Excitable Cell and Tissue Modelling using CellML/FML

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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 \( \mu \text{M} \) E-4031

Control
E-4031
E-4031 Fit

**Control**

- Voltage (mV)
- Current (pA/pF)
- Time (s)
- Model (blue)
- Data (red)

**E4031 Block**

- Voltage (mV)
- Current (pA/pF)
- Time (s)
- Model (blue)
- Data (red)
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

Parameter Selection Interface:

- Current Value:
  - Val: $1E0$
  - Lower Limit: $\infty$
  - Upper Limit: $\infty$
- Options:
  - Not Fitted
  - Shared Value
  - Data Spec.

Setting Parameter Limit:

- Unconstrained
- By Value
  - Lower Limit: $\infty$
  - Upper Limit: $\infty$
- Percentage (%): $\%$

Buttons:
- Confirm
- Cancel
Optimisation Progress

- Optimisation Result
- Shared Parameters
  - time_independent_outward_current_i_k1_calculation_P0
  - g_s_07.csv
  - slow_inward_current_g_s
  - g_s_10.csv
  - slow_inward_current_g_s
- Cost
  - Raw cost
  - Weighted cost

Optimiser Choice

<table>
<thead>
<tr>
<th>slow_inward_current_g_s</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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</tbody>
</table>

Optimisation Result

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- Shared Parameters
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Optimisation paused. Press "Confirm" when modification is done.
Optimisation of peripheral SAN AP using Noble (1962) Model

RMS = 0.78mV

![Graph showing raw data and optimised result with RMS = 1.21 mV.](image)

- **Membrane Voltage (millivolt)**
- **Time (second)**

**RMS = 1.21 mV**
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.
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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