Membrane Systems and Their Application to Systems Biology

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1 Introduction

P-systems, or membrane systems [1], were introduced by George Păun as a class of unconventional computing devices of distributed, parallel and nondeterministic type, inspired by the compartmental structure and the functioning of living cells. The basic model consists of a membrane structure, described by a finite string of well matching parentheses, and graphically represented as regions on the plane, hierarchically embedded within an external region. Each membrane contains a multiset of *objects* (representing chemical substances) that evolve according to given *evolution rules* (representing reactions). Objects are described as symbols or strings over a given alphabet, evolution rules are given as rewriting rules. The rules act on objects, by modifying and moving them, and they can also affect the membrane structure, by dissolving the membranes. A computation in P systems starts from an initial configuration, identified by the membrane structure, the objects and the rules initially present inside each membrane, and then letting the system evolve. Assuming an universal clock, rules are applied in a nondeterministic and maximal parallel manner: all the applicable rules are used at each step to modify all objects which can be the subject of a rule, and this is done in parallel for all membranes; the evolved objects are then communicated to the regions specified by the rules. When no rule can be further applied, the computation halts and the output is defined in terms of the objects sent out of the external membrane or, alternatively, collected inside a specified membrane. No output is obtained if the computation never halts (that is, whenever a rule can be continuously applied). A comprehensive overview of basic P systems and of other classes appeared in [1], an updated bibliography can be found in the P systems Web Page ([2]). As a model of computation inspired by biological mechanisms, P systems have been extensively studied in the area of Natural Computing from the point of view of their computational power, and compared with other models like DNA computing or splicing systems. However, they can also be considered as a powerful tool to model complex systems and to simulate processes taking place inside them. In this view, they have been applied in various research areas, ranging from Biology to Linguistics to Computer Science (see, e.g., [3]), but very promising results have been obtained in simulating cellular phenomena, hence returning meaningful and useful information to biologists, in the frame of systems biology.

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2 Stochastic Modelling

In this view, it is important to take into account the role of stochastic noise in modelling and simulating coupled chemical reactions (see the classical Gillespie algorithm [4]) and, in a more general frame, in cellular processes involving few molecules as, e.g., signal transduction pathways, and the working of transcription or translation machinery [5]. For this reason, in [6] the class of dynamical probabilistic P systems (DPPs) has been introduced for the analysis and simulation of the behavior of complex systems. DPPs are discrete and stochastic models, where probability values are associated with the rules, and such values change during the evolution according to the current state of the system. A different approach to stochastic modeling of biological systems has been given in [7].

3 Simulation Results

In order to check both the effectiveness and the correctness of the models, we designed and implemented a software simulator, that hopefully will become a tool for biologists for testing known data, predicting unknown scenarios and returning meaningful information. The last version of the simulator uses a novel method, called *tau leaping*, introduced by Gillespie et al. [8] and then adapted by Cazzaniga et al. [9] to work in the framework of P Systems (this new method is named tau-DPPs). Using tau-DPPs, we can simulate systems structured by several volumes, tracing the simulated time of the compartments as well as time line of the whole system. This gives us the possibility to quantitatively and qualitatively describe biological systems. Our model was able to simulate properly the Ras protein cycle, the activation of adenylate cyclase, the production of cyclic AMP and the activation of cAMP-dependent protein kinase in a single yeast cell of the yeast *Saccharomyces cerevisiae*. The results are compared with the experimental data and give information on the key regulatory elements of this signalling network. Another application was to metapopulation modeling [10]. A slightly different approach to modeling biological systems with P-systems can be found in [11].

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