

PhysioDesigner: A versatile platform for multilevel modeling of physiological systems network.

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Integrated physiology and systems biology have been developing as new interdisciplinary scientific fields, in which the importance of multilevel modeling of physiological systems is rapidly increasing. To develop such models increasing in size and complexity, systematical supports from software is necessary. For example, SBML (<http://sbml.org>) is currently de facto standard to describe subcellular biochemical phenomena, and CellDesigner (<http://www.celldesigner.org>) is the most used software to edit and simulate SBML models. CellML (<http://www.cellml.org>) is for modeling of physiological system, among others.

In the same direction, we have been developing PhysioDesigner as a common platform on which users can develop multilevel models with interdisciplinary collaborations. PhysioDesigner enables users to build hierarchical multi-layer models. Each of models includes multiple modules representing a component of physiological functions. PhysioDesigner is freely available at <http://physiodesigner.org>. Models built on PhysioDesigner are written in PHML (Physiological Hierarchy Markup Language) format, which is an XML based specification to describe hierarchy of systems in comprehensive biological models, and which is a partially convertible with CellML. In PHML, each of biological and physiological elements represented in a model is called a module, and structural and functional relationships among modules are defined by edges. A group of modules can be treated as a module at a higher level. By this recursive definition of the modules, a hierarchical structure found in the physiological systems is expressed in a model. Modules also form a big network representing functional connectivity among physiological functions. Each module is quantitatively characterized by several physical quantities, such as, states defining the system's dynamics, and variable and static parameters. Definition of the dynamics such as ordinary differential equations, or functions of physical-quantities are explicitly described by mathematical equations. Morphometric and time series data can be integrated to modules as well. It is possible to import a SBML model in a module. Such an SBML-PHML hybrid model can represent a multilevel biophysiological system incorporating different technologies.

Simulations can be performed by Flint, which can read not only PHML models, but also SBML and SBML-PHML hybridized models. There is also a cloud-based simulation service powered by Flint, called Flint K3, which is in-service at <http://flintk3.org>.