Modeling miRNA-mediated translation control

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***Short Abstract* — This work is concerned with modeling of miRNA-mediated regulation of gene expression. We propose a novel approach based on queuing systems theory. The model describes changes of probabilities of different numbers of ribosomes associated with a given transcript. This allows to compare simulation results with experimental observations of polysome profiles and determine the type of control exerted by miRNA on the translation process.**

***Keywords* — miRNA, translation control, queuing systems.**

I. Introduction

ONE of the molecular components regulating gene expression is microRNA – a small (21-25 nt) single-stranded non coding RNA molecule. The main function of this molecule is post-transcriptional regulation of gene expression through gene silencing. It is achieved either by inhibition of translation or by degradation of mRNA [1]. The detailed mechanisms employed include inhibition of attaching the 60s ribosomal subunit, premature ribosome drop-off or inhibition of protein elongation process, cleavage of mRNA or destabilization of mRNA [2-3].This regulation appears to be used in control of cellular responses to stress, e.g. induced by irradiation. Despite many efforts, however, detailed mechanisms employed in such case are still not fully understood. Development and analysis of mathematical model of miRNA-mediated mechanisms of control of gene expression should advance the research in this field.

II. Preparation of Abstracts

In the literature, one can find several models of regulatory networks, in which miRNAs are involved. Some of them describe specific miRNA interactions, while others attempt at creating a generic model of these processes [3-5]. In this work, a different approach is proposed, inspired by our own experimental results, showing different polysome profiles observed for reporter genes containing miRNA binding sites (using the technique described in [6]). The model is focused on the mRNA processing by the ribosome complexes, a number of which may produce proteins from one mRNA template in parallel. When there is more than one ribosome on a mRNA, such construct is called a polysome [7]. Measuring polysome, together with respective protein levels may lead to conclusions about the type and power of miRNA-mediated control specific gene expression as well as provide information about highly processed transcripts.

The approach proposed in this paper is based on a queuing systems theory. Each transcript is processed in such system, with ribosomes viewed as service stations. There are discrete events of ribosome binding, movement along a mRNA strand, finishing translation, thus producing a single protein molecule, and ribosome stop, either random or caused by miRNA complex attached to a respective binding site. Binding of miRNA molecules to mRNA is also modeled as a discrete event, probability of which depends on the level of mRNA and its type.

The system state is defined by a n-dimensional vector P. Each variable $P_i(t)$ represents probability of i ribosomes being attached to mRNA at the moment t. Thus, simulation results can be directly compared with the experimentally observed distribution of polysome fractions. The dimension of the state vector is defined by the size of mRNA,

III. Conclusion

In this work a novel approach of modeling regulatory mechanisms of gene expression is proposed. It consists in describing a process of translation within the framework of queuing systems theory. Stationary distribution of polysomes observed in biological experiments were well represented by the simulation results in preliminary studies.

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