Cell Illustrator 2.0: A Platform for Biopathway Modeling and Simulation

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1 Introduction

In the post-genome era, biopathway information processing is one of the most important issues in bioinformatics. Development of Genomic Object Net ([5] is our approach to this issue. This software aims at describing and simulating structurally complex dynamic causal interactions and processes such as metabolic pathways, signal transduction cascades, gene regulations. In Dec/2002, we have released Java based software Genomic Object Net 1.0 [1, 3]. The software was based on Hybrid Functional Petri net (HFPN) [2]. With HFPN, we can model rule based biological processes in biopathways, e.g. gene regulation and also ODEs-based kinetics, e.g. chemical processes in biopathways. In fact, with HFPN, we have modeled and simulated: the glycolytic pathway of Escherichia coli, gene regulation of circadian rhythms in Drosophila, boundary formation by notch signaling in Drosophila, and apoptosis induced by Fas ligand.

2 Architecture

However, when modeling biopathways with HFPN, we have realized that three extensions will be useful for modeling and simulating more complicated biopathway processes (e.g. activities of enzymes for a multi-modification protein) and other biological processes that are not normally treated in biopathways (e.g. alternative splicings, frameshiftings). The first is, an entity should be extended to contain more than one value, such as list and pair, because, (i) every part in a cell should contain 3D information, e.g. position and speed, (ii) proteins often have many modified states, e.g. p53 has known sixteen phosphorylation positions and two acetylation positions and modified states of p53 can be $2^{18}$. In HFPN, an entity can contain only one value. The second is, HFPN should be extended to handle other primitive types, e.g. boolean, string, because major parts in a cell contain information similar to strings such as DNA sequences, mRNA sequences and protein sequences. In HFPN, an entity has only two types, discrete (non-negative integers) and continuous (non-negative real numbers). The third is, HFPN should be extended to handle more advanced type, object that consists of variables and methods. Many parts in a cell, e.g. DNA, mRNA, protein, have known functions, e.g. translation, transcription, degradation, and modification. Thus, if an entity takes the type object that has the methods with these known functions, each process that connects to the entity only needs to call a method of the object in the entity. To realize these three extensions, we have defined two special components; entity and process, called generic entity and generic process, respectively. We name this extension of Petri net hybrid functional Petri net with extension (HFPNe) [4]. With these extended architecture HFPNe, we have developed Cell Illustrator.
2.0 while extensively updating the following features: (i) biological elements are introduced for easy biopathway modelings, (ii) major chemical equations are included for better compatibility with other differential equation based softwares, (iii) automatic pathway layout functionalities are developed for large-scale biopathway modeling and simulation. The application supports the one of open XML formats for biopathway modeling and simulation named Cell System Markup Language 1.9 (https://www.csml.org/). On the new version, we are modeling large scale biopathways, e.g. signaling pathways in endothelial cell (see Fig.1 (a)) and MAPK signaling pathways for various kind of stress response in budding yeast (see Fig.1 (b)).

References


