconsistent Gröbner basis may contain remainders that are polynomials in the parameters and are free of variables.

The inconsistent case is illustrated by the pair $\{x - 1, x - 2\}$ which gives the S-polynomial 1. This gives the quotient 0 and remainder 1 when divided by either $x - 1$ or $x - 2$.

Buchberger and many other authors have improved the basic algorithm to allow more efficient computation of Gröbner bases of polynomials in practical applications. For a recent summary see [46]. Variations in the algorithm can lead to slightly different Gröbner bases for the same problem that do, however, yield the same set of roots. For example, the MATHEMATICA statement equation (4) reverses the sign on the second and third polynomials relative to equation (3). Also, some variations of the algorithm converts the pair of polynomials, equation (24), to

$$h_1 = x + y^4 - 6y^3 + 10y^2 - 9,$$
$$h_2 = y^3 - 6y^2 + 12y - 8. \quad (26)$$

This characterizes a situation that is accommodated by the following final step to ensure a unique result. It uses a further detail of the reduction algorithm that was not needed in the earlier examples, because all of these ended with a zero remainder. Here, the leading term of h_1 is not divisible by the leading term of h_2, and conversely. However, the terms y^4 and $-6y^3$ in h_1 are divisible by y^3, the leading term in h_2. Accordingly, we move the term(s) preceding these in h_1, i.e. x, into a 'global' remainder, and divide the residue $y^4 - 6y^3 + 10y^2 - 9$ by h_2. This gives the quotient y and the local remainder $-2y^2 + 8y - 9$. None of the terms in this is divisible by y^3, so we add it to the interim global remainder, and accept the result

$$h_1 = yh_2 + r, \quad r = x - 2y^2 + 8y - 9 \quad (27)$$

as the final *reduced* basis comprising equation (25), where the polynomials have been renamed g_5 and g_6 for consistent style. This final reduction can go through several steps in more complicated examples.

The Gröbner basis of $f_1 = x + ay - 1$ and $f_2 = x + by - 1$ illustrates a problem of degeneracy that can occur when the polynomials contain symbolic coefficients (in this case a and b). Their Gröbner basis is $\{y, x - 1\}$. This implies the common roots $(x, y) = (1, 0)$. However, if $a = b$, then $f_1 = f_2$, the Gröbner basis is the one-element set $\{x + ay - 1\}$, and the common roots are $\{1 - ay, y\}$, where y ranges freely over all complex numbers. This kind of problem is called a specialization problem. It is discussed in [47]. Weispfenning introduced 'comprehensive Gröbner bases' to address it [48].

Earlier, we mentioned the possibility of triangular sets of polynomials that are not Gröbner bases. For example, referring to the g_1, g_2, g_3 in equation (12), consider the further polynomials

$$h_1 = g_1, \quad h_2 = g_2, \quad h_3 = g_3 + (y + z)g_2. \tag{28}$$

These are triangular. They have the same set of solutions as g_1, g_2, g_3 and, in consequence, f_1, f_2, f_3. The triple $\{h_1, h_2, h_3\}$ does not comprise a Gröbner basis, however, because the S-polynomial condition is not satisfied. In particular,

$$\begin{aligned} S(h_1, h_3) = &-6xy^2z^2 + 11xy^2z - 6xy^2 - xyz^4 + 6xyz^3 - xz^5 \\ &+ 6xz^4 - 12xz^3 - y^3z^3 - y^2z^4 + 6y^2z^3 - yz^5 \\ &+ 6yz^4 - 12yz^3 - z^4 + 6z^3. \end{aligned} \tag{29}$$

Reducing this modulo h_1, h_2, h_3 gives

$$S(h_1, h_3) = q_1h_1 + q_2h_2 + q_3h_3 + r, \tag{30}$$

where

$$\begin{aligned} q_1 &= -xyz + 6xy - xz^2 + 6xz - 12x - y^3, \\ q_2 &= -6xz^2 + 11xz - 6x - 6yz^2 + 11yz - 6y, \\ q_3 &= 0, \\ r &= -6xz^2 + 11xz - 6x - 6yz^2 + 11yz - 6y + 11z^2 - 6z. \end{aligned} \tag{31}$$

Since $r \neq 0$, the triple h_1, h_2, h_3 does not constitute a Gröbner basis. Application of the Buchberger algorithm to equation (31) does reduce it to a Gröbner basis.

Note, too, that given a set of polynomials f_i, it is possible to form a triangular Gröbner basis with common roots that are a superset of the common roots of the f_i. For example, the polynomial g_3 in equation (3), which factors to $(z - 1)(z - 2)(z - 3)$ can be replaced by g_3^2. This triple retains the Gröbner basis property. The common roots of f_1, f_2, f_3 are amongst the common roots of g_1, g_2, g_3, but the latter include each of these twice.

The final steps of the solution of the very simple pair of polynomials comprising equation (14) by the method of Gröbner bases fits into the overall scheme that has been described. Following the construction of $S(f_3, f_4) = y \times (x - 1) - 1 \times (xy - 2) = -y + 2$, reduction of this modulo $\{f_3, f_4\}$ leaves $f_5 = -y + 2$. Hence the extended list of polynomials $\{x - 1, xy - 2, -y + 2\}$. The second of these is removed because its leading term is divisible by the leading term of the first. Hence $\{x - 1, -y + 2\}$. Then normalization gives $\{x - 1, y - 2\}$. Correspondingly, for equation (14), $S(f_1, f_2) = 1/2 \times (2x + 3y - 5) - 1 \times (x + y - 3) = y/2 + 1/2$. Neither f_1 nor f_2 divides this, so the extended list of polynomials is $\{2x + 3y - 5, x + y - 3, y/2 + 1/2\}$. The leading term of the first divides the leading term of the second, which is removed accordingly. Hence $\{2x + 3y - 5, y/2 + 1/2\}$. Normalization gives $\{x + 3/2y - 5/2, y/2 + 1/2\}$ and the final reduction converts this to $\{x - 4, y + 1\}$. Solving three linear equations in $\{x, y, z\}$ becomes even more cumbersome, involving intermediate expressions that are nonlinear. However, the early formulation of the Buchberger algorithm in [34] does contain a branch that avoids nonlinear intermediates in this case, and follows Gaussian elimination closely.

To give an example of a non-triangular Gröbner basis, consider the polynomials $p_1 = x^2 + y^2 + z^2$ and $p_2 = yz + x$. Here, the terms are arranged in decreasing order of total exponent, with ties broken by the criterion used earlier. Then $\{p_1, p_2\}$ constitute a Gröbner basis, because the S-polynomial is $x^2yz/x^2p_1 - x^2yz/yzp_2 = yzp_1 - x^2p_2 = y^3z$. But the pair $\{p_1, p_2\}$ is not triangular. The 'total degree ordering' in this example is much more efficient than the 'lexicographic' ordering used elsewhere in this paper, when the objective is just to determine if a given polynomial can be reduced to zero by a Gröbner basis.

Heck [49] provides a very thorough account of Gröbner bases in the context of MAPLE programming, which takes a more conventional approach to the build up of terminology and conventions. Recent texts that discuss the underlying theory in a mathematical setting include [35, 45, 47, 50].

Buchberger has sent us the following definition. 'A Gröbner basis, with respect to a particular ordering of power products, is a set of polynomials $G = \{g_1, \ldots, g_m\}$ such that the leading power product [i.e. leading term with coefficient replaced by 1] of any polynomial f which can be written as $f = h_1 \cdot g_1 + \cdots + h_m \cdot g_m$ is a multiple of the leading power product in one or more of the polynomials in G.' A practical application usually starts with a set of polynomials $\{f_1, \ldots, f_n\}$ that is not a Gröbner basis and uses Buchberger's algorithm to convert this set to a Gröbner basis $\{g_1, \ldots, g_m\}$. A fundamental relationship between the initial polynomials and their Gröbner basis is that the set of all combinations $h_1 \cdot f_1 + \cdots + h_n \cdot f_n$ and the set of all combinations $h_1 \cdot g_1 + \cdots + h_m \cdot g_m$ are the same. Algebraists call this set the ideal generated by the polynomials $f_1, \ldots, f_n$, or equivalently by $g_1, \ldots, g_m$, as mentioned earlier. Also, Gröbner bases have an 'elimination property' which is stronger, for some purposes, than triangularization. It has many practical consequences, for example our present focus on the result that given a set F of polynomials and a corresponding Gröbner basis G, then the set of roots of F is equal to the set of roots of G, and the multiplicity (number of repetitions) of each root is the same in F and G.

The proofs of this elimination property are difficult and the original proof led to the characterizing property of S-polynomials that we have used, rather than proceeding from it. The proofs that many problems in algebraic geometry, invariant theory, statistics, discrete optimization, coding theory, systems theory, cryptography, theorem proving, summation and several other areas of mathematics can be reduced to the construction of Gröbner bases from given sets of polynomials are difficult, too.

6. Some chemical applications

6.1. *Stereochemistry and conformational analysis*

An important line of work on protein folding and ligand docking follows from the combined use of

(1) the treatment of an organic molecule as a linkage by Go and Scheraga [51],
(2) the Denavit–Hartenberg formulas for the inverse kinematics of robot limbs—see e.g. [52],
(3) Gröbner basis and resultant methods for solving the polynomial equations that describe ring closure, folding and docking.

Emiris and Mourrain [2] and Finn and Kavraki [3] provided early detailed overviews in relation to drug design. Manocha is continuing a substantial project in this area, following his early work [6, 7]. Coutsias *et al.* recently showed that 'Monte Carlo minimization is made severalfold more efficient (for an eight-residue loop) by employing the local moves generated by [a] loop closure algorithm' based on the inverse kinematic linkage approach [1]. They focused attention on the behaviour of a chain molecule that undergoes changes in the torsional angles of six backbone bonds that comprise three coterminal pairs. Their algorithm manipulates the torsion angles at three consecutive C_α atoms along a peptide backbone, in the simplest case. Earlier work of other authors dealt with this and several variants. The new work, however, covers models with arbitrary structures between the coterminal pairs. For loop closure models that allow variation in n torsion angles with $n > 6$, a heuristic method is used to search over $n - 6$ degrees of freedom. Then the analytic method is used to solve for the remaining 6 torsion angles. Possible extensions of this work are also described in [1]. A Fortran 95 routine that implements the algorithm can be downloaded from the web. The kinematic formulation and the solution of the polynomial equations by the method of resultants are included in the paper and comprise useful prototypes for further studies, including solution using Gröbner bases.

Computer algebraists have given considerable attention to showing that cyclohexane can exist in boat and chair forms. This originated in the PhD thesis of Oosterhoff on intramolecular electrostatic forces [53], and his subsequent paper with Hazebroek [54]. The monograph *Modern Computer Algebra* by von zur Gathen and Gerhard [45] devotes an entire section to this problem. The cyclic structure of C_6H_{12} together with the use of standard, uniform bond angles and uniform bond lengths leads to an overdetermined system of equations. The Gram determinant which expresses this is expanded to a set of algebraic equations that are polynomial in dot products of the vectors which describe the orientation of the bonds. Triangularization leads to a quadratic equation which implies two stable regions of the solution space. Heck also presents the problem on p. 699 of his text [49]. Levelt extends this approach to explore the stereochemistry of cycloheptane [4]. All of this work used Gröbner bases. Extending it succesfully to ring systems with the greater flexibility that occurs with 9 or more ring atoms would be of greater interest, and even more with a double bond in the ring.

Polynomial equations also occur in the treatment of stereochemical problems by classical linkage theory. In this regard, Lewis and Bridgett discuss conic tangency equations and Apollonius problems in biochemistry and pharmacology, although they use resultant methods to solve the equations [5].

Determining the number of possible conformations and, in particular, the possibility of stereochemical homogeneity, requires the determination of just the number of distinct roots or, at times, a lower bound, which affects the choice of algorithm.

6.2. *Reaction kinetics*

The study of chemical reaction mechanisms and the determination of rate and equilibrium constants give rise to multivariate polynomials in several ways.

6.2.1. *Pseudo steady state sequential enzyme reactions*

A method of refining rate constants using Gröbner bases is illustrated by a recent study of the three-step conversion of glucose and creatine to NADPH by Yildirim *et al.* [12]. They measured the amount of NADPH that was formed over the course of an *in vitro* experiment. The system of single step rate equations, given by the law of mass action, was coupled by the pseudo-steady assumption that v, the overall rate of formation of NADPH, was constant over short periods of time. The equations were structured as polynomial in v and the concentrations of the metabolites, with integer exponents and coefficients which depended on the three single step rate constants and the concentration of NADPH. This set of polynomials was triangularized, using the Gröbner basis function of MAPLE. The basis included a polynomial in v of degree 11, which was free of metabolite concentrations.

For each recorded result, the polynomial was solved numerically for v using a set of first approximations to the three single step rate constants. Each root was back substituted into the other polynomials that comprised the basis, and the resulting equations for the metabolite concentrations were solved numerically. Values of v which led to negative concentrations were discarded. This left just one root for each time interval, and this was used to integrate forward to compute the amount of NADPH that would be expected next. These computed values were compared with the observed values in a least-squares iteration towards self-consistent evaluation of the rate constants.

This study formed part of an ongoing line of work which was begun at the University of Bath by Bennett *et al.* [9], continued there by Bayram for his PhD [8], and then by Yildirim in his PhD with Bayram [10]. Several further papers by these authors on pseudo steady state enzyme kinetics are cited in the Supplementary Material. Related work includes the affinity binding studies of Grinfeld and co-workers [55, 56].

6.2.2. *Reaction networks*

Feinberg has studied the mechanisms of reaction networks for several decades and he has published extensive accounts of the pivotal role of multivariate polynomial systems in the analysis of these systems. A major concern in this work is the determination of whether a network can support one steady state, multiple steady states, oscillatory states or none of these. For surveys see [57–60]. A recent paper discussed the discrimination between proposed mechanisms for the ethylene hydrogenation on rhodium [61]. Ellison and Feinberg do not use Gröbner bases, but one of his systems was used by Heck in a simple example in network analysis involving the steady state of a reaction system comprising 5 species, 3 reversible reactions and 2 irreversible reactions (see p. 698 of [49]).

Clarke also considered reaction networks from an algebraic viewpoint [62]. Eiswirth refers to the work of Ellison and Feinberg and of Clarke in the theoretical part of his ongoing work on electrocatalysis and Langmuir–Hinshelwood mechanisms—see e.g. [63]. Gatermann discussed algebraic properties of polynomial systems in some related work that made use of Gröbner bases [64]. Lustfeld studied the kinetics of small molecule reactions that create tropospheric pollutants [22]. Melenk *et al.* reported early work on the symbolic solution of large stationary chemical kinetics problems [65].

6.2.3. *Polymerization*

Nakao *et al.* considered the kinetics of non-equilibrium condensation polymerization of substituted monomers, en route to the computation of the molecular mass distribution in the end product [23]. They used the cascade theory, enumerated the different kinds of cross-links that are formed, and constructed the corresponding rate equations. A numerical calculation was carried through for a single species polymerization, and then the probability generating function (pgf) was computed for a multi-unit system such as phenol-formaldehyde. The process is characterized by monomer–monomer reactions which are much faster than the other competing reactions. An alternative formulation is discussed which involves the Gröbner basis of the pgf and increases computational efficiency.

Further aspects of chemical kinetics are considered in sections 6.3 and 6.7 below. Looking to the future, particularly with gas phase reaction sequences which involve small molecules, it may be possible to

(1) use spectroscopic and other methods to measure the concentrations of intermediates and end products at extremely short time intervals,
(2) treat the one-step rate equations as polynomial equations in which the one-step rate parameters are the 'unknowns' and the coefficients contain symbols for the metabolite concentrations,
(3) use GBs to solve for the rate constants in terms of the (symbolic) concentrations,
(4) substitute the observed values of these concentrations.

6.3. *Compartmental analysis and identifiability*

'A compartmental system [consists] of a finite number of macroscopic subsystems each of which is homogeneous and well-mixed [that] interact by exchanging material. There may be inputs from ... and outputs to the environment' [66]. Many authors represent compartmental models by block diagrams. The equations for all the transfers between compartments comprise a system of coupled differential or difference equations. Standard methods for solving these require the solution of polynomial algebraic equations, hence an opportunity to use Gröbner basis software.

'Identifiability' is an important issue in compartmental analysis. If the equations that relate the parameters in a model to measurable data can be solved uniquely for these parameters then the model is globally identifiable. If there are a finite number of solutions greater than 1, the model is locally identifiable. If an infinite number of solutions is possible, the model is unidentifiable. The determination of identifiability often can be done by finding the number of roots of a polynomial in a Gröbner basis.

Several authors have reported compartmental modelling and identifiability calculations for work on metabolic systems, pharmacokinetics and spectrscopy that use Gröbner bases.

Raksanyi *et al.* discussed first pass effects of drugs after oral administration using Michaelis–Menten elimination kinetics [20]. They present an example that involves triangularization very clearly.

Chappell *et al.* compared and contrasted Taylor series and similarity transformation approaches [17]. Their examples include Michaelis–Menten elimination kinetics, a two-compartment model with one nonlinear elimination pathway and a seven-compartment model of tumour targeting by antibodies.

Ljung and Glad approached the problem using differential algebra [18].

Margaria *et al.* did so, too, with detailed discussion of models of bovine mastitis and cattle immunization [19].

Cobelli's group discuss a system to compute identifiability [15, 16]. Their examples include zinc, bilirubin, lipoprotein and apolipoprotein B metabolism, using 7, 6, 7 and 11 linear compartment models and nonlinear models of drug kinetics and glucose control by insulin, glucose metabolism in the brain based on PET measurements, involving 2, 3 and 3 nonlinear compartment models, respectively.

Heck works the structural identifiability of the three-compartment model of cadmium transfer through the human body on p. 701 *et seq* of his text [49].

Within the field of spectroscopy, time-resolved fluorescence methods are used to study the kinetics of excited-state processes, which can be modelled by a compartmental system. To improve the parameter recovery and to obtain a better model discrimination power a simultaneous analysis of related decay curves is advocated [67]. In the so-called target analysis of the resulting fluorescence decay surface the data are fitted directly to the parameters of the compartmental model [68]. This type of analysis triggered the identifiability analysis of the compartmental models describing excited-state reactions [69, 70]. Over 40 papers by Ameloot, Beechem, Boens, Kowalczyk, Molski, Novikov and co-workers during the past two decades report on identifiability problems in fluorescence spectroscopy and its applications. In general a set of polynomial equations was constructed in the course of determining the experimental conditions involving excitation and emission wavelengths and co-reactant concentrations, which can lead to a unique solution for all the unknown spectral parameters related to absorption and emission, and rate constants. Identifiability issues that were addressed in earlier papers include reversible diffusion-mediated excited-state association, time resolved fluorescence of glucagon, kinetic parameters of single species quenching and related schemes in diffusion related association, and fluorimetric determination of the concentrations of Na^+, K^+ and Ca^{2+}. The recent work by Boens *et al.* used similarity transformations in testing the identifiability of a compartment model for reversible intermolecular two-state excited-state processes [21].

6.4. *Thermodynamics*

Levelt *et al.* computed the critical curve for phase change in a binary mixture using the van der Waals one-fluid approach that extends the one-component equation of state by the one-fluid approach, with the further assumption of the geometric mean law for the cross-coefficient [25]. Levelt *et al.* repeat all the relevant formulas, with citations to the classical and the more recent work on the problem. Automatic differentiation of some of the formulas leads to a system of polynomial equations. Gröbner bases did not deal with these very well, but resultant methods gave useful results. The calculation is presented as a prototype for further thermodynamic studies.

6.5. *Quantum chemistry*

Čížek and Bracken transformed the Bethe equation for finite cycles in lattice spin models with an isotropic Heisenberg Hamiltonian into a system of algebraic equations which they solved using Gröbner bases [24]. This gave a characteristic polynomial in the energy which they solved for all states. They also considered the anisotropic case.

6.6. *Chemical biology*

Recently, Sturmfels and his co-workers reported applications of polynomial systems in statistical studies of genetic linkage analysis [71], biological sequence analysis [31, 32] and phylogenetic invariants [33]. Related papers are cited on Pachter's website [72].

6.7. *Partial differential equations and differential Gröbner bases*

This topic is of major importance. The identifiability work of Margaria *et al*. [19] provides a convenient entry point. They give several sets of PDEs, containing symbolic parameters, which are converted to triangular systems of PDEs by a process analogous to the algorithm described in section 4. The identifiability of particular parameters follows trivially from an inspection of the elements of the basis of increasing complexity.

On a more general front, differential Gröbner bases provide a major enhancement to the Lie symmetry methods which have come into focus as a very powerful approach to studying systems of PDEs. References to introductory texts and software surveys that cover these topics, and to applications to coupled nonlinear Schrödinger equations, to Boltzmann, Fokker–Planck, magneto-gas-hydrodynamic and Navier–Stokes equations are given in section 15.2 of [73]. Further work includes studies of self-written waveguides by Poladian *et al*. [74], hemoprotein–ligand diffusion dynamics by Sastry and Sabareesh [75], Lotka–Volterra systems by Brenig [76], and by Brenig, Comte and Diels on electrical discharges in a gas where the Poisson equation for the electrical field is coupled to the equations of motion of the charged particles, themselves coupled to the ODEs (ordinary differential equations) describing the kinetics of ionizing collisions [77]. Also, Hillgarter developed extensive lists of the symmetry groups for second-order PDEs in one-dependent and two-dependent variables [78].

A simple Gröbner basis treatment of the van der Pol equation by series expansion is given by Heck on p. 700 of his text [49].

6.8. *Other topics*

To increase awareness of the ability to solve sets of simultaneous polynomial algebraic equations among future chemists, courses on numerical methods of physical chemistry could include examples which relate to

(1) properties of solutions and multi-component mixtures that are polynomial in the concentrations of the components (e.g. computing the composition that will have prescribed values for a selection of these properties),
(2) the design mensuration of industrial plant for chemical reactions and separation, capsules for drug delivery, containers for laboratory benchwork, magnetic and electrostatic force fields in scientific equipment,
(3) electrostatic interactions within molecules and between molecules, and other problems that require the algebraic description of geometry.

Looking further afield, the use of Chebyschev and Taylor series for inter- and intra-molecular force fields that bind small ligands, leading to (overdetermined) systems of polynomial equations by simple differentiation warrants exploration. 'Visibility' problems were mentioned in section 1. Further progress will depend, in part, on more widespread understanding of the algebraic principles. The theory that underlies the structure of Gröbner bases and the Buchberger algorithm provide a convenient entry point to this material which we hope this present paper will lead readers to pursue.

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References

[1] Coutsias, E. A., Seok, C., Jacobson, M. P., and Dill, K. A., 2004, *J. comp. Chem.*, **25,** 510.
[2] Emiris, I., and Mourrain, B., 1999, *Algorithmica*, **25,** 372.
[3] Finn, P. W., and Kavraki, L. E., 1999, *Algorithmica*, **25,** 347.
[4] Levelt, A. H. M., 1998, The cycloheptane molecule, a challenge to computer algebra, invited lecture, *ISSAC '97*; www-math.sci.kun.nl/medewerkers/ahml/engels.pdf.
[5] Lewis, R. H., and Bridgett, S., 2003, Conic tangency equations and {A}pollonius problems in biochemistry and pharmacology, *Math. Comput. Simulation*, **61**(2), 101.
[6] Manocha, D., and Zhu, Y., 1994, *Proceedings of the 2nd International Conference on Molecular Biology*, pp. 285–294 (downloadable from www.cs.unc.edu/ dm/).
[7] Manocha, D., Zhu, Y., and Wright, W., 1995, *Comput. Appl. biol. sci. (CABIOS)*, **11,** 71 (downloadable from www.cs.unc.edu/ dm/).
[8] Bayram, M., Bennett, J. P., and Dewar, M. C., 1993, *Acta. Biotheoret*., **41,** 53.
[9] Bennett, J. P., Davenport, J. H., Dewar, M. C., Fisher, D. L., Grinfeld, M., and Sauro, M., 1991, *Lect. Notes Cont. Inf. Sci*., **165,** 23.
[10] Yildirim, N., and Bayram, M., 2000, *Appl. Math. Comput*., **112,** 41.
[11] Yildirim, N., and Bayram, M., 2000, *Appl. Math. Comput*., **112,** 255.
[12] Yildirim, N., Çiftçi, M., and Küfrevioğlu, Ö. İ., 2002, *J. math. Chem*., **31,** 121.
[13] Yildirim, N., 2002, *J. math. Chem*., **32,** 271.
[14] Yildirim, N., Ankaralioglu, N., Yidrim, D., and Akcay, F., 2003, *Appl. Math. Comput*., **137,** 67.
[15] Audoly, S., Bellu, G., D'Angiò, L., Saccomani, M. P., and Cobelli, C., 2001, *IEEE Trans. Biomed. Eng*., **48,** 55.
[16] Audoly, S., D'Angiò, L., Saccomani, M. P., and Cobelli, C., 1998, *IEEE Trans. Biomed. Eng*., **45,** 36.
[17] Chappell, M. J., Godfrey, K. R., and Vajda, S., 1990, *Math. Biosci*., **102,** 41.

[18] Ljung, L., and Glad, T., 1994, *Automatica*, **30,** 265.
[19] Margaria, G., Riccomagno, E., Chappell, M. C., and Wynn, H. P., 2001, *Math. Biosci.*, **174,** 1.
[20] Raksanyi, A., Lecourtier, Y., Walter, E., and Venot, A., 1985, *Math. Bisosci.*, **77,** 245.
[21] Boens, N., Szubiakowski, J., Novikov, E., and Ameloot, M., 2000, *J. chem. Phys.*, **112,** 8260.
[22] Lustfeld, H., 1998, Lecture Notes in Physics, Vol. 503 (New York: Springer), pp. 292–304.
[23] Nakao, T., Tanaka, F., and Kohjiya, S., 2002, *Macromol.*, **35,** 5649.
[24] Čížek, J., and Bracken, P., 1996, *Phys. Rev. Lett.*, **77,** 211.
[25] Levelt, A. H. M., 1995, *Proceedings of the SCAFI Seminar on Computer Algebra in Industry 2: Problem Solving in Practice*, Amsterdam, Netherlands, edited by A. M. Cohen, L. Van Gastel, S. M. Verduyn Lunel (London: Wiley), pp. 227–238.
[26] Gardner, R. J., and Gritzmann, P., 1997, *Trans. Am. math. Soc.*, **349,** 2271.
[27] Theobald, T., 2003, *Algorithmic and Quantitative Real Algebraic Geometry, DIMACS Series*, Vol. 60, edited by S. Basu and L. Gonzalez-Vega (Providence, RI: American Mathematical Society), pp. 207–219.
[28] Butcher, J., Carminati, J., and Vu, K. T., 2003, *Comput. Phys. Comm.*, **155,** 92.
[29] Mansfield, E. L., Reid, G. J., and Clarkson, P. A., 1998, *Comput. Phys. Comm.*, **115,** 460.
[30] Senthilvelan, M., Poladian, L., and de Sterke, C. M., 2002, *Phys. Rev.* E, **65,** 066607.
[31] Pachter, L., and Sturmfels, B., 2004, Parametric inference for biological sequence analysis, http://arxiv.org/abs/q-bio.GN/0401033.
[32] Pachter, L., and Sturmfels, B., Tropical geometry of statistical models, http://arxiv.org/abs/q-bio.QM/0311009
[33] Sturmfels, B., and Sullivant, S., 2004, Toric ideals of phylogenetic invariants, http://arxiv.org/abs/q-bio.PE/0402015.
[34] Buchberger, B., 1970, *Aequationes Math.*, **4/3,** 374.
[35] Buchberger, B., and Winkler, F. (eds), 1998, *Gröbner Bases and Applications*, London Mathematical Society Lecture Notes Series, Vol. 251 (New York: Cambridge University Press).
[36] Canny, J., 1988, *ACM Doctoral Dissertation Awards* (Cambridge, MA: MIT Press).
[37] Canny, J., 1990, *J. symb. Comp.*, **9,** 241.
[38] Macaulay, F. S., 1916, *The Algebraic Theory of Modular Systems* (Cambridge: Cambridge Mathematical Library).
[39] Freniere, E. R., 1980, *SPIE radiat. Scattering opt. Syst.*, **19,** 26–40.
[40] Deilamiann, K., Gillaspy, J. D., and Kelleher, D. E., 1992, *Appl. Opt.*, **31,** 2820.
[41] Lipkin, H., 1965, Lie Groups for Pedestrians (Amsterdam: North-Holland).
[42] Buchberger, B., 2001, *J. multimensional Syst. signal Process.*, **12,** 223.
[43] Buchberger, B., 2001, *Proceedings of EUROCAST* (*8th International Conference on Computer Aided Systems Theory*), *Lecture Notes in Computer Science*, Vol. 2178, edited by R. Moreno-Diaz, B. Buchberger and J. L. Freier (Berlin: Springer), pp. 1–19.
[44] Levelt, A. H. M., 1995, *Proceedings of the SCAFI Seminar on Computer Algebra in Industry 2: Problem Solving in Practice*, edited by A. M. Cohen, L. Van Gastel, S. M. Verduyn Lunel (New York: Wiley), pp. 43–59.
[45] von zur Gathen, J., and Gerhard, J., 2003, *Modern Computer Algebra*, 2nd Edn (New York: Cambridge University Press).
[46] Weispfenning, V., 2001, *Computer Algebra Handbook: Foundations, Applications, Systems*, edited by J. Grabmeier, E. Kaltofen and V. Weispfening (Berlin: Springer), pp. 28–32.
[47] Cox, D., Little, J., and O'Shea, D., 1997, *Ideals, Varieties and Algorithms: an Introduction to Computational Algebraic Geometry and Communicative Algebra*, 2nd Edn (New York: Springer).
[48] Weispfenning, V., 1992, *J. symb. Comp.*, **114,** 1.
[49] Heck, A., 2003, *Introduction to MAPLE*, 3rd Edn (New York: Springer).
[50] Winkler, F., 1998, *Polynomial Systems in Computer Algebra* (New York: Springer).
[51] Go, N., and Scheraga, H. A., 1973, *Macromol.*, **6,** 273.
[52] Murray, R. M., Li, Z., and Shastry, S. S., 1994, *A Mathematical Introduction to Robotic Manipulation* (Boca Raton: CRC Press).
[53] Oosterhoff, L. J., 1949, PhD thesis, University of Leiden, Netherlands.
[54] Hazebroek, P., and Oosterhoff, L. J., 1951, *Disc. Faraday Soc.*, **10,** 88.
[55] Bennet, J. P., Grinfeld, M., and Hubble, J., 1993, *J. symb. Comput.*, **15,** 79.
[56] Grinfeld, M., Bennet, J., and Hubble, J., 1997, *IAM J. Math. Appl. Bus. Ind.*, **8,** 157.
[57] Feinberg, M., http://www.che.eng.ohio-state.edu/FEINBERG/LecturesOnReactionNetworks.
[58] Feinberg, M., 1981, *Modelling of Chemical Reaction Systems. Springer Series in Chemical Physics*, Vol. 18 (New York: Springer), pp. 55–68.
[59] Feinberg, M., 1987, *Chem. Eng. Sci.*, **42,** 2229.
[60] Schlosser, P. M., and Feinberg, M., 1994, *Chem. Eng. Sci.*, **49,** 1749.
[61] Ellison, P., and Feinberg, M., 2000, *J. molec. Catalysis* A, **154,** 155.
[62] Clarke, B. L., 1980, *Adv. chem. Phys.*, **43,** 1.
[63] Eiswirth, M., Bürger, J., Strasser, P., and Ertl, G., 1996, *J. phys. Chem.*, **100,** 19118.
[64] Gatermann, K., http://www.zib.de/gatermann/public.html#PUBLICATIONS.
[65] Melenk, H., Moller, H. M., and Neun, W., 1989, *Impact Comput. Sci. Eng.*, **1,** 138.
[66] Jacquez, J. A., 1996, *Compartmental Analysis in Biology and Medicine* (Ann Arbor: BioMedware).
[67] Beecham, J. M., Gratton, E., Ameloot, M., Knutson, J. R., and Brand, L., 1989, *Flourscence Spectroscopy*, edited by J. Lakowicz (New York: Plenum Press).
[68] Beechem, J. M., Ameloot, M., and Brand, L., 1985, *Chem. Phys. Lett.*, **120,** 466.
[69] Ameloot, M., Beechem, J. M., and Brand, L., 1986, *Chem. Phys. Lett.*, **129,** 211.
[70] Ameloot, M., Boens, N., Andriessen, R., Van den Bergh, V., and De Schryver, F. C., 1991, *J. phys. Chem.*, **95,** 2041.

[71] HALLGRÍMSDÓTTIR, I. B., and STURMFELS, B., 2004, Resultants in genetic linkage analysis, http://arxiv.org/abs/q-bio.QM/0405001.
[72] PACHTER, L., http://math.berkeley.edu/lpachter/275/.
[73] BARNETT, M. P., CAPITANI, J. F., VON ZUR GATHEN, J., and GERHARD, J., 2004, *Int. J. quant. Chem.*, **100,** 80.
[74] POLADIAN, L., SENTHILVELAN, M., BESLEY, J. A., and DE STERKE, C. M., 2004, *Phys, Rev.* E, **69,** 016608.
[75] SASTRY, G. M., and SABAREESH, V., 2003, *Chem. Phys. Lett.*, **369,** 691.
[76] BRENIG, L., 2004, On a constructive approach to the solution of dynamical systems, private communication.
[77] BRENIG, L., 2004, private communication.
[78] HILLGARTER, E., 2002, Dissertation, RISC, Johannes Kepler University, Linz, Germany.