CellML: current status and future directions

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Te Whare Wānanga o Tāmaki Makaurau


cellML

What is CellML?

The purpose of CellML is to store and exchange computer-based **mathematical models**. CellML allows scientists to share models even if they are using different modelling tools. It also enables them to reuse components from one model in another, thus accelerating model development.

- MathML within a modular, reusable framework.
- Unambiguous and tool-independent description of a set of mathematical equations.
- Typically describing a system of differential algebraic equations.
- Units, units, units...

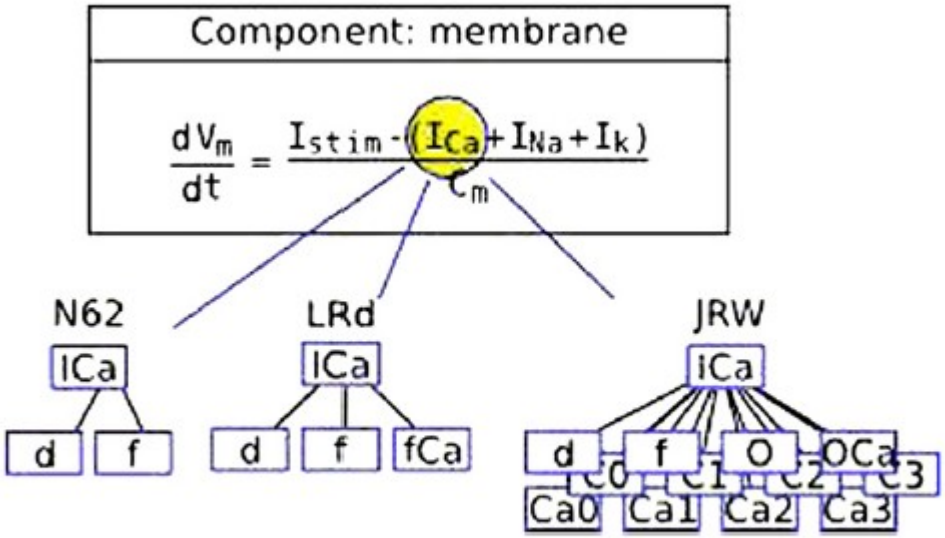


Fig. 1. An illustrative example of CellML encapsulation. The membrane component requires a value for I_{Ca}, the value could come from many potential sources with three possibilities shown (N62: Noble (1962); LRd: Luo and Rudy (1994); and JRW: Jafri et al.

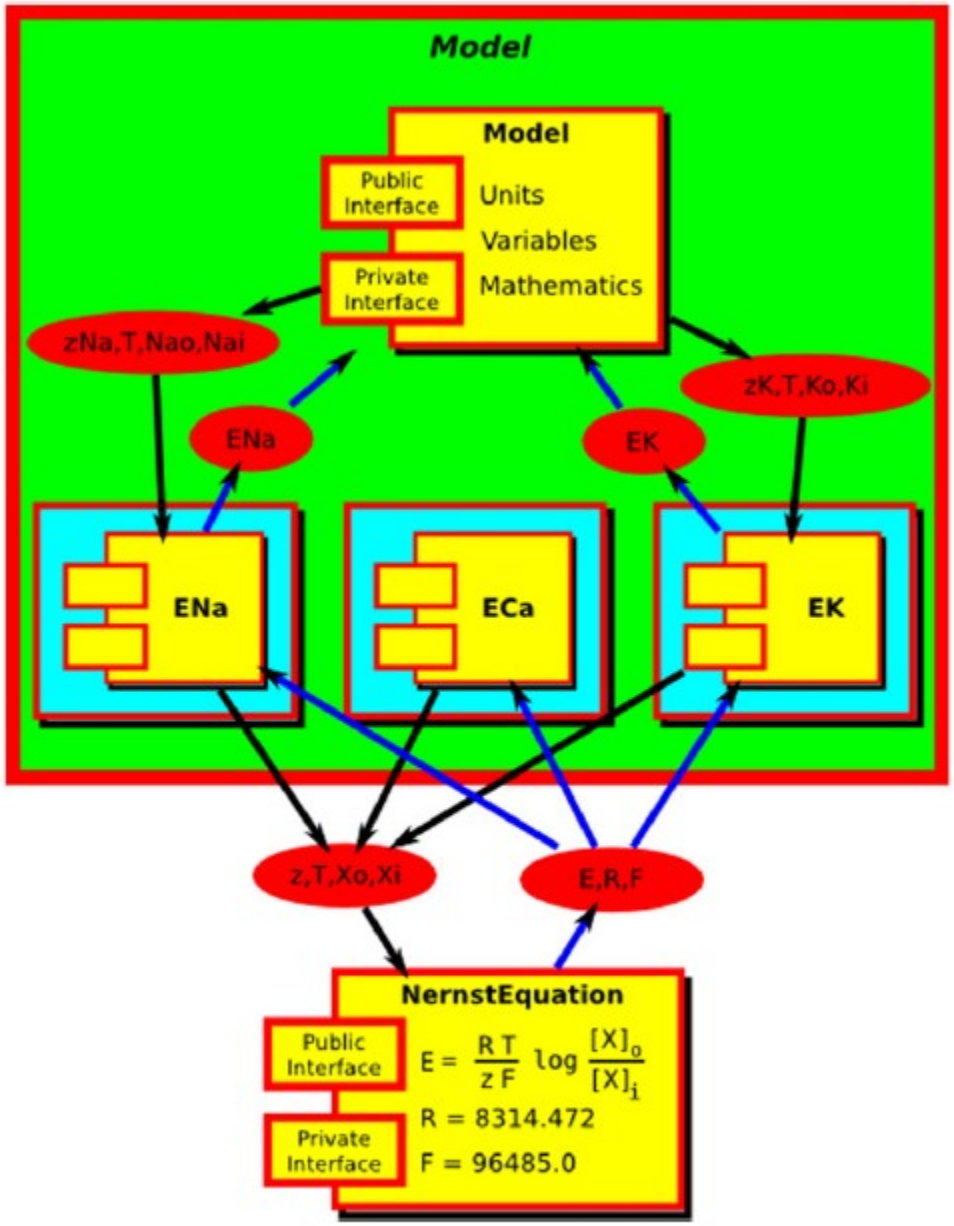
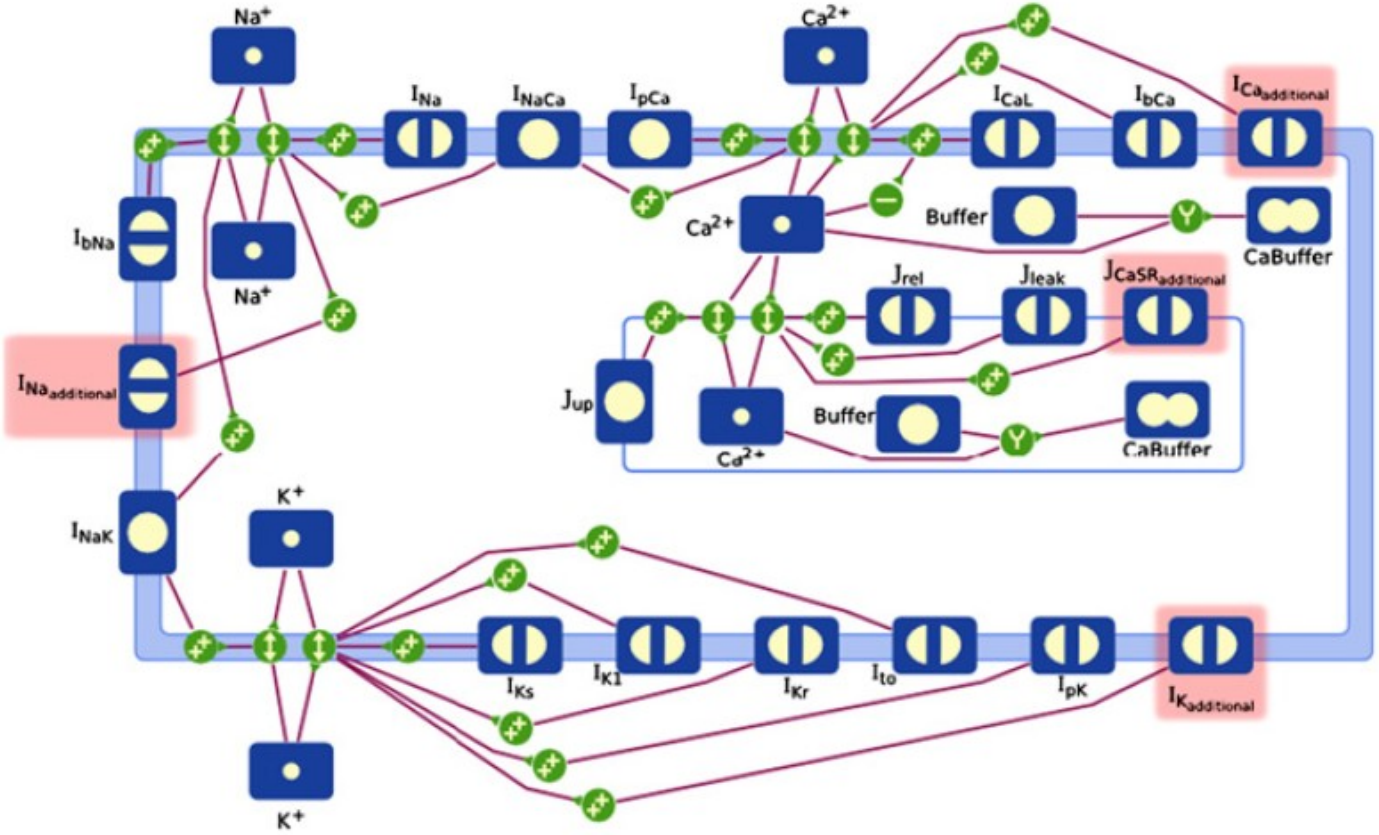
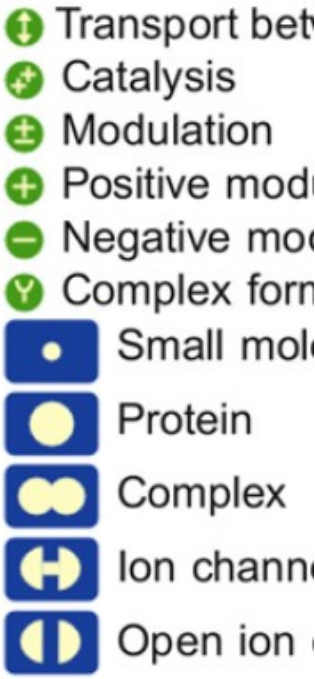
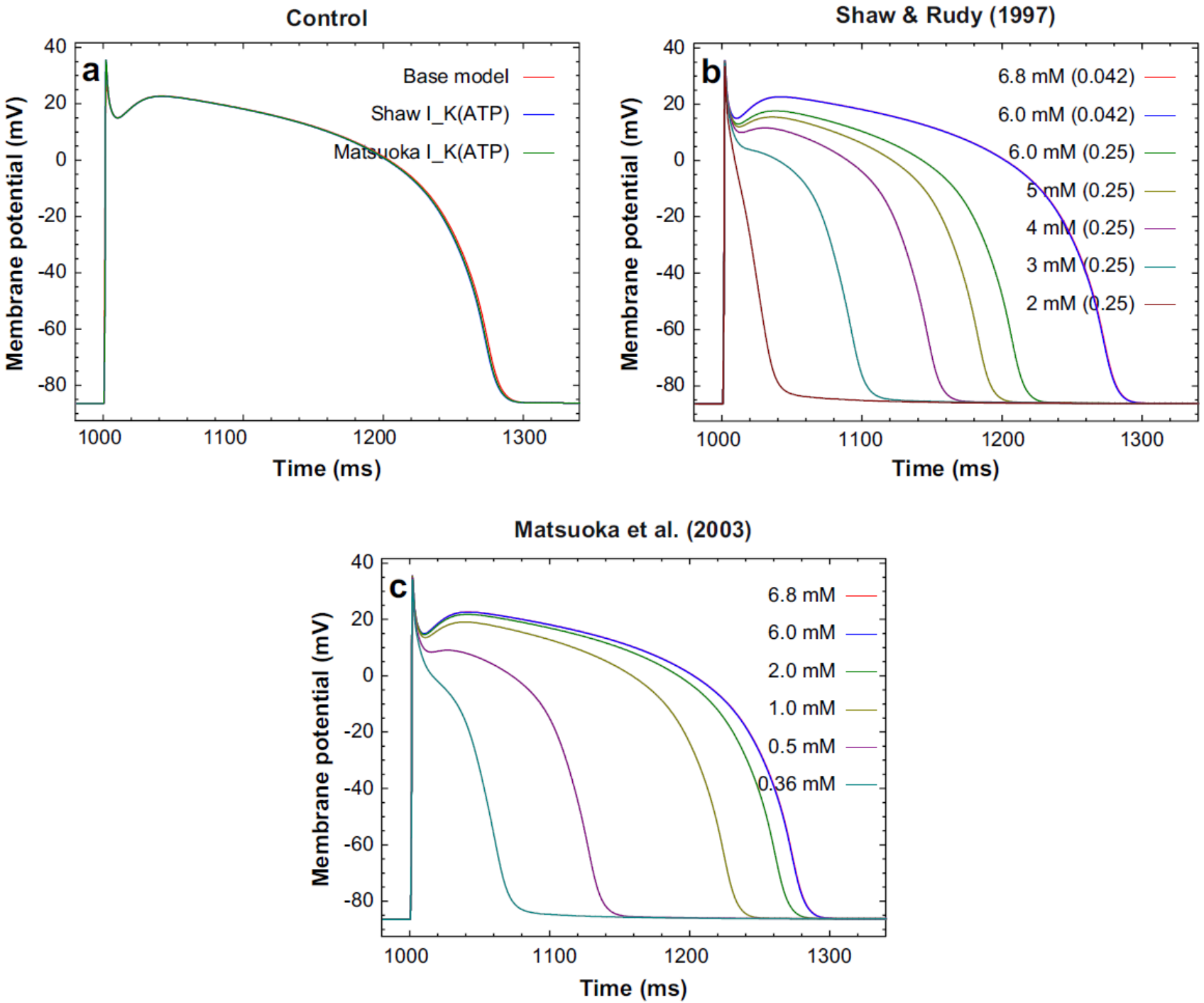


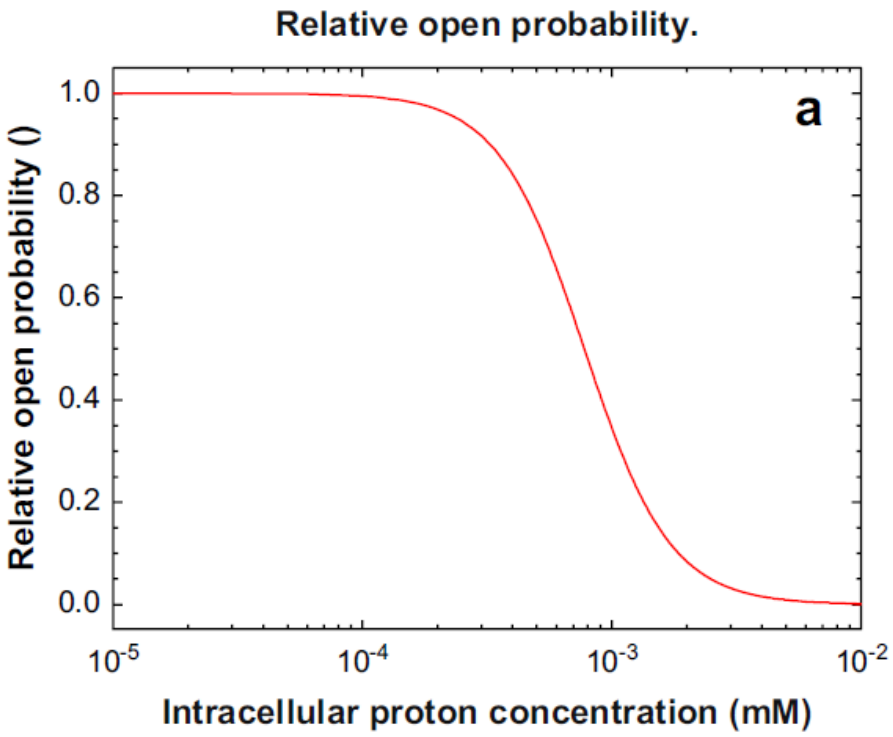
Fig. 2. An example cellular electrophysiology model which includes the dynamics of sodium, calcium, and potassium ions. In this model the standard Nernst Equation

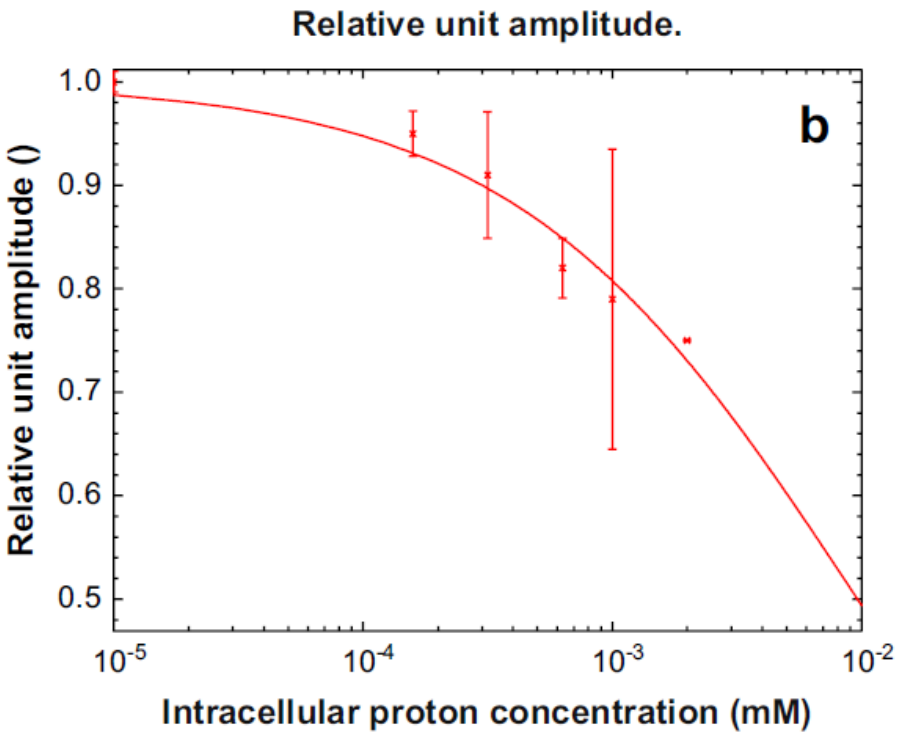




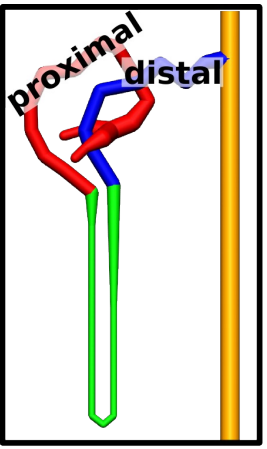
se TNNP model as described by ten Tusscher et al. (2004). See the key on the right for the definition of the symbols used


Control
a
Base model
Shaw I_K(ATP)
Matsuoka I_K(ATP)
Membrane potential (mV)
Time (ms)
Shaw & Rudy (1997)
b
6.8 mM (0.042)
6.0 mM (0.042)
6.0 mM (0.25)
5 mM (0.25)
4 mM (0.25)
3 mM (0.25)
2 mM (0.25)
Membrane potential (mV)
Time (ms)
Matsuoka et al. (2003)
c
6.8 mM
6.0 mM
2.0 mM
1.0 mM
0.5 mM
0.36 mM
Membrane potential (mV)
Time (ms)





The effects of changing pH$_i$ on the inward rectifier K^+ current I_{K1}. Experimental data from Ito et al. (1992): (b) also illustrates the annotation of simulatio



finite element nephron model

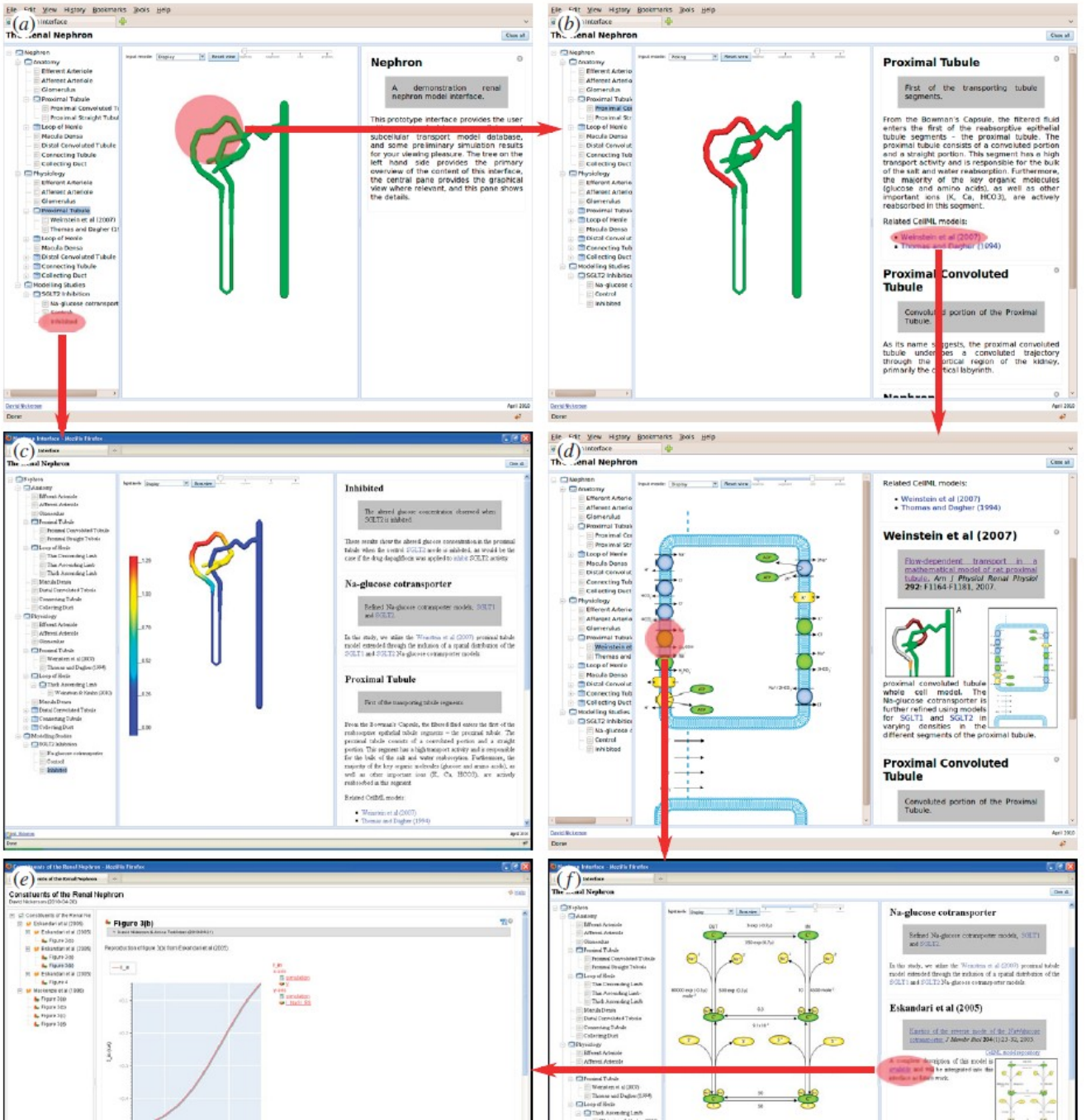
proximal

distal

proximal cell model

Na-glucose
transporter model

distal cell model


(a)
Nephron
A demonstration renal nephron model interface.
This prototype interface provides the user subcellular transport model database, and some preliminary simulation results for your viewing pleasure. The tree on the left hand side provides the primary overview of the content of this interface, the central pane provides the graphical view where relevant, and this pane shows the details.
(b)
Proximal Tubule
First of the transporting tubule segments.
From the Bowman's Capsule, the filtered fluid enters the first of the reabsorptive epithelial tubule segments – the proximal tubule. The proximal tubule consists of a convoluted portion and a straight portion. This segment has a high transport activity and is responsible for the bulk of the salt and water reabsorption. Furthermore, the majority of the key organic molecules (glucose and amino acids), as well as other important ions (K, Ca, HCO3), are actively reabsorbed in this segment.
Related CellML models:
Weinstein et al (2007)
Thomas and Dagher (1994)
Proximal Convoluted Tubule
Convoluted portion of the Proximal Tubule.
(c)
Inhibited
Na-glucose cotransporter
Proximal Tubule
(d)
Related CellML models:
Weinstein et al (2007)
Thomas and Dagher (1994)
Weinstein et al (2007)
Proximal Convoluted Tubule
Convoluted portion of the Proximal Tubule.
(e)
Constituents of the Renal Nephron
Figure 3(b)
(f)
Na-glucose cotransporter
Eskandari et al (2005)

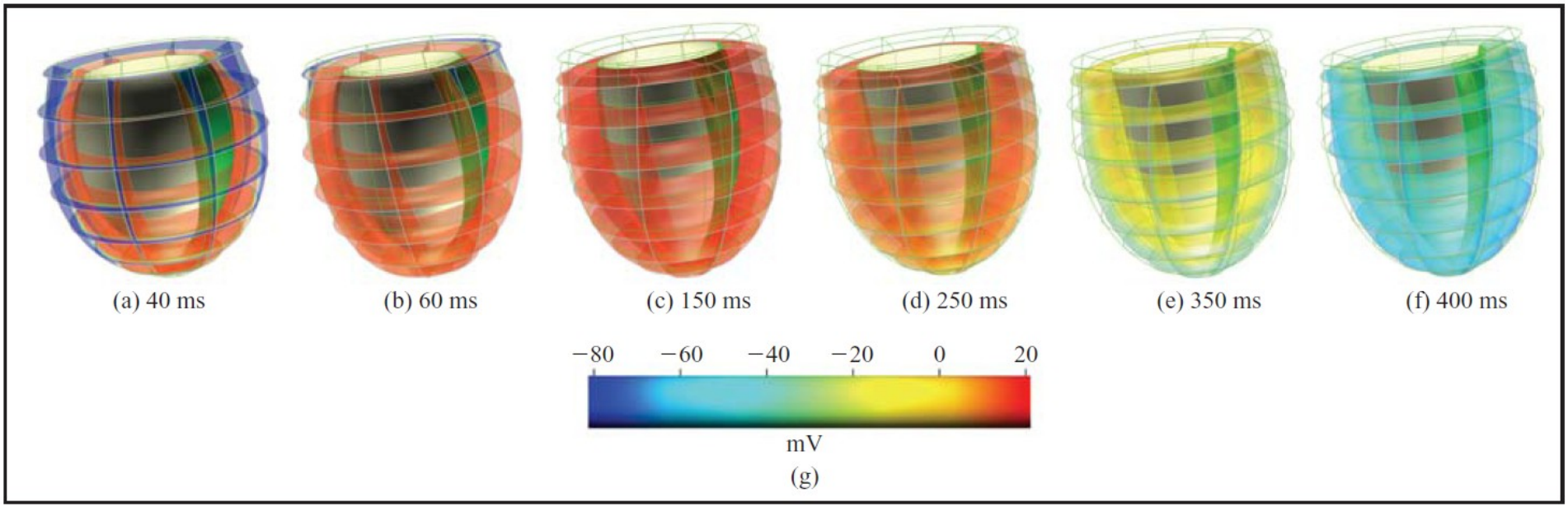
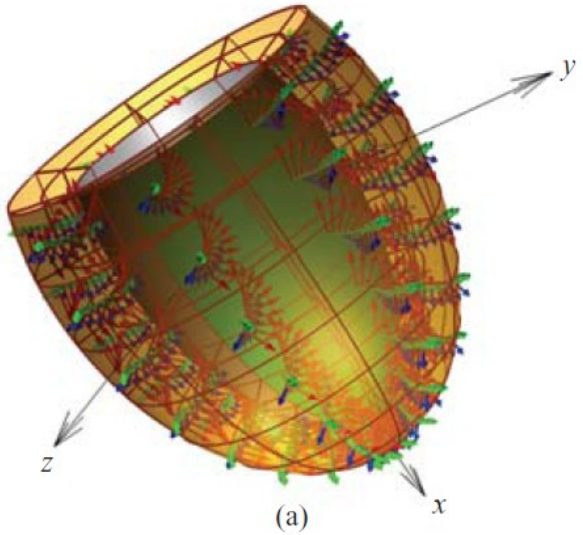
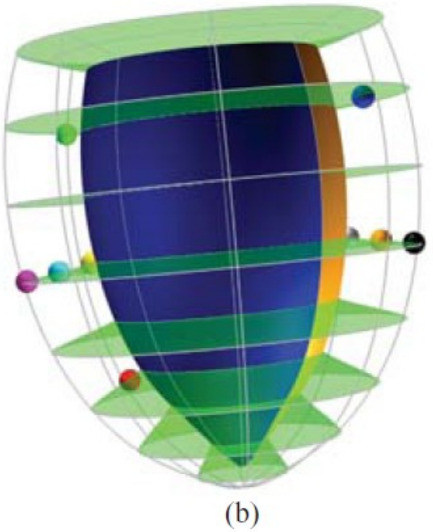


Figure 10

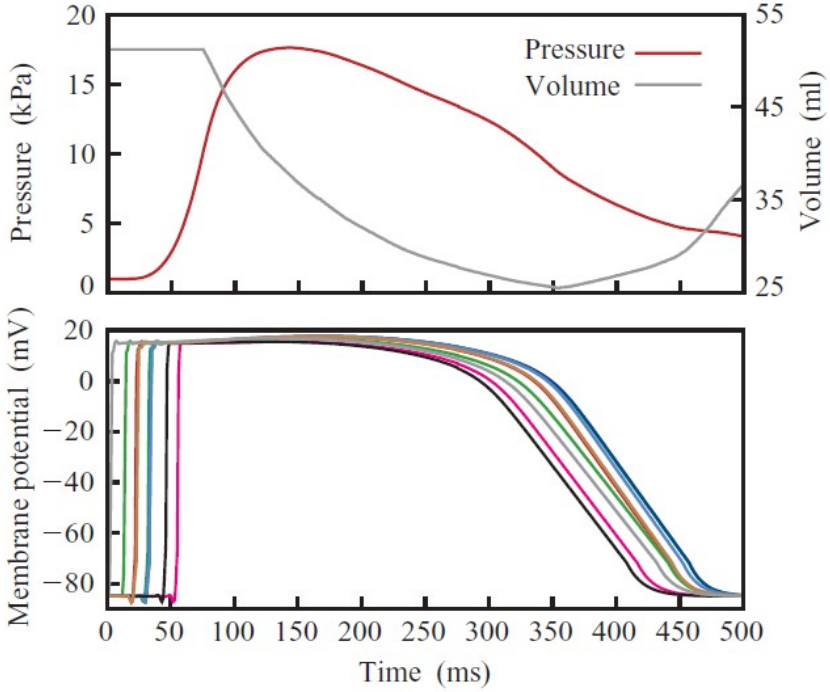
Simulation results of the active contraction and ejection of blood using the rotationally symmetric left-ventricular geometry shown in Figure 9(a). The green lines show the undeformed geometry and the colored surfaces indicate membrane electrical potential, using the color scale in (g).

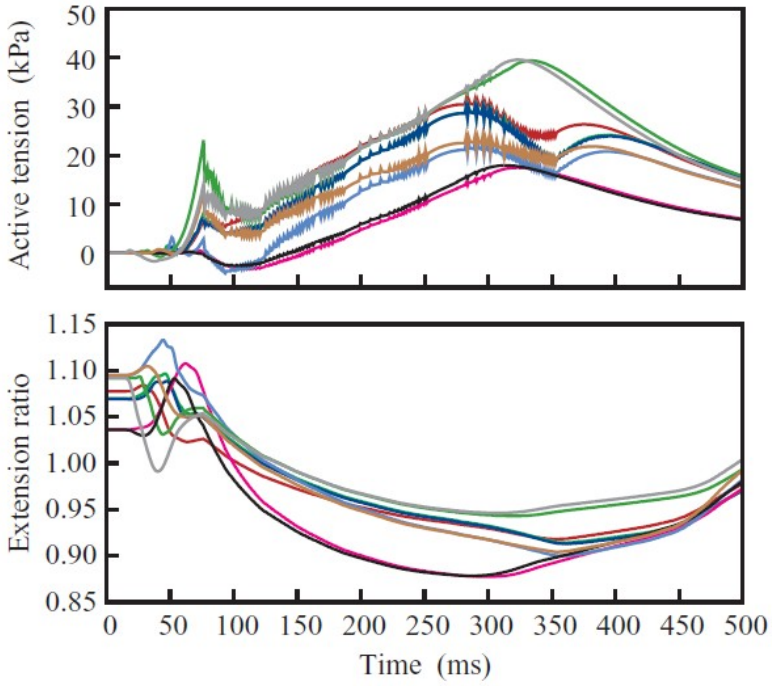

y
z
x

(a)



(b)


Pressure
Volume
Pressure (kPa)
Volume (ml)
Membrane potential (mV)
Time (ms)


Active tension (kPa)
Extension ratio
Time (ms)

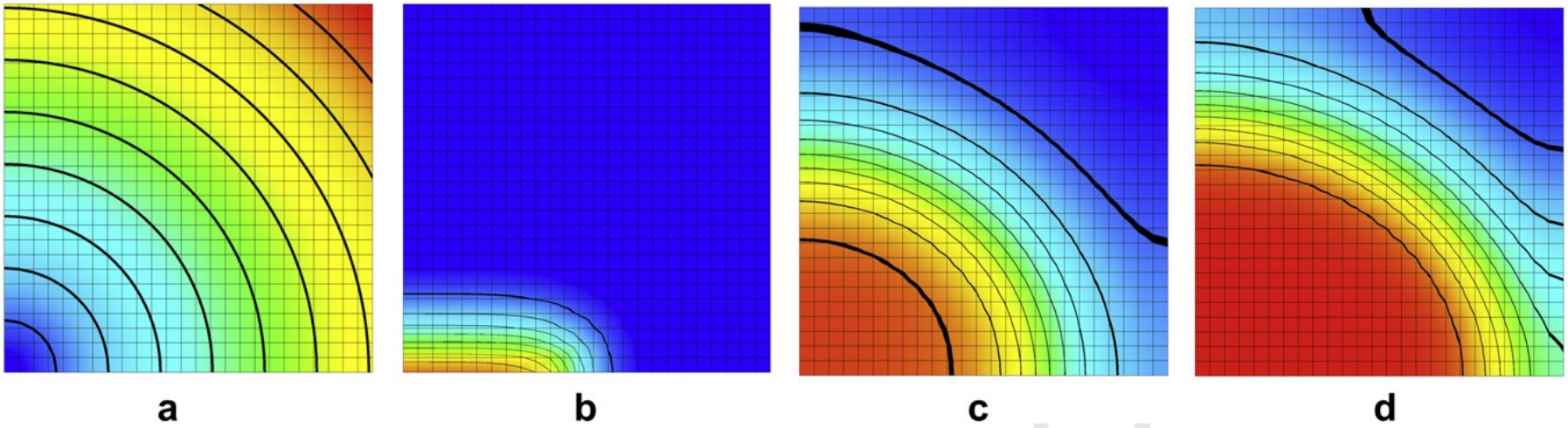


Fig. 7. (a) A plot of the fast sodium channel conductance, g_{Na} throughout the monodomain solution domain. The conductance varies in a radial fashion from 100% of its normal value of 3.855×10^{-5} mS mm^{-2} (blue) to 300% of its normal value (red). (b) A plot of the transmembrane voltage immediately after the stimulation pulse has finished. The following two

Beyond CellML 1.1

- A broad specification of “fundamental CellML concepts”
  - MathML plus the core CellML elements and attributes
- Secondary specifications narrow the scope of the fundamental concepts
  - Typically to enable computational simulation of a specific class of mathematical model(s).
  - For example: index-1 DAE models which do not invlove simultaneous equations and only use a restricted subset of MathML 2.0 elements.

CellML 1.2

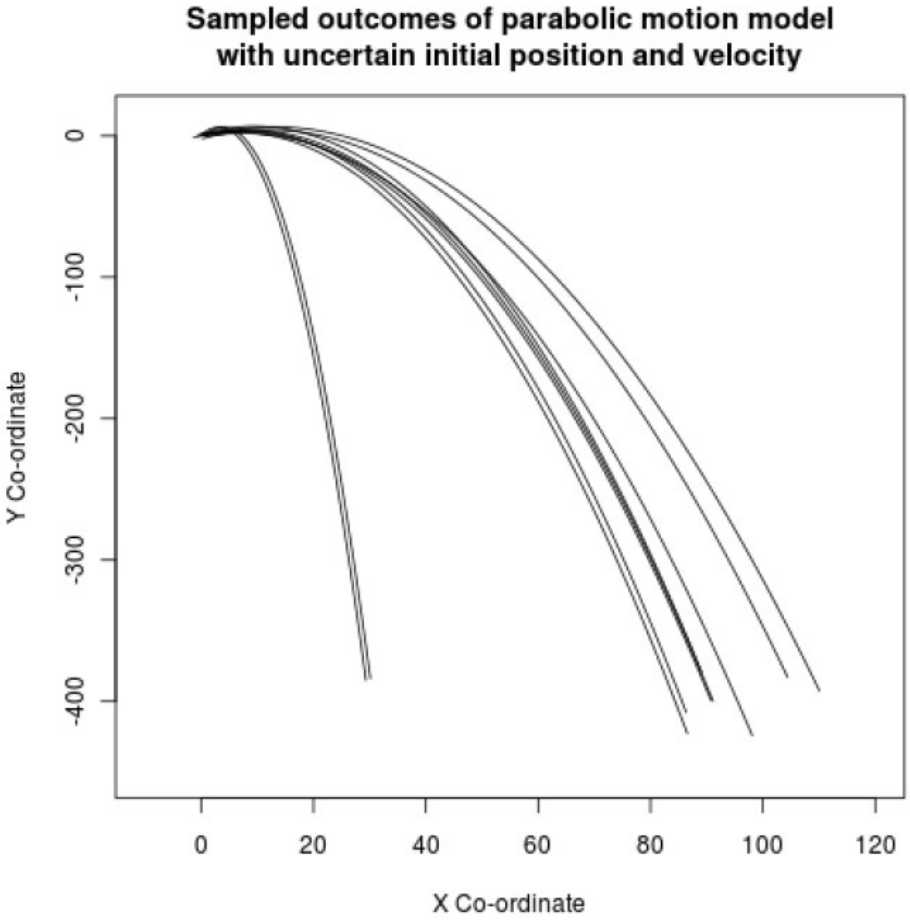
- Released as the fundamental concepts specification plus a collection of secondary specifications.
- Scope similar to what is currently supported by the CellML Integration Service with some notable additions:
  - Variable typing
  - Reset rules
  - Delays
  - Stochastic variation
  - Minor corrections and updates.

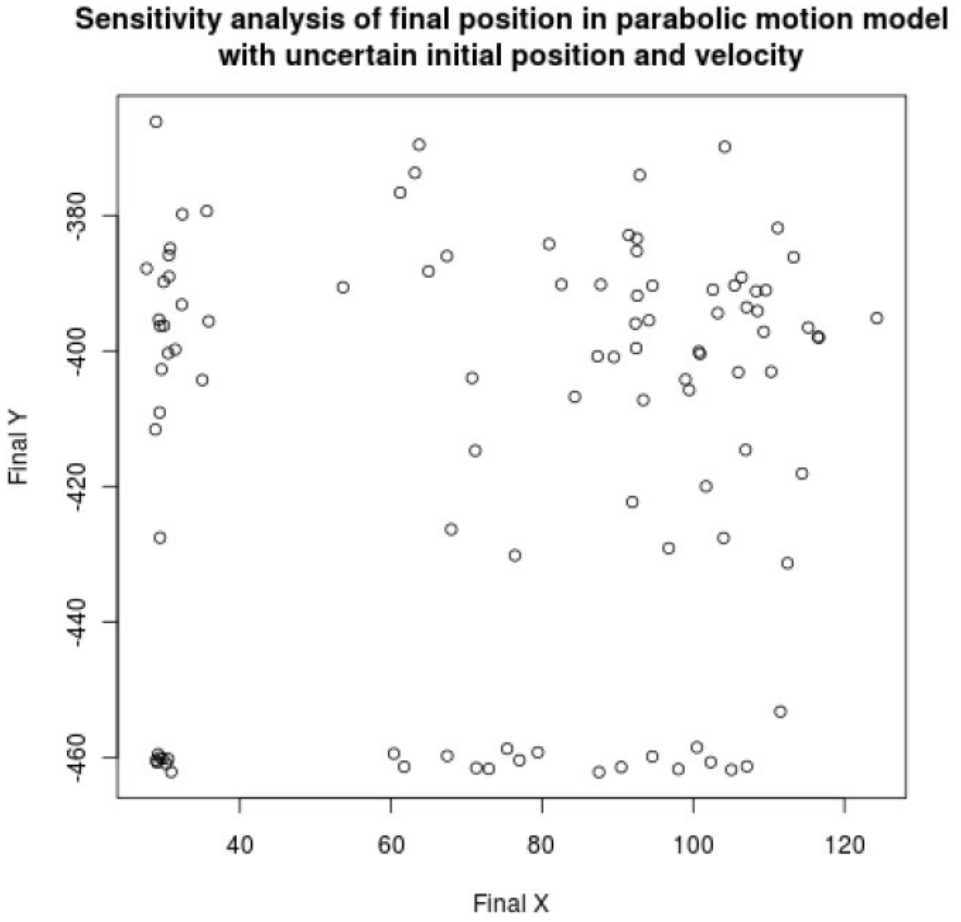
Variable typing

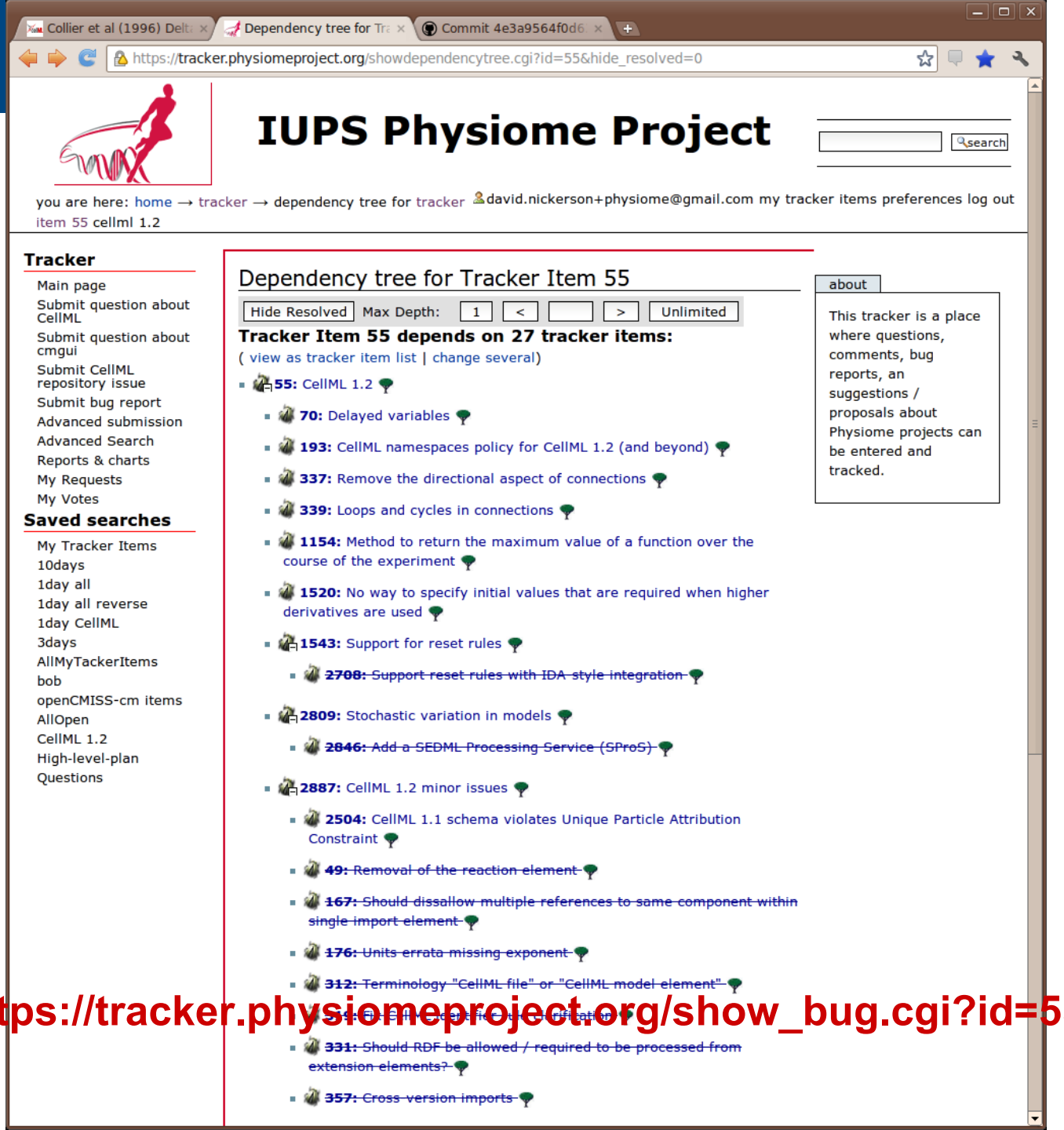
- Fundamental concepts allows arbitrary types.
  - Type attribute added to variables, value is a URI which defines the type.
- Secondary specification restricts this to real and boolean types only.
- Interaction of types with units
  - Must be defined if type real, must be absent when type boolean.
- Future relaxation to allow vectors, matrices, etc., without needing to change fundamental concepts specification.

Representing Parameter Uncertainty in CellML

- Often, parameters will be determined experimentally.
- Experimental error means that there is inherent uncertainty in experimentally determined parameters.
- Some parameters vary between individuals in a population; even if the mean value for a population is known, the value for an individual might not be.
- Sometimes, only a sensible range for parameter values is known; the exact value is unknown. In this case, a modeller might want to say a parameter is uncertain and equally likely to take any value in the range.
- Proposal from Andrew Miller.


Sampled outcomes of parabolic motion model
with uncertain initial position and velocity
Y Co-ordinate
0
-100
-200
-300
-400
0
20
40
60
80
100
120
X Co-ordinate


Sensitivity analysis of final position in parabolic motion model
with uncertain initial position and velocity
Final Y
-380
-400
-420
-440
-460
40
60
80
100
120
Final X



https://tracker.physiomeproject.org/show_bug.cgi?id=55

Electing a CellML Editorial Board

- Recent call for nominees resulted in 10 nominees standing for election to the CellML Editorial Board.
- Spanning the globe from New Zealand to the UK.
- Soon to be a call for votes!
- http://www.cellml.org/community/boardnominees
- http://lists.cellml.org/mailman/listinfo/cellml-discussion

The Physiome Model Repository

- http://models.physiomeproject.org
- A repository for models as part of the Physiome, VPH, VPR projects and pretty much any one else.
- CellML specific models available via: http://models.cellml.org
- FieldML specific models available via: http://models.fieldml.org

PMR2

- Workspace – data agnostic mercurial repository
- Changeset – a representation of a single revision of the content of a workspace
- Exposure – a permanent link to a specific changeset with data rendered for the web
- Exposure plug-ins – an extensible framework for rendering workspace content for web presentation
- Plone CMS – workflow manager; user access controls; web presentation; etc.

Embedded Workspaces

- Intended to manage the separation of modules which are integrated to create a model
- Facilitate the sharing and reuse of model components independently from the source model
- Enables the development of the modules to proceed independently, thus the version of the workspaces embedded is also tracked
- Allows authors to make use of relative URIs when linking data resources providing a file system agnostic method to describe complex module relationships in a portable manner

Embedded Workspaces

- Workspaces can be embedded at a specific revision or set to track the most recent revision of the source workspace
- Changes made to the source workspace will not affect the embedding workspace until the author explicitly chooses to update the embedded workspace
- Provides the author with the opportunity to review the changesets and make an informed decision regarding alterations to embedded revisions

Collier et al (1996) Delt | Tracker Item 2898 – St | Control of the pacemak

50.18.64.32/e/70/

You are here: Home › Exposures › Collier et al (1996) Delta-Notch model

David Nickerson

contents | view | sharing

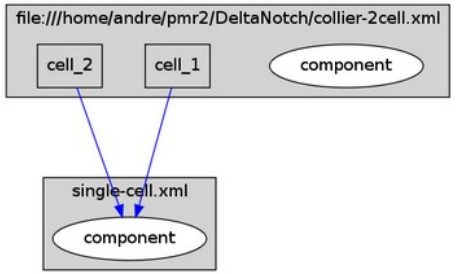
actions | display | add new... | state: pending review

Info Item state changed.

Collier et al (1996) Delta-Notch model

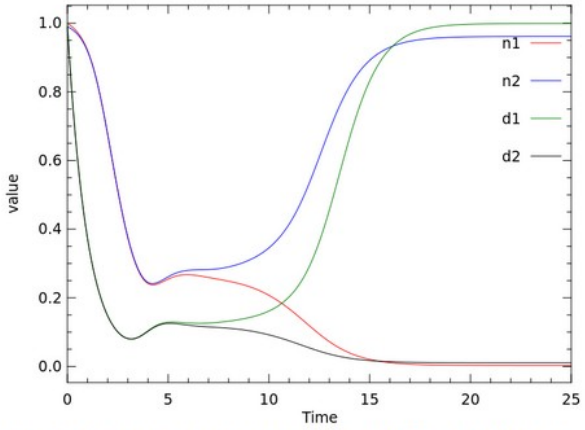
by David Nickerson — last modified Sep 01, 2011 08:40 AM — History

An initial attempt to demonstrate one use of CellML with multicellular models using the Delta-Notch model of Collier et al (1996) as an example. In the current state of this workspace, I show the two cell variant of the Collier model as described in Figure 3 of the Collier article. In this encoding of the model, we use CellML 1.1 to separate the single cell dynamics from the population model. In the single cell model I have encoded the two ODEs which make up the dynamics (Equation 2 in the Collier paper) and left the initial conditions and parameters undefined. The population model (collier-2cell.xml) uses the CellML import feature to *"instantiate"* two cells, as shown in the diagram below:



Model hierarchy (generated using CellML2Dot) of the two cell variant of the Collier et al Delta-Notch signalling model. The two single cell models are then connected together in the two cell variant of the Collier model. The parent model defines the parameters to be used in both instances of the single cell model along with the different initial conditions for each cell. I define a neighbourhood average for delta for each of the cells, which for the two cell variant simply consists of the delta value from the other cell and the zero boundary condition. The connections between the single cell models can be seen in the figure below:

Model connections (generated using CellML2Dot) of the two cell variant of the Collier et al Delta-Notch signalling model. The common model parameters can be seen as well as the initial conditions for the individual cells. Simulations of the two cell variant of the Collier model can be performed to demonstrate that the model is correctly encoded. A reproduction of the results from Figure 3 of the Collier et al (1996) article can be seen below, using the two cell variant as encoded in CellML.



Simulation results (generated using CellMLSimulator) of the two cell variant of the Collier Delta-Notch signalling model. These results correspond to those shown in Figure 3 of the Collier et al (1996) article.

Model Curation

Curation Status:

Source

Derived from workspace Delta-Notch Intercellular Signalling at changeset 0fee83ae6e42.

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single-cell.xml

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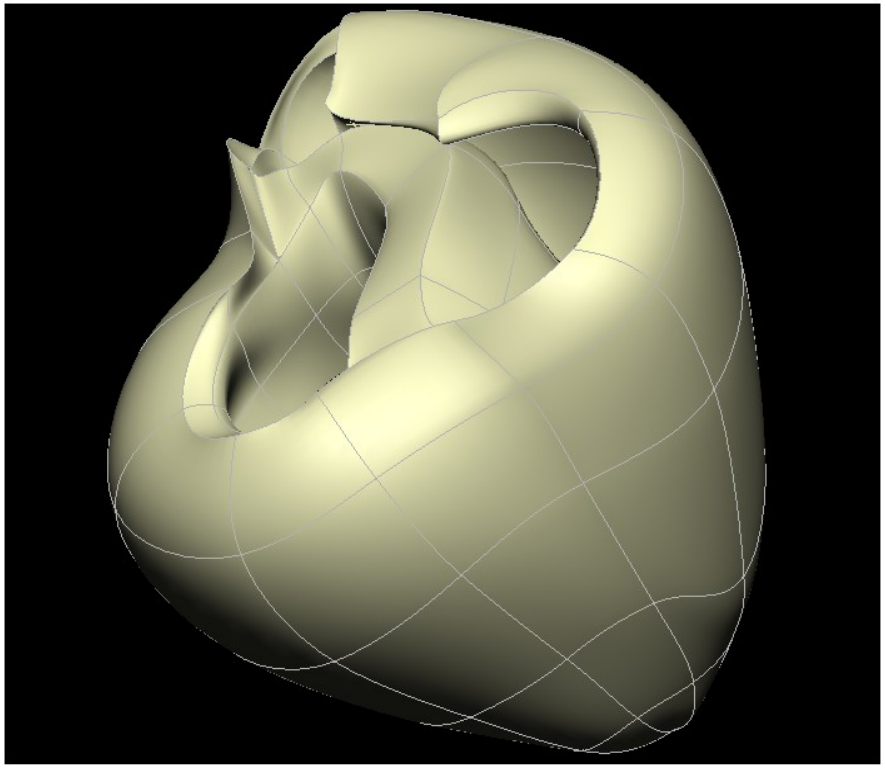

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Views available

FieldML Metadata

Source View

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50.18.64.32/workspace/a1/cellml_simulator/fdb3693c38ff7d21160566a685f6ed31d4b115fc/tutorial/csim-reference-des

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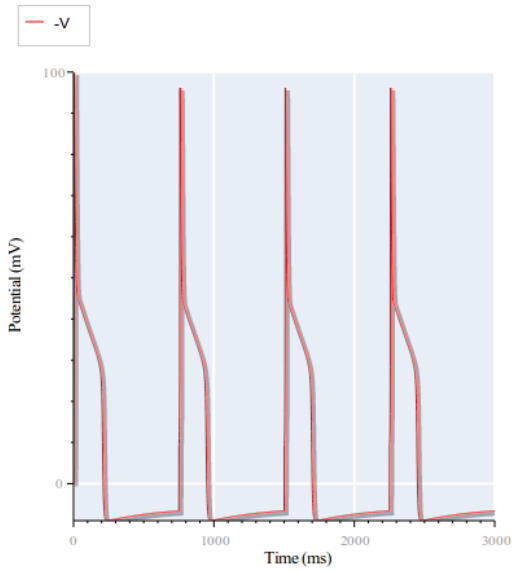
A series of cardiac cellular electrophysiological modelling case studies in the use of CellML and associated metadata.

David Nickerson (2009-07-05)

Help

- A series of cardiac cellular ele
  - Modifying Hodgkin & Huxle
    - HH Model Validation
      - Sodium Channel Ki
        - INa Gating Rate
        - INa Steady State
      - Potassium Channel
      - Voltage Clamp Vali
      - Action Potential Val
    - Modification toward No
      - Action Potentials
      - Membrane Currents
      - Gating Variables
      - Gating Variables
  - TNNP stimuli
    - Periodic
    - S1-S2 restitution
      - Untitled metadata

Action Potentials



-V
x-axis
simulation
time
y-axis
simulation
minus_V

HH Model Validation

+ Last modified: 2009-07-05, David Nickerson (Created: 2009-07-05, David Nickerson)

This is the parent task for the simulation experiments used to validate the base Hodgkin & Huxley model implemented for this tutorial. The model has been previously implemented and is available online from the Computational Bioengineering Laboratory at the National University of Singapore.

The original source of these models is http://www.bioeng.nus.edu.sg/compbiolab/p3/. All the graphs illustrated here are simulated directly from the data described on the NUS server.

Tasks:

- Sodium Channel Kinetics Validation
- Potassium Channel Kinetics Validation
- Voltage Clamp Validation

Generated by: CellMLSimulator (version: CellMLSimulator 0.3.0-devel-json - revision 211:217 - Thu Jun 11 11:43:39 NZST 2009) at Tue Jul 07 2009 14:42:38 GMT+0200 (CEST)

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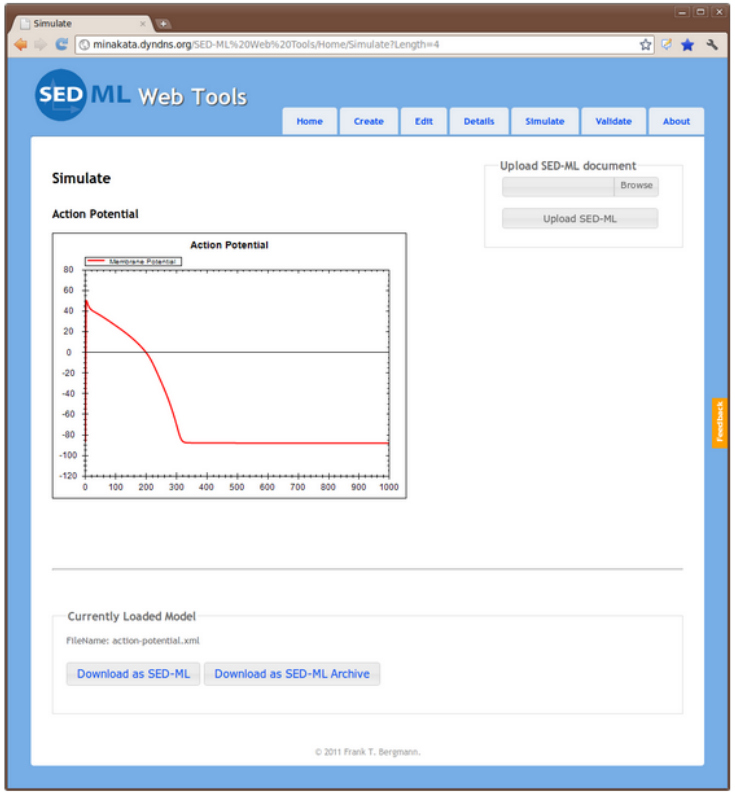
The ORd human ventricular action potential model

This workspace houses a CellML 1.0 encoding of the 2011 O'Hara, Virág, Varró, & Rudy 2011 human cardiac ventricular action potential model (ORd). The original article is available at: http://www.ncbi.nlm.nih.gov/pubmed/21637795. This model was encoded based on the Matlab version of the code available from: http://rudylab.wustl.edu/research/cell/.

The CellML 1.0 encoding of the ORd model was contributed by Steven Niederer. While the units in the CellML encoding are not yet perfect, it is a match for the Matlab code and matches the simulation output for a single beat perfectly. The figure below shows the output of the simulation experiment action-potential.xml encoded in SED-ML using the original version of the model from Steve. This output is generated by running the simulation experiment using the SED-ML Web Tools.



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Curation Status:

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Derived from workspace An encoding of the human ORd model by Steve Neiderer at changeset a96ef0c61614.

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Navigation

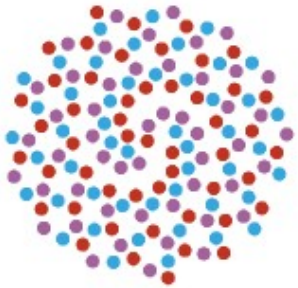
- Ohara_Rudy_2011.cellml
- action-potential.xml

FieldML: a meta-language for field interchange

- A standard format for interchanging field descriptions and data between different software.
- Able to describe fields of arbitrary complexity.
- Efficient.
- Extensible.
- Reusable model components.
- http://precedings.nature.com/documents/5901/version/1

Acknowledgements

- Poul Nielsen
- Peter Hunter
- Tommy Yu
- Andrew Miller
- Randall Britten
- Alan Garny
- Mike Cooling
- The CellML community
- Auckland Bioengineering Institute



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