The CellML Model Repository as a Resource for Cardiac Modelling

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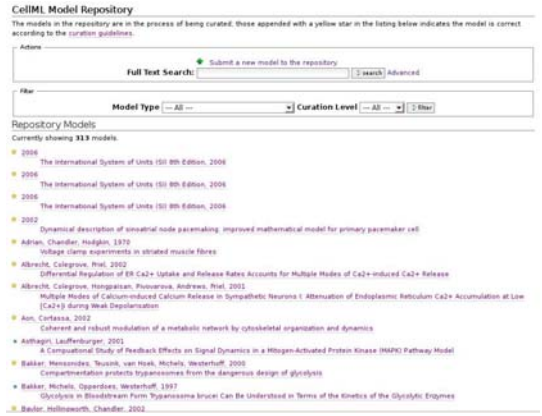
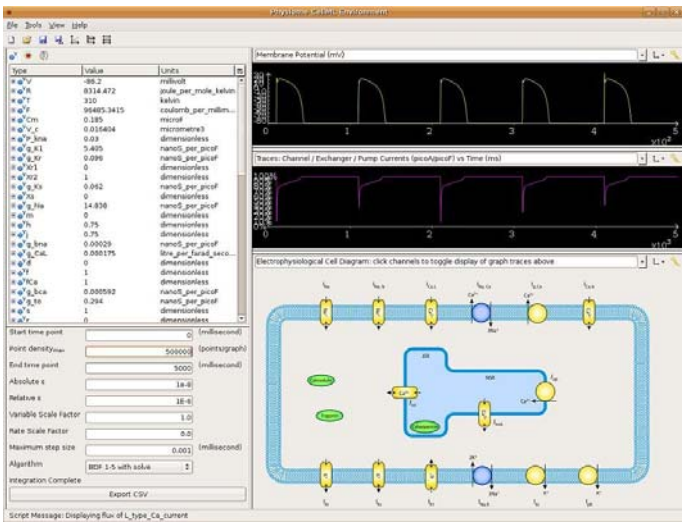
CellML Model Repository: The CellML model repository at http://www.cellml.org/models contains upwards of 300 unique computational models of biological systems. Among these are a number of well curated models of cardiac biology and physiology at the cellular and subcellular level including models of cardiac electrophysiology, excitation-contraction coupling, myofilament mechanics, signalling systems and combinations thereof.

The purpose of this repository is to provide a comprehensive resource for researchers to permanently store models as they are published, and to access authoritative versions of other models. Making computational models freely available to the research community in a standardised format facilitates model reuse, error correction, the update of parameters and equations as new experimental data is produced and the checking of assumptions inherent in the model.



The CellML model repository model listing

Model Curation: Models are coded into CellML using the relevant journal publication as a reference with the aim of reproducing the output of the model as shown in figures and graphs in the publication. There are frequently errors in the equations and values of variables and parameters, and resolving these issues often requires correspondence with the author of the publication [1]. The curation process aims to ensure that models are reproduced in the state intended by the author, although issues such as unit consistency and biophysical constraints such as mass and charge balance need to be addressed so as to make the model physiologically and physically consistent.



Tools: A CellML application programming interface (API) has also been developed and a number of free, open-source software tools for developing and simulating CellML models are available, including Physiome CellML Environment (PCEnv) and Cellular Open Resource (COR) [2]. Other modelling environments such as JSim and Virtual Cell also support the CellML format. Information on further tools such as validators, debuggers and simulation specific packages can be found at *www.cellml.org/tools.* COR also able to generate procedural code from the CellML in languages such as C++, FORTRAN77 and Java. PCEnv is also able to store graphical layouts in 'session' files: shown to the left is a screenshot of a session file for the Ten Tusscher et al. 2004 model [3]. The top graph shows action potentials produced by the model, while clicking on channels or pumps in the cell diagram brings up current traces in the middle graph.

Screenshot of a PCEnv session: Ten Tusscher et al. 2004 model with interactive SVG cell diagram.

The CellML Repository and Multiscale Modelling of the Heart: The CellML model repository serves as a resource for ready-to-implement computational models of cardiac physiology. These CellML models are imported into programs such as CMISS to describe cellular behaviour in tissue level simulations; alternatively, procedural code can be generated and incorporated into larger models [4]. Models at the biochemical and intracellular signalling level can be incorporated in a modular fashion into cellular level models. For example, a module describing energy metabolism and another describing the beta-adrenoreceptor signalling pathway could be added to a model of cardiac myocyte electrophysiology to create a model that is able to give an appropriate response to simulated pharmacological stimulation. New software for the CellML repository is currently being developed that will allow models to reference and import other models within the repository. This will facilitate the decomposition of major models into a 'LEGO set' of curated, standardised components such as ion channels, signalling pathway modules, receptors, etc. which can be used for building new models.

1. Le Novère et al. "Minimum Information Requested in the Annotation of Biochemical Models (MIRIAM)" *Nature Biotechnology* Dec 2005 23(12) 1509-1515
2. Garny et al. "Cellular Open Resource (COR): a Public CellML Based Environment for Modeling Biological Function" *International Journal of Bifurcation & Chaos* Dec 2003 13(12) 3579-3590
3. Ten Tusscher et al. "A model for human ventricular tissue" *American Journal of Heart and Circulatory Physiology* Apr 2004 286(4) 1573-1589
4. Nickerson et al. " Using CellML in Computational Models of Multiscale Physiology" *Conf. Proc.: 27th Annual International Conference of the IEEE Engineering in Medicine and Biology* Sept 2005 6096-6099.

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