Requirements for a language for multiscale cell model development

Upi Bhalla
NCBS Bangalore
Levels of description

- Behaviour
  \[ g = g_{\text{max}} \cdot t/\tau_p \cdot \exp(1-t/\tau_p) \]

- Systems
  \[ g = g_{\text{max}} \cdot m^x \cdot h^y \]

- Areas
  \[ 1-m \left\langle \frac{\alpha(V)}{\beta(V)} \right\rangle m \]

- Circuits
  \[ \tau_m \frac{\partial V}{\partial t} = E - V + \lambda^2 \frac{\partial^2 V}{\partial x^2} \]
  \[ E = RT/zF \cdot \ln([\text{out}]/[\text{in}]) \]

- Neurons
  \[ \frac{\partial \phi}{\partial t} = D \nabla^2 \phi(\vec{r}, t) \]

- Dendrites
  \[ A + B \iff C \]
  \[ \frac{dA}{dt} = -kf.A.B + kb.C \]

- Synapses
  Stochastic forms
  Brownian motion

- Molecules

Mechanics:
- Tensegrity
- Bending moments
- Motors
- Bulk flow
A typical multiscale model

Network

Cell

Biophysics

Molecules

Spine: Receptor traffic

Network activity

Electrode stimulus

Dendrite: MAPK feedback

G_{AMPAR}

Ca^{2+}

G_{KA}
Biophysically-detailed network model
The Multiscale Object-Oriented Simulation Environment
http://moose.ncbs.res.in,
http://sourceforge.net/projects/moose/
LGPL but uses GPL modules
C++/Python/Qt/GSL/OpenGL and many many more…
MOOSE supports standards

MOOSE supports the following standards:

- MPI
- MUSIC
- NeuroML
- Python
- SBML

Other related tools:

- BioModels
- DOQCS
- neuroConstruct
- NumPy
- PyNN
- NeuronDB
User interfaces

External I/O

Databases

Model files

SBW, other model systems

Input

Start

Stop

Model

Simulation entities, e.g., molecules

Parsers

Shell

Multiprocessor scheduler

Internode messaging

To other nodes

Solvers
Modelling across scales

Single particle (Smoldyn plugin)  Compartmental ODE and stochastic Steady-state solver  Cellular biophysics  Network

Multiscale: biophysical network
Multiscale: SigNeur
Multiscale language requirements

- Composition specification:
  - Single NeuroML model
  - Multiple SBML models
    - Diffusion specification
    - Entity mapping

- Interface specification
  - Molecules -> channel properties
  - Ion flux (Ca) -> Signaling effects
  - Synaptic input -> Ligand molecules
  - Molecular gradients/junctions

- Geometry specification
  - Spines
  - Junctions
  - Caps
  - Mapping to detailed morphology
  - Spatial transforms and writhing

- Mechanics specification

- Control specifications:
  - Solvers
  - Runtime
  - Output variables
1. Composition specification

a. Identify model sources
b. Identify where each one goes
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a. Identify model sources
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c. Diffusion along compartments
d. Diffusion into spines
1. Composition specification

a. Identify model sources
b. Identify where each one goes
c. Diffusion along compartments
d. Diffusion into spines
e. Entity mapping: Unique
f. Entity mapping: complex
2. Interface specification

a. Molecules -> Channel conductance
b. Molecules -> Channel kinetics
c. Ion flux (Ca) -> Signaling effects
d. Synaptic input -> Ligand molecules
2. Interface specification

a. Molecules->Channel conductance
b. Molecules-> Channel kinetics
c. Ion flux (Ca) -> Signaling effects
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e. Molecular gradients/junctions

All involve scaling, offset, unit conversion and so on.
Geometry specification

a. Spines
b. Junctions
Geometry specification

- a. Spines
- b. Junctions
- c. Caps
- d. Detailed morphology: meshes
- e. Detailed morphology: mappings
Geometry specification

a. Spines
b. Junctions
c. Caps
d. Detailed morphology: meshes
e. Detailed morphology: mappings
f. Spatial transforms
g. Writhing
4. Mechanics specification
5. Control

a. Solvers
b. Runtime control
c. Output variables and formats

Vs.

SEDM
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Ease of use: Sensible defaults
Options

• Will SEDML handle arbitrary model control?
• NeuroML vs composition ML?
• Problem-specific compositionML, or are there generic ways to assemble MLs?
• Forget the compositionML.
  – Use Python or script, local to simulator
  – Push for modularity in other MLs.
Thank You

Siji, Harsha, Aditya, Niraj, Oliver Subhasis, [Karan, Pragati, Arnold]