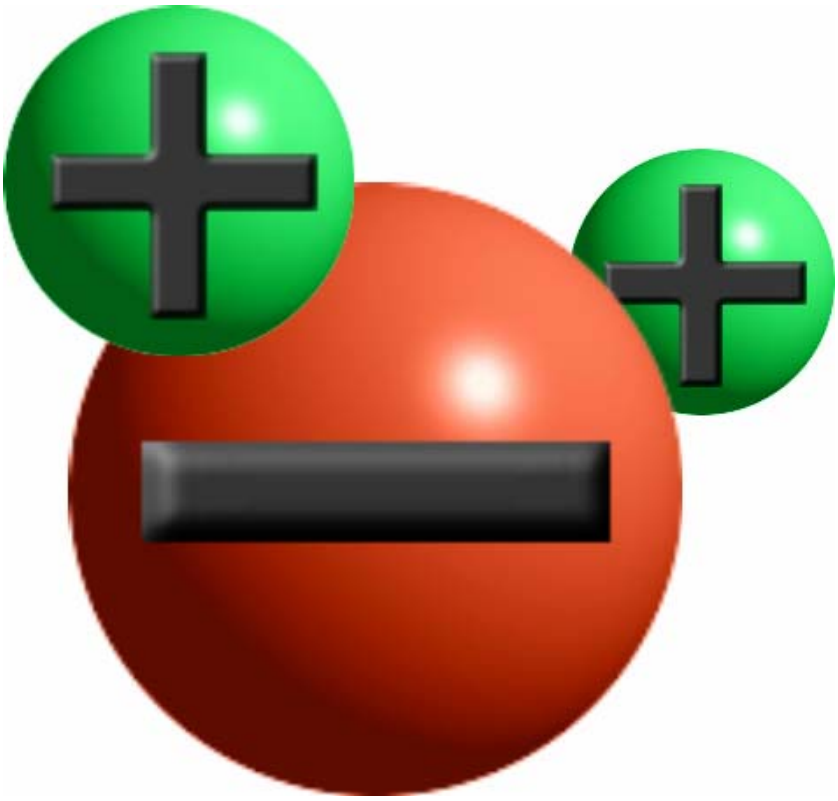
ISIM Interface™



User's Manual

Release 1.4

June 22, 2007

Website: https://simtk.org/home/isim_interface

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Introduction

This document is a work in progress.

General Information

Ion Simulator Interface is a graphical user interface to the programs ISIM and APBS, for computing the electrostatic potential in the vicinity of a macroion (macromolecule) in the presence of mobile dissolved ions.

Documentation and source code for the programs APBS and ISIM can be found on the web at http://apbs.sourceforge.net/ and at http://mccammon.ucsd.edu/isim/, respectively. See the License section of this document for information about use, duplication, and distribution of this software.

The Poisson-Boltzmann equation

The Poisson-Boltzman equation is important in the theory of electrostatic potential.

Equation 1: Poisson's equation, relating the charge density to the electrostatic potential and to the dielectric.

$$\nabla \cdot \left[\varepsilon(\vec{r})\nabla\phi(\vec{r})\right] = \rho(\vec{r})$$

Equation 2: Poisson-Boltzmann equation, relating charge density to ion concentrations.

$$\nabla \cdot \varepsilon(\vec{r})\nabla\phi(\vec{r}) = \rho_{macro}(\vec{r}) + \sum_i q_i n_i^0 e^{-q_i\phi(\vec{r})/kT}$$

r: a position in space

$\rho(r)$: charge density at position r

$\rho_{\text{macro}}(r)$: charge density of a fixed macroion

q_i: the charge on ion type i

n_i: the bulk concentration of ion type i

$\phi(r)$: the electrostatic potential at position r

$\varepsilon(r)$: the dielectric at position r

T: temperature (degrees Kelvin)

k: Boltzmann's constant

Task Flow In ISIM

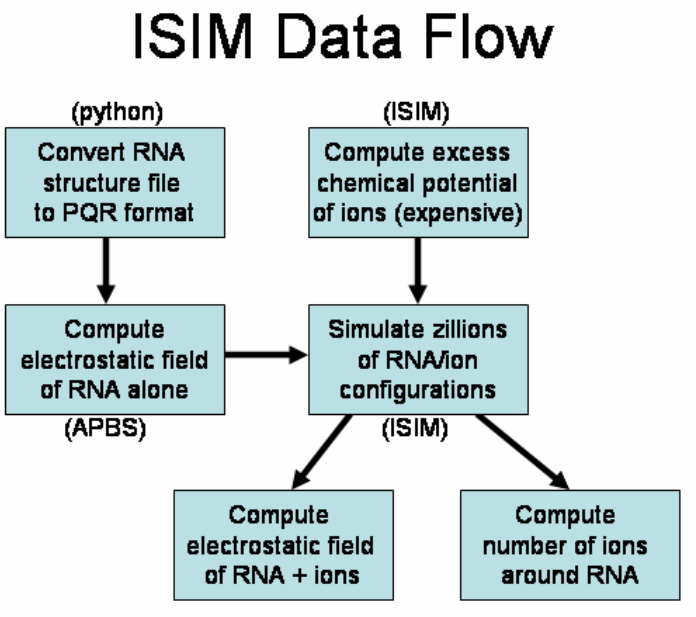


Figure 1: ISIM data flow

System Requirements

- The Ion Simulator Interface runs the programs ISIM and APBS on your local computer, so you will need to have adequate memory and other resources for the simulation. In general a larger molecule will require more memory.
- Java 1.3 or later runtime environment installed on your computer (available from java.sun.com)

Tutorial

Start the program

- Go to the https://simtk.org web site, type Isim under “Search Simtk.org” and click “Go”.

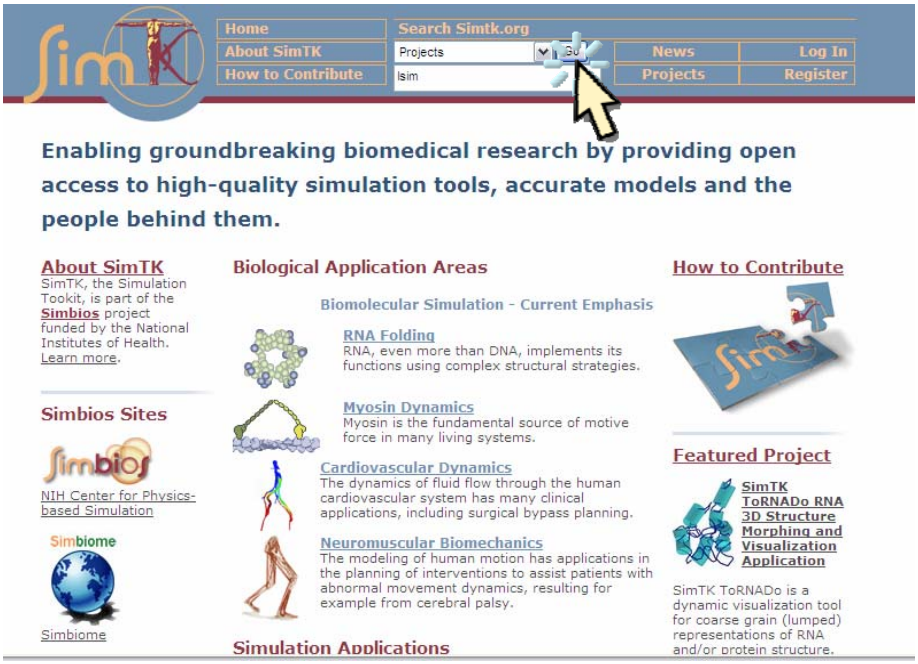


Figure 2: https://simtk.org home page

- Click on Ion Simulator Interface.

Figure 3: Ion Simulator Interface link

- The Ion Simulator Interface page will come up.
- Click on “Downloads” on the upper left side menu.
- Then under “Download Links” on the right hand side, click on IsimInterface1.3.278.jnlp.

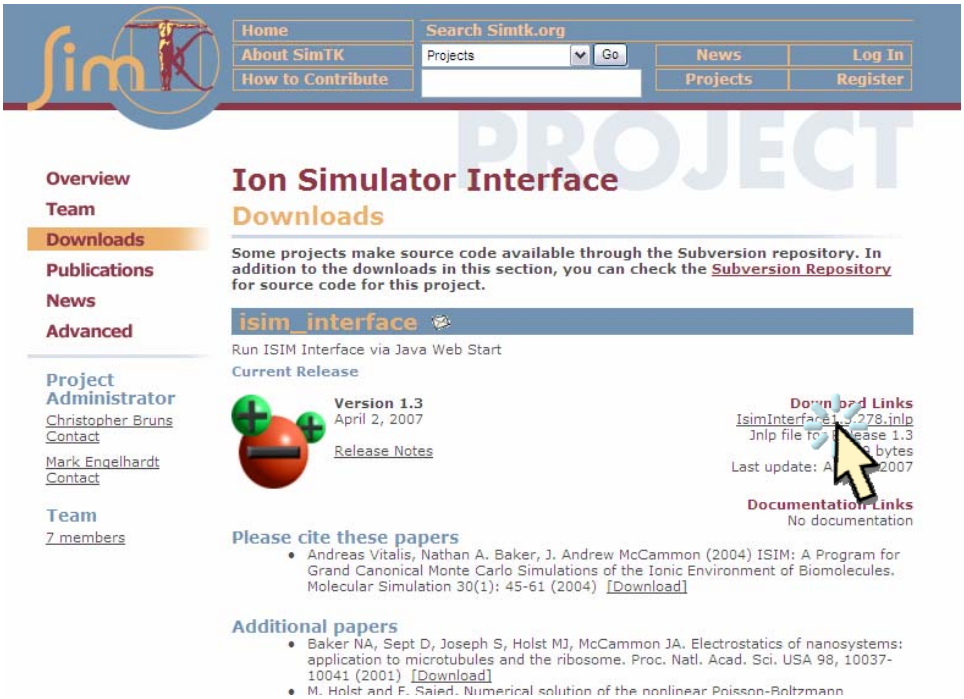


Figure 4: Ion Simulator Interface download page

- ISIM will begin to download automatically.
- The initial window will come up.

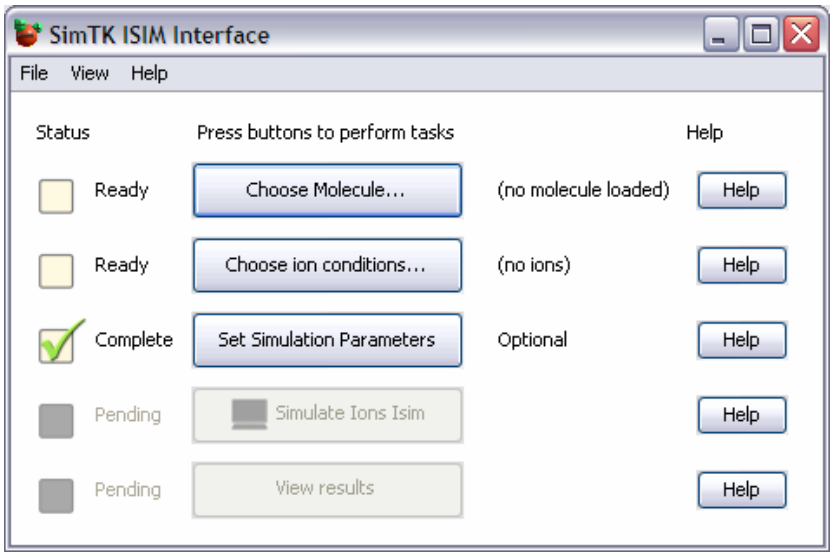


Figure 5: Ion Simulator Interface as it appears when first launched.

Choose a molecule

- You must choose a molecule about which to compute the ionic environment.
- Usually this molecule is RNA, DNA, or protein.
- Press the "Choose Molecule" Button to load a macromolecular structure file.
- The file can be either in Protein Data Bank (PDB) format, or in PQR format.
- PQR format contains partial charge information for each atom, while PDB format does not.

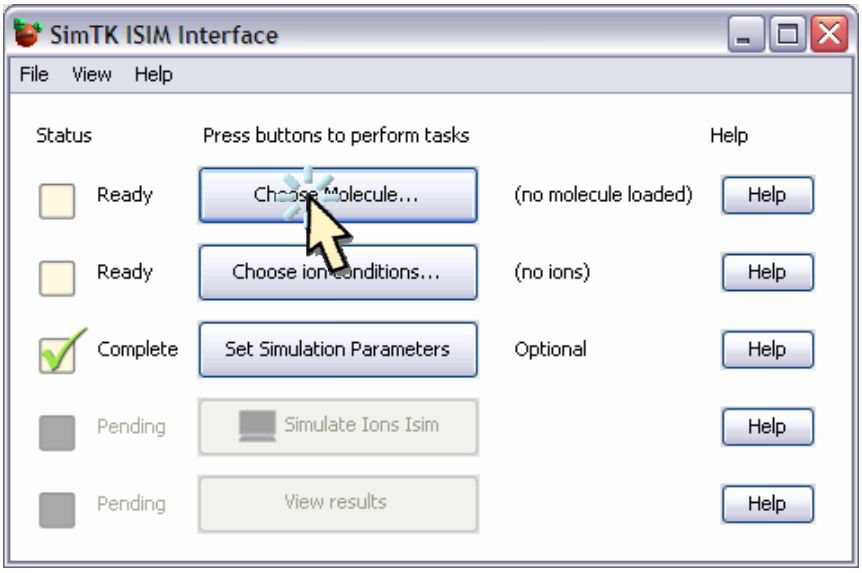


Figure 6: Click on "Choose Molecule..." to select a fixed macroion for the simulation.

- The “Choose Molecule” window will come up.

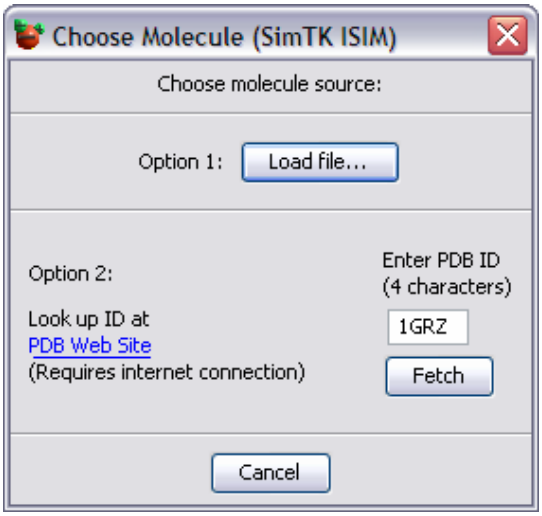


Figure 7: The Choose Molecule Source dialog window.

- Load the molecule:
    - Option 1: click on the **Load file** button to choose a molecule saved locally.
    - Option 2: enter the molecule ID (PDB ID) and click the **Fetch** button to load molecule from the PDB Web Site (requires internet connection). A sample valid PDB ID (1GRZ) is provided for your convenience.
- After this step is complete, a green check should appear next to the "Choose Molecule" button.

Choose ion conditions

Click the "Choose Ion Conditions" button.

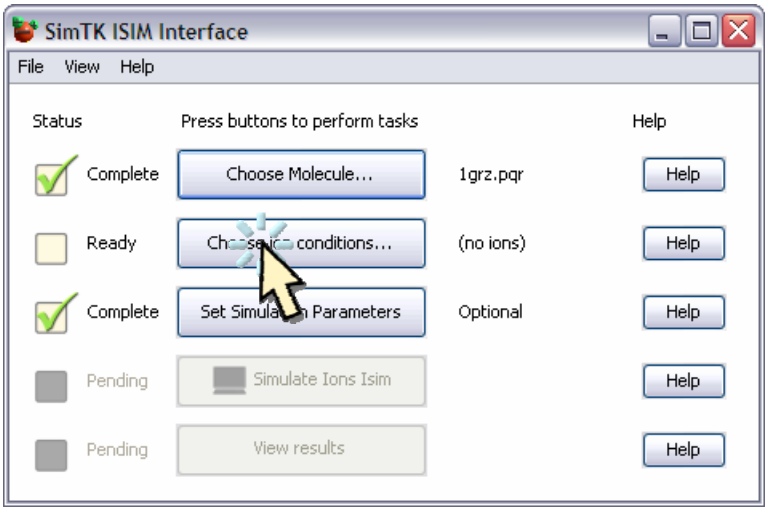


Figure 8: Click the "Choose ion conditions..." button to select ion type.

- The "Choose Ions" window will come up.

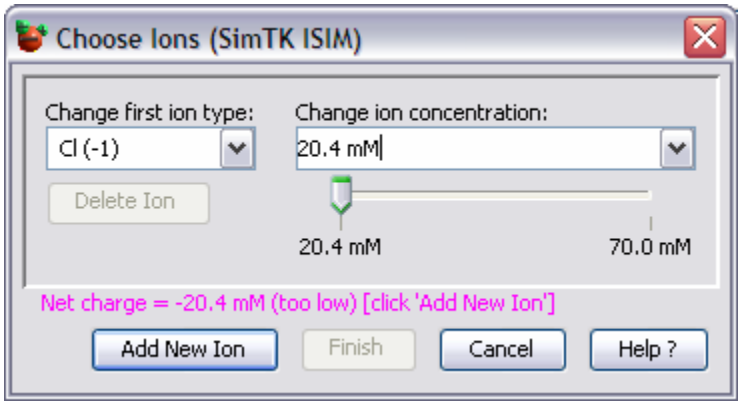


Figure 9: Choose Ions Window

- Choose ion type from the first drop down menu.

- Choose concentration from the second drop down menu, or use the slide bar to change ion concentrations, (concentrations are specified in units of millimols per liter (mM)).

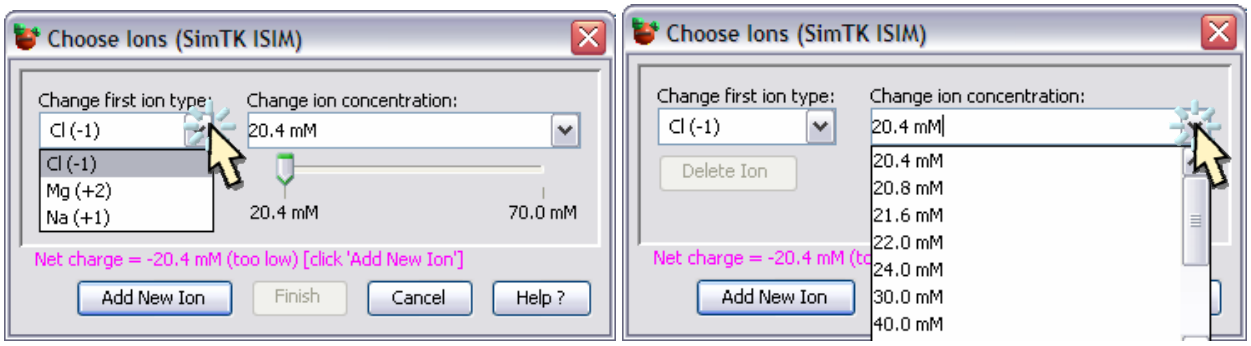


Figure 10: Select ion conditions from the pull-down menus

- You can add up to three ion types by clicking on the “Add New Ion” button.
- You need to adjust the concentration so that the “Net Charge” (shown in magenta above the “Add New Ion button) is = 0 in order to continue onto the next step.

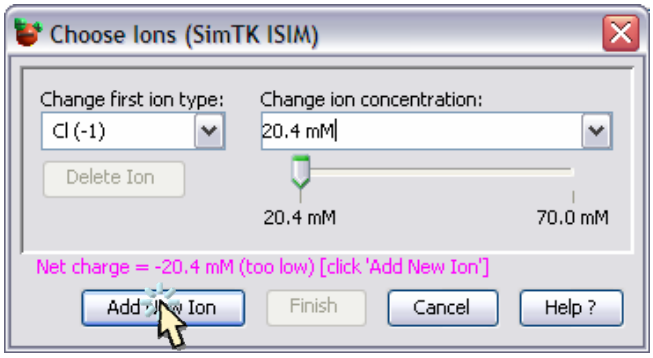


Figure 11: To “Add New Ion” and Net charge should be = 0.

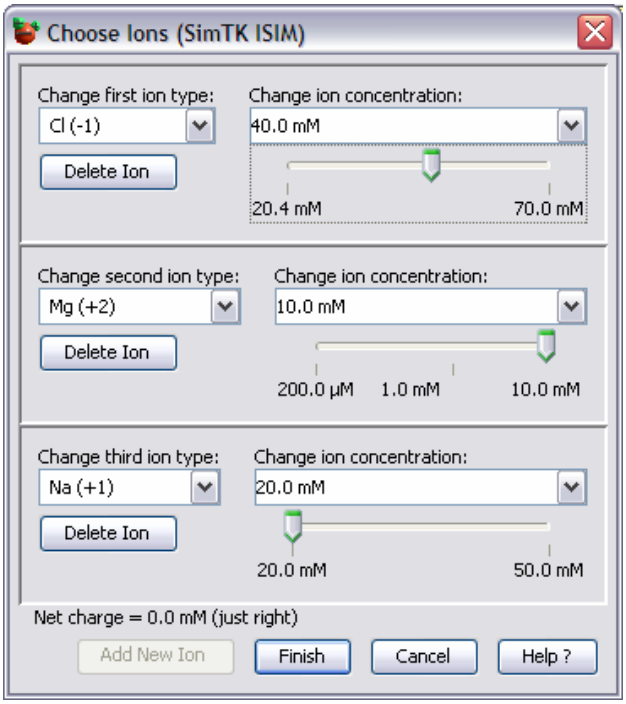


Figure 12: Ions and concentrations with Net charge 0 mM selected

- Click on the "Finish" button, a green check will appear next to the "Choose Conditions" button.
- NOTE – you must select all three ion types, because no parameters for conditions with less than three ions have been precomputed.

Simulation Parameters

Setting Simulation Parameters is optional, that is why you automatically see a green check on the "Set Simulation Parameters" button.

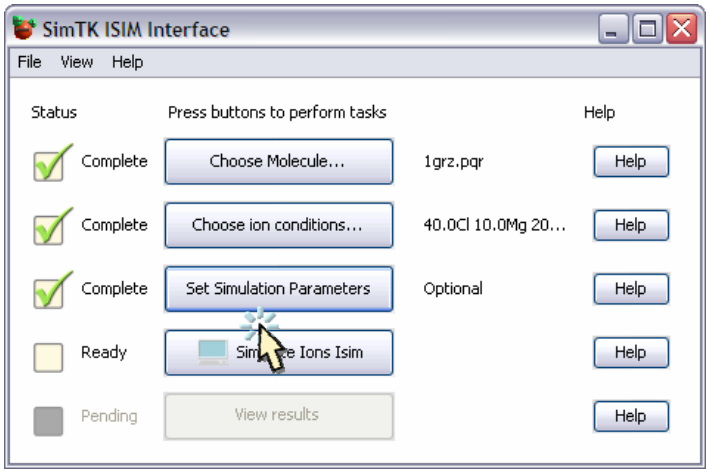


Figure 13: Click on "Set Simulation Parameters" button (optional step)

- Click the “Set Simulations Parameters” button.
- The “Simulation Parameter” window will come up, make changes as desired and click on “Done”.
- HINT – For a short test run, set the number of Monte Carlo steps to a much lower number, such as 500 or 1000.

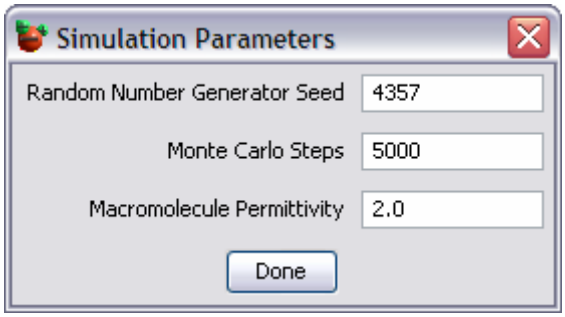


Figure 14: “Simulation Parameters” Window

Ion Simulation

- Click the “Simulate Ions Isim” button to start the computation (completing this step takes minutes to a few hours depending on the parameters).
- The program ISIM will now run.
- The amount of time this step takes will depend upon the complexity of the simulation.
- The elapsed time for this step is indicated to the left of the button.
- A green check will appear when the step is complete.

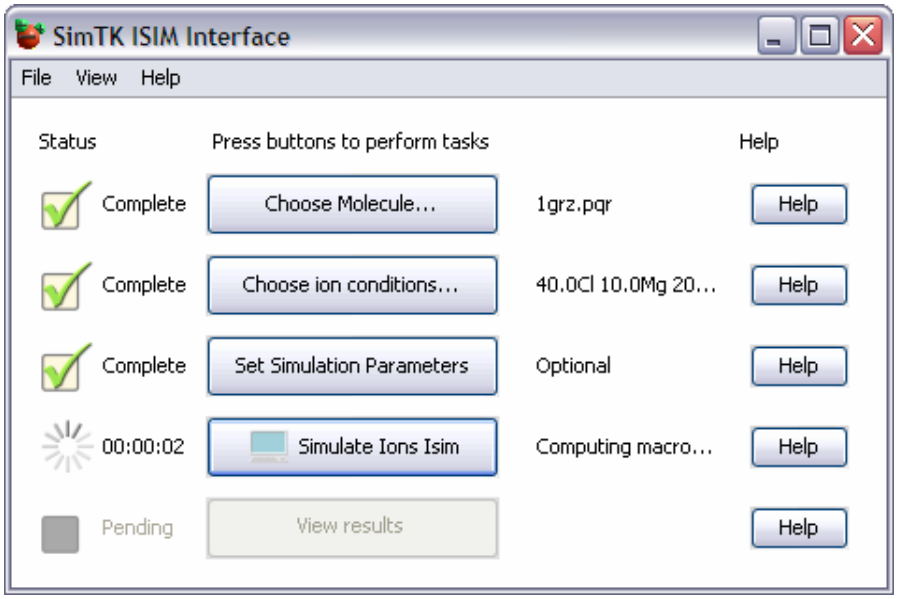


Figure 15: Elapsed time shown on the left side of the button.

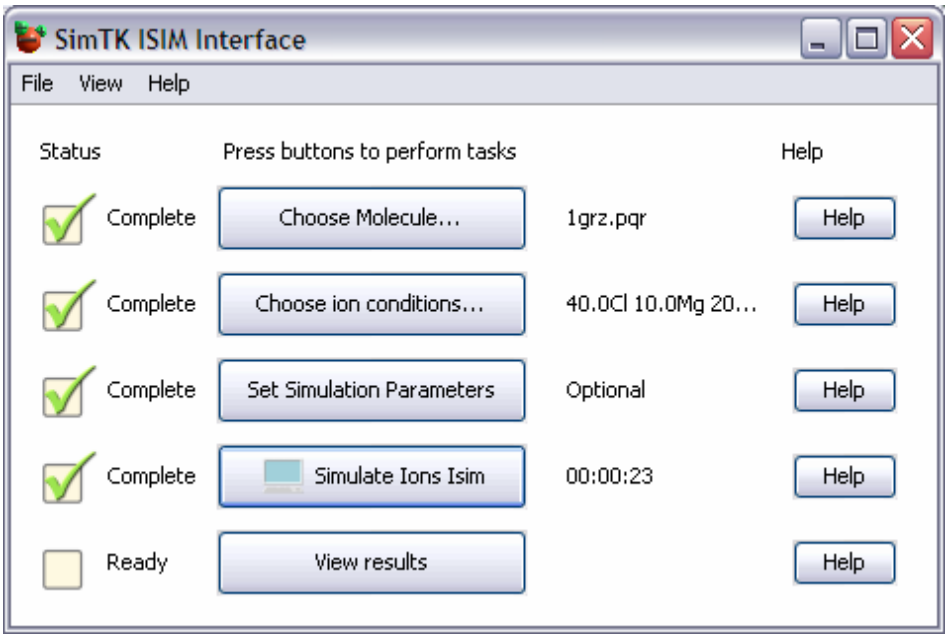


Figure 16: Simulation complete.

View Results

- Click on the "View Results" button.

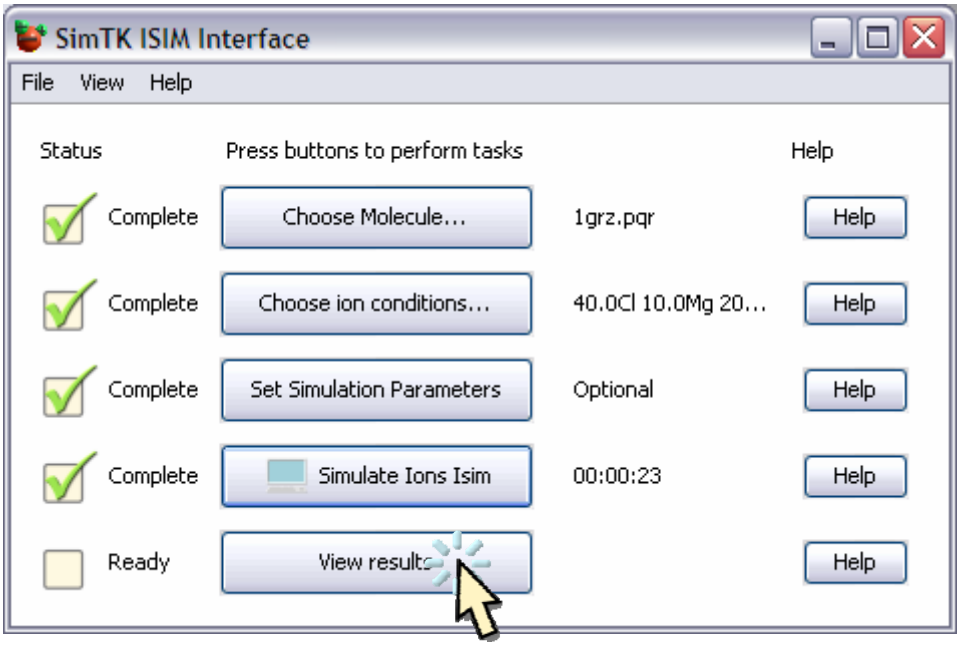


Figure 17: Click on "View results" button

- The "Ions Count" window will come up showing the various calculations for the ion types previously picked.

- The “Ions Count” window has additional buttons to provide more detail and information.

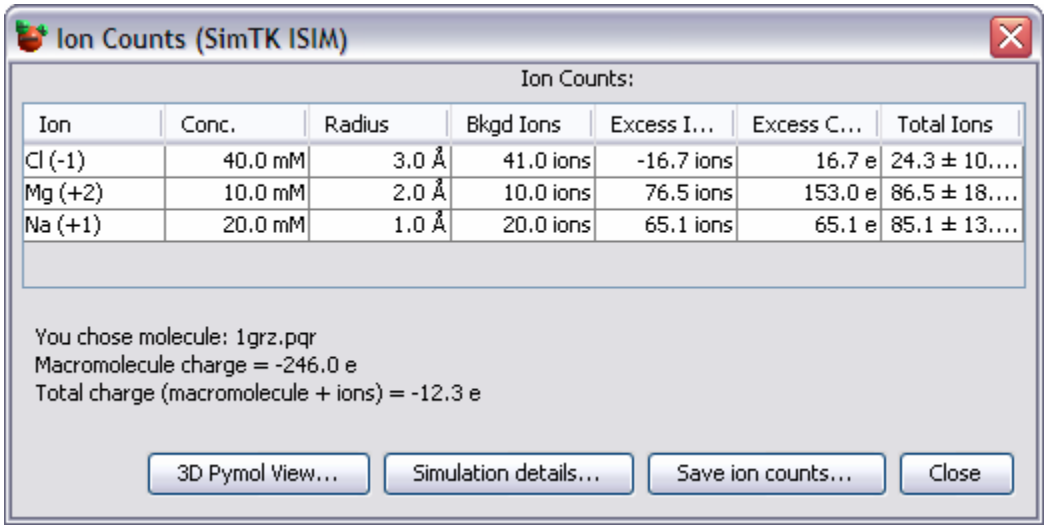


Figure 18: Ion Counts Window with various results.

- Save ions counts... button:

  Saves the results into a .csv file that should open in excel.
- Simulation details... button:
  - This will give you the simulation details as shown in Figure 19.

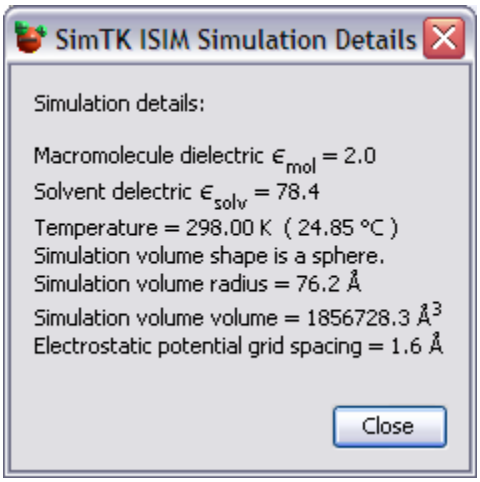


Figure 19: Simulation details

- 3D Pymol View... button:
  - When you click on this button and do not have Pymol installed, you will get the window in Figure 20 and you will need to install Pymol.

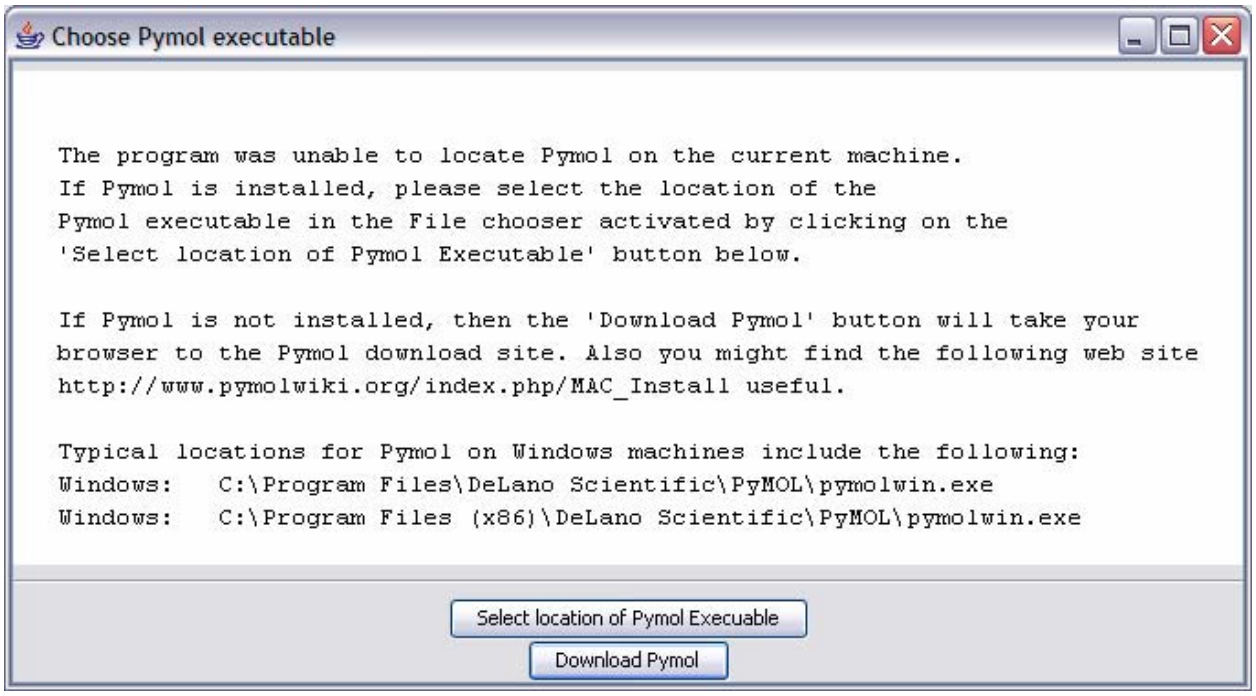


Figure 20: Pymol not installed, instructions how to download

Troubleshooting

(error messages)

Java Version

Isim Interface requires Java version 1.5 to run. Some users have reported trouble when using Java version 1.6. If you experience problems with ISIM Interface and you have Java 1.6 installed, first try clearing your Web Start cache (see sections below), then run ISIM Interface again. If problems remain, consider installing Java 1.5 instead of Java 1.6.

General Troubleshooting

Some problems can be diagnosed by examining the log window, which records the progress of Ion Simulator Interface (see figure).

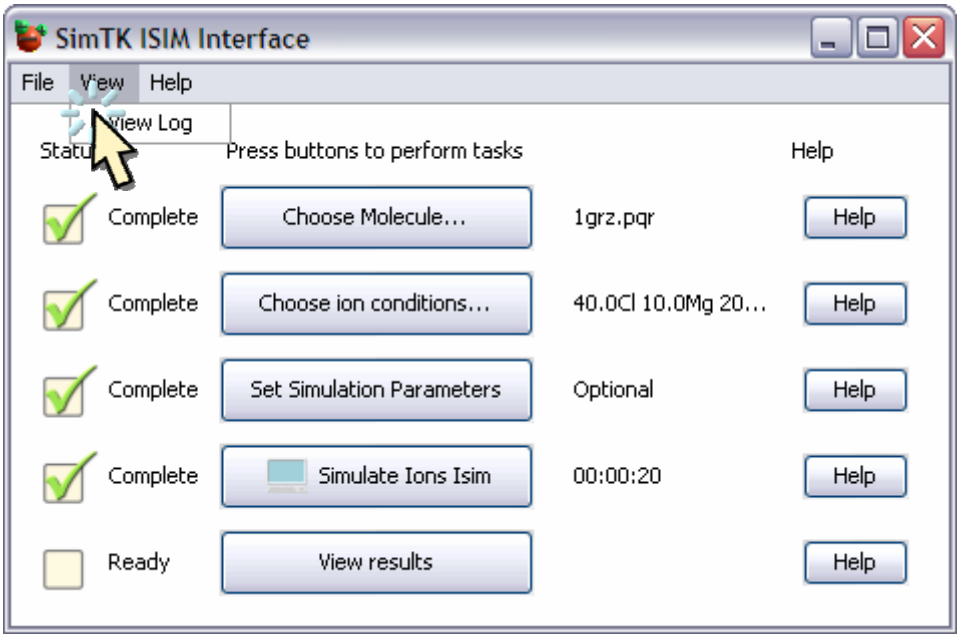
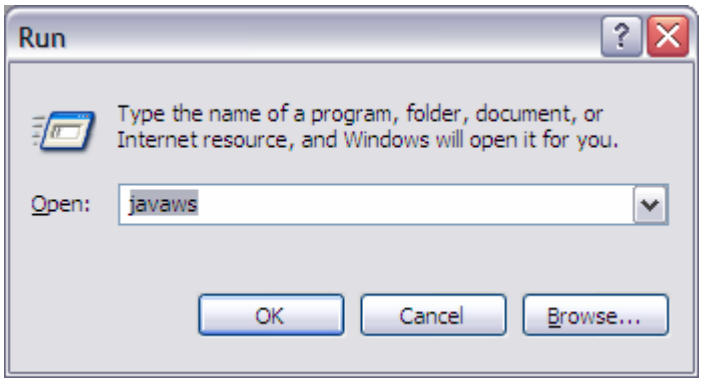


Figure 21: Examine the run log to help identify problems with the simulation.

PC Instructions -- Why am I not getting the latest version of Ion Simulator Interface using webstart?



Webstart is supposed to fetch the latest version of the program from the simtk server, but sometimes it does not update to the latest version. In this situation, you can get the latest version the next time you run by clearing the webstart cache. Run Java Web Start by itself by typing "javaws" at the command line, or by finding and clicking Java Web Start on your system.

Figure 32: Command line window

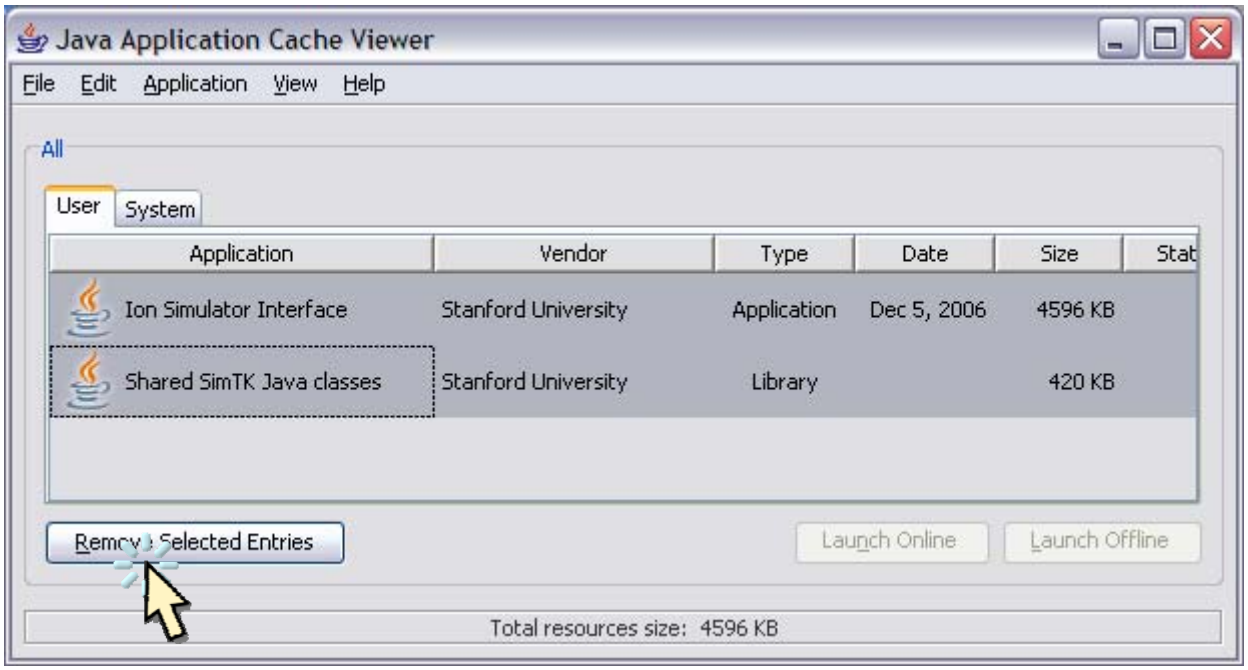


Figure 23: To force an update to the latest version of the program, run Java Web Start by itself, then remove the ISIM application and any Shared SimTK Java Classes from the application cache.

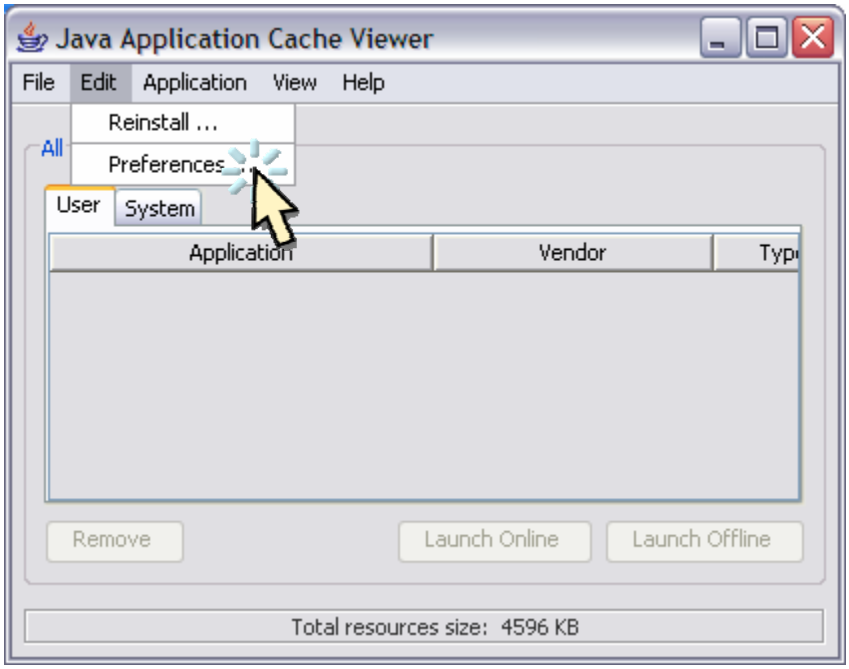


Figure 24: If the ISIM application is not shown in the Java Web Start Application Manager, you will be unable to remove just the ISIM application from the application cache. In this case, clear the entire application cache using the Preferences menu.

MAC Instructions -- Why am I not getting the latest version of Ion Simulator Interface using webstart?

Webstart is supposed to fetch the latest version of the program from the simtk server, but sometimes it does not update to the latest version. In this situation, you can get the latest version the next time you run by clearing the webstart cache. Run Java Web Start by doing the following:

- Find the "Utilities" folder by going to the "File" menu, click on "Find" and type "utilities" on the search area.
- In the "Utilities" folder find the "Java" folder and expand it.
- In the Java folder select the J2SE folder.
- Double Click on "Java Cache Viewer" to run the application.

- The Viewer will come up:

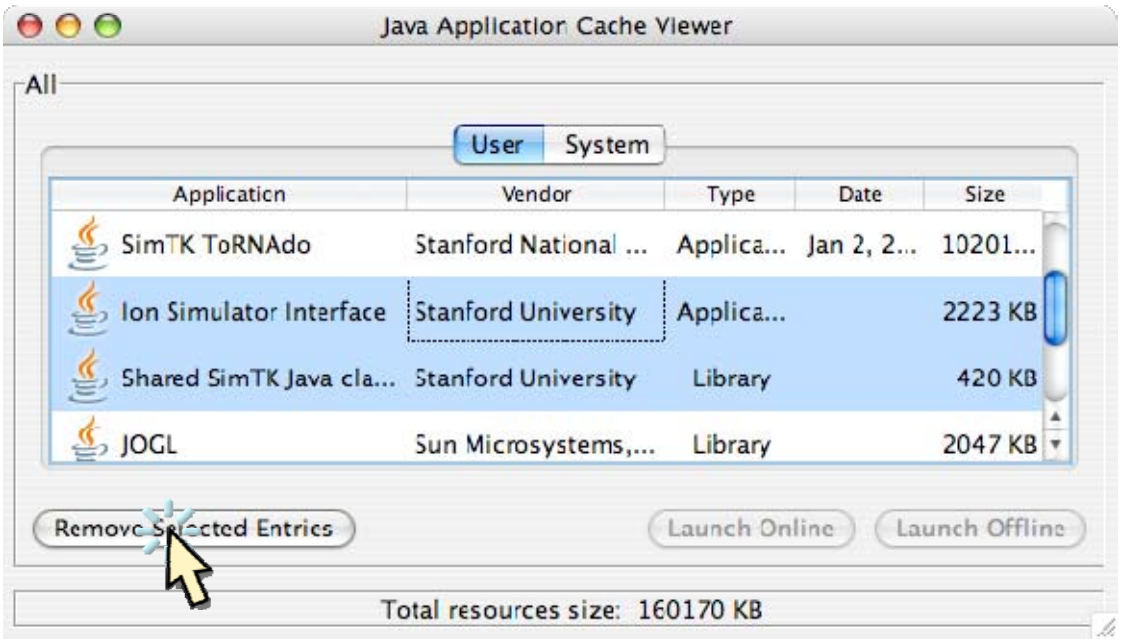


Figure 25: To force an update to the latest version of the program, then remove the ISIM application and any Shared SimTK Java Classes from the application cache.

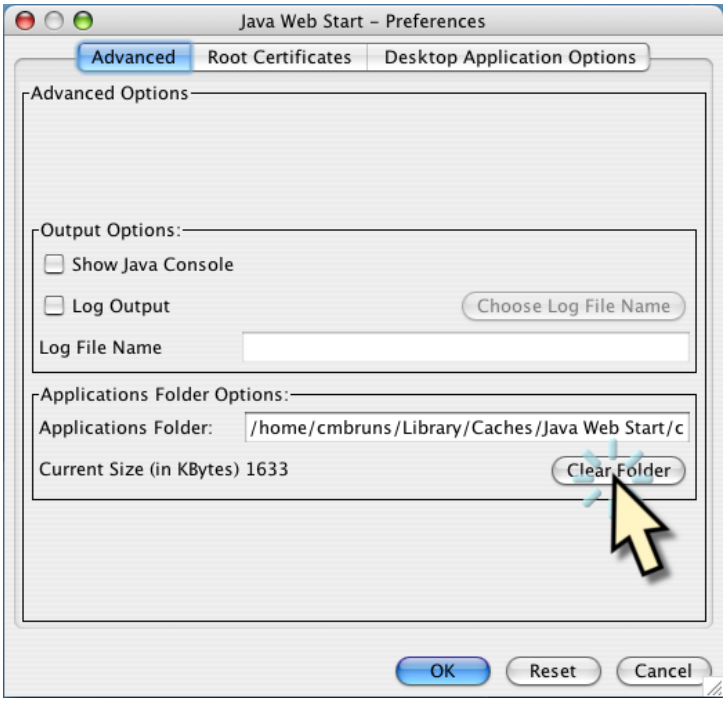


Figure 26: If you cannot find the Isim application, you can clear all applications by running Java Web Start in Utilities > Java > Java Web Start and selecting Preferences from the top menu.

Submitting Problem Reports and Enhancement Requests

If you observe a problem with the program, or if you would like to request a new behavior in future versions, please file a bug or feature report at SimTK.org.
You can do this by selecting Help > Report a program Problem (bug) or Help > Request a new program feature directly from the application.

You can also file a bug or report a feature by going to the Isim Interface project page (https://simtk.org/home/isim_interface), select Advanced > ”Features & Bugs” > ”Bugs” or “Features” > ”Submit New”, fill in the report and click “Submit”.

Thank you for helping us to improve the program.

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ABPS license

APBS binaries are included as part of the Ion Simulator Interface distribution.

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ISIM License

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Washington University, St. Louis

References

APBS

http://apbs.sourceforge.net/

Baker NA, Sept D, Joseph S, Holst MJ, McCammon JA. Electrostatics of nanosystems: application to microtubules and the ribosome. *Proc. Natl. Acad. Sci. USA* **98**, 10037-10041 2001.

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M. Holst and F. Saied, Numerical solution of the nonlinear Poisson-Boltzmann equation: Developing more robust and efficient methods. *J. Comput. Chem.* **16**, 337-364, 1995.

ISIM

http://mccammon.ucsd.edu/isim/

Andreas Vitalis, Nathan A. Baker, J. Andrew McCammon (2004) ISIM: A Program for Grand Canonical Monte Carlo Simulations of the Ionic Environment of Biomolecules. *Molecular Simulation* **30**(1): 45-61