A TORIC PERSPECTIVE ON COMPLEX BALANCING

OSKAR HENRIKSSON

These expository notes are meant to serve as an accessible introduction to the notions of *complex balanced steady states* and *deficiency* in chemical reaction network theory. The perspective we take is that of *toric dynamical systems*, which provides a geometric interpretation of the deficiency in terms of toric geometry. Along the way, we recall the basic concepts from reaction network theory, as well as some of the key results from toric geometry that are relevant for understanding the toric interpretation of deficiency.

1. Introduction

Chemical reaction network theory (CRNT) has its roots in a series of papers published by Horn, Jackson and Feinberg in 1970's [20, 11, 19], and is, at its essence, the study of dynamical systems induced by *networks of interacting species* (for instance chemical substances, cells or humans). Since these equations often involve parameter values that are unknown or hard to determine, classical techniques such as numerical simulations or sampling often become infeasible, and an important goal of CRNT is therefore to develop *qualitative* methods that let us understand the dynamics in terms of the *structure* of the network. This is often done using tools and language from graph theory and algebraic geometry; an overview of the use of algebraic geometry in CRNT is given in [8]. There has also been attempts to use numerical algebraic geometry to study concrete reaction networks; for recent examples in a biomedical context, see [15].

A topic of central importance in CRNT is the existence and behavior of so-called *steady states*. Phenomena such as multistationarity and bifurcations play important roles in synthetic biology and systems biology, where they are believed to account for cellular differentiation and decision making [25, 26]. Much work has gone into finding qualitative conditions for when multistationarity can and cannot be displayed by a network, and into finding the region in parameter space where this happens. Some recent progress in this direction includes a characterization for small networks using Newton polytopes [24], as well as methods for finding parameter values that allow multistationarity, based on degree theory and rational parametrizations [9].

Example 1.1. An example of a reaction network that we will later analyze in more detail, and in a more general form (this is the special case $N = 1$), is the *McKeithan network*, that appears in [27] as a model for so-called *kinetic proofreading* at T-cell receptors. The network takes the form

$$\mathrm{T} + \mathrm{M} \underset{\kappa_4}{\overset{\kappa_1}{\rightleftharpoons}} \mathrm{C} \xrightarrow{\kappa_2} \mathrm{D}\,, \qquad \mathrm{D} \xrightarrow{\kappa_3} \mathrm{T} + \mathrm{M}$$

Date: October 18, 2020.

where T is a T-cell receptor, M is an antigen-presenting complex, C is an inactive form of the complex that arises when M binds to T, and D is an active form, that sets off an immunological response. The arrows represent biochemical transformations, and the labels $\kappa_1, \dots, \kappa_4$ are (unknown) rate constants that control the rate of each transformation. Under so-called mass-action kinetics, the concentration (denoted by c) of each species will vary over time according to the following system of ODE's:

$$\begin{aligned}
\dot{c}_{\mathrm{C}} &= \kappa_1 c_{\mathrm{T}} c_{\mathrm{M}} - \kappa_4 c_{\mathrm{C}} + \kappa_2 c_{\mathrm{C}} \\
\dot{c}_{\mathrm{D}} &= \kappa_2 c_{\mathrm{C}} - \kappa_3 c_{\mathrm{D}} \\
\dot{c}_{\mathrm{T}} &= -\kappa_1 c_{\mathrm{T}} c_{\mathrm{M}} + \kappa_4 c_{\mathrm{C}} + \kappa_3 c_{\mathrm{D}} \\
\dot{c}_{\mathrm{M}} &= -\kappa_1 c_{\mathrm{T}} c_{\mathrm{M}} + \kappa_4 c_{\mathrm{C}} + \kappa_3 c_{\mathrm{D}} \,.
\end{aligned}$$

A *steady state* of this system corresponds to a solution of the polynomial system that arises when we set the derivatives in the left-hand sides equal to 0.

The topic of these notes goes back to the early works by Jackson, Horn and Feinberg on the notions of *complex balancing* and *deficiency*. In particular, we will discuss the so-called *deficiency zero theorem*, which gives simple conditions under which remarkably strong statements about the dynamics of a network are true, including incapability of displaying multistationary behavior.

In practice, networks that fulfill these conditions are not very common, but the underlying ideas have laid the foundation for other results, applicable to other and wider classes of networks, for instance the classical *deficiency one theorem* [13], or the more recent notion of *disguised toric dynamical systems* introduced in [2]. At the same time, a big advantage of the deficiency zero theorem is that the conditions are simple to verify computationally, and it is therefore used as a basic building block in software such as the CRNToolbox [23].

Example 1.2. If we enter the McKeithan network described above as input in the CRNToolbox, we get a report as output that includes the following information:

```
This is a weakly reversible deficiency zero network.  The
DEFICIENCY ZERO THEOREM gives the following information:  For
ANY assignment of pos- itive rate constants to the individual
reactions, the corresponding mass action differential equations
admit PRECISELY ONE steady state (in each positive stoichiometric
compatibility class); that steady state is ASYMPTOTICALLY
STABLE; and there are NO CYCLIC COMPOSITION TRAJECTORIES.
```

Our goal in this text will be to introduce the relevant terminology behind the deficiency zero theorem, and to explain a more modern perspective on complex balancing and deficiency in terms of binomial ideals and toric geometry, that was first presented in a paper from 2009 by Craciun, Dickenstein, Shiu, and Sturmfels [7].

The notes are organized as follows: In Section 2, we introduce some of the basic results in the theory of affine toric varieties that are used in the rest of the notes. In Section 3 we give the formal definition of a chemical reaction network, and introduce the notion of steady states, complex balancing and deficiency. We also state and prove the matrix–tree theorem, and indicate by giving an example how it can be used to find conditions for when a network admits complex balancing steady states. Finally, in Section 4, we give a geometric interpretation of deficiency following [7], and relate this to the classical deficiency zero theorem.

2. Preliminaries from toric geometry

Toric varieties are a particularly well-studied class of varieties, whose underlying combinatorial structure allows for very explicit calculations. In this section we introduce the notion of an *affine* toric variety, and describe the ideals of such varieties. Our presentation is based on that in [6] and [18].

2.1. **Algebraic tori.**

The algebraic prototype for our tori will be the algebraic group $(\mathbb{C}^*)^n \cong V(x_1y_1 - 1, \dots, x_ny_n - 1) \subseteq \mathbb{C}^{2n}$, which has coordinate ring $\mathbb{C}[x_1^{\pm 1}, \dots, x_n^{\pm 1}]$. By an n-dimensional ***torus*** we will mean an affine algebraic group T that is isomorphic to $(\mathbb{C}^*)^n$. An important tool in the study of toric varieties is algebraic group homomorphisms between tori. It turns out that these are easy to characterize.

Proposition 2.1. *A map $\Phi\colon (\mathbb{C}^*)^n \to (\mathbb{C}^*)^s$ is an algebraic group homomorphism if and only if it takes the form $\boldsymbol{t} \mapsto (\boldsymbol{t}^{\boldsymbol{m}_1}, \dots, \boldsymbol{t}^{\boldsymbol{m}_s})$, for some $\boldsymbol{m}_1, \dots, \boldsymbol{m}_s \in \mathbb{Z}^n$.*

Proof. It is easy to see that all maps of this form are algebraic group homomorphisms. Conversely, if $\Phi\colon (\mathbb{C}^*)^n \to (\mathbb{C}^*)^s$ is an algebraic group homomorphism, then, on the level of coordinate rings, it is clear that the $\mathbb{C}$-algebra homomorphism $\Phi^*\colon \mathbb{C}[y_1^{\pm 1}, \dots, y_s^{\pm 1}] \to \mathbb{C}[x_1^{\pm 1}, \dots, x_n^{\pm 1}]$ must send units to units, i.e. $\Phi^*(y_i) = \lambda_i \boldsymbol{x}^{\boldsymbol{m}_i}$ for some $\lambda_i \in \mathbb{C}$ and $\boldsymbol{m}_i \in \mathbb{Z}^n$ for each $i = 1, \dots, s$. But since Φ is a group homomorphism, it holds that $\Phi(1, \dots, 1) = (1, \dots, 1)$, and we conclude that $\lambda_i = 1$. □

A ***character*** of a torus T is an algebraic group homomorphism $\chi\colon T \to \mathbb{C}^*$. The set $M = \mathrm{Hom}_{\mathbf{AlgGrp}}(T, \mathbb{C}^*)$ of all characters is called the ***character lattice*** of T, and has the structure of an abelian group under pointwise multiplication. By Proposition 2.1, there is a one-to-one correspondence between tuples $\boldsymbol{m} = (a_1, \dots, a_n) \in \mathbb{Z}^n$ and characters

$$\chi_{\boldsymbol{m}}\colon (\mathbb{C}^*)^n \to \mathbb{C}^*, \quad (t_1, \dots, t_n) \mapsto t_1^{a_1} \cdots t_n^{a_n}\,.$$

If we for a general n-dimensional torus T fix an isomorphism $T \cong (\mathbb{C}^*)^n$, this observation gives an isomorphism $M \cong \mathbb{Z}^n$, and we conclude that a character lattice is always a free abelian group of rank equal to the dimension of the torus. Indeed, one can go further and show that $\mathrm{Hom}_{\mathbf{AlgGrp}}(\square, \mathbb{C}^*)$ gives an antiequivalence of categories between algebraic tori and free finitely generated abelian groups, with inverse functor $\mathrm{Hom}_{\mathbf{Ab}}(\square, \mathbb{C}^*)$.

We end this subsection by recording two other important results about tori. For proofs of these facts, we refer to [21, §16].

Theorem 2.2. *Let $\Phi\colon T_1 \to T_2$ be an algebraic group homomorphism between tori. Then $\mathrm{im}(\Phi) \subseteq T_2$ is a closed subset and a torus.*

Theorem 2.3. *Let T be a torus, and $H \subseteq T$ be an irreducible subvariety that is also a subgroup. Then H is a torus.*

2.2. **Affine toric varieties.**

Definition 2.4. An ***affine toric variety*** is an irreducible affine variety X containing a torus T as a Zariski open (and therefore dense) subset, in such a way that the multiplication $T \times T \to T$ extends to an algebraic action $T \times X \to X$.

Remark 2.5. Note that $\dim(X) = \dim(T)$ must hold, since the dimension of a non-empty Zariski open subset of an irreducible affine variety always coincides with the dimension of the variety. In particular, $\dim(X) = n$ if $T \cong (\mathbb{C}^*)^n$.

Example 2.6. The curve $X = V(y^3 - x^2)$ is an affine toric variety with torus $T = X \cap (\mathbb{C}^*)^2 \cong \mathbb{C}^*$ via $(t^2, t^3) \mapsto t$. It is clear that the multiplication on T (induced from $\mathbb{C}^*$) extends to an action $T \times X \to X$ with $((t^2, t^3), (a, b)) \mapsto (t^2 a, t^3 b)$.

We now describe a useful method for constructing affine toric varieties. Let $\mathcal{A} \in \mathbb{Z}^{n \times s}$ be a matrix, with columns $\boldsymbol{m}_1, \dots, \boldsymbol{m}_s \in \mathbb{Z}^n$. By Proposition 2.1, every such matrix gives rise to an algebraic group homomorphism

$$\Phi_{\mathcal{A}} \colon (\mathbb{C}^*)^n \to (\mathbb{C}^*)^s \,, \quad \boldsymbol{t} \mapsto (\boldsymbol{t}^{\boldsymbol{m}_1}, \dots, \boldsymbol{t}^{\boldsymbol{m}_s}) \,.$$

Let $Y_{\mathcal{A}}$ be the Zariski closure of the image $T := \mathrm{im}(\Phi_{\mathcal{A}})$ in $\mathbb{C}^s$.

Proposition 2.7 ([6, Prop. 1.1.8])**.** *The affine variety $Y_{\mathcal{A}}$ constructed above is an affine toric variety, with torus $T = \mathrm{im}(\Phi_{\mathcal{A}})$ and $\dim(Y_{\mathcal{A}}) = \mathrm{rank}(\mathcal{A})$.*

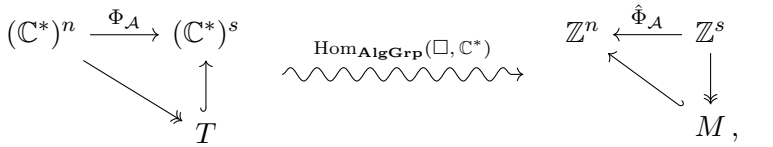
Proof. It follows by Theorem 2.2 that T is a torus, and that it is closed in $(\mathbb{C}^*)^s$. This implies that $T = Y_{\mathcal{A}} \cap (\mathbb{C}^*)^s$, so that T is open in $Y_{\mathcal{A}}$. We also note that $Y_{\mathcal{A}}$ is irreducible, since T is irreducible.

Next, we describe an action of T on $Y_{\mathcal{A}}$. Since $T \subseteq (\mathbb{C}^*)^s$, we can let every $\boldsymbol{s} = \Phi_{\mathcal{A}}(\boldsymbol{t}) \in T$ act on all of $\mathbb{C}^s$ via multiplication. This action takes Zariski closed sets to Zariski closed sets:

$$\boldsymbol{s}.V(f_1, \dots, f_r) = V(f_1(\boldsymbol{t}^{-\boldsymbol{m}_1} x_1, \dots, \boldsymbol{t}^{-\boldsymbol{m}_s} x_s), \dots, f_r(\boldsymbol{t}^{-\boldsymbol{m}_1} x_1, \dots, \boldsymbol{t}^{-\boldsymbol{m}_s} x_s)) \,.$$

In particular, $\boldsymbol{s}Y_{\mathcal{A}}$ will be Zariski closed for every $\boldsymbol{s} \in T$. Note that $T = \boldsymbol{s}T$, and that $\boldsymbol{s}T \subseteq \boldsymbol{s}Y_{\mathcal{A}}$ (since $T \subseteq Y_{\mathcal{A}}$). Hence, $T \subseteq \boldsymbol{s}Y_{\mathcal{A}}$. By definition of the Zariski closure, we therefore have that $Y_{\mathcal{A}} \subseteq \boldsymbol{s}Y_{\mathcal{A}}$. Similarly, we obtain $Y_{\mathcal{A}} \subseteq \boldsymbol{s}^{-1}Y_{\mathcal{A}}$, which after multiplication by $\boldsymbol{s}$ gives $\boldsymbol{s}Y_{\mathcal{A}} \subseteq Y_{\mathcal{A}}$. Hence, we conclude that $\boldsymbol{s}Y_{\mathcal{A}} = Y_{\mathcal{A}}$. This shows that the multiplication in T extends to an algebraic action of all of $\mathbb{C}^s$ which, in turn, restricts to an action on $Y_{\mathcal{A}}$.

Finally, we investigate the dimension of $Y_{\mathcal{A}}$. Recall that $\dim(Y_{\mathcal{A}}) = \dim(T)$ and that $\dim(T)$ is the rank of $M = \mathrm{Hom}_{\mathbf{AlgGrp}}(T, \mathbb{C}^*)$. The map $\Phi_{\mathcal{A}}$ gives rise to a commutative diagrams



where $\hookrightarrow$ and $\twoheadrightarrow$ denote injective and surjective maps, respectively, whereas $\mathbb{Z}^n$ and $\mathbb{Z}^s$ are shorthands for the character lattices of $(\mathbb{C}^*)^n$ and $(\mathbb{C}^*)^s$, respectively. The injectivity of the induced map $M \to \mathbb{Z}^n$ follows from the surjectivity of $(\mathbb{C}^*)^n \to T$. The surjectivity of the induced map $\mathbb{Z}^s \to M$ follows by applying $\mathrm{Hom}_{\mathbf{Ab}}(\square, \mathbb{C}^*)$ to

$$\mathbb{Z}^s \longrightarrow M \twoheadrightarrow \mathrm{coker}(\mathbb{Z}^s \to M)$$

and observing that the injectivity of $T \hookrightarrow (\mathbb{C}^*)^s$ together with the fact that $\mathrm{Hom}_{\mathbf{Ab}}(\mathrm{Hom}_{\mathbf{AlgGrp}}(\square, \mathbb{C}^*)) \cong \mathrm{id}_{\mathbf{Tori}}$ gives that $\mathrm{Hom}_{\mathbf{Ab}}(\mathrm{coker}(\mathbb{Z}^s \to M), \mathbb{C}^*) = 0$, which in turn implies $\mathrm{coker}(\mathbb{Z}^s \to M) = 0$. We can now note that $\hat{\Phi}_{\mathcal{A}}(\boldsymbol{e}_i) = \boldsymbol{m}_i$, since $\chi_{\boldsymbol{e}_i} \circ \Phi_{\mathcal{A}} = \chi_{\boldsymbol{m}_i}$. Hence, $\mathrm{im}(\hat{\Phi}_{\mathcal{A}}) = \mathrm{col}_{\mathbb{Z}}(\mathcal{A})$. By the first isomorphism theorem of abelian groups, and the commutativity of the rightmost diagram, it holds that $M \cong \mathrm{im}(M \to \mathbb{Z}^n) = \mathrm{im}(\hat{\Phi}_{\mathcal{A}}) = \mathrm{col}_{\mathbb{Z}}(\mathcal{A})$. This concludes the proof. □

Remark 2.8. One can show that *every* affine toric variety is isomorphic to $Y_{\mathcal{A}}$ for some integer matrix $\mathcal{A}$; see [6, Thm. 1.1.17] for a proof.

Remark 2.9. We note that the real part $Y_{\mathcal{A}} \cap \mathbb{R}^n$ of an affine toric variety $Y_{\mathcal{A}}$ is Zariski dense in $Y_{\mathcal{A}}$. This follows from [1, Prop. 3.3.16], since $Y_{\mathcal{A}}$ is irreducible and $(1, \dots, 1)$ is a smooth real point of $Y_{\mathcal{A}}$ (indeed, the entire open subset $Y_{\mathcal{A}} \cap (\mathbb{C}^*)^n \cong (\mathbb{C}^*)^{\mathrm{rk}(\mathcal{A})}$ is smooth, since smoothness is a local property that is preserved by isomorphism). In particular, the real dimension of $Y_{\mathcal{A}} \cap \mathbb{R}^n$ coincides with the complex dimension of $Y_{\mathcal{A}}$ which is $\mathrm{rk}(\mathcal{A})$.

2.3. **Binomial ideals and lattice ideals.** Our next goal will be to determine the ideal $I(Y_{\mathcal{A}}) \subseteq \mathbb{C}[x_1, \dots, x_s]$, where $Y_{\mathcal{A}}$ is as in the previous subsection. Before that we give a brief introduction to the theory of binomial ideals.

A (pure) ***binomial*** in the polynomial ring $\mathbb{C}[\boldsymbol{x}] = \mathbb{C}[x_1, \dots, x_n]$ we will mean a difference of monomials $\boldsymbol{x}^{\boldsymbol{u}} - \boldsymbol{x}^{\boldsymbol{v}}$ for $\boldsymbol{u}, \boldsymbol{v} \in \mathbb{Z}^n_{\geqslant 0}$. An ideal $I \subseteq \mathbb{C}[\boldsymbol{x}]$ generated by binomials is called a ***binomial ideal***. It is easy to see that such an ideal is generated by *finitely many* binomials. Indeed, since $\mathbb{C}[\boldsymbol{x}]$ is Noetherian, every ideal I admits some finite set of generators, each of which can be written as a finite $\mathbb{C}[\boldsymbol{x}]$-linear combination of binomial ideals.

Proposition 2.10 ([18, Thm. 3.6])**.** *Any binomial ideal, with respect to any monomial ordering, admits a Gröbner basis consisting of binomials.*

Proof. Apply Buchberger's algorithm to a finite set of binomial generators, note that the S-polynomial of two binomials is a binomial, and use that the remainder of a binomial with respect to a set of binomials can be taken to be a binomial. □

A particular class of binomial ideals is so-called lattice ideals. By a ***lattice***, we here mean a subgroup $L \subseteq \mathbb{Z}^n$. Let L be a lattice. For any $\boldsymbol{\ell} \in L$ gives rise to a binomial $\boldsymbol{x}^{\boldsymbol{\ell}_+} - \boldsymbol{x}^{\boldsymbol{\ell}_-} \in \mathbb{C}[\boldsymbol{x}]$, where

$$\boldsymbol{\ell}_+ = \sum_{\ell_i > 0} \ell_i \boldsymbol{e}_i \,, \quad \boldsymbol{\ell}_- = \sum_{\ell_i < 0} (-\ell_i) \boldsymbol{e}_i \,.$$

The ideal $I_L = \langle \boldsymbol{x}^{\boldsymbol{\ell}_+} - \boldsymbol{x}^{\boldsymbol{\ell}_-} : \boldsymbol{\ell} \in L \rangle$ is called the ***lattice ideal*** associated to L. It is easy to verify that $I_L = \langle \boldsymbol{x}^{\boldsymbol{u}} - \boldsymbol{x}^{\boldsymbol{v}} : \boldsymbol{u}, \boldsymbol{v} \in \mathbb{Z}^n_{\geqslant 0}, \boldsymbol{u} - \boldsymbol{v} \in L \rangle$.

Proposition 2.11. *Let $L \subseteq \mathbb{Z}^n$ be a lattice, and let $\mathscr{B}$ be a basis for L. Then*

$$I_L = \langle \boldsymbol{x}^{\boldsymbol{\ell}_+} - \boldsymbol{x}^{\boldsymbol{\ell}_-} : \boldsymbol{\ell} \in \mathscr{B} \rangle : (x_1 \cdots x_n)^\infty \,.$$

Proposition 2.12. *Let $L \subseteq \mathbb{Z}^n$ be a lattice. Then I_L is prime if and only if $\mathbb{Z}^n / L$ is torsion-free.*

For proofs of these facts, see [18, §3.3].

2.4. **Toric ideals.** Let $\mathcal{A} \in \mathbb{Z}^{n \times s}$ be an integer matrix with columns $\boldsymbol{m}_1, \dots, \boldsymbol{m}_s \in \mathbb{Z}^n$, and let $Y_{\mathcal{A}}$ be the closure of the image of the morphism $\Phi \colon (\mathbb{C}^*)^s \to \mathbb{C}^n$, $\boldsymbol{t} \mapsto (\boldsymbol{t}^{\boldsymbol{m}_1}, \dots, \boldsymbol{t}^{\boldsymbol{m}_s})$. We now give two different descriptions of the ideal $I(Y_{\mathcal{A}}) \subseteq \mathbb{C}[x_1, \dots, x_s]$.

The first description is straight-forward: we simply observe that $I(Y_{\mathcal{A}}) = \ker(\Phi^*_{\mathcal{A}})$, where

$$\Phi^*_{\mathcal{A}} \colon \mathbb{C}[x_1, \dots, x_s] \to \mathbb{C}[t_1^{\pm 1}, \dots, t_n^{\pm 1}] \,, \quad x_j \mapsto \boldsymbol{t}^{\boldsymbol{m}_j}$$

is the induced $\mathbb{C}$-algebra homomorphism between the coordinate rings.

The second description is a little bit more intricate: it turns out that $I(Y_{\mathcal{A}})$ is the lattice ideal corresponding to the lattice $L = \ker_{\mathbb{Z}}(\mathcal{A}) \subseteq \mathbb{Z}^s$. The proof we give here, using monomial orderings, is based on that given in [30, Lemma 4.1].

Proposition 2.13 ([6, Prop. 1.1.9])**.** *In the situation above,* $I(Y_{\mathcal{A}}) = I_L$.

Proof. We begin by showing the inclusion "$\supseteq$". Note that any generator $\boldsymbol{x}^{\boldsymbol{\ell}_+} - \boldsymbol{x}^{\boldsymbol{\ell}_-}$ of I_L vanishes on $\mathrm{im}(\Phi_{\mathcal{A}})$:

$$(\boldsymbol{x}^{\boldsymbol{\ell}_+} - \boldsymbol{x}^{\boldsymbol{\ell}_-})(\Phi_{\mathcal{A}}(\boldsymbol{t})) = \prod_{\ell_i>0} (\boldsymbol{t}^{\boldsymbol{m}_i})^{\ell_i} - \prod_{\ell_i<0} (\boldsymbol{t}^{\boldsymbol{m}_i})^{-\ell_i} = \boldsymbol{t}^{\mathcal{A}\boldsymbol{\ell}_+} - \boldsymbol{t}^{\mathcal{A}\boldsymbol{\ell}_-} = 0\,.$$

By definition of the Zariski closure, it follows that $\boldsymbol{x}^{\boldsymbol{\ell}_+} - \boldsymbol{x}^{\boldsymbol{\ell}_-} \in I(Y_{\mathcal{A}})$.

To show "$\subseteq$", we assume for a contradiction that $I_L \not\subseteq I(Y_{\mathcal{A}})$, and fix a monomial ordering $\preccurlyeq$ on $\mathbb{C}[\boldsymbol{x}]$. We can then choose an $f \in I(Y_{\mathcal{A}}) \setminus I_L$ with minimal leading monomial. Suppose the leading monomial of f is $\boldsymbol{x}^{\boldsymbol{u}} = x_1^{u_1} \cdots x_s^{u_s}$. Without loss of generality, we can assume that this is the leading *term* of f (if not, just multiply by a scalar). Now, note that $f(\Phi_{\mathcal{A}}(\boldsymbol{t})) = f(\boldsymbol{t}^{\boldsymbol{m}_1}, \dots, \boldsymbol{t}^{\boldsymbol{m}_s}) = 0$ in $\mathbb{C}[t_1^{\pm 1}, \dots, t_n^{\pm 1}]$. This means that the term $\boldsymbol{x}^{\boldsymbol{u}}(\Phi_{\mathcal{A}}(\boldsymbol{t}))$ is cancelled in the evaluation, so f must contains a monomial $\boldsymbol{x}^{\boldsymbol{v}} = x_1^{v_1} \cdots x_s^{v_s} \prec \boldsymbol{x}^{\boldsymbol{u}}$ such that $\boldsymbol{x}^{\boldsymbol{u}}(\Phi_{\mathcal{A}}(\boldsymbol{t})) = \boldsymbol{x}^{\boldsymbol{v}}(\Phi_{\mathcal{A}}(\boldsymbol{t}))$. But then $(\boldsymbol{t}^{\boldsymbol{m}_1})^{u_1} \cdots (\boldsymbol{t}^{\boldsymbol{m}_s})^{u_s} = (\boldsymbol{t}^{\boldsymbol{m}_1})^{v_1} \cdots (\boldsymbol{t}^{\boldsymbol{m}_s})^{v_s}$, which implies $\boldsymbol{t}^{\mathcal{A}\boldsymbol{u}} = \boldsymbol{t}^{\mathcal{A}\boldsymbol{v}}$. Hence, $\mathcal{A}\boldsymbol{u} = \mathcal{A}\boldsymbol{v}$, which implies $\boldsymbol{u} - \boldsymbol{v} \in L$ and $\boldsymbol{x}^{\boldsymbol{u}} - \boldsymbol{x}^{\boldsymbol{v}} \in I_L$. This gives that $f - \boldsymbol{x}^{\boldsymbol{u}} - \boldsymbol{x}^{\boldsymbol{v}} \in I(Y_{\mathcal{A}}) \setminus I_L$. However, the leading monomial of this polynomial is strictly smaller that that of f with respect to $\preccurlyeq$, which is a contradiction. □

An ideal of the form $I(Y_{\mathcal{A}})$ for some $\mathcal{A} \in \mathbb{Z}^{n\times s}$ is called a ***toric ideal***. It turns out that we have the following concrete characterization of toric ideals.

Proposition 2.14 ([6, Prop. 1.1.11])**.** *An ideal* $I \subseteq \mathbb{C}[x_1, \dots, x_s]$ *is a toric ideal if and only if it is binomial and prime.*

Proof. We first show the "only if" part. Suppose $I = I(Y_{\mathcal{A}})$ for some $\mathcal{A} \in \mathbb{Z}^{n\times s}$ and $n \in \mathbb{Z}_{\geqslant 0}$. By Proposition 2.13, I is the lattice ideal associated to $\ker_{\mathbb{Z}}(\mathcal{A})$ and therefore a binomial ideal. Furthermore, $Y_{\mathcal{A}}$ is irreducible by Theorem 2.7, which implies that I is prime.

Next, we prove the "if" part. For this end, let $I = \langle \boldsymbol{x}^{\boldsymbol{u}^i} - \boldsymbol{x}^{\boldsymbol{v}^i} : i = 1, \dots, r \rangle$ for some $\boldsymbol{u}^i, \boldsymbol{v}^i \in \mathbb{Z}^s_{\geqslant 0}$ be a binomial prime ideal. Note that $T := V(I) \cap (\mathbb{C}^*)^s \neq \varnothing$ (e.g. $(1, \dots, 1) \in T$), and that it is a subgroup of $(\mathbb{C}^*)^s$. Since $V(I) \subseteq \mathbb{C}^s$ is irreducible, we have that $T = V(I) \cap (\mathbb{C}^*)^s$ is irreducible in $(\mathbb{C}^*)^s$. By Theorem 2.3, this implies that T is a torus. Suppose that the dimension of T is n, pick an isomorphism $(\mathbb{C}^*)^n \to T$, and consider the composition $\Phi\colon (\mathbb{C}^*)^n \to T \hookrightarrow (\mathbb{C}^*)^s$. Note that Φ is an algebraic group homomorphism between tori. By Proposition 2.1, this means that there exists a matrix $\mathcal{A} \in \mathbb{Z}^{n\times s}$ such that $\Phi = \Phi_{\mathcal{A}}$, with notation as in Section 2.2. Note that $\mathrm{im}(\Phi) = T$ is an open subset of $V(I)$ (since $(\mathbb{C}^*)^s$ is open in $\mathbb{C}^s$). Because $V(I)$ is irreducible, this implies that the closure of T in $V(I)$ (and hence also in $\mathbb{C}^s$) is equal to $V(I)$. Again using the notation from Section 2.2, we now have $Y_{\mathcal{A}} = V(I)$. Since I is prime (and hence radical), Hilbert's Nullstellensatz gives $I = I(V(I)) = I(Y_{\mathcal{A}})$. □

3. Reaction networks and complex balancing

In this section, we introduce some of the core concepts in the theory of chemical reaction networks, with focus on their steady states. In particular, we introduce the notion of a complex balancing steady state, and discuss the properties of reaction networks that admit such steady states.

3.1. **Basic definitions and examples.** A ***reaction network*** consists of three finite ordered sets:

- A set $\mathcal{S} = \{X_1, \dots, X_n\}$ of ***species***.
- A set $\mathcal{C} = \{\boldsymbol{y}_1, \dots, \boldsymbol{y}_m\} \subseteq \mathbb{Z}^n_{\geqslant 0}$ of ***complexes*** of the network. A complex $(\lambda_1, \dots, \lambda_n) \in \mathcal{C}$ will be interpreted as a linear combination $\sum_{i=1}^n \lambda_i X_i$ of the species, with non-negative integer coefficients.
- A set $\mathcal{R} = \{R_1, \dots, R_r\} \subseteq (\mathcal{C} \times \mathcal{C}) \setminus \{(\boldsymbol{y}, \boldsymbol{y}) : \boldsymbol{y} \in \mathcal{C}\}$ of ***reactions***. A reaction $(\boldsymbol{y}_i, \boldsymbol{y}_j)$ will be denoted $\boldsymbol{y}_i \to \boldsymbol{y}_j$, and if $(\boldsymbol{y}_i, \boldsymbol{y}_j), (\boldsymbol{y}_j, \boldsymbol{y}_i) \in \mathcal{R}$ we write $\boldsymbol{y}_i \rightleftharpoons \boldsymbol{y}_j$.

A reaction network $\mathcal{N} = (\mathcal{S}, \mathcal{C}, \mathcal{R})$ gives rise to a directed graph $G = (\mathcal{C}, \mathcal{R})$ with vertices $\mathcal{C}$ and edges $\mathcal{R}$. We will often identify the network with this digraph (and let $\mathcal{S}$ be understood from the context). In particular, we will use terminology from graph theory to describe our networks (e.g. *connected components* and *strong connectedness*).

If not stated otherwise, we will always let n denote the number of species in a network, m the number of complexes, r the number of reactions and ℓ the number of connected components.

Example 3.1. A simple reaction network that describes the decomposition of ozone into oxygen is given by

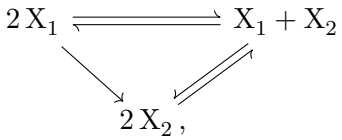
$$\mathrm{O_3} \rightleftharpoons \mathrm{O_2} + \mathrm{O}\,, \quad \mathrm{O_3} + \mathrm{O} \longrightarrow 2\,\mathrm{O_2}\,.$$

In our formalism, it corresponds to

$$\mathcal{S} = \{\mathrm{O_3}, \mathrm{O_2}, \mathrm{O}\}\,,\ \mathcal{C} = \{(1,0,0), (0,1,1), (1,0,1), (0,2,0)\}\,,$$
$$\mathcal{R} = \{((1,0,0),(0,1,1)), ((0,1,1),(1,0,0)), ((1,0,1),(0,2,0))\}\,.$$

It has two connected components, one of which is strongly connected and one of which is not strongly connected.

Example 3.2. A more abstract example is this network:



which corresponds to

$$\mathcal{S} = \{\mathrm{X_1}, \mathrm{X_2}\}\,,\ \mathcal{C} = \{(2,0), (1,1), (0,2)\}\,,$$
$$\mathcal{R} = \{((2,0),(1,1)), ((1,1),(2,0)), ((1,1),(0,2)), ((2,0),(0,2))\}\,,$$

and is strongly connected.

Example 3.3. The following example comes up in [12, §4.2] as a simplification of a the classical *Edelstein example* that first appeared in [10], as a simple example of a network that admits multiple steady states. Feinberg's simplified network is given by

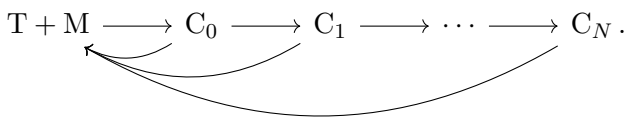
$$\mathrm{A} \rightleftharpoons 2\,\mathrm{A}\,, \quad \mathrm{A} + \mathrm{B} \rightleftharpoons \mathrm{C} \rightleftharpoons \mathrm{B}\,,$$

and corresponds to

$$\mathcal{S} = \{\mathrm{A}, \mathrm{B}, \mathrm{C}\}\,,\ \mathcal{C} = \{(1,0,0), (2,0,0), (1,1,0), (0,0,1), (0,1,0)\}\,,$$
$$\mathcal{R} = \{((1,0,0),(2,0,0)), \dots, ((0,0,1),(0,1,0))\}\,.$$

It has two connected components, both of which are strongly connected.

Example 3.4. As a final example, we again consider McKeithan's model for kinetic proofreading, proposed in [27], here in its full form, with N inactive intermediate steps from binding to the active complex:



It is strongly connected, and involves $N + 2$ complexes.

3.2. **Kinetics and stoichiometry.** Given a reaction network $\mathcal{N} = (\mathcal{S}, \mathcal{C}, \mathcal{R})$, we will be interested in modelling the concentrations of the species over time. The concentrations will be assembled into a vector $\boldsymbol{x} = (x_1, \dots, x_n)$, where x_i denotes the concentration of ith species. The concentrations are assumed to satisfy an autonomous system

$$\dot{\boldsymbol{x}} = \sum_{(\boldsymbol{y}_i \to \boldsymbol{y}_j) \in \mathcal{R}} (\boldsymbol{y}_j - \boldsymbol{y}_i)\, v_{ij}(\boldsymbol{x})\,, \quad \boldsymbol{x} \in \mathbb{R}^n_{\geqslant 0}\,, \tag{3.1}$$

where $\boldsymbol{v} \colon \mathbb{R}^n_{\geqslant 0} \to \mathbb{R}^r_{\geqslant 0}$ is a C^1-function, with components indexed by $\mathcal{R}$, that describes the rate of each reaction as a function of the concentrations. Such a function is called a ***kinetics*** for $\mathcal{N}$.

We can rewrite the system (3.1) as $\dot{\boldsymbol{x}} = N\,\boldsymbol{v}(\boldsymbol{x})$, where $N \in \mathbb{R}^{n \times r}$ is the so-called ***stoichiometric matrix*** of $\mathcal{N}$, defined by letting the pth column be $\boldsymbol{y}_j - \boldsymbol{y}_i$ if $R_p = (\boldsymbol{y}_i \to \boldsymbol{y}_j)$. The column space $S = \mathrm{col}(N) \subseteq \mathbb{R}^n$ is called the ***stoichiometric subspace***, and its dimension is denoted s. Given an initial condition $\boldsymbol{x}_0 \in \mathbb{R}^n_{\geqslant 0}$, it is easy to see that the system will develop inside the parallel translate $\boldsymbol{x}_0 + S$, which we will call the ***stoichiometric compatibility class*** of $\boldsymbol{x}_0$.

Example 3.5. For the reaction network in Example 3.2, we obtain

$$N = \begin{pmatrix} -1 & 1 & -1 & 1 & -2 \\ 1 & -1 & 1 & -1 & 2 \end{pmatrix}, \quad S = \mathrm{span}_{\mathbb{R}} \left\{ \begin{pmatrix} 1 \\ -1 \end{pmatrix} \right\},$$

and hence $s = \dim_{\mathbb{R}}(S) = 1$.

An important aspect of the dynamics of a reaction network, under the assumption of a kinetics, is the ***steady states*** of the network, by which we mean points $\boldsymbol{x}^* \in \mathbb{R}^n_{\geqslant 0}$ for which $\dot{\boldsymbol{x}} = \boldsymbol{0}$, i.e. solutions to the system $N\,\boldsymbol{v}(\boldsymbol{x}) = \boldsymbol{0}$.

3.3. **Mass action networks.** As is common in most parts of CRNT, we will here restrict our attention to so-called ***mass action kinetics***, in which each component of $\boldsymbol{v} \colon \mathbb{R}^n_{\geqslant 0} \to \mathbb{R}^r_{\geqslant 0}$ is given by $v_{ij}(\boldsymbol{x}) = \kappa_{ij} \boldsymbol{x}^{\boldsymbol{y}_i}$ for some ***rate constant*** $\kappa_{ij} \in \mathbb{R}_{>0}$. A ***mass action network*** $\mathcal{N} = (\mathcal{S}, \mathcal{C}, \mathcal{R}, \boldsymbol{\kappa})$ is a reaction network with mass action kinetics, where $\boldsymbol{\kappa} = (\kappa_{ij})_{(\boldsymbol{y}_i \to \boldsymbol{y}_j) \in \mathcal{R}} \in \mathbb{R}^r_{>0}$ is the tuple of rate constants (with the same ordering as $\mathcal{R}$). We can view a mass-action network as a digraph $(\mathcal{C}, \mathcal{R})$ where the edges are labeled by the rate constants.

Remark 3.6. Mass-action kinetics is based on the idea of collision theory, and goes back to work by Guldberg and Waage (see e.g. [16]). It is usually regarded as a reasonable approximation for the dynamics of a reaction network, but relies, among other things, on isothermal, well-stirred conditions. For a discussion on the limitations of mass-action kinetics in a biochemical context, we refer to [17].

The system of ODE's associated of a mass action network is given by

$$\dot{\boldsymbol{x}} = \sum_{(\boldsymbol{y}_i \to \boldsymbol{y}_j) \in \mathcal{R}} (\boldsymbol{y}_j - \boldsymbol{y}_i)\, \kappa_{ij} \boldsymbol{x}^{\boldsymbol{y}_i}\,, \quad \boldsymbol{x} \in \mathbb{R}^n_{\geqslant 0}\,.$$

The steady states correspond to the zeros of the right-hand side. Note that this gives rise to a system of polynomial equations, which can be studied with methods from algebraic geometry. It is, however, worth noting that the system is also partly linear in nature. A common way to emphasize this, is via the factorization

$$\dot{\boldsymbol{x}} = Y\, A_{\boldsymbol{\kappa}}\, \Psi(\boldsymbol{x})\,, \tag{3.2}$$

where

- $Y \in \mathbb{R}^{n\times m}$ has $\boldsymbol{y_j}$ as its jth column. (This matrix tells us how much there is of every species in every complex.)
- $A_{\boldsymbol{\kappa}} \in \mathbb{R}^{m\times m}$ is the ***Laplacian*** of of the labeled digraph associated to $\mathcal{N}$. The (i,j)-th entry, for $i \neq j$, is given by κ_{ji}, whereas the diagonal entries are taken so that each columns sums to 0. (Loosely speaking, the jth column tells us the inflow of the different complexes caused by the reactions where $\boldsymbol{y}_j$ is the reactant.)
- $\Psi(\boldsymbol{x}) \in \mathbb{R}^m$ is the column vector of monomials in the concentrations corresponding to each complex, i.e. $\Psi(\boldsymbol{x}) = (\boldsymbol{x}^{\boldsymbol{y}_1}, \ldots, \boldsymbol{x}^{\boldsymbol{y}_m})^t$.

Under this factorization, the steady states of the mass-action network form a semi-algebraic set $V_{\geqslant 0}(Y A_{\boldsymbol{\kappa}} \Psi(\boldsymbol{x})) \subseteq \mathbb{R}^n_{\geqslant 0}$. Two of the main questions about steady states that are studied in CRNT are these:

(i) How many steady states are there in each stoichiometric compatibility class, i.e. what does $V_{\geqslant 0}(Y A_{\boldsymbol{\kappa}} \Psi(\boldsymbol{x})) \cap (\boldsymbol{x}_0 + S)$ look like for different choices of $\boldsymbol{x}_0$ and $\boldsymbol{\kappa}$?

(ii) Are the steady states locally attracting, i.e. given $\boldsymbol{x}^* \in V_{\geqslant 0}(Y A_{\boldsymbol{\kappa}} \Psi(\boldsymbol{x}))$, and $\boldsymbol{x}(0) \in (\boldsymbol{x}^* + S)$ sufficiently close to $\boldsymbol{x}^*$, does it hold that $\boldsymbol{x}(t) \to \boldsymbol{x}^*$ as $t \to \infty$?

The answers typically depend on both the rate constants and the stoichiometric compatibility class. Since both of these are often unknown (especially in biochemical applications), the study of the steady states can be quite challenging. For a survey on the main problems, techniques and recent developments (especially with regards to multistationarity) we refer to [8].

Remark 3.7. It is interesting to note that systems of ODE's that do not *a priori* have anything to do with chemistry can be realized as the autonomous system of a mass-action network. A simple example is the equations in the epidemiological SIR model:

$$\dot{S} = -\beta I S\,, \quad \dot{I} = \beta I S - \gamma I\,, \quad \dot{R} = \gamma I\,,$$

which corresponds to the mass-action network

$$\mathrm{S} + \mathrm{I} \xrightarrow{\beta} 2\,\mathrm{I}\,, \quad \mathrm{I} \xrightarrow{\gamma} \mathrm{R}\,.$$

Necessary and sufficient conditions for when an autonomous system corresponds to a mass-action network can be found in [22]. In particular, these conditions exclude some well-known systems with particularly pathological dynamics, such as the Lorentz system

$$\dot{x} = \sigma y - \sigma x\,, \quad \dot{y} = \rho x - x z - y\,, \quad \dot{z} = x y - \beta z\,,$$

with parameters $\sigma, \rho \in \mathbb{R}_{>0}$. Here the second equation breaks the conditions given in [22, Thm. 3.1]. This could be seen as a first indication that the study of mass-action networks is more than the mere study of polynomial autonomous systems.

3.4. **Complex balancing.** The main focus of this text will be reaction networks that admit steady states that satisfy the following two additional properties:

(i) The steady state involves the whole network, i.e. $\boldsymbol{x}^* \in \mathbb{R}^n_{>0}$.
(ii) The reaction rates are balanced already at the level of complexes, i.e. $A_{\boldsymbol{\kappa}}\Psi(\boldsymbol{x}^*) = \mathbf{0}$.

Such a steady state is said to be ***complex balancing***. As we will soon see, mass-action networks that admit such steady states have remarkably well-behaved dynamics.

Definition 3.8. Let $\mathcal{N} = (\mathcal{S}, \mathcal{C}, \mathcal{R}, \boldsymbol{\kappa})$ be a mass-action network. The corresponding autonomous system $\dot{\boldsymbol{x}} = Y A_{\boldsymbol{\kappa}} \Psi(\boldsymbol{x})$ is called a ***toric dynamical system*** if it admits a complex balancing steady state.

The term *toric* is fairly modern terminology that was introduced in [7]. It alludes to a certain toric structure in the set of rate constants for which a network $\mathcal{N}$ gives rise to a toric dynamical system; this is the main topic of Section 4 of these notes.

Theorem 3.9. *Suppose $\mathcal{N} = (\mathcal{S}, \mathcal{C}, \mathcal{R}, \boldsymbol{\kappa})$ is a mass-action network that gives rise to a toric dynamical system $\dot{\boldsymbol{x}} = Y A_\kappa \Psi(\boldsymbol{x})$. Then the following holds:*

(i) Every stoichiometric compatibility class has a unique positive steady state.
(ii) Every positive steady state is complex balancing.
(iii) Every steady state is locally attracting.

For proofs of these facts we refer to [20].

Remark 3.10. Conjecturally, point (iii) in the theorem above can be strengthened to say that complex balancing steady states are *globally* attracting. This so-called ***global attractor conjecture*** was first formulated in [19].

The next result gives a remarkably simple sufficient condition for when a reaction network gives rise to a toric dynamical system. The theorem is usually attributed to Feinberg, and a classical reference is [12, Lecture 5].

Theorem 3.11 (Deficiency zero theorem)**.** *Suppose that $\mathcal{N} = (\mathcal{S}, \mathcal{C}, \mathcal{R})$ is a reaction network that satisfies the following two conditions:*

(i) Every connected component of $\mathcal{N}$ is strongly connected.
(ii) It holds that $\delta := m - \ell - s = 0$, where m is the number of complexes, ℓ is the number of connected components, and s is dimension of the stoichiometric subspace.

Then the mass-action network $(\mathcal{S}, \mathcal{C}, \mathcal{R}, \boldsymbol{\kappa})$ gives rise to a toric dynamical system for any choice of rate constants $\boldsymbol{\kappa} \in \mathbb{R}^r_{>0}$.

A graph satisfying condition (i) in the theorem is called ***weakly reversible***, and the quantity $\delta = m - \ell - s$ is called the ***deficiency*** of the network. In Chapter 4 we will go through a modern proof of this theorem, based on results from toric geometry, and at the same time give a geometric interpretation of the deficiency.

3.5. **The kernel of the Laplacian.** An important idea in both the classical proof of the deficiency zero theorem, and the more modern toric approach we will take in the next chapter, is to exploit the partially linear structure of the system (3.2). In this subsection, we will therefore investigate the kernel of the Laplacian. Throughout, we will let $G = (V, E)$ be a digraph with $V = \{1, \dots, m\}$ and positive labels $\boldsymbol{\kappa} = (\kappa_{ij})_{(i\to j)\in E}$. We also recall that the Laplacian $A_{\boldsymbol{\kappa}} \in \mathbb{R}^{m\times m}$ for G is given by

$$(A_{\boldsymbol{\kappa}})_{ji} = \begin{cases} \kappa_{ij} & \text{if } (i \to j) \in E \text{ and } i \neq j \\ 0 & \text{if } (i \to j) \notin E \text{ and } i \neq j \\ -\Big(\displaystyle\sum_{(i\to \ell)\in E} \kappa_{i\ell} \Big) & \text{if } i = j\,. \end{cases} \tag{3.3}$$

It is easy to see that if $\ker(A_{\boldsymbol{\kappa}}) \cap \mathbb{R}^m_{>0} \neq \varnothing$, then every strongly connected component must be terminal, or, equivalently: G must be weakly reversible. We will therefore restrict our attention to this case.

The key to understanding the kernel in the weakly reversible case will be to study certain subgraphs of G. By a ***subtree*** of G we will mean a directed subgraph without cycles, and a subtree will be called an ***i-tree*** it has the vertex i as its unique sink. For any subtree T of G, let $\boldsymbol{\kappa}^T = \prod_{(i\to j)\in E(T)} \kappa_{ij}$, and for each $i = 1, \dots, m$, let

$$K_i = \sum_{\substack{T \text{ maximal} \\ i\text{-tree}}} \boldsymbol{\kappa}^T\,.$$

With this notation at hand, we are now able to prove the *matrix–tree theorem*, which gives an explicit basis for $\ker(A_{\boldsymbol{\kappa}})$. The proof we give here is based on a lemma proved in [29, §2.2.1]. For another proof, and a discussion on the historical context of the matrix–tree theorem, we refer to [28].

Lemma 3.12. *Let $G = (V, E)$ be a strongly connected digraph with $V = \{1, \dots, m\}$ and positive labels $\boldsymbol{\kappa} = (\kappa_{ij})_{(i\to j)\in E}$. Then the (i, j)-th cofactor of the Laplacian $A_{\boldsymbol{\kappa}}$ is given by $c_{ij} = (-1)^{m-1}K_j$ for every $i, j \in \{1, \dots, m\}$.*

Proof. Let $M(i, j)$ be the (i, j)-th minor of $A_{\boldsymbol{\kappa}}$, i.e. the determinant of the submatrix obtained by removing the ith row and the jth column. Recall that $c_{ij} = (-1)^{i+j}M(i, j)$. The proof now consists of the following steps.

Step 1: We begin by reducing to the case $i = 1$, by observing that $c_{ij} = c_{1j}$ for all $i, j \in \{1, \dots, m\}$. To see this, note that each column of $A_{\boldsymbol{\kappa}}$ sums to 0, so we can obtain $M(1, j)$ from $M(i, j)$ by adding the rows 2 through $m - 1$ to the first row, negating it and the reordering the rows via $i - 2$ transpositions of the columns. This implies $M(i, j) = (-1)^{1+(i-2)}M(1, j)$, which gives the desired equality.

Step 2: We now reduce to the case $j = 1$. Let $\hat{G}$ be the graph obtained by switching the labels 1 and j, and let $\hat{M}$ denote the corresponding minors. Then $M(1, j) = \hat{M}(j, 1)$. At the same time, the observations we made in Step 1 give $(-1)^{j+1}\hat{M}(j, 1) = \hat{M}(1, 1)$, which evaluates to $(-1)^{m-1}K_j$, if the lemma is valid for $(i, j) = (1, 1)$.

Step 3: Observe that edges going out of the vertex 1 neither affect $M(1, 1)$ nor K_1. Form a new digraph G' by removing all such edges. Note that $|E(G')| \geqslant m - 1$ by the strong connectivity of G.

Step 4: Note that $|E(G')| = m-1$ if and only if G' is a maximal 1-tree of G. In this case, we can reorder the vertices so that each edge goes from a vertex with higher index to a vertex with lower index, which turns the submatrix corresponding to $M(1, 1)$

into an upper triangular matrix with diagonal entries $-\kappa_{st}$ for all $(s \to t) \in E(G')$, which readily yields the desired equality.

Step 5: If $|E(G')| > m-1$, then there are vertices of G that have outdegree greater than 2. For each such vertex, choose precisely one edge going out of it. By making all possible combinations of such choices at all vertices, we get a collection of subgraphs $G^{(1)}, \dots, G^{(r)}$ that are precisely the maximal i-trees of G. By the multilinearity of the determinant, it follows that $M(i,j)$ is the sum of the (i,j)-th minors of the subgraphs $G^{(1)}, \dots, G^{(r)}$. Combined with Step 4, this proves the lemma. □

Theorem 3.13 (Matrix–tree theorem)**.** *Let $G = (V, E)$ be a weakly reversible digraph with positive labels $\boldsymbol{\kappa} = (\kappa_{ij})_{(i\to j)\in E}$, and connected components $G_1, \dots, G_\ell$. Then* $\dim(\ker(A_{\boldsymbol{\kappa}})) = \ell$*, and a basis is given by $\{\boldsymbol{w}_1, \dots, \boldsymbol{w}_\ell\}$, where*

$$\boldsymbol{w}_\nu = \sum_{i \in V(G_\nu)} K_i \boldsymbol{e}_i \,, \quad \nu = 1, \dots, \ell \,.$$

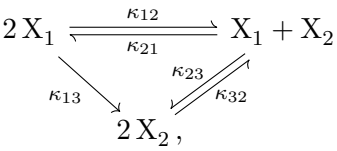
Proof. We begin by noting that the weak reversibility implies that if we reorder the vertices by connected components, then the Laplacian $A_{\boldsymbol{\kappa}}$ becomes a block-diagonal matrix $A_{\boldsymbol{\kappa}} = A_{\boldsymbol{\kappa}}(G_1) \oplus \cdots \oplus A_{\boldsymbol{\kappa}}(G_\ell)$, and it suffices to compute the kernel of the Laplacian for each connected component of G. Thus we only need to prove the theorem for the case $\ell = 1$.

We do this by observing that the rows of $A_{\boldsymbol{\kappa}}$ all sum to 0, so $\det(A_{\boldsymbol{\kappa}}) = 0$. At the same time, the strong connectivity implies the existence of an i-tree for every $i \in V$, so that $K_i \neq 0$. The previous lemma therefore shows that all $(m-1)\times(m-1)$-minors are non-zero, and we conclude that $\operatorname{rank}(A_{\boldsymbol{\kappa}}) = m - 1$.

The results now follows if we can prove that $(K_1, \dots, K_m)^t \in \ker(A_{\boldsymbol{\kappa}})$. To see this, recall that the adjugate matrix of $A_{\boldsymbol{\kappa}}$ is given by $\operatorname{adj}(A_{\boldsymbol{\kappa}}) = (c_{ji})$, where c_{ji} is the (j,i)-th cofactor. The lemma then gives that the columns of $\operatorname{adj}(A_{\boldsymbol{\kappa}})$ are $(-1)^{m-1}(K_1, \dots, K_m)^t$. Since the adjugate matrix satisfies $\operatorname{adj}(A_{\boldsymbol{\kappa}})A_{\boldsymbol{\kappa}} = \det(A_{\boldsymbol{\kappa}})I$, and $\det(A_{\boldsymbol{\kappa}}) = 0$, this gives $A_{\boldsymbol{\kappa}}(K_1, \dots, K_m)^t = \mathbf{0}$. □

The following example illustrates how the matrix–tree theorem can be used to find a (necessary) condition for when a certain reaction network gives rise to a toric dynamical system.

Example 3.14. The reaction network in Example 3.2, with rate constants as below, has the following Laplacian:



$$A_{\boldsymbol{\kappa}} = \begin{pmatrix} -(\kappa_{12}+\kappa_{13}) & \kappa_{21} & 0 \\ \kappa_{12} & -(\kappa_{21}+\kappa_{23}) & \kappa_{32} \\ \kappa_{13} & \kappa_{23} & -\kappa_{32} \end{pmatrix} .$$

By the matrix–tree theorem, we have $\ker(A_{\boldsymbol{\kappa}}) = \operatorname{span}_{\mathbb{R}}\{(K_1, K_2, K_3)^t\}$, where

$$K_1 = \kappa_{32}\kappa_{21} \,, \quad K_2 = \kappa_{13}\kappa_{32} + \kappa_{12}\kappa_{32} \,, \quad K_3 = \kappa_{12}\kappa_{23} + \kappa_{13}\kappa_{23} + \kappa_{21}\kappa_{13} \,.$$

Suppose that the system associated to this network is a toric dynamical system, and that $\boldsymbol{x}^* = (x_1, x_2) \in V_{>0}(A_{\boldsymbol{\kappa}}\Psi(\boldsymbol{x}))$. Then $\Psi(\boldsymbol{x}) = (x_1^2, x_1x_2, x_2^2)^t = \lambda(K_1, K_2, K_3)^t$ for some $\lambda > 0$, which implies $K_1K_3 = K_2^2$. In Example 4.11, we will show that the autonomous system associated to this network is a toric dynamical system *if and only if* $K_1K_3 = K_2^2$. That an equation like this determines whether the system is a toric dynamical system is related to the fact that $\delta = 1$ for this network.

4. An algebro-geometric approach

In this section, we present an interesting connection between complex balancing and toric geometry, that was first described in [7]. Our presentation will be inspired by that in [7], [3, §5] and [4].

4.1. **The complex balancing ideal.** Let $\mathcal{N} = (\mathcal{S}, \mathcal{C}, \mathcal{R}, \boldsymbol{\kappa})$ be a mass-action network as before. The goal will be to give an algebro-geometric condition on the values of $\boldsymbol{\kappa}$ that turn the autonomous system associated on $\mathcal{N}$ into a toric dynamical system.

Throughout the rest of this section, we will assume that $\mathcal{N}$ is weakly reversible, since it otherwise will not have any complex balancing steady states. Let $\mathcal{N}_1, \dots, \mathcal{N}_\ell$ be networks corresponding to the connected components (each with $\mathcal{S}$ as the set of species), and let $\mathcal{C} = \mathcal{C}_1 \cup \dots \cup \mathcal{C}_\ell$ be the corresponding partition of the complexes.

In what follows, we will regard both the concentrations and the rate constants as variables, and work in the polynomial ring $\mathbb{Q}[\boldsymbol{x}, \boldsymbol{\kappa}] = \mathbb{Q}\big[\{x_k\}_{k=1}^n \cup \{\kappa_{ij}\}_{(i\to j)\in\mathcal{R}}\big]$. We are interested in the positive zero locus of the ideal $\langle A_{\boldsymbol{\kappa}}\Psi(\boldsymbol{x})\rangle \subseteq \mathbb{Q}[\boldsymbol{x}, \boldsymbol{\kappa}]$.

To avoid the steady states where some of the species are extinct (which are less interesting from a chemical point of view, and at the same time complicates the picture significantly), we will consider the saturation $C_{\mathcal{N}} = \langle A_{\boldsymbol{\kappa}}\Psi(\boldsymbol{x})\rangle : (x_1 \cdots x_n)^\infty \subseteq \mathbb{Q}[\boldsymbol{x}, \boldsymbol{\kappa}]$. We will call this the ***complex balancing ideal*** of $\mathcal{N}$. Note that by properties of the saturation,

$$V(A_{\boldsymbol{\kappa}}\Psi(\boldsymbol{x})) \setminus V(x_1 \cdots x_n) \subseteq V(C_{\mathcal{N}}) \subseteq V(A_{\boldsymbol{\kappa}}\Psi(\boldsymbol{x}))\,,$$

which ensures that $V_{>0}(C_{\mathcal{N}}) = V_{>0}(A_{\boldsymbol{\kappa}}\Psi(\boldsymbol{x}))$.

4.2. **The toric balancing ideal.** We will now use the matrix–tree theorem to do a simplifying change of variables with the purpose of revealing the underlying toric geometry.

Suppose that $\boldsymbol{\kappa}^* \in \mathbb{R}^r_{>0}$ is a tuple of rate constants such that $\mathcal{N} = (\mathcal{S}, \mathcal{C}, \mathcal{R}, \boldsymbol{\kappa}^*)$ gives rise to a toric dynamical system, with a complex balancing steady state $\boldsymbol{x}^* \in \mathbb{R}^n_{>0}$. By the matrix–tree theorem (with notation as before), it then holds that $\Psi(\boldsymbol{x}^*) \in \operatorname{span}_{\mathbb{R}}\{\boldsymbol{v}_1, \dots, \boldsymbol{v}_\ell\}$, from which it is easy to see that $K_i^*(\boldsymbol{x}^*)^{\boldsymbol{y}_j} = K_j^*(\boldsymbol{x}^*)^{\boldsymbol{y}_j}$ needs to hold for all i, j such that $\boldsymbol{y}_i$ and $\boldsymbol{y}_j$ belong to the same connected component of $\mathcal{N}$. Motivated by this, we introduce a new ideal

$$I_{\mathcal{N}} = \big\langle K_i\boldsymbol{x}^{\boldsymbol{y}_j} - K_j\boldsymbol{x}^{\boldsymbol{y}_i} : i, j \in \{1, \dots, m\} \text{ with } \boldsymbol{y}_i, \boldsymbol{y}_j \in \mathcal{C}_\nu \text{ for some } \nu \in \{1, \dots, \ell\}\big\rangle$$

in the subring $\mathbb{Q}[\boldsymbol{x}, \boldsymbol{K}] = \mathbb{Q}\big[\{x_i\}_{i=1}^n \cup \{K_i\}_{i=1}^m\big] \subseteq \mathbb{Q}[\boldsymbol{x}, \boldsymbol{\kappa}]$. The following lemma shows that we can view $\mathbb{Q}[\boldsymbol{x}, \boldsymbol{K}]$ as a polynomial ring in its own right.

Lemma 4.1 ([7, Lemma 5])**.** *The polynomials $K_1, \dots, K_m \in \mathbb{Q}[\boldsymbol{\kappa}]$ are algebraically independent over $\mathbb{Q}$.*

Proof. Assume towards a contradiction that $\lambda_1 K_1 + \dots + \lambda_m K_m = 0$, for $\lambda_i \in \mathbb{Q}$. We will now identify all rate constants κ_{ij} that correspond to reactions *from* the same complex; formally, we substitute $\kappa'_i = \kappa_{ij}$ for all i, j to obtain new polynomials $K'_i \in \mathbb{Q}[\kappa'_1, \dots, \kappa'_m]$. Note that $K'_i = t_i \cdot \prod_{j\neq i} \kappa'_j$, where t_i is the number of i-trees in $\mathcal{N}$. Also note that $\lambda_1 K'_1 + \dots + \lambda_m K'_m = 0$. Dividing by $\kappa'_1 \cdots \kappa'_m$ now gives $\lambda_1 t_1 \frac{1}{\kappa'_1} + \dots + \lambda_m t_m \frac{1}{\kappa'_m}$. This would be an algebraic relation between $(\kappa'_1)^{-1}, \dots, (\kappa'_m)^{-1}$ in $\mathbb{Q}[(\kappa'_1)^{\pm 1}, \dots, (\kappa'_m)^{\pm 1}]$, which is a contradiction. □

As in the previous subsection, we form the saturation $T_{\mathcal{N}} = I_{\mathcal{N}} : (x_1 \cdots x_n)^\infty$, and note that $V_{>0}(I_{\mathcal{N}}) = V_{>0}(T_{\mathcal{N}})$. We will now show that $T_{\mathcal{N}}$ is a *toric* ideal in $\mathbb{Q}[\boldsymbol{x}, \boldsymbol{K}]$ (note that this is *not* true in general if we view it as an ideal in $\mathbb{Q}[\boldsymbol{x}, \boldsymbol{\kappa}]$, nor if we consider $I_{\mathcal{N}}$ instead of $T_{\mathcal{N}}$). Motivated by this, we will refer to it as the ***toric balancing ideal*** of the $\mathcal{N}$.

The idea of the proof will be to show that $T_{\mathcal{N}}$ is the toric ideal associated to a particular integer matrix. Recall that, by assumption, $\mathcal{N}$ has (strongly) connected components $\mathcal{N}_1, \ldots, \mathcal{N}_\ell$. For each $\nu \in \{1, \ldots, \ell\}$, let Y_ν be the matrix whose columns are the complexes $\boldsymbol{y} \in \mathcal{C}_\nu$. Note that, up to reordering of the complexes, $Y = (Y_1 \ \cdots \ Y_\ell)$. We can now form the matrix

$$\mathrm{Cay}'(\mathcal{N}) = \begin{pmatrix} I_n & Y_1 & Y_2 & \cdots & Y_\ell \\ \mathbf{0} & \mathbf{1} & \mathbf{0} & \cdots & \mathbf{0} \\ \mathbf{0} & \mathbf{0} & \mathbf{1} & \cdots & \mathbf{0} \\ \vdots & \vdots & \ddots & \vdots & \\ \mathbf{0} & \mathbf{0} & \mathbf{0} & \cdots & \mathbf{1} \end{pmatrix} \in \mathbb{Z}^{(n+\ell)\times(n+m)},$$

which in [7, §2] is introduced as the ***extended Cayley matrix***. Here, $\mathbf{0}$ and $\mathbf{1}$ denote row vectors of appropriate length, consisting of zeros and ones, respectively. The toric ideal associated to $\mathrm{Cay}'(\mathcal{N})$ is the kernel of the $\mathbb{Q}$-algebra homomorphism

$$\varphi\colon \mathbb{Q}[\boldsymbol{x}, \boldsymbol{K}] \to \mathbb{Q}[\boldsymbol{x}, t_1, \ldots, t_\ell]$$

defined by $x_i \mapsto x_i$ and $K_i \mapsto \boldsymbol{x}^{\boldsymbol{y}_i} t_\nu$ when $\boldsymbol{y}_i \in \mathcal{C}_\nu$.

Proposition 4.2 ([4, Prop. 4.2])**.** *The toric balancing ideal T_G is the toric ideal in $\mathbb{Q}[\boldsymbol{x}, \boldsymbol{K}]$ associated to $\mathrm{Cay}'(\mathcal{N})$.*

Proof. We begin by showing the inclusion "$\subseteq$". Note that $I_{\mathcal{N}} \subseteq \ker(\varphi)$, since

$$\varphi(K_i \boldsymbol{x}^{\boldsymbol{y}_j} - K_j \boldsymbol{x}^{\boldsymbol{y}_i}) = \varphi(K_i)\varphi(\boldsymbol{x}^{\boldsymbol{y}_j}) - \varphi(K_j)\varphi(\boldsymbol{x}^{\boldsymbol{y}_i}) = \boldsymbol{x}^{\boldsymbol{y}_i}\boldsymbol{x}^{\boldsymbol{y}_j} t_\nu - \boldsymbol{x}^{\boldsymbol{y}_j}\boldsymbol{x}^{\boldsymbol{y}_i} t_\nu = 0$$

if $\boldsymbol{y}_i, \boldsymbol{y}_j \in \mathcal{C}_\nu$. Now, let $f \in \mathbb{Q}[\boldsymbol{x}, \boldsymbol{K}]$ be such that $f \cdot (x_1 \cdots x_n)^N \in I_{\mathcal{N}}$ for some $N \in \mathbb{Z}_{\geqslant 0}$. Then $0 = \varphi(f \cdot (x_1 \cdots x_n)^N) = \varphi(f) \cdot (x_1 \cdots x_n)^N$, which implies $\varphi(f) = 0$.

Next, we show the inclusion "$\supseteq$". To simplify the notation, we let $A_\nu = \{i \in \{1, \ldots, m\} : \boldsymbol{y}_i \in \mathcal{C}_\nu\}$. For every $\nu = 1, \ldots, \ell$, pick an $i_\nu \in A_\nu$. Then for any $i \in A_\nu$, it is easy to verify the equality

$$K_i = \frac{1}{\boldsymbol{x}^{\boldsymbol{y}_{i_\nu}}}(K_i \boldsymbol{x}^{\boldsymbol{y}_{i_\nu}} - K_{i_\nu} \boldsymbol{x}^{\boldsymbol{y}_i}) + K_{i_\nu} \boldsymbol{x}^{\boldsymbol{y}_i - \boldsymbol{y}_{i_\nu}}$$

in the ring $\mathbb{Q}[\boldsymbol{x}^{\pm 1}, \boldsymbol{K}]$. This means that any $f \in \mathbb{Q}[\boldsymbol{x}, \boldsymbol{K}]$ can be expressed as

$$f = \sum_{\nu=1}^{\ell} \sum_{i \in A_\nu \setminus \{i_\nu\}} b_i (K_i \boldsymbol{x}^{\boldsymbol{y}_{i_\nu}} - K_{i_\nu} \boldsymbol{x}^{\boldsymbol{y}_i}) + r\,,$$

where $b_i \in \mathbb{Q}[\boldsymbol{x}^{\pm 1}, \boldsymbol{K}]$ for $i = 1, \ldots, m$, and $r \in \mathbb{Q}[\boldsymbol{x}^{\pm 1}, K_{i_1}, \ldots, K_{i_\ell}]$. For a sufficiently large $N \in \mathbb{Z}_{\geqslant 0}$, we get

$$(x_1 \cdots x_n)^N f = \sum_{\nu=1}^{\ell} \sum_{i \in A_\nu \setminus \{i_\nu\}} c_i (K_i \boldsymbol{x}^{\boldsymbol{y}_{i_\nu}} - K_{i_\nu} \boldsymbol{x}^{\boldsymbol{y}_i}) + s\,, \tag{4.1}$$

where $c_i \in \mathbb{Q}[\boldsymbol{x}, \boldsymbol{K}]$ for $i = 1, \ldots, m$, and $s \in \mathbb{Q}[\boldsymbol{x}, K_{i_1}, \ldots, K_{i_\ell}]$.

Now, suppose that $f \in \ker(\varphi)$. Then

$$0 = \varphi((x_1 \cdots x_n)^N f) = \sum_{\nu=1}^{\ell} \sum_{i \in A_\nu \setminus \{i_\nu\}} \varphi(c_i) \overbrace{\varphi(K_i \boldsymbol{x}^{\boldsymbol{y}_{i_\nu}} - K_{i_\nu} \boldsymbol{x}^{\boldsymbol{y}_i})}^{=0} + \varphi(s)\,,$$

from which we conclude that $\varphi(s) = 0$.

We now want to show that this implies $s = 0$. To see this, suppose that

$$s = \sum_{a_1,\ldots,a_\ell \geqslant 0} s_{a_1,\ldots,a_\ell}(\boldsymbol{x}) K_{i_1}^{a_1} \cdots K_{i_\ell}^{a_\ell}$$

for polynomials $s_{a_1,\ldots,a_\ell}(\boldsymbol{x}) \in \mathbb{Q}[\boldsymbol{x}]$. Applying φ then gives

$$\begin{aligned} 0 &= \sum_{a_1,\ldots,a_\ell \geqslant 0} s_{a_1,\ldots,a_\ell}(\boldsymbol{x}) \varphi(K_{i_1})^{a_1} \cdots \varphi(K_{i_\ell})^{a_\ell} \\ &= \sum_{a_1,\ldots,a_\ell \geqslant 0} s_{a_1,\ldots,a_\ell}(\boldsymbol{x}) (\boldsymbol{x}^{\boldsymbol{y}_{i_1}} t_1)^{a_1} \cdots (\boldsymbol{x}^{\boldsymbol{y}_{i_\ell}} t_\ell)^{a_\ell} \\ &= \sum_{a_1,\ldots,a_\ell \geqslant 0} s_{a_1,\ldots,a_\ell}(\boldsymbol{x}) \boldsymbol{x}^{a_1 \boldsymbol{y}_{i_1} + \cdots + a_\ell \boldsymbol{y}_{i_\ell}} t_1^{a_1} \cdots t_\ell^{a_\ell}\,, \end{aligned}$$

which implies $s_{a_1,\ldots,a_\ell}(\boldsymbol{x}) \boldsymbol{x}^{a_1 \boldsymbol{y}_{i_1} + \cdots + a_\ell \boldsymbol{y}_{i_\ell}} = 0$ and therefore $s_{a_1,\ldots,a_\ell}(\boldsymbol{x}) = 0$ for all $a_1, \ldots, a_\ell \geqslant 0$. Hence, we conclude that $s = 0$, and (4.1) then shows that $(x_1 \cdots x_n)^N f \in I_{\mathcal{N}}$, i.e. $f \in T_{\mathcal{N}}$. □

Remark 4.3. We can also view $T_{\mathcal{N}}$ as the lattice ideal corresponding to $L = \ker_{\mathbb{Z}}(\mathrm{Cay}'(\mathcal{N})) \subseteq \mathbb{Z}^{n+m}$. It is easy to verify that

$$L = \left\{ (-Y\boldsymbol{u}, \boldsymbol{u})^t : \begin{array}{c} \boldsymbol{u} = \left(u_1^{(1)}, \ldots, u_{m_1}^{(1)}, \ldots, u_1^{(\ell)}, \ldots, u_{m_\ell}^{(\ell)}\right)^t \in \mathbb{Z}^m \\ u_1^{(\nu)} + \cdots + u_{m_\nu}^{(\nu)} = 0\,, \;\; \nu = 1 \ldots, \ell \end{array} \right\}.$$

From this we get a generating set of $T_{\mathcal{N}}$ consisting of binomials $\boldsymbol{x}^{(Y\boldsymbol{u})_-} \boldsymbol{K}^{\boldsymbol{u}_+} - \boldsymbol{x}^{(Y\boldsymbol{u})_+} \boldsymbol{K}^{\boldsymbol{u}_-}$ for $\boldsymbol{u} \in \mathbb{Z}^m$ of this form. An alternative way of finding these generators, that relies on Proposition 2.11 and Propsoition 2.12, is given in the proof of [7, Prop. 6]. Another characterization of $T_{\mathcal{N}}$ is given in [4], where they view $T_{\mathcal{N}}$ as the defining ideal of the multi-Rees algebra $\mathcal{R}_{\mathbb{Q}[\boldsymbol{x}]}(\langle \mathcal{C}_1 \rangle \oplus \cdots \oplus \langle \mathcal{C}_\ell \rangle)$.

The following proposition ensures that $T_{\mathcal{N}}$ encodes the same information as $C_{\mathcal{N}}$ about the conditions under which our networks gives rise to a toric dynamical system.

Proposition 4.4 ([3, Prop. 5.30])**.** *Let $(\boldsymbol{x}^*, \boldsymbol{\kappa}^*) \in \mathbb{R}^n_{>0} \times \mathbb{R}^r_{>0}$ and let $\boldsymbol{K}^* \in \mathbb{R}^m_{>0}$ be the tuple of constants obtained from $\boldsymbol{\kappa}^*$ via the matrix–tree theorem. Then*

$$(\boldsymbol{x}^*, \boldsymbol{\kappa}^*) \in V_{>0}(C_{\mathcal{N}}) \iff (\boldsymbol{x}^*, \boldsymbol{K}^*) \in V_{>0}(T_{\mathcal{N}})\,.$$

Proof. The implication " $\Longrightarrow$ " follows from the reasoning leading up to the construction of $T_{\mathcal{N}}$. For the implication " $\Longleftarrow$ ", we note that the quantity $(\boldsymbol{x}^*)^{\boldsymbol{y}_i}/K_i^*$ only depends on the connected component of $\boldsymbol{y}_i$. Let λ_ν be the value obtained for a component G_ν. Then $\Phi(\boldsymbol{x}^*) = \sum_{\nu=1}^{\ell} \lambda_\nu \sum_{\boldsymbol{y}_k \in V(G_\nu)} K_k^* \boldsymbol{e}_k = 0$, by the matrix–tree theorem. □

4.3. **The toric moduli ideal.** We are mainly interested in values of the rate constants for which our network give rise to a toric dynamical system, not the particular complex balancing steady states. We therefore want to understand the image of $V_{>0}(T_{\mathcal{N}})$ under the projection $\mathbb{R}^n \times \mathbb{R}^m \to \mathbb{R}^m$. The algebraic analog of this is to consider the elimination ideal $M_{\mathcal{N}} = T_{\mathcal{N}} \cap \mathbb{Q}[\boldsymbol{K}] \subseteq \mathbb{Q}[\boldsymbol{K}]$. We will call this the ***toric moduli ideal*** of $\mathcal{N}$.

Remark 4.5. The moduli ideal is a toric ideal in $\mathbb{Q}[\boldsymbol{K}]$ (but not necessarily $\mathbb{Q}[\boldsymbol{\kappa}]$). It is prime because $T_{\mathcal{N}}$ is prime. To see that it is binomial, recall that a generating set for $T_{\mathcal{N}}$ can be obtained as a subset of a Gröbner basis of $C_{\mathcal{N}}$ with respect to lex. By Proposition 2.10, $C_{\mathcal{N}}$ admits such a Gröbner basis consisting solely of binomials.

We will now show that $V_{>0}(M_{\mathcal{N}})$ is precisely the set of tuples $\boldsymbol{K}^* \in \mathbb{R}^m_{>0}$ for which our network gives rise to a toric dynamical system. We will therefore call this semialgebraic set the ***toric moduli space***.

Theorem 4.6 ([7, Thm. 7])**.** *Let $\mathcal{N} = (\mathcal{S}, \mathcal{C}, \mathcal{R})$ be a weakly reversible reaction network. For $\boldsymbol{\kappa}^* \in \mathbb{R}^r_{>0}$, it holds that the mass-action network $(\mathcal{S}, \mathcal{C}, \mathcal{R}, \boldsymbol{\kappa}^*)$ gives rise toric dynamical system if and only if $\boldsymbol{K}^* \in V_{>0}(M_{\mathcal{N}})$.*

Proof. The "only if" part is easy; if $\boldsymbol{\kappa}^* \in \mathbb{R}^r_{>0}$ gives us a toric dynamical system, then there exists an $\boldsymbol{x}^* \in \mathbb{R}^n_{>0}$ such that $(\boldsymbol{x}^*, \boldsymbol{K}^*) \in V_{>0}(T_{\mathcal{N}})$, which implies that $\boldsymbol{K}^* \in V_{>0}(M_{\mathcal{N}})$.

We now turn to the "if" part of the statement. Let $\boldsymbol{K}^* \in V_{>0}(M_{\mathcal{N}})$. We want to show that there exists an $\boldsymbol{x}^* \in \mathbb{R}^n_{>0}$ such that $(\boldsymbol{x}^*, \boldsymbol{K}^*) \in V_{>0}(T_{\mathcal{N}})$. The key idea, following the presentation in [3, §5], will be to work over $\mathbb{C}$, and use that both $T_{\mathcal{N}}$ and $M_{\mathcal{N}}$ are toric ideals, so that $V_{\mathbb{C}}(T_{\mathcal{N}})$ and $V_{\mathbb{C}}(M_{\mathcal{N}})$ are affine toric varieties by Proposition 2.14, with tori $V_{\mathbb{C}}(T_{\mathcal{N}}) \cap (\mathbb{C}^*)^{n+m}$ and $V_{\mathbb{C}}(M_{\mathcal{N}}) \cap (\mathbb{C}^*)^m$, respectively.

We begin by noting that the projection $\pi \colon V_{\mathbb{C}}(T_{\mathcal{N}}) \to V_{\mathbb{C}}(M_{\mathcal{N}})$ associated to the elimination has Zariski dense image; this follows by the closure theorem [5, Thm. 4.4.4]. Also note that, on the level of the tori, π is an algebraic group homomorphism $V_{\mathbb{C}}(T_{\mathcal{N}}) \cap (\mathbb{C}^*)^{n+m} \to V_{\mathbb{C}}(M_{\mathcal{N}}) \cap (\mathbb{C}^*)^m$. Theorem 2.2 therefore tells us that $\pi(V_{\mathbb{C}}(T_{\mathcal{N}}) \cap (\mathbb{C}^*)^{n+m})$ is closed in $V_{\mathbb{C}}(M_{\mathcal{N}}) \cap (\mathbb{C}^*)^m$. But at the same time, $\pi(V_{\mathbb{C}}(T_{\mathcal{N}}) \cap (\mathbb{C}^*)^{n+m})$ is dense in $V_{\mathbb{C}}(M_{\mathcal{N}}) \cap (\mathbb{C}^*)^m$, since $\pi(V_{\mathbb{C}}(T_{\mathcal{N}}))$ is dense in $V_{\mathbb{C}}(M_{\mathcal{N}})$. From this we conclude that $\pi(V_{\mathbb{C}}(T_{\mathcal{N}}) \cap (\mathbb{C}^*)^{n+m}) = V_{\mathbb{C}}(M_{\mathcal{N}}) \cap (\mathbb{C}^*)^m$. Since $\boldsymbol{K}^* \in V_{\mathbb{C}}(M_{\mathcal{N}}) \cap (\mathbb{C}^*)^m$, we know that there exists some $(z_1, \dots, z_n) \in (\mathbb{C}^*)^n$ such that $(z_1, \dots, z_n, \boldsymbol{K}^*) \in V_{\mathbb{C}}(T_{\mathcal{N}}) \cap (\mathbb{C}^*)^{n+m}$. But since $T_{\mathcal{N}}$ is generated by binomials and $\boldsymbol{K}^* > 0$, it is easy to see* that we must also have $(|z_1|, \dots, |z_n|, \boldsymbol{K}^*) \in V_{\mathbb{C}}(T_{\mathcal{N}}) \cap (\mathbb{C}^*)^{n+m}$. This implies $(|z_1|, \dots, |z_n|, \boldsymbol{K}^*) \in V_{>0}(T_{\mathcal{N}})$. □

We already know that $M_{\mathcal{N}} \subseteq \mathbb{Q}[\boldsymbol{K}]$ is a toric ideal from the observation we made above. However, we will now show this more explicitly, by realizing $M_{\mathcal{N}}$ as the toric ideal corresponding to the matrix

$$\mathrm{Cay}(\mathcal{N}) = \begin{pmatrix} Y_1 & Y_2 & \cdots & Y_\ell \\ \mathbf{1} & \mathbf{0} & \cdots & \mathbf{0} \\ \mathbf{0} & \mathbf{1} & \cdots & \mathbf{0} \\ \vdots & \vdots & \ddots & \vdots \\ \mathbf{0} & \mathbf{0} & \cdots & \mathbf{1} \end{pmatrix},$$

*Indeed, if $z_1^{u_1} \cdots z_n^{u_n} K_1^{u_{n+1}} \cdots K_m^{u_{n+m}} = z_1^{v_1} \cdots z_n^{v_n} K_1^{v_{n+1}} \cdots K_m^{v_{n+m}}$ holds, then taking the modulus on both sides gives $|z_1|^{u_1} \cdots |z_n|^{u_n} K_1^{u_{n+1}} \cdots K_m^{u_{n+m}} = |z_1|^{v_1} \cdots |z_n|^{v_n} K_1^{v_{n+1}} \cdots K_m^{v_{n+m}}$.

which is obtained by deleting the n first columns of $\mathrm{Cay}'(\mathcal{N})$. In [7], this matrix is referred to as the ***Cayley matrix***. The corresponding toric ideal is given by the kernel of the $\mathbb{Q}$-algebra homomorphism

$$\psi\colon \mathbb{Q}[\boldsymbol{K}] \to \mathbb{Q}[\boldsymbol{x}, t_1, \dots, t_\ell]\,, \quad K_i \mapsto \boldsymbol{x}^{\boldsymbol{y}_i} t_\nu \text{ when } \boldsymbol{y}_i \in \mathcal{C}_\nu\,.$$

Theorem 4.7 ([7, Thm. 9])**.** *In the situation above, it holds that $M_\mathcal{N}$ is the toric ideal associated to* $\mathrm{Cay}(\mathcal{N})$*.*

Proof. Simply note that $\psi = \varphi\big|_{\mathbb{Q}[\boldsymbol{K}]}$, where $\varphi\colon \mathbb{Q}[\boldsymbol{x}, \boldsymbol{K}] \to \mathbb{Q}[\boldsymbol{x}, t_1, \dots, t_\ell]$ is the map discussed in the previous section, and $\mathbb{Q}[\boldsymbol{K}]$ is regarded as a subring of $\mathbb{Q}[\boldsymbol{x}, \boldsymbol{K}]$. It then follows immediately that

$$\ker(\psi) = \ker(\varphi) \cap \mathbb{Q}[\boldsymbol{K}] = T_\mathcal{N} \cap \mathbb{Q}[\boldsymbol{K}] = M_\mathcal{N}\,. \qquad \square$$

This concrete description of $M_\mathcal{N}$ allows us to determine the dimension of the corresponding moduli space.

Proposition 4.8 ([14, Prop. 3])**.** *The rank of* $\mathrm{Cay}(\mathcal{N})$ *equals $\ell + s$, where ℓ is the number of connected components of $\mathcal{N}$, and $s = \dim_\mathbb{R}(S)$.*

Proof. We begin by noting that $\ker(\mathrm{Cay}(\mathcal{N})) = \ker(Y) \cap \mathrm{im}(A_\mathcal{N})$, where $A_\mathcal{N}$ is the complex–reaction incidence matrix; this follows readily by observing that

$$\mathrm{im}(A_\mathcal{N}) = \left\{ \left(u_1^{(1)}, \dots, u_{m_1}^{(1)}, \dots, u_1^{(\ell)}, \dots, u_{m_\ell}^{(\ell)}\right)^t \in \mathbb{Z}^m : \sum_{i=1}^{m_\nu} u_i^{(\nu)} = 0\,,\ \nu = 1, \dots, \ell \right\}.$$

Moreover, we note that $\ker(N)/\ker(A_\mathcal{N}) \cong \ker(Y) \cap \mathrm{im}(A_\mathcal{N})$ by applying the first isomorphism theorem to the map $\psi\colon \ker(N) \to \mathbb{Z}^m$, with $\boldsymbol{w} \mapsto A_\mathcal{N}\boldsymbol{w}$. The claim now follows from the fact that $\dim\ker(N) = r - s$, and $\dim\ker(A_\mathcal{N}) = r - (m - \ell)$. $\square$

A consequence of the previous result, combined with Theorem 2.7, is that $V_\mathbb{C}(M_\mathcal{N})$ has dimension $\ell + s$. This gives the following interpretation of the deficiency of the network.

Corollary 4.9. *The codimension of $V_\mathbb{C}(M_\mathcal{N})$ in $\mathbb{C}^m$ equals $\delta = m - \ell - s$.*

Together with Remark 2.9, this shows that $V_\mathbb{R}(M_\mathcal{N})$ has codimension δ in $\mathbb{R}^m$. In particular, if $\delta = 0$, we obtain $V_{>0}(M_\mathcal{N}) = \mathbb{R}^m_{>0}$, i.e. the network gives rise to a toric dynamical system for *any* choice of positive rate constants; this recovers the classical deficiency zero theorem (Theorem 3.11).

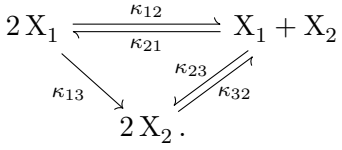
4.4. **Some examples.** We end the report by revisiting the examples that we encountered in Section 3.1.

Example 4.10. The ozone network from Example 3.1,

$$\mathrm{O_3} \rightleftharpoons \mathrm{O_2} + \mathrm{O}\,, \quad \mathrm{O_3} + \mathrm{O} \longrightarrow 2\,\mathrm{O_2}\,,$$

is not weakly reversible, and it therefore does not admit any complex balancing steady states.

Example 4.11. Recall the two-species network from Example 3.2 that we also studied in Example 3.14:



It is strongly connected and has deficiency $\delta = 3 - 1 - 1 = 1$. Its toric balancing ideal is given by

$$\begin{aligned} T_{\mathcal{N}} &= \langle K_1 x_1 x_2 - K_2 x_1^2, K_1 x_2^2 - K_3 x_1^2, K_2 x_2^2 - K_3 x_1 x_2 \rangle : (x_1 x_2)^\infty \\ &= \langle K_1 K_3 - K_2^2, -K_2 x_2 + K_3 x_1, -K_1 x_2 + K_2 x_1 \rangle , \end{aligned}$$

where the last line is a reduced Gröbner basis with respect to lex. From this it is easy to see that

$$M_{\mathcal{N}} = T_{\mathcal{N}} \cap \mathbb{Q}[\boldsymbol{K}] = \langle -K_1 K_3 + K_2^2 \rangle .$$

Another way to see this is to observe that the Cayley matrix for this network is

$$\mathrm{Cay}(\mathcal{N}) = \begin{pmatrix} 2 & 1 & 0 \\ 0 & 1 & 2 \\ 1 & 1 & 1 \end{pmatrix} ,$$

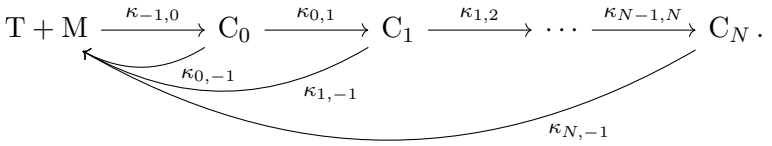
and that $\ker_{\mathbb{Z}}(\mathrm{Cay}(\mathcal{N}))$ is generated by $(1, -2, 1)^t = (1, 0, 1)^t - (0, 2, 0)^t$, which by Proposition 2.11 implies that

$$M_{\mathcal{N}} = \langle K_1 K_3 - K_2^2 \rangle : (K_1 K_2)^\infty = \langle K_1 K_3 - K_2^2 \rangle .$$

From this we conclude that corresponding mass-action system admits a steady state if and only if the rate constants satisfies the equation $K_1 K_3 = K_2^2$. Using our analysis from Example 3.14, this corresponds to the equation

$$\kappa_{32}\kappa_{21}(\kappa_{12}\kappa_{23} + \kappa_{13}\kappa_{23} + \kappa_{21}\kappa_{13}) = (\kappa_{13}\kappa_{32} + \kappa_{12}\kappa_{32})^2 .$$

Example 4.12. We finally consider McKeithan's network from Example 3.4, with complexes numbered $-1, 0, 1, \ldots, N$ and rate constants numbered accordingly, as indicated by this diagram:



We have $m = N + 2$ and $\ell = 1$, and it is easy to verify that a basis for S is given by $\{\boldsymbol{y}_0 - \boldsymbol{y}_{-1}, \ldots, \boldsymbol{y}_N - \boldsymbol{y}_{N-1}\}$, meaning that $s = N + 1$. Hence, $\delta = 0$, and we expect the moduli ideal $M_{\mathcal{N}}$ to be trivial. That this indeed is the case can be seen from the Cayley matrix, which in this case takes the form

$$\mathrm{Cay}(\mathcal{N}) = \begin{pmatrix} 1 & & & & \\ 1 & & & & \\ & 1 & & & \\ & & 1 & & \\ & & & \ddots & \\ & & & & 1 \\ 1 & 1 & 1 & \cdots & 1 \end{pmatrix}$$

and clearly satisfies $\ker_{\mathbb{Z}}(\mathrm{Cay}(\mathcal{N})) = \{\boldsymbol{0}\}$, which gives $M_{\mathcal{N}} = \langle 0 \rangle$, and we conclude that this network gives rise to a toric dynamical system for *all* values of the rate constants.

References

1. J. Bochnak, M. Coste, and M. Roy, *Real algebraic geometry*, Ergebnisse der Mathematik und ihrer Grenzgebiete (3), vol. 36, Springer-Verlag, 1998. MR 1659509 — Cited on page 5.
2. L. Brustenga i Moncusí, G. Craciun, and M.S. Sorea, *Disguised toric dynamical systems*, preprint available at `arxiv.org/abs/2006.01289` (2020). — Cited on page 2.
3. D.A. Cox, *Applications of Polynomial Systems*, CBMS Regional Conference Series in Mathematics, Conference Board of the Mathematical Sciences, 2020. — Cited on pages 13, 15, and 16.
4. D.A. Cox, K.-N. Lin, and G. Sosa, *Multi-rees algebras and toric dynamical systems*, Proceedings of the American Mathematical Society **147** (2019), no. 11, 4605–4616. — Cited on pages 13, 14, and 15.
5. D.A. Cox, J. Little, and D. O'Shea, *Ideals, Varieties, and Algorithms: An Introduction to Computational Algebraic Geometry and Commutative Algebra*, Undergraduate Texts in Mathematics, Springer International Publishing, 2015. — Cited on page 16.
6. D.A. Cox, J.B. Little, and H.K. Schenck, *Toric Varieties*, Graduate studies in mathematics, American Mathematical Society, 2011. — Cited on pages 3, 4, and 6.
7. G. Craciun, A. Dickenstein, A. Shiu, and B. Sturmfels, *Toric dynamical systems*, J. Symbolic Comput. **44** (2009), 1551–1565. — Cited on pages 2, 10, 13, 14, 15, 16, and 17.
8. A. Dickenstein, *Biochemical reaction networks: an invitation for algebraic geometers*, Mathematical Congress of the Americas 2013, Contemporary Mathematics, vol. 656, American Mathematical Society, 2016, p. 65–83. — Cited on pages 1 and 9.
9. A. Dickenstein, M.P. Millán, A. Shiu, and X. Tang, *Multistationarity in structured reaction networks*, Bulletin of Mathematical Biology **81** (2019), no. 5, 1527–1581. — Cited on page 1.
10. B.B. Edelstein, *Biochemical model with multiple steady states and hysteresis*, Journal of Theoretical Biology **29** (1970), no. 1, 57–62. — Cited on page 7.
11. M. Feinberg, *Complex balancing in general kinetic systems*, Archive for Rational Mechanics and Analysis **49** (1972), no. 3, 187. — Cited on page 1.
12. M. Feinberg, *Lectures On Chemical Reaction Networks*, 1979, available online at `https://crnt.osu.edu/LecturesOnReactionNetworks`. — Cited on pages 7 and 10.
13. M. Feinberg, *The existence and uniqueness of steady states for a class of chemical reaction networks*, Archive for Rational Mechanics and Analysis **132** (1995), no. 4, 311. — Cited on page 2.
14. E. Feliu, D. Cappelletti, and C. Wiuf, *Node balanced steady states: Unifying and generalizing complex and detailed balanced steady states*, Mathematical Biosciences **301** (2018), 68–82. — Cited on page 17.
15. E. Gross, B. Davis, K.L. Ho, D.J. Bates, and H.A. Harrington, *Numerical algebraic geometry for model selection and its application to the life sciences*, Journal of The Royal Society Interface **13** (2016), no. 123. — Cited on page 1.
16. C.M. Guldberg and P. Waage, *Über die chemische Affinität*, Journal für praktische Chemie **19** (1879), 69–114. — Cited on page 8.
17. J. Gunawardena, *Theory and mathematical methods*, Comprehensive Biophysics **9** (2012), 243–267. — Cited on page 8.
18. J. Herzog, T. Hibi, and H. Ohsugi, *Binomial Ideals*, Graduate Texts in Mathematics, Springer International Publishing, 2018. — Cited on pages 3 and 5.
19. F. Horn, *The dynamics of open reaction systems*, Mathematical Aspects of Chemical and Biochemical Problems and Quantum Chemistry, Proceedings of the SIAMAMS, vol. 8, 1974, pp. 125–137. — Cited on pages 1 and 10.
20. F. Horn and R. Jackson, *General mass action kinetics*, Archive for Rational Mechanics and Analysis **47** (1972), 81–116. — Cited on pages 1 and 10.
21. J.E. Humphreys, *Linear Algebraic Groups*, Graduate Texts in Mathematics, Springer, 1975. — Cited on page 3.
22. V. Hárs and J. Tóth, *On the inverse problem of reaction kinetics*, Colloquia Mathematica Societatis János Bolyai 30., Qualitative Theory of Differential Equations, Szeged (Hungary), 1979, pp. 363–379. — Cited on pages 9 and 10.
23. H. Ji, P. Ellison, D. Knight, and M. Feinberg, *CRNToolbox version 2.35*, 2018, available at `http://crnt.osu.edu/CRNTWin`. — Cited on page 2.

24. B. Joshi and A. Shiu, *Which small reaction networks are multistationary?*, SIAM Journal on Applied Dynamical Systems **16** (2017), no. 2, 802–833. — Cited on page 1.
25. M. Kaufman, C. Soulé, and R. Thomas, *A new necessary condition on interaction graphs for multistationarity*, Journal of Theoretical Biology **248** (2007), no. 4, 675 – 685. — Cited on page 1.
26. V.B. Kothamachu, E. Feliu, L. Cardelli, and O.S Soyer, *Unlimited multistability and boolean logic in microbial signalling*, Journal of the Royal Society, Interface **12** (2015), no. 108, 20150234. — Cited on page 1.
27. T.W. McKeithan, *Kinetic proofreading in T-cell receptor signal transduction*, Proceedings of the National Academy of Sciences of the United States of America **92** (1995), no. 11, 5042–5046. — Cited on pages 1 and 8.
28. I. Mirzaev and J. Gunawardena, *Laplacian dynamics on general graphs*, Bulletin of mathematical biology **75** (2013), no. 11, 2118–2149. — Cited on page 11.
29. A.J. Shiu, *Algebraic methods for biochemical reaction network theory*, Ph.D. thesis, University of California, Berkeley, 2010, available at `https://www.math.tamu.edu/~annejls/Thesis_AnneShiu.pdf`. — Cited on page 11.
30. B. Sturmfels, *Gröbner bases and convex polytopes*, Memoirs of the American Mathematical Society, American Mathematical Society, 1996. — Cited on page 5.