An Identification Procedure for Piecewise-Affine Models of Genetic Regulatory Networks

Samuel Drulhe$^{1,2,*}$, Riccardo Porreca$^3$, Giancarlo Ferrari Trecate$^{3,4}$, Hidde de Jong$^1$

**Genetic regulatory networks in brief**

- Genetic Regulatory Networks (GRNs) underlie functioning and development of living organisms.
- Components: genes, proteins, metabolites, and their mutual regulatory interactions.
- Genes code for proteins. Gene expression is controlled by concentration of regulatory proteins in cell.
- Experimental techniques in biology have led to the production of enormous amounts of data on the dynamics of gene expression: DNA microarrays, gene reporter systems.
- System identification problem: derive a model of the regulatory interactions from measurements and model structure.
- Among classes of systems that were used for modeling biological networks [2], we focus on Piecewise Affine (PWA) systems of GRNs introduced by [6]:
  - the concentration space is divided into hyperrectangular regulation domains separated by thresholds on the concentration variables;
  - each domain corresponds to an affine mode of operation.
- We are using the data model described on Figure 1. The identification problem is then to reconstruct from the noisy dataset:
  - the number of modes (b) all rate parameters (c) all switching thresholds.
- Algorithms for PWA systems identification have been proposed [5], but existing identification methods are generic in nature and do not exploit features and constraints of PWA models of GRNs.
- The method we present focuses on the problem of detecting switches among different modes of operation in gene expression data [9] and on the reconstruction of switching thresholds associated with regulatory interactions [4]: Such an identification method is designed for output-error systems where the observations are noisy time-series measurements of concentration levels inside a cell: it is described on Figure 2.

**E. coli carbon starvation response**

The performance of our approach has been analyzed using synthetic data produced by a simplified model of the carbon starvation response in the bacterium Escherichia coli [10]. In particular, we evaluated the impact of the noise level and sampling time on the identified systems. Our results show that the method, coupled with the carbon starvation response in the bacterium E. coli, is described on Figure 2.

**PWA systems identification**

- The concentration space is divided into hyperrectangular regulation domains separated by thresholds on the concentration variables.
- Each domain corresponds to an affine mode of operation.
- We are using the data model described on Figure 1. The identification problem is then to reconstruct from the noisy dataset:
  - the number of modes (b) all rate parameters (c) all switching thresholds.
- Algorithms for PWA systems identification have been proposed [5], but existing identification methods are generic in nature and do not exploit features and constraints of PWA models of GRNs.
- The method we present focuses on the problem of detecting switches among different modes of operation in gene expression data [9] and on the reconstruction of switching thresholds associated with regulatory interactions [4]: Such an identification method is designed for output-error systems where the observations are noisy time-series measurements of concentration levels inside a cell: it is described on Figure 2.

**Simple example**

\[
\begin{align*}
\dot{x}_1(t) &= f_1(x) - \gamma_1 x_1 - \gamma_2 x_2 x_3 \\
\dot{x}_2(t) &= f_2(x) - \gamma_3 x_1 x_2 + \gamma_4 x_1 x_2 x_3 \\
\dot{x}_3(t) &= f_3(x) - \gamma_5 x_1 x_2 + \gamma_6 x_1 x_2 x_3
\end{align*}
\]

**References**