Software Environment and Technologies for Cell Physiological Modelling

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Contents

- Cybow Modeller
  a software suite for cell modelling

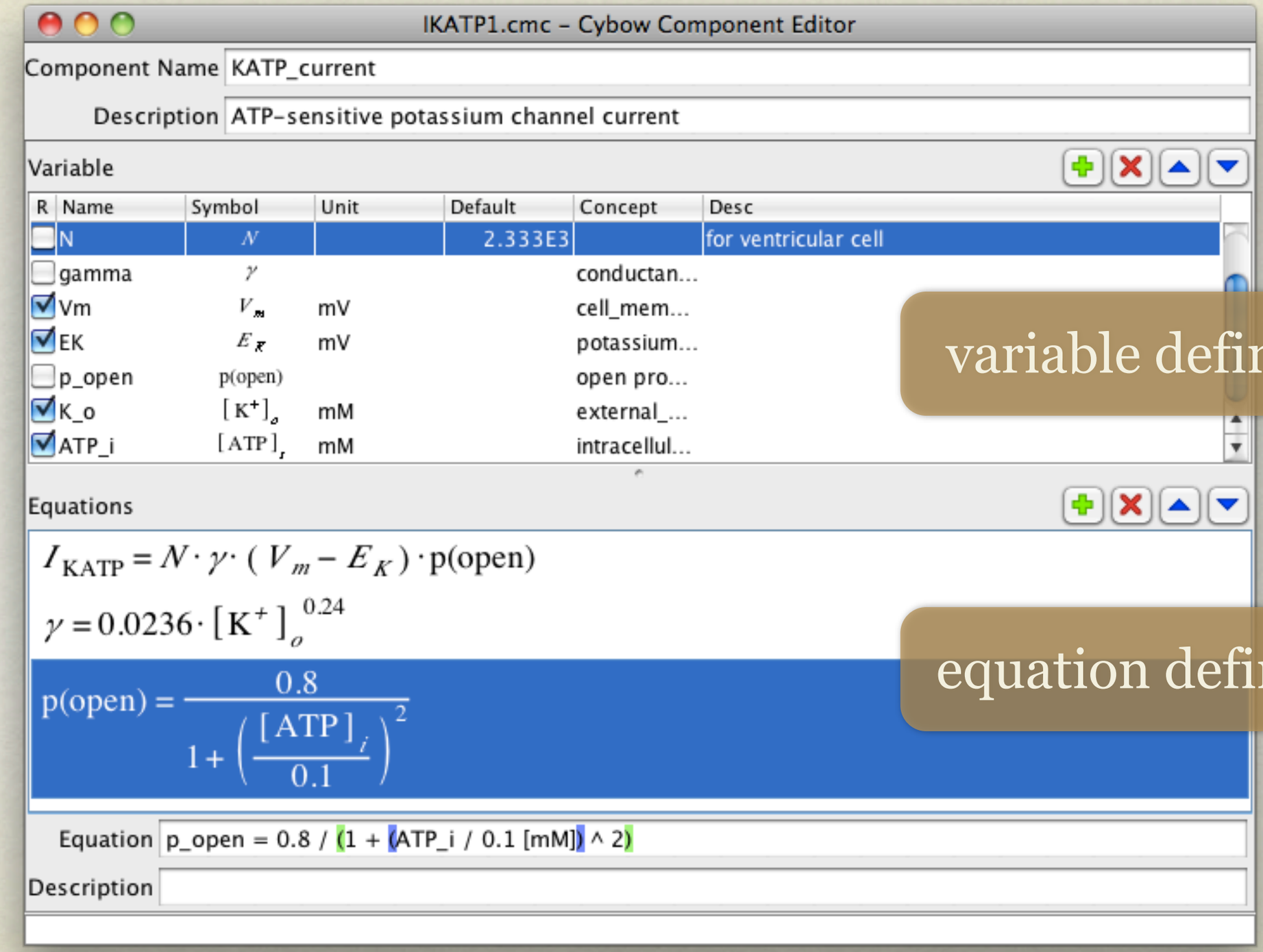
- Cell Physiology Ontology (CPO)
  ontology on physical quantities in cell physiology

- 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



Component Editor

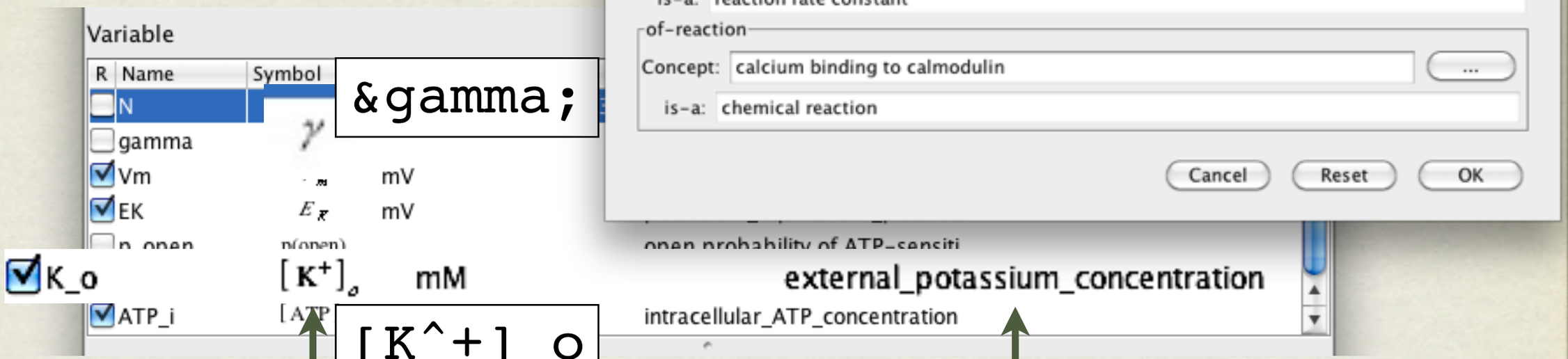
Variable definitions

Variable

R	Name	Symbol	Unit	Default	Concept	Desc
☐	N	N		2.333E3		for ventricular cell
☐	gamma	γ			conductance of ATP-sensitive p...	
☑	Vm	V_m	mV		cell_membrane_potential	
☑	EK	E_K	mV		potassium_equilibrium_potential	
☐	p_open	p(open)			open probability of ATP-sensiti...	
☑	K_o	$[K^+]_o$	mM		external_potassium_concentration	
☑	ATP_i	$[ATP]_i$	mM		intracellular_ATP_concentration	

Component Editor

Variable definitions



Component Editor

Equation definitions

Equations

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

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

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

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

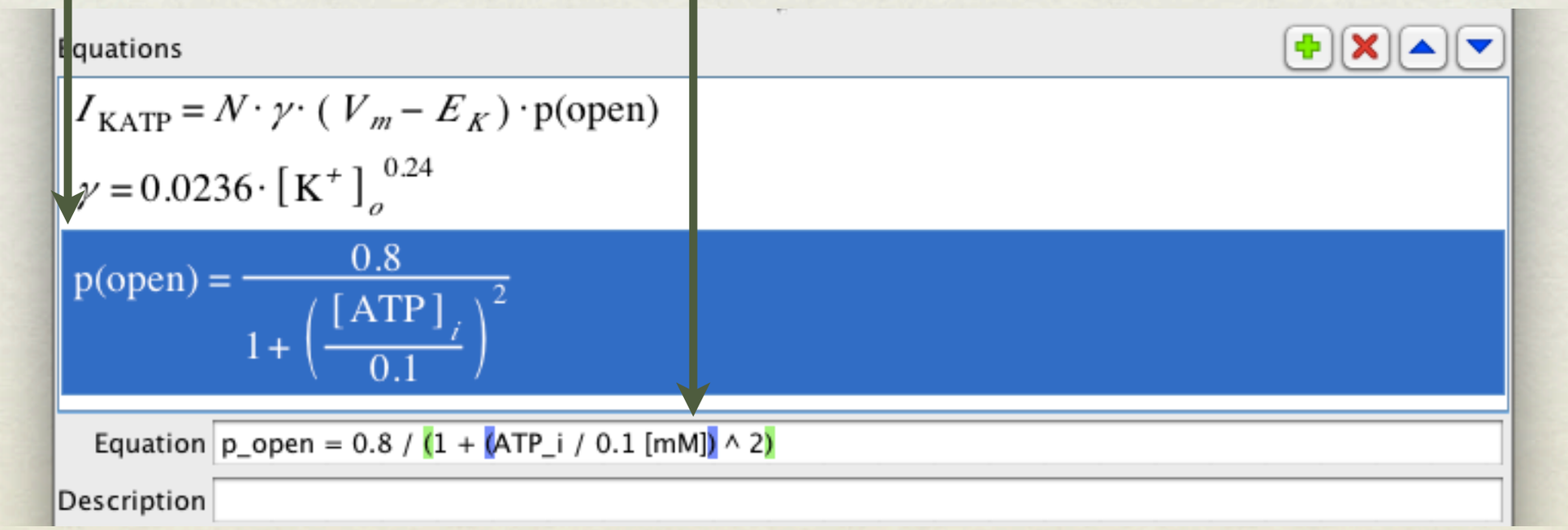
Description:

Component Editor

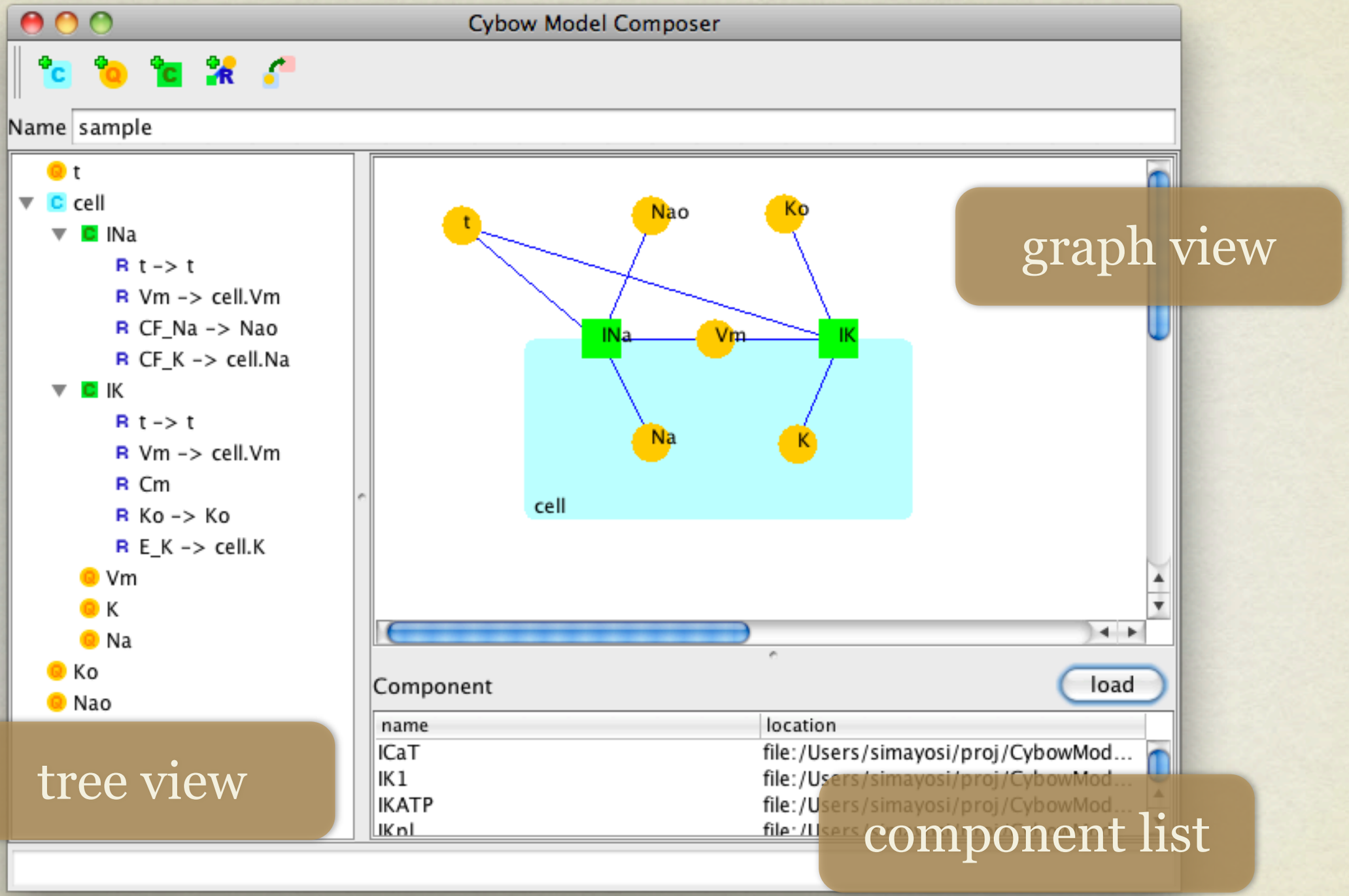
Equation definitions

Text input

Graphic expression



Model Composer



Model Composer

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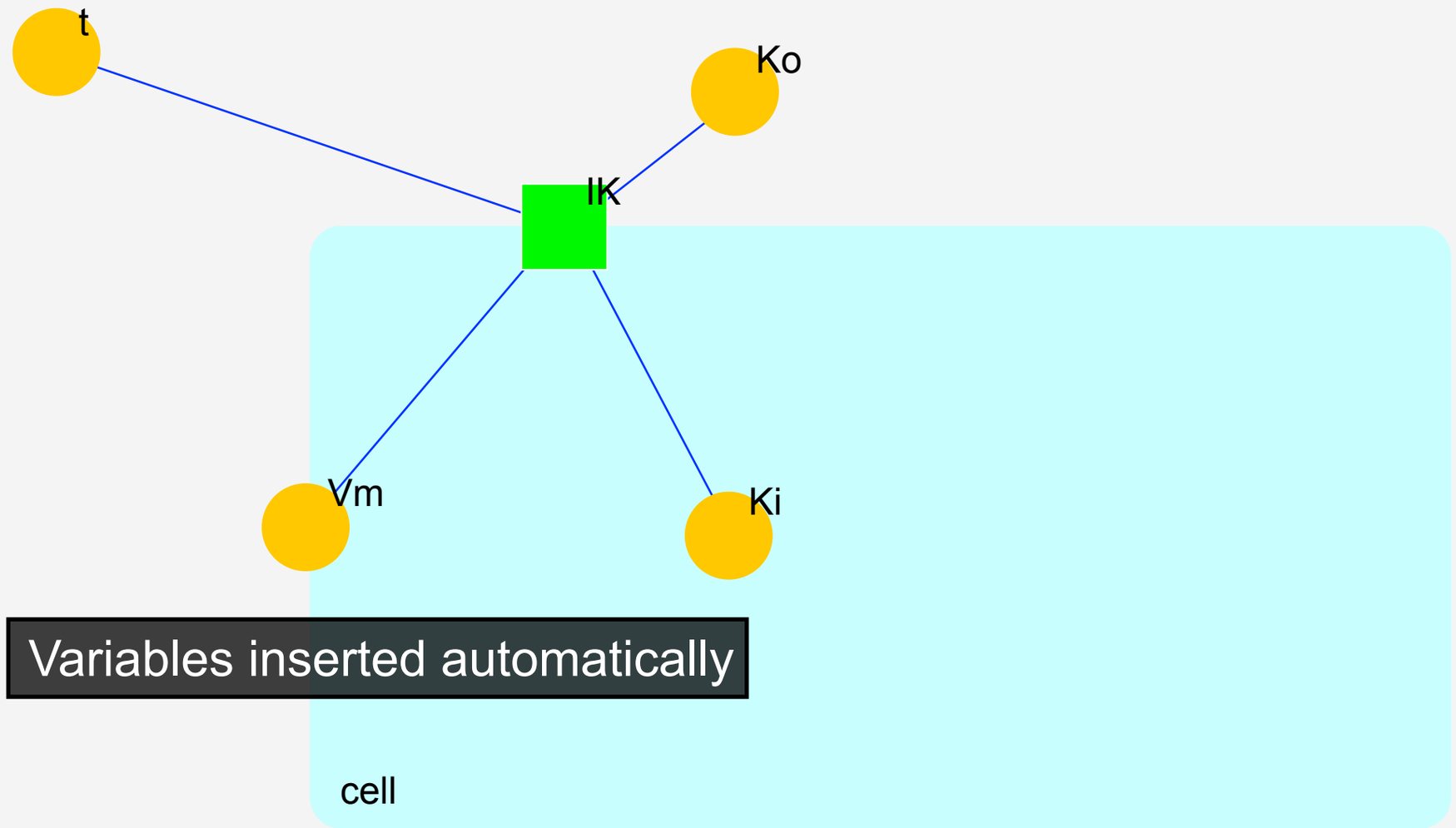
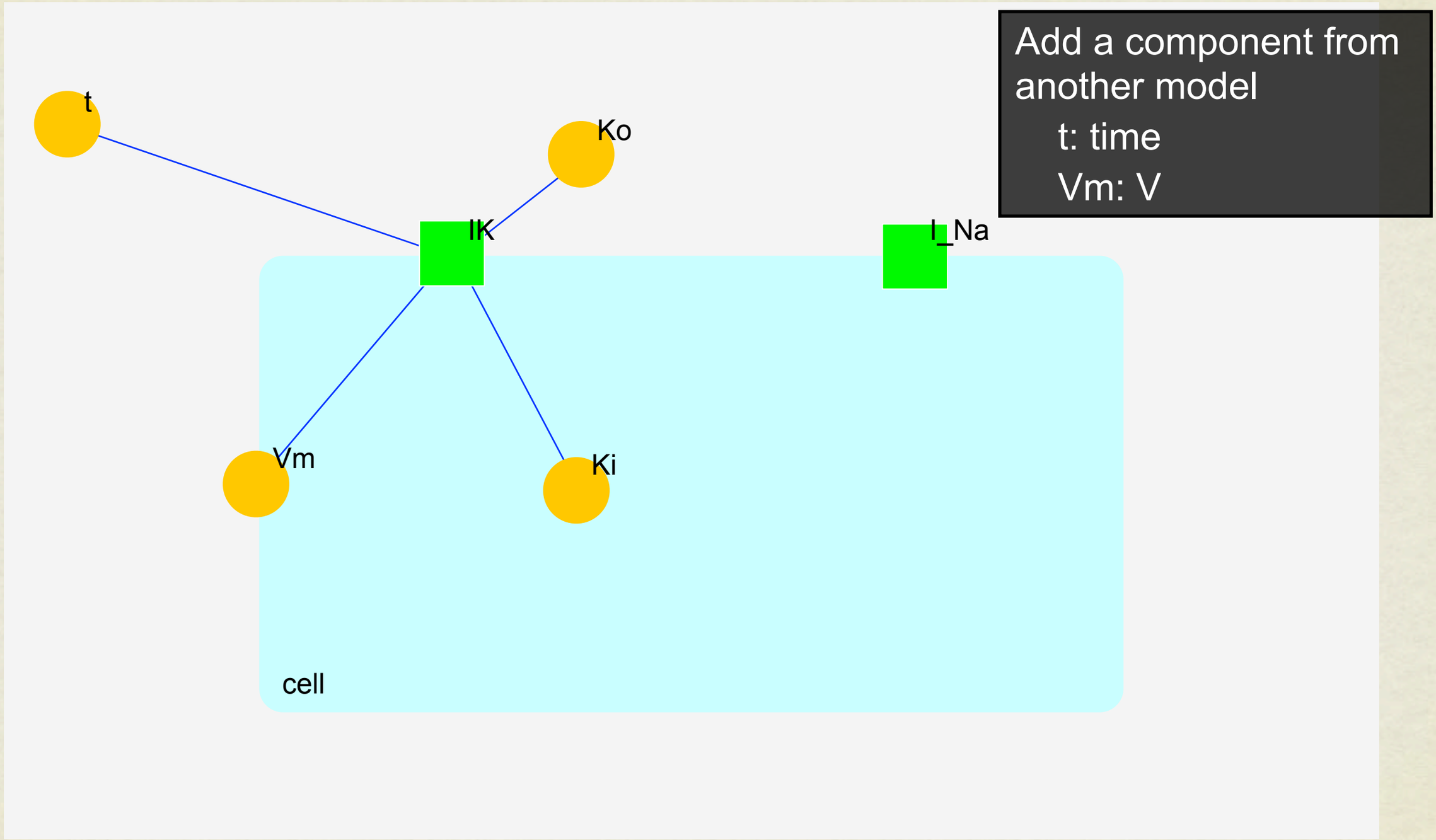
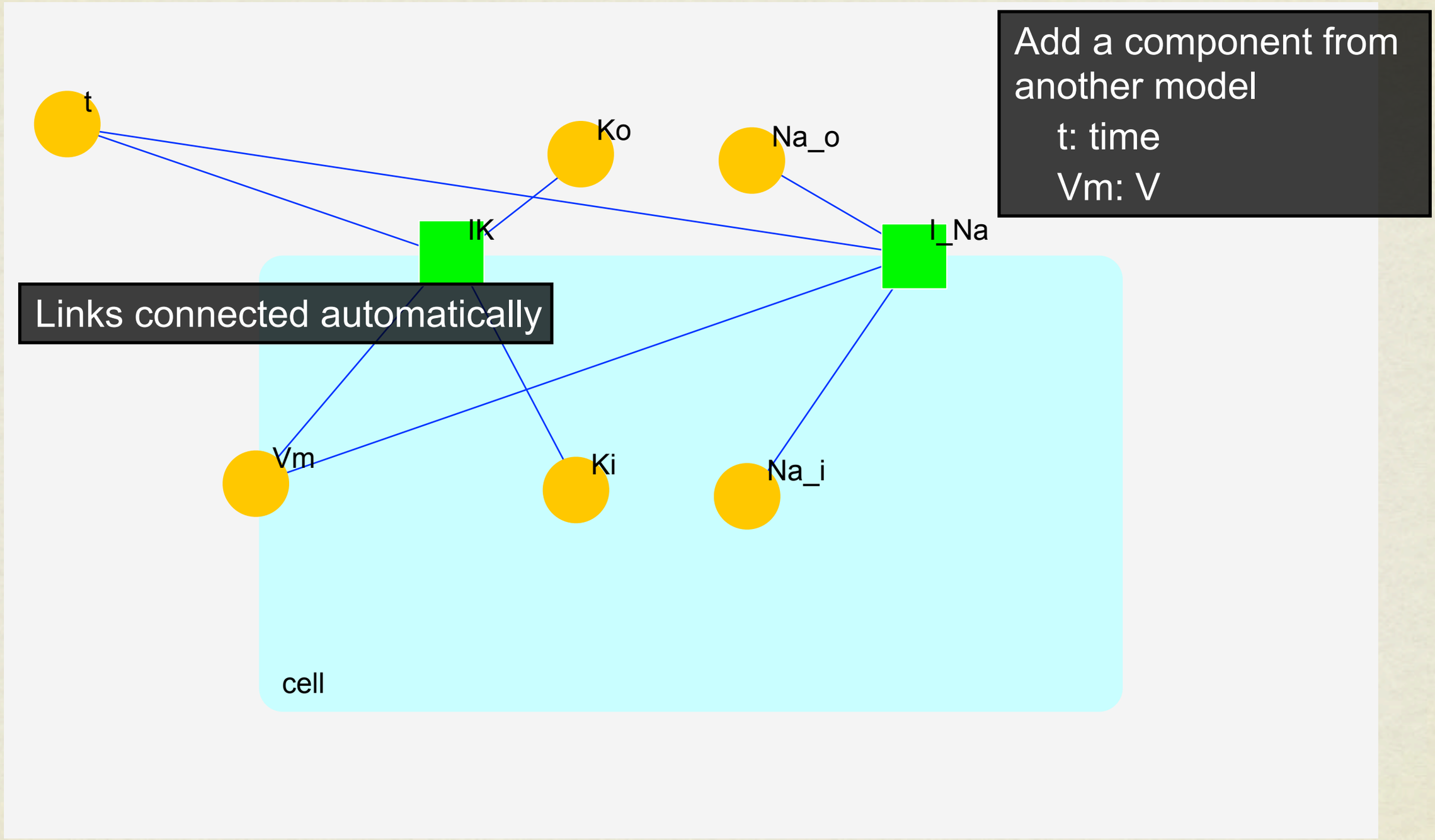


Model Composer



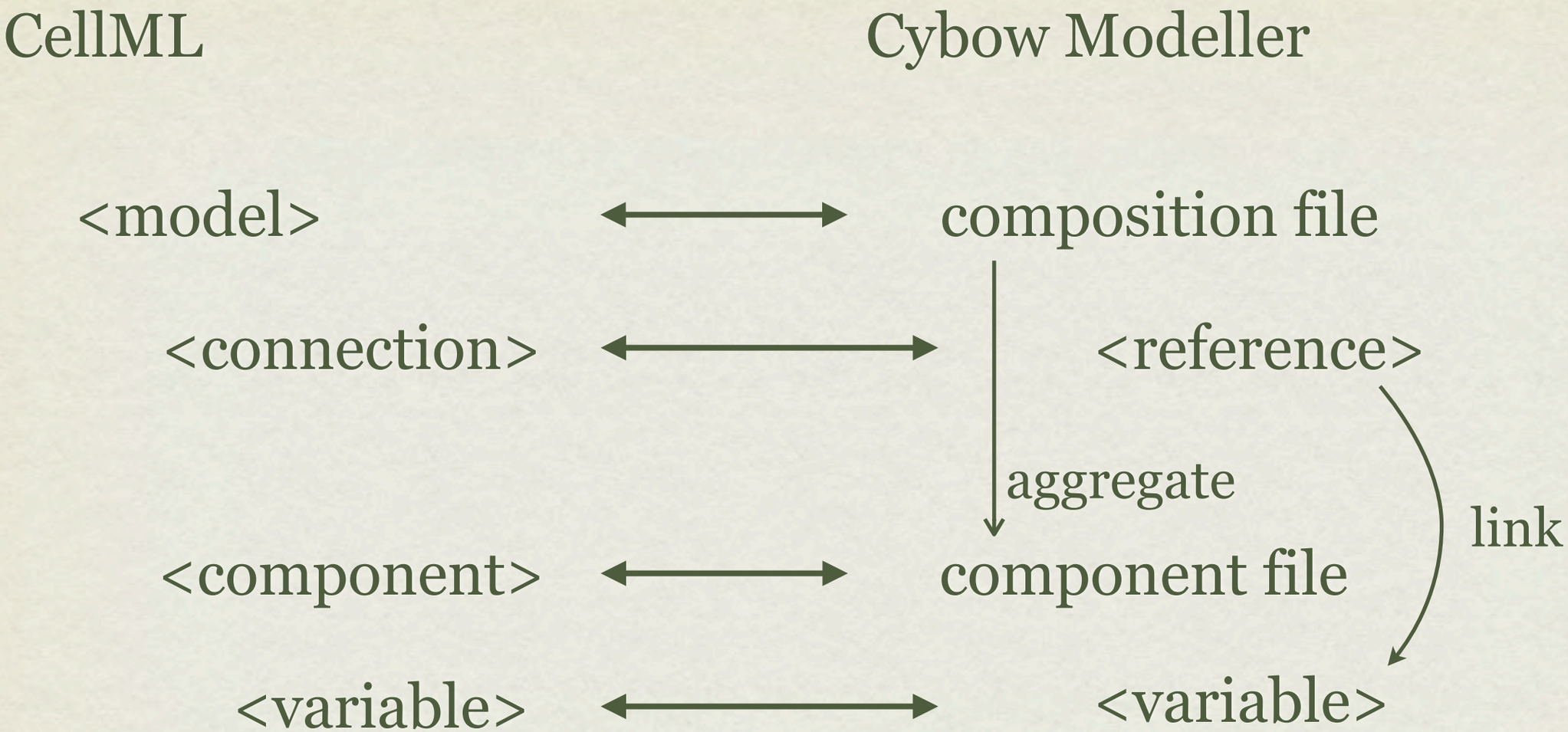
Model Composer



Tools for Computation

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

Conversion with CellML



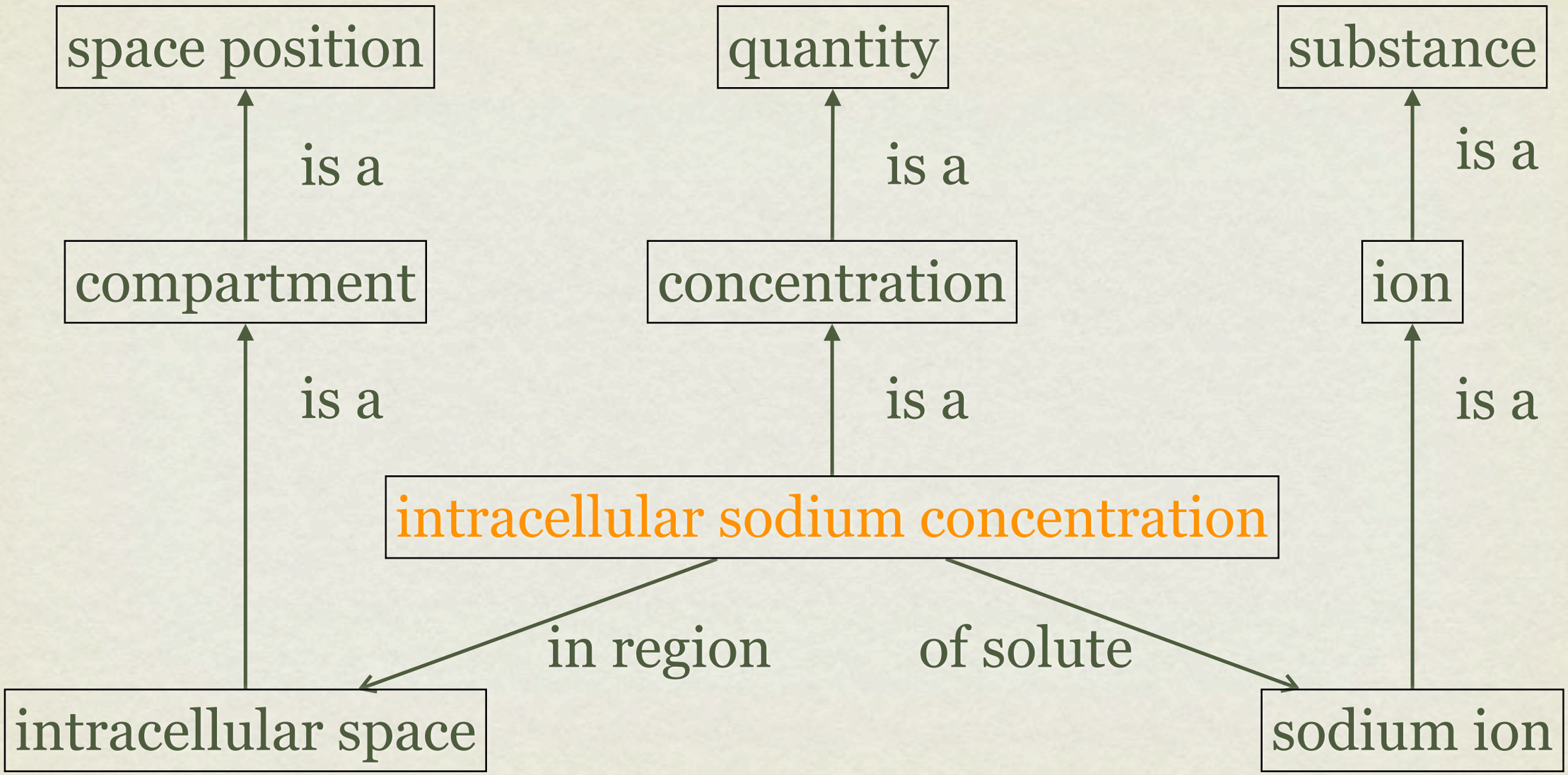
Availability

- 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`

Cell Physiology Ontology

- On physical quantities referred in cell physiology, e.g.
  - ATP-sensitive potassium current
  - intracellular sodium concentration
  - cellular contractile force

Concept Hierarchy



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/`

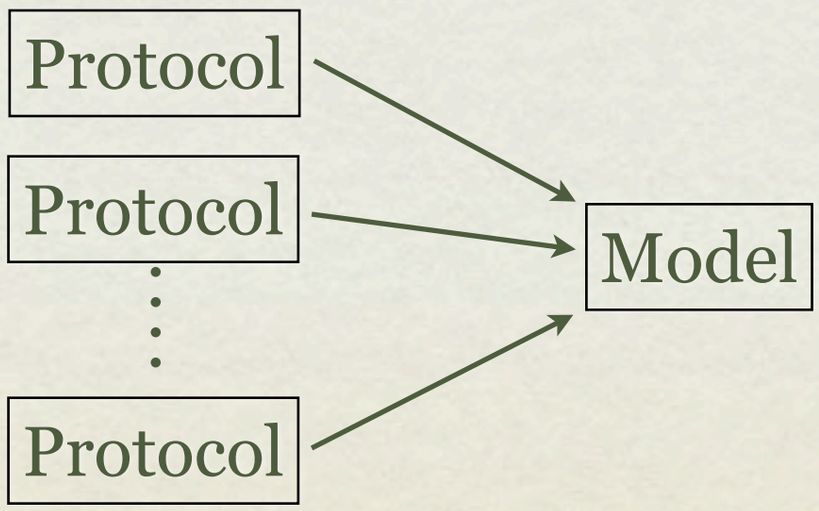
- Download OWL file
- Browse concepts using OWLDoc

PEPML

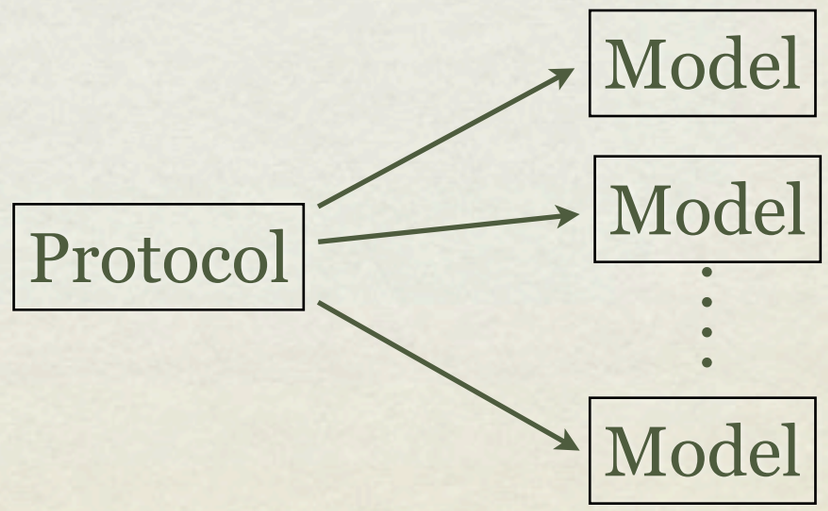
Physiological Experimental Protocol Markup Language

- XML-based format
- Specialised for explicit description of experimental procedures

Validation



Comparison



Impossibility of Arithmetic Definition

- Example: muscle contraction

- Procedure

  initially

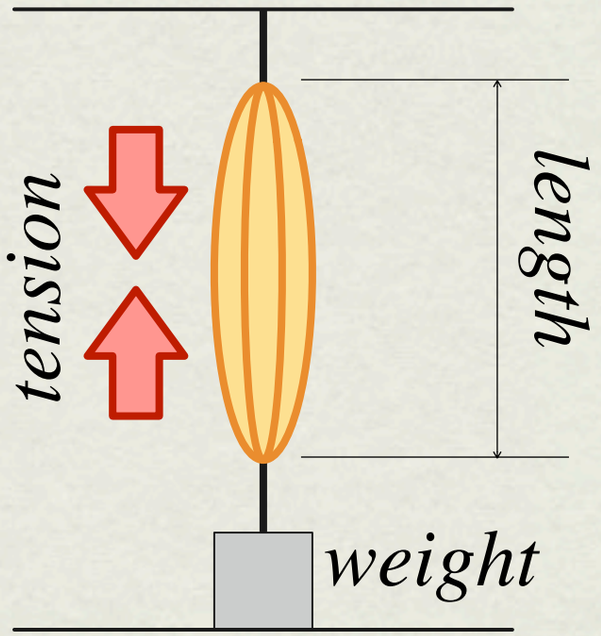
  length = *initial-length*

  after *tension* ≥ *weight*

  tension = *weight*

  after *length* ≥ *initial-length*

  length = *initial-length*



Example: periodic stimuli

```
<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>
```

$$I_{\text{ext}} := 0$$

$$\textbf{if}(t_{\text{onset}} \le (t \bmod T_{\text{stim}}) < (t_{\text{onset}} + d_{\text{stim}})) \{$$

$$\quad I_{\text{ext}} := A_{\text{stim}}$$

$$\}$$

Example: periodic stimuli

```
<protocol ...>
  <event id="default">
    <condition>...</condition>
    <action>...</action>
  </event>
  <event id="stimulus">
    ...
    <condition>...</condition>
    <action>...</action>
  </event>
</protocol>
```

Example: periodic stimuli

```
<event id="default">
  <condition>
    <literal type="bool" value="true" units="" />
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  <action>
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      <literal value="0" units="mV" />
    </set_value>
  </action>
</event>
```

$I_{ext} := 0$

if$(t_{onset} \leq (t \bmod T_{stim}) < (t_{onset} + d_{stim}))$ {

$I_{ext} := A_{stim}$

}

Example: periodic stimuli

```
<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>
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  </condition>
  <action>
    <set_value>
      <var id="Iext" />
      <ref name="stim_amplitude" />
    </set_value>
  </action>
</event>
```

parameters

function

parameter reference

function evaluation

$I_{ext} := 0$

if$(t_{onset} \leq (t \bmod T_{stim}) < (t_{onset} + d_{stim}))$ {

$I_{ext} := A_{stim}$

}

Current Status

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