A New Framework for Modeling Complex Biological Systems

CORDERO F (1, 2), MANINI D (2), GRIBAUDO M (3), BALBO G (2)

(1) Department of Clinical and Biological Sciences - University of Torino, Torino, Italy
(2) Department of Computer Science, University of Torino, Torino, Italy
(3) Department of Electronics and Computer Science - Polytechnic of Milano, Milano, Italy

Motivation

The use of mathematical modeling in systems biology is a crucial approach for describing and analyzing the temporal dynamics of the phenomena under study. Unfortunately when the formalism adopted to describe the biological mechanism is non-trivial, the model design may require a substantial effort from biologists, thus making it less effective. Here we present a framework based on object-oriented mean field analysis, that allows the biologists to visually describe and analyze the system under study. We propose a Graphical User Interface (GUI) that provides a practical instrument for representing the biological entities composing the system.

Methods

An object-oriented like mean field model is a representation that describes the behavior of a system composed by a large number of interacting objects in an intuitive manner. When applied within the context of systems biology objects representing the biological entities are divided into classes. All the objects belonging to a given class have exactly the same behavior and are influenced by the distribution of the others in the system. Each object is modeled by a Continuous Time Markov Chain (CTMC), whose transition rates may depend on the state of the whole system. All the objects belonging to the same class are characterized by the same infinitesimal generator and the same parameters. If two objects perform the same actions at different rates, they must belong to different classes. We propose a framework able to compute the time evolution of the number of objects for each biological entity. The modeling approach we propose has two specific features with respect to those present in literature: capability to represent in several ways the same biological system according to the user’s point of view, and the technical solution able to scale large systems. The former allows the user to describe a biochemical reaction not only as an interaction among different entities (as provided by many tools), but also by analyzing entity behaviors in terms of CTMC states. The latter supplies simple and accurate approximations capable of computing the solution of complex models, characterized by large concentration of entities, in reasonable times.
Results

Our framework provides as output a data file, and a web page with the related graphs, reporting the time evolution of the concentration of each entity. Moreover, auxiliary web pages showing the classification of the input model are created. The main advantages lie in the intuitive system representation provided by the object-oriented approach with the support of the GUIs and in the flexibility of the tool modeling approach. This framework can be used to simulate different types of biochemical kinetics as well as complex bio-pathways characterized by the interaction among entities with different behaviors. We present this modeling process through the description of two kinetics, the Michaelis-Menten and an inhibitory kinetic, and the analysis of a complex system such as the switch of LAC operon in conjunction with the glycolysis pathway. The figure depicts a snapshot of our framework where the representation of the Michaelis-Menten kinetic is shown. In particular, we report three panels: the whole model, the enzyme’s CTMC, and the available entity list.

Availability

http://www.di.unito.it/~manini/OBAM-Tool-Draw

Contact email
manini@di.unito.it