Chem 2312H **September 29, 2022**

Accessing and Navigating MacroModel (via Maestro) at MSI via Linux

You will need to access Maestro (using MacroModel, a module within Maestro, although the name of that module may be being phased out) at MSI for doing the molecular mechanics minimization computation of the menthone isomers. Maestro may be accessed via the Nice remote desktop client or via the NoMachine application.

Here are instructions for setting up that access on your laptop. You will need to be either on the campus network or connected via VPN in order to do this.

1. Make sure you have verified with MSI that you are "registered" by following the instructions in the email message that you received from MSI.

To access MSI via Nice on a lab computer, see section **2a**.

2a. Nice is already installed on the desktop computers on the right hand bench in 491K computer room. Open Chrome and you will see the bookmark (or type the url address: nice.msi.umn.edu). A window opens asking for your x500 and your x500 password. You now will be seeing a Linux session at MSI.

To access MSI via Nice on your computer, see section **2b**.

2b. You will need to load Nice onto your Mac or PC. Nice is a remote desktop client.
You will also need to download and install the DCV client named "DCV Endstation."

a. Go to https://www.nice-dcv.com/.

Open the "NICE DCV 2022.1 Client" dropdown menu

If you are using Windows, download and install the "Windows (x86_64 and x86) Version 2022.1-8261" (not the Windows Portable) version.

If you are using Mac, select and download and install the "macOS (x86_64) Version 2022.1-4279".

c. Go to https://www.msi.umn.edu/support/faq/how-do-i-obtain-graphical-connection-using-nice-system and follow the instructions there, which have been expanded upon below.

d. To get to Maestro, open the Nice engine frame at http://nice.msi.umn.edu.

e. Open a "non-GPU" session by selecting (any) one from the "Services" drop-down menu in the left panel. Do not click more than once otherwise multiple sessions will simultaneously begin.

If you have difficulty with one or more of these steps on your own computer, you can go to the MSI Help Desk (staffed from 9-4 weekdays), which is located on the 5th floor (587) of Walter Library (Digital Technology Center), the building just to the north of Smith Hall. Have your computer with you so they can help you past the hang-up. (https://www.msi.umn.edu/content/helpdesk)

Once you are viewing the desktop via Nice, here is how you can access Maestro.

a. Select a non-GPU option under Services. A new desktop window will open. Expand the Home folder by clicking on its small icon. Under File in the top menu, select Open Terminal Here. A new Linux terminal window will open.

This gives you a command line from which you can load Maestro. (Instructions for doing this are at https://www.msi.umn.edu/sw/schrodinger), but here they are:

IMPORTANT: To connect to one of the supercomputers (Mesabi or Mangi), you must undertake the additional step of establishing an ssh connection. Note that inputs in the Linux terminal are case sensitive. In the terminal, type, exactly (including spaces):

```
ssh -Y mesabi [hit return or enter]
```

You should then be prompted to enter your UMN x500 password, after which, you will press return or enter. You are now connected to the Mesabi cluster.

b. In the new command line, type, exactly:

```
module load schrodinger [hit return or enter]
maestro [hit return or enter]
```

Maestro release 2021-3 should load, although this can be a VERY slow process; be patient (and ignore any "Warnings").

3. Create an input geometry for menthone (the trans-diastereomer) and carry out a conformational search with molecular mechanics in MacroModel.

Create a working directory:

a. Go to *File* → *Change Working Directory* (to open the file explorer) → *Create New Folder* (folder icon in right hand side of top menu bar) Change the directory label to "menthonemaster_dir." Open the menthone master directory and again click the "Create New Folder*"* button and change the directory label to 'menthonesub_dir.'
Select the 'menthonesub_dir' directory (single click to highlight, don't double-click to open) and click "choose" (button at bottom right) to set the working directory for computational files associated with menthone.

Create an input structure and carry out a conformational search:

b. Go to *Edit* → *2D Sketcher*. Draw menthone in the right hand workspace; specify the relative configuration of the two stereocenters. Now change the title to 'menthoneinitial_geometry' and click "Save as new." Close the 2D Sketcher window.

c. Open the "Tasks" button (upper right on the menu bar) and browse/navigate to "conformational search." A window will open that displays the possible options that can be modified for the conformational search.

d. Select the "Force Field" tab, select MMFF, and select water as the solvation model (the closest solvent to methanol, the polar protic solvent in which you have measured the equilibrium ratio).

e. Select the "CSearch" tab at the top. Change the method to Torsional Sampling (MCMM). Uncheck the Multiligand box and, then, the Perform Automatic Setup During Calculation box. Click the "Perform Automatic Setup" button. Change the torsional sampling options to Extended.

f. Delete the default job name and enter "menthone-csearch." Do not use spaces, back-slashes or forward slashes in file names. Select "Run" to begin the conformational search.

g. Click the *Jobs* → *Monitor* buttons (located to the left of tasks), and a monitor window will open that displays the progress of the conformational search.

h. View the structures of the family of unique conformers by selecting *Project* → *Show Table* to display the Project Table window.

i. Select *Show* → *All* to display information from the conformational search.

j. Inspect the column named "Minimization Converged-(force field)" to ensure that each conformer has converged, as evidenced by a checked box for each conformer. Also, for each conformer reported in the Project Table, inspect the column named "Times Found-(force field)" to ensure that each conformer was found at least ten times.

k. Record the energies for each conformer found in the "Potential Energy" (not "Relative Potential Energy") into your Excel spreadsheet.

For additional help on performing the molecular mechanics computation using Maestro (the GUI for MacroModel), read "Operation 1" on p 646, Box 3 (p 647), and pp 649-651 in the following publication: A guide to small molecule structure assignment through computation of (^{1}H and ^{13}C) NMR chemical shifts. Willoughby, P. H.; Jansma M. J.; Hoye, T. R. *Nature Protocols* **2014**, *9*, 643–660. (You can link to this at https://www.nature.com/articles/nprot.2014.042 if you are connecting on a campus WiFi or internet or via VPN from off campus.)