HAL open science

A FEW ASPECTS OF MASS-ACTION SHEAVES

Alexandru Iosif

To cite this version:

Alexandru Iosif. A FEW ASPECTS OF MASS-ACTION SHEAVES. 2019. hal-02296867

HAL Id: hal-02296867

https://hal.science/hal-02296867

Preprint submitted on 25 Sep 2019

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

A FEW ASPECTS OF MASS-ACTION SHEAVES

ALEXANDRU IOSIF

Abstract. We emphasize that the set of mass-action networks on a fixed set of species should be regarded as a monoid, for the mass-action approximation works under the homogeneity assumption, while in real systems this is only locally true. Hence, if one seeks a meaningful global approximation of mass-action form, one should regard mass-action networks as local pictures of a more general object. In this article we propose sheaves as a natural framework for evolving chemical reaction networks.

1. Introduction

A *chemical reaction network* $\mathcal{N}$ is a finite directed graph whose vertices are labelled by distinct monomials $m_1, \ldots, m_s \in \mathbb{Z}[x_1, ..., x_n]$, called chemical complexes, and whose edges are labelled by real positive parameters $k_1, \ldots, k_r$, called *rate constants*. We refer to [7] for a detailed introduction to these networks. Here the variables $x_1, \ldots, x_n$ play the role of concentrations of chemical species and the chemical complexes are of the form $m_i = x^{y_i} := \prod_j x_j^{(y_i)_j}$ for some column vector $y_i \in \mathbb{Z}^n_{\geq 0}$ and $i \in [s]$. We interpret this by saying that the ith complex has $(y_i)_j$ units of species j. The *zero complex* is the monomial 1. The source of a reaction is called an *educt complex* and the sink of a reaction is called a *product complex*. Let Y_e and Y_p denote the matrices whose columns are the exponents of the educt and produc complexes, respectively, ordered by k. Then, any chemical reaction network $\mathcal{N}$ can be uniquely identified by a quadruple (Y_e, Y_p, k, x). In this paper we are concerned with *mass-action networks* for which the kinetics is of the form

$$\dot{x} = (Y_p - Y_e)\text{diag}(k)x^{Y_e}.$$

A solution x of $(Y_p - Y_e)\text{diag}(k)x^{Y_e} = 0$ is called a *steady state*. As the coordinates of x represent concentrations of chemical species, one usually requires that x is either nonnegative or positive. Note that the set of steady states of a mass-action network forms an algebraic variety (or a semialgebraic variety if one requires that $x \geq 0$ or $x > 0$).

Sometimes it is interesting to take several chemical reaction networks, put them together, and give some of the properties of the resulting chemical reaction network in terms of the properties of the former chemical reaction networks. An example of this procedure can be found in [5], where the authors apply it to the identifiability and

2010 *Mathematics Subject Classification.* Primary: 37N25, 92B99, 92C42.

Key words and phrases. Polynomial systems in biology, chemical reaction networks, steady states.

steady state invariants of chemical reaction networks. Suppose we would like to join two reactions. The output depends on the reactions and it can be classified into four cases:

- Case 1: The reactions have different educts and products.
- Case 2: The reactions have the same educts and different products.
- Case 3: The reactions have different educts and the same products.
- Case 4: The reactions have the same educts and products.

The following definition is an intent to cover these four cases and it is a generalization of the definition of union of chemical reaction networks introduced in [5].

Definition 1.1. The *sum* $\mathcal{N}_1 + \mathcal{N}_2$ of two chemical reaction networks $\mathcal{N}_1$ and $\mathcal{N}_2$ is the union of $\mathcal{N}_1$ and $\mathcal{N}_2$ where equally labelled vertices are identified and equally directed parallel arrows sum over the rate constants. Let X denote a (possibly infinite) set of chemical species. The set of all chemical reaction networks on X with $+$ is a monoid $(X, +)$ with identity element the empty reaction 0 for which $\dot{x} = 0 \ \ \forall x \in X$.

Remark 1.2. The way we define the sum of reactions only works if the summands are independent. This is not always the case in chemistry: It is well known that there exist inert systems which start to react after adding them a set of catalysts. This more general situation is not considered in this article and it will be analyzed in a future work.

Remark 1.3. Note that, by allowing generalized mass-action dynamics with real rate constants (rather than positive), $(X, +)$ becomes a group.

It could happen that two chemical reaction networks represent essentially the same object, labelled in different ways. Two chemical reaction networks $\mathcal{N}_1$ and $\mathcal{N}_2$, both on n species and r arrows, are *equivalent* (written $\mathcal{N}_1 \sim \mathcal{N}_2$) if there are permutations $\sigma \in \Sigma_r$ and $\tau \in \Sigma_n$ such that $Y^T_{\bullet,\mathcal{N}_1} = \tau(\sigma Y_{\bullet,\mathcal{N}_2})^T$, for $\bullet \in \{e, p\}$. $\sim$ is an equivalence relation. However note that elements of the same class might have different physical meaning.

2. Chemical reaction sheaves

Let $C \subseteq \mathbb{R}^3$ be a container in which a set of chemical reactions takes place and suppose that the set of chemical reactions can change in time but the shape and position of the container are constant. We model the chemistry taking place in C as a topological space $X = \mathbb{R}^3 \times \mathbb{R}$ (three dimensions for space and one for time) with the product topology and some extra data: to each open subset U of X we associate a submonoid $\nu(U)$ of $\mathfrak{N}$ such that for each inclusion $U \subseteq V$ of open sets of X we have $\nu(U) \subseteq \nu(V)$ and, if U is $\emptyset$ or an open subset of $X - C \times \mathbb{R}$, then $\nu(U) = \{0\}$.

Definition 2.1. The data (X, ν) is called a *chemical reaction sheaf* if every stalk ν_P has the form $\{0, \mathcal{N}_P\}$, where $\mathcal{N}_P \neq 0$ if $P \in C \times \mathbb{R}$ and $\mathcal{N}_P = 0$ otherwise. A *finite chemical reaction sheaf* if a chemical reaction sheaf for which $\nu(X)$ is finite.

Remark 2.2. By associating $\{0, \mathcal{N}\}$ to each nonempty open set that intersects $C \times \mathbb{R}$, and $\{0\}$ to each other open set, $\mathcal{N}$ can be regarded as a finite chemical reaction sheaf. Actually note that every finite chemical reaction sheaf is of this form.

Experimentally, we can only hope to measure a finite set of temporal restrictions $\nu|_{\mathbb{R}^3\times t_1}, \dots, \nu|_{\mathbb{R}^3\times t_n}$ of a chemical reaction sheaf. As $\mathbb{R}^3 \times t_i \simeq \mathbb{R}^3$, by sending (x, t_i) to x, $\nu|_{\mathbb{R}^3\times t_i}$ can be regarded as a sheaf ν_{t_i} over $\mathbb{R}^3$. This motivates the following definition.

Definition 2.3. An *algebraic path* between $\nu|_{\mathbb{R}^3\times t_1}$ and $\nu|_{\mathbb{R}^3\times t_2}$ is any morphism between the sheaves ν_{t_1} and ν_{t_2}. An algebraic path is called *reversible* if it is an isomorphism, otherwise it is called *irreversible*.

3. Mass-action sheaves

Definition 3.1. A *mass-action sheaf* is a chemical reaction sheaf in which every chemical reaction network is a mass-action network.

Mass-action networks which are described by the same set of ODEs are indistinguishable: two reaction networks $\mathcal{N}_1$ and $\mathcal{N}_2$ are dynamically equivalent, written $\mathcal{N}_1 \dot{\sim} \mathcal{N}_2$, whenever their dynamics are described by the same set of ODEs. We denote the set of equivalence classes of $\mathfrak{N}$ with respect to $\dot{\sim}$ by

$$\dot{\mathfrak{N}} = \mathfrak{N}/\dot{\sim}.$$

A central problem in mass-action networks is the classification of parameters with respect to the existence of multiple steady states. From this angle, it is interesting to have a good description of the variablity of the chemical reaction graphs inside each class of $\dot{\mathfrak{N}}$. We refer to [1, 2] for results in this direction.

Remark 3.2. Unless some differentiability conditions are required, ν need not be described by PDEs. However this is not necessary, as many Biological processes are not globally smooth (e.g., the cell can suddenly start a mechanism based on external stimuli).

4. Steady state sheaves

As every mass-action network has an associated steady state variety, whenever one is only interested in the steady states, one can approximate the evolution between two mass-action networks by a morphism between two steady state varieties. At the level of sheaves, when one restricts the analysis to steady states, the object of interest is a sheaf of steady states. At the level of steady states it is enough to keep information about the *steady state ideal* $\langle (Y_p - Y_e)\mathrm{diag}(k)x^{Y_e}\rangle$ and about the *conservation relations* (actually, if one requires that $x > 0$, one only needs saturated ideals). Moreover, if one is only interested in strictly positive steady states, then almost every ideal represents the set of steady states of a chemical system [3]. In particular, up to a saturation, every binomial ideal can be regarded as the steady state ideal of a mass-action network [6, Corollary 1.8]. However, by doing so, information about the dynamics might be lost. Yet, it would be interesting to have a nice graphical description of the elements of the same class, when two reactions are considered equivalent if they have the same steady states (or the same nonnegative or positive steady states). A possible approach might be through the study of the Gröbner bases structures of these ideals [4].

5. Discussion

While the previous constructions are very general, when modelling "evolving biological systems" one would like to restrict algebraic paths to chemically relevant ones. For instance, for long intervals of time, one might wish to achieve stable autocatalytic reactions. This also suggests the need for a good definition of entropy. In such a framework the algebraic paths which increase the entropy of the system would define the direction of time. Besides, if $\mathfrak{P}_{t_1,t_2}$ denotes the set of all algebraic paths between $\nu_{\mathbb{R}^3\times t_1}$ and $\nu_{\mathbb{R}^3\times t_2}$, it would be interesting to find the elements of $\mathfrak{P}_{t_1,t_2}$ which optimize the entropy. Note that entropy might break the reversibility of algebraic paths.

Finally, we propose the following problems:

Problem 5.1. *Find conditions for a mass-action sheaf to be globally described by PDEs.*

Problem 5.2. *Find conditions for a steady state sheaf to be a scheme.*

Acknowledgement

This research was done while the author was a PhD student at Otto-von-Guericke-Universität in Magdeburg. She would like to thank her PhD advisors, Carsten Conradi and Thomas Kahle, for giving her the opportunity to think of this problem. This project was funded by the Deutsche Forschungsgemeinschaft, 284057449, and by the DFG-RTG "MathCore", 314838170. Now the author has a full postdoctoral position at the Joint Research Center for Computational Biomedicine in Aachen.

References

1. Gheorghe Craciun and Casian Pantea, *Identifiability of chemical reaction networks*, Journal of Mathematical Chemistry **44** (2008), no. 1, 244–259.
2. Gheorghe Craciun, Casian Pantea, and Grzegorz A Rempala, *Algebraic methods for inferring biochemical networks: a maximum likelihood approach*, Comput biol chem **33** (2009), no. 5, 361–367.
3. Alicia Dickenstein, *Biochemical reaction networks: An invitation for algebraic geometers*, Mathematical Congress of the Americas, vol. 656, American Mathematical Soc., 2016, pp. 65–83.
4. Elizabeth Gross, *Personal communication at FoCM*, 2017.
5. Elizabeth Gross, Heather A Harrington, Nicolette Meshkat, and Anne Shiu, *Joining and decomposing reaction networks*, preprint arXiv:1810.05575 (2018).
6. Alexandru Iosif, *Algebraic methods for the study of multistationarity in mass-action networks*, Ph.D. thesis, Otto-von-Guericke-Universität Magdeburg, 2019.
7. Anne Shiu, *Algebraic methods for biochemical reaction network theory*, Ph.D. thesis, University of California, Berkeley, 2010.

Joint Research Center for Computational Biomedicine, Aachen, Germany
E-mail address: `iosif@aices.rwth-aachen.de`