Development of model-based publication for scientific communication.

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Problem

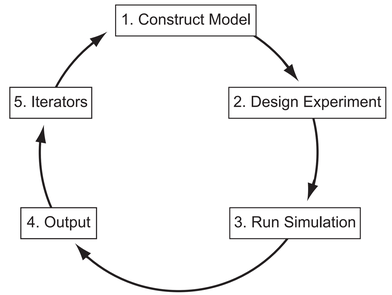
Currently, both paper and digital publication lack model comparison tools, model lineage inspection tools, model verification tools, and replication of results is greatly complicated. Consequently, peer review is only phenomenological, models can not be progressively improved, and science cannot advance.

How can different models be compared?
How can emergent properties of a model be quantitatively distinguished from those for which a model is tuned?
How do publications add to scientific knowledge, by their descriptive narrative or their computational extensions?

Solution

We are developing a new set of computational tools to support the evaluation, understanding, sharing, and publication of computational models of the nervous system. This is intended to lay the ground work for making models, rather than, as at present, the written description of models, the base for scientific publication in neuroscience. The Publication System is designed to be platform independent as it adheres to the CBI federated software architecture [2].

User-Workflow



1. Construct Model: Simple models can be created directly within the G-Shell by entering commands. More complex models can be imported into the G-Shell from either the GENESIS model libraries or from external model libraries. The model can also be explored, checked, and saved. Changes made to the components of a model during a research project include changes to cell morphology (e.g. spines) and membrane conductances.

2. Design Experiment: Set model parameter values specific to a given simulation, the stimulus parameters for a given simulation run or 'experiment', and/or the variables to be stored for subsequent analysis.

3. Run Simulation: Configure runtime options, check, run, reset simulation, and save model state. The model state can be saved at any simulation time step to allow it to be imported into a subsequent GENESIS session. Output is flushed to raw result storage for subsequent data analysis.

4. Output: Check simulation output and the validity of results to determine whether simulation output exists in the correct locations. Output can be analyzed either within GENESIS or piped to external applications such as Matlab, Grace, or Mathematica.

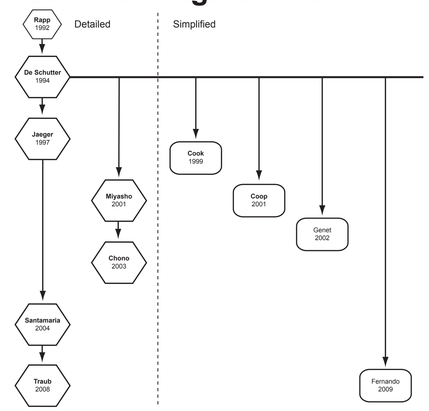
5. Iterators: Close the loop between output of results and model construction in the GENESIS users workflow. Iterators connect experimental results and model output and include for example, automated construction of simulations and batch files, static parameter searching, and active parameter searching using the dynamic clamp.

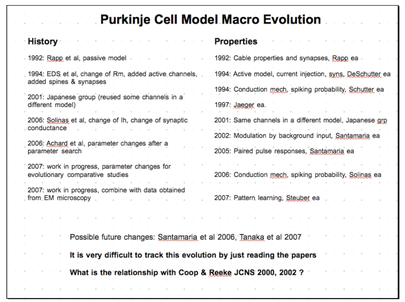
Supports micro-evolution tracking of a model during a research project.

Creation

By extension, the Publication System will allow model lineage browsing and defines multiple possible roles for a reader (i.e., global administrator, chief editor, article editor, reviewer, PI, collaborator, external reader) to comment on particular aspects of a model. This starts a dialog about the model, for example, an author could designate those who could comment on the model or comments could be restricted to those whose components are included in the model, or who have published similar models. The system becomes ultimately a new way to discourse about science and scientific results.

Model Lineage Browser





Purkinje Cell Model Micro Evolution

Morphology compartmentalization
Changes to Rm
Insertion of active conductances
Updates of maximal channel conductances

Exploration of parameter space

Cerebellar Purkinje cell [1]
One of the first "Community Models".

Coupled equations: 25,471

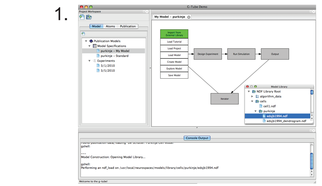
Morphological compartments: 1600
Spines (2 compartments each): 1,474
ODEs: 16,039
Soma voltage gates: 13

Main dendrite:
Compartments: 9
Voltage gates/compartment: 14
Smooth dendrites
Compartments: 105
Voltage gates/compartment: 10
Spiny dendrites
Compartments: 1485
Voltage gates/compartment: 10

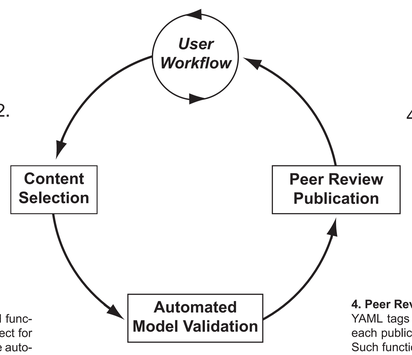
[Ca] Exponential decay eqns: 1,600
Voltage gates/compartment: 1
Ligand-gated channels, 2nd order ODEs: 1,474
Parallel fibers/spine: 1
Ligand-gated channels, 2nd order ODEs: 10
Basket cell axon/main dendritic compartment: 1
Ligand-gated channels, 2nd order ODEs: 1695
Stellate axons/smooth dendritic compartment: 2
Stellate axons/spiny dendritic compartment: 1
Ligand-gated channels, 2nd order ODEs: 105
Climbing fibers/smooth dendtiric compartment: 1

Publication-Workflow

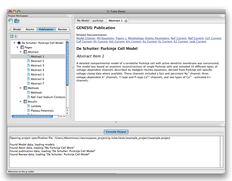
Supports macro-evolution tracking of a model between research projects.



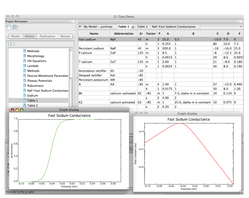
1. User-Workflow
A new project is initiated at the beginning of the User-Workflow and can either be created from scratch or based on a previously published model. During completion of the User-Workflow, the GUI automatically creates a project record by tracking all models, simulation configurations, and results of a given research project as well as maintaining a graph of ancestry during the lifetime of a model. The GUI also provides interface access to a project including: the model, model configuration, stimulation protocols and simulation configuration repositories and links workflow output selected records to a simulation schedule that defines reproducible runs of one or more simulations.

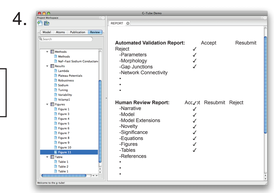


2. Content Selection
Publications are built from "publication atoms" generated by an investigator during completion of the User-Workflow. They are the smallest components of a project and are equivalent to Abstract items, sections in the Introduction, Methods, Results, Discussion, or a Table or Figure of a traditional paper based publication. An investigator uses the GUI to flag the components of a project to be incorporated into a publication.



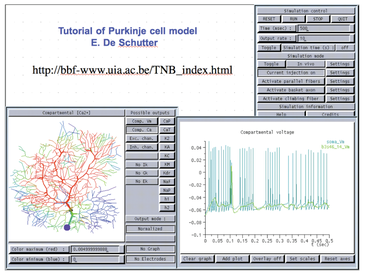
3. Automated Model Validation
Once completed, a project employs automated functionality to organize, check, and prepare a project for review. The review process is augmented by the automated verification that all figures are generated by the same model. The system will also implement other forms of semi-automatic testing, including determining the 'normality' of the range of basic parameters and an assessment of how fragile model parameters are or tests of whether a new model is significantly different from existing models. The ability to quantify where a model is located with respect to both its own parameters and those of other models is also valuable. It allows the robustness of model behavior to particular parameters to be characterized. It will be possible to designate whether or not parameters are well constrained by experimental data.

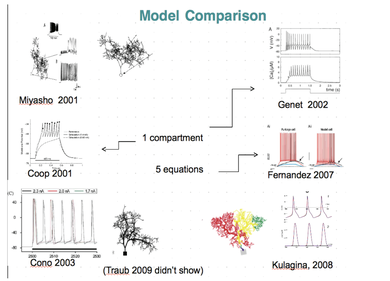




4. Peer Review and Publication
YAML tags inserted into the descriptor file associated with each publication atom assist in guiding the review process. Such functionality generates a summary of project contents that is designed to simplify peer review by providing a reader flow for a reviewer and automatically generated validation reports. Prior to manuscript submission, this review functionality can be employed by collaborators to track project development.

The Publication Workflow organizes model evolution to enable full lineage browsing.





Through the user-workflow, each individual research project becomes a tutorial of model exploration. The tutorials can then be used for convenient comparisons across research projects between models that were constructed for different targets, such as performance optimization, functional (phenomenological) correctness and anatomical and morphological completeness.

The reader roles supported by the publication system enables new ways for collaborations and provides a valuable resource the construction of reports and presentations.

The model publication database can be used to automate the discovery of relationships between models and otherwise hidden features, and to identify critical new research paths for modeling and experiment.

Conclusion

Electronic model publication enables quantitative model lineage tracking and model comparison at both macro and micro levels, detailed author attribution, objective impact measures, and thus a clear path for progress in scientific knowledge and communication

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