

Sharing physiological models

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Physiological systems are inherently complex, involving the dynamic interaction of many entities over a wide range of spatial and temporal scales. Reliably forecasting the behavior of such systems is difficult for all but the simplest processes. When a system is comprised of multiple interacting processes, one must use mathematical modeling to make quantitative predictions of behavior. The development of such multi-scale modelling frameworks to represent our knowledge of physiological systems is one of the primary aims of the IUPS Physiome Project (see <http://physiomeproject.org/>). These frameworks require standards and tools for representing, sharing, combining, and solving models. Much progress has been made over the past decade to fulfill these requirements:

- CellML (<http://www.cellml.org/>) is a language for representing physiological systems that can be approximated as well-mixed compartments of interacting species. Such systems are typically described by coupled differential/algebraic equations. CellML represents models of such systems using a high-level mathematical notation, Content MathML (<http://www.w3.org/Math/>), that is automatically translatable into standard human-readable mathematical notation and computer executable code. The CellML language includes constructs that facilitate modular decomposition of models into submodels, and the integration of models into supermodels. These facilities encourage model reuse, enabling physiologists to build and explore the behavior of new models using well-tested and curated components;
- The CellML Model Repository (<http://models.cellml.org/cellml/>) is an open public library of more than 500 peer-reviewed models of diverse physiological processes (*e.g.* calcium dynamics, cardiovascular circulation, cell cycle, cell migration, circadian rhythms, electrophysiology, endocrine, excitation-contraction coupling, gene regulation, hepatology, immunology, ion transport, mechanical constitutive laws, metabolism, myofilament mechanics, neurobiology, pH regulation, PK/PD, signal transduction) represented in the CellML format. The repository is searchable and includes information about the original publications, governing mathematical equations, metadata, and the curation status. Facilities are provided for the collaborative development of new models, enabling controlled access to information throughout the model creation process. Tools are also provided for automatically generating code in a variety of computer languages;
- OpenCOR (<http://www.opencor.ws/>) is an open-source cross-platform application for creating, editing, annotating, solving, and analysing CellML models. It provides a unified environment to access models from the CellML Model Repository, combine and modify models, view models in a number of useful representations, check models for consistency, and solve models using a variety of numerical integrators. Although still under active development, documentation and code are available for download from the developer site (<http://www.opencor.ws/developer/>);
- FieldML (<http://physiomeproject.org/software/fieldml/>) is an emerging declarative language for representing models of general spatio-temporally varying systems. It focusses on describing hierarchical models involving interactions between generalized mathematical fields. FieldML can be used to represent the dynamic 3D geometry and solution fields from computational models of cells, tissues, and organs. It provides a common format for model interchange within the bioengineering and general engineering analysis communities. Some FieldML model examples are available in the model repository (<http://models.fieldml.org/fieldml/>);
- OpenCMISS (<http://physiomeproject.org/software/opencmiss/>) is a mathematical modelling environment that enables the application of finite element analysis techniques to a variety of complex bioengineering problems. While still under active development, it currently supports the solution of coupled models of large deformation solid mechanics and fluid mechanics. It incorporates reaction-diffusion solvers, enabling simulation of, for example, electrical activation problems. Facilities exist to embed CellML models, providing a flexible way to couple complex point-wise processes within large-scale spatio-temporally varying models.

The above languages, tools, and repositories are significant contributions to the the Physiome Project, providing the scientific community with the means to integrate quantitative knowledge of physiological systems within a consistent, flexible, freely available, framework.