

CellML: Cellml.org, Tools and Community

Lawson, J.¹ Britten, R.² Crampin, E.³ Halstead, H.⁴ Hunter, P.⁵ Nielsen, P.⁶

1. CellML Group, Bioengineering Institute, University of Auckland, New Zealand
2. CellML Group, Bioengineering Institute, University of Auckland, New Zealand
3. Systems Biology and Cell Modelling Group, Bioengineering Institute, University of Auckland, New Zealand
4. CellML Group, Bioengineering Institute, University of Auckland, New Zealand
5. Director, Bioengineering Institute, University of Auckland, New Zealand
6. CellML Group, Bioengineering Institute, University of Auckland, New Zealand

The purpose of CellML is to store and exchange computer-based mathematical models of as wide a range of scale and subject as possible. For example, biochemical signalling and metabolic systems can be embedded in electrophysiological models of excitable cells in CellML. The CellML language is an open standard based on the XML markup language and is being developed by the Bioengineering Institute at the University of Auckland and affiliated research groups [1].

The majority of computational biology publications aim to discuss their model but often fail to provide a comprehensive set of instructions for recreating the model, or include errors preventing reproduction of published model outputs. Publishing a paper with a link to a CellML model facilitates the wide distribution and recreation of that model, and additionally forces the modeller to carefully consider matters such as unit consistency.

The CellML specification and application programming interfaces (API) are driven by a core team, but a growing international community is involved in work related to CellML. A community website (www.cellml.org) has been set up as a focal point for the community and also functions as a model repository. A number of groups are developing software tools for CellML and using the language for research in computational biology.

A repository of almost 300 unique CellML models is available at www.cellml.org/models: these are computational models from peer-reviewed publications that have been coded into CellML. These models are undergoing an active curation process based on the MIRIAM standard, proposed by the international biological modelling community [2]. This process includes 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. The CellML community strongly supports collaboration with other groups to continue to set standards for curation and distribution of biological models.

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). 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.

In the near future, models in the cellml.org model repository will be completely annotated with ontologies such as BioPaX and references to databases such as UniProt. Models will be broken down into the components from which they are comprised, and these components will themselves be curated, providing a toolbox of standardised computational parts from which new models can be created, in an *in silico* analogy to the MIT Registry of Standard Biological parts

(http://parts.mit.edu/registry/index.php/Main_Page). 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.

For more information, please join the CellML community mailing list at <http://www.cellml.org/mailman/listinfo/cellml-discussion>.

- 1.) Cuellar, A.A., Lloyd, C. M., Nielsen, P. F., Bullivant, D. P., Nickerson, D. P., Hunter, P. J. "An Overview of CellML 1.1, a Biological Model Description Language" *Simulation*, 2003, **79**, No. 12, 740-747
- 2.) Le Novère, N., Finney, A., Hucka, M., Bhalla, U.S., Campagne, F., Collado-Vides, J., Crampin, E.J., Halstead, M., Klipp, E., Mendes, P., Nielsen, P., Sauro, H., Shapiro, B., Snoep, J.L., Spence, H.D., Wanner, B.L. "Minimum information requested in the annotation of biochemical models (MIRIAM)" *Nature Biotechnology*, 2005, **23** 1509-1515