



Generalized Epithelial Transport Modeling: Computational Physiology

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Introduction

We are developing a set of tools that will provide a generalized framework for the development and application of epithelial transport models. Where possible, our user interface attempts to hide the mathematical and computational details from the novice modeler.

We are creating a library of reusable renal epithelial transport models. Users will be able to search this library for appropriate pre-existing models, or templates, to incorporate into their own work. The library includes models from small molecules and membrane transporters, through to whole cell models.

Collaborative and open science

Community standards are used to encode the mathematical models, simulation experiments, and associated biological information and experimental data. Using such standards ensures that models built using our tools are interchangeable with other tools.

Our tools make use of distributed version control systems to manage the encoded data (Miller *et al.* 2011). This ensures users are able to share their work with collaborators while maintaining accurate provenance records.

Current prototype implementation of our tools provides custom client-server software. Our aim is to integrate our prototype implementation into the Physiome Model Repository (Yu *et al.* 2011). This will enable users to contribute their work to the scientific community at large, providing opportunity for application of such work in novel applications.

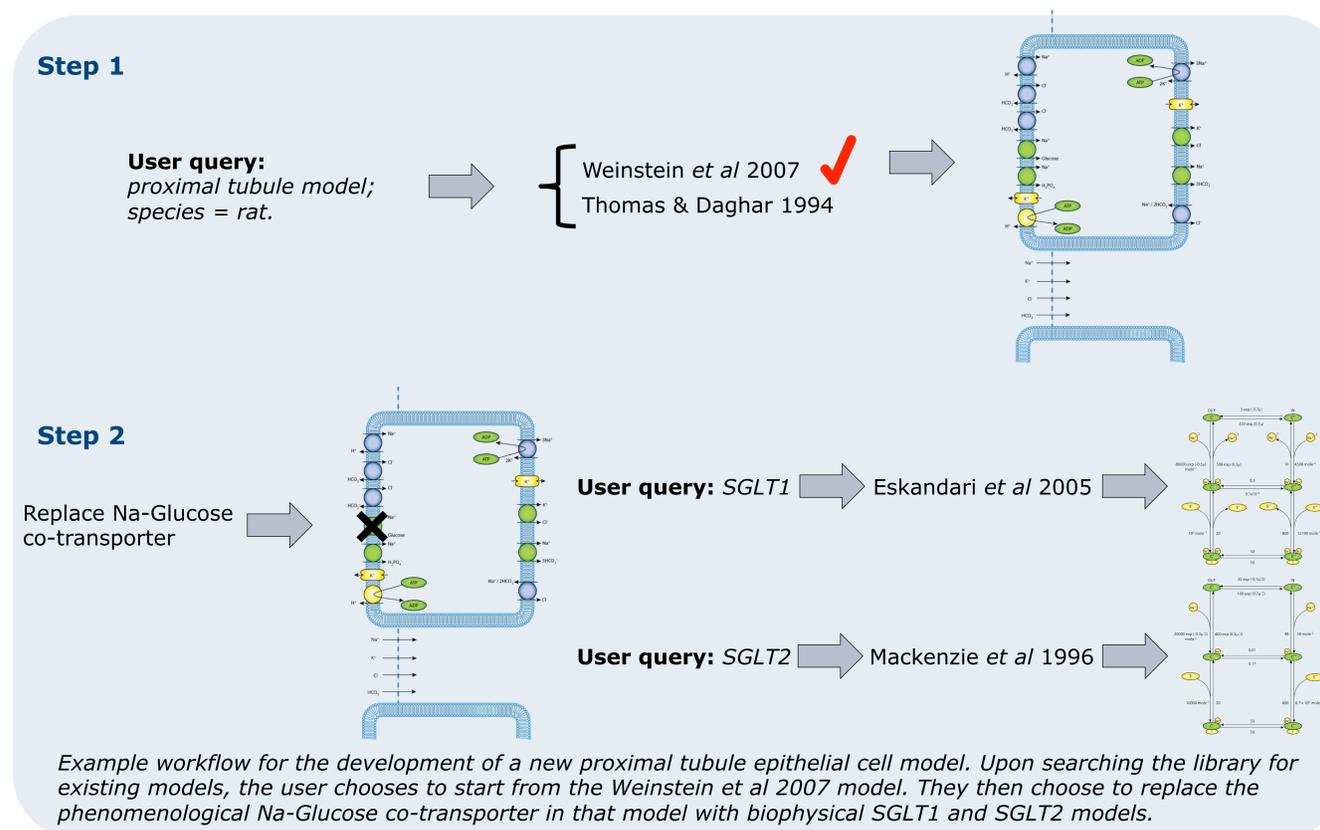
Experimental protocols & validation

Simulation experiments can be defined to correspond to specific experimental protocols. Such simulation definitions can be stored in the library as templates ready for application to specific models. If "expected" data is associated with the simulation description, we are able to use the data to aid the validation of new models to which the simulation is applied.

Methods

Our tools and model library make use of CellML (<http://cellml.org>) to encode the mathematical models and SED-ML (<http://sed-ml.org>) to encode the simulation experiments. Encoded data are annotated with additional information to describe the model beyond the mathematical relationships. Such information may include: the specific biology a given part of a model is representing; the identity of the person who encoded the model; or a link to the published article in which the model was first published (or subsequent publications refining the model).

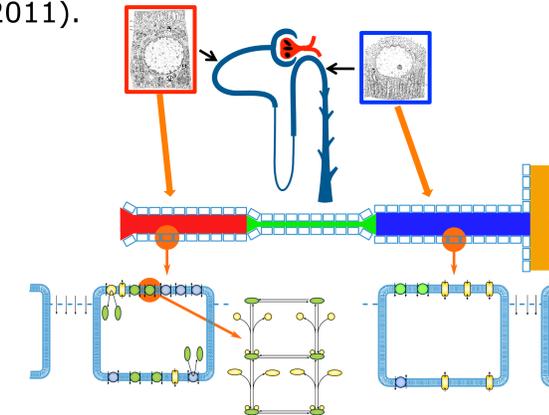
The model library consists of encoded models designed to be modular and reusable. Complex models may be created through the assembly of existing modules from the model library, and then contributed back to the library for future use. Model annotations are used to guide the user as to appropriate models to use for a given purpose and to automate the model assembly process, as shown below.



In addition to making use of existing whole cell models from the library, users are able to make use of *empty* or template cell models. The user will then be able to add the desired collection of ionic species and transport processes from the library to the appropriate compartments and membranes of the template cell model. Such models can be assembled and simulated following the method of Latta *et al* 1984 to ensure conservation of mass and maintenance of electroneutrality.

Future work

By making use of accepted community standards to encode and annotate the data in our library, we ensure that models developed using our tools are available for use in other contexts. In particular, we are developing a finite element nephron model which will be able to directly make use of models from the library as shown below. This work is being performed under the OpenCMISS software project (Bradley *et al* 2011).



References

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Acknowledgements

Supported by the Virtual Physiological Rat Project, NIH grant P50-GM094503.