Application of piecewise deterministic Markov processes to stochastic gene expression models

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Abstract

This doctoral dissertation is devoted to the issue of piecewise deterministic Markov processes (PDMP) and their applications in models of stochastic gene expression. One of the classical models describing protein synthesis by a single gene is the Goodwin model. In a two-dimensional version, it can be presented as a nonlinear system of ordinary differential equations, in which the variables correspond to the levels of concentration of mRNA and protein molecules. The level of protein molecules regulates the production of new mRNA molecules by means of a nonlinear regulation function. In this paper we focus on two types of Goodwin models with different regulation functions. Additionally, our models include the stochastic disturbance associated with the switching of the gene between the active and inactive state. This means that the discussed models can be considered as PDMPs.

First, we recall the basic concepts related to Markov processes and introduce the general definition of PDMP. Then, we provide the theory of Markov semigroups used to study the asymptotic behavior of piecewise deterministic Markov processes. We also present basic gene expression models that are PDMPs and that are an inspiration for the models discussed in this dissertation.

In Chapter 2, we present a two-dimensional Goodwin model of stochastic gene expression with negative feedback loop. The regulation function in this system is considered to be the decreasing Hill function. For this model we define a stochastic process which is PDMP. The main result of this chapter is the proof of the fact that the Markov semigroup generated by this process is asymptotically stable. It means that the densities of the distributions of this process converge to the unique invariant density.

In the next model discussed in the paper, the regulation function is considered to be the increasing Hill function, which induces a positive feedback loop. We prove that the Markov semigroup generated by the stochastic process for this model is sweeping from the family of all compact subsets of the set $R^2_+ \setminus \{(0,0)\} \times \{0,1\}$. It means that the probability that trajectories of the process remain in any such compact subset converges to zero.

In addition, in the last chapter we consider possible use of the theory of piecewise deterministic Markov processes to analyze the dynamics of a group of genes conected in a regulatory network. An example model of interaction between two genes and the related PDMP process are described.