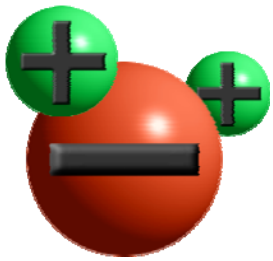
User's Guide for Ion Simulator (ISIM) Interface

pre ALPHA test version 0.9.9



Contents

Introduction

This is a pre-alpha version of the Ion Simulator Interface software

*** IMPORTANT NOTICE ***
This document refers to a pre-alpha version of the Ion Simulator Interface software. As such, only minimal functionality is provided. Please help us to identify bugs and identify weaknesses.

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.

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

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

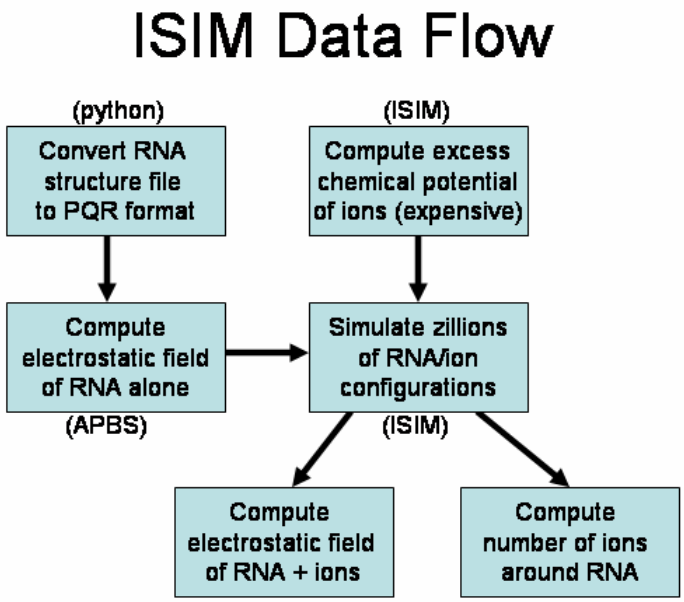


Figure 1: ISIM data flow

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.

Tutorial

Start the program

Ion Simulator Interface can be run in either of two ways:

1. Double click on the executable jar file downloaded from SimTK.org. This requires that you have a Java 1.4 or later runtime environment installed on your computer (available from java.sun.com).

OR,

2. Run it directly from the SimTK.org web site using Java Web Start. This requires that you have a Java 1.3 or later runtime environment installed on your computer (available from java.sun.com)

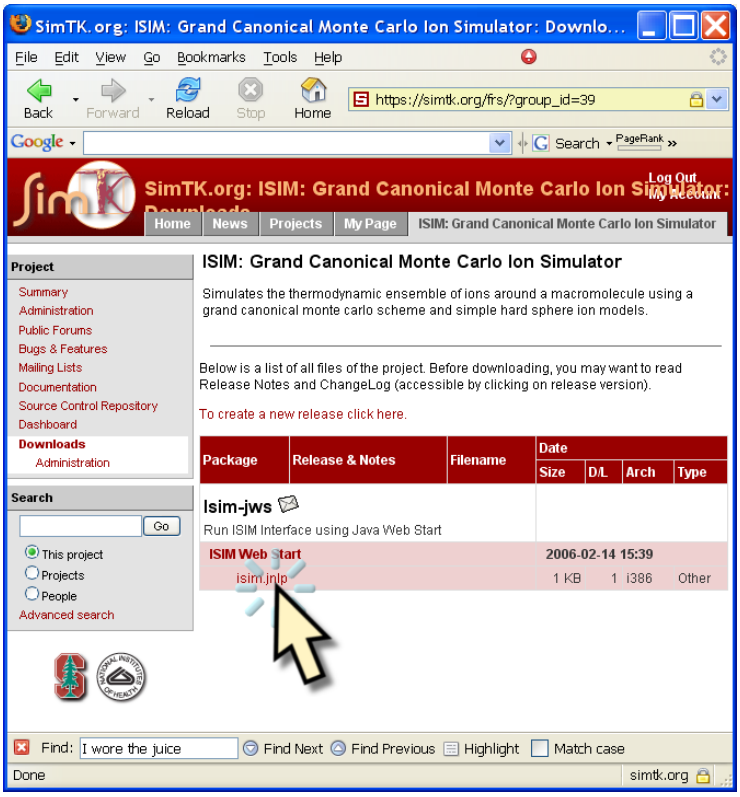


Figure 2: Run Ion Simulator Interface over the web using Java Web Start at simtk.org

The initial window should look something like this:

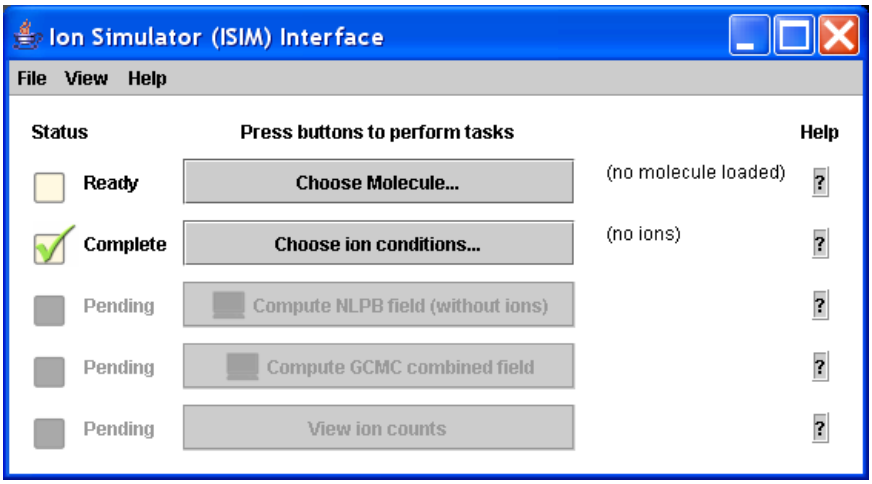


Figure 3: Ion Simulator Interface as it appears when first launched.

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.

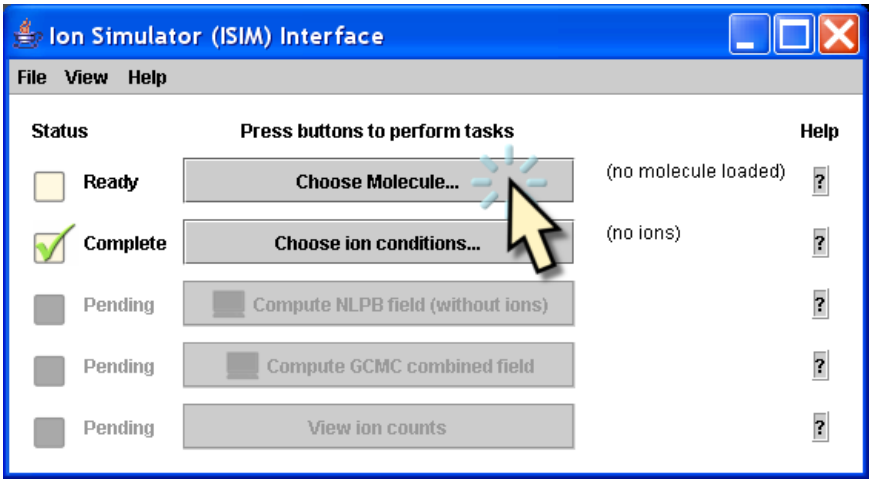


Figure 4: Click on "Choose Molecule..." to select a fixed macroion for the simulation.

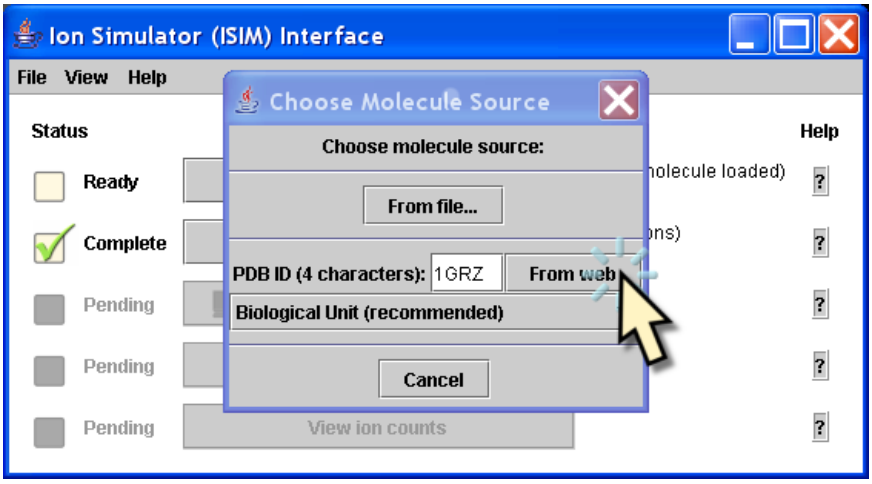


Figure 5: The Choose Molecule Source dialog window permits you to load a structure file either from your computer, or remotely from the Protein Data Bank (PDB http://www.rcsb.org/pdb/). In this example, PDB entry 1GRZ (Tetrahymena type I intron) will be loaded.

Choose ion conditions

Select the set of dissolved ions in the solution. Concentrations are specified in units of millimols per liter (mM). Other parameters include temperature, permittivity of the

solvent, and permittivity of the macroion. Excess chemical potentials for each ionic condition are expensive to calculate, so they are pre-computed.

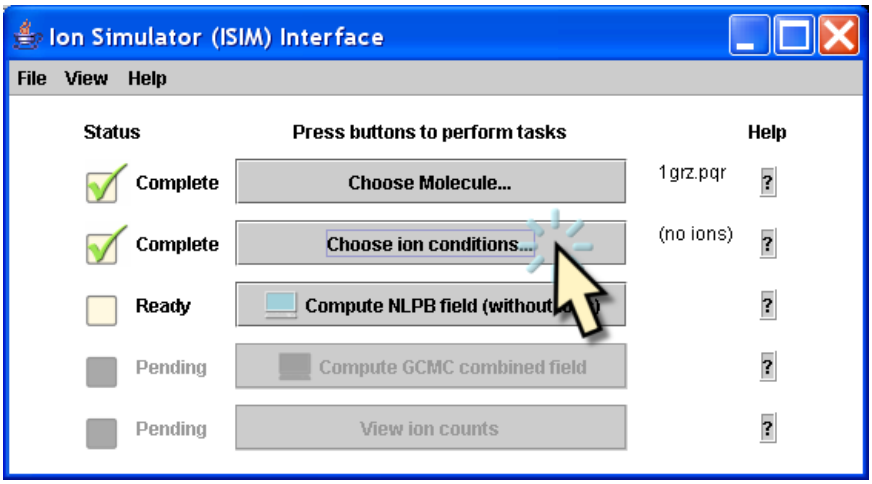


Figure 6: Click the "Choose ion conditions..." button to select the dissolved salt ions in the simulation.

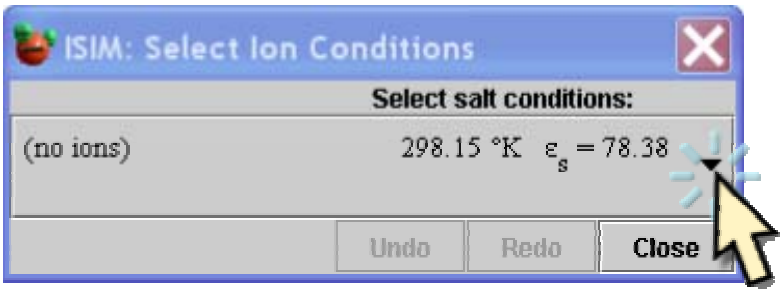


Figure 7: Select ion conditions from the pull-down menu

Compute electrostatic field of the molecule (APBS)

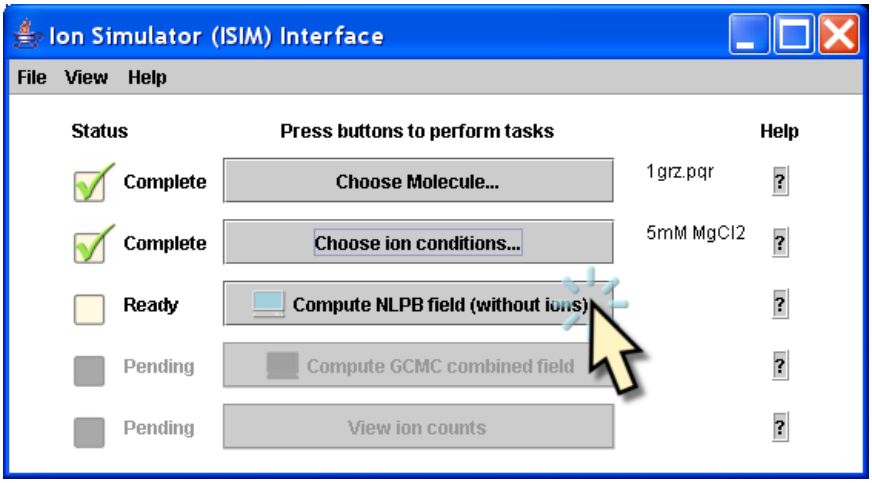


Figure 8: Click the "Compute NLPB field" button to begin the non-linear Poisson-Boltzmann computation of the electrostatic potential field about the macroion in isolation.

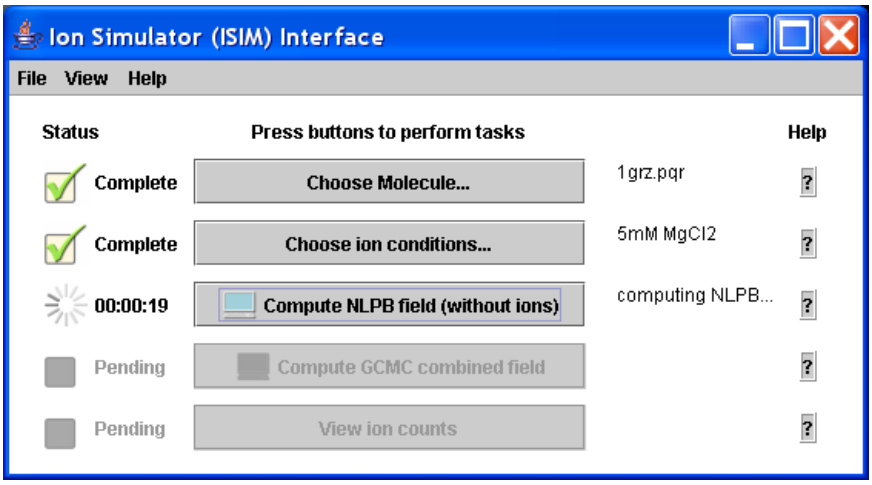


Figure 9: The elapsed time of the computation is shown to the left of the button.

Compute electrostatic field of the system (ISIM)

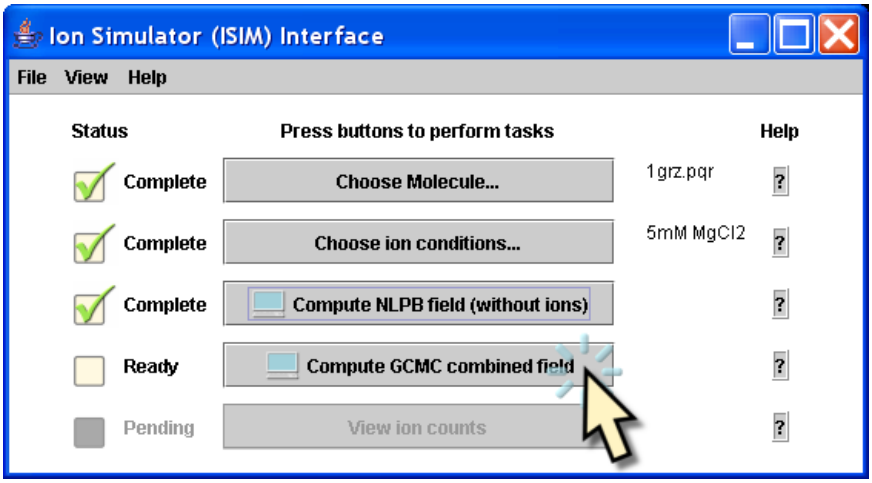


Figure 10: Click the "Compute GCMC" to begin computing the ensemble of ion positions using the program ISIM.

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 at the same position when the step is complete.

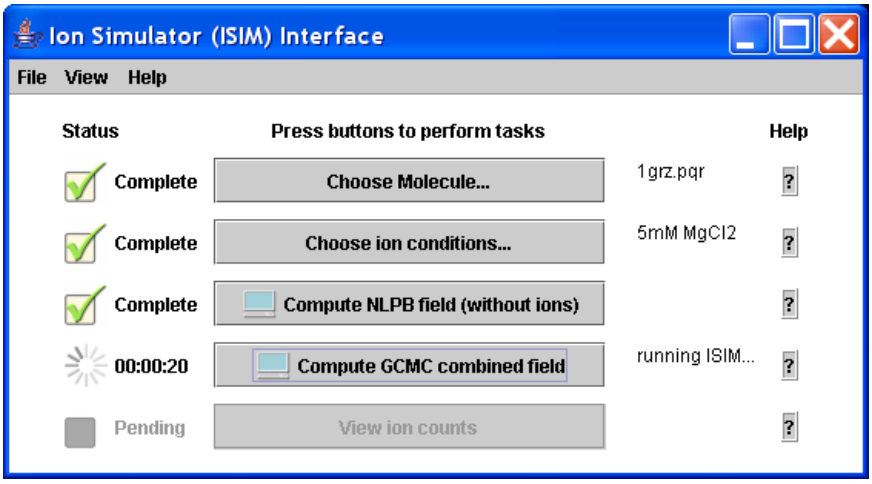


Figure 11: Elapsed time is shown to the left of the button

View the results

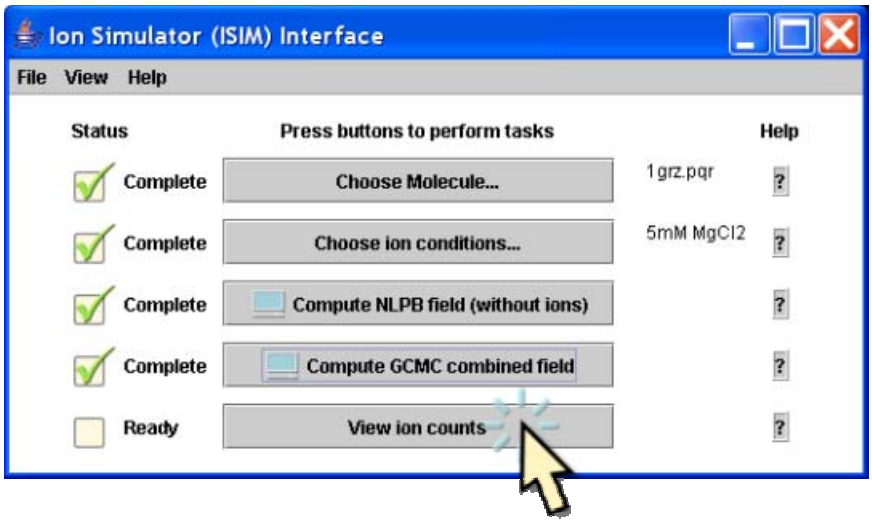


Figure 12: Click "View ion counts" to show a table of the average number of each ion type in the simulation volume.

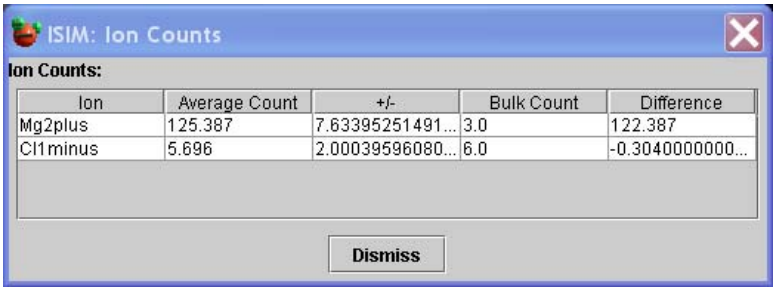


Figure 13: Summary of average ion counts during the simulation.

Troubleshooting

(error messages)

General Troubleshooting

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

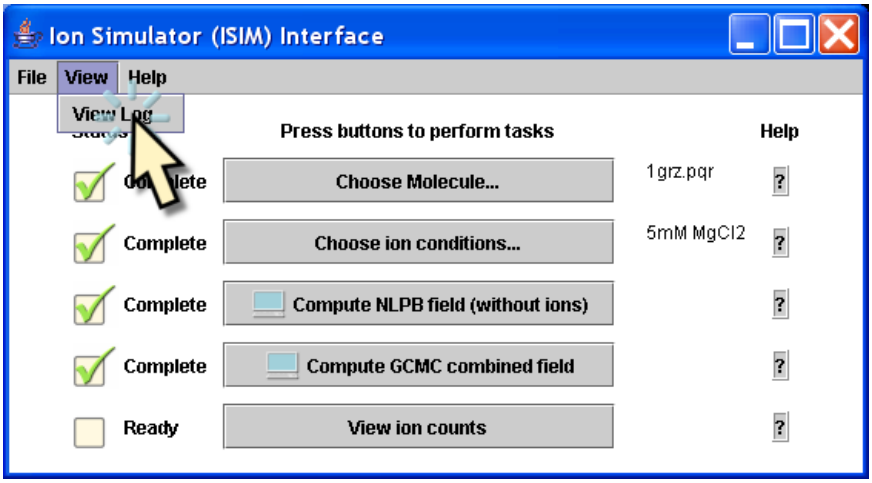


Figure 14: Examine the run log to help identify problems with the simulation.

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 and I do not know why. 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.

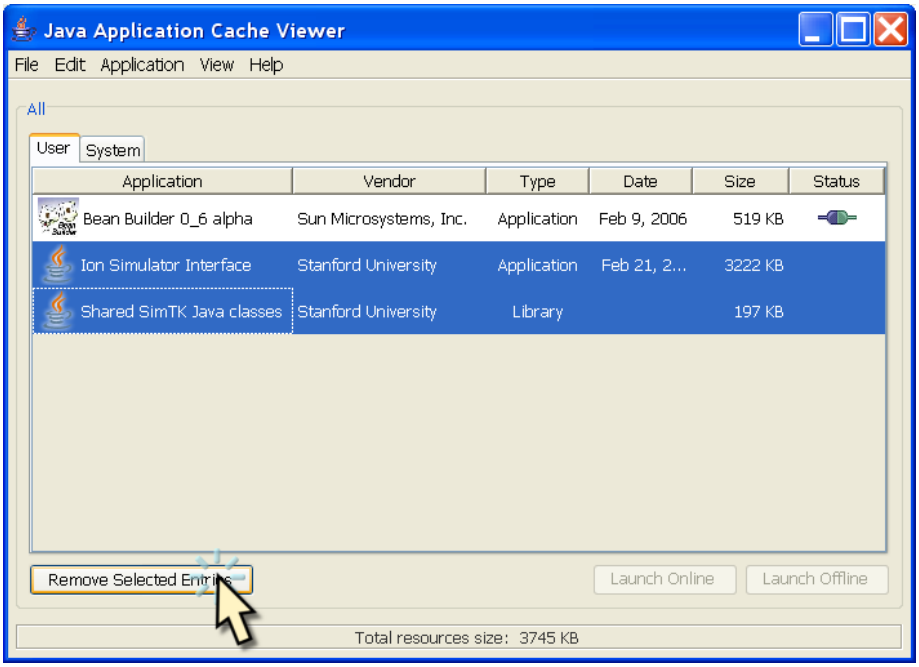


Figure 15: To force an update to the latest version of the program, run Java Web Start by itself, then remove the application and any associated dependencies from the application cache.

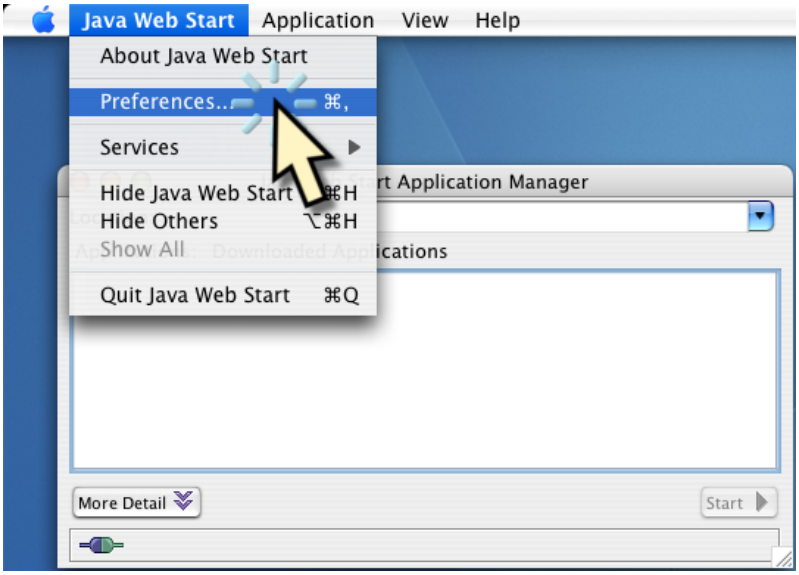


Figure 16: If the ISIM application is not shown in the Java Web Start Application Manager, you will be unable to remove just the ISIM application from the application cache. In this case, clear the entire application cache using the Preferences menu (next figure).

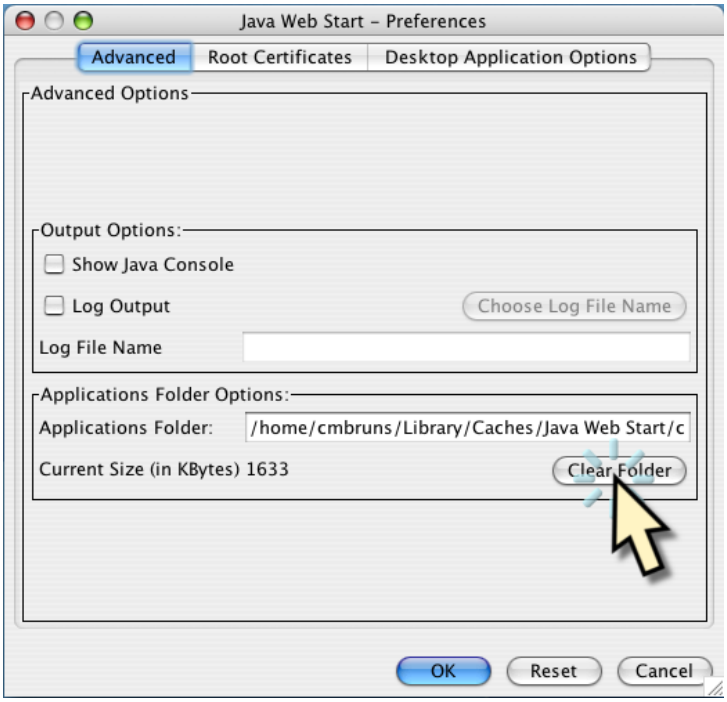


Figure 17: If it is impossible to remove just the ISIM application, you can clear all applications from the Java Web Start Application Cache using the preferences menu.

About this guide

version 0.50 Feb 14, 2006 Christopher Bruns, Stanford University

Software Used in Ion Simulator Interface

JDom

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The Ion Simulator Interface software consists of distinct components, each with a different distribution license. Use and redistribution of the Ion Simulator Interface software is subject to the conditions of all of these licenses.

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ABPS license

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

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ISIM License

ISIM binaries are included as part of the Ion Simulator Interface distribution. These ISIM binaries are distributed under the terms of the following license:

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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.

M. Holst and F. Saied, Multigrid solution of the Poisson-Boltzmann equation. *J. Comput. Chem.* **14**, 105-113, 1993.

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