BPE: Biopathway Executer for Large-Scale Biopathway Modeling and Simulation

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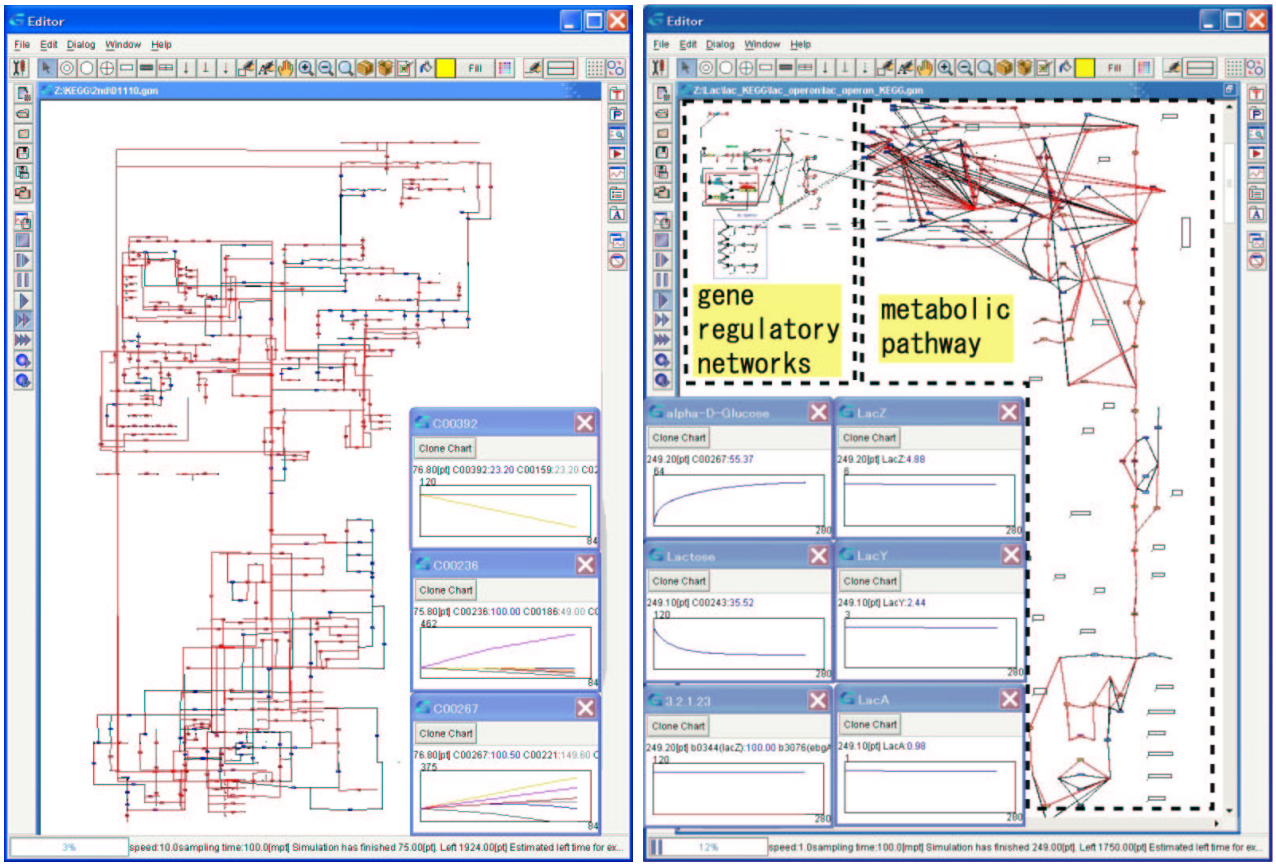
1 Introduction

Biopathway databases have been developed, such as KEGG [6] and EcoCyc [3], that compile interaction structures of biopathways together with biological annotations. However, these biopathways are not directly editable and simulatable. Thus, we are developing an application, the Biopathway Executer (BPE) [5], that reconstructs these two major biopathway databases to XML formats of modeling and simulation platforms. BPE is developed with JAVA and has a database of executable biopathways that integrates some parts of biopathway information, KEGG and BioCyc, and other databases, e.g. MIPS and BRENDA. Currently, BPE employs the XML format (GONML) of a Hybrid Functional Petri net (HFPN) for the output. The features of HFPN are: (i) biopathways that contain discrete and continuous processes can be modeled, (ii) all biopathways that are modeled with ordinary differential equations (ODEs) can be remodeled, (iii) biopathways can be modeled while keeping readability by human. Other XML formats of biopathways, SBML [7] and CellML [2] are subsets of GONML. Thus, BPE can bridge major biopathway databases and major modeling and simulating softwares.

2 Results and Discussion

To demonstrate the effectiveness/usability of BPE, two examples are created and simulated on Genomic Object Net [4] which is based on the HFPN architecture [1]. Fig. 1(a) is a snapshot of the executable large-scale metabolic pathway with 2D plotting graphs and animations by BPE. The map compiles thirty maps that are categolized into carbohydrate metabolism in KEGG. The executable map contains more than 10000 HFPN components. Many substrates and products exist on the map but not displayed, because they are also removed in original KEGG map for human readability. Fig. 1(b) ia an executable metabolic pathway with gene regulatory networks. The biopathway consists of right and left boxed parts. The right part is a metabolic pathway by BPE. The pathway consists from two KEGG maps: glycolysis/gluconeogenesis and galactose metabolism. The left part is the gene regulatory network of *lac* operon that is modeled by a user. These examples show that BPE is a useful tool for integrating biopathway databases for large-scale modeling and simulation.



(a) (b)

Figure 1: (a) KEGG 2nd metabolic pathway map recreated with the BPE. (b) A BPE generated metabolic pathway with gene regulatory networks.

Our aim of BPE is to automatically generate editable, executable biopathways including signal transduction pathways, e.g. gene regulatory networks. Thus, we need to extend current BPE to integrate other signal transduction pathway data in KEGG and BioCyc, signal induction reactions data, e.g. CSNDB, TRANSPATH, and GeneNet. In addition, we need to create conversion processes for reactions in signal transduction pathways.

References

[1] Matsuno, H., Doi, A., Nagasaki, M., and Miyano, S., Hybrid Petri net representation of gene regulatory netowrk, *Genome Informatics*, 10:341–352, 2000.

[2] `http://www.cellml.org/`

[3] `http://www.ecocyc.org/`

[4] `http://www.genomicobject.net/`

[5] `http://www.genomicobject.net/BPE/`

[6] `http://www.kegg.org/`

[7] `http://www.sbml.org/`