BioSim - A Semi-Quantitative, Qualitative Simulation Environment for Molecular Biology

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Several genome sequencing projects have been completed or are on the way, e.g., the human genome project. The results of these projects will reveal a growing number of diseases that are genetically determined, so that physicians will be able to improve diagnostics and therapy, and the pharmaceutical industry can develop more effective drugs. Computer simulation models can facilitate analysis and interpretation of genomic and proteomic information, e.g., they can be used for analysing and understanding observed behaviours, and once a simulation model has been validated it can be used to test hypotheses, or to explore the properties of a simulation model under different conditions.

Traditionally, biochemical systems are modelled using kinetics and differential equations in a quantitative simulator. However, for many biological processes detailed quantitative information is not available. Another problem is the building of a simulation model of a biological system. Model building is an inevitable and time consuming task that even can turn the building of a putatively simple model into a major task.

Qualitative reasoning techniques (Dague, 1995) can be used for model building and simulation when only qualitative or fuzzy statements about the nature of interactions are known (Heidtke and Schulze-Kremer, 1998). Based on these techniques, we present a simulation environment that allows the combined use of quantitative and qualitative information. Furthermore, we present a Model Description Language to facilitate the model building task. This language allows to set up a structured and object-oriented domain library that holds templates describing molecular biology primitives, e.g. enzyme kinetics, using semi-quantitative and qualitative mathematical constraints. These templates are used to translate a selected item of interest from a molecular biology knowledge base into simulation objects and processes. Currently, the simulation environment is connected to EcoCyc (Karp et al., 1997), Encyclopedia of *E. coli* genes and metabolism, from which a simulation model can be derived or assembled individually, respectively.

We show that semi-quantitative, qualitative reasoning can be combined with automatic transformation of contents of genomic databases into simulation models to give an interactive modelling system that reasons about the relations and interactions of biological entities.

References

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