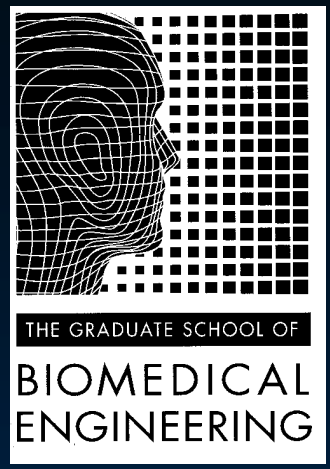

Excitable Cell and Tissue Modelling using CellML/FML

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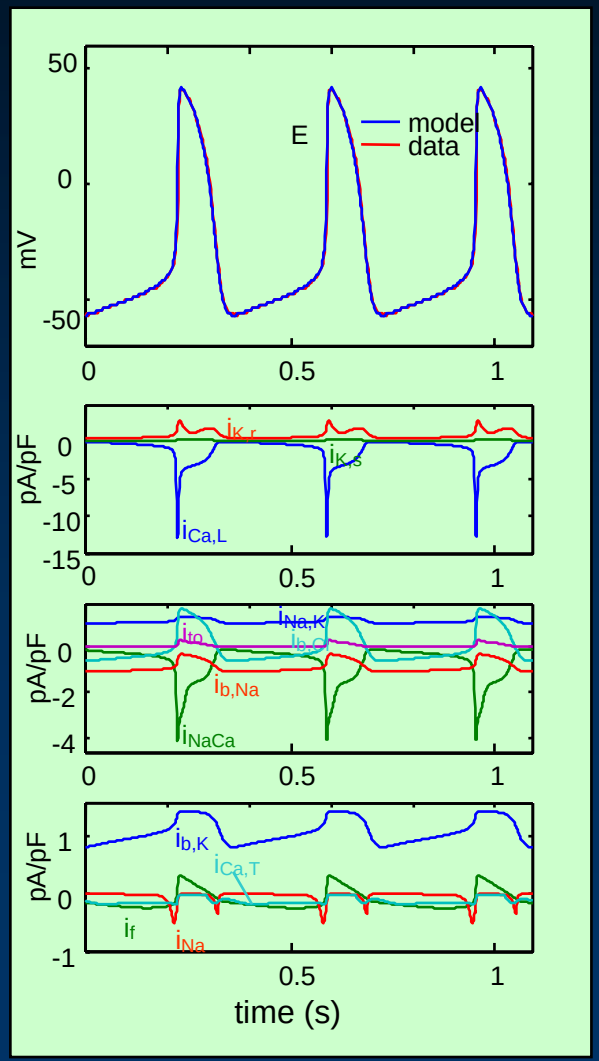
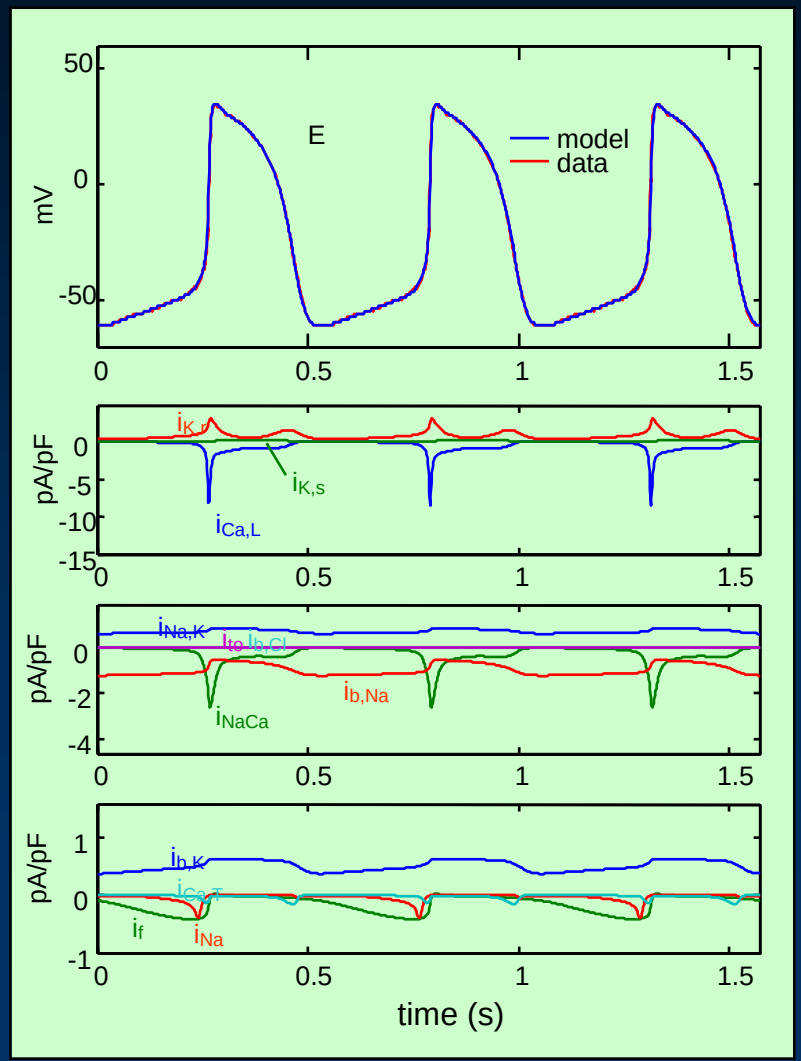
David Chang, & Nigel H Lovell

Graduate School of Biomedical Engineering, UNSW

Parameter Optimisation of Excitable Cell Models

Large-scale non-linear least-squares fitting:

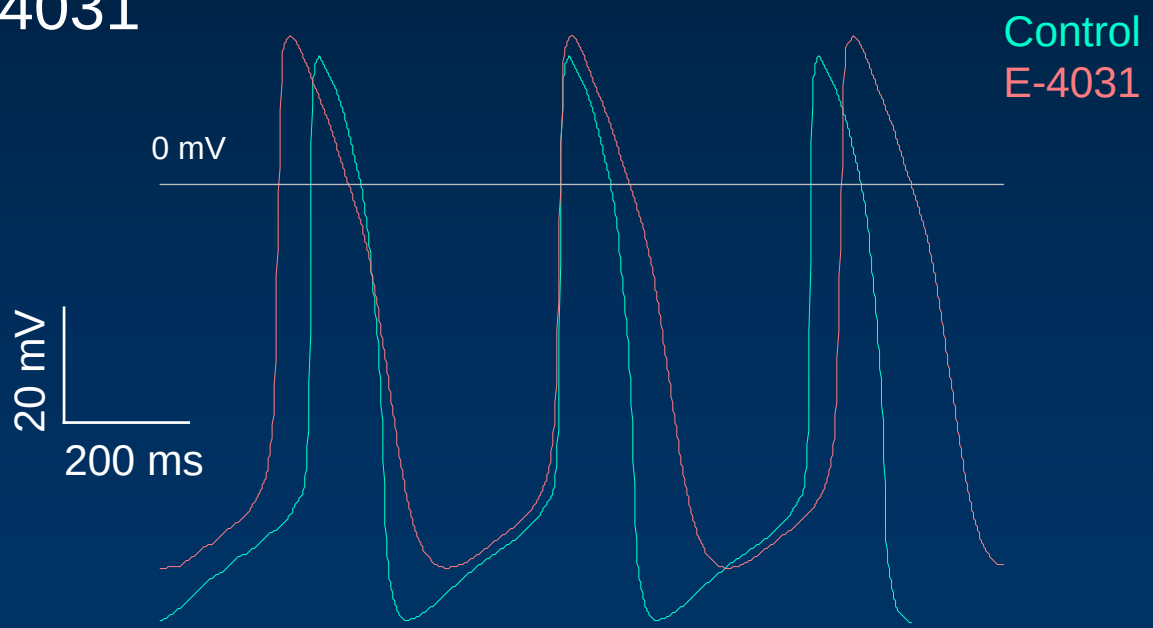




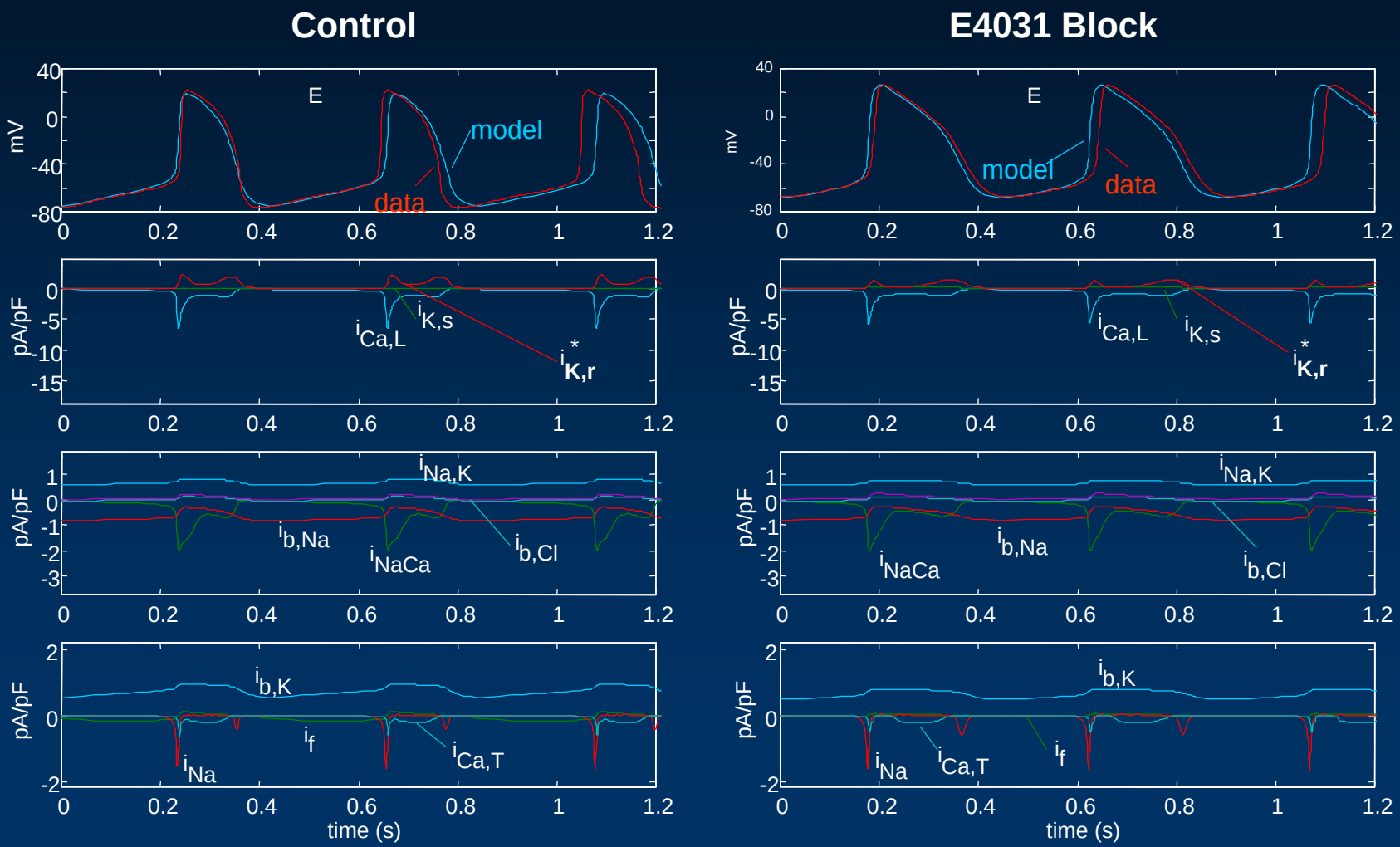
Parameter optimisation using multiple data sets

Effect of E-4031 on Peripheral SAN Myocytes

0.1 μM E-4031



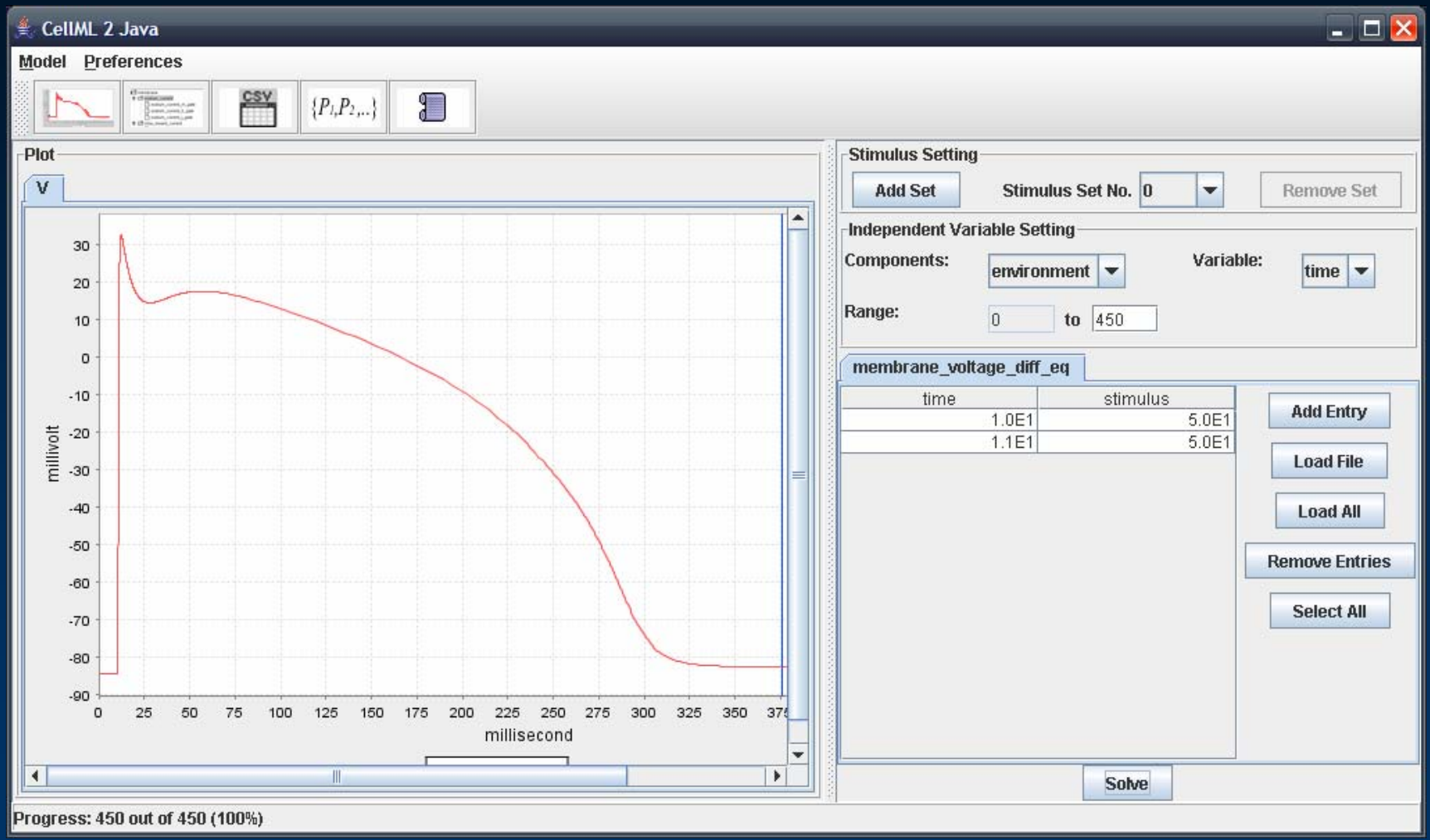
E-4031 Fit


Control
E4031 Block
E
model
data
mV
pA/pF
$i_{Ca,L}$
$i_{K,s}$
$i^*_{K,r}$
$i_{Na,K}$
$i_{b,Na}$
i_{NaCa}
$i_{b,Cl}$
$i_{b,K}$
i_{Na}
i_f
$i_{Ca,T}$
time (s)

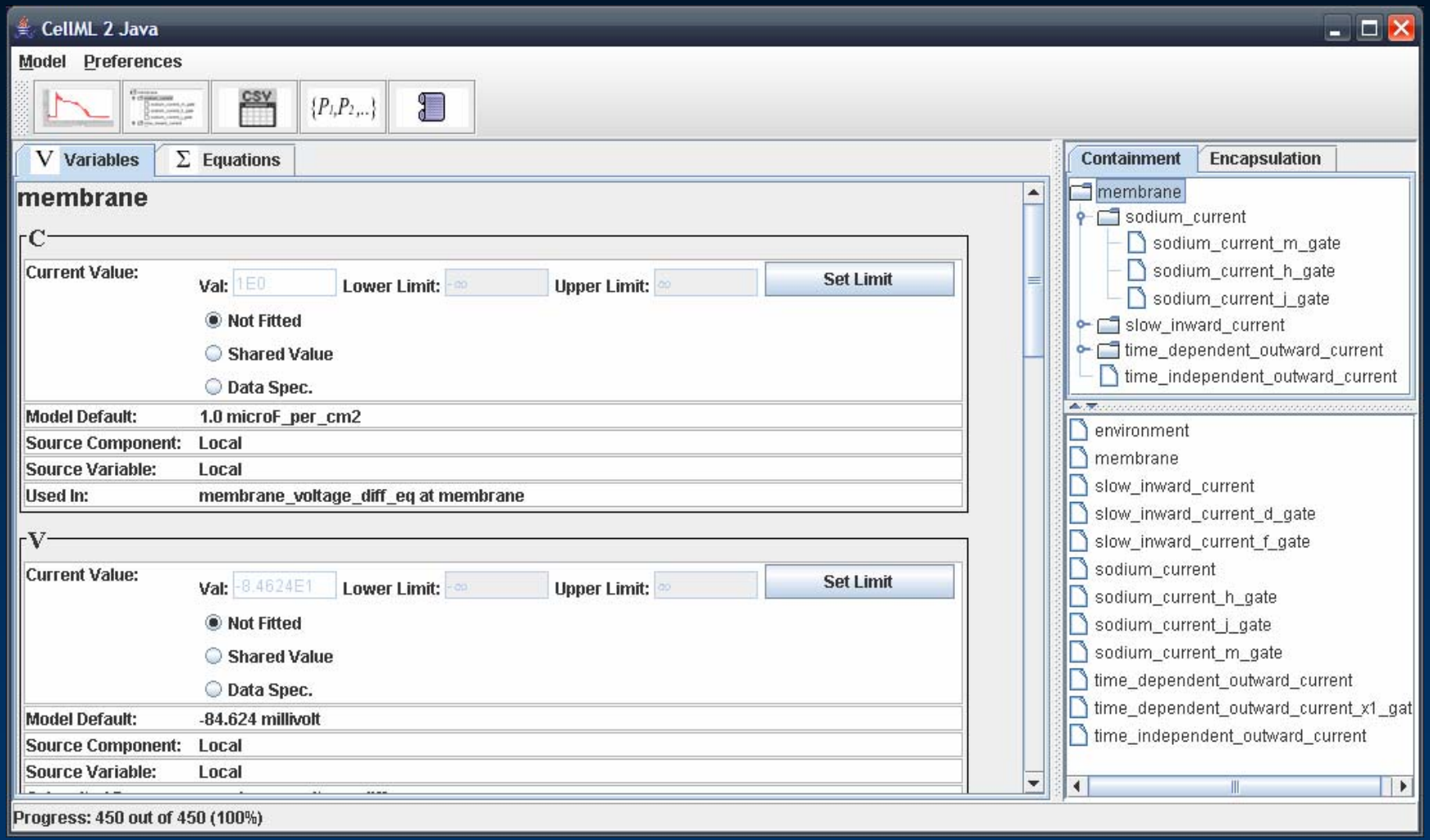
CellML for Parameter Optimisation

- **Large repository of excitable cell models**
  - **Valid, bug free**
- **Models easily accessible**
- **CellML parser can be incorporated into parameter fitting software**
  - **current and future models can be optimised without model-specific re-coding of routines**

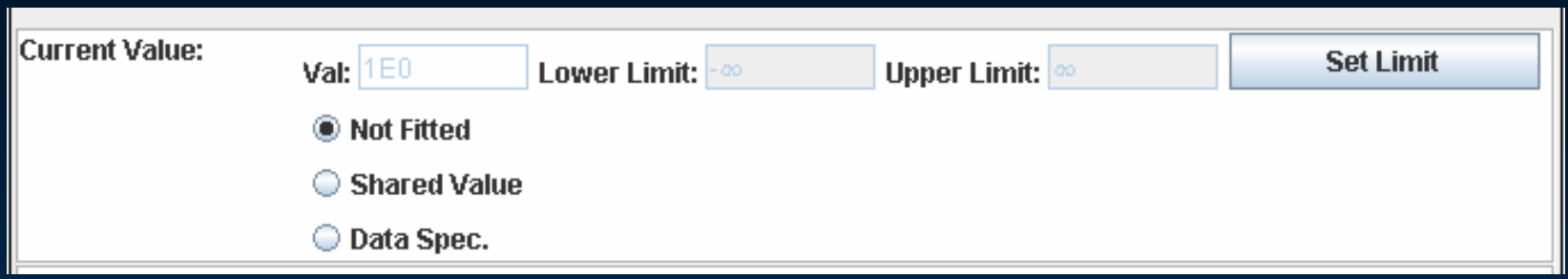
CellML Parameter Optimiser

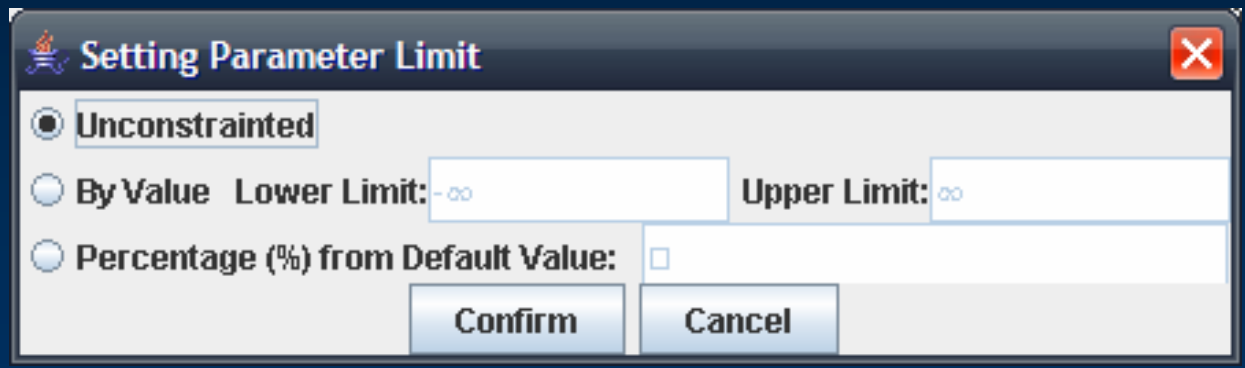


Component Viewer

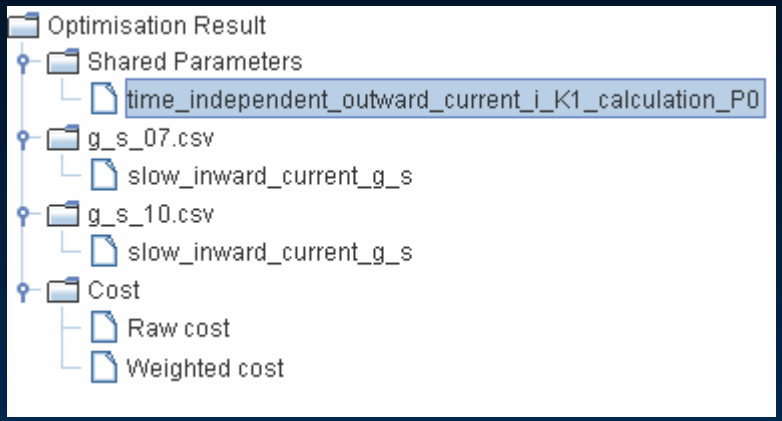


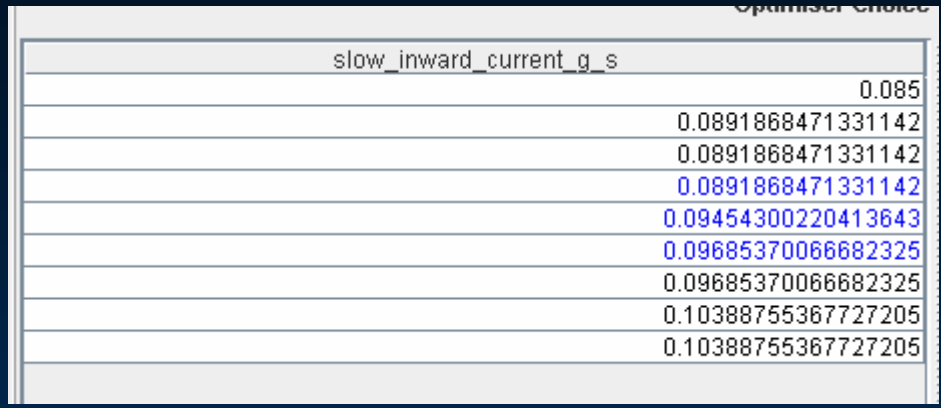
Parameter Selection

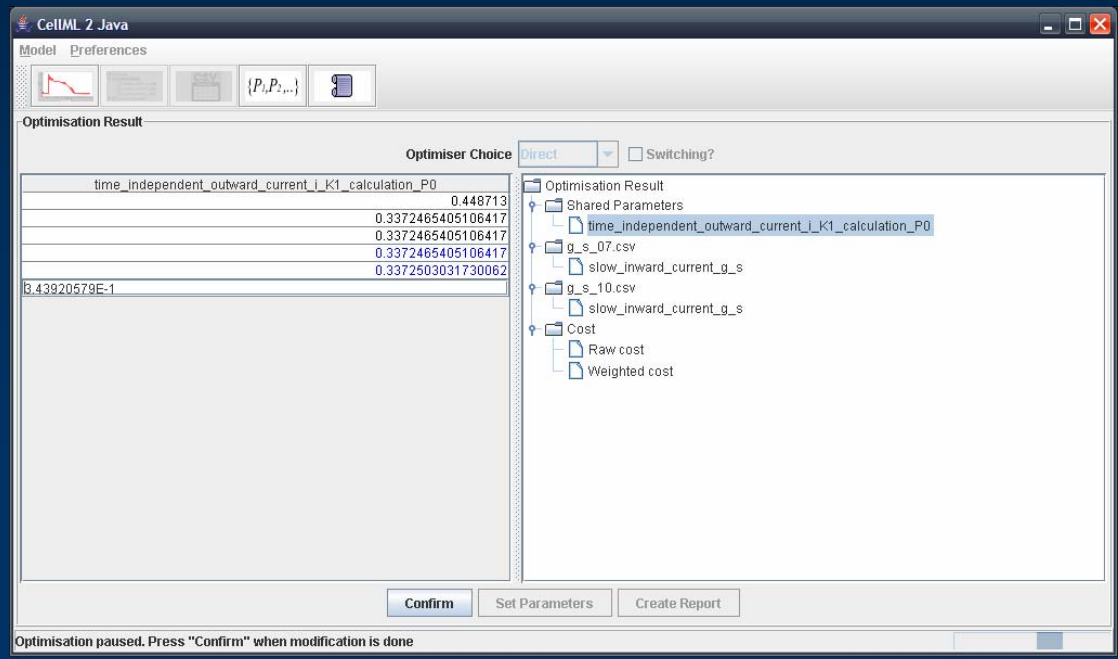




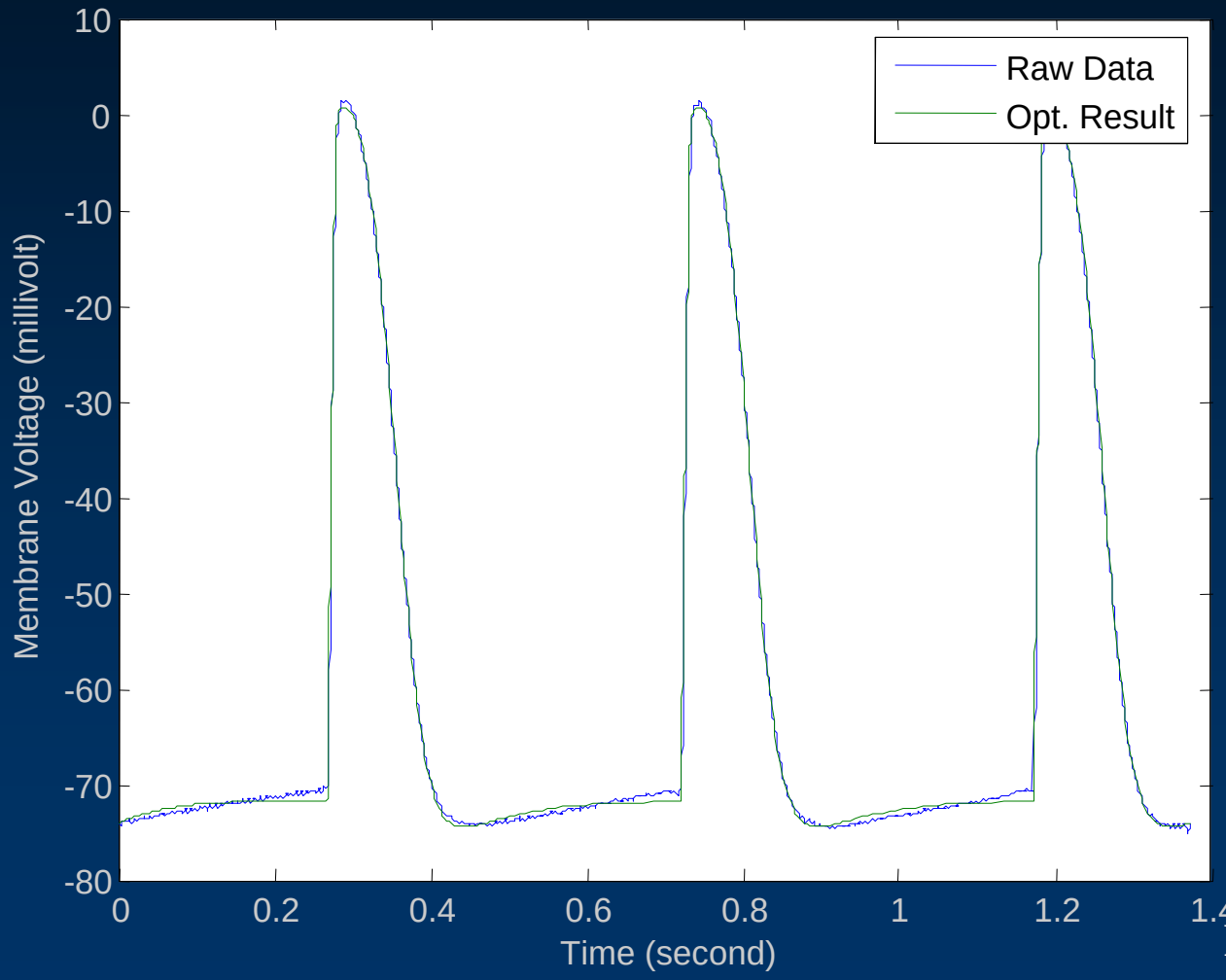
Optimisation Progress





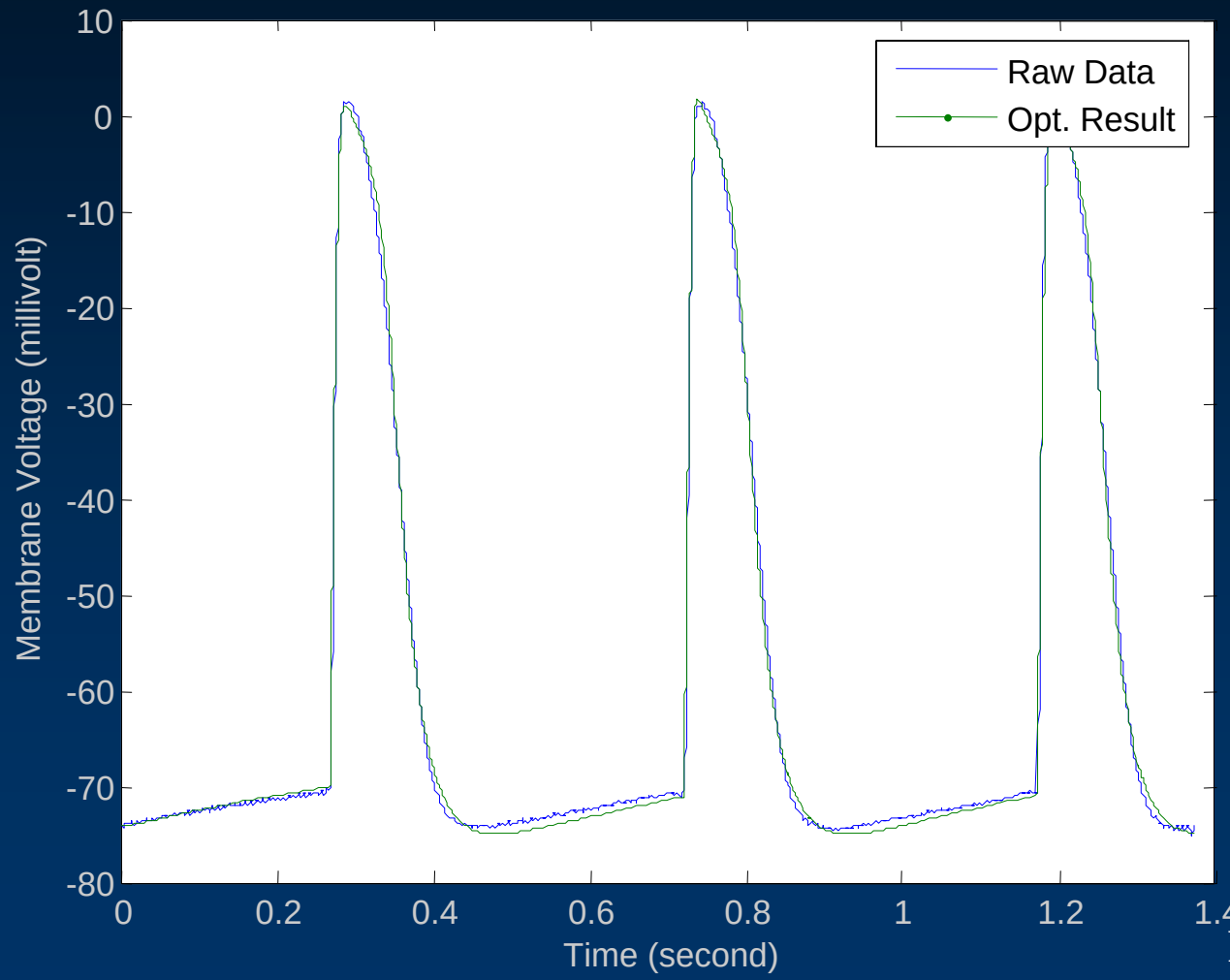


Optimisation of peripheral SAN AP using Noble (1962) Model



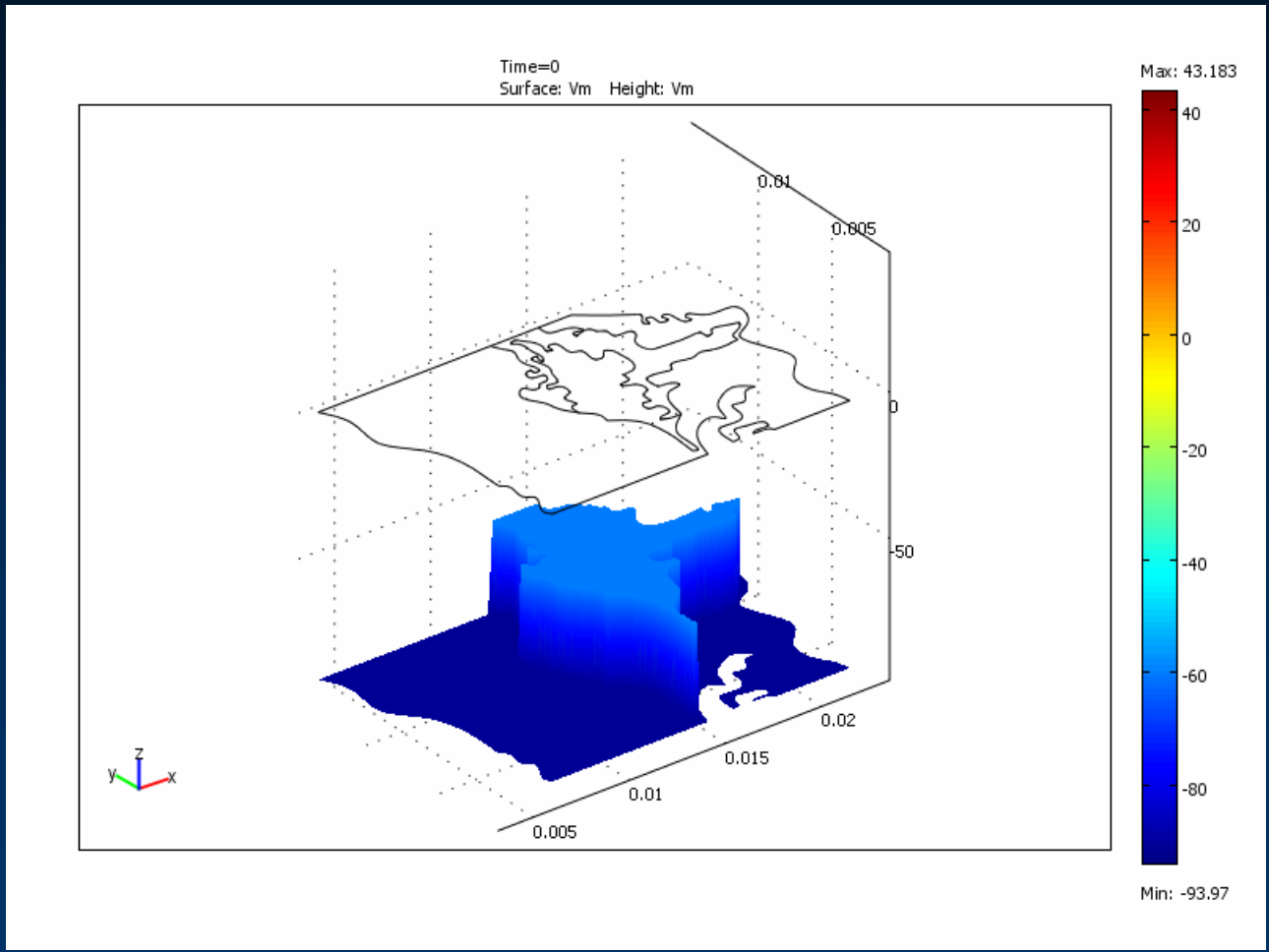
RMS = 0.78mV

Optimisation of peripheral SAN AP using Lovell *et al* (2004) Model



RMS = 1.21mV

Excitable Tissue Modelling Using FML/ModelML



MML Framework

- **FML and ModelML**
  - **FML describes Geometry/Field information**
  - **ModelML describes the relational aspects of a multi-scale biological model**
- **Share common syntax**
  - **<Import> branch**
  - **<declaration> branch**
    - **Expressions, variables, functions, data set declarations.**

FML <frame>

<frame>
<cell_list>
<dim0>
<dim1>
<dim2>
<dim3>
<b_rep>
<mesh>
<fields>
<dimension>

- **Cell Objects – Lines, PolyLine, Curves, Bezier Curves**
  - **Can Attach Attributes such as Scalar, Vector etc to create data set**

FML (geometric models)

- **B-Rep (adjacency information)**
  - **Vertex-Edge, Edge-Face**
  - **Parametric**
  - **Domain Information**
- **Mesh**
  - **1 Dim, 2 Dim, 3 Dim, cell objects reference**
  - **Neighbouring information**
  - **Domain Information**
- **Fields**
  - **Field Function, basis function mapping**
  - **Data organisation**

FML <mapping>

- **Combine/reuse FML models by using <mapping>.**
- **Operations including <scale>, <shift>, <rotate> etc**
  - **Restrictions apply**

ModelML (Overview)

- **Relational Grouping (Subdomain/Boundary/Point etc) between CellML and FML**
- **Describes General Mathematical Model under <system>**
- **Responsible for naming and accessing objects between imported models**

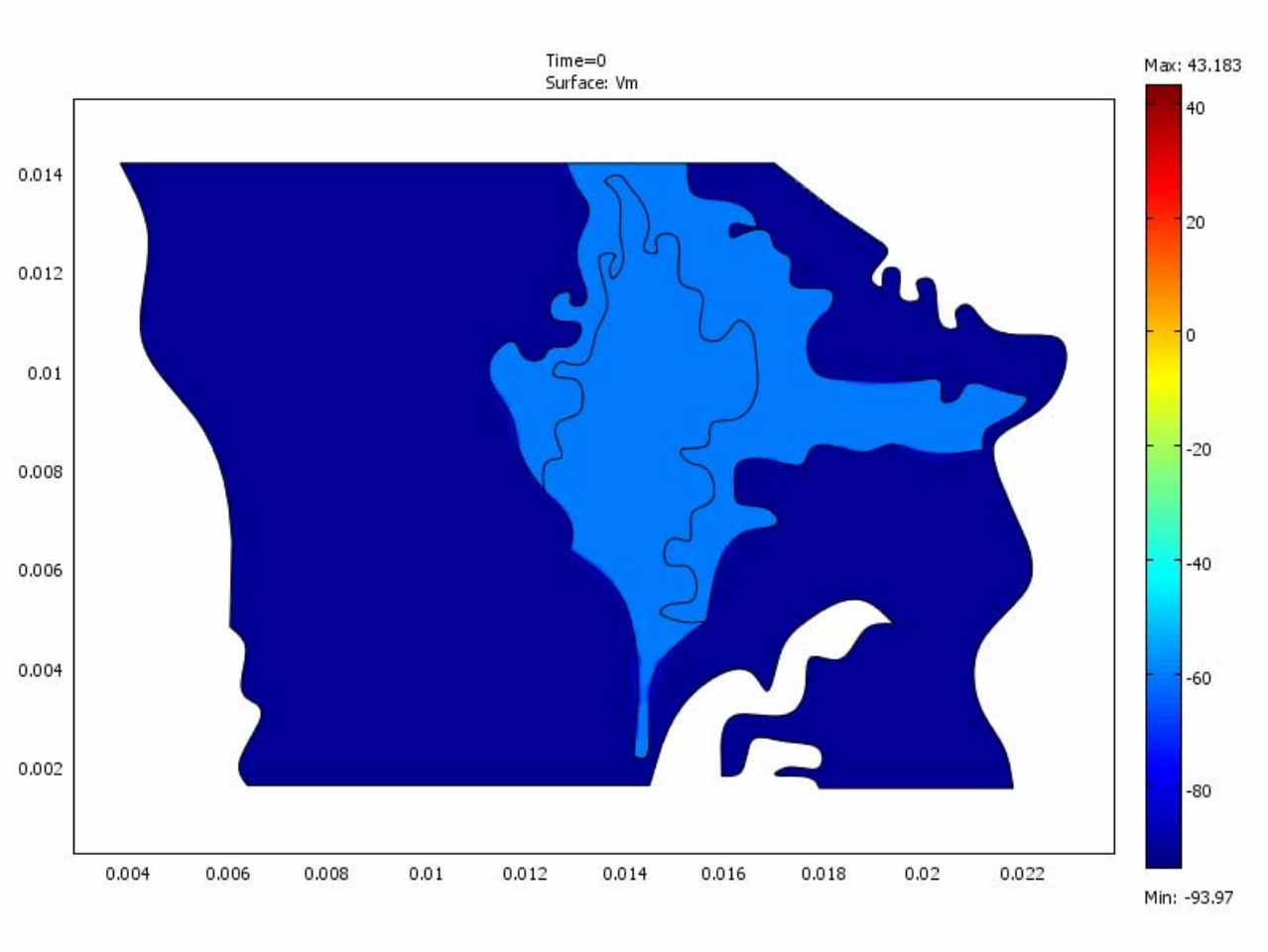
ModelML <import>

- **<import>**
- **Currently support FML and CellML**
- **For CellML, need to declare**
  - **Dependent variable**
  - **Time variable**
- **CellML modifications**
  - **Variable value overrides**
  - **Attach/Modify equations from CellML**

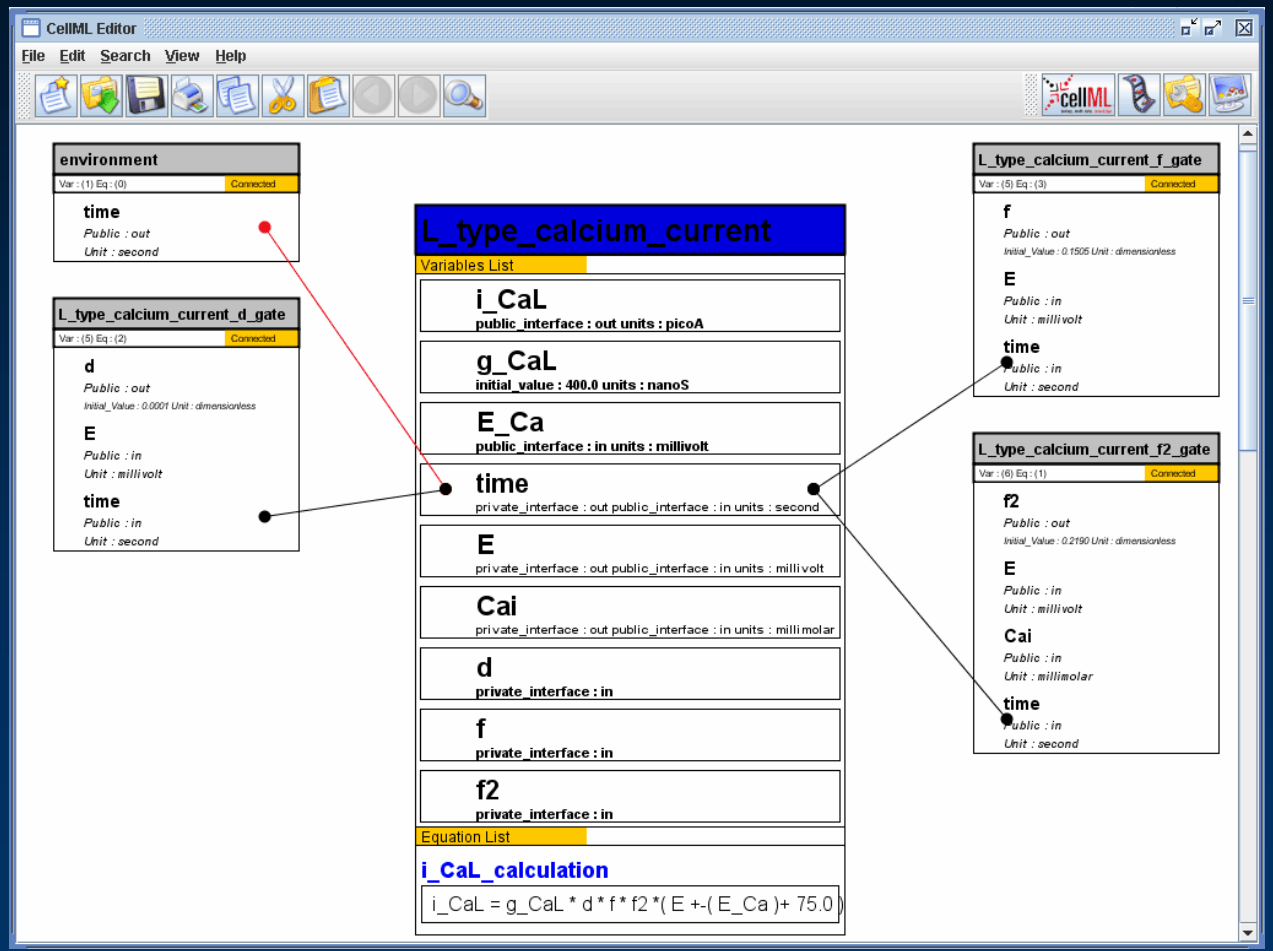
ModelML <system>

- **Describes an ODE system**
- **can be fully described from one CellML model, or from a subset of ODE equations from a CellML model**
- **Allows us to combine/utilise different CellML models together.**

2D Cardiac Pacemaker Using FML/ModelML



Development of a CellML Editor, Incorporating Component Visualization



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