Lab0:

(7) Using FFE options under “Modeling Commands”, run the “Analyze”, “Minimize” and “Spacefill” programs on the ibuprofen structure. What is the value of the van der Waals surface area of ibuprofen in square Angstroms? How about the accessible surface area, and the “contact-reentrant” (smooth molecular) area?

Tinker-FFE version 8.10.1 Results

I downloaded from Pubchem but the structure from Cactus has tiny bit higher energy

Analyze ibuprofen before Minimization:

Analysis Types [E]

Total Potential Energy : 21.0277 Kcal/mole

Analyze ibuprofen after Minimization:

Analysis Types [E]

Total Potential Energy : 12.2922 Kcal/mole

Running spacefill (FFE-Tinker version 8.10.1) on minimized energy structure. Realized that for *Probe Radius in Angstroms (Leave blank for van der Waals Area and Volume)* this needs to be added to work for (2) and (3) below.

(1) Van der Waals Area and Volume: works WITHOUT & WITH probe radii

```
$ ~/tools/Tinker-FFE/tinker/bin/spacefill ~/tools/Tinker-FFE/NIHdownloads/ibuprofen.xyz $(echo 1
N) -k ~/tools/Tinker-FFE/NIHdownloads/ibuprofen.key # $(echo <my_in1> <my_in2> …) does same as
stdin

Van der Waals Surface Area and Volume :
Total Area :             240.174 Square Angstroms
Total Volume :           232.243 Cubic Angstroms

$ ~/tools/Tinker-FFE/tinker/bin/spacefill ~/tools/Tinker-FFE/NIHdownloads/ibuprofen.xyz $(echo 1
1.4 N) -k ~/tools/Tinker-FFE/NIHdownloads/ibuprofen.key

Van der Waals Surface Area and Volume :
Total Area :             240.174 Square Angstroms
Total Volume :           232.243 Cubic Angstroms
```

(2) Accessible Area and Excluded Volume: works only WITH probe radii

```
# this will ask to input the Probe Radius anyway and in FFE it just stalls at “Enter a Value for
the Probe Radius [1.4 Ang] :”
$ ~/tools/Tinker-FFE/tinker/bin/spacefill ~/tools/Tinker-FFE/NIHdownloads/ibuprofen.xyz $(echo 2
N) -k ~/tools/Tinker-FFE/NIHdownloads/ibuprofen.key

# this works
$ ~/tools/Tinker-FFE/tinker/bin/spacefill ~/tools/Tinker-FFE/NIHdownloads/ibuprofen.xyz $(echo 2
1.4 N) -k ~/tools/Tinker-FFE/NIHdownloads/ibuprofen.key
```

```
Accessible Surface Area and Excluded Volume :
Total Area :             428.639 Square Angstroms
Total Volume :           693.930 Cubic Angstroms
```

(3) Contact-Reentrant Area and Volume: works only WITH probe radii

```
# this will ask to input the Probe Radius anyway and in FFE it just stalls at “Enter a Value for
the Probe Radius [1.4 Ang] :”
$ ~/tools/Tinker-FFE/tinker/bin/spacefill ~/tools/Tinker-FFE/NIHdownloads/ibuprofen.xyz $(echo 3
N) -k ~/tools/Tinker-FFE/NIHdownloads/ibuprofen.key

# this works
$ ~/tools/Tinker-FFE/tinker/bin/spacefill ~/tools/Tinker-FFE/NIHdownloads/ibuprofen.xyz $(echo 3
1.4 N) -k ~/tools/Tinker-FFE/NIHdownloads/ibuprofen.key

Contact-Reentrant Surface Area and Volume :
Total Area :             229.593 Square Angstroms
Total Volume :           238.914 Cubic Angstroms
```

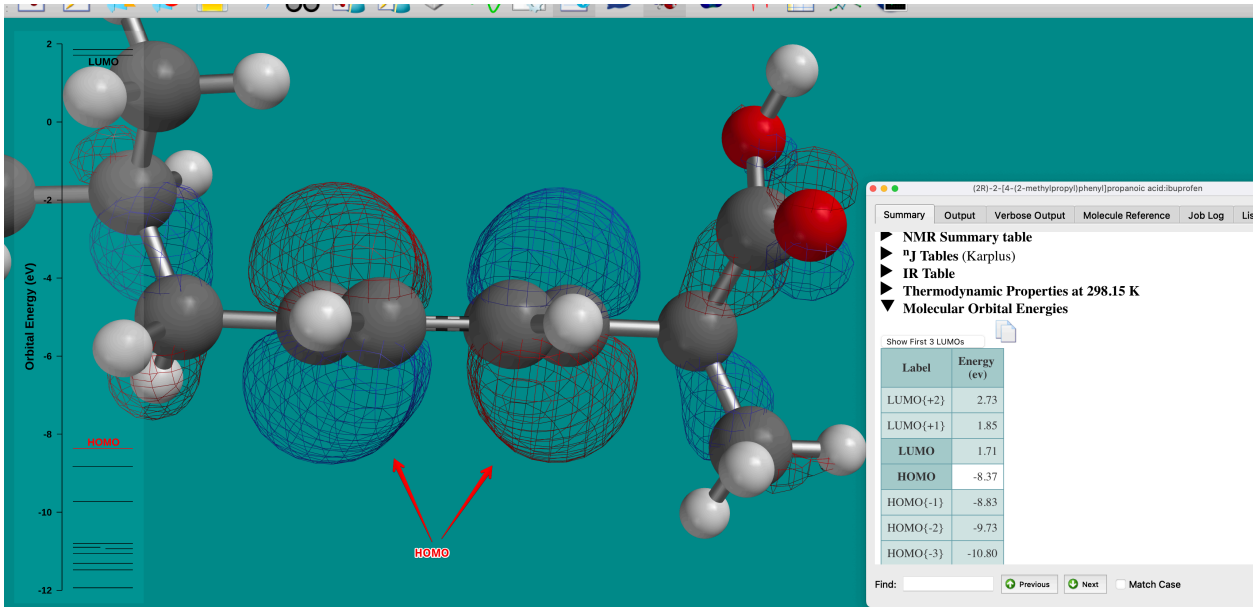
Conclusions:

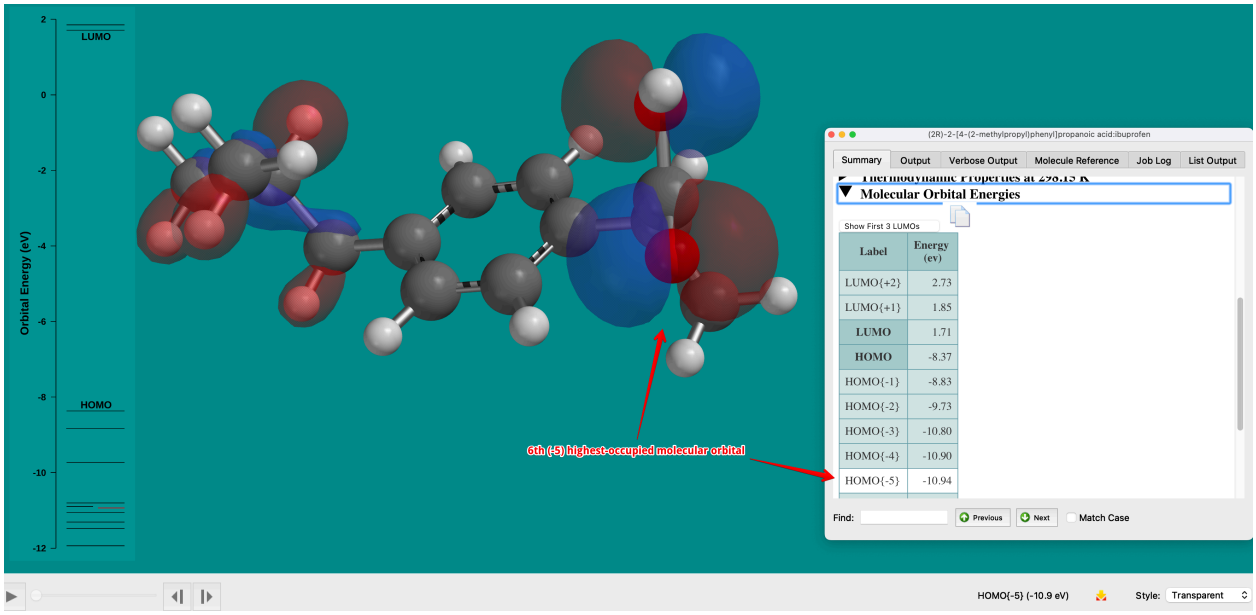
Contact-Reentrant Area much closer to VDW surface area/volume than SASA, makes sense.

(8) Open the Spartan Student program, and use its structure building menu to construct the ibuprofen molecule. You can then run a Hartree-Fock molecular orbital calculation using the STO-3G basis set for this molecule. Look at several of the highest energy occupied orbitals for ibuprofen. Save a picture of the highest occupied p-type orbital. Use the “Command-Shift-4” key combination to do a screen capture, drag the mouse over the screen area to be saved.

Spartan (ibuprofen)

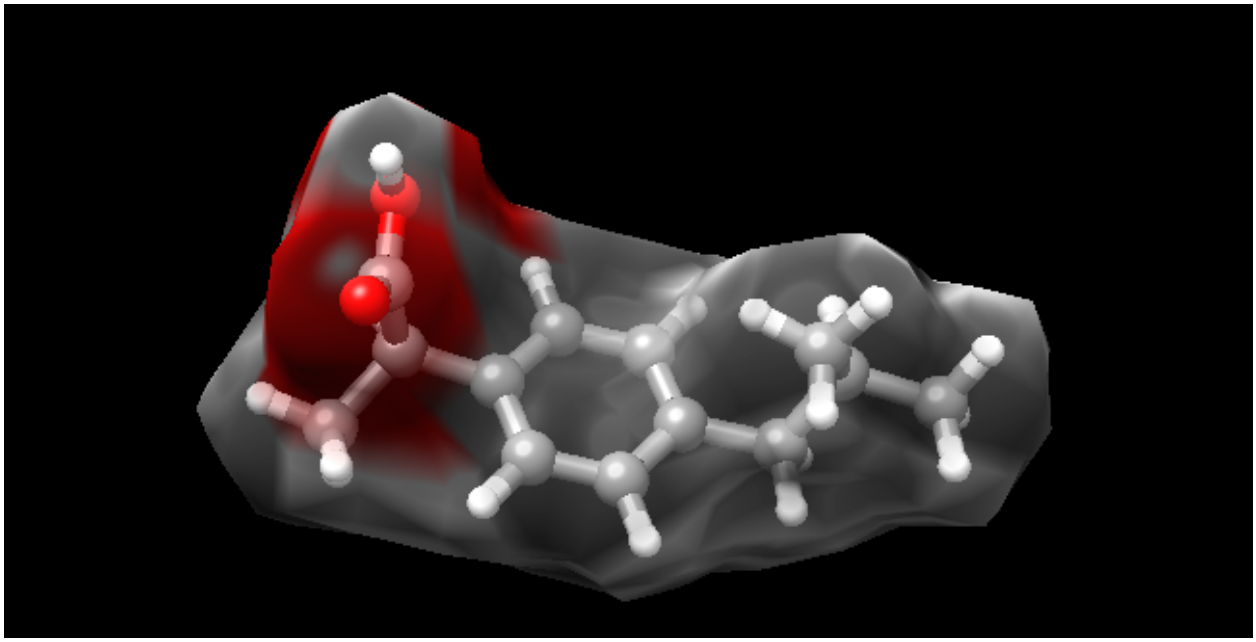
Changing from HOMO where the π-orbital is localized on the benzene ring to HOMO{-5} then π-orbital is localized to -COOH group.



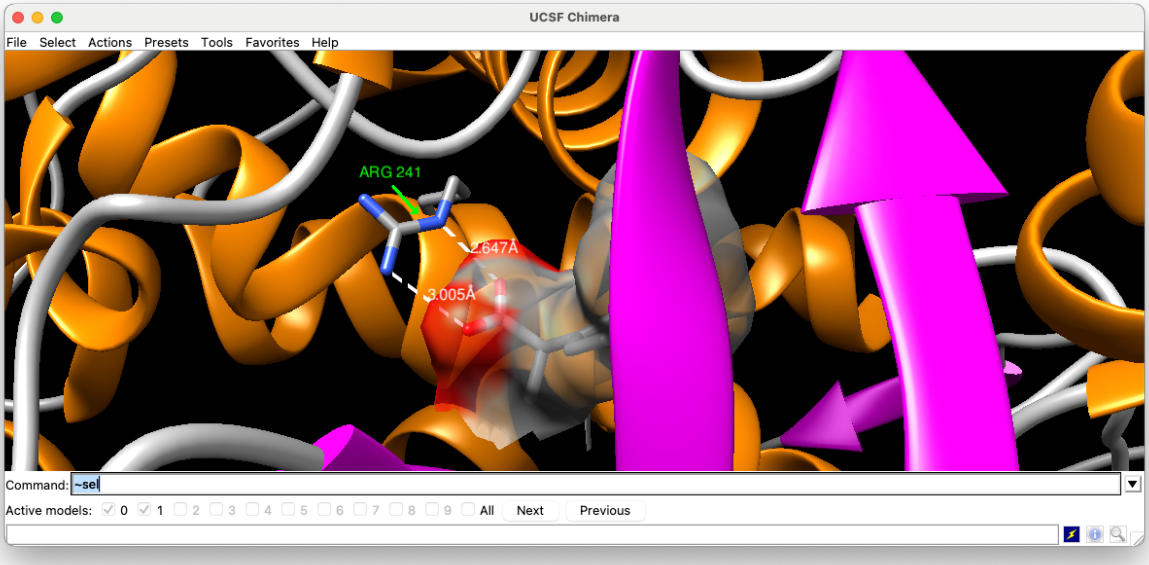


(9) Two visualization programs that are widely used for biomolecular structures are Chimera and VMD. We will use both of these packages later in the course. Both programs have online tutorials: “Chimera Getting Started” and “Using VMD Tutorial”, which are found in the Software Resources area of the course website.

UCSF Chimera



Electrostatic potential and surface of ibuprofen (canonical blue=positive, white=neutral, red=negative)



PDB 3VM4: carboxyl of ibuprofen hydrogen bonding to 241Arg of Cytochrome P450SP alpha (CYP152B1) in *Sphingomonas paucimobilis.* (note that hydrogens of Arginine are not shown in the visualization)