Virtual Cell Quick Start Guide

**Go to https:// vcell.org**   Select the Download tab

Click on one of the links to download and install the VCell launcher for Windows, MAC or Linux.   The software will download, please follow the installer instructions.

> Tip: Whenever you launch VCell from the local shortcut and are connected to the Internet, it will automatically check for and download any updated version.

> Tip: You can run the local VCell application without an Internet connection and without logging in to the model database, however, you will only be able to save your work using File > Export and your models will not be saved to the database.

The VCell workspace has 4 panes.

1. Model Navigation (upper left) to access different parts of a Biomodel.
2. Database Navigation (lower left) to find public or private models or to import models from external databases.
3. Main Workspace (upper right) where components of the model are described and edited.
4. Properties (lower right) that describe the detailed properties of selected model components and error warnings.
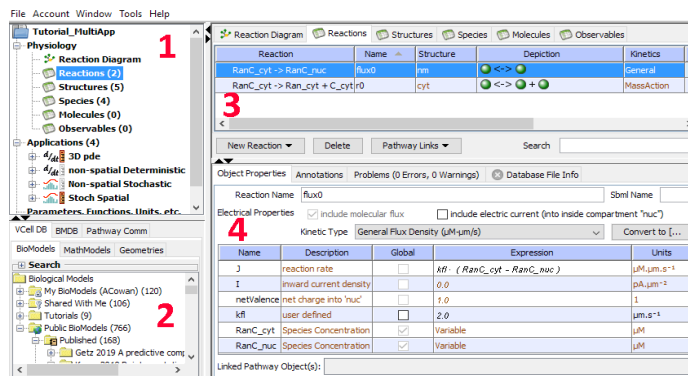
> Tip: There are multiple views for browsing and creating elements of a model.   For example, species can be specified and edited in both Structure and Reaction Diagram views. Clicking on Species leads to the list of all species in the model.

> Tip: Select any element in the top right panel and you can view/edit its Object Properties in the bottom right panel. The "Search" field provides an easy way to find any specific item in what might be a long list, e.g. 10's to 100's of parameters or reactions.

A Searchable Help Manual can be opened from the Help Menu

Working with VCell BioModels:

An "empty" BioModel appears when VCell starts; you can create a new BioModel by selecting File >New > BioModel. A ***BioModel*** consists of the "*Physiology*" (conceptual representation of the model: structures, molecules, connectivity, kinetics) and one or more "*Applications*" (virtual experiments that can be simulated: initial conditions, actual morphologies, electrical protocols, etc.). An Application can be either continuous, stochastic or rule-based, and either compartmental or spatial using a "*Geometry*". A "*Geometry*", is a representation of a spatial structure that a BioModel Application (or a MathModel) can use for spatially resolved simulations. It can be 1-D, 2-D, or 3-D, and either analytically defined or based on a digital image.   Each application has a mathematical representation that is automatically generated and can be viewed. For each "Application" you can specify one or more "Simulations" (time length, resolution, solvers to use, parameter overrides, etc.) that will run and produce Results. Results can be viewed in VCell or exported .
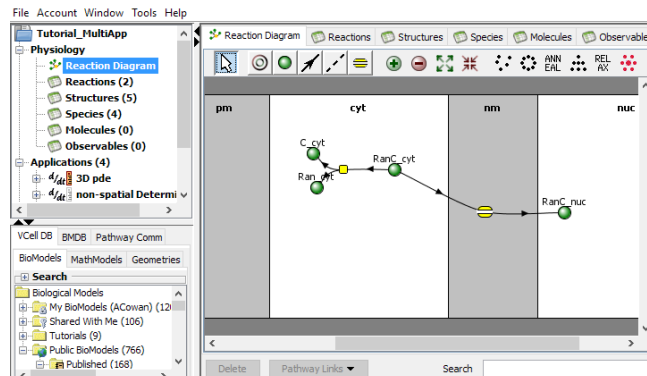
Start from an existing VCell BioModel: From the Database navigation pane (bottom left) navigation bar, or click on and open a public or shared BioModel from "Shared Models" (organized in folders by user names), "Education" (associated with classes and teaching resources) or Tutorials (created to introduce users to VCell). Save your private copy: (File > SaveAs) with a new name.

Import an existing model from other software: Models in the BioModels.net repository can be imported using the **BioModels.net** tab in the Database navigation pane; select a model and click the **Import** button.   To import other models, from VCell choose **File** > **Import**; VCell supports VCML and SBML files; import will create a new BioModel from the imported data.

Create/edit a BioModel:

- ♦   create the Physiology
- ♦   create one or more Applications
- ♦   create one or more Simulations for each Application
- ♦   run Simulations
- ♦   view Results   ⇒   (optionally) export Results
- ♦   keep expanding and modifying your BioModel

**BioModels are saved in a database.**

By default, all newly created BioModels are private. A pop-up menu for a selected model in the **Database Navigation** pane (see above) is used to make any of your models public (accessible to all users) or shared (accessible to one or more specific users). Public or shared access is read-only; only the owner can modify or delete items and other users must save their private copy to make changes.

Tip: A BioModel must be internally consistent and are automatically saved to the database whenever you want to run Simulations. You will be prompted to take action in one of three cases: (i) the BioModel was never saved – you will be prompted to provide a name, (ii) when there are inconsistencies that prevent successful math generation – you will be presented an error message, or (iii) when saving will overwrite existing Simulation Results due to upstream changes to the BioModel (and not due just to direct changes to a Simulation) – you will be given the choice to overwrite, save a new edition of the BioModel, or save under a new name.

Tip: When making changes upstream they automatically propagate downstream. For example, creating a new compartment in the Physiology will propagate to all Applications and spatial Applications will need to have the extra compartment mapped to the Geometry. For another example, setting a molecular concentration as fixed in an Application will remove it from the list of variables from all Simulations of that Application. A consequence is that if you already have simulation results, often some (or all) become invalidated by changes and must be re-run. It is important to keep in mind the tree-like hierarchy of the BioModel (Physiology > Applications > Simulations) to understand VCell behavior during saves and the effects of editing at various levels.

Working with the Physiology:

Select *Physiology* in the **Model Navigation** pane, and use either Structures (table view) or Reaction Diagram tab in the **Main Workspace** pane to add compartments and membranes. Populate compartments and membranes with molecular species (molecules, complexes, or states thereof). Species can also be added in the Species tab (table view), Reaction Diagram tab or will be automatically created when creating reactions. Reactions or fluxes are created in the Reaction Diagram or Reactions (table view) tabs. Within the Reaction Diagram, select different icons for adding species (green ball), compartments (circle), reactions (solid line with arrow), reaction modifiers (dashed line) or fluxes (yellow pore) .
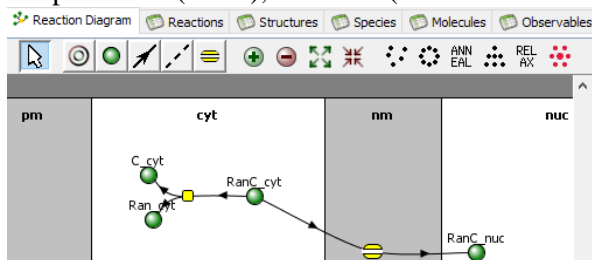
Tip: All items in the Physiology window and reaction editor have context menus that pop up on right mouse button click.

Tip: You can open more than one BioModel at a time and you can cut and paste molecules or reactions between them.

Tip: You can search the database for molecules and reactions already defined in all of your models and models accessible to you (public or shared with you).

Working with Applications:

Right click *Applications* in the **Model Navigation** pane, select New Application (Deterministic, Stochastic, etc...). By default, every new Deterministic and Stochastic Application is compartmental (i.e., every compartment is treated as homogenous and without spatial information, and are all mapped to a standard non-spatial geometry)

Tip: Compartmental Applications require proper specifications of the surface and volumes of compartments (e.g. a spherical cell with a 10 micron diameter is 523.33 micrometers cubed).

Tip: Even if your primary goal is to create spatial Applications, compartmental Applications are often a useful starting point to find or verify parameters for a stable initial state of the system.

To make an Application spatial, select the Geometry, Geometry Definition tabs from the **Main Workspace** pane, click "Add Geometry" and select "New", or "Open from.." an existing geometry.

Tip: Spatial Geometries must be created, edited, and saved in the context of a Bio or Math-Model. A Geometry that is being used in a BioModel Application (and/or a MathModel) cannot be deleted or modified from the database; if you edit a geometry in use, it will be saved as a new edition associated with the model.

Tip: Structure Mapping in spatial Applications is done manually. Map every compartment in the Physiology to a domain (region) in the Geometry; every region must have at least one compartment mapped to it. A child compartment can be mapped to the same region as its parent (unresolved, "distributed").

Tip: Always use the surface viewer to inspect 3-D Geometries, especially ones derived from image stacks; there might be more regions then you think there are, and regions might have illegal common boundaries in places you weren't aware of.
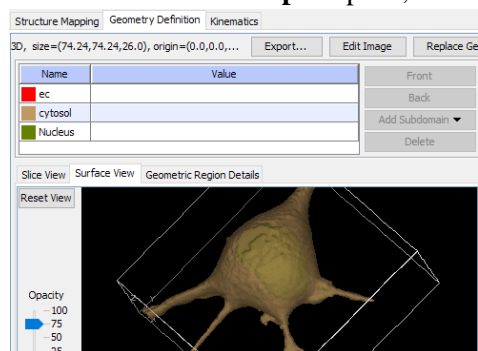
Select the Specifications tab to complete specifying the Application before moving to the Simulation tab. You can specify boundary conditions, initial concentrations and enable/disable reactions. Edit default values as needed. Use the Protocols tab to set up events and electrophysiology protocols, etc.

Tip: Do not forget diffusion constants for spatial applications. They default to zero for each molecular species, which may be appropriate in some cases, but is always illegal when a molecule is involved in a membrane flux.

Tip: You can specify uneven initial concentrations in spatial Applications by using an expression (including Boolean expressions) involving x, y, and z coordinates.

Tip: You can specify use of an equilibrium approximation for a reaction by checking the "Fast" checkbox.

Working with Simulations:

Create and manipulate Simulations using the Add 📄, Copy 📄, Edit 📝, and Delete 📄 buttons on the top left. When creating new Simulations, always check that the defaults are appropriate for time, solver, and mesh (in spatial models). The top right buttons will select Run ▶ get Info 🛈 access Results 📊 or Quick Run 🔵 (without saving).
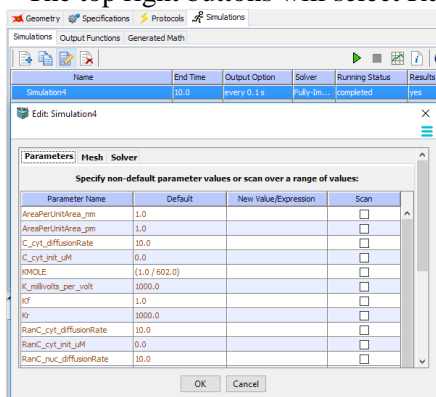
Tip: Use the Ctrl and Shift keys to select multiple Simulations in the list.

Tip: Timestep is very important for spatial Simulations – if it is too big, the solver will fail, if it is too small, it may take too long to run.

Tip: It is rarely useful to save >100 timepoints for spatial Simulations or >1000 for compartmental ones.

Tip: When spatial simulations run slowly, first experiment with coarse meshes.

Tip: For compartmental applications, try the CVODE solver when stiffness and numerical instability are an issue.

Tip: For large compartmental models, try the Quick Run option to get quick results without saving the model to the database. Remember to save your model to the database afterwards.

Use the "Parameters" tab in the edit simulation window to create Simulations in which specific parameter values are overridden.

Tip: Parameter Scan allows you to run simulations in which one or more parameters vary according to a specified list or range of values.

Simulation Results can be viewed in a separate window invoked by clicking on the "Results" icon.

Tip: Results can be viewed while a Simulation is running; the data display will update automatically at the same time with the Simulation status.

Tip: Line plot windows can display more then one variable at a time – use the Ctrl or Shift keys to select multiple variables for the Y axis.

Tip: When viewing spatial data, use the point and line tools to mark the display area and fetch spatial or time data for the selections; time plots and kymographs are often very.

Tip: You can download data from Simulation Results in a variety of formats from the "Export" tab of Results windows.

Tip: When exporting spatial data into movie formats, you can display more than one variable in the same movie by selecting the "overlay" checkbox option.

Tip: The NRRD format supports export of full spatial datasets including for 3-D simulations (values for all variables at all time points and at all points in space).

Tip: Line plot windows have a button to display tabular values that can be copied and pasted directly into other applications such as a spreadsheet.
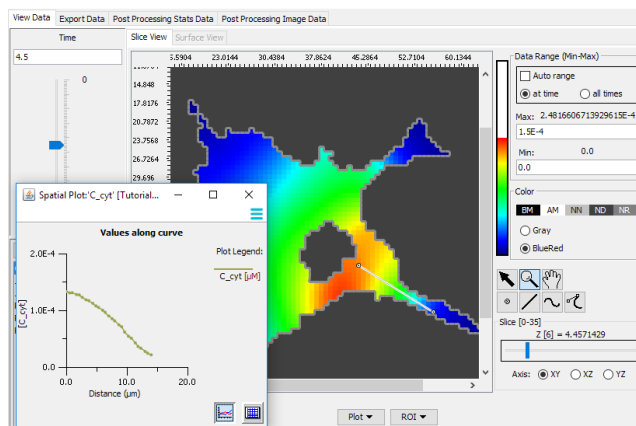
Model Storage:

The database supports multiple editions of documents. By default all saved entries are private, but the owner can use 'Permissions...' functions under the File menu to make them public or accessible to other specified VCell users. Public and shared access is read-only, users can only change their own copies of VCell documents.

Export and Import:

Use File > Export or File > Import to export and import BioModels to and from local files. Tabs or pop-up menus can be used to export components of a model. Simulation results can be exported as Quick Time movies or as image files, surface information for Geometries can be exported in STL and AVS formats, and the Physiology can be exported as a cartoon in GIF format.

Tip: MatLab format supports math export from compartmental Applications.

Tip: Select PDF format to generate a printable description of the BioModel

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