

Kinetic realization of delayed dynamical models

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1 Introduction

The nonnegative system classes are important tools in modeling such space/time varying phenomena, where the state variables are naturally positive (e.g. biochemical processes, reaction networks, compartmental systems). In engineering practice it is often necessary that the delays appearing in the operation of processes (e.g. signal propagation, material flow) are modeled appropriately in order to describe the dynamic behavior precisely [1].

There are existing necessary and sufficient conditions for an ordinary dynamical system to be realizable as a CRN [2], but for a given kinetic system there might exist more than one structurally different realization with the same dynamical behavior. These reaction networks connected by a positive definite diagonal linear transformation are called linearly conjugate realizations of a kinetic system. It is an important task to find realizations with special structural properties. We can compute realizations containing minimal and maximal number of reactions (so-called sparse and dense realizations) and so-called weakly reversible realizations, and there exists algorithms which is able to compute all possible realizations of a kinetic system.

In this work we propose the generalization of these results and algorithms to delayed kinetic systems and CRNs. Our goal is to solve the inverse problem, i.e. to compute reaction graphs which realize a given delayed kinetic dynamicity by extending earlier results [3, 4].

2 Mathematical background

2.1 Mass-action reaction networks with time delays

Delayed CRNs consist of elementary reaction steps $\mathcal{R}_j$, $j = 1, \dots, r$, taking place between n chemical species denoted by $X_1, \dots, X_n$ of the form

$$\mathcal{R}_j : \sum_{i=1}^n y_{ij} X_i \xrightarrow{\kappa_j, \tau_j} \sum_{i=1}^n y'_{ij} X_i. \quad (1)$$

where the nonnegative integers y_{ij} and y'_{ij} are the stoichiometric coefficients, the positive numbers κ_j are the reaction rate constants, and the nonnegative numbers τ_j are the time delays.

The linear combinations of species on the left and right hand sides of the reaction steps (1) are called complexes (source complex and product complex, respectively)

$$C_j = \sum_{i=1}^n y_{ij} X_i \quad C'_j = \sum_{i=1}^n y'_{ij} X_i. \quad (2)$$

Note that the zero complex can also be present in the set of complexes, we can use it to represent the effects of the environment. The mass action law states that the reaction rate of the reaction step (1) is

$$\varrho_j(x) = \kappa_j \prod_{i=1}^n x_i^{y_{ij}} \quad (3)$$

where x_i denotes the concentration of the specie X_i .

2.2 Graph representation of mass-action systems with time delays

We can assign a weighted directed graph $D^\tau = (V_d, E_d^\tau) = (V_d, E_d^{\tau_0=0}, E_d^{\tau_1}, \dots, E_d^{\tau_p})$ to the reaction network (1), where:

1. The vertices correspond to the complexes, i.e. $V_d = \{C_1, \dots, C_m\}$.
2. The directed edges represent reactions, i.e. $(C_j, C_l) \in E_d^{\tau_i}$, if C_j transforms into C_l in the network with time delay τ_i .
3. The reaction rates are assigned as positive weights to the edges.

2.3 Delay differential equations of mass-action systems with time delays

The dynamics of a delayed CRN with reaction steps (1) is described by a system of delay differential equations (DDEs) of the form

$$\dot{x}(t) = \sum_{i=0}^p Y A_i \psi(x(t - \tau_i)) \quad (4)$$

where $x \in \mathbb{R}^n$ is the concentration vector of the species, $Y \in \mathbb{R}^{n \times m}$ stores the stoichiometric composition of the complexes, $A_i \in \mathbb{R}^{m \times m}$, $i = 0, \dots, p$ contains information corresponding to the weighted directed graph and ψ is the monomial mapping defined by

$$\psi_j(x) = \prod_{i=1}^n x_i^{y_{ij}}, \quad j = 1, \dots, m. \quad (5)$$

The exact structure of A_i is

$$[A_0]_{jk} = \begin{cases} -\sum_{i=0}^p \sum_{l=1}^m \kappa_{jl}^{\tau_i}, & j = k \\ \kappa_{kj}, & j \neq k \end{cases} \quad (6)$$

$$[A_i]_{jk} = \kappa_{kj}^{\tau_i} \quad i = 1, \dots, p. \quad (7)$$

where $\kappa_{kj}^{\tau_i}$ is the weight of the $(C_k, C_j) \in E_d^{\tau_i}$ edge.

Note that if $\tau_i = 0$, $i = 1, \dots, p$, then the above system reduces to a system of ODEs describing an ordinary CRN with $A = \sum_{i=0}^p A_i$ containing the weighted directed edges.

3 Delayed linearly conjugate realization

Let us consider a dynamical system with time delays

$$\dot{x}(t) = \sum_{i=0}^p M_i \psi(x(t - \tau_i)). \quad (8)$$

Such a system is uniquely characterized by the $(p + 2)$ -tuple $(Y, M_0, \dots, M_p)$.

Definition 1. A realization described by the matrices $Y, A'_0, \dots, A'_p$ is linearly conjugate to the delayed kinetic system $(Y, M_0, \dots, M_p)$ if there exists a positive diagonal matrix $T \in \mathbb{R}^{n \times n}$ such that

$$\sum_{i=0}^p Y A'_i \psi(x(t - \tau_i)) = \sum_{i=0}^p T^{-1} M_i \Psi_T \psi(x(t - \tau_i)). \quad (9)$$

where $\Psi_T \in \mathbb{R}^{m \times m}$ is such a positive diagonal matrix, that $[\Psi_T]_{ii} = \psi_i(T \cdot \mathbf{1})$.

By using the notation $A_i = A'_i \Psi_T^{-1}$, $i = 0, \dots, p$, we can say that a realization described by the matrices $Y, T, A_0, \dots, A_p$ is linearly conjugate to the delayed kinetic system $(Y, M_0, \dots, M_p)$ if $Y A_i = T^{-1} M_i$, holds for $i = 0, \dots, p$.

The above realization is uniquely characterized by the $(p + 3)$ -tuple $(Y, T, A_0, \dots, A_p)$.

Proposition 1. Let us consider a delayed kinetic system $(Y, M_0, \dots, M_p)$. There exists a $(Y, T, A_0, \dots, A_p)$ linearly conjugate realization if and only if $M_0 \psi(x(t))$ is kinetic and M_i has only nonnegative elements, $i = 1, \dots, p$.

The following definitions and theorems will help us understand the exact structure of the linearly conjugate realizations of a delayed kinetic system.

Proposition 2. Let us consider a delayed kinetic system $(Y, M_0, \dots, M_p)$. The set of $(Y, T, A_0, \dots, A_p)$ linearly conjugate realizations is a convex set.

Definition 2. Let us consider a delayed kinetic system $(Y, M_0, \dots, M_p)$ and a linearly conjugate realization $(Y, T, A_0, \dots, A_p)$. It is said that $(Y, A_0, \dots, A_p)$ is

1. a sparse realization, if it contains minimal number of reactions,
2. a dense realization, if it contains maximal number of reactions.

Definition 3. Let us consider a delayed kinetic system $(Y, M_0, \dots, M_p)$ and a linearly conjugate realization $(Y, T, A_0, \dots, A_p)$. It is said that $(Y, T, A_0, \dots, A_p)$ has a superstructure property if its reaction graph contains the reaction graph of all other dynamically equivalent realizations of the delayed kinetic system as subgraphs.

Using the above we can now state the following very important theorem.

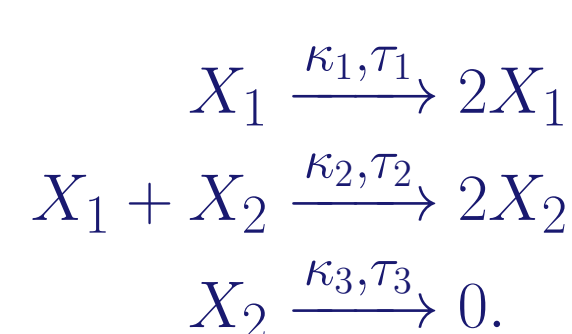
Proposition 3. Let us consider a delayed kinetic system $(Y, M_0, \dots, M_p)$ and a dense linearly conjugate realization $(Y, T^d, A_0^d, \dots, A_p^d)$. Then $(Y, T, A_0^d, \dots, A_p^d)$ has superstructure property.

The following corollary makes us able to compute all of the structurally different linearly conjugate realizations of a delayed kinetic system

Corollary 1. Let us consider a delayed kinetic system $(Y, M_0, \dots, M_p)$ and a dense linearly conjugate realization $(Y, T^d, A_0^d, \dots, A_p^d)$. Then the structure of the unweighted directed reaction graph of the dense realization is unique.

4 Example: Lotka-Volterra reaction with time delay

Let us consider a classical Lotka-Volterra model in kinetic form with delayed reactions



The DDEs describing the dynamics are the following

$$\dot{x}(t) = \begin{bmatrix} -\kappa_1 x_1(t) - \kappa_2 x_1(t) x_2(t) + 2\kappa_1 x_1(t - \tau_1) \\ -\kappa_2 x_1(t) x_2(t) - \kappa_3 x_2(t) + 2\kappa_2 x_1(t - \tau_2) x_2(t - \tau_2) \end{bmatrix}.$$

Figure 1(a) shows the solution of the system defined by the tuple $(Y, A_0, \dots, A_3)$ with initial conditions $x(0) = [1 \ 2]^T$ and Figure 1(b) shows the reaction graph of the system.

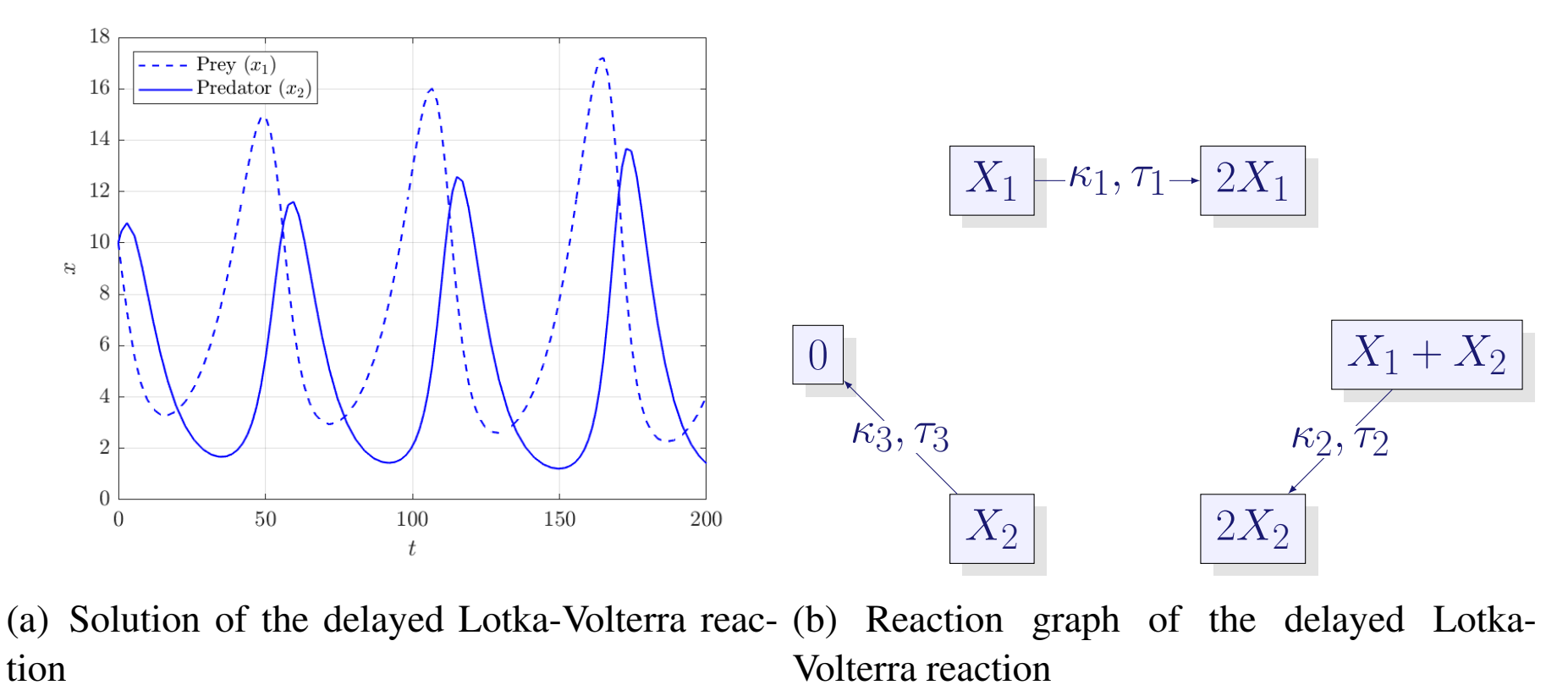


Figure 1: Delayed Lotka-Volterra reaction with $\kappa_1 = 0.1$, $\kappa_2 = 0.02$, $\kappa_3 = 0.15$ and $\tau_1 = 0.2$, $\tau_2 = 0.1$

4.1 Computation of possible reaction graph structures

The algorithms were implemented in Python 3.6.4 using the Gurobi Optimization package. The computations were tested on workstation with a 2.7 GHz Intel Core i7-7500U processor and 8 Gb RAM (DDR4 2133 MHz, 0.5 ns).

Figure 2 shows the reaction graph of the dense realization of the delayed Lotka-Volterra reaction. The delayed reaction with $\tau_1 = 0.2$ and $\tau_2 = 0.1$ delays are shown with dashed, blue and red arrows, respectively.

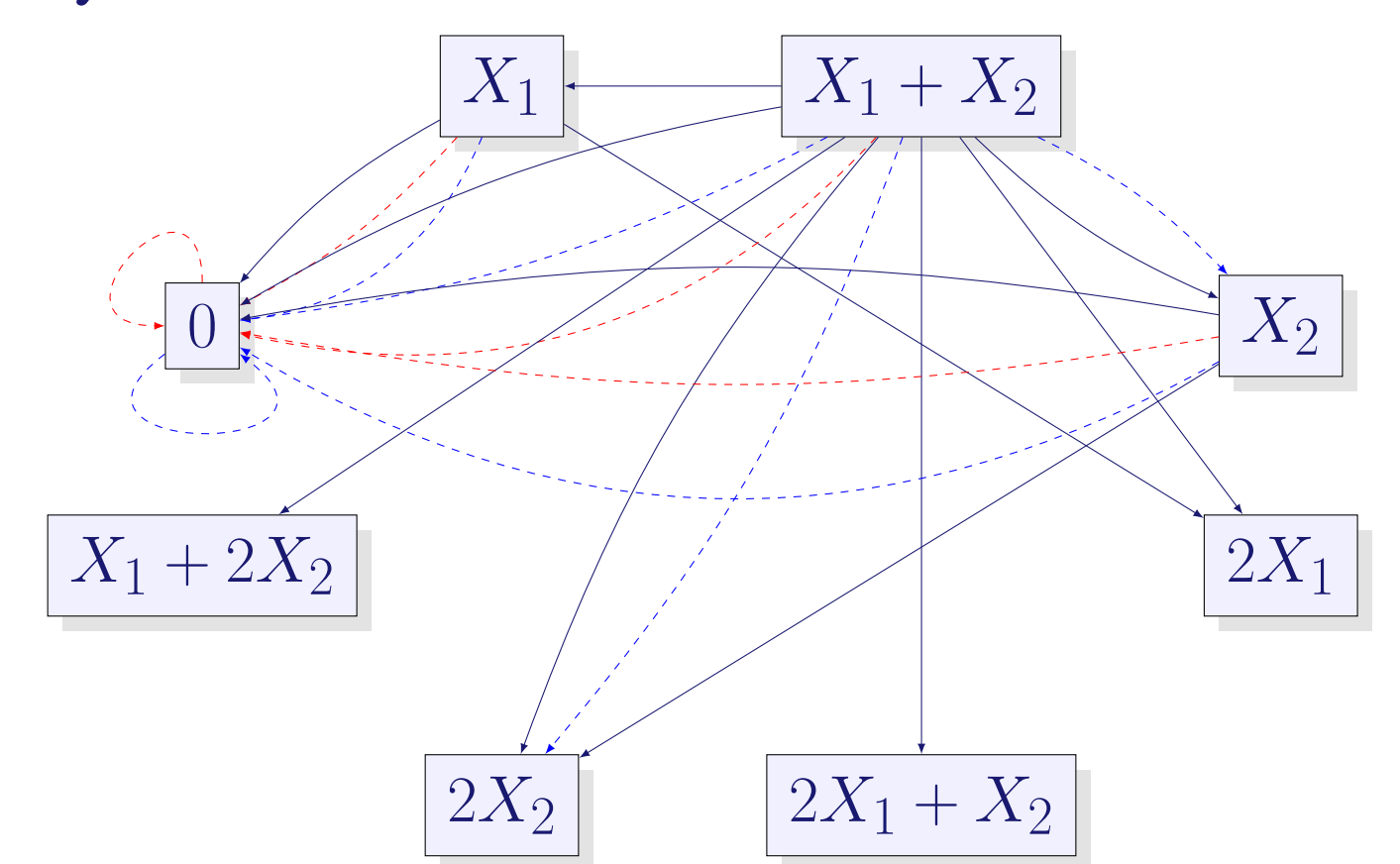


Figure 2: Reaction graph of the dense linearly conjugate realization

Figure 3 shows the distribution of structurally different realizations depending on the number of reactions.

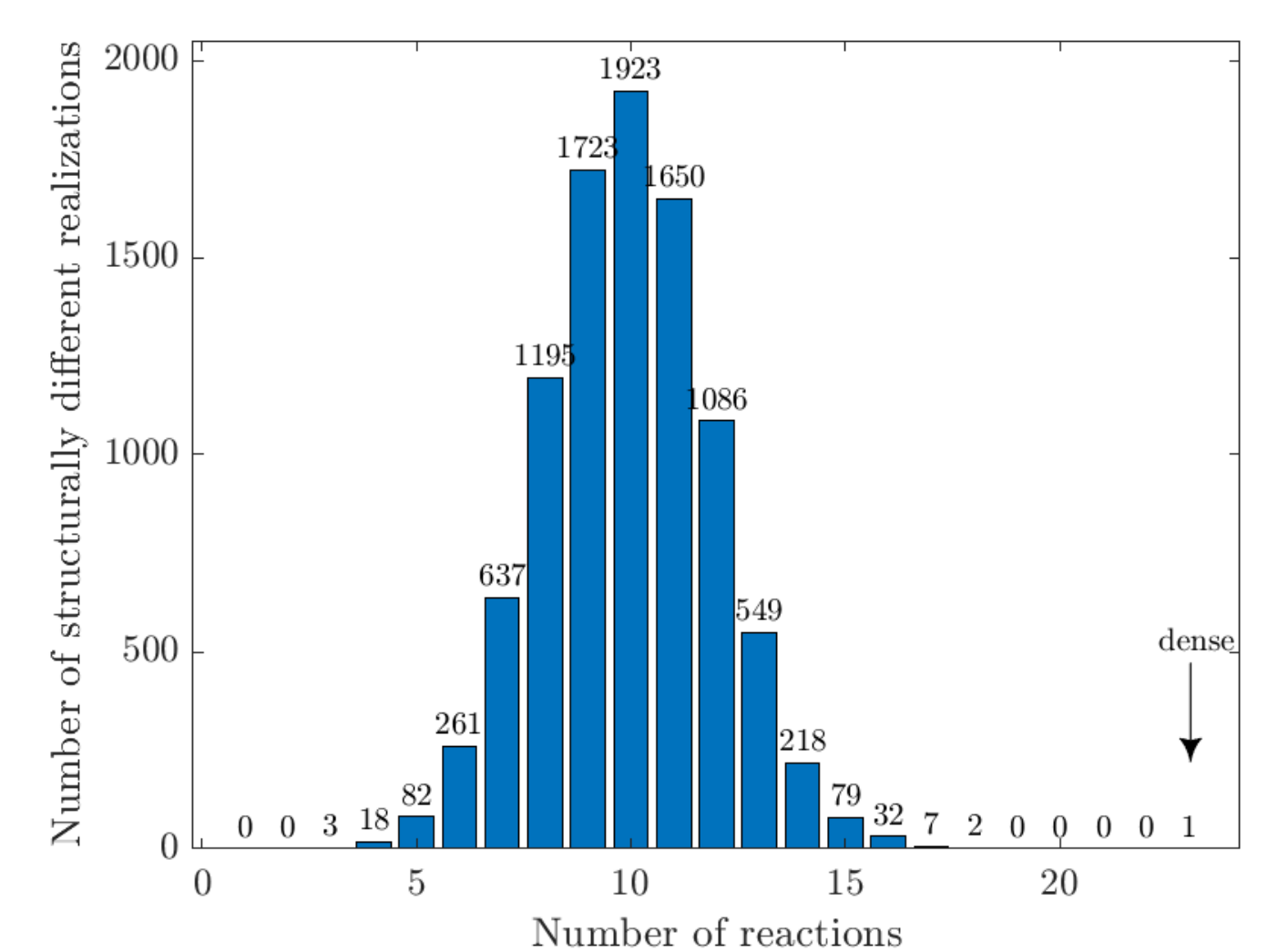


Figure 3: Distribution of structurally different realizations

5 Conclusion

In this work we generalized the optimization model and linear programming algorithms to compute the dense linearly conjugate realization and all of the realizations of a delayed kinetic system. For the extending of the methods it was proven that delayed, dense linearly conjugate realizations form a superstructure among delayed linearly conjugate realizations, assuming a fixed set of complexes.

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