

**Quantitative and Computational Cell Biology: The Virtual Cell Approach**  
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The *Virtual Cell* is a unique software environment for quantitative cell biological research that is being developed at the National Resource for Cell Analysis and Modeling (<http://www.nrcam.uhc.edu>). It provides a sophisticated framework for analyzing, modeling, and simulating cellular function that can range from simple molecular motors to tissue-wide processes. It is deployed as a distributed application to be used over the Internet, being freely accessible to all members of the scientific community.

The *Virtual Cell* has been specifically designed to be a tool for a wide range of scientists – from experimental cell biologists to theoretical biophysicists. On the one hand, models of cell biological processes can be easily created, allowing quick testing of simple models to evaluate hypotheses or to interpret experimental data. On the other hand, the *Virtual Cell* provides an integrated framework that facilitates building of large, multi-layered models to probe the predicted behavior of complex, highly non-linear systems (e.g. spatial oscillatory calcium waves, cell cycle regulation by intracellular signaling networks). One of the unique strengths of the *Virtual Cell* is that models can be based on both experimental data (biochemistry, molecular biology, imaging, etc.) and purely theoretical assumptions by using a very general conceptual structure of a model as a collection of arbitrary processes. These are defined in terms of which molecules or molecular complexes are involved (ranging from elemental species such as sodium or calcium, to large macromolecular structures), where they are located (defined areas within a tissue, cell, organelle, etc., or well mixed compartments), and how they interact with each other (simple kinetic reactions, transport fluxes, diffusion, electrical forces, etc.). The user can build complex models with a web-based interface to specify compartmental topology and geometry, molecular characteristics, and relevant interaction parameters; the *Virtual Cell* then automatically converts the specified biological mechanisms to a corresponding mathematical system of ordinary and/or partial differential equations. The mathematics-savvy user may directly specify the complete mathematical description of the model, bypassing the schematic interface. The system will automatically solve the equations by applying numerical solvers and generate appropriate software code to perform and analyze simulations. The simulations are run on a powerful multi-node, multi-processor computer cluster that is used as a dedicated server for computationally intensive applications. Results of the simulations can be displayed and analyzed on-line or downloaded to the user's computer in a variety of formats, from raw data to QuickTime movie files. The models and their applications and simulations are all stored in a secure database that maintains user privacy. Moreover, the database provides mechanisms for sharing models for collaborations and publishing of specific versions. Links to external databases (such as KEGG or SwissProt) facilitate incorporation of existing data when building models. A powerful set of tools based on XML technology is also available to compare and edit models; the XML representation also facilitates the use of other tools – we support both emerging standards for biological modeling languages, SBML and CellML for either import or export into/from the *Virtual Cell*.

An overview of the technologies used, the user interface, and several applications of the *Virtual Cell* will be presented, including experiments and modeling of calcium dynamics and phosphoinositide signaling in neuronal cells.

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