Summary of meeting to discuss possible future NeuroML/SBML interactions

Location:	European Bioinformatics Institute, Hinxton, UK
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Attendees:	**EBI:** Nicolas le Novere, Michele Mattioni, Sarah Keating, Nicolas Rodriguez; **UCL:** Padraig Gleeson, Angus Silver, Guy Billings; **Univ. Hertfordshire:** Volker Steuber; **Textensor Limited:** Robert Cannon
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Motivation for meeting

It is becoming increasingly clear that models in computational neuroscience can benefit from including models of biochemical reactions, and that computational neuroscientists need to interact more closely with the systems biology community. The most productive way of interacting will involve the exchange of models between computational neuroscientists and systems biologists and therefore requires the use of common model description languages. This meeting was arranged between users/developers of NeuroML and SBML to exchange ideas on how more detailed models of neuronal systems might be produced in the future, which fall within the scope of both NeuroML and SBML.

Discussion

The meeting opened with introductions and an update of the current status of each of the languages. Development of Level 3 of SBML is continuing, which will have a more modular structure than previous Levels. The draft specification of Level 3 Core has recently been released, and work on each of the packages is proceeding, some of which have reached the draft proposal stage. While the Spatial Diffusion and Geometry packages have relevance for spatially distributed biochemical signalling models, no package is specifically addressing electrophysiological modelling.

The NeuroML specifications have been stable at version 1.8.1 for the past number of months and work is proceeding towards v2.0 of the language. Working Groups have been set up in the areas of Morphologies, Channels and Synapses, and NeuroML developers are involved with the INCF initiative on standards for large scale network descriptions.

Possible scenarios for NeuroML-SBML interaction

A number of options were discussed for how to standardise the representation of biochemical signalling pathways in neuronal models:

1) Extend NeuroML with the ability to express biochemical signalling pathways (i.e. build in a subset of SBML)
2) Extend the Spatial Diffusion and/or Geometry packages of SBML to allow cable modelling & introduce a concept of membrane potential
3) Keep the focus of NeuroML on neuronal modelling & provide a generic framework for interacting with internal & external pathways expressed in SBML (possibly having the framework generic enough for interacting with CellML also).
4) Develop a new model description language from scratch.

Of these options, there was general agreement that option 3) was the way to proceed, as the computational neuroscience community has more to gain from this interaction than the wider systems biology community. Also, keeping the signalling pathway elements as valid SBML allows existing tools for that language to be used for analysis of these parts of the model.

A proposal for incorporating SBML in NeuroML cell description files

In line with this option, a proposal was made to incorporate information on signalling pathways into NeuroML version 2.0 cell description files. The overall structure of the file would look something like:

< cell definition starts>
    <segments & segment groups>
    <channel distributions in terms of groups>
    <signalling pathways in terms of groups>
<end of cell definition>

i.e. in addition to statements like "NaP channels are present on group dendrites with density XXX" (as is possible in NeuroML v1.x Level 2 cell descriptions), statements like: "Pathway from file CaSignalling.sbml is present on group dendrites" should be allowed.

Potential Issues

What is missing from this description is information on the spatial discretisation to use for the signalling models, i.e. if there are 100 compartments used by the simulator for the electrical part of the simulation will this correspond to 100 instances of the SBML model? A larger or smaller spatial discretisation may be needed for the signalling part, as well as potentially a different timestep. It was generally agreed that the discretisation is not an issue for the simulator independent model description, it should be left up to the simulator to decide (this is still an open issue for electrical discretisation). Whatever way the cell is modelled, there should be an unambiguous way to reference variables according to the NeuroML description, i.e. if ca is a species in the SBML description, "the value of ca at 0.5 along segment x" should be mapped by the simulator to the correct variable in its set of signalling models.

In a cell with spatial extent there can be transfer of species between adjacent modelled compartments. Some specification of diffusion rate between these should be included in the cell description and the simulated pathways modelled appropriately.

A generic SBML file can contain a number of compartments in which species are described. It may be the case that restrictions need to be placed on the compartment names in an SBML file used in an NeuroML cell description. It is interesting however to consider the case where a pathway is present on group "spines", and the SBML model contains compartments spine_head, spine_neck, etc. This involves a problematic distribution of the morphological information between the NeuroML and SBML elements of the model description, with associated difficulties for supporting software.

Current work in this area

The concepts described here will only be useful if there is support in simulation tools for kinds of models covered. The MOOSE simulator (http://moose.sourceforge.net) is developing reading/writing capabilities for SBML and native NeuroML support is planned, using a library in early stages of development, libNeuroML, for loading such model components.

The NEURON simulator is planning on support for biochemical reaction-diffusion models (http://www.neuron.yale.edu/phpBB/viewtopic.php?f=40&t=1495). Also, a utility in Python has been developed (SBML2NEURON) to run basic SBML models on this platform: http://www.neuroml.org/neuron_tools.php.

Future plans

These concepts will be discussed further at the INCF Multiscale Modelling Meeting in Bangalore in November, which some of the participants to this meeting will attend. Prior to that, these initial ideas for including signalling pathways in NeuroML cell descriptions will be extended further, and initial implementations of these concepts on NEURON and MOOSE are planned. Future work on support for SBML model components in NeuroML will be carried out in the NeuroML Working Groups which interested parties are encouraged to join (http://www.neuroml.org/roadmap.php).