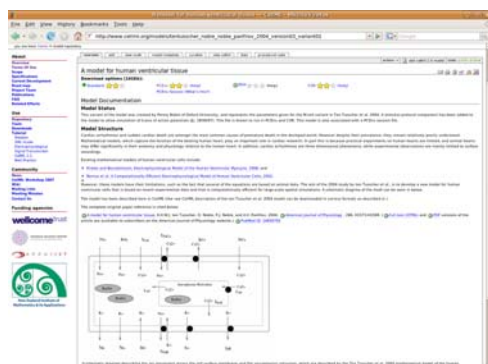


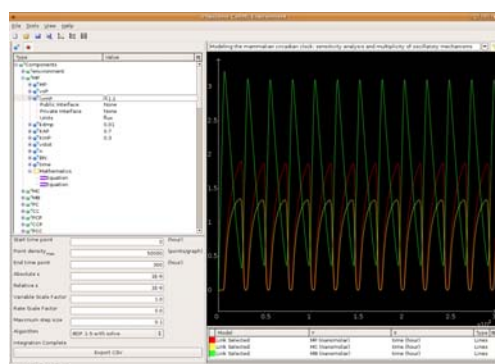
CellML: The purpose of CellML is to store and exchange computer-based mathematical models encompassing a wide a range of scales and subjects. For example, biochemical signalling and metabolic pathways can be embedded within electrophysiological models of excitable cells in CellML. The CellML language^[1] is an open standard based on the XML markup language and is being developed by an open community including the Auckland Bioengineering Institute and affiliated research groups. Many computational biology publications aim to discuss their model but fail to provide a comprehensive set of instructions for recreating the model, or may include errors preventing reproduction the published results. Publishing a paper with a link to CellML code provides an unambiguous description of a model and facilitates its wide distribution and replication, allowing it to be reviewed and improved by others.



Screenshot of a model page from CellML.org repository showing documentation.

Cellml.org: The website www.cellml.org provides a focal point for the community and contains the CellML specifications, member profiles, wikis, FAQs, roadmaps, etc. A repository of almost 300 models is also available at www.cellml.org/models. These are models from peer-reviewed publications that have been coded into CellML. These models are undergoing an active curation process based on MIRIAM^[2], a set of standards proposed by the international biological modelling community. This process involves provision of comprehensive documentation, annotation with citation and model author metadata, maintenance of file modification histories, and correspondence with model authors to ensure that models define all required initial conditions and parameters. A screenshot of a page from the repository is shown to the left, complete with documentation describing the model and its curation status; such a page exists for each model on the site.

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)^[3]. 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 provides a text-based editing environment which represents the CellML in a simplified format, and is also able to generate procedural code from the CellML in languages such as C++, FORTRAN77 and Java. PCEnv and COR use the CVOLE integrator and allow the user to access to several algorithms and adjust integration parameters. PCEnv is also able to store graphical layouts in 'session' files. These files are accessible from the model repository, allowing users to easily load reproductions of publication figures, as shown below.



PCEnv 'session' screenshot showing the tree-based graphical CellML editor and the graphed output of a circadian rhythm model.



COR screenshot showing the text based editorial mode (bottom) including a rendering of an ordinary differential equation (top).

Community: 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. Issues such as unit consistency and biophysical constraints such as mass and charge balance need to be addressed in many models if they are to be synthesised into new, larger models^[4]. The CellML community espouses an open-source approach to these problems, drawing on the diverse skills of its members in an international, multidisciplinary collaboration. The CellML email discussion list can be found at www.cellml.org/mailman/listinfo/cellml-discussion.

Future: In the near future, models in the Cellml.org repository will be annotated with references to the BioPAX ontology and databases such as UniProt. An API has recently been developed for software tools to allow interaction between CellML and SVG diagrams of models, such as biochemical pathway schematics, and work is also underway to standardise graphical representations of CellML models. Models will also be broken down into their constituent components, and these components will themselves undergo curation, providing a toolbox of standardised computational building blocks from which new models can be created, in an *in silico* analogy to the *in vitro* MIT "Registry of Standard Biological Parts."

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