

SynBioSS Desktop Simulator

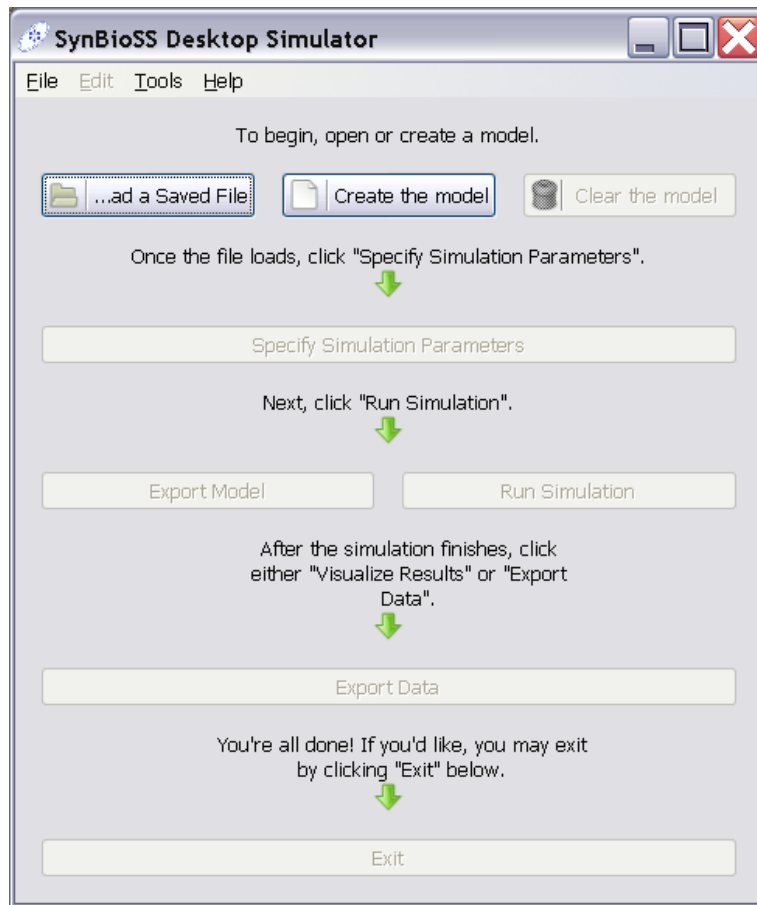


Figure 1 – The main window of SynBioSS Desktop as it appears immediately after opening the application. As each “level” of the simulation is completed, starting by opening an existing model or defining a new one, the appropriate options on the next level will become available.

Figure 1 depicts the main window of the SynBioSS Desktop as it appears immediately after launching the application. This window is the primary means by which users interact with the application. A new model can be opened (in SBML or NetCDF format) through the “Read a Saved File” button at top-left, or a new model can be created using the “Create the model” button at top-center. In either case, the model can be edited, and the edit/create window is shown in Figure 2.

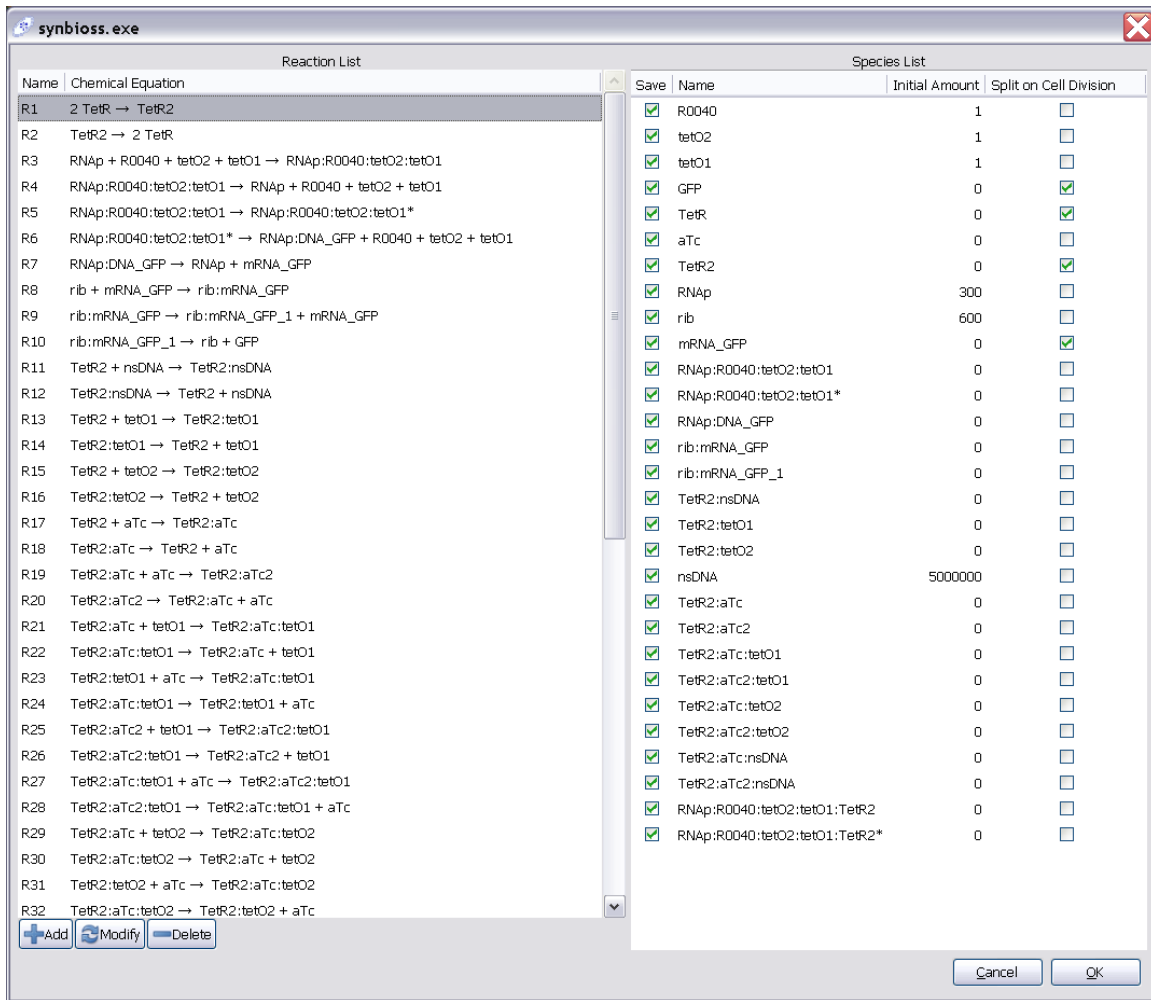


Figure 2 – The network creation/editing window of SynBioSS Desktop Simulator.

Reactions are shown in the left pane and species are shown in the right pane. The left pane also contains three buttons: “Add”, “Modify” and “Delete”. These buttons modify the list of reactions by adding a reaction, modifying the selected reaction or deleting the selected reaction. If either “Add” or “Modify” is clicked, a reaction detail dialog box appears. The reaction detail dialog box contains a kinetic description of the reaction. The rate kinetic rate law is set by choosing an appropriate elementary reaction type from the drop-down box. The corresponding rate equation is then shown below the drop-down box. Reactants, products and stoichiometries are then specified below the rate equation. The $x_0 \dots x_n$ labels apply to the concentrations in the rate equation. If more reactants or products are needed, clicking the appropriate button below either the reactants or products will suffice. The

kinetic parameters are entered in scientific notation for the corresponding constant in the displayed rate equation. Finally, a name may be given to the reaction, but this is optional. Changes are applied by clicking either the “Apply” or “OK” buttons and either “Cancel” or “OK” dismisses the dialog box. If the reaction being edited is a new reaction, an additional button appears between “Cancel” and “Apply” allowing an additional reaction to be created without closing the dialog box.

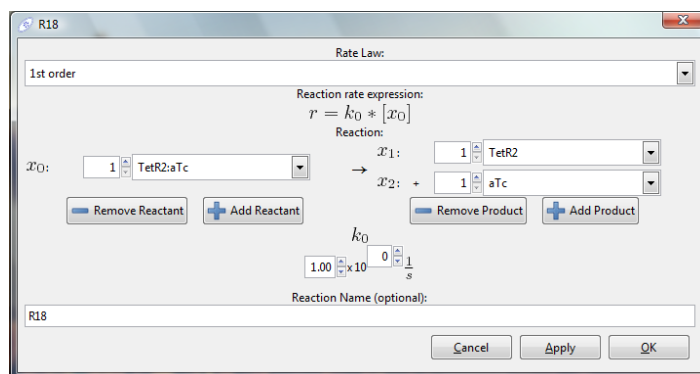


Figure 3 – The reaction detail dialog box.

After the model (reactions stoichiometry, kinetics, and initial conditions) has been specified, the second level option on the main window, “Specify Simulation Parameters,” becomes active. Users must then click on this button to interact with the window shown in Figure 4, specifying the length of the simulation, the number of trajectories to simulate, and other important parameters.

In the “Advanced Options” panel, the cell volume, doubling time and standard deviation of the doubling time can be set. Also in the “Advanced Options” panel, the integration time step and save times may be set. The integration time step affects the simulation time required, the numerical accuracy of the simulation and the memory required for simulation. If you find that a simulation is crashing (producing no output, despite apparently finishing), try decreasing the integration time step. If you have a long simulation and find that even starting the simulation is taking too long, try increasing the save time interval.

In the “More Advanced Options” panel, the numerical integrator is chosen in a drop-down menu. The Milstein (Adaptive-step) integrator should be the best compromise between robustness and simulation time. The exact SSA algorithm is an implementation of the Next-Reaction variant of Gillespie’s Stochastic Simulation Algorithm. It will not crash, but may take a very long time to get simulation results. The other two fixed-step integrators may or may not be faster than Milstein (Adaptive-step), but if the integration time step is too large, the results may not be accurate or even cause the simulation to crash. The adaptive-step Milstein algorithm will automatically adjust its integration step to ensure numerical accuracy. The remaining parameters are algorithm specific, and more information can be found on the Hy3S website or the Hy3S article in BMC Bioinformatics.

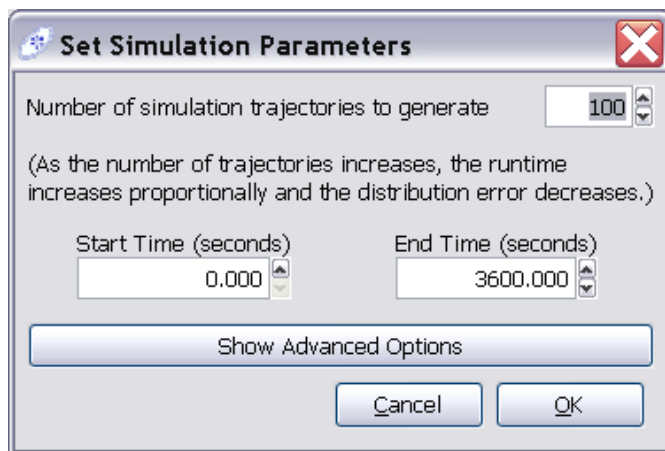


Figure 4 – The dialog box used to specify simulation parameters other than the model itself.

After the model has been defined and the auxiliary parameters specified, the third level of options of Figure 1 become available. At this point, users may export the model to a new NetCDF or SBML file, or they may run the simulation. After the simulation has been run, the data may be exported to a set of .csv files (comma separated values, one file per species) for analysis in any plotting package of the user’s choice.