

Requirements for a language for multiscale cell model development



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Levels of description

Behaviour
Systems
Areas
Circuits
Neurons
Dendrites
Synapses
Molecules

$$g = g_{\max} \cdot t/\tau_p \cdot \exp(1-t/\tau_p)$$

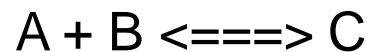
$$g = g_{\max} \cdot m^x \cdot h^y$$

$$1-m \begin{matrix} \swarrow \alpha(V) \\ \searrow \beta(V) \end{matrix} m$$

$$\tau_m \frac{\partial V}{\partial t} = E - V + \lambda^2 \frac{\partial^2 V}{\partial x^2}$$

$$E = RT/zF \cdot \ln([\text{out}]/[\text{in}])$$

$$\frac{\partial \phi}{\partial t} = D \nabla^2 \phi(\vec{r}, t)$$



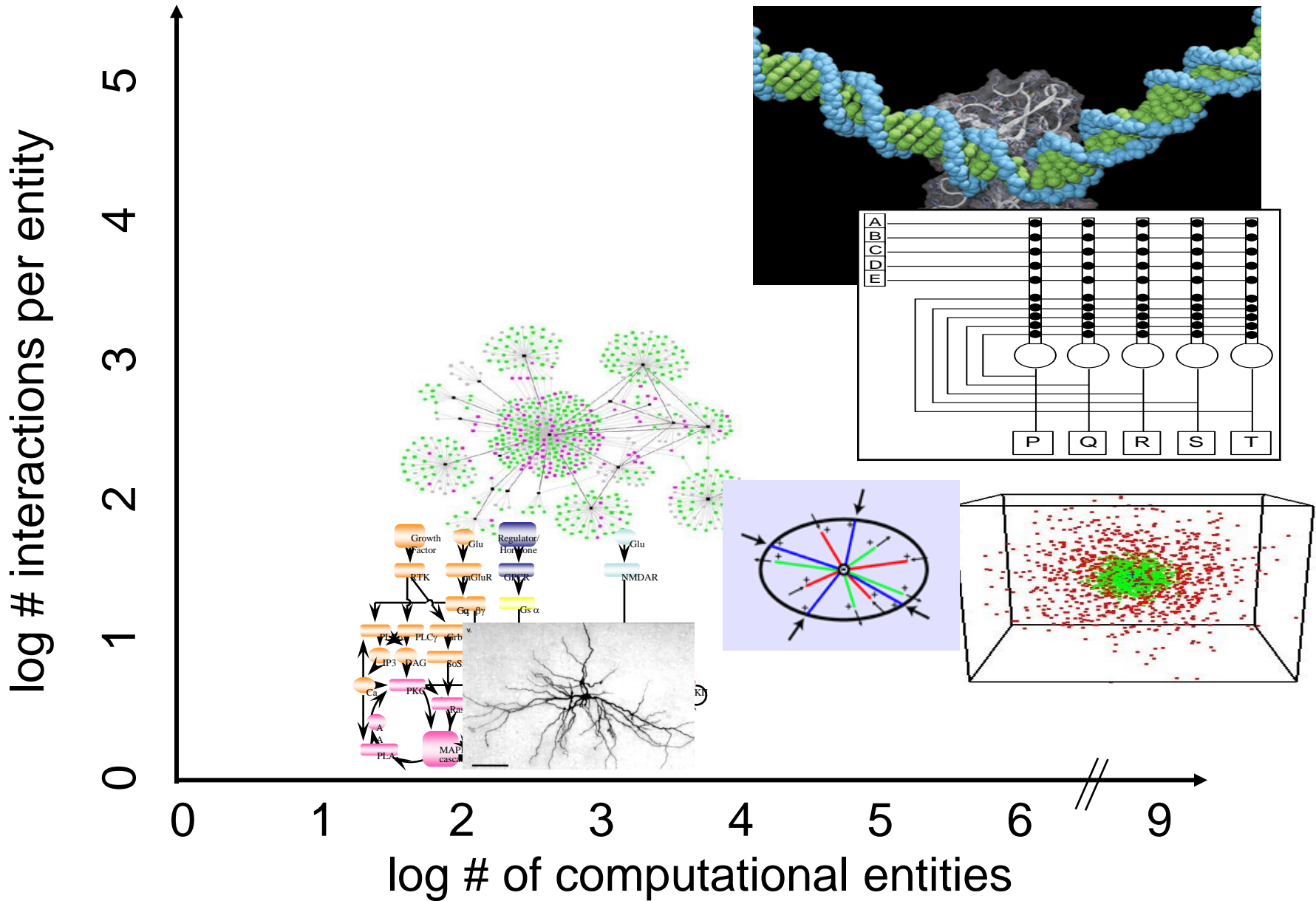
$$dA/dt = -k_f \cdot A \cdot B + k_b \cdot C$$

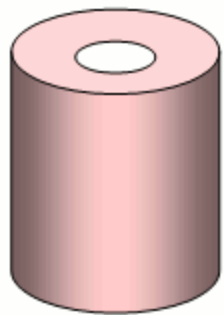
Stochastic forms

Brownian motion

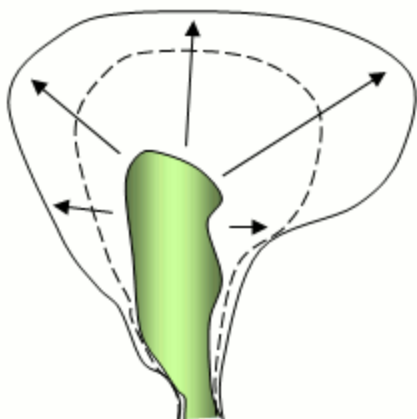
Mechanics:
 Tensegrity
 Bending moments
 Motors
 Bulk flow

Problem sizes

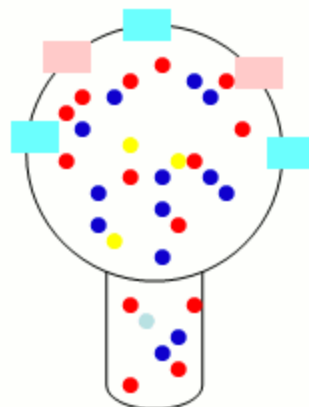




ChannelML



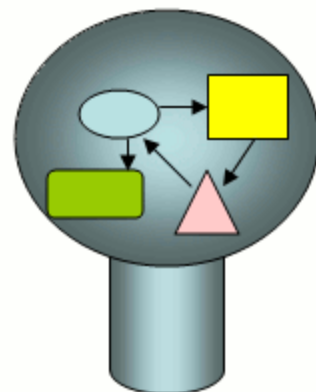
MechML



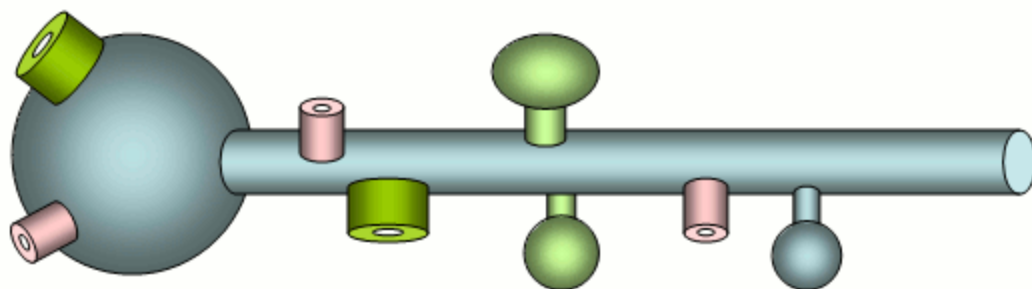
3DMCML



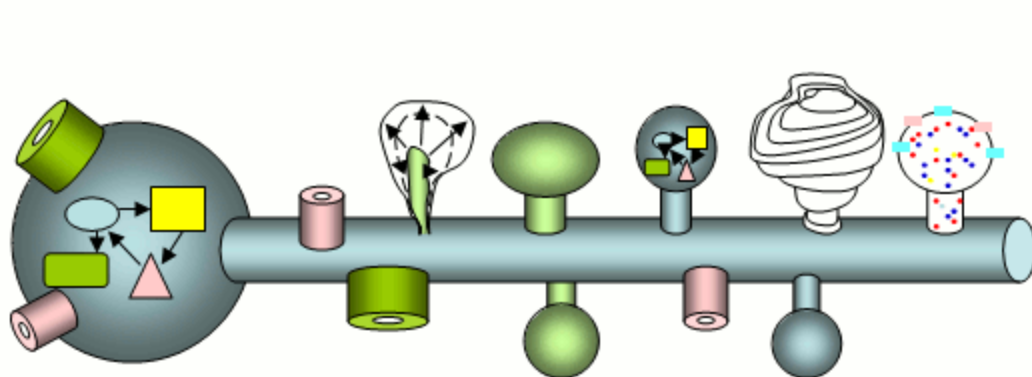
MeshML



SBML



NeuroML

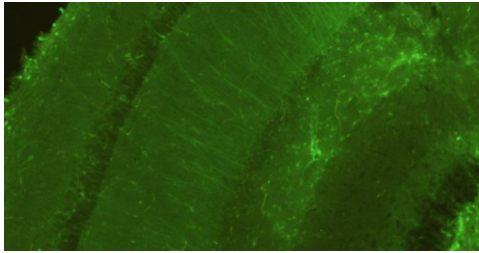


SEDML

Composition
Math
How to link
How to solve

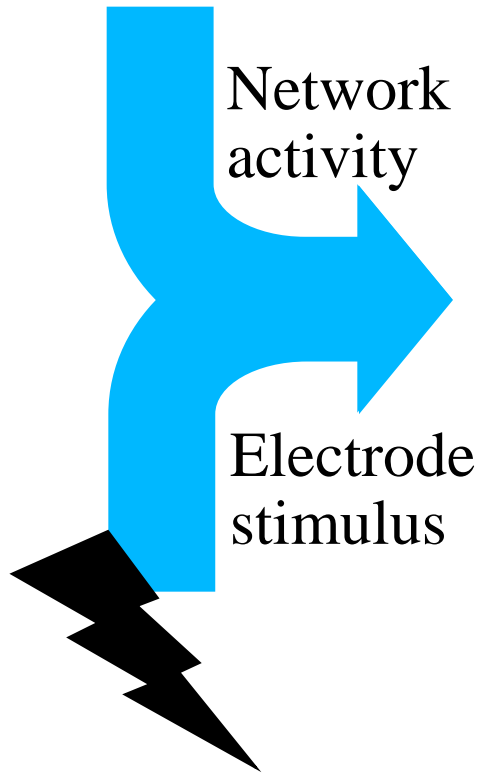
A typical multiscale model

Network

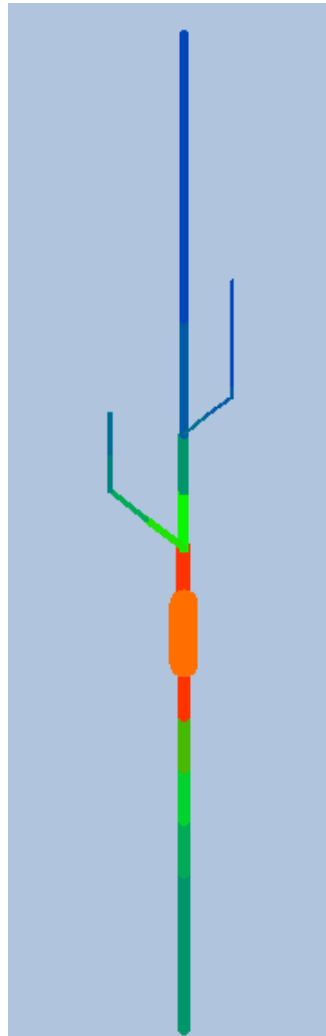


Network activity

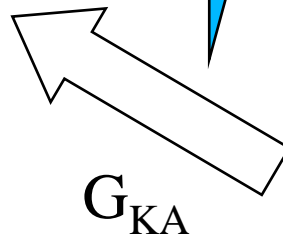
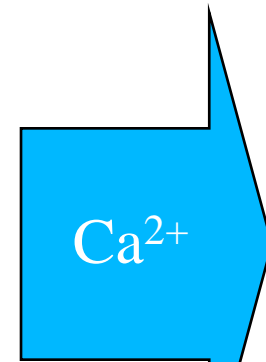
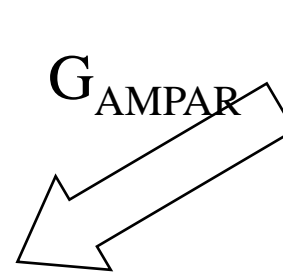
Electrode stimulus



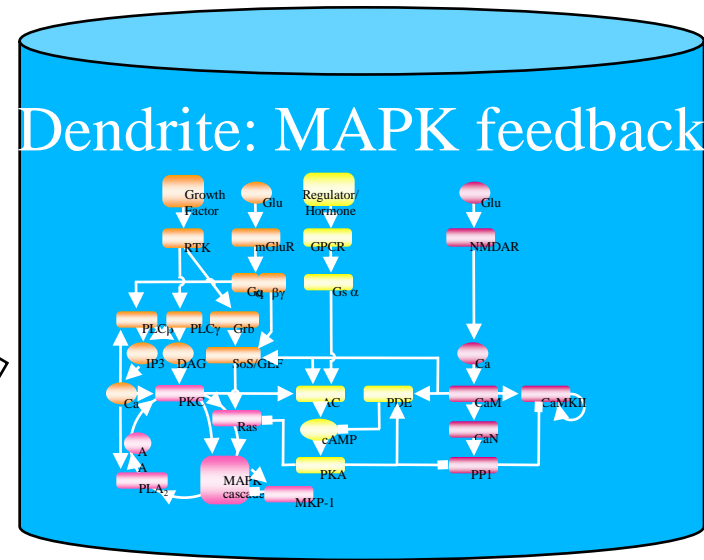
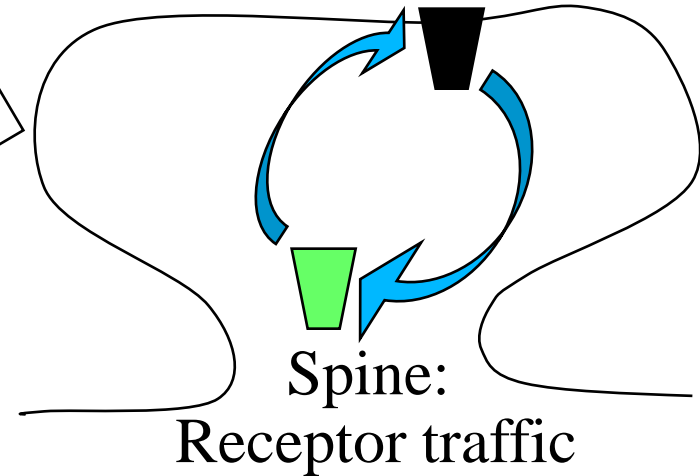
Cell



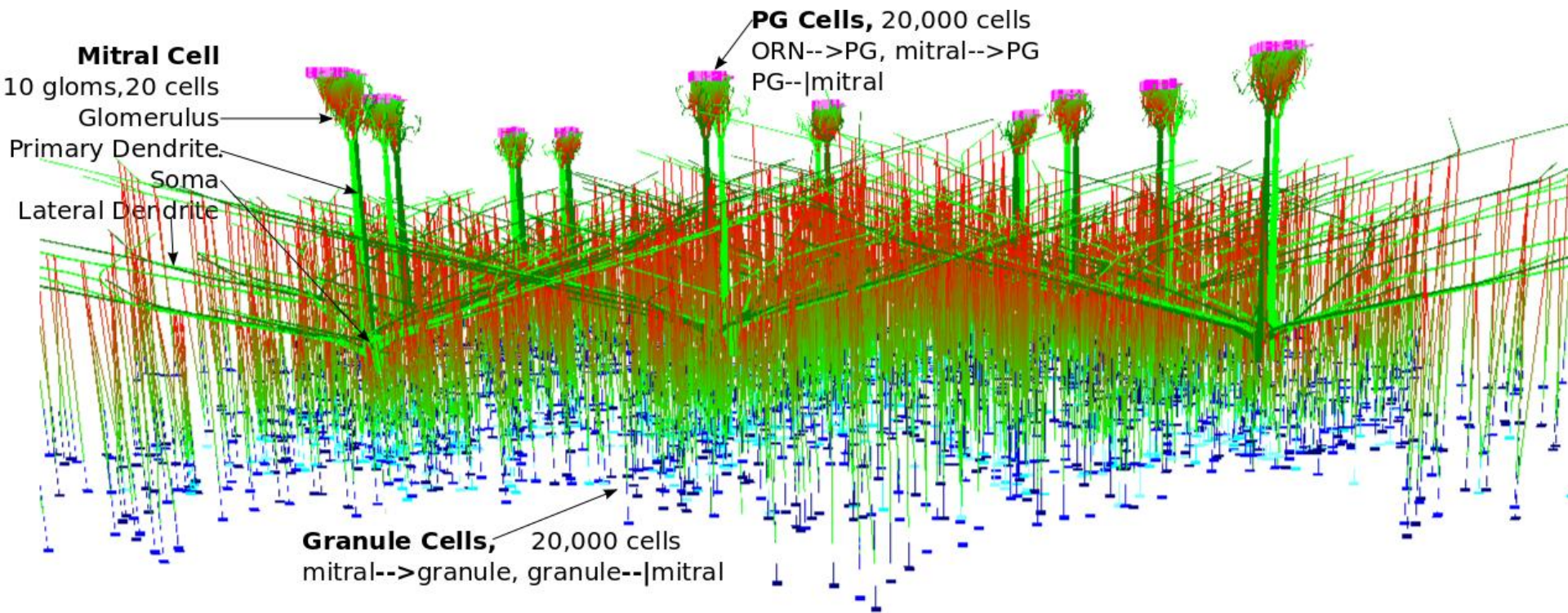
Biophysics

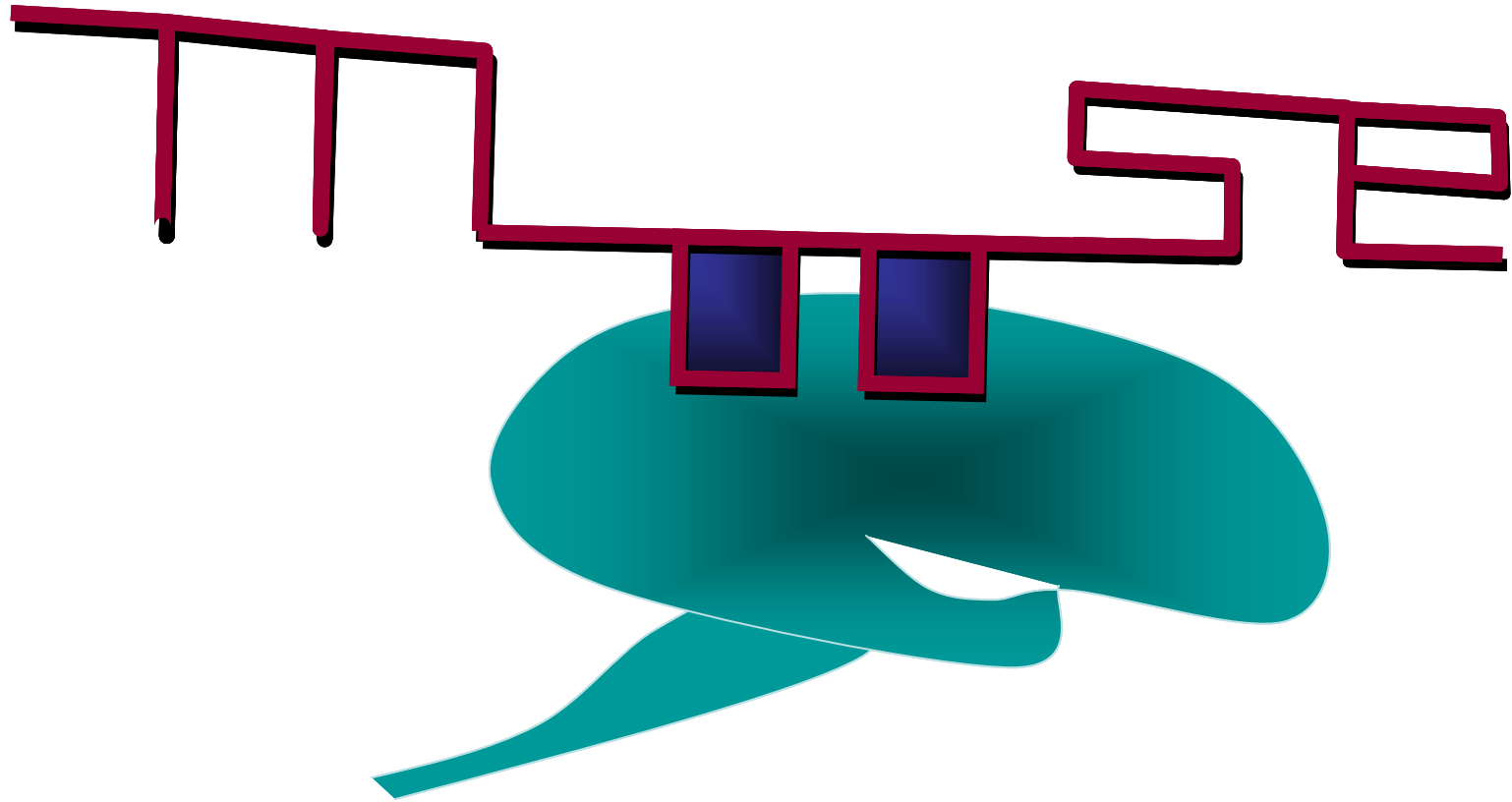


Molecules



Biophysically-detailed network model





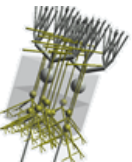
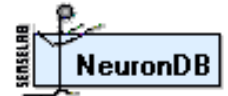
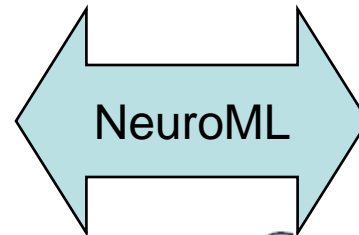
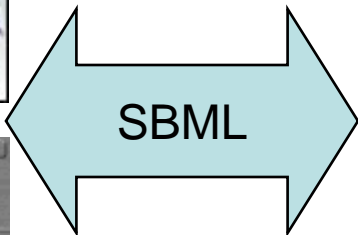
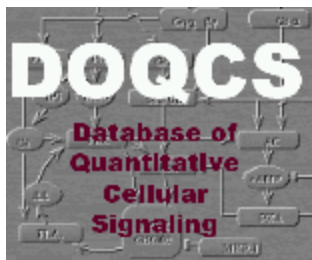
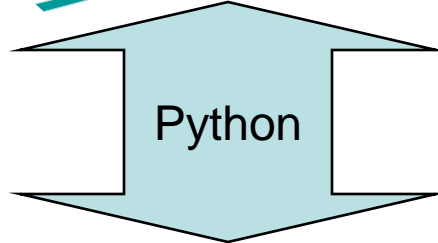
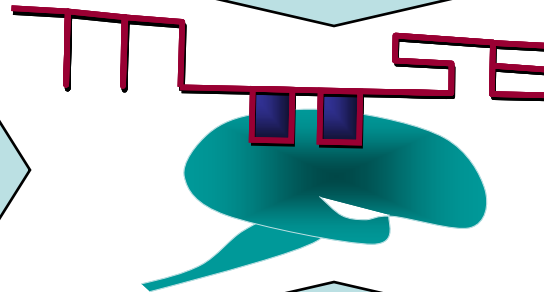
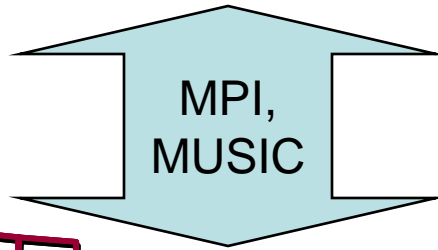
The Multiscale Object-Oriented Simulation Environment

<http://moose.ncbs.res.in>,
<http://sourceforge.net/projects/moose/>

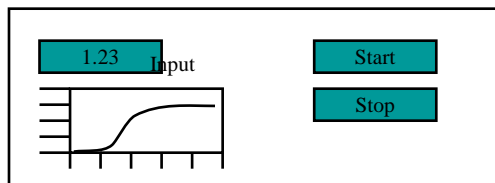
LGPL but uses GPL modules

C++/Python/Qt/GSL/OpenGL and many many more...

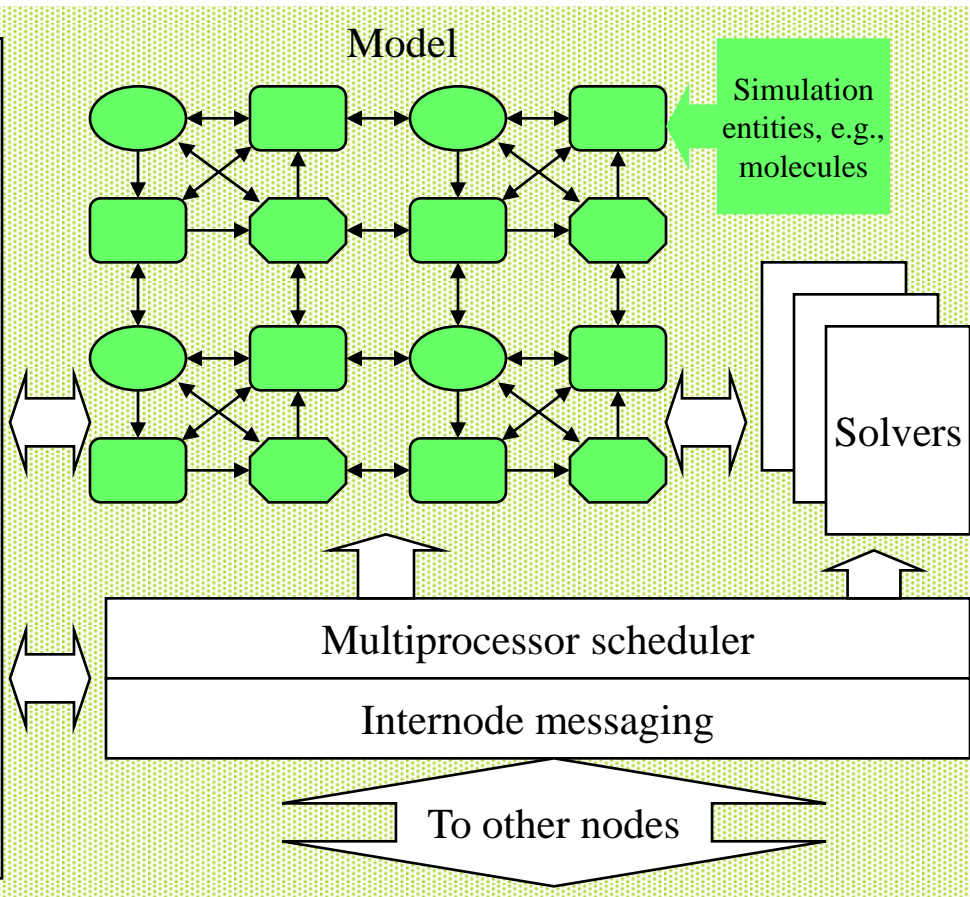
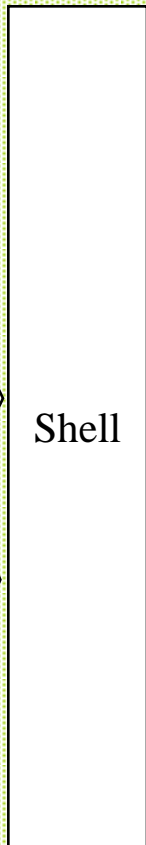
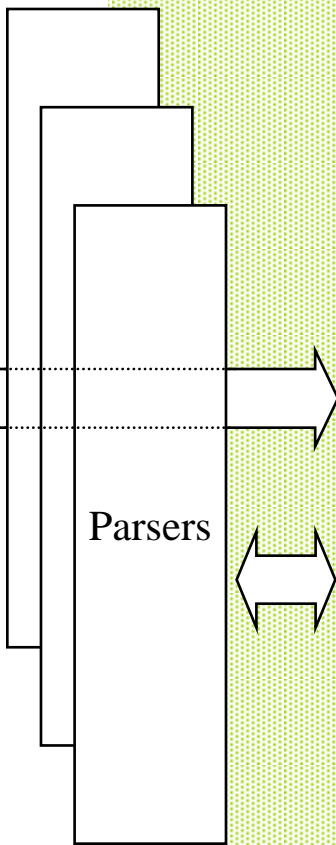
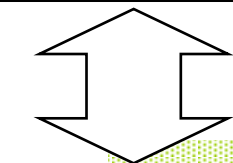
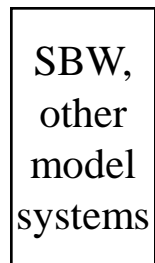
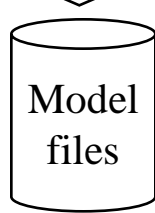
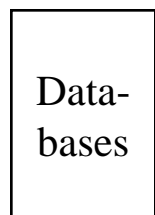
MOOSE supports standards



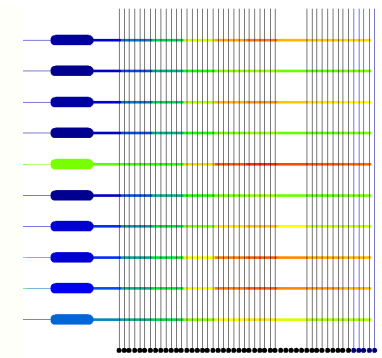
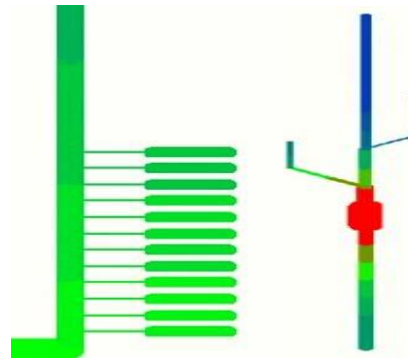
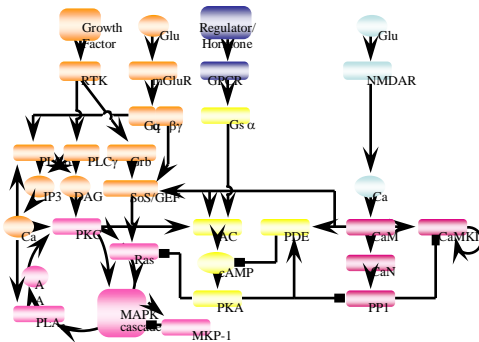
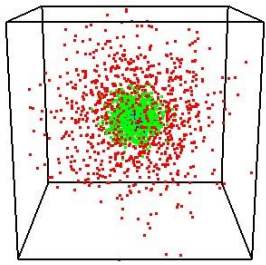
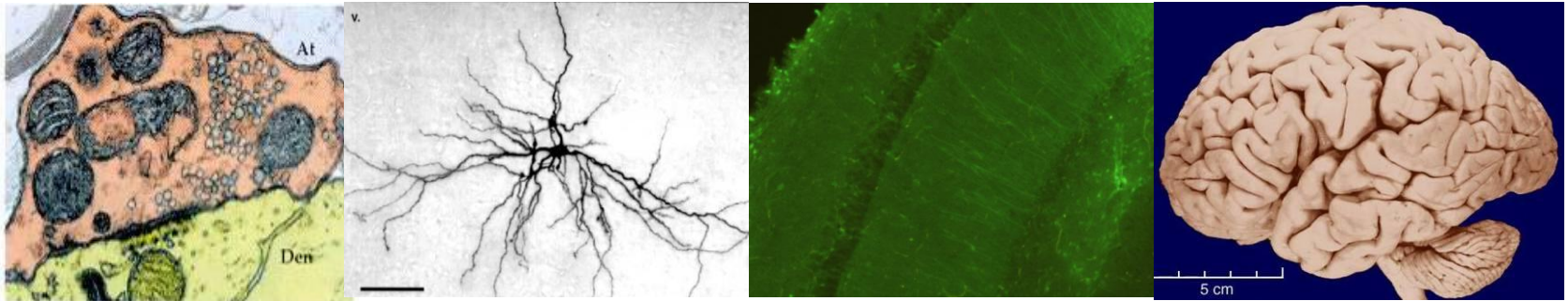
User interfaces



External I/O



Modelling across scales



Single particle
(Smoldyn plugin)

Compartmental
ODE and stochastic
Steady-state solver

Cellular biophysics

Network

Multiscale: biophysical network

Multiscale: SigNeur



Man in light blue shirt and glasses.

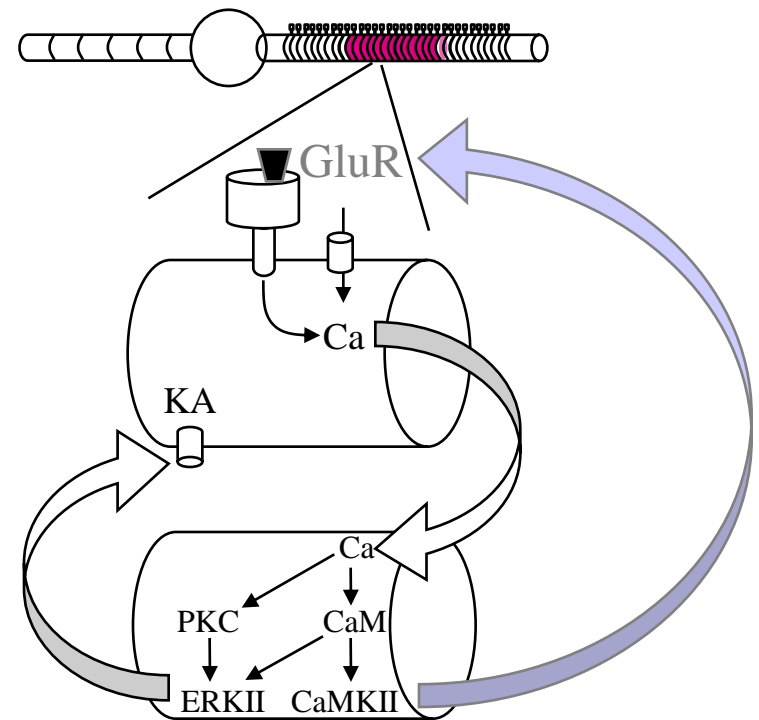
Man in green t-shirt and jeans, touching the moose's head. ID badge visible.

Large taxidermy specimen of a moose with large antlers.

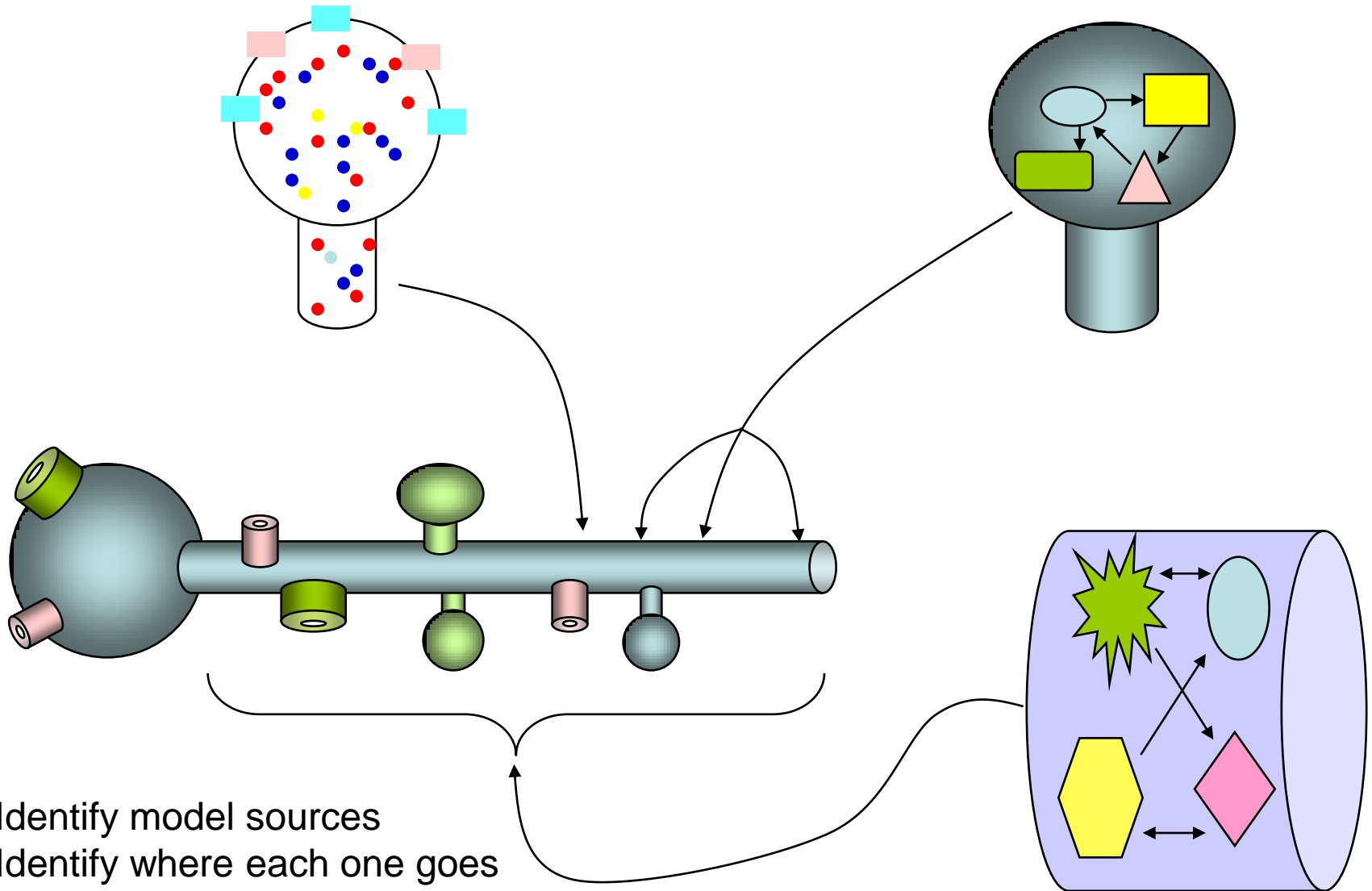
CFR 2008
Portland
Oregon
USA

Multiscale language requirements

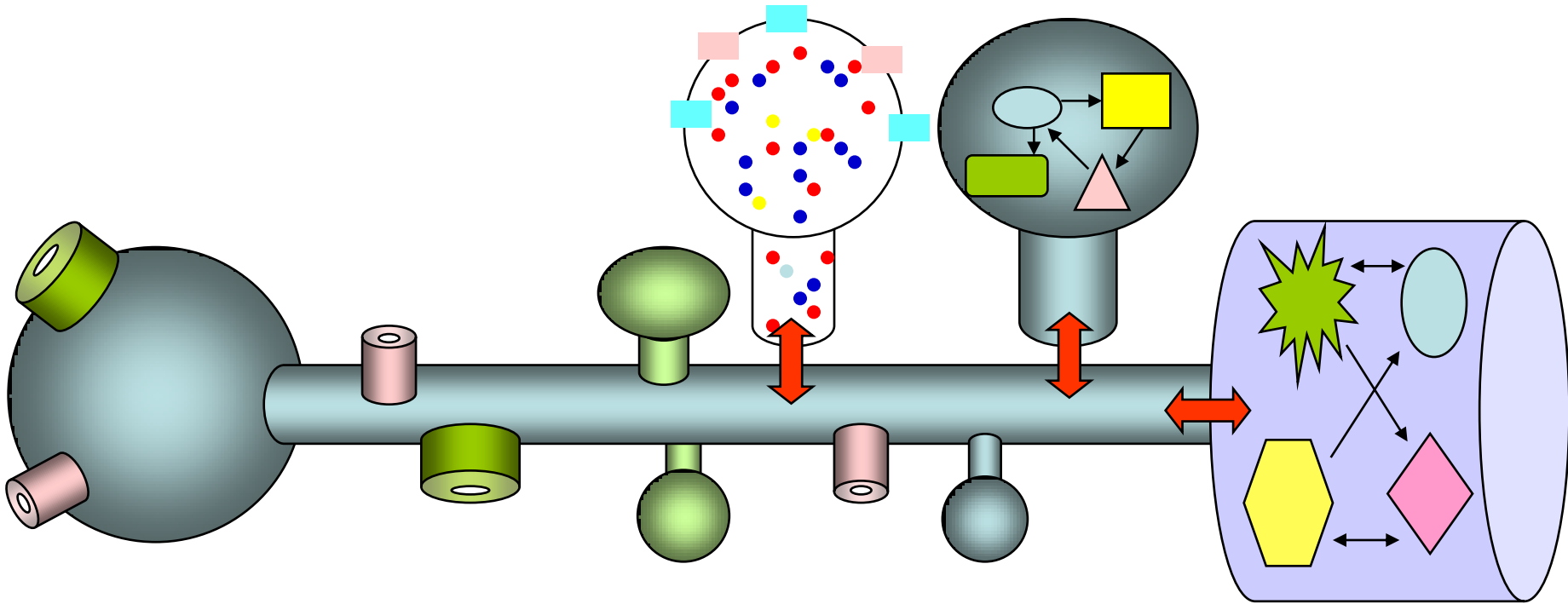
- Composition specification:
 - Single NeuroML model
 - Multiple SBML models
 - Diffusion specification
 - Entity mapping
- Interface specification
 - Molecules -> channel properties
 - Ion flux (Ca) -> Signaling effects
 - Synaptic input -> Ligand molecules
 - Molecular gradients/junctions
- Geometry specification
 - Spines
 - Junctions
 - Caps
 - Mapping to detailed morphology
 - Spatial transforms and writhing
- Mechanics specification
- Control specifications:
 - Solvers
 - Runtime
 - Output variables





1. Composition specification

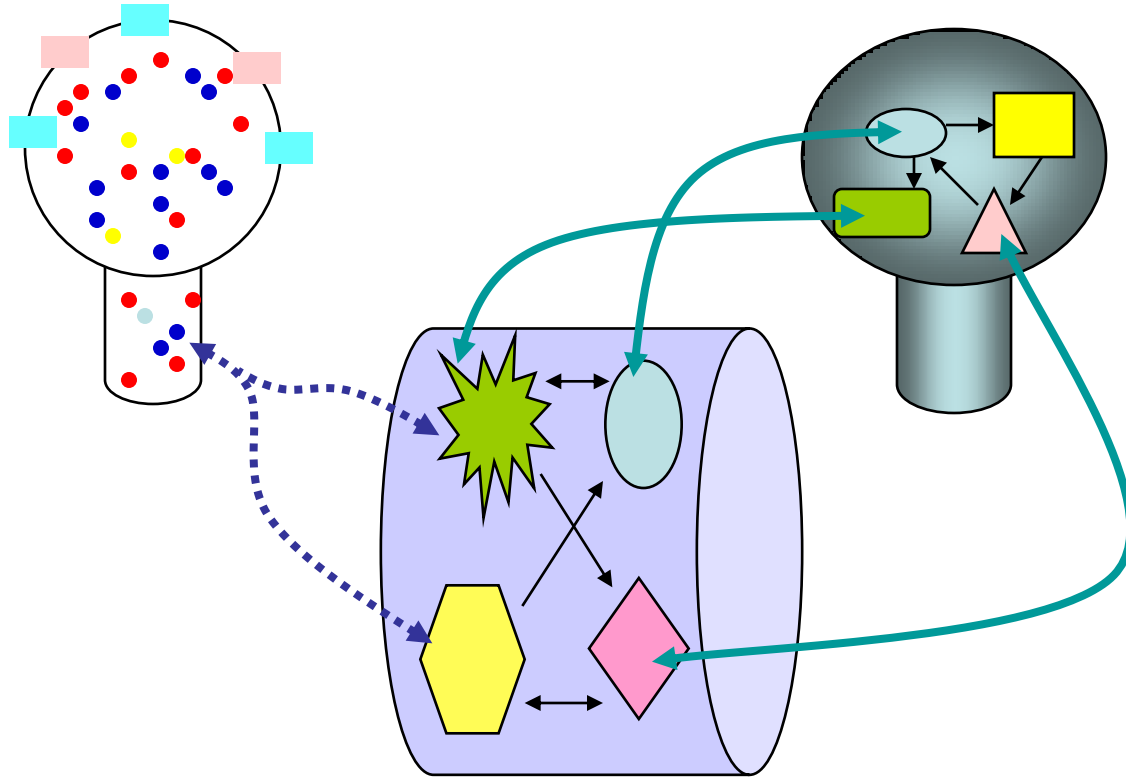




1. Composition specification

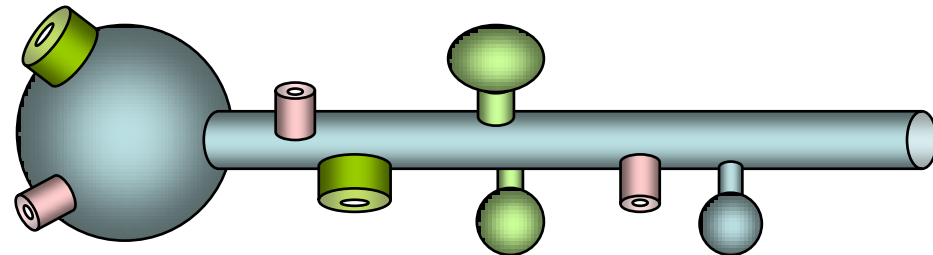


- a. Identify model sources
- b. Identify where each one goes
- c. Diffusion along compartments 
- d. Diffusion into spines 

1. Composition specification

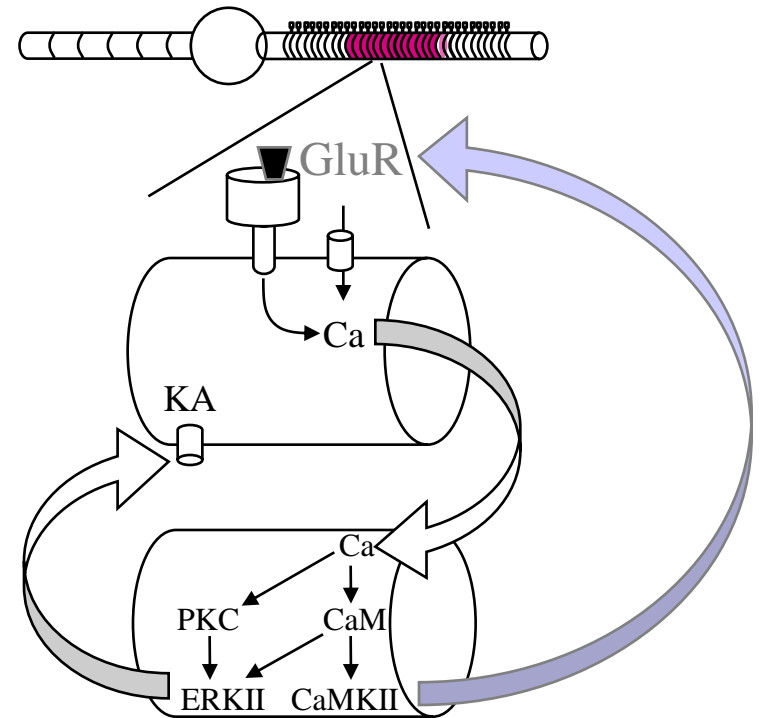


- Identify model sources
- Identify where each one goes
- Diffusion along compartments
- Diffusion into spines
- Entity mapping: Unique 
- Entity mapping: complex 



2. Interface specification

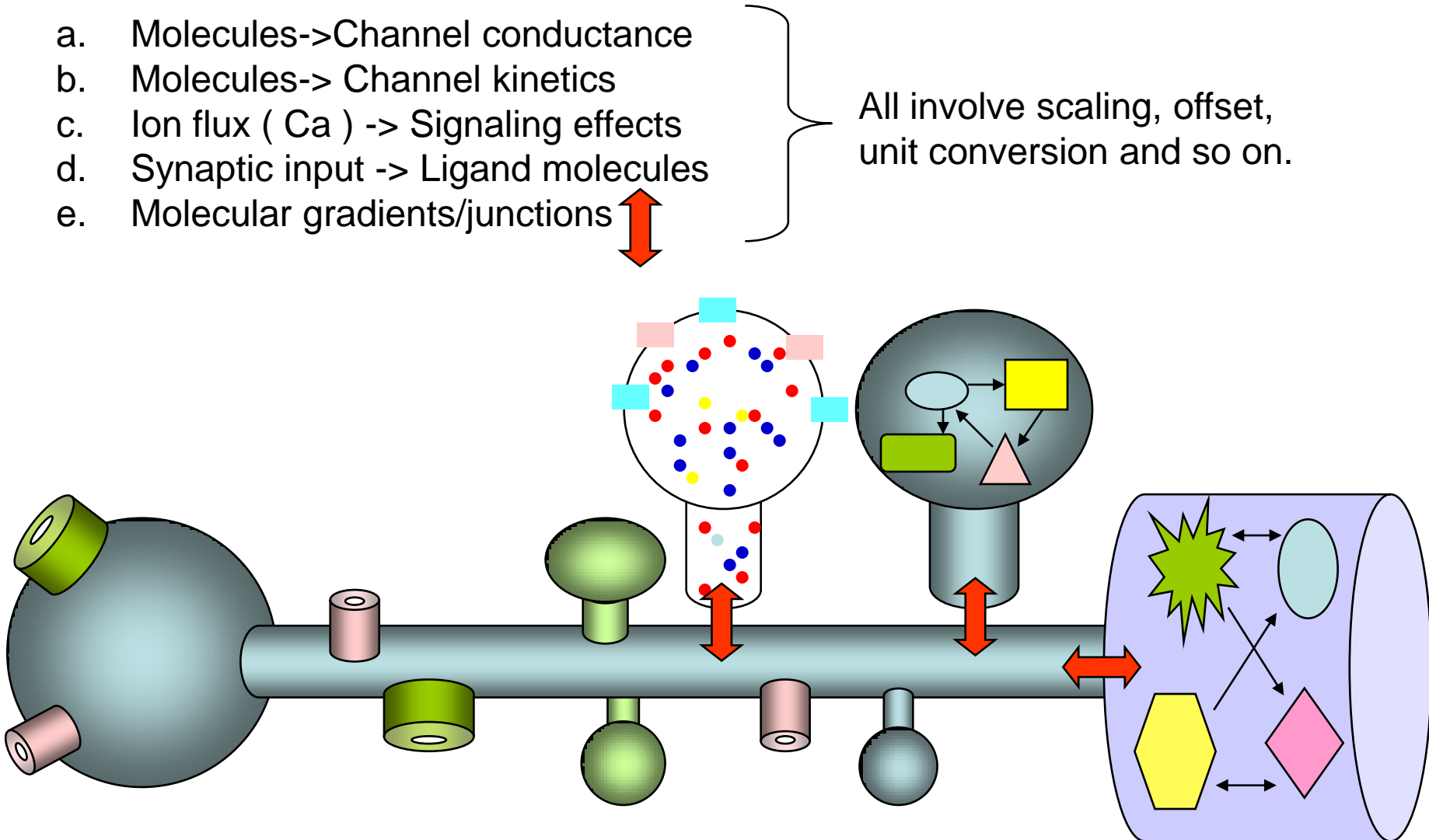
- a. Molecules->Channel conductance
- b. Molecules-> Channel kinetics
- c. Ion flux (Ca) -> Signaling effects
- d. Synaptic input -> Ligand molecules



2. Interface specification

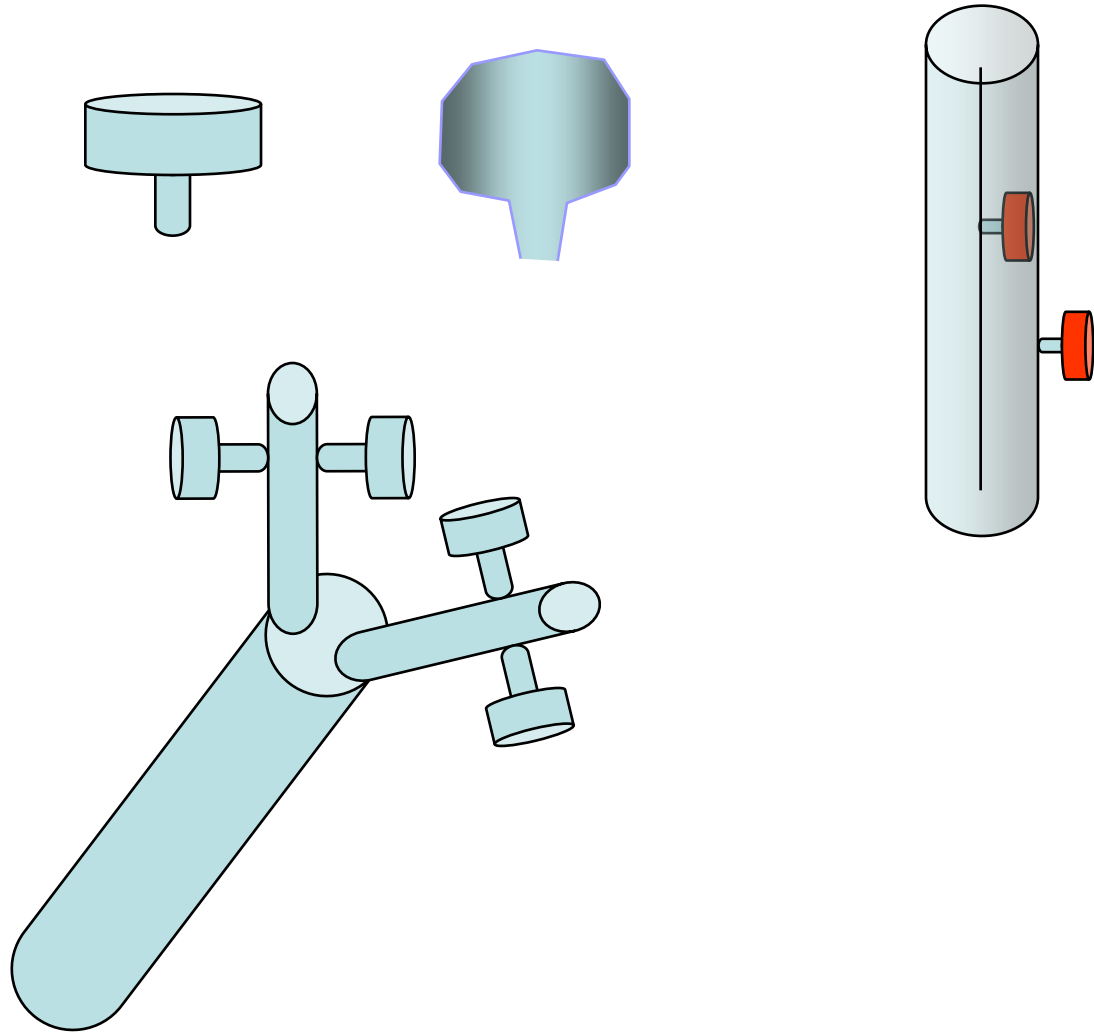
- a. Molecules->Channel conductance
- b. Molecules-> Channel kinetics
- c. Ion flux (Ca) -> Signaling effects
- d. Synaptic input -> Ligand molecules
- e. Molecular gradients/junctions

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



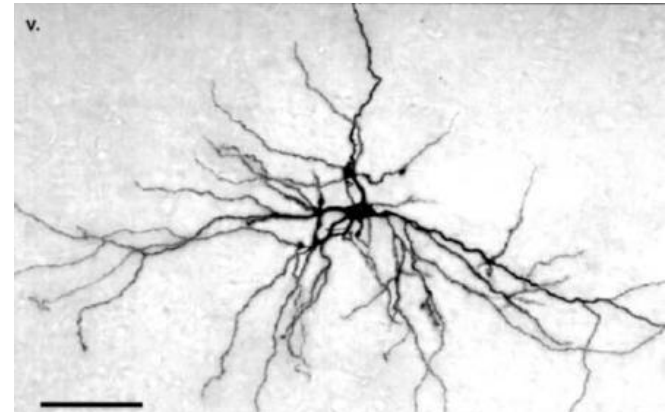
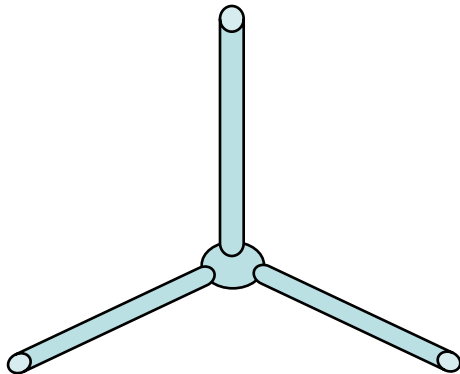
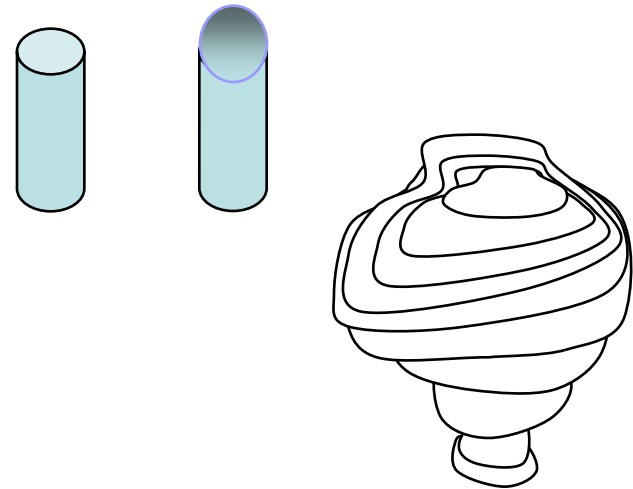
Geometry specification

- a. Spines
- b. Junctions



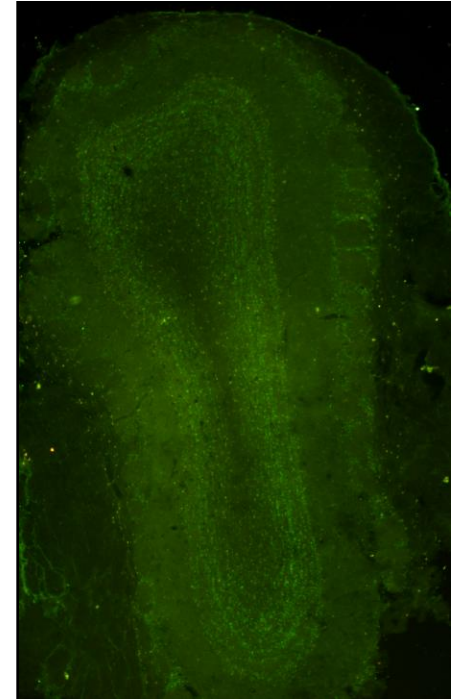
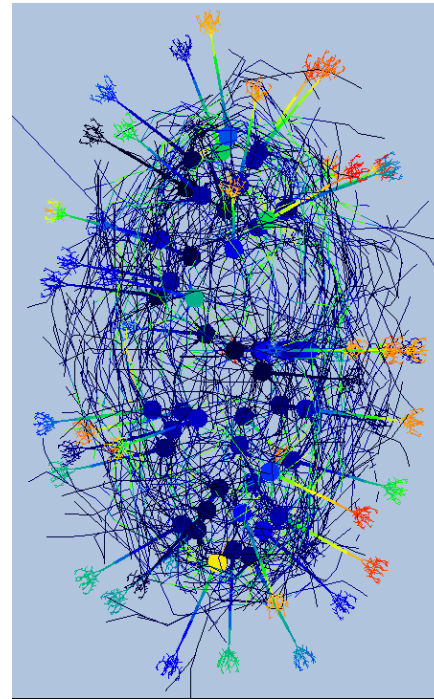
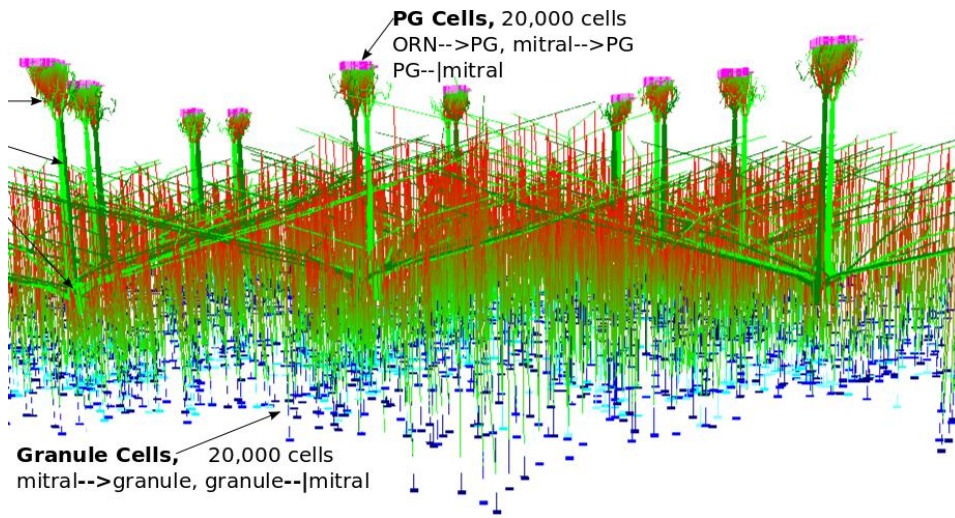
Geometry specification

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

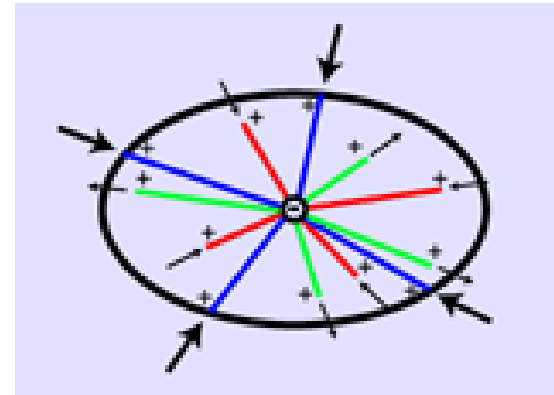
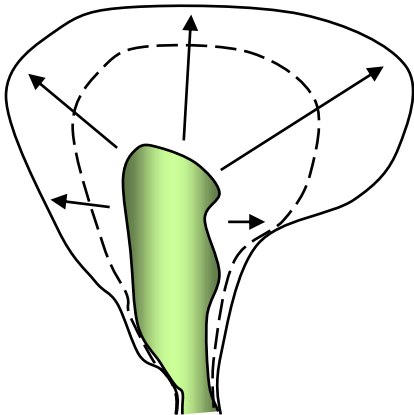


Geometry specification

- Spines
- Junctions
- Caps
- Detailed morphology: meshes
- Detailed morphology: mappings
- Spatial transforms
- Writhing

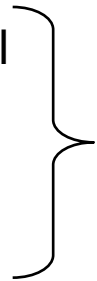


4. Mechanics specification

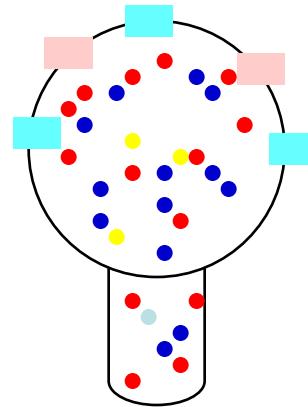


5. Control

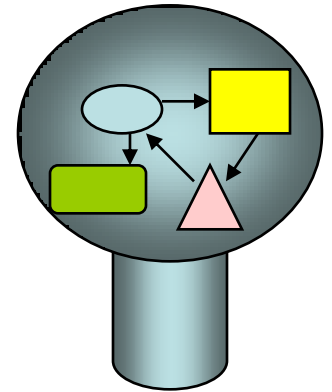
- a. Solvers
- b. Runtime control
- c. Output variables and formats



SEDML



Vs.



Multiscale language requirements

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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

INCF
SBCNY
NCBS/TIFR
DAE
DBT
EU-India Grid

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

