Introduction

The Biochemical Simulation Environment (BISEN) package provides a framework for constructing mathematical models to simulate and analyze the kinetics of biochemical systems, integrating data on biochemical thermodynamics and kinetics into a set of model equations and computer codes (see figure 1). This package can generate systems of differential equations for user-specified multicompartments of enzymes and transporters accounting for proton and metal cation binding, electrophysiology, distribution of biochemical reactants (e.g., [ATP]) into multiple rapidly converting chemical species (e.g., [H-ATP], [K-ATP], [Mg-ATP]), buffering of protons and metal cations, and the effect of temperature, ionic strength and reaction thermodynamics. For large systems, manual construction of such models is error prone.

Large scale model

To put BISEN to the test, a model of the tricarboxylic acid cycle and oxidative phosphorylation was successfully reproduced as a BISEN model.

Fig. 4: Left: Schematic of the TCA cycle model (Wu et al. 2007). Right: Simulations (lines) and data (symbols) for state 2 and state 3 respiration.

For the large scale example the input file consisted of roughly 50 declarations while the output model corresponded to 1200 lines of MATLAB code. Models of this size and larger cannot realistically be built without a tool like this. The modularity of the approach enables the user to compare different models for different enzymes and transporters while maintaining a database of model components. Models are collected at http://www.biocoda.org (see figure 5).

Fig. 5: Biological components databank website

Future work

Features to export BISEN models in the Systems Biology Markup Language (SBML) and CellML formats are planned for future updates of the package. We are currently working with the CellML developers so that the next CellML specification is engineered to fit with the thermodynamic and ion dissociation databases.

Availability

BISEN can be obtained at: http://bbc.mcw.edu/BISEN

References


Funding: This work was funded by NIH grant HL072011.