Efficient Methods to Compute Hopf Bifurcations in Chemical Reaction Networks Using Reaction Coordinates

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Abstract. In the paper we build an our previous work to compute Hopf bifurcation fixed point for chemical reaction systems on the basis of reaction coordinates. For determining the existence of Hopf bifurcations the main algorithmic problem is to determine whether a single multivariate polynomial has a zero for positive coordinates. For this purpose we provide heuristics on the basis of the Newton polytope that ensure the existence of positive and negative values of the polynomial for positive coordinates. We apply our method to the example of the Methylene Blue Oscillator (MBO).

1 Introduction

In the paper we build an our previous work [1] to compute Hopf bifurcation fixed point for chemical reaction systems on the basis of reaction coordinates. In that paper algorithmic ideas introduced by El Kahoui and Weber [2], which already had been used for mass action kinetics of small dimension [3], have been combined with methods of stoichiometric network analysis (SNA) introduced by Clarke in 1980 [4] that had been used in several "hand computations" in a semi-algorithmic way for parametric systems, the most elaborate being described in [5]. The algorithmic method presented in [1] uses and combines the ideas of these methods and extends them to a new approach for computing Hopf bifurcation in complex systems using reaction coordinates also allowing systems with linear constraints.

However, the used criteria of determining Hopf bifurcation fixed points with empty unstable manifold involving an equality condition on the principal minor

$\Delta_{n-1} = 0$ in conjunction with inequality conditions on $\Delta_{n-2} > 0 \wedge \cdots \wedge \Delta_1 > 0$ (and positivity conditions on the variables and parameters) still turned out to become diffecult problems for general quantifier elimination algorithm even for moderate dimensions.

In this paper we use the rather basic observation that the condition for existence of Hopf bifurcation fixed points when using convex coordinates is given by the single polynomial equation $\Delta_{n-1} = 0$ (together with positivity conditions on the convex coordinates) (dropping resp. delaying a test for having unstable empty manifold on already determined witness points for Hopf bifurcations). Hence the main algorithmic problem is to determine whether a single multivariate polynomial has a zero for positive coordinates.

For this purpose we provide heuristics on the basis of the Newton polytope that ensure the existence of positive and negative values of the polynomial for positive coordinates cf. Sect. 2.2.

We apply our method to the example of the Methylene Blue Oscillator (MBO) in Sect. 3.

2 Condition for a Hopf bifurcation

Consider a parameterized autonomous ordinary differential equation of the form $\dot{x} = f(u, x)$ with a scalar parameter u. By a classical result of Hopf, this system exhibits at the point (u_0, x_0) a Hopf bifurcation, i. e. an equilibrium transforms into a limit cycle, if $f(u_0, x_0) = 0$ and the Jacobian $D_x f(u_0, x_0)$ has a simple pair of pure imaginary eigenvalues and no other eigenvalues with zero real parts [6, Thm. 3.4.2].[6] The proof of this result is based on the center manifold theorem. From a physical point of view, the most interesting case is that the unstable manifold of the equilibrium (u_0, x_0) is empty. However, for the mere existence of a Hopf bifurcation, this assumption is not necessary.

In [2] it is shown that for a parameterized vector field $f(u, x)$ and the autonomous ordinary differential system associated with the semi-algebraic description of the set of parameters values for which a Hopf bifurcation (with empty unstable manifold) occurs for the system can be expressed by the following first-order formula:

$$\begin{aligned} &\exists x (f_1(u, x) = 0 \wedge f_2(u, x) = 0 \wedge \cdots \wedge f_n(u, x) = 0 \\ &\quad \wedge a_n > 0 \wedge \Delta_{n-1}(u, x) = 0 \wedge \Delta_{n-2}(u, x) > 0 \wedge \cdots \wedge \Delta_1(u, x) > 0) \end{aligned} \quad (1)$$

In this formula a_n is $(-1)^n$ times the Jacobian determinant of the matrix $Df(u, x)$, and the $\Delta_i(u, x)$'s are the i^{th} Hurwitz determinants of the characteristic polynomial of the same matrix $Df(u, x)$.

The proof uses a formula of Orlando [7], which is discussed also in several monographs, e.g. in [8] or [9]. However, a closer inspection of the two parts of the proof of [2, Theorem3.5] shows even the following: for a fixed point (given in

[6] We ignore here the non-degeneracy condition that this pair of eigenvalues crosses the imaginary axis transversally, as it is in realistic models always satisfied.

possibly paramterized form) the condition that there is a pair of purely complex eigenvalues is given by the condition $\Delta_{n-1}(u,x) = 0$ and the condition that all other eigenvalues have negative real part is given by $\Delta_{n-2}(u,x) > 0 \wedge \cdots \wedge \Delta_1(u,x) > 0$. This statement (without referring to parameters explicitly) is also contained in [10, Theorem2], in which a different proof technique is used.

Hence if we drop the condition of Hopf bifurcation points that they have empty unstable manifold a semi-algebraic description of the set of parameters values for which a Hopf bifurcation occurs for the system is given by the following formula:

$$\begin{aligned} &\exists x(f_1(u,x) = 0 \wedge f_2(u,x) = 0 \wedge \cdots \wedge f_n(u,x) = 0 \\ &\quad \wedge a_n > 0 \wedge \Delta_{n-1}(u,x) = 0) \end{aligned} \tag{2}$$

Notice that when the quantifier-elimination procedure yields sample points for existientially quantified formulae—as is the cased for the virtual substitution based method provided by REDLOG—then the condition $\Delta_{n-2}(u,x) > 0 \wedge \cdots \wedge \Delta_1(u,x) > 0$) can be tested for the sample points later on, i.e. one can then test whether this Hopf bifurcation fixed point has empty unstable manifold.

Example: Lorenz system. The famous "Lorenz System" [12, 6, 13] is given by the following system of ODEs:

$$\dot{x}(t) = \alpha\,(y(t) - x(t)) \tag{3}$$

$$\dot{y}(t) = r\,x(t) - y(t) - x(t)\,z(t) \tag{4}$$

$$\dot{z}(t) = x(t)\,y(t) - \beta\,z(t) \tag{5}$$

It is named after Edward Lorenz at MIT, who first investigated this system as a simple model arising in connection with fluid convection.

After imposing positivity conditions on the parameters the following answer is obtained using the combination of REDLOG and formula simplification using SLFQ for the test of a Hopf bifurcation fixed point:

$$\begin{aligned} (-\alpha^2 - \alpha\beta + \alpha r - 3\alpha - \beta r - r = 0 \vee -\alpha\beta + \alpha r - \alpha - \beta^2 - \beta = 0) \wedge \\ -\alpha^2 - \alpha\beta + \alpha r - 3\alpha - \beta r - r \leq 0 \wedge \\ \beta > 0 \wedge \alpha > 0 \wedge -\alpha\beta + \alpha r - \alpha - \beta^2 - \beta \geq 0 \end{aligned} \tag{6}$$

When testing for Hopf bifurcation fixed with empty unstable manifold we obtain the following formulae:

$$\begin{aligned} &\alpha^2 + \alpha\beta - \alpha r + 3\alpha + \beta r + r = 0 \wedge \\ &\quad \alpha r - \alpha - \beta^2 - \beta \geq 0 \wedge \\ &\quad 2\alpha - 1 \geq 0 \wedge \beta > 0 \end{aligned} \tag{7}$$

These formulae are not equivalent and hence for the case of the Lorenz system not all Hopf bifurcation fixed points have unstable empty manifold.

2.1 Using Reaction Coordinates

In [1] a new approach for computing Hopf bifurcation in complex systems using reaction coordinates also allowing systems with linear constraints has been given. The Jacobian matrix of subsystem formed by d-faces is given by the equation 8, where $\mathcal{S}$, $\mathcal{K}$ and $\mathcal{E}$ denote respectively the stoichiometric matrix, kinetic matrix and the set of extreme currents.

$$\mathrm{Jac}(x) = \mathcal{S}\mathrm{diag}(\sum_{i}^{d} j_i\mathcal{E}_i)\mathcal{K}^t\mathrm{diag}(1/x_1, ..., 1/x_n) \tag{8}$$

.

If we check for existence of Hopf bifurcation fixed points (without requireing empty unstable manifolds) then we have to decide the following formula :

$$\exists j_1 \cdots j_d \exists x_1 \cdots x_n (\Delta_{n-1}(j,x) = 0 \wedge j_1 \geq 0 \wedge \cdots j_d \geq 0 \wedge x_1 > 0 \wedge \cdots x_n > 0)$$

Hence the algorithmic task is to determine whether the single multivariate polynomial equation $\Delta_{n-1}(j,x) = 0$ has a solution for all variables being non-negative.

We discuss sufficient conditions and their efficient algorithmic realizations in the next section.

Remark 1. If the method provides sample points (if the exstential formula is satisfiable) then those can be tested for having empty unstable manifold by substituting them into the condition

$$\Delta_{n-2}(j,x) > 0 \wedge \cdots \wedge \Delta_1(j,x) > 0.$$

2.2 Sufficient Conditions for a Positive Solution of a Single Multivariate Polynomial Equation

The method discussed in this section is summarized in an algorithmic way in Alg. 1, which uses Alg. 2 as a subalgorithm.

Given $f \in \mathbb{Z}[x_1, \ldots, x_m]$, our goal is to heuristically certify the existence of at least one zero $(z_1, \ldots, z_m) \in]0, \infty[^m$ for which all coordinates are strictly positive. To start with, we evaluate $f(1, \ldots, 1) = f_1 \in \mathbb{R}$. If $f_1 = 0$, then we are done. If $f_1 < 0$, then it suffices by the intermediate value theroem to find $p \in]0, \infty[^m$ such that $f(p) > 0$. Similarly, if $f_1 > 0$ it suffices to find $p \in]0, \infty[^m$ such that $(-f)(p) > 0$. This algorithmically reduces our original problem to finding for given $g \in \mathbb{Z}[x_1, \ldots, x_m]$ at least one $p \in]0, \infty[^m$ such that $g(p) = f_2 > 0$.

We are going to accompany the description of our method with the example $g_0 = -2x_1^6 + x_1^3x_2 - 3x_1^3 + 2x_1x_2^2 \in \mathbb{Z}[x_1, x_2]$. Fig. 1 shows an implicit plot of this polynomial. In addition to its variety, g_0 has three sign invariant regions, one bounded one and two unbounded ones. One of the unbounded regions contains our initial test point $(1, 1)$, for which we find that $g_0(1, 1) = -2 < 0$. Thus our goal is to find one point $p \in]0, \infty[^2$ such that $g_0(p) > 0$.

Algorithm 1: pzerop

Input: $f \in \mathbb{Z}[x_1, \ldots, x_m]$

Output: $\bot$, $+$, $-$, 1, or (π, ν). A result $\bot$ means that this incomplete procedure failed; $+$ or $-$ mean that f has been identified as positive or negative definite on $]0, \infty[^m$, resp., and 1 means that $f(1, \ldots, 1) = 0$. Otherwise $\nu = (p, f(p))$, $\pi = (q, f(q))$, where p, $q \in]0, \infty[^m$ with $f(p) < 0 < f(q)$.

```
1  begin
2      f_1 := f(1, ..., 1)
3      if f_1 = 0 then
4          return 1
5      else if f_1 < 0 then
6          π := pzerop_1(f)
7          ν := ((1, ..., 1), f_1)
8          if π ∈ {⊥, −} then
9              return π
10         else
11             return (ν, π)
12     else
13         π := ((1, ..., 1), f_1)
14         ν' := pzerop_1(−f)
15         if ν' = ⊥ then
16             return ⊥
17         else if ν' = − then
18             return +
19         else
20             (p, f(p)) := ν'
21             ν := (p, −f(p))
22             return (ν, π)
```

Algorithm 2: pzerop_1

Input: $f \in \mathbb{Z}[x_1, \ldots, x_m]$

Output: $\bot$, $-$, or π. A result $\bot$ means that this incomplete procedure failed; $-$ means that f has been identified as negative definite on $]0, \infty[^m$. Otherwise $\pi = (q, f(q))$, where $q \in]0, \infty[^m$ with $0 < f(q)$.

```
1  begin
2      F⁺ := { d ∈ frame(f) | sgn(d) = 1 }
3      if F⁺ = ∅ then
4          return −
5      foreach (d_1, ..., d_m) ∈ F⁺ do
6          L := {d_1 n_1 + ··· + d_m n_m − c = 0}
7          foreach (e_1, ..., e_m) ∈ frame(f) \ F⁺ do
8              L := L ∪ {e_1 n_1 + ··· + e_m n_m − c ≤ −1}
9          if L is feasible with solution (n_1, ..., n_m, c) ∈ Q^{m+1} then
10             g := the principal denominator of n_1, ..., n_m
11             (N_1, ..., N_m) := (g n_1, ..., g n_m) ∈ Z^m
12             f̄ := f[x_1 ← ∞^{N_1}, ..., x_m ← ∞^{N_m}] ∈ Z(∞)
13             assert lc(f̄) > 0 when using non-exact arithmetic in the LP solver
14             k := min{ k ∈ N | f̄(2^k) > 0 }
15             return ((2^{kN1}, ..., 2^{kN_m}), f̄(2^k))
16     return ⊥
```

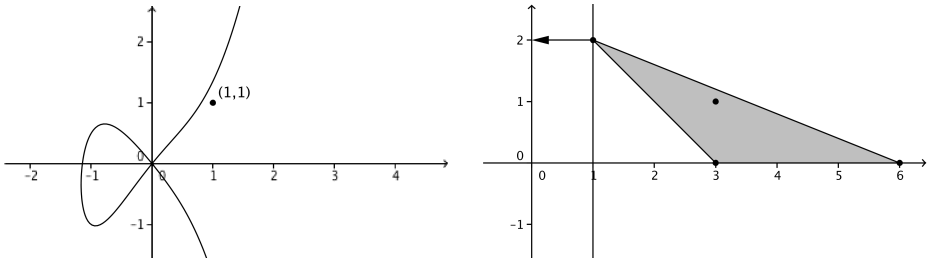

Fig. 1. We consider $g_0 = -2x_1^6 + x_1^3x_2 - 3x_1^3 + 2x_1x_2^2$. The left hand shows the variety $g_0 = 0$. The right hand side shows the frame, the Newton polytope, and a separating hyperplane for the positive monomial $2x_1x_2^2$ with its normal vector.

In the spirit of tropical geometry—and we refer to [14] as a standard reference with respect to its applications for polynomial system solving—we take an abstract view of

$$g = \sum_{d \in D} a_d x^d := \sum_{(d_1,\ldots,d_m) \in D} a_{d_1,\ldots,d_m} x_1^{d_1} \cdots x_m^{d_m}$$

as the set $\text{frame}(g) = D \subseteq \mathbb{N}^m$ of all exponent vectors of the contained monomials. For each $d^* \in \text{frame}(g)$ we are able to determine $\text{sgn}(d) := \text{sgn}(a_d) \in \{-1, 1\}$. The set of vertices of the convex hull of the frame is called the *Newton polytope* $\text{newton}(g) \subseteq \text{frame}(g)$. In fact, the existence of at least one point $d \in \text{newton}(g)$ with $\text{sgn}(d) = 1$ is sufficient for the the existence of $p \in]0, \infty[^m$ with $g(p) > 0$.

In our example we have $\text{frame}(g_0) = \{(6,0), (3,1), (3,0), (1,2)\}$ and $\text{newton}(g_0) = \{(6,0), (3,0), (1,2)\} \subseteq \text{frame}(g_0)$. We are particularly interested in $d^* = (d_1^*, d_2^*) = (1,2)$, which is the only point there with a positive sign as it corresponds to the monomial $2x_1x_2^2$.

In order to understand this sufficient condition, we are now going to compute a suitable point p. We construct a hyperplane $H : n^T x = c$ containing d such that all other points of $\text{newton}(g)$ are not contained in H and lie on the same side of H. We choose the normal vector $n \in \mathbb{R}^m$ such that it points into the halfspace not containing the Newton polytope. The vector $c \in \mathbb{R}^m$ is such that $\frac{c}{|n|}$ is the offset of H from the origin in the direction of n.

In our example H is the line $x = 1$ given by $n = (-1, 0)$ and $c = -1$. Fig. 1 pictures the situation.

It turns out that generally $\langle n|d^* \rangle = \max\{ \langle n|d \rangle \mid d \in \text{newton}(g) \}$, and that this maximum is strict. For the monomials of the original polynomial $g = \sum_{d \in D} a_d x^d$ and a symbol ∞ this observation translates via the following identity:

$$\bar{g} = g[x \leftarrow \infty^n] = \sum_{d \in D} a_d \infty^{\langle n|d \rangle} \in \mathbb{Z}(\infty).$$

Hence plugging into $\bar{g}$ a number $\beta \in \mathbb{R}$ corresponds to plugging into g the point $\beta^n \in \mathbb{R}^m$ and from our identity we see that in $\bar{g}$ the exponent $\langle n|d^* \rangle$ corresponding to our chosen point $d^* \in \text{newton}(g)$ dominates all other exponents so that

for large β the sign of $\bar{g}(\beta) = g(\beta^n)$ equals the positive sign of the coefficient a_{d^*} of the corresponding monomial. To find a suitable β we successively compute $\bar{g}(2^k)$ for $k \in \mathbb{N}$.

In our example we obtain $\bar{g} = 2\infty^{-1} - 2\infty^{-3} - 2\infty^{-6}$, we obtain $\bar{g}(1) = -2$, but already $\bar{g}(2) = \frac{23}{32} > 0$. In terms of the original g this corresponds to plugging in the point $p = 2^{(-1,0)} = \left(\frac{1}{2}, 1\right) \in]0, \infty[^2$.

It remains to be clarified how to construct the hyperplane H. Consider $\text{frame}(g) = \{\, (d_{i1}, \ldots, d_{im}) \in \mathbb{N}^m \mid i \in \{1, \ldots, k\} \,\}$. If $\text{sgn}(d) = -1$ for all $d \in \text{frame}(g)$, then we know that g is negative definite on $]0, \infty[^m$. Otherwise assume without loss of generality that $\text{sgn}(d_{11}, \ldots, d_{1m}) = 1$. We write down the following linear program:

$$\begin{pmatrix} d_{11} & \ldots & d_{1m} & -1 \end{pmatrix} \cdot \begin{pmatrix} n_1 \\ \vdots \\ n_m \\ c \end{pmatrix} = 0, \quad \begin{pmatrix} d_{21} & \ldots & d_{2m} & -1 \\ \vdots & \ddots & \vdots & \vdots \\ d_{k1} & \ldots & d_{km} & -1 \end{pmatrix} \cdot \begin{pmatrix} n_1 \\ \vdots \\ n_m \\ c \end{pmatrix} \leq -1.$$

This is feasible if and only if $(d_{11}, \ldots, d_{1m}) \in \text{newton}(g)$. In the negative case, we know that $(d_{11}, \ldots, d_{1m}) \in \text{frame}(g) \setminus \text{newton}(g)$, and we iterate with another $d \in \text{frame}(g)$ with $\text{sgn}(d) = 1$. If we finally fail on all such d, then our incomplete algorithm has failed. In the positive case, the solution provides a normal vector $n = (n_1, \ldots, n_m)$ and the offset c for a suitable hyperplane H. Our linear program can be solved with any standard LP solver. For our purposes here we have used Gurobi[7]; it turns out that the dual simplex of Glpsol[8] performs quite similarly on the input considered here.

For our example $g_0 = -2x_1^6 + x_1^3x_2 - 3x_1^3 + 2x_1x_2^2$, we generate the linear program

$$\begin{aligned} n_1 + 2n_2 - c &= 0 \\ 6n_1 - c &\leq -1 \\ 3n_1 + n_2 - c &\leq -1 \\ 3n_1 - c &\leq -1, \end{aligned}$$

for which Gurobi computes the solution $n = (n_1, n_2) = (-0.5, 0)$, $c = -0.5$. Notice that the solutions obtained from the LP solvers are typically floats, which we lift to integer vectors by suitable rounding and gcd computations.

Note that we do not explicitly contruct $\text{newton}(g)$ with a convex hull algorithm but favour a linear programming approach for several reasons. Firstly, we do not need that comprehensive information, but is sufficient to find one vertex with a positive sign the convex hull. Secondly, for the application dicussed here it turns out that there a typically only few (around 10%) such candidate points at all. Finally, it is known that for high dimensions the subset of $\text{frame}(g)$ establish-

[7] www.gurobi.com
[8] www.gnu.org/software/glpk

ing vertices of the convex hull gets comparatively large. Practical experiments with QuickHull[9] on our data support these theoretical considerations.

2.3 Summarizing the Algorithm for Checking the Existence of Hopf Bifurcations

Computing Hopf bifurcation fixed point for high dimensional systems and systems with conservation laws has been proven to be difficult in practice. To overcome this difficulty for systems arising from chemical reaction networks we introduced in our previous paper [1] an algorithm based on using the reaction coordinates instead of concentration coordinates and the technique of quantifier elimination on real closed field. It enables us to decide the occurrence of Hopf bifurcation in different chemical systems even with conservation laws. However it is still difficult to simplify the quantified formulae of some chemical networks with complex dynamic (e.g: Methylene Blue Oscillator) with the currently available quantifier elimination packages. In this section we summarize our new efficient algorithmic approach for computing the Hopf bifurcation in complex chemical systems. The new approach uses also the reaction coordinates and improves the previous algorithm by simplifying the formula expressing Hopf-existence condition as shown in 2 and solving it by the method described in 2.2. The pre-processing step and the steps 2-6 presented in [1] remain the same. After Computing characteristic polynomial of each Jacobian matrix, we compute the $n-1^{\text{th}}$ Hurwitz determinant of the characteristic polynomial and we apply the algorithm 1 "pzerop", which uses algorithm 2 "pzerop$_1$" as a subalgorithm to find the positive solution of the polynomial equation $\Delta_{n-1} = 0$. The pseudo code given in Alg. 3 outlines the main steps of the new approach and integrates the algorithms "pzerop" and "pzerop$_1$".

3 Algorithmic Determination of Hopf bifurcations in the Methylene Blue Oscillator System

As a complex example we consider the autocatalytic system "Methylen Blue Oscillator" (MBO), which isdefined by the following reaction equations:

[9] www.qhull.org

Algorithm 3: Algorithms for Computing Hopf Bifurcations in Chemical Reaction Networks Using Reaction Coordinates

Input: $\mathcal{N}$. A chemical reaction network with $\dim(\mathcal{N}) = n$.

Output: true, false or unknown. A statement about the existence of Hopf-bifurcation.

begin
- Generate the stoichiometric matrix $\mathcal{S}$ and kinetic matrix $\mathcal{K}$ from the reaction network.
- Compute the minimal set $\mathcal{E}$ of the vectors generating the flux cone.
- **for** $d = 1 \dots n$ **do**
  - Compute all d-faces and of the flux cone (subsystems).
- **for** *each subsystem* $\mathcal{N}_i$ **do**
  - **do**
  - Compute the transformed Jacobian Jac_i of $\mathcal{N}_i$ using $\mathcal{K}$, $\mathcal{S}$ and flux cone coordinates j_i's
  - **if** Jac_i *is singular* **then**
    - compute the reduced manifold of Jac_i calling the result also Jac_i
  - Compute the characteristic polynomial of Jac_i
  - Compute the the $n - 1^{\text{th}}$ Hurwitz determinant of the characteristic polynomial.
  - Compute $\mathcal{F}_i := \text{pzerop}(\Delta_{n-1}(j, x))$ using algorithm 1.
- The disjunction of $\mathcal{F}_i$ yields a criterion for the existance of a Hopf bifurcation fixed point, It can be computed lazily for increasing d and the subsystems.

$$
\begin{aligned}
MB^+ + HS^- &\longrightarrow MB + HS \\
H_2O + MB + HS^- &\longrightarrow MBH + HS + OH^- \\
HS + OH^- + MB^+ &\longrightarrow MB + S + H_2O \\
H_2O + 2MB &\longrightarrow MB^+ + MBH + OH^- \\
HS^- + O_2 &\longrightarrow HS + O_2^- \\
HS + O_2 + OH^- &\longrightarrow O_2^- + S + H_2O \\
H_2O + HS^- + O_2^- &\longrightarrow HO_2^- + HS + OH^- \\
O_2^- + HS &\longrightarrow HO_2^- + S \\
H_2O_2 + 2HS^- &\longrightarrow 2HS + 2OH^- \\
MB + O_2 &\longrightarrow MB^+ + O_2^- \\
HS^- + MB + H_2O_2 &\longrightarrow MB^+ + HS + 2OH^- \\
OH^- + 2HS &\longrightarrow HS^- + S + H_2O \\
MB + HS &\longrightarrow MBH + S \\
H_2O + MBH + O_2^- &\longrightarrow MB + H_2O_2 + OH^- \\
&\longrightarrow O_2
\end{aligned}
$$

The MBO reaction systems contains eleven species (not counting water) and fifteen reactions O_2, O_2^-, HS, MB^+, MB, MBH,HS^-, OH^-,S,$H2O2$ and HO_2^-. It may be reduced to six dimensional system by considering only the essential species O_2, O_2^-, HS, MB^+, MB and MBH. The pre-processing step of our algorithm yields the following two matrices describing the reaction laws: stoichiometric matrix $\mathcal{S}$ and kinetic matrix $\mathcal{K}$.

$$
\mathcal{S} = \begin{pmatrix}
1 & -1 & 1 & -2 & 0 & 0 & 0 & 0 & 0 & -1 & -1 & 0 & -1 & 1 & 0 \\
-1 & 0 & -1 & 1 & 0 & 0 & 0 & 0 & 0 & 1 & 1 & 0 & 0 & 0 & 0 \\
1 & 1 & -1 & 0 & 1 & -1 & 1 & -1 & 2 & 0 & 1 & -2 & -1 & 0 & 0 \\
0 & 1 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & -1 & 0 \\
0 & 0 & 0 & 0 & -1 & -1 & -1 & 0 & 0 & -1 & 0 & 0 & 0 & 0 & 1 \\
0 & 0 & 0 & 0 & 1 & 1 & 0 & -1 & 0 & 1 & 0 & 0 & 0 & -1 & 0
\end{pmatrix}
$$

$$
\mathcal{K} = \begin{pmatrix}
0 & 1 & 0 & 2 & 0 & 0 & 0 & 0 & 0 & 1 & 1 & 0 & 1 & 0 & 0 \\
1 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 1 & 0 & 0 & 1 & 0 & 1 & 0 & 0 & 0 & 2 & 1 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 \\
0 & 0 & 0 & 0 & 1 & 1 & 1 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 1 & 0
\end{pmatrix}
$$

The flux cone of this Model is generated by 31 extreme currents. We tried to compute Hopf bifurcation in all subsystems involving 2-faces and 3-faces by the algorithmic approach described in [1], but the generated quantified formulae could not be solved by Redlog (on our currently used hardware).

Using our new approach the algorithmic test sketched in Sect. 2.2 could be performed in less than 2 minutes of computation time for all instances resulting from 2-faces. In only 3% of the cases no definite answer could be obtained; in 67% of the cases it could be excluded that the resulting polynomial has a zero, whereas in 30% of the cases it could be verified that the resulting polynomial has a zero. Hence for (at least) 30% of the 2-faces there are Hopf bifurcations on these faces.

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