Computer simulation of biomolecular processes using stochastic process algebra

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Computational analysis of sequence and structure information has proved to be extremely successful. The existence of a formal, unifying language to describe the relevant data has played a major role in these advancements. Recently, much interest is focused on system level studies of networks of interacting proteins. These biochemical processes mediate the interaction of cells with their environment and are responsible for most of the information processing inside the cell. Currently, however, there is no formal language to describe such processes. They are analyzed either by simulating the continuous, mass-action differential equations, or by various discrete, Monte-Carlo simulations.

In previous work (1) we have suggested a novel formal non-deterministic and discrete way for modeling biochemical networks using the π-calculus. π-Calculus (2) is a process algebra, originally used in the study of distributed computer systems. Our π-calculus model for biochemical processes is mathematically well-defined, while remaining biologically faithful and transparent. Our model is amenable to computer simulation, analysis and formal verification using a combination of existing and self-developed tools (Logix/FCP, 3). In addition to studying particular systems, it also provides a platform for formalizing higher-level questions regarding modularity, abstraction and comparison of biochemical processes.

In this work, we extend the framework to allow accurate quantitative modeling of biochemical networks. A new computer simulation language and system, called Psi, was developed - which is based on the stochastic version of π-calculus. In this model, actions in the original π-calculus specification are assigned rates, according to the corresponding biochemical reactions. We illustrate our modified system through a study of a model of the circadian clock, proposed recently (4).

A major advantage of the π-calculus formalism is its ability to alternate between different levels of complexity. The modular design of biological systems is best captured by such a description. To illustrate this, we have studied the circadian machinery at two levels of abstraction. First, we model the molecular interactions explicitly. Second, we identify a functional module in the system - a hysteresis module - and describe the system using this functional module. By using two Psi programs, we show that both levels of description are equally good at capturing the behavior of the system.

References

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