Software Environment and Technologies for Cell Physiological Modelling

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**Contents**

- **Cybow Modeller**
  a software suite for cell modelling

- **Cell Physiology Ontology (CPO)**
  ontology on physical quantities in cell physiology

- **PEPML**
  a description format of experimental protocols
Cybow Modeller

- Software toolkit
  - Editors of cell models
  - Imports & exporters of other formats (inc. CellML)
  - Code generators
Component Editor

### Variable Definitions

<table>
<thead>
<tr>
<th>Name</th>
<th>Symbol</th>
<th>Unit</th>
<th>Default</th>
<th>Concept</th>
<th>Desc</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>( N )</td>
<td></td>
<td>2.333E3</td>
<td></td>
<td>for ventricular cell</td>
</tr>
<tr>
<td>( \gamma )</td>
<td>( \gamma )</td>
<td></td>
<td></td>
<td>conductan...</td>
<td>cell_mem...</td>
</tr>
<tr>
<td>Vm</td>
<td>( V_m )</td>
<td>mV</td>
<td></td>
<td></td>
<td>potassium...</td>
</tr>
<tr>
<td>EK</td>
<td>( E_K )</td>
<td>mV</td>
<td></td>
<td></td>
<td>open pro...</td>
</tr>
<tr>
<td>( p_{open} )</td>
<td>p(open)</td>
<td></td>
<td></td>
<td></td>
<td>external...</td>
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<tr>
<td>( [K^+]_o )</td>
<td>([K^+]_o)</td>
<td>mM</td>
<td></td>
<td></td>
<td>intracell...</td>
</tr>
<tr>
<td>ATP_i</td>
<td>([ATP_i])</td>
<td>mM</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Equation Definitions

\[
I_{KATP} = N \cdot \gamma \cdot (V_m - E_K) \cdot p(open)
\]

\[
\gamma = 0.0236 \cdot [K^+]_o^{0.24}
\]

\[
p(open) = \frac{0.8}{1 + \left( \frac{[ATP_i]}{0.1} \right)^2}
\]

Equation: \( p_{open} = 0.8 / \left(1 + [ATP_i] / 0.1 \text{ [mM]} \right)^2 \)

Description: p_open = 0.8 / (1 + ATP_i / 0.1 [mM])^2
Component Editor

Variable definitions

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<td>(N)</td>
<td></td>
<td>2.333E3</td>
<td>for ventricular cell</td>
<td></td>
</tr>
<tr>
<td>gamma</td>
<td>gamma</td>
<td>(\gamma)</td>
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<td></td>
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<tr>
<td>Vm</td>
<td>Vm</td>
<td>(V_m)</td>
<td>mV</td>
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<td>cell_membrane_potential</td>
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<tr>
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<td>EK</td>
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<td>mV</td>
<td></td>
<td>potassium_equilibrium_potential</td>
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</tr>
<tr>
<td>p_open</td>
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<td>p(open)</td>
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<td></td>
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<tr>
<td>K_o</td>
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<td>([K^+]_o)</td>
<td>mM</td>
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<td>external_potassium_concentration</td>
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</tr>
<tr>
<td>ATP_i</td>
<td>ATP_i</td>
<td>([ATP]_i)</td>
<td>mM</td>
<td></td>
<td>intracellular_ATP_concentration</td>
<td></td>
</tr>
</tbody>
</table>
Component Editor

Variable definitions

- \( \gamma \)
- \( [K^+]_o \)

Graphic symbol

denoted physical quantity (CPO)
Component Editor

Equation definitions

\[ I_{\text{KATP}} = N \cdot \gamma \cdot (V_m - E_K) \cdot p(\text{open}) \]
\[ \gamma = 0.0236 \cdot [\text{K}^+]_o^{0.24} \]

\[ p(\text{open}) = \frac{0.8}{1 + \left( \frac{[\text{ATP}]_i}{0.1} \right)^2} \]

Equation: \[ p_{\text{open}} = 0.8 / \left( 1 + \left[ \frac{\text{ATP}_i}{0.1 \text{ mM}} \right]^2 \right) \]
Component Editor

Equation definitions

Graphic expression

Text input
Model Composer

- Tree view
- Graph view
- Component list
Model Composer

cell
Model Composer
Model Composer

Variables inserted automatically
Add a component from another model

t: time
Vm: V
Add a component from another model

- t: time
- Vm: V

Links connected automatically
Tools for Computation

- Code Generator for time-series simulation
- Exporter of XPPAut ODE file for bifurcation analysis
Conversion with CellML

CellML

<model>
<connection>
<component>
<variable>

Cybow Modeller

composition file
<reference>
aggregate
component file
link
<variable>
Availability

- Source codes of most tools are available at http://sourceforge.net/projects/cybowmodeller/
- Other tools are in preparation for opening
- Contact simayosi@astem.or.jp
On physical quantities referred in cell physiology, e.g.

- ATP-sensitive potassium current
- Intracellular sodium concentration
- Cellular contractile force
intracellular sodium concentration

- compartment
- concentration
- ion

- space position
- quantity
- substance

- intracellular space
- in region
- of solute

- is a
- is a
- is a
Definition Example

rapidly activating delayed rectifier potassium current

- is-a-subclass-of: current by ion channel

- is-a-current-component-of: delayed rectifier potassium current

- is-carried-through: Kv11.1
Availability

http://cpo.dynabios.org/

- Download OWL file
- Browse concepts using OWLDoc
Physiological Experimental Protocol Markup Language

- XML-based format
- Specialised for explicit description of experimental procedures
- Example: muscle contraction

- Procedure

  initially
  \[ \text{length} = \text{initial-length} \]
  after tension \( \geq \) weight
  \[ \text{tension} = \text{weight} \]
  after length \( \geq \) initial-length
  \[ \text{length} = \text{initial-length} \]
Example: periodic stimuli

\[
I_{\text{ext}} := 0
\]

\[
\text{if}(t_{\text{onset}} \leq (t \mod T_{\text{stim}}) < (t_{\text{onset}} + d_{\text{stim}})) \{ \\
\quad I_{\text{ext}} := A_{\text{stim}} \\
\}
\]

<protocol ...>
  <event id="default">
    <condition>
      <literal type="bool" value="true" units="" />
    </condition>
    <action>
      <set_value><var id="Iext" rdf:type="&cpo;Injected_Current" /><literal value="0" units="mV" /></set_value>
    </action>
  </event>
  <event id="stimulus">
    <param name="stim_period" units="ms" />
    <param name="stim_duration" units="ms" />
    <param name="stim_onset" units="ms" />
    <param name="stim_amplitude" units="mA" />
    <define id="phase">
      <arg name="time" />
      <mod><ref name="time" /><ref name="stim_period" /></mod>
    </define>
    <condition>
      <and>
        <ge><eval href="#phase"><var id="time" rdf:type="&cpo;time" /></eval><ref name="stim_onset" /></ge>
        <lt>
          <eval href="#phase"><var id="time" /></eval><add><ref name="stim_onset" /><ref name="stim_duration" /></add>
        </lt>
      </and>
    </condition>
    <action>
      <set_value><var id="Iext" /><ref name="stim_amplitude" /></set_value>
    </action>
  </event>
</protocol>
Example: periodic stimuli

```xml
<protocol ...>
  <event id="default">
    <condition>...</condition>
    <action>...</action>
  </event>
  <event id="stimulus">
    ...
    <condition>...</condition>
    <action>...</action>
  </event>
</protocol>
```
Example: periodic stimuli

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I_{\text{ext}} := 0 \\
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Example: periodic stimuli

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\text{if}(t_{\text{onset}} \leq (t \mod T_{\text{stim}}) < (t_{\text{onset}} + d_{\text{stim}})) \{ \\
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\}
\]
Current Status

- XML Schema definition (β) will be available soon
- Draft of specification will be prepared later