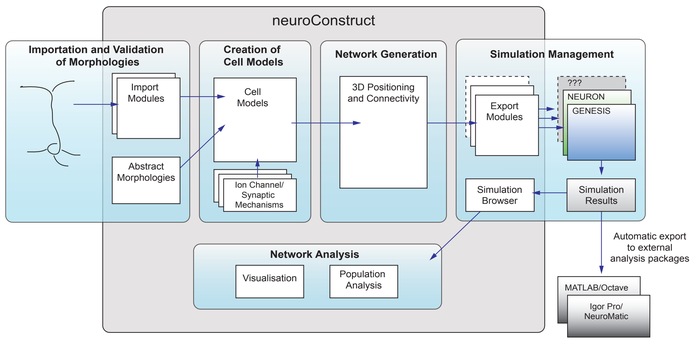
Parallel simulations of a 3D cerebellar network created with neuroConstruct

Padraig Gleeson[1], Volker Steuber[1,2], R. Angus Silver[1]

[1]Department of Physiology, University College London, UK
[2]Science and Technology Research Institute, University of Hertfordshire, UK

neuroConstruct

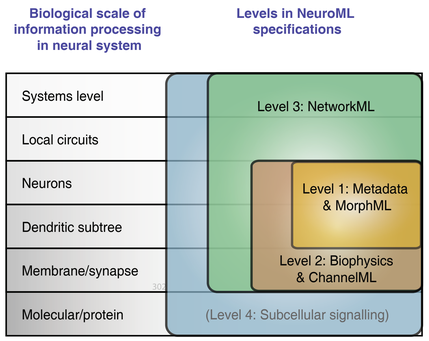
The properties of ion channels and synapses can have a profound effect on higher level behaviour of neural systems. Linking these low level mechanisms to higher level neural network behaviour can be aided by the development of biophysically realistic computational models. However, such models are very complex and can require large computational resources. We have developed a software application, neuroConstruct, which facilitates the construction of such network models. Models of cells with detailed morphologies and voltage and concentration-dependent membrane conductances can be created through a graphical user interface, and are based on open standards (NeuroML) ensuring transparency of the underlying physiological parameters and portability of the models to multiple simulation platforms. Complex connectivity patterns between groups of cells in 3D can also be generated. neuroConstruct automatically generates code for the numerical simulation on either NEURON or GENESIS. neuroConstruct projects can be generated and controlled either through the GUI or a command line interface based on Jython.



The main functional areas of neuroConstruct and the interaction with simulation environments and external packages

NeuroML

The NeuroML project is an international collaboration to allow greater access to and reuse of models of neuronal systems. The current focus of the project is on standardising a number of key objects which are common to many simulators, allowing an unambiguous description of the physiological concepts being modelled. The standards are currently specified as Schemas describing the contents of XML (Extensible Markup Language) documents. There are currently 3 Levels of compliance to the NeuroML standards. These deal with different levels of description of the nervous system.

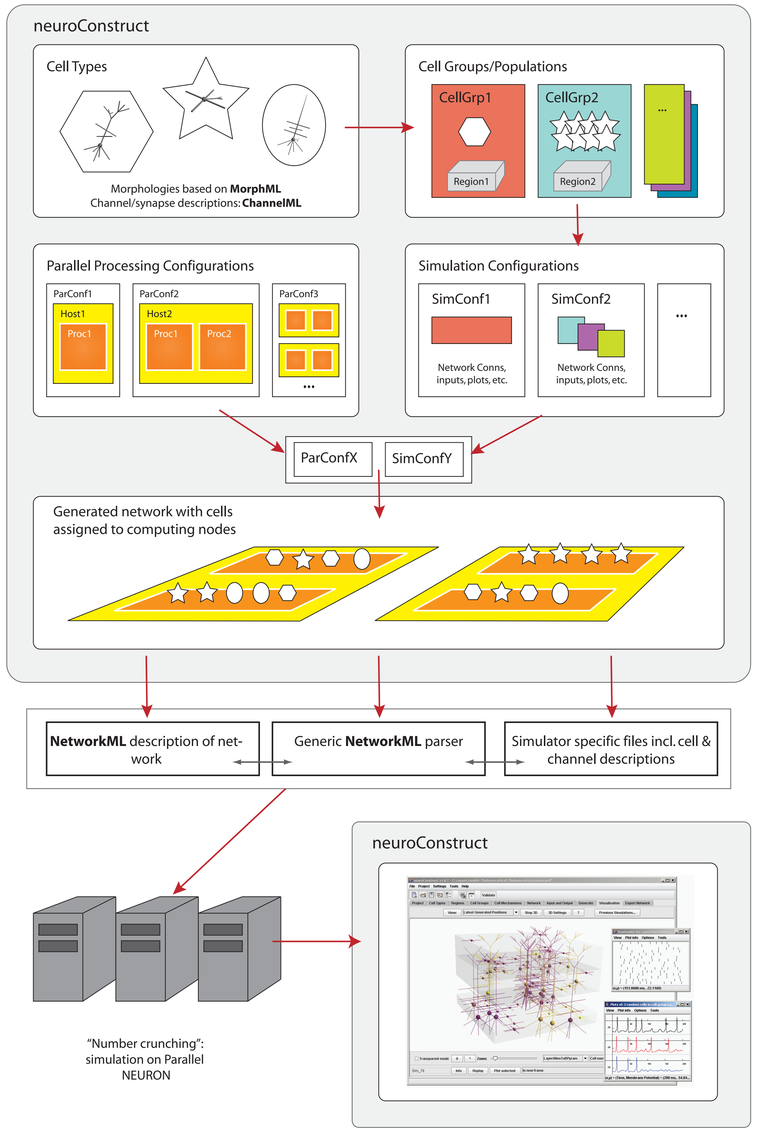


The relationship between the Levels in the NeuroML standards and the various scales at which models of neuronal information processing are commonly created

Level 1: This Level of the standards defines Metadata (contributing authors, citations, generic properties, etc.) which can be used to provide background information on objects at any of the Levels. It also defines MorphML, which is used to describe neuroanatomical information, in particular the branching structure of neurons.

Level 2: This builds on Level 1 and allows specification of the biophysical properties of neurons (e.g. specific capacitance, membrane/cytoplasmic resistance, location and density of membrane conductances, etc.). ChannelML allows the description of models of voltage and ligand gated ion channels, synaptic mechanisms and the dynamics of internal ion concentrations.

Level 3: This level allows specification of the positions in 3D space of neurons, their interconnectivity and electrical inputs. Positions and connectivity of cells can be specified either with an explicit list or implicitly by specifying an algorithm for defining cell packing and connectivity rules, etc.



Schematic illustrating the independent specification of network structure and Parallel Configurations and the generation of distributed networks with neuroConstruct

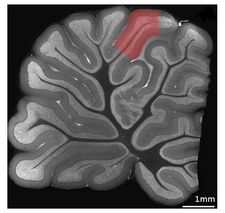
Parallel network simulations

A neuroConstruct project can have multiple Cell Types, the structures of which are specified in a simulator independent format, closely linked to MorphML. Cell Groups consist of a Cell Type, the 3D Region in which they are placed and a specification of the packing pattern to use. Simulation Configurations are sets of Cell Groups, together with Network Connections, electrical inputs and lists of variables to plot and/or save during the simulation. A project can have many of these, each designed to illustrate a different aspect of the behaviour of the cells in the network, e.g. activity of single cells, small networks of a subset of Cell Groups, large scale network activity.

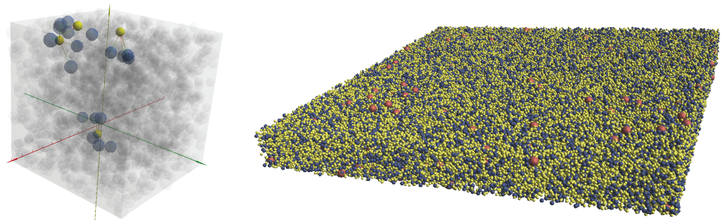
The various configurations of the parallel computing environment in which network simulations can be run are separate from any specific Simulation Configuration. These Parallel Configurations can include: a single processor on the local machine, a number of local processors, or a set of hosts each of which can have multiple processors. At the time of generation, the cells and connections for a particular Simulation Configuration are created first, and then the cells are assigned to the computing nodes as defined in the chosen Parallel Configuration.
To create an executable simulation, a NetworkML file specifying the network structure plus distribution across the nodes is created, along with a generic NetworkML parser written in Python (appropriate for any NetworkML file and any simulator supporting Python) and files specific for the simulator, to create the cells and manage the simulation. Currently Parallel NEURON is supported, but the scheme could be extended for other simulators, potentially accessing them through a standard interface such as PyNN.

Cerebellar Granule Cell Layer Model

The ability to execute simulations in parallel environments allows larger scale simulations to be generated. The system we are currently focussing on is the granule cell (GrC) layer of the cerebellum. To this end we are collaborating with Zoltan Nusser's lab to obtain detailed anatomical data on the densities of GrCs, mossy fiber terminals and Golgi cells in the GrC layer of P30 rats, to age match the electrophysiolgical data collected in the Silver lab.
The latest version of neuroConstruct has allowed us to extend the initial 3D GrC layer model from Gleeson et al 2007 to reflect a more realistic anatomy and to scale up the size of the simulation. We have constructed a model of a 1mm by 1mm patch of GrC layer, a volume sufficiently large to encompass a number of distinct receptive fields within the fractured somatotopic map (Bower and Kassel, 1990). A smaller scale version of the network with the same cell densities and conenctivity can be used when multiple simulation runs are needed to investigate the influence of anatomy and synaptic plasticity on signal processing in this brain region.



Region of cerebellar vermis under investigation. Data: Andrea Lorincz, Zoltan Nusser



Two versions of the cerebellar granule cell layer model incorporating realistic cell densities and connectivity. Left: cube of side 100μm containing 2560 cells. Right: 1mm square by 100μm thick patch containing over a quarter of a million cells. Granule cells are in yellow, mossy fiber terminals in blue, Golgi cells in red.

Conclusions

- **We have extended neuroConstruct to automatically generate code for running simulations on multiple processors using the Python scripting version of Parallel NEURON.**
- **This allows the generation of networks of hundreds of thousands of cells.**
- **Simulations can be created on a scale much closer to real biological networks**
- **neuroConstruct can be freely downloaded from http://www.neuroConstruct.org. Email p.gleeson@ucl.ac.uk about obtaining a beta release of the parallel version of neuroConstruct. The latest NeuroML specifications can be found at http://www.NeuroML.org.**

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University of Hertfordshire · NeuroML XML for Computational Neuroscience · neuroConstruct Biophysical Neural Network Modelling Software