PhysioDesigner, an open platform for multilevel modeling applicable to computational neuroscience

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Abstract — An open platform, PhysioDesigner for enhancing multilevel modeling of physiological functions in the field of integrated life-science, which is also applicable to computational neuroscience, has been developed. Users combine and build mathematical models of biological and physiological functions on PhysioDesigner. Users can also integrate morphometric data on a model, which is used, for example, to define a domain on which partial differential equations are solved. The models developed by PhysioDesigner is stored in insilicoML (ISML) format which is an XML-based specification, to describe wide variety of models of biological and physiological functions with hierarchical structure.

Keywords — PhysioDesigner, Multilevel modeling, Integrated life science, Computational neuroscience

1 Introduction

Mathematical multi-level modeling of biological and physiological phenomena is crucial for integrating pieces of biological and physiological knowledge[1, 2]. The models developed in the relevant scientific field are getting larger in size and higher in accuracy. A collaborative framework should be developed. We have been developing an open platform called PhysioDesigner (Fig. 1), as a successor of insilicoIDE[3] developed by Physiome.jp initiative (www.physiome.jp), on which users can build a new model by combining existing models and integrating morphometric data. Simulations of these models can be performed by an accompanying simulator (insilicoSim) which supports parallel computing in a MPI-available environment. There is also a database of models, timeseries and morphometric data on Physiome.jp website. Anyone can freely download them. The high reusability of models is one of outstanding features of PhysioDesigner.

2 Basic Concepts

PhysioDesigner uses ISML[4] (insilicoML) to store models internally, which has been developed in the framework of insilico platform[2]. ISML is partially compatible with CellML which is one of the pioneering languages developed in IUPS Physiome project[5]. ISML is especially designed to structuralize the targeting physiological phenomena and to represent their hierarchical structure based on modularity. A module represents a conceptual physiological entity, such as ion channel, cell membrane, neuron, neuronal nucleus and so on. A group of modules can be treated as a

Figure 1: PhysioDesigner snapshot. PhysioDesigner shows a Hodgkin-Huxely model in nesting diagram (right upper), the same mode but in the tree diagram (right lower) and component list tree (left upper). Square like objects in nesting or tree diagrams represent modules in which several physical quantities are defined with equations and values.

Figure 2: A model is represented as an aggregate of modules. Each module is quantitatively characterized by physical-quantities.
module which is at one level above. This definition allows to express a situation such as a neuronal nucleus is composed of many neurons. Consequently, a model is represented as an aggregation of modules.

Each module is characterized by several physical-quantities, that can represent dynamical variables (so called state) used in differential equations to determine dynamics, time varying parameters, and constants. Usually the physical-quantities are defined by equations such as algebraic equations, ordinary/partial differential equations, numbers or morphometric data. Programming like expression such as IF-THEN syntax can be also defined in physical-quantities.

Relationships between modules are defined by edges. Two types of edges are defined in ISML. One is a functional edge representing a relationship that one module gives values (physical quantities) to the other module. The receiver module can utilize the values in equations. The other type is called a structural edge, defining spatial or logical hierarchical relationship.

3 Various modeling

PhysioDesigner can deal with models based on ordinary differential equations (ODEs) in a sophisticated manner. The methods to handle morphological information and partial differential equations (PDEs) can spread the targets to be modeled. Models including PDEs and morphometric data developed on PhysioDesigner can be exported in FreeFEM++ [6] format and solved with the finite element method by it (Fig. 3).

Systems biology markup language (SBML) [7] has been developed as a pioneering effort to develop an unified methodology to develop mathematical models of biological functions mainly in the subcellular level, such as gene expression/regulation and signal processing in cells. As shown in Fig. 4 PhysioDesigner can import a SBML model in a module. And modules can form a network with functional/structural edges to represent phenomena in the physiological levels such as cell network, tissue and organs. The hybridization modeling between SBML and ISML can be a good methodology for multi-level modeling.

There are still open challenges for further development on other modeling techniques such as multi-agent systems, though currently the platform can support these techniques for limited cases. We have introduced a template/instance framework which can be helpful to build a large scale model with high-efficiency. Once we define a cluster of modules as a template, we can create a kind of ”copy”s (instances) as the modules, whose properties follow the one of the template, and can have some personality.

4 Conclusion

We have been developing an open platform as a comprehensive versatile information infrastructure for enhancing the integrative life science, which can be applicable to computational neuroscience as well. Such framework can also work to sustain the quality and soundness of the models.

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References