Conditions for Solvability in Chemical Reaction Networks at Quasi-Steady-State

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Abstract

The quasi-steady-state assumption (QSSA) is a widely used approximation in chemistry and chemical engineering to simplify reaction mechanisms. The key step in the method requires a solution by radicals of a system of multivariate polynomials. Pantea et al. [8] showed that there exist mechanisms for which the associated polynomials are not solvable by radicals. We present a class of chemical reaction networks for which solvability is guaranteed and provide minimal examples of CRNs for which the QSSA method fails.

1 Introduction

Many important reactions in chemistry are described by large reaction mechanisms, collections of small intermediate steps which combine to form the overall reaction. These reactions give rise to a system of differential equations which allow the behavior of the reaction to be predicted and analyzed. Due to their complexity, it is often useful to simplify the mechanisms so that calculations can be performed more quickly. One of the most well-known methods for reducing mechanisms is the quasi-steady-state assumption (QSSA), which replaces some of the differential equations with polynomial equations (in several variables). After solving these equations, the concentrations of some species to be removed from the model by substitution.

However, QSSA is only possible when this system of polynomials admits a finite number of solutions, all expressible in radicals. In practice, this is often the case, and it was noticed only recently that such a reduction cannot always be done. In 2014, Pantea et al. presented two mechanisms for which it was shown that QSSA cannot be performed [8]. One mechanism was constructed, but the other is an actual mechanism arising from chemistry, with a chemically reasonable choice of intermediates.

The technique is still taught today, and remains one of the most fundamental and simple methods of model reduction ([5], as PSSH). Given the widespread use of the method, we are interested in knowing when it is possible to guarantee that QSSA can be performed. We present conditions on the kinetics of the system and the structure of a graph derived from the mechanism which guarantee that QSSA can be performed. These are sufficient to demonstrate the minimality of the examples presented by Pantea et al. with respect to

kinetics, number of intermediates, number of species, and a particular structural property of the network. The class of CRNs and intermediates we describe, while small, describes many common networks. In part, these results explain why, historically, this issue was not noticed.

The paper is organized as follows. In Section 2, notation and definitions used to discuss chemical reaction networks and the QSSA method are introduced. We begin Section 3 by recalling several basic facts from commutative algebra, and apply them to show that, under some mild conditions, QSSA is possible for a networks with few intermediates. Subsequently, we show that if QSSA is "locally" possible, then it can be extended to the entire network if it satisfies certain structural and algebraic properties. This is followed by a series of illustrative examples. We conclude the paper with a discussion of the results in a historical context, and further problems suggested by this work.

2 Background

We begin with an overview of chemical reaction networks and the oriented species-reaction graph. This is followed by an introduction to QSSA and the notation we need to discuss them.

2.1 Chemical Reaction Networks

First we state several important definitions used for describing CRNs, following the presentation in [4], and the construction of the oriented species-reaction graph [3].

Definition 2.1. A *chemical reaction network (CRN)* is described by the following information:

1. A set of species, denoted $\mathcal{S}$.
2. A set of complexes, which are formal linear combinations of species with coefficients in $\mathbb{R}_{\geq 0}$, denoted $\mathcal{C}$. These can be identified with functions in $\mathbb{R}^{\mathcal{S}}$ or vectors in $\mathbb{R}^{\mathcal{S}}$ where all values are nonnegative.
3. A set of reactions, denoted $\mathcal{R}$, which can formally be viewed as a subset of $\mathcal{C} \times \mathcal{C}$, where a reaction $c \to c'$ is identified with the pair (c, c').

Treating the complexes as vectors, we use c_s to denote the coefficient of species s in complex c. Further, this paper will always assume the coefficients of the complexes are taken from $\mathbb{Z}_{\geq 0}$; as we will see later, this is necessary to obtain problems involving polynomials.

Reversible reactions are split into separate forward and reverse reactions.

As a matter of convention, specific species are often denoted by capital letters or combinations thereof ($A, B, A \cdot B, ...$) and their concentrations with square brackets ($[A], [B], [A \cdot B], ...$).

Definition 2.2. The complex on the left of a reaction arrow may be referred to as the *reactants*, and those on the right as the *products* of that particular reaction.

Definition 2.3. The kinetics of a CRN associate each reaction $c \to c'$ in a CRN with a *reaction rate*, $K_{c\to c'}$, which is a function of the species concentrations.

These functions describe the rate of change of concentrations in the system. Taken together, they provide the *rate function* for the CRN, a system of first order differential equation describing the rate of change of the concentrations:

$$\frac{d\mathbf{s}}{dt} = \Phi(\mathbf{s}) = \sum_{c\to c'\in\mathcal{R}} (c' - c)K_{c\to c'}(\mathbf{s})$$

The vector product in the summation is performed entry-wise.

Definition 2.4. A $\mathbb{Q}$-linear dependence among the differential equations in the rate function is called a *linear conservation law* (LCL). This means, for each $s \in \mathcal{S}$, there exists some rational number a_s such that:

$$0 = \sum_{s\in\mathcal{S}} a_s \Phi(\mathbf{s})_s = \sum_{s\in\mathcal{S}} a_s \frac{d[s]}{dt} = \frac{d}{dt} \sum_{s\in\mathcal{S}} a_s[s],$$

which is equivalent to saying

$$\sum_{s\in\mathcal{S}} a_s[s] = T,$$

where T is a constant determined by the initial conditions as

$$T = \sum_{s\in\mathcal{S}} a_s[s]_0$$

As the name indicates, LCLs are linear polynomials in concentration. When $\mathcal{Q} \subseteq S$, we define $LCL(\mathcal{R}, \mathcal{Q})$ as the maximal independent set of LCLs arising from the rate equations for each $q \in \mathcal{Q}$.

Definition 2.5. A CRN is *at-most-bimolecular* if no reactant has more than two nonzero terms.

Such kinetics are common in chemistry: for an "elementary" mechanism, each reaction corresponds to the collision and subsequent reaction of the reactants. The probability of a 3-way collision occurring is so small that such reactions are not common in practice, and proceed very slowly when they do appear.

Definition 2.6. One of the most well-studied kinetics is *mass-action kinetics*, where the rate of reaction is proportional to the product of the reactants:

$$K_{c\to c'}(\mathbf{s}) = k_{c\to c}\mathbf{s}^c$$

The term $k_{c\to c'}$ is the rate constant, a positive real number associated with the reaction.

The previously mentioned restriction to integer coefficients in complexes makes the term $\mathbf{s}^c$ a monomial in several variables. Note that under these kinetics, each rate constant is associated to a unique monomial.

If a CRN with mass-action kinetics is also at-most-bimolecular, then all of the polynomials in its differential equations have degree at most two.

$$\mathrm{E} + \mathrm{S} \underset{\mathrm{k_{-1}}}{\overset{\mathrm{k_1}}{\rightleftharpoons}} \mathrm{E \cdot S} \xrightarrow{\mathrm{k_2}} \mathrm{E} + \mathrm{P}$$

$$\begin{aligned}
\frac{d[E]}{dt} &= -k_1[E][S] + k_{-1}[E \cdot S] + k_2[E \cdot S] \\
\frac{d[S]}{dt} &= -k_1[E][S] + k_{-1}[E \cdot S] \\
\frac{d[E \cdot S]}{dt} &= k_1[E][S] - k_{-1}[E \cdot S] - k_2[E \cdot S] \\
\frac{d[P]}{dt} &= k_2[E \cdot S]
\end{aligned}$$

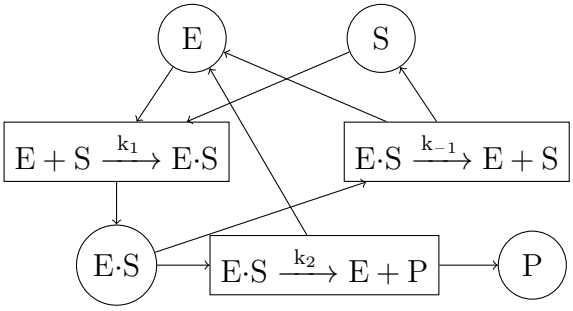

Figure 1: Example of a mechanism with the corresponding differential equations and OSR graph.

Next, we define an associated graph, whose structure is closely related to the structure of the differential equations. The definition here largely coincides with that in [3], but reversible reactions are treated as two separate reactions.

Definition 2.7. The *oriented species-reaction graph (OSR graph)* diagrams the relationships between species and reactions. Structural properties of this graph are closely related to properties of the system of equations.

The vertices of the graph are given by the (disjoint) union of $\mathcal{S}$ and $\mathcal{R}$. For each reaction $c \to c'$, an edge is drawn from s to $c \to c'$ if $c(s)$ is nonzero, and an edge from $c \to c'$ to s if $c'(s)$ is nonzero. Edges are weighted by the value of $c(s)$ or $c'(s)$.

When drawn, species are generally enclosed in circles, and reactions in rectangles. A small example is depicted in Figure 1.

2.2 Quasi-Steady-State-Assumption

2.2.1 Overview

Working with large CRNs is challenging: the corresponding system of differential equations is difficult to solve, and many of the species in the mechanism have concentrations which are hard to measure experimentally. Often, most rate constants cannot be measured, further complicating the use of the model. It is useful to have a way to simplify the network to obtain a more tractable system of differential equations and eliminate particular species.

One of the most popular methods for this elimination is the quasi-steady-state-assumption (QSSA). In this method, a collection of species are identified as fast-reacting intermediates. Because they react so much more quickly than the other species, we assume that at any point in time their concentrations are at steady state with respect to the other concentrations in the system.

This corresponds to setting the differential equations for these species equal to zero. In the case of mass-action kinetics with integer coefficients in each complex, this results in

a system of polynomial equations with variables corresponding to the rates of reaction of these species. Solving them allows for expressions in terms of the remaining species to be substituted into the remaining differential equations, eliminating the fast-reacting species from the model. Fast-reacting species are difficult to measure, but also good candidates for elimination by QSSA. By eliminating them, the species present in the model are more likely to coincide with those which can be determined experimentally, making it simpler to test the accuracy of the model.

For example, in Figure 1, the enzyme-substrate complex $E \cdot S$ may be an unstable structure, and hence a good candidate for elimination by QSSA. Apply the QSSA by setting the derivative equal to zero:

$$\frac{d[E \cdot S]}{dt} = k_1[E][S] - k_{-1}[E \cdot S] - k_2[E \cdot S] = 0 \Longrightarrow [E \cdot S] = \frac{k_1}{k_{-1} + k_2}[E][S]$$

This can be substituted into the remaining three differential equations, eliminating the intermediate from them. The reduced system is simpler to solve by exact or numerical methods, and only involves the concentrations of the slow-reacting species. When there are multiple solutions, it is usually possible to eliminate some based on physical constraints (e.g. imaginary or negative concentrations) and then determine which remaining roots best fit experimental data.

For this process to be useful, we need a solution by radicals of the intermediates in terms of the slow species and rate constants. In practice many mechanisms are solvable, but Pantea et al. presented two mechanisms for which they showed that the system does not have a solution in radicals. This naturally leads us to ask for which CRNs we can guarantee that QSSA is or is not possible.

2.2.2 Definitions

To makes these notions precise and simplify the upcoming discussion, we introduce several definitions.

Let $(\mathcal{S}, \mathcal{C}, \mathcal{R})$ be a CRN and $\mathcal{Q} \subseteq \mathcal{S}$ the set of species identified as intermediates to eliminate by QSSA. Further, we restrict to mass-action kinetics and integer coefficients in each complex; it follows that each entry of the rate function is a polynomial in the reaction rate constants and species concentrations.

Definition 2.8. For QSSA, we are interested in solvability with respect to a particular ground field, $\Bbbk_{\mathcal{Q}}$:

$$\Bbbk_{\mathcal{Q}} = \mathbb{Q}(\{c_s \mid s \in \mathcal{S} - \mathcal{Q}\} \cup \{k_{c \to c'} \mid c \to c' \in \mathcal{R}\} \cup \{T \mid T \text{ a constant term of } f \in LCL(\mathcal{R}, \mathcal{Q})\})$$

The c's and k's are algebraically independent parameters corresponding to the concentrations of the nonintermediate species and rate constants, respectively. To simplify the notation, these parameters are generally indexed by integers. The terms from the conservation laws are algebraically independent as well.

The subscript on $\Bbbk_{\mathcal{Q}}$ will often be omitted when it is clear from context.

Definition 2.9. Computations will take place in one of two polynomial rings: $A_{\mathcal{Q}} = \Bbbk[x_q \mid q \in \mathcal{Q}]$ or $B_{\mathcal{Q}} = \Bbbk^a[x_q \mid q \in \mathcal{Q}]$, where $\Bbbk^a$ denotes the algebraic closure. To perform QSSA, we are interested in solving a system of polynomial equations in $A_{\mathcal{Q}}$. This is exactly the same as finding the zeros of the *quasi-steady-state ideal*, $I_{\mathcal{Q}}$, the ideal generated by the polynomials corresponding to each intermediate in the rate function, along with any conservation laws:

$$I_{\mathcal{Q}} = \langle \{\Phi_q \mid q \in \mathcal{Q}\} \cup LCL(\mathcal{R}, \mathcal{Q}) \rangle$$

We can view $I_{\mathcal{Q}}$ as an ideal of either $A_{\mathcal{Q}}$ or $B_{\mathcal{Q}}$. Where this is not clear from the context, it will be specified.

Notation 2.1. For an ideal I in $k[x_1, ..., x_n]$, we use $V(I)$ to denote the set of points in k^n on which every polynomial in I vanishes, and $V^a(I)$ when we take the points from $(k^a)^n$.

Definition 2.10. We say that a solution $\alpha \in V^a(I_{\mathcal{Q}})$ is *degenerate* if any of its coordinates are zero. This is an indicator that a poor choice of intermediates was made, as it means that the steady state requires some intermediate to be absent from the system.

Remark 2.1. Under our definition of QSSA, the LCLs are included as constraints in the system. We restrict to LCLs involving only the intermediates: this is because the QSSA implies the intermediates react on a different time scale than the slow species, and hence the linearity of differentiation fails.

There are both advantages and disadvantages to treating systems which require LCLs. On one hand, it allows us to treat a wider range of systems. On the other, the constants associated to the LCLs can be difficult or impossible to measure in practice, and generally species for which there are LCLs are poor candididates for elimination by QSSA.

As such, it may be preferable to say that QSSA is impossible for a collection of intermediates which require LCLs. The only results which depend on the inclusion of the LCLs are those about the number of steady states. Naturally, these apply to this definition of QSSA if either "the set $LCL(\mathcal{R}, \mathcal{Q})$ is empty" or "there are no LCLs among the intermediates" are added to the hypotheses.

As an example of these rings and ideals, consider the CRN from Figure 1, where we pick $\mathcal{Q} = \{E \cdot S\}$. The nonintermediate concentrations are c_E, c_S, c_P. The variable we use for the intermediate is $x_{[E \cdot S]}$, which for simplicity will just be called x.

First we determine $\Bbbk$. The concentrations are as above, and the rate constants are k_{-1}, k_1, and k_2. The linear conservation laws are

$$x + c_E = T_1$$

$$c_E - c_S - c_P = T_2$$

Since neither LCL involves only concentrations in $\mathcal{Q} = \{E \cdot S\}$, they are ignored. This means $\Bbbk = \mathbb{Q}(c_E, c_S, c_P, k_{-1}, k_1, k_2)$. As there are no LCLs, the ideal $I_{\mathcal{Q}}$ is just generated by $\Phi_{[E \cdot S]}$:

$$I_{\mathcal{Q}} = \langle k_1 c_E c_S - k_{-1} x - k_2 x \rangle$$

The ideal lives in either $A_{\mathcal{Q}} = \Bbbk[x]$ or $B_{\mathcal{Q}} = \Bbbk^a[x]$. As demonstrated earlier, $I_{\mathcal{Q}}$ vanishes on one point, and the solution is solvable over $\Bbbk$ (in fact, contained in it).

We are interested in the CRNs and sets of intermediates for which elimination by QSSA is possible. By "QSSA is possible" we mean that:

1. there are finitely many solutions to the corresponding system of polynomials, that is, $V^a(I_{\mathcal{Q}})$ is finite
2. the solutions can be obtained by radicals; for each point $(\alpha_1, ..., \alpha_m) \in V^a(I_{\mathcal{Q}})$, the extension $\Bbbk(\alpha_i)$ is solvable

This is not the only possible definition. As discussed previously, it would not be unreasonable to require that there are no LCLs. We could also weaken the definition to only require finiteness and solvability for real solutions. This can be further weakened to nonnegative or nonzero concentrations.

3 Main Results

This section presents the main results on CRN polynomials. First, we discuss some useful properties of the coefficients of the rate law polynomials (Φ_s), some of which address the role LCLs play in QSSA. Next, we present simple solvability criteria for the CRN polynomials, as well as a finiteness conditions. This section concludes with a graph-theoretical construction which allows the previous results to be extended to larger networks.

3.1 Properties of Rate Law Polynomials

Here we collect some useful, well-known facts about the rate law polynomials of mass-action CRNs.

Fact 3.1. Every term in the coefficients of the rate law polynomials has a $k_{c\to c'}$ factor.

Proof. Every reaction is attached to some rate constant $k_{c\to c'}$, and their sum gives rise to the coefficient. □

Fact 3.2. Given a rate law polynomial Φ_s, if any term is negative, then it must be divisible by x_s.

Proof. Under mass-action kinetics, it is not possible for a species to be consumed at a constant rate. We can also see this from the definition of the rate function:

$$\Phi_s(\mathbf{s}) = \sum_{c\to c'} (c' - c) k_{c\to c'} \mathbf{s}^c$$

A negative sign can only come from the $(c' - c)$ term, and only if species s is present in complex c, which means that x_s will divide $\mathbf{s}^c$. □

Fact 3.3. Each monomial can be associated with a unique collection of rate constant parameters.

Proof. Each rate constant $k_{c\to c'}$ is associated with exactly one reaction. Furthermore, the reactant complex c determines the monomial with which it appears, and so $k_{c\to c'}$ cannot be in the coefficeint of any other monomial. □

Fact 3.4. Any collection of (nonzero) coefficients of distinct monomials is algebraically independent, even when they are taken from different rate law polynomials.

Proof. From the previous fact, we know that the set of rate constants appearing in each of the coefficients mentioned above are disjoint. Any nonzero relation among the coefficients would induce one among their component rate constants, which is a contradiction. □

Fact 3.5. Suppose that Φ_r and Φ_s each have the same degree, at least two nonzero terms, and one divides the other. Then $\Phi_r = \alpha\Phi_s$ where $\alpha \in \mathbb{Q}$.

Proof. Since one divides the other, let $\alpha = \Phi_r/\Phi_s$, which is necessarily in $\Bbbk$. Let a, a' and b, b' be the corresponding pairs of coefficients of two nonzero terms. Comparing terms, we see that:

$$a = \alpha a', b = \alpha b'$$
$$ab' = ba'$$

Because the ks are uniquely associated with each coefficient, this is not possible unless $b'|b$. Both are linear polynomials in the $k_{c\to c'}$ and so it must be the case that one one is rational multiple of the other. This means $\alpha \in \mathbb{Q}$, as desired. □

Note that this fact implies $\Phi_r - \alpha\Phi_s = 0$, and hence the existence of a linear conservation law.

3.2 Specialization of parameters

In defining $\Bbbk$, we chose algebraically independent rate constants. Their independence is crucial in later results, but in practice some of their values may be known, and hence we need to verify that specializing the rate constants to certain values does not alter solvability.

In one sense, this isn't essential, as QSSA is generally applied before the k_i are known, and so they must be treated as parameters. On the other hand, if any of them are known, these specializations can simplify some computations.

It was remarked by Pantea et al. that it is clear that specialization preserves solvability because it is possible to just specialize in the general solution. However, consider the following "counterexample":

$$f(x) = tx^2 + x + 1$$

which has roots

$$\frac{-1 \pm \sqrt{1-4t}}{2t}$$

If we specialize at $t = 0$, the root doesn't exist in this form, and so we might worry that there exist more pathological cases in which this could somehow cause solvability to be lost. It turns out this is not the case, as we will show below.

The more significant problem is that specialization will *not* preserve the finiteness of $V^a(I_{\mathcal{Q}})$, a problem which arises even in simple CRNs. This becomes important in later sections.

Lemma 3.1. *Suppose $\mathbb{L}/\Bbbk$ is a Galois extension. If we specialize the parameters in $\Bbbk$ to obtain the field k, it is possible to extend the specialization to $\mathbb{L}$, resulting in some field L. If $\mathbb{L}/\Bbbk$ is solvable, so is L/k.*

Proof. Number the rate constants $k_1, ..., k_n$ and the values to which they should be specialized as $t_1, ..., t_n$. First, we lift $\mathbb{L}/\Bbbk$ to $\mathbb{L}(t_1, ..., t_n)/\Bbbk(t_1, ..., t_n)$. This lifting induces an embedding of $G = \mathrm{Gal}(\mathbb{L}(t_1, ..., t_n)/\Bbbk(t_1, ..., t_n)$ into $\mathrm{Gal}(\mathbb{L}/\Bbbk)$.

Let $A = \mathbb{Q}(...)(t_1, ..., t_n)k_1, ..., k_n]$ (i.e. the subring of k consisting of polynomials in the k_i), B its integral closure in $\mathbb{L}$. Let $\mathfrak{p} = \langle k_1 - t_1, ..., k_n - t_n\rangle$. Note that $\mathfrak{p}$ is maximal and that $A/\mathfrak{p} \cong k$. Let $\mathfrak{P}$ be a maximal ideal of B lying over $\mathfrak{p}$. Then let $L = B/\mathfrak{P}$. By construction, it extends the specialization of parameters, and L/k is a field extension. Furthermore, there is a surjective homomorphism from $G_{\mathfrak{P}}$ to $\mathrm{Gal}(L/k)$ (Proposition 14, [7]).

Subgroups and homomorphic images of solvable groups are solvable. Since G can be identified with a subgroup of the solvable group $\mathrm{Gal}(\mathbb{L}/\Bbbk)$, it is solvable. Similarly, $G_{\mathfrak{P}}$ is solvable because it is a subgroup of G. Finally, the extension we are interested in is solvable because there is a surjection from $G_{\mathfrak{P}}$ onto it. □

Remark 3.1. To apply these results, note that the Gröbner basis calculation can be performed without dividing by any coefficients (this avoids issues in which something is specialized to zero). For a generator of $I \cap k[x_i]$, specialization preserves it solvability. As long as finiteness is preserved, this polynomial is nonzero and hence all the solutions in that coordinate are solvable.

This result allows us to work with many CRNs at once by treating the rate constants as parameters. Unfortunately, there is no version of this lemma for insolvable groups, as they are not closed under subgroups and homomorphic images. In particular, there can be specializations of the coefficients which lead to solvable Galois groups, even though the Galois group is insolvable when the coefficients are parameters. This makes classifying insolvable networks more difficult, as any such theory would have to also consider the possible specializations of the coefficients. Any complete classification of the networks for which QSSA is possible would also need to cover these cases, for which our techniques are not as useful.

3.3 Simple Solvability Criteria

While there is a solvability criterion for single-variable polynomials, the Φ_q polynomials obtained from applying the QSSA are rarely univariate, so a crucial first step is to reduce to that case.

Proposition 3.1. *Suppose I is an ideal in $A = k[x_1, ..., x_n]$, where k is a field. Then $V^a(I)$ is finite (i.e. I is a zero-dimensional ideal) if and only if $I \cap k[x_i] \neq \{0\}$ for each $1 \leq i \leq n$.*

Proof. $\Rightarrow$: If $V^a(I)$ is empty, $I = A$ so there is nothing to prove. Assume otherwise.

Write $V(I) = v_1, ..., v_m$ and denote the jth component of v_i by v_{ij}. For each coordinate j, define the following polynomial:

$$f(x_j) = \prod_{1 \leq i \leq m} \mathrm{irr}(v_{ij}, k, x_j),$$

where $\mathrm{irr}(\alpha, k, x)$ is the minimal polynomial of α over k in the variable x.

By construction, $f(x_j)$ is a nonzero polynomial in $k[x_j]$ which vanishes everywhere on $V^a(I)$. By the Nullstellensatz some power of f is in I, so $k[x_j] \cap I \neq \{0\}$.

$\Leftarrow$: Since $I \cap k[x_j]$ is nontrivial for each x_j, we can pick a nonzero $f(x_j) \in I \cap k[x_j]$. By definition, f vanishes on every point in $V^a(I)$, and f has only finitely many roots, so there are only finitely many choices for each coordinate of any point in $V^a(I)$. □

In most practical cases, there are only finitely many steady states, and so $|V^a(I_{\mathcal{Q}})|$ is typically finite. When there are infinitely many solutions, QSSA will fail anyway, as this makes it impossible to pick concentrations for the intermediates to substitute into the remaining equations. Furthermore, it suggests that some of the concentrations can be selected approximately freely at steady-state, which is not typical behavior, especially for well-chosen intermediates.

Reducing to the single variable case allows us to determine solvability by computing the Galois groups corresponding to the splitting field of a generator of $I_{\mathcal{Q}} \cap k[x_j]$ over k. The computation of those generators requires the following proposition.

Proposition 3.2. *Let I as above, and G a reduced Gröbner basis for I with respect to the the lexicographic ordering with*

$$x_1 > x_2 > ... > x_n$$

Then $I \cap k[x_n]$ is generated by $G \cap k[x_n]$, which only contains one element.

Proof. If $I \cap k[x_n]$ is empty, then $G \cap k[x_n]$ is necessarily empty as well.

Otherwise, there exists some nonzero $f(x_n)$ in $k[x_n]$. By definition, the leading terms with respect to $>$ of the polynomials of G divide the leading terms of every polynomial in I. Let $g \in G$ be a polynomial whose leading term divides that of f. This means its leading term is of the form x_n^r, so by the choice of ordering, none of its other terms are divisible by x_i when $i < n$, so g is contained in $k[x_n]$.

Furthermore, g is unique; if there were another $g' \in G \cap k[x_n]$, one of the leading terms would divide the other, but G is a reduced Gröbner basis. □

This is a special case of the Elimination Theorem [2]. This computation also results in the polynomial of smallest degree in $I \cap k[x_n]$, somewhat reducing the difficulty of detreminngi the Galois groups. Since it is possible to compute Gröbner bases and Galois groups over $\Bbbk$, this suggests a very basic criterion for applying QSSA.

Proposition 3.3. *QSSA can be performed if and only if both $I_{\mathcal{Q}} \cap \Bbbk[x_q] \neq \{0\}$ for each $q \in \mathcal{Q}$ and the generator of that intersection is solvable over $\Bbbk$. These conditions can be verified algorithmically.*

Proof. As remarked earlier, QSSA fails if $V^a(I_{\mathcal{Q}})$ is infinite. If it is finite, Proposition 3.1 shows that $I_{\mathcal{Q}} \cap \Bbbk[x_i]$ is nontrivial for each variable x_i.

Let g_i be a generator of $I_{\mathcal{Q}} \cap \Bbbk[x_i]$ as an ideal of $\Bbbk[x_i]$, then the solutions to g_i are expressible in radicals if and only if the Galois group of g_i is solvable over $\Bbbk$. Because $g_i \in I_{\mathcal{Q}}$, it vanishes everywhere on $V^a(I_{\mathcal{Q}})$, and so when g_i is solvable, every possible component of the ith coordinate is also solvable over $\Bbbk$.

The conditions can be verified in two steps:

1. Compute a reduced Gröbner basis of $I_{\mathcal{Q}}$ with respect to

$$x_1 > ... > x_{j-1} > x_{j+1} > ... > x_n > x_j$$

For each j, let g_j be the unique element of $G \cap k[x_j]$. If there is no such element for some j, QSSA is not possible (by Prop. 3.1, this would imply $V^a(I_{\mathcal{Q}})$ is not finite).

2. Compute the Galois group of g_j over $\Bbbk$, and test for solvability.

By definition, if QSSA is possible, there are finitely many solutions, all expressible by radicals.

□

While this proposition provides a straightforward test for solvability, it is computationally expensive. We compute n Gröbner bases, the complexity of which is doubly exponential in the degree and number of variables (however, there are ways to do this with just one Gröbner basis calculation). While some of our later results suggest that the computational complexity is smaller for CRNs, it is preferable to avoid these computations when possible. For almost all examples, the computation of the Galois group is the most time-consuming step; in one example, we did not find the Galois group even after several hours. This is a further motivation to develop criteria for solvability based on the structure of the CRN.

The Galois group of a polynomial f of degree n is determined by its action on the n roots of f, and so it naturally embeds into S_n. As the coefficients of the polynomials which generate $I_{\mathcal{Q}}$ are parameters, we might generically expect the Galois groups obtained above to be isomorphic to some S_n. If $n \leq 4$, the Galois group will be solvable, so a degree bound can guarantee solvability. This does not always work, as we will see later, but it is a reasonable heuristic.

Proposition 3.4. *Suppose we have a CRN with at-most-bimolecular kinetics, at most two intermediates, and for which $V^a(I_{\mathcal{Q}})$ is finite. Then it is possible to perform QSSA on this system.*

Proof. If there is just one intermediate, we have a linear or quadratic univariate polynomial, which is certainly solvable.

When there are two intermediates, we work in $\Bbbk[x_1, x_2]$. By hypothesis, $I_{\mathcal{Q}} \cap \Bbbk[x_1]$ and $I_{\mathcal{Q}} \cap \Bbbk[x_2]$ are both generated by nonzero polynomials g_1, g_2, respectively. It suffices to show both polynomials have solvable Galois groups.

The choice of kinetics means that there are two generators of $I_{\mathcal{Q}}$, each with degree at most 2. The product of their degrees bounds the maximum degree of a member of the Gröbner basis by Bézout's theorem. This means both degrees are at most 4, and hence g_1 and g_2 have solvable Galois groups over $\Bbbk$. □

3.4 Criterion for Finiteness

All the results thus far highlight the importance of ensuring that $V^a(I_{\mathcal{Q}})$ is finite in applying QSSA. This motivates the following theorem, which shows that it is also possible to ensure the finiteness of $V^a(I_{\mathcal{Q}})$ for two intermediates with slightly stronger hypotheses.

Physically, we would not expect CRNs to have infinitely many steady states, so it seems reasonable that Theorem 3.1 will generalize (perhaps under slightly different hypotheses) but the method of proof does not appear to generalize well, even to the case of three intermediates. On the other hand, this theorem shows that there are finitely many solutions in the algebraic closure, but real CRNs can only have solutions which are positive real numbers. It is possible that there is a network with a choice of intermediates for which there are infinitely many solutions in $\Bbbk^a$ but only finitely many which can embedded in $\mathbb{R}$ or $\mathbb{R}_{\geq 0}$.

As mentioned earlier, such results are useful from a computational perspective. It is known that the computational complexity of finding a Gröbner basis is much lower for zero dimensional ideals [6], so this would indicate that calculating steady states arising from CRNs is a more tractable problem. Since the algorithm outlined above requires computing n Gröbner bases, it would be helpful to have a reasonable assurance that the Gröbner basis calculations will be quick, even if the Galois group is insolvable.

Theorem 3.1. *Suppose we have a CRN with at-most-bimolecular kinetics and exactly two intermediates, q_1 and q_2, such that between Φ_{q_1} and Φ_{q_2}, both variables x_{q_1} and x_{q_2} appear, and at least one of them has a nonzero constant term. Then $V^a(I_{\mathcal{Q}})$ is finite.*

Proof. For simplicy of notation, we will use x and y instead of x_{q_1} and x_{q_2}.

To show that $V^a(I_{\mathcal{Q}})$ is finite, we want $I_{\mathcal{Q}}$ to be a zero dimensional ideal in $B_{\mathcal{Q}}$. Since $B_{\mathcal{Q}}$ is Noetherian, this would imply $B_{\mathcal{Q}}/I_{\mathcal{Q}}$ is Artin, and hence has finitely many maximal ideals, which means $I_{\mathcal{Q}}$ is contained in finitely many maximal ideals of $B_{\mathcal{Q}}$. Each maximal ideal in $B_{\mathcal{Q}}$ containing $I_{\mathcal{Q}}$ corresponds to a point in $V^a(I_{\mathcal{Q}})$, so when it is contained in a finite number of them, $V^a(I_{\mathcal{Q}})$ is finite.

To prove that $I_{\mathcal{Q}}$ is zero-dimensional, it suffices to find two elements $h_1, h_2 \in I_{\mathcal{Q}}$ such that $h_1 \neq 0$ and h_2 is not a zero divisor modulo h_1. When we have such elements, two applications of Krull's Principal Ideal Theorem (Corollary 11.17 in [1]) to them show that the height of a minimal prime of $I_{\mathcal{Q}}$ is at least two. This means the Krull dimension of $A_{\mathcal{Q}}/I_{\mathcal{Q}}$ is 0 or -1, both of which imply $V^a(I_{\mathcal{Q}})$ is finite (though the last says there are no solutions).

This is easiest if we can find an h_1 which is irreducible, as then the ideal it generates is prime, and so will suffice to check that $h_2 \notin \langle h_1 \rangle$.

Let the generators of $I_{\mathcal{Q}}$ be

$$g_1(x,y) = \Phi_{q_1}(x,y) = ax^2 + by^2 + cxy + dx + ey + f$$

$$g_2(x,y) = \Phi_{q_2}(x,y) = a'x^2 + b'y^2 + c'xy + d'x + e'y + f'$$

Case 1. There is an LCL. It is linear, so we can write it as

$$l(x,y) = rx + sy + t$$

where $r, s \in \mathbb{Q}$ and t is a parameter. It has a root at $(0, -t/s)$, so it suffices to show that this is not a root of g_1:

$$g_1(0, -t/s) = \frac{t^2}{s^2}b - \frac{t}{s}e + f$$

But the coefficients of g_1 are algebraically independent, so this is a contradiction unless $f = 0$. Similarly, if $l(x,y)$ also divides g_2, then neither generator has a constant term, a

contradiction. As a result, we get an irreducible, $l(x, y)$ and some polynomial not in the ideal it generates, which is sufficient, as noted above.

If $s = 0$ the argument can be repeated with $(-t/r, 0)$ as a root instead.

Case 2. One of g_1, g_2 is linear - WLOG, assume it is g_1.

Note that if g_1 does not have a constant term, it cannot divide g_2, as otherwise, g_2 would have no constant term either, contradicting the hypotheses. This guarantees $g_2 \notin \langle g_1 \rangle$, and so we're done in this case.

If they are both linear, then g_1 cannot divide g_2. If it did, Lemma 3.5 implies the existence of an LCL, covered by the previous case. We can write $g_1 = dx + ey + f$, and at least one of d, e is nonzero (f must be nonzero by the previous paragraph). Assume $e \neq 0$, as the other argument is symmetric. This means g_1 has a root at $(0, -f/e)$. Substitute this into g_2 and clear the denominator:

$$b'f^2 - ee'f' + f'e^2 = 0$$

From the algebraic independence of the coefficients, this is only possible when $b' = 0$. Since $e \neq 0$, we rearrange to get

$$e'f = ef'$$

This is only possible if $f' = \alpha f$ for some rational α or $e' = f' = 0$. The former implies the constant term of g_1 is a rational number, which is not possible. The latter implies

$$g_2 = x(a'x + c'y + d'),$$

If $g_1 | g_2$, then it must divide $a'x + c'y + d'$. Write $\alpha(dx + ey + f) = a'x + c'y + d'$ and compare coefficeints

$$\frac{c'}{e} = \alpha = \frac{d'}{f},$$

so $ed' = fc'$, which requires $d' = c' = 0$. This is an immediate contradiction, as then $\alpha e = c' = 0$, but by hypothesis e is nonzero.

Case 3. Both g_1 and g_2 are quadratic. Assume, without loss of generality, that g_1 has a nonzero constant term. We will show that it is irreducible or univariate.

1. $a \neq 0$: by Gauss's lemma, it suffices to show it is irreducible over $\mathbb{k}^a(y)[x]$. As g_2 is degree 2, it suffices to show it has no root in $\mathbb{k}^a(y)$, which can be done by showing the discriminant is not a square. We will assume that it is reducible, and show that this implies it is univariate.

   $$\Delta = (cy + d)^2 - 4a(by^2 + ey + f) = (c^2 - 4ab)y^2 + (2cd - 4ae)y + (d^2 - 4af)$$

   If this were a square, it would be of the form

   $$(\alpha y + \beta)^2 = \alpha^2 y^2 + 2\alpha\beta y + \beta^2$$

   We compute $\alpha^2\beta^2$ in two ways, comparing coefficients above:

   $$\alpha^2\beta^2 = (\alpha\beta)^2 = (cd - 2ae)^2 = c^2d^2 + 4a(-cde + ae^2)$$

$$\alpha^2\beta^2 = (\alpha^2)(\beta^2) = (c^2 - 4ab)(d^2 - 4af) = c^2d^2 + 4a(4abf - bd^2 - fc^2)$$

Which leads to another relation between the coefficients:

$$4a(4abf - bd^2 - fc^2 + cde - ae^2) = 0$$

Cancel $4a$, as it is nonzero. Then it must be the case that $e = 0$ or it would not be possible for the e^2 term to be eliminated. Then we obtain

$$4abf - bd^2 - fc^2 = 0$$

from which it follows that $b = 0$ (first term) and $c = 0$, and hence g_1 is univariate in x.

2. $b \neq 0$: this is similar to the above, but with $\mathbb{k}^a(x)[y]$ instead.
3. $a, b = 0, c \neq 0$. Just as above, reduce to $\mathbb{k}^a(y)[x]$. The polynomial is linear in this field, hence irreducible.

We know that g_1 does not divide g_2. If it did, we could write $g_1 = \alpha g_2$ because the degrees are the same. Assume that $a \neq 0$, as any other case is identical. Comparing coefficients, we see $af' = a'f$, so either $\alpha \in \mathbb{Q}$, implying the existence of an LCL, or $f = f' = 0$, contradicting the assumption that one of the constant terms is nonzero.

Since g_1 doesn't divide g_2, for the cases when g_1 is irreducible, we are done by the earlier remarks.

Alternatively, when g_1 is univariate, we can substitute each root of g_1 into g_2 and solve for the roots. This leads to only finitely many solutions unless this substitution turns g_2 into the zero polynomial. However, this cannot happen: g_1 is irreducible in $\mathbb{k}[x_1]$, because it has no roots in $\mathbb{k}$. This makes g_1 the minimal polynomial of its roots. As a result, the substitution only kills the coefficents of y and y^2 in g_2 (written as a polynomial in y) if g_1 divides both of those coefficients. This would make the degree of g_2 at least 3, a contradiction.

□

Corollary 3.1. *With at-most-bimolecular kinetics, QSSA is always possible when there is just one intermediate, or when there are two intermediates satisfying the hypotheses of Theorem 3.1.*

Proof. For one intermediate, we get a quadratic univariate equation, which certainly has finitely many solutions, all of which are solvable. For two intermediates, the premises and conclusion of this proposition imply the hypotheses of Proposition 3.4. □

Note that the hypothesis of at-most-bimolecular kinetics is not a significant limitation of these results. The kinetics are only relevant insofar as they restrict the degrees of the intermediates, so the theorems still apply in the case that the restriction of the CRN to $\mathcal{Q}$ is at-most-bimolecular. This is almost always the case; in chemistry, the highest degree that can arise in an elementary mechism is three, but such reactions are very slow. If such reactions are not crucial to the formation of the final product, they can often be neglected, and when they are, they will almost certainly cause an accumulation of their reactants. In this case, none of those reactants would be good candidates for elimination by QSSA, and so the corresponding degree three monomial would not be appear in a generator of $I_{\mathcal{Q}}$.

3.5 Graph-Theoretical Criteria for Solvability

The previous results only apply when there are at most two intermediates. We will now give certain structural criteria on the OSR graph which allow these results to be extended to larger networks.

Recall our previous definition of degeneracy:

Definition 3.1. We say that a steady-state is *degenerate* if it requires some concentrations to be zero.

We might similarly require that it be possible to experimentally achieve the steady states:

Definition 3.2. Similarly, a steady-state is *achievable* or *physically meaningful* if the concentrations involved are nonnegative and nonimaginary.

Our later results will show that QSSA is possible for the nondegenerate, acheivable steady states when their OSR graphs are treelike, in a way that will be made more precise later.

Definition 3.3. Let G be the oriented species-reaction graph G, corresponding to a CRN $(\mathcal{S}, \mathcal{C}, \mathcal{R})$. For any subset $\mathcal{Q} \subseteq \mathcal{S}$, let $G(\mathcal{Q})$ be the induced subgraph of G given by deleting the species vertices not in $\mathcal{Q}$ (i.e. removing slow species). This can be referred to as the *restriction of the OSR to* $\mathcal{Q}$, or, in the context of QSSA, the *QSSA OSR (QOSR).*

On the QOSR graph, we would like to group together species which interact with each other. Such groupings reflect the distribution of variables among the rate law polynomials.

Definition 3.4. If $\sim$ is an equivalence relation on a QOSR graph $G(\mathcal{Q})$, we say that it is *compatible* when it satisfies the following conditions for $s, s' \in \mathcal{Q}$ and $r, r' \in \mathcal{R}$:

1. For all $s \in \mathcal{S}$ and $r \in \mathcal{R}$, $s \not\sim r$.
2. The relation respects directed adjacency; $x \to y$ implies $[x] \to [y]$.
3. For all $s, s' \in \mathcal{S}$ and $r, r' \in \mathcal{R}$: if $s \to r$ and $s' \to r'$ are edges, then $s \sim s'$ if and only if $r \sim r'$.

The first condition ensures that $G/\sim$ preserves adjacencies in G. The last two ensure that each equivalence class is closed with respect to species which react together; if $A + B \to C$ is in the CRN, then we are guaranteed that $A \sim B$. The converse does not necessarily hold, as if $A \sim B$ then either $A + B$ is a complex, or there are two reactions $r \sim r'$ such that $A \to r$ and $B \to r'$.

The motivation for the following theorem is as follows: if the QOSR graph is approximately treelike, we can start at a root of the tree, solve for the associated concentrations, and substitute those values into the remaining equations. Substituting solvable roots into solvable roots should result in another solvable root.

Theorem 3.2. *Let G be the OSR graph of a CRN, $\mathcal{Q}$ a set of intermediates such that $LCL(\mathcal{R}, \mathcal{Q})$ is empty, and $H = G(\mathcal{Q})$ some QOSR graph. Suppose there exists a compatible relation on H such that*

1. *$H/\sim$ has no directed cycles*

2. *QSSA is possible in each equivalence class*

3. *for each equivalence class $[q]$, specialization constant terms of the generators of $I_{[q]}$ with values algebraic over $\Bbbk_{\mathcal{Q}-[q]}$ does not make $V^a(I_{[q]})$ infinite.*

Then QSSA is possible for $\mathcal{Q}$.

Proof. We proceed by induction on the number of equivalence classes of intermediates. If there is just one, then it is all of $\mathcal{Q}$, and so QSSA is possible.

Since $H/\sim$ has no directed cycles, pick some $[q] \in \mathcal{Q}$ such that there is no path from $[q]$ to any other member of $\mathcal{Q}/\sim$ in $H/\sim$.

By hypothesis, QSSA is possible for $I_{\mathcal{Q}-[q]}$, and all of it solutions will be solvable over $\Bbbk_{\mathcal{Q}}$ because the compatibility condition ensures the concentrations corresponding to members of $[q]$ do not appear in the generators of $I_{\mathcal{Q}-[q]}$, and hence are not needed in computing the Gröbner basis.

Take any partial solution $(\alpha_1, ..., \alpha_m)$ of $I_{\mathcal{Q}-[q]}$. We can perform the Gröbner basis calculations to find the univariate polynomials in $I_{[q]}$ without division (in case some values become zero). Since finiteness is preserved, these univariate polynomials must remain nonzero. They are solvable by hypothesis, which is preserved by solvability, so we can extend it to a solution solvable over $\Bbbk(\alpha_1, ..., \alpha_m)$. Solvable towers are solvable, and so the new solution is solvable by radicals as well.

This means any solution is solvable in each coordinate, and we only gain finitely many more in extending from $I_{\mathcal{Q}-[q]}$ to $I_{\mathcal{Q}}$. Therefore, QSSA is possible. □

Any collection of intermediates for which there is a linear conservation law must be excluded because it is possible for the LCL to "split" across equivalence classes.

Note that the theorem remains true if we weaken "QSSA is possible" by restricting to any combination of nondegenerate, nonzero, nonnegative, or real-valued concentrations.

Lemma 3.2. *Suppose we have a CRN with intermediates $\mathcal{Q}$ and a compatible equivalence relation $\sim$. If the intermediates in each equivalence class satisfy the conditions of Corollary 3.1, any specialization of the constant term at a nondegenerate and achievable steady state is nonzero.*

Proof. Note that so long as the constant term is nonzero, the theorem only requires that the algebraic independence relation among coefficients of different monomials be preserved. Since the specialization is with values algebraic over a field over which the independence relation is preserved, we are done.

The constant term can be written as a polynomial in the other concentrations. All the terms are positive, because we are working with a CRN and it is only possible to consume a species if it participates in the reaction. In order for the constant term to be zero, one of three things must happen: either all the (substituted) concentrations are zero, some are negative, or the products of some pairs of them are negative. The first implies degeneracy, the second and third that they are not achievable. □

Corollary 3.2. *For some CRN, let $\mathcal{Q}$ be a set of intermediates and G its OSR graph. If there exists a compatible relation on $G(\mathcal{Q})$ for which $[q] \in \mathcal{Q}$ satisfies 3.1, then there are finitely many physically meaningful nondegenerate steady states, all expressible by radicals.*

The restriction to achievable nondegenerate steady states in this theorem does suggest that there could exist CRNs with infinitely many steady states in the algebraic closure, but finitely many of actual interest. It may be the case, however, that only nondegeneracy is required in the preceeding lemma, as the only known "counterexamples" require some concentrations to be equal to zero.

3.6 Examples

First, we will discuss the CRNs originally presented by Pantea et al. in the context of what we have proven. Following this, we will provide some examples of CRNs with "interesting" properties. This includes Galois groups, such as $S_4 \times \mathbb{Z}_2$ and D_8, and reducible univariate polynomials, neither of which we would typically expect with generic coefficients. We conclude with an example of a mechanism which demonstrates the necessity of the nondegeneracy condition in Corollary 3.2.

For several examples, Maple code is available which demonstrates the computation. We have implemented a version of the algorithm outlined in Proposition 3.3, which computes the Galois groups associated to a mechanism, given the QSSA ideal. Several examples also go through the algorithm manually to help clarify the technical details of implementing it.

Example 3.1. This is the "original" insolvable mechanism [8]:

$$\begin{aligned}
2\,\mathrm{Y} &\underset{\mathrm{k}_{-1}}{\overset{\mathrm{k}_1}{\rightleftharpoons}} 2\,\mathrm{B} \\
\mathrm{Y} + \mathrm{B} &\xrightarrow{\mathrm{k}_2} \mathrm{Z} + \mathrm{A} \\
\mathrm{Z} + \mathrm{B} &\underset{\mathrm{k}_{-3}}{\overset{\mathrm{k}_3}{\rightleftharpoons}} 2\,\mathrm{X} \\
\mathrm{A} + \mathrm{X} &\xrightarrow{\mathrm{k}_4} \mathrm{Y} + \mathrm{B} \\
2\,\mathrm{Z} &\underset{\mathrm{k}_{-5}}{\overset{\mathrm{k}_5}{\rightleftharpoons}} 2\,\mathrm{A},
\end{aligned}$$

for which $\mathcal{Q} = \{X, Y, Z\}$ were chosen as intermediates. The QOSR graph is plotted in 2

The mechanism is at-most-bimolecular, and there are 3 intermediates. The univariate polynomial in $z = [Z]$ obtained by computing a Gröbner basis with respect to

$$x > y > z,$$

is degree 8, demonstrating the sharpness of the bound used in Proposition 3.4. The corresponding Galois group is isomorphic to S_8, which is insolvable. Corollary 3.1 shows that this is the minimum number of intermediates necessary to have an insolvable Galois group, as for two intermediates we can almost always guarantee solvability.

Furthermore, five total species is chemically reasonable when there are three intermediates, as we expect at least one "overall reactant" and one "overall product", neither of

which are intermediates. Additionally, we can see from the QOSR graph, Figure 2, that this network has a cycle between X, Y, and Z. The only way to remove a cycle with a compatible relation is to place all its members in one equivalence class, which prevents the application of Corollary 3.2.

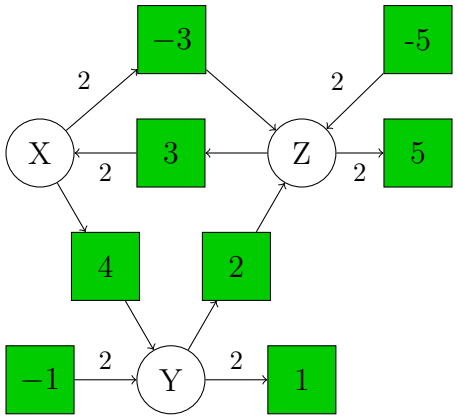

Figure 2: QOSR graph for the first mechanism from Pantea et. al [8]

Example 3.2. In fact, we can break the cycle from Pantea's example by deleting the edge $(2, Z)$. This is the same as changing the reaction

$$\mathrm{Y} + \mathrm{B} \xrightarrow{\mathrm{k_2}} \mathrm{Z} + \mathrm{A} \quad \text{into} \quad \mathrm{Y} + \mathrm{B} \xrightarrow{\mathrm{k_2}} \mathrm{A}.$$

We can then define a compatible relation such that $X \sim Z$ and $Y \sim Y$, which allows the application of Theorem 3.2. To simplify the calculations and illustrate an interesting point about degenerate soutions, we also remove the backwards reaction -5.

This is more clear in Figure 3. If we group the intermediates in each marked region, QSSA is possible with respect to them alone. When the $2 \to Z$ edge is deleted (marked in red) there is no longer a cycle between these regions. No specialization of its constant term affects solvability or finiteness for $I_{\{Y\}}$ (due to the incoming edge from -1) and so we are guaranteed that QSSA is possible for $\mathcal{Q} = \{X, Y, Z\}$.

This example is particularly interesting in that it leads to a degree 8 polynomial which has a Galois group isomorphic to $S_4 \times \mathbb{Z}_2$ rather than S_8.

Let $x = [X], y = [Y], z = [Z]$ and $a = [A], b = [B]$. The rate equations for the intermediates are:

$$\begin{aligned}
\frac{dx}{dt} &= -2k_{-3}x^2 - k_4ax + 2k_3bz \\
\frac{dy}{dt} &= -2k_1y^2 - k_2by + 2k_{-1}b^2 + k_4ax \\
\frac{dz}{dt} &= -2k_5z^2 - k_3bz + k_{-3}x^2
\end{aligned}$$

There are no LCLs among the intermediates, so we have all of the constants, and hence:

$$\Bbbk_{\mathcal{Q}} = \mathbb{Q}(a, b, k_1, k_{-1}, k_2, k_3, k_{-3}, k_4, k_5) \quad \text{and} \quad A_{\mathcal{Q}} = \Bbbk_{\mathcal{Q}}[x, y, z],$$

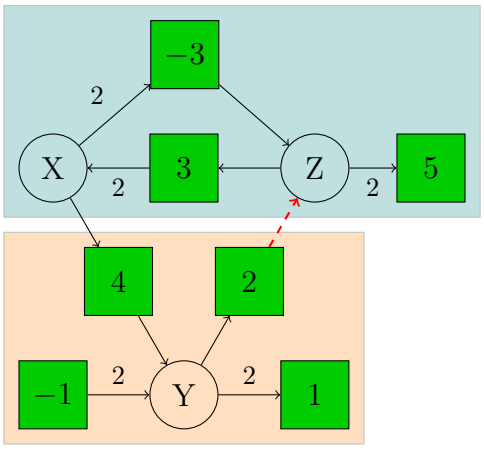

Figure 3: QOSR graph for the modified Pantea mechanism of Example 3.2. The deleted edge is dashed and marked in red, and regions are drawn around the graph to denote equivalence classes used in applying Theorem 3.2

.

with the following QSSA ideal:

$$I_{\mathcal{Q}} = \langle -2k_{-3}x^2 - k_4ax + 2k_3bz, -2k_1y^2 - k_2by + 2k_{-1}b^2 + k_4ax, -2k_5z^2 - k_3bz + k_{-3}x^2 + 2k_{-5}a^2 \rangle.$$

We already know that the Galois groups are solvable, but we can follow the algorithm outlined in 3.3 to calculate them them. The Galois groups (over $\mathbb{k}$) for the irreducible factors of the univariate polynomials in each coordinate are as follows:

var.	Galois group
x	S_3 or $\{e\}$
y	$S_4 \times \mathbb{Z}_2$ or $\mathbb{Z}_2$
z	S_3 or $\{e\}$

There are two Galois groups in each case because the polynomials obtained from the Gröbner bases are reducible.

There is even more that can be said about these results. As Corollary 3.2 highlights, there may be some interest in removing the degenerate steady states from the analysis. In this case, the Galois groups $\{e\}$ and $\mathbb{Z}_2$ only occur for a degenerate solutions where $x = 0$ or $y = 0$. It is possible to rule out such solutions ahead of time by modifying $I_{\mathcal{Q}}$. We can compute the saturation

$$I'_{\mathcal{Q}} = I_{\mathcal{Q}} : \langle xyz \rangle^{\infty}$$

$$\begin{aligned} I'_{\mathcal{Q}} = &\langle ak_4x + 4k_5z^2, -ak_4x + 2bk_3z - 2k_{-3}x^2, abk_3k_4 + 2ak_4k_5z + 4k_{-3}k_5xz, \\ &a^2k_4^2k_5x + ab^2k_3^2k_4 + 4ak_{-3}k_4k_5x^2 + 4k_{-3}^2k_5x^3, -ak_4x - 2b^2k_{-1} + bk_2y + 2k_1y^2 \rangle \end{aligned}$$

While the generating set is now much more complex, the degenerate solutions have been eliminated. When we check the Galois groups again for $I'_{\mathcal{Q}}$, only S_3 and $S_4 \times \mathbb{Z}_2$ remain.

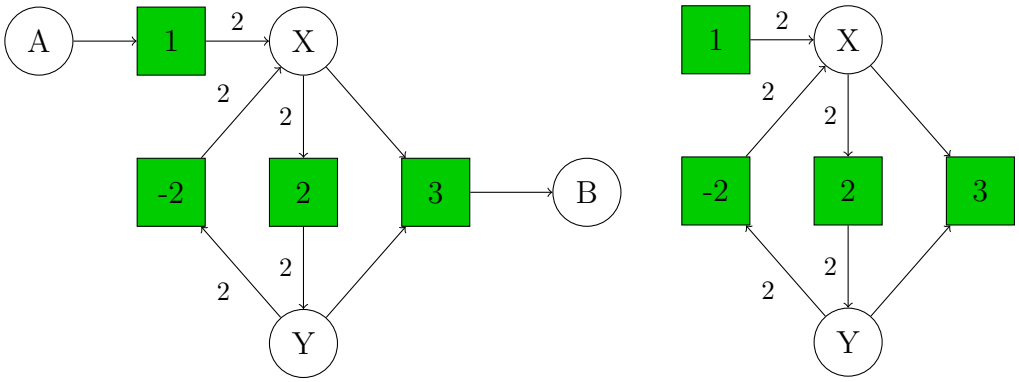

Figure 4: The OSR and QOSR graphs for the third example.

Example 3.3. This is a very small mechanism:

$$\mathrm{A} \xrightarrow{\mathrm{k_1}} 2\,\mathrm{X} \underset{\mathrm{k_{-2}}}{\overset{\mathrm{k_2}}{\rightleftharpoons}} 2\,\mathrm{Y}$$
$$\mathrm{X} + \mathrm{Y} \xrightarrow{\mathrm{k_3}} \mathrm{B}$$

Its OSR and QOSR graphs are presented in Figure 4

This system is readily seen to satisfy Corollary 3.1, as the reaction $\mathrm{A} \xrightarrow{\mathrm{k_1}} 2\,\mathrm{X}$ results in a nonzero constant term in Φ_x, and the kinetics are at-most-bimolecular. Let $x = [X]$. The corresponding univariate polynomial is

$$\begin{aligned} f(x) =& (8k_{-2}k_2^2 - 3k_2k_3^2)x^4 + (8k_{-2}k_2k_3)x^3 \\ &+ (-8ak_{-2}k_1k_2 + ak_1k_3^2 - 4k_{-2}^2k_2)x^2 \\ &- (2k_{-2}k_1ak_3)x + (2a^2k_{-2}k_1^2) \end{aligned}$$

Contrary to the remarks motivating Proposition 3.4, the Galois group is D_8, rather than S_4. While the system itself is very simple, it is not immediately clear why the Galois group is not a symmetric group. On the other hand, if we ignore the first reaction, the QOSR graph is very symmetric, so it could be the case that the structure of this graph is in some way related to that of the Galois group.

Additionally, the Galois group associated to $[Y]$ is also isomorphic to D_8. This seems even more surprising, as the structure of the OSR graph is not similar between X and Y. On the other hand, there is a reversible reaction converting X to Y, and they react together to form B. In some sense, this makes them exchangeable, which might explain the similarity of their Galois groups.

This is exactly what we see in practice: due to the structure of the network, we can show that solutions in y are multiples of those in x. Letting $a = [A]$, we know:

$$\Phi_x(x, y) = 0 = -2k_2x^2 - k_3xy + 2k_{-2}y^2 + k_1a$$

$$\Phi_y(x, y) = 0 = -2k_{-2}y^2 - k_3xy + 2k_2x^2$$

Add the two equations, and solve for y in terms of x:

$$2k_3xy = k_1a \Longrightarrow y = \frac{k_1a}{2k_3}\frac{1}{x},$$

which implies they have the same Galois group. This is largely a consequence of symmetries in the graph which let us cancel all of the quadratic terms from the rate law polynomials.

Example 3.4. Finally, we present an example of a mechanism which shows that nondegeneracy is necessary in Corollary 3.2.

$$\begin{aligned}
\mathrm{Z} &\xrightarrow{\mathrm{k_1}} \mathrm{X} \\
\mathrm{X} &\xrightarrow{\mathrm{k_2}} \mathrm{X} + \mathrm{Y} \\
\mathrm{Y} &\xrightarrow{\mathrm{k_3}} \mathrm{X} + \mathrm{Y} \\
\mathrm{Z} &\xrightarrow{\mathrm{k_4}} \mathrm{X} + \mathrm{Y} \\
\mathrm{X} + \mathrm{Y} &\xrightarrow{\mathrm{k_5}} \mathrm{C}
\end{aligned}$$

We choose intermediates $\mathcal{Q} = \{X, Y, Z\}$. Note that this is already a "bad" choice of intermediates, as it is clear that it will only be at steady state when $[Z] = 0$. Let $x = [X]$, $y = [Y]$, and $z = [Z]$. The rate law polynomials are:

$$\begin{aligned}
\Phi_x(x, y, z) &= -k_5xy + k_1z + k_4z \\
\Phi_y(x, y, z) &= -k_5xy + k_2x + k_4z \\
\Phi_z(x, y, z) &= -k_1z - k_4z
\end{aligned}$$

In principle, we can group $\{X, Y\}$ and $\{Z\}$ to apply the corollary. However, the only steady state for Z is at $z = 0$. We can make the substitution:

$$\begin{aligned}
\Phi_x(x, y, 0) &= -k_5xy \\
\Phi_y(x, y, 0) &= -k_5xy + k_2x
\end{aligned}$$

This system has infinitely many solutions, and so QSSA is not possible.

We do not know of any examples which demonstrate the necessity of requiring real and nonnegative solutions, and it is suspected that only nondegeneracy is needed. For instance, suppose a solution involves $(k_1 - k_2)$ or $\sqrt{k_1 - k_2}$. There are no restrictions on the relative magnitudes of the rate constants, so we do not lose any generality by assuming $k_1 > k_2$, making both values positive and real. This suggests that it would be difficult to construct a "counterexample" which shows that requiring the roots be positive and real is necessary.

Example 3.5. This example complements the previous in that it comes very close to a nondegenerate counterexample.

$$\begin{aligned}
\mathrm{A} &\xrightarrow{\mathrm{k_1}} \mathrm{X} + \mathrm{Y} \\
\mathrm{X} &\xrightarrow{\mathrm{k_2}} \mathrm{Z} \\
\mathrm{Y} &\xrightarrow{\mathrm{k_3}} 2\,\mathrm{Y} + \mathrm{Z}
\end{aligned}$$

Choose $\mathcal{Q} = \{X, Y, Z\}$ as intermediates, and set $x = [X]$, $y = [Y]$, and $z = [Z]$, as usual (it is clear that Z is not a "good" intermediate, as it can only accumulate). Then we see that

$$\Phi_z(x, y, z) = k_2 x + k_3 y$$

and at quasi-steady-state,

$$x = \frac{k_1}{k_2} a \qquad y = -\frac{k_1}{k_3} a$$

Upon substitution into Φ_z, we get

$$k_4 a - k_4 a = 0$$

and hence there are infinitely many solutions in z. However, this system does not satisfy the conditions of Theorem 3.2. In particular, the only possible grouping is $\mathcal{Q}_1 = \{X, Y\}$ and $\mathcal{Q}_2 = \{Z\}$, but QSSA is not possible for $\mathcal{Q}_2$, since $I_{\mathcal{Q}_2} = A_{\mathcal{Q}_2}$. If we make it possible by including a reaction with Z, such as $\mathrm{Z} \xrightarrow{\mathrm{k_4}} \mathrm{B}$, then there are only finitely many solutions.

4 Discussion

This paper provides partial answers several of the questions raised in the original paper discussing the relationship between insolvability and QSSA [8]. Corollary 3.1 shows that both mechanisms presented in that paper are minimal with respect to the number of intermediates (given at-most-bimolecular kinetics), and Theorem 3.2 further shows that they are minimal with respect to the structure of the QOSR graph as well: the mechanisms have a cycle among three intermediates. It is not necessarily minimal with respect to the Galois group, as A_5 is the smallest insolvable group. As mentioned earlier, we generally expect the degree bound to be sharp and that the Galois group be S_n, where n is the degree. There are examples which do have smaller insolvable Galois groups.

The results also begin to answer the question of why, historically, these problems in applying QSSA were not noticed. For many mechanisms, the number of intermediates is not too large, especially when the computations are performed by hand. For more complicated systems and more general kinetics, other techniques exist which do not necessarily require solutions in radicals. Furthermore, Theorem 3.2 allows QSSA to be extended to larger systems under certain structural constraints.

In fact, these results suggest that finiteness of the number of steady states is in some ways more critical than solvability. For all of these results, we require finiteness as the first step to showing that the solution is expressible in radicals. Its failure to be preserved by specialization makes it difficult to extend solvability among subsets of the intermediates to the entire system. There are several interesting questions that could be asked in this direction:

1. Does Theorem 3.1 generalize to larger sets of intermediates? We suspect it would, but the necessity of restricting to achievable steady states in Corollary 3.2 suggests that it may not

2. How important is nondegeneracy to finiteness? The only "counterexamples" to Corollary 3.2 are degenerate steady states, so it may be possible to generalize it to negative and/or complex-valued concentrations

3. Does there exist some analog of Theorem 3.2, but for finiteness?

While the generalizing to negative or complex concentrations may seem unnecessary, CRNs can model other kinds of systems, where this information may be useful. We also saw that it is possible to remove degenerate solutions with saturation, but the same is not possible for negative or complex steady states.

Another area of interest would be the relationship between other properties of the CRN and its associated Galois groups. At the moment, the computation of the Galois groups is the most difficult task, so a firmer understanding of the Galois groups which arise from CRNs (without specialization) may be useful. This suggests several questions:

1. Are there any other properties of the Galois group which can be related to the OSR or other graphs?

2. What relationships exist between the Galois groups of different species?

3. Is it possible to determine some Galois groups outright from the structure? (the OSR graph seems a good candidate, but it could be some other graph)

4. For a group G, does there exist a CRN and choice of intermediates such that G is a Galois group associated to one of the intermediates?

The first and second questions seem the most approachable, and it is possible that they could be leveraged in such a way as to allow the Galois groups from CRNs to be computed even when they are of high degree.

The third question is likely very difficult to answer, but it would be extremely useful. At the moment, the computation of the Galois groups is the slowest step in the algorithm outlined earlier. Further, we know of no software which can compute Galois groups over fields of rational functions in $\mathbb{Q}$ for polynomials of degree greater than 8. This bound is hit very quickly, even for small numbers of intermediates with at-most-bimolecular kinetics. It may be possible that there is enough extra structure in the chemical reaction networks to make this possible.

The fourth is of less practical interest, and its answer would likely necessitate progress on the other three. Even without the restricting to at-most-bimolecular kinetics, we suspect that not all groups are realizable by QSSA. For instance, we know of no examples of a nontrivial Galois group of odd order.

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I would like to thank Dr. Anne Shiu for her mentorship and many valuable insights. I am also grateful to Ola Sobieska for her helpful conversations. This research was conducted as part of Texas A&M University's Mathematics REU on Algebraic Methods in Computational Biology, funded by the National Science Foundation through REU grant DMS-1460766.

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Dependencies

Defined Functions

Example Usage

Rate constants are written as k_i = ki, and k_{-i} = ji

To use this code, run all the cells from 'Dependencies' and 'Defined Functions', then use define the QSSA ideal and use the QSSA groups to determine the Galois groups associated to each coordinate as shown below.

It is not recommended to run every cell, as some of the examples take several minutes to complete the Galois group computation.

Several of these examples are also worked out in separate worksheets in case the provided function does not provide all the desired information.

Original Pantea Mechanism

This is the first mechanism from the Pantea paper. Here we do not make their specialization of the rate constants, so the computations are somewhat slow.

[example 3.1 from report]

```
> Px := -2*j3*x^2 - k4*a*x + 2*k3*b*z
```

$$Px := -k4\,a\,x + 2\,k3\,b\,z - 2\,j3\,x^2 \quad \textbf{(3.1.1)}$$

```
> Py := -2*k1*y^2 - k2*b*y + 2*j1*b^2 + k4*a*x
```

$$Py := k4\,a\,x + 2\,j1\,b^2 - k2\,b\,y - 2\,k1\,y^2 \quad \textbf{(3.1.2)}$$

```
> Pz := -2*k5*z^2 - k3*b*z + j3*x^2 + k2·b·y
```

$$Pz := k2\,b\,y - k3\,b\,z + j3\,x^2 - 2\,k5\,z^2 \quad \textbf{(3.1.3)}$$

```
> J := PolynomialIdeal({Px, Py, Pz})
```

$$J := \langle -k4\,a\,x + 2\,k3\,b\,z - 2\,j3\,x^2,\ k4\,a\,x + 2\,j1\,b^2 - k2\,b\,y - 2\,k1\,y^2,\ k2\,b\,y - k3\,b\,z + j3\,x^2 - 2\,k5\,z^2\rangle \quad \textbf{(3.1.4)}$$

```
> QSSAGroups(J, [x, y, z], false)
```

$$[[x, ["8T50", \{"S(8)"\}, "-", 40320, \{"(1\ 8)", "(2\ 8)", "(3\ 8)", "(4\ 8)", "(5\ 8)", "(6\ 8)", "(7\ 8)"\}]], [y, ["8T50", \{"S(8)"\}, "-", 40320, \{"(1\ 8)", "(2\ 8)", "(3\ 8)", "(4\ 8)", "(5\ 8)", "(6\ 8)", "(7\ 8)"\}]], [z, ["8T50", \{"S(8)"\}, "-", 40320, \{"(1\ 8)", "(2\ 8)", "(3\ 8)", "(4\ 8)", "(5\ 8)", "(6\ 8)", "(7\ 8)"\}]]] \quad \textbf{(3.1.5)}$$

Three Variables: S3, S4 x Z2, S3 (features saturation)

This example is from the modified Pantea mechanism, where the loops is broken by changing the second reaction from Y + B -> Z + A into Y + B -> A, as well as

removing the -5 reaction.
It demonstrates the usage of saturation to remove degenerate solutions, which removes less interesting Galois groups.

[example 3.2 from report]

```
> Px := -2*j3*x^2 - k4*a*x + 2*k3*b*z
```

$$Px := -k4\,a\,x + 2\,k3\,b\,z - 2\,j3\,x^2 \quad \textbf{(3.2.1)}$$

```
> Py := -2*k1*y^2 - k2*b*y + 2*j1*b^2 + k4*a*x
```

$$Py := k4\,a\,x + 2\,j1\,b^2 - k2\,b\,y - 2\,k1\,y^2 \quad \textbf{(3.2.2)}$$

```
> Pz := -2*k5*z^2 - k3*b*z + j3*x^2
```

$$Pz := -k3\,b\,z + j3\,x^2 - 2\,k5\,z^2 \quad \textbf{(3.2.3)}$$

```
> J := PolynomialIdeal({Px, Py, Pz})
```

$$J := \langle -k3\,b\,z + j3\,x^2 - 2\,k5\,z^2,\ -k4\,a\,x + 2\,k3\,b\,z - 2\,j3\,x^2,\ k4\,a\,x + 2\,j1\,b^2 - k2\,b\,y - 2\,k1\,y^2 \rangle \quad \textbf{(3.2.4)}$$

without saturation

```
> QSSAGroups(J, [x, y, z], false)
```

```
[[x, ["3T2", {"S(3)"}, "-", 6, {"(1 3)", "(2 3)"}, "1T1", {"Id"}, "+", 1,
    {""}]], [y, ["6T11", {"2S_4(6)", "2 wr S(3)", "[2^3]S(3)"}, "-", 48,
    {"(3 6)", "(1 5)(2 4)", "(2 4 6)(1 3 5)"}, "2T1", {"S(2)"}, "-", 2,
    {"(1 2)"}]], [z, ["1T1", {"Id"}, "+", 1, {""}, "3T2", {"S(3)"}, "-", 6,
    {"(1 3)", "(2 3)"}]]]
```

(3.2.1.1)

with saturation

```
> QSSAGroups(J, [x, y, z], true)
```

```
[[x, ["3T2", {"S(3)"}, "-", 6, {"(1 3)", "(2 3)"}]], [y, ["6T11", {"2S_4(6)",
    "2 wr S(3)", "[2^3]S(3)"}, "-", 48, {"(3 6)", "(1 5)(2 4)",
    "(2 4 6)(1 3 5)"}]], [z, ["3T2", {"S(3)"}, "-", 6, {"(1 3)", "(2 3)"}]]]
```

(3.2.2.1)

Two Variables: both D8

This is a simple 2 intermediate system. By applying the quadratic formula to Py, we can see that the y solutions are multiples of the x solutions, which explains why the Galois groups are identical.
It is not entirely understood why the Galois groups are D_8 instead of S_4, since the polynomials seem very generic.

[example 3.3 from report]

```
> Px := k1·a - 2·k2·x^2 + 2·j2·y - k3·x·y
```

$$Px := -2\,k2\,x^2 - k3\,x\,y + k1\,a + 2\,j2\,y \quad \textbf{(3.3.1)}$$

```
> Py := k2·x^2 - 2 j2·y^2 - k3·x·y
```

$$Py := -2\,j2\,y^2 + k2\,x^2 - k3\,x\,y \quad \textbf{(3.3.2)}$$

```
> J := PolynomialIdeal({Px, Py})
```

$$J := \langle -2\,j2\,y^2 + k2\,x^2 - k3\,x\,y,\ -2\,k2\,x^2 - k3\,x\,y + a\,k1 + 2\,j2\,y \rangle \quad \textbf{(3.3.3)}$$

```
> QSSAGroups(J, [x, y], false)
```

[[x, ["4T3", {"D(4)"}, "-", 8, {"(1 3)", "(1 2 3 4)"}]], [y, ["4T3", {"D(4)"}, "-", 8, {"(1 3)", "(1 2 3 4)"}]]] **(3.3.4)**

Three Variables: large groups which are not Sn

This is the modified Pantea mechanism without the removal of the -5 reaction. This makes the y Galois group larger, and leads to a slow computation.

[example 3.2 from report without removing reaction -5]

```
> Px := -2*j3*x^2 - k4*a*x + 2*k3*b*z
```

$$Px := -a\,k4\,x + 2\,b\,k3\,z - 2\,j3\,x^2 \quad \textbf{(3.4.1)}$$

```
> Py := -2*k1*y^2 - k2*b*y + 2*j1*b^2 + k4*a*x
```

$$Py := a\,k4\,x + 2\,j1\,b^2 - k2\,b\,y - 2\,k1\,y^2 \quad \textbf{(3.4.2)}$$

```
> Pz := -2*k5*z^2 - k3*b*z + j3*x^2 + 2·j5·a^2
```

$$Pz := 2\,j5\,a^2 - b\,k3\,z + j3\,x^2 - 2\,k5\,z^2 \quad \textbf{(3.4.3)}$$

```
> J := PolynomialIdeal({Px, Py, Pz})
```

$$J := \langle -a\,k4\,x + 2\,b\,k3\,z - 2\,j3\,x^2,\ a\,k4\,x + 2\,j1\,b^2 - k2\,b\,y - 2\,k1\,y^2,\ 2\,j5\,a^2 - b\,k3\,z + j3\,x^2 - 2\,k5\,z^2 \rangle \quad \textbf{(3.4.4)}$$

```
> QSSAGroups(J, [x, y, z], false)
```

[[x, ["4T5", {"S(4)"}, "-", 24, {"(1 4)", "(2 4)", "(3 4)"}]], [y, ["8T44", {"[2^4]S(4)"}, "-", 384, {"(4 8)", "(1 8)(4 5)", "(1 2 3 8)(4 5 6 7)"}]], [z, ["4T5", {"S(4)"}, "-", 24, {"(1 4)", "(2 4)", "(3 4)"}]]] **(3.4.5)**

```
> with(PolynomialIdeals)
```

[<,>, Add, Contract, EliminationIdeal, EquidimensionalDecomposition, Generators, HilbertDimension, IdealContainment, IdealInfo, IdealMembership, Intersect, IsMaximal, IsPrimary, IsPrime, IsProper, IsRadical, IsZeroDimensional, MaximalIndependentSet, Multiply, NumberOfSolutions, Operators, PolynomialIdeal, PrimaryDecomposition, PrimeDecomposition, Quotient, Radical, RadicalMembership, Saturate, Simplify, UnivariatePolynomial, VanishingIdeal, ZeroDimensionalDecomposition, in, subset] **(1)**

```
> with(Groebner)
```

[Basis, FGLM, HilbertDimension, HilbertPolynomial, HilbertSeries, Homogenize, InitialForm, InterReduce, IsBasis, IsProper, IsZeroDimensional, LeadingCoefficient, LeadingMonomial, LeadingTerm, MatrixOrder, MaximalIndependentSet, MonomialOrder, MultiplicationMatrix, MultivariateCyclicVector, NormalForm, NormalSet, RationalUnivariateRepresentation, Reduce, RememberBasis, SPolynomial, Solve, SuggestVariableOrder, Support, TestOrder, ToricIdealBasis, TrailingTerm, UnivariatePolynomial, Walk, WeightedDegree] **(2)**

```
> Px := -2*j3*x^2 - k4*a*x + 2*k3*b*z
```

$$Px := -k4\,a\,x + 2\,k3\,b\,z - 2\,j3\,x^2 \quad \textbf{(3)}$$

```
> Py := -2*k1*y^2 - k2*b*y + 2*j1*b^2 + k4*a*x
```

$$Py := k4\,a\,x + 2\,j1\,b^2 - k2\,b\,y - 2\,k1\,y^2 \quad \textbf{(4)}$$

```
> Pz := -2*k5*z^2 - k3*b*z + j3*x^2 + k2·b·y
```

$$Pz := k2\,b\,y - k3\,b\,z + j3\,x^2 - 2\,k5\,z^2 \quad \textbf{(5)}$$

```
> J := PolynomialIdeal({Px, Py, Pz})
```

$$J := \langle -k4\,a\,x + 2\,k3\,b\,z - 2\,j3\,x^2,\ k4\,a\,x + 2\,j1\,b^2 - k2\,b\,y - 2\,k1\,y^2,\ k2\,b\,y - k3\,b\,z + j3\,x^2 - 2\,k5\,z^2\rangle \quad \textbf{(6)}$$

```
> fx := Basis(J, plex(y, z, x))[1]
```

$$fx := 16\,k1\,k5^2\,x^8\,j3^4 + 32\,a\,k1\,k4\,k5^2\,x^7\,j3^3 + 24\,a^2\,j3^2\,k1\,k4^2\,k5^2\,x^6 + (8\,a^3\,j3\,k1\,k4^3\,k5^2 + 8\,a\,b^2\,j3^2\,k1\,k3^2\,k4\,k5)\,x^5 + (a^4\,k1\,k4^4\,k5^2 + 8\,a^2\,b^2\,j3\,k1\,k3^2\,k4^2\,k5 + 4\,b^4\,j3^2\,k2^2\,k3^2\,k5)\,x^4 + (2\,a^3\,b^2\,k1\,k3^2\,k4^3\,k5 + 4\,a\,b^4\,j3\,k2^2\,k3^2\,k4\,k5)\,x^3 + (a^2\,b^4\,k1\,k3^4\,k4^2 + a^2\,b^4\,k2^2\,k3^2\,k4^2\,k5)\,x^2 - a\,b^6\,k2^2\,k3^4\,k4\,x - 4\,b^8\,j1\,k2^2\,k3^4 \quad \textbf{(7)}$$

```
> fy := Basis(J, plex(z, x, y))[1]
```

$$fy := 64\,k5\,y^8\,k1^4\,j3^2 + 128\,b\,j3^2\,k1^3\,k2\,k5\,y^7 + (32\,a^2\,j3\,k1^3\,k4^2\,k5 - 256\,b^2\,j1\,j3^2\,k1^3\,k5 + 96\,b^2\,j3^2\,k1^2\,k2^2\,k5)\,y^6 + (48\,a^2\,b\,j3\,k1^2\,k2\,k4^2\,k5 - 384\,b^3\,j1\,j3^2\,k1^2\,k2\,k5 + 32\,b^3\,j3^2\,k1\,k2^3\,k5)\,y^5 + (4\,a^4\,k1^2\,k4^4\,k5 \quad \textbf{(8)}$$

$$-96\,a^2\,b^2\,j1\,j3\,k1^2\,k4^2\,k5+24\,a^2\,b^2\,j3\,k1\,k2^2\,k4^2\,k5+384\,b^4\,j1^2\,j3^2\,k1^2\,k5$$
$$-192\,b^4\,j1\,j3^2\,k1\,k2^2\,k5+4\,b^4\,j3^2\,k2^4\,k5)\,y^4+(4\,b\,k2\,a^4\,k1\,k4^4\,k5$$
$$-96\,b^3\,k2\,a^2\,j1\,j3\,k1\,k4^2\,k5+4\,b^3\,k2^3\,a^2\,j3\,k4^2\,k5+384\,b^5\,k2\,j1^2\,j3^2\,k1\,k5$$
$$-32\,b^5\,k2^3\,j1\,j3^2\,k5)\,y^3+(-8\,a^4\,b^2\,j1\,k1\,k4^4\,k5+2\,a^4\,b^2\,k1\,k3^2\,k4^4$$
$$+a^4\,b^2\,k2^2\,k4^4\,k5+96\,a^2\,b^4\,j1^2\,j3\,k1\,k4^2\,k5-24\,a^2\,b^4\,j1\,j3\,k2^2\,k4^2\,k5$$
$$-256\,b^6\,j1^3\,j3^2\,k1\,k5+96\,b^6\,j1^2\,j3^2\,k2^2\,k5)\,y^2+(-4\,a^4\,b^3\,j1\,k2\,k4^4\,k5$$
$$-a^4\,b^3\,k2\,k3^2\,k4^4+48\,a^2\,b^5\,j1^2\,j3\,k2\,k4^2\,k5-128\,b^7\,j1^3\,j3^2\,k2\,k5)\,y$$
$$+4\,a^4\,b^4\,j1^2\,k4^4\,k5-2\,a^4\,b^4\,j1\,k3^2\,k4^4-32\,a^2\,b^6\,j1^3\,j3\,k4^2\,k5$$
$$+64\,j1^4\,k5\,j3^2\,b^8$$

```
> fz := Basis(J, plex(x, y, z))[1]
```

$$fz := 512\,k1^2\,k5^4\,j3^2\,z^8+(-128\,a^2\,j3\,k1^2\,k4^2\,k5^3+256\,b^2\,j3^2\,k1\,k2^2\,k5^3)\,z^6 \quad (9)$$
$$-64\,a^2\,b\,j3\,k1^2\,k3\,k4^2\,k5^2\,z^5+(8\,a^4\,k1^2\,k4^4\,k5^2-16\,a^2\,b^2\,j3\,k1\,k2^2\,k4^2\,k5^2$$
$$-256\,b^4\,j1\,j3^2\,k1\,k2^2\,k5^2+32\,b^4\,j3^2\,k2^4\,k5^2)\,z^4+(8\,a^4\,b\,k1^2\,k3\,k4^4\,k5$$
$$+48\,a^2\,b^3\,j3\,k1\,k2^2\,k3\,k4^2\,k5)\,z^3+(2\,a^4\,b^2\,k1^2\,k3^2\,k4^4$$
$$+2\,a^4\,b^2\,k1\,k2^2\,k4^4\,k5+32\,a^2\,b^4\,j1\,j3\,k1\,k2^2\,k4^2\,k5+4\,a^2\,b^4\,j3\,k2^4\,k4^2\,k5$$
$$-64\,b^6\,j1\,j3^2\,k2^4\,k5)\,z^2+(-a^4\,b^3\,k1\,k2^2\,k3\,k4^4-16\,a^2\,b^5\,j1\,j3\,k1\,k2^2\,k3\,k4^2$$
$$-2\,a^2\,b^5\,j3\,k2^4\,k3\,k4^2)\,z-2\,a^4\,b^4\,j1\,k1\,k2^2\,k4^4-4\,a^2\,b^6\,j1\,j3\,k2^4\,k4^2$$
$$+32\,b^8\,j1^2\,j3^2\,k2^4$$

```
> galois(fx, x)
```

"8T50", {"S(8)"}, "-", 40320, {"(1 8)", "(2 8)", "(3 8)", "(4 8)", "(5 8)", "(6 8)", "(7 8)"} **(10)**

```
> galois(fy, y)
```

"8T50", {"S(8)"}, "-", 40320, {"(1 8)", "(2 8)", "(3 8)", "(4 8)", "(5 8)", "(6 8)", "(7 8)"} **(11)**

```
> galois(fz, z)
```

"8T50", {"S(8)"}, "-", 40320, {"(1 8)", "(2 8)", "(3 8)", "(4 8)", "(5 8)", "(6 8)", "(7 8)"} **(12)**

```
> with(PolynomialIdeals)
```

[<,>, Add, Contract, EliminationIdeal, EquidimensionalDecomposition, Generators, HilbertDimension, IdealContainment, IdealInfo, IdealMembership, Intersect, IsMaximal, IsPrimary, IsPrime, IsProper, IsRadical, IsZeroDimensional, MaximalIndependentSet, Multiply, NumberOfSolutions, Operators, PolynomialIdeal, PrimaryDecomposition, PrimeDecomposition, Quotient, Radical, RadicalMembership, Saturate, Simplify, UnivariatePolynomial, VanishingIdeal, ZeroDimensionalDecomposition, in, subset] **(1)**

```
> with(Groebner)
```

[Basis, FGLM, HilbertDimension, HilbertPolynomial, HilbertSeries, Homogenize, InitialForm, InterReduce, IsBasis, IsProper, IsZeroDimensional, LeadingCoefficient, LeadingMonomial, LeadingTerm, MatrixOrder, MaximalIndependentSet, MonomialOrder, MultiplicationMatrix, MultivariateCyclicVector, NormalForm, NormalSet, RationalUnivariateRepresentation, Reduce, RememberBasis, SPolynomial, Solve, SuggestVariableOrder, Support, TestOrder, ToricIdealBasis, TrailingTerm, UnivariatePolynomial, Walk, WeightedDegree] **(2)**

```
> Px := -2*j3*x^2 - k4*a*x + 2*k3*b*z
```

$$Px := -a\,k4\,x + 2\,b\,k3\,z - 2\,j3\,x^2 \quad \textbf{(3)}$$

```
> Py := -2*k1*y^2 - k2*b*y + 2*j1*b^2 + k4*a*x
```

$$Py := a\,k4\,x + 2\,j1\,b^2 - k2\,b\,y - 2\,k1\,y^2 \quad \textbf{(4)}$$

```
> Pz := -2*k5*z^2 - k3*b*z + j3*x^2
```

$$Pz := -b\,k3\,z + j3\,x^2 - 2\,k5\,z^2 \quad \textbf{(5)}$$

```
> J := PolynomialIdeal({Px, Py, Pz})
```

$$J := \langle -b\,k3\,z + j3\,x^2 - 2\,k5\,z^2,\ -a\,k4\,x + 2\,b\,k3\,z - 2\,j3\,x^2,\ a\,k4\,x + 2\,j1\,b^2 - k2\,b\,y - 2\,k1\,y^2\rangle \quad \textbf{(6)}$$

```
> K := Saturate(J, {x·y·z})
```

$$K := \langle a\,k4\,x + 4\,k5\,z^2,\ -a\,k4\,x + 2\,b\,k3\,z - 2\,j3\,x^2,\ a\,b\,k3\,k4 + 2\,a\,k4\,k5\,z + 4\,j3\,k5\,x\,z,\ a^2\,k4^2\,k5\,x + a\,b^2\,k3^2\,k4 + 4\,a\,j3\,k4\,k5\,x^2 + 4\,j3^2\,k5\,x^3,\ -a\,k4\,x - 2\,b^2\,j1 + b\,k2\,y + 2\,k1\,y^2\rangle \quad \textbf{(7)}$$

```
> fx1 := Basis(K, plex(y, z, x))[1]
```

$$fx := a^2\,k4^2\,k5\,x + a\,b^2\,k3^2\,k4 + 4\,a\,j3\,k4\,k5\,x^2 + 4\,j3^2\,k5\,x^3 \quad \textbf{(8)}$$

```
> fy1 := Basis(K, plex(z, x, y))[1]
```

$$fy := 32\,j3^2\,k5\,y^6\,k1^3 + 48\,b\,j3^2\,k1^2\,k2\,k5\,y^5 + (16\,a^2\,j3\,k1^2\,k4^2\,k5 - 96\,b^2\,j1\,j3^2\,k1^2\,k5 + 24\,b^2\,j3^2\,k1\,k2^2\,k5)\,y^4 + (16\,a^2\,b\,j3\,k1\,k2\,k4^2\,k5 - 96\,b^3\,j1\,j3^2\,k1\,k2\,k5 + 4\,b^3\,j3^2\,k2^3\,k5)\,y^3 + (2\,a^4\,k1\,k4^4\,k5 \quad \textbf{(9)}$$

$$-32\,a^2\,b^2\,j1\,j3\,k1\,k4^2\,k5+4\,a^2\,b^2\,j3\,k2^2\,k4^2\,k5+96\,b^4\,j1^2\,j3^2\,k1\,k5$$
$$-24\,b^4\,j1\,j3^2\,k2^2\,k5)\,y^2+(a^4\,b\,k2\,k4^4\,k5-16\,a^2\,b^3\,j1\,j3\,k2\,k4^2\,k5$$
$$+48\,b^5\,j1^2\,j3^2\,k2\,k5)\,y-2\,a^4\,b^2\,j1\,k4^4\,k5+a^4\,b^2\,k3^2\,k4^4$$
$$+16\,a^2\,b^4\,j1^2\,j3\,k4^2\,k5-32\,b^6\,j1^3\,j3^2\,k5$$

```
> fz1 := Basis(K, plex(x, y, z))[1]
```

$$fz := -b\,k3\,a^2\,k4^2-2\,k5\,z\,a^2\,k4^2+16\,k5^2\,j3\,z^3 \quad \textbf{(10)}$$

```
> galois(fx1, x)
```

"3T2", {"S(3)"}, "-", 6, {"(1 3)", "(2 3)"} **(11)**

```
> galois(fy1, y)
```

"6T11", {"2S_4(6)", "2 wr S(3)", "[2^3]S(3)"}, "-", 48, {"(3 6)", "(1 5)(2 4)", **(12)**
"(2 4 6)(1 3 5)"}

```
> galois(fz1, z)
```

"3T2", {"S(3)"}, "-", 6, {"(1 3)", "(2 3)"} **(13)**