Modelling and simulation of the E.coli-Lambda interactions

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Motivation

Bacteriophage Lambda is a virus that infects E. coli. Upon infection, the phage can propagate choosing between two different programs that depend by environmental conditions. If, for example, the cell is exposed to agents that damage DNA by endangering the existence of bacteriophage itself, the Lambda can activate a program that allows its propagation outside the hosting cell. An approach to understand the behaviour of biological systems consist in the cooperation of biomedical and computer scientists. The integration of the knowledge from the two fields allows the modeling of a biological system of interest and to run the in-silico simulation of this biological prototype in different scenarios. It is the aim of Systems biology [2] to analysis, model and simulate biological systems and processes, through the supply of mathematical and computational models. In the context of LITBIO (http://www.litbio.org) project, we are modelling several biological systems, among those we have analysed and modelled the behaviour of Lambda virus attaching an E. coli bacterium. LITBIO offers a virtual desk, to progressively engineer models of biological systems and to simulate and validate them [3]. The proposed work has been split in two main steps: first, we have studied the literature in order to identify actors, functions and environmental variables involved within the E.coli-Lambda interactions. The second step was dedicated to define the model and simulate the behaviour of the biological system. Thanks to the expressiveness of some informatics tools like modelling languages and timed automata model checking we were able to effectively represents compartments and understand the system dynamics. The final model allows to simulate the activities of Lambda attacking the E. coli and to acquire new knowledge about latency period, infection and virus reaction time.

Methods

The definition of a model that match as much as possible the reality of a complex biological system requires a step-by-step approach. To this end, computer science offers formal and automatic tools to obtain an intuitive and precise representation of complex systems [4,5]. The E.coli-Lambda system, first has been analysed and represented by UML diagrams. This model allowed a coarse-grain representation of the system through the identification of its main stages. Then, each stage has been analysed with a fine-grain approach. The formal description of the system has been obtained by UPPAL. The UML diagrams help to better understand the interactions that occur between Bacteriophage Lambda and E. coli bacterium, and their autonomous behaviour. The analytical study of the system has been conducted by using the timed automata model checking tool UPPAAL (http://www.uppaal.org). We created a set of finite state automata, to represent the cell compartments autonomous behaviour and the behaviour of E.coli-Lambda interactions (see Figure). UPPAAL is a graphical tool that provides immediate overview of the dynamic evolution of the system. The use of this tool in the first case of simulation, has been useful to validate the proposed model of the E.coli-Lambda system. Moreover, it provides a more detailed and complete description of the system behaviour.

Results

The UML diagrams and UPPAAL timed automata model checking have been reveled useful tools to obtain an effective model of a biological system of the E.coli-Lambda system. The model allows to study the dynamic behaviour of the systems interactions. The proposed model can be considered the starting point to study and analyse a more complex systems.

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