Chapter VIII

On a Formal Model of the T Cell and Its Biological Feedback

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ABSTRACT

In this chapter a model of the molecular networks, created by using a network of communicating automata, is described as a dynamic structure, discrete event system, and interesting theoretical results are provided. This formal model provides a detailed approach of the biological system, and its implementation is able to handle large amounts of data. This model is applied to T cell signalling networks. T cell shows a hierarchical organization depending on various factors. Some mechanisms are still unresolved, including contribution of each signalling pathway to each response type. The software tool produced is used to simulate and analyze the T cell behaviour. The simulation reflects, quite faithfully, the process of T cell activation and T cell responses. This increases the confidence in using this model and its implementation both as descriptive and prescriptive tools. The interactions that govern the T cell behaviour are simulated and analyzed, providing statistical correlations according to software experiments, together with new insights on signalling networks that
trigger immunological responses. The software tool allows users to systematically perturb and monitor the components of a T cell molecular network, capturing biological information relevant to immunology.

INTRODUCTION

Systems biology is a new holistic view of molecular biology. The challenge for systems biology is to discover answers to molecular biology’s questions, and to identify the principles that lead to the actual combination of molecular mechanisms. Today we have long lists of genes and encoded proteins, but simply listing the molecules explains neither how these molecules interact and form molecular networks, nor how the cell processes are triggered and regulated. A useful idea is to add new abstractions, discrete models, and methods able to help our understanding of the biological phenomena, giving us predictive power, useful classifications, possibly new molecular computing paradigms, algorithmic analysis of biomolecular protocols, and a new perspective on the dynamics of the membrane systems.

The understanding of complex molecular networks is difficult due to the great number of molecules, proteins and enzymes, pathways, and feedback loops involved in cellular control. Systems biology aims to have a modular understanding of biological phenomena, focusing on system structure and behaviour analysis. In a systemic way, complex molecular networks can be decomposed into smaller meaningful units; then the process of modelling is understood as a combination of parts along two coordinates: structure and behaviour. This chapter defines a network of communicating automata, including more quantitative details. This approach offers an appropriate framework for modelling and provides considerable theoretical power. It is useful to connect this approach to a general theory of modelling and simulation defined by the discrete event system formalism (Zeigler et al., 2000).

In this chapter, we refer to both the behaviour dynamics and structure dynamics of the T cell signalling network. The system’s behaviour is represented as time-varying input/output segments. Given the behaviour of a causal, time-invariant system, we use some abstraction mechanisms to support compositional modelling. Moreover, we consider that our system can change its structure by adapting a rule according to the previous steps. Everything is expressed in a distributed environment making the model compositional, highly adaptable, and realistic. In this way, we can predict unobserved behaviours according to a theoretical framework of discrete-event modelling.
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