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Stepwise Construction of a Metabolic Network in Event-B: the Heat Shock Response

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Abstract

There is a high interest in constructing large, detailed computational models for biological processes. This is often done by putting together existing submodels and adding to them extra details/knowledge. The result of such approaches is usually a model that can only answer questions on a very specific level of detail, and thus, ultimately, is of limited use. We focus instead on an approach to systematically add details to a model, with formal verification of its consistency at each step. In this way, one obtains a set of reusable models, at different levels of abstraction, to be used for different purposes depending on the question to address. We demonstrate this approach using Event-B, a computational framework introduced to develop formal specifications of distributed software systems. We first describe how to model generic metabolic networks in Event-B. Then, we apply this method for modeling the biological heat shock response in eukaryotic cells, using Event-B refinement techniques. The advantage of using Event-B consists in having refinement as an intrinsic feature; this provides as a final result not only a correct model, but a chain of models automatically linked by refinement, each of which is provably correct and reusable. This is a proof-of-concept that refinement in Event-B is suitable for biomodeling, serving for mastering biological complexity.

Keywords: Biomodeling, Model refinement, Model hierarchy, Heat shock response, Event-B, Rodin

1. Introduction

The general problem we address in this paper is how to systematically add details to a biological model so that the model may be used at different levels of abstraction depending on the question to be addressed. Our approach to
 5 this problem is based on model refinement. The idea is to specify the model

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