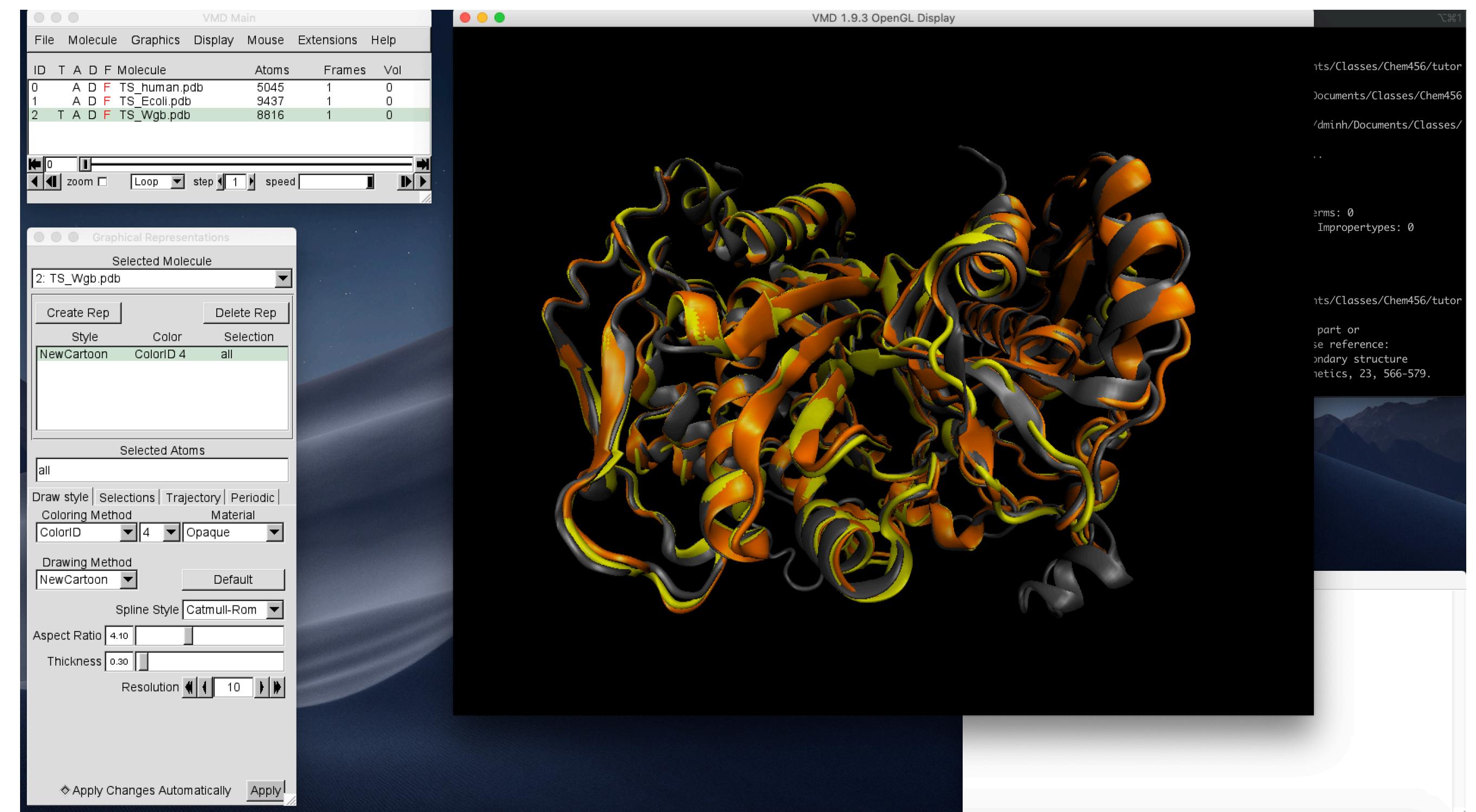
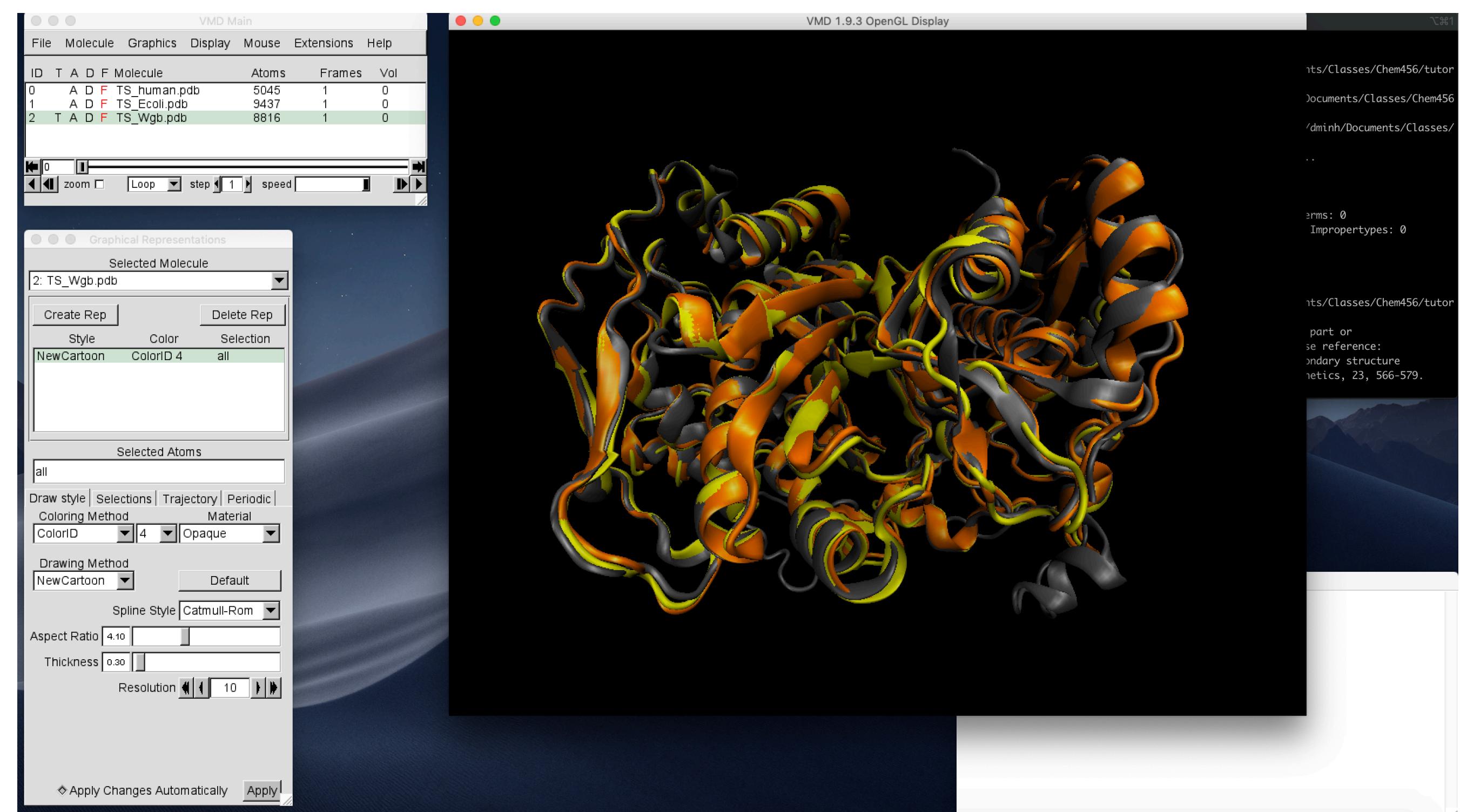


1.2.3 Exercise: Visualizing Electrostatic Potentials with VMD

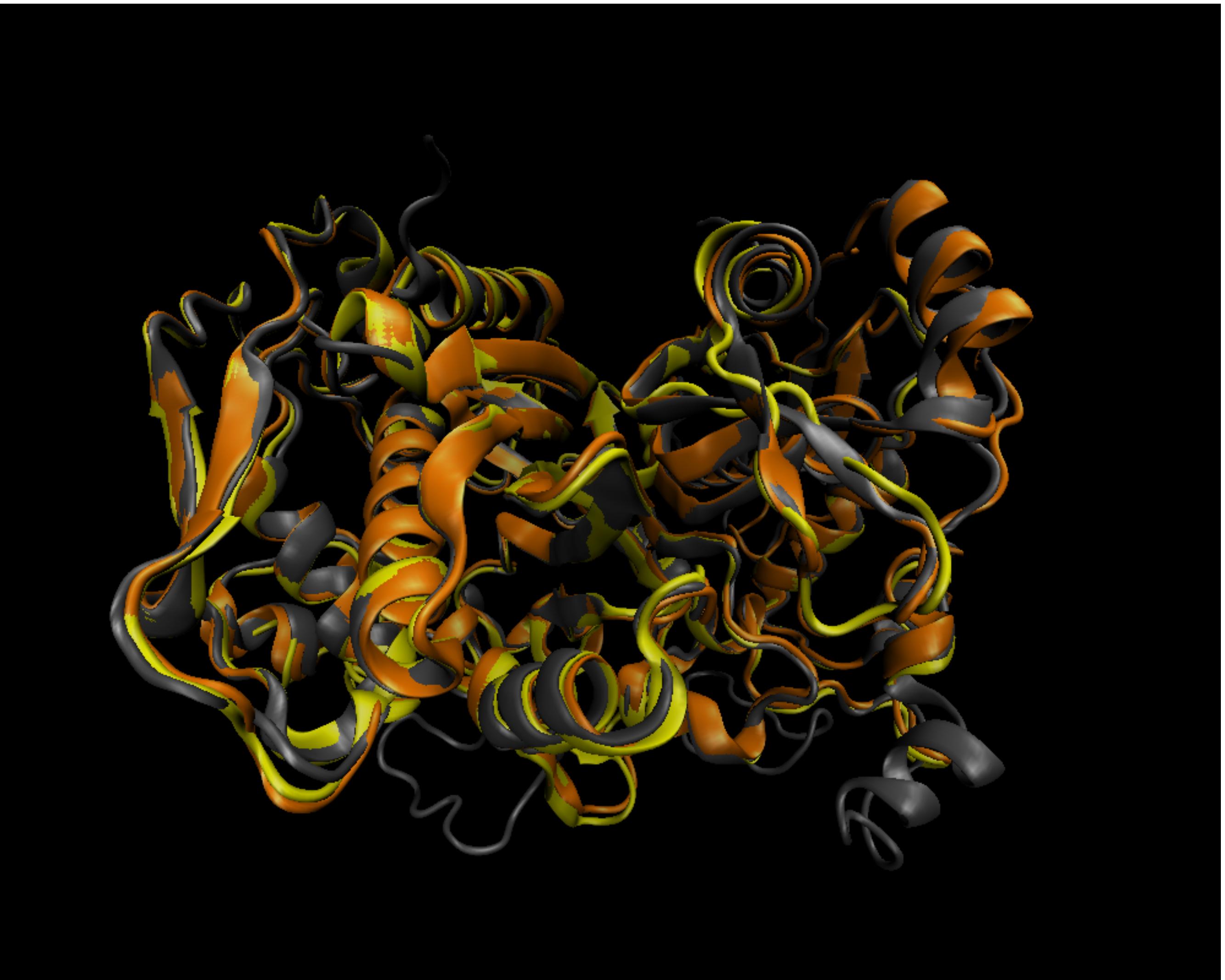
- Load the models of TS from human, E. coli, and W.g.b. The files are available in the modelingworkshop/exercises/thymidylate-synthase/ directory.
- Use the “NewCartoon” representation and color human gray (2), E. coli orange (3), and W.g.b. yellow (4)
- Your display should look something like the image to the right
- Which of the enzymes is least like the others?



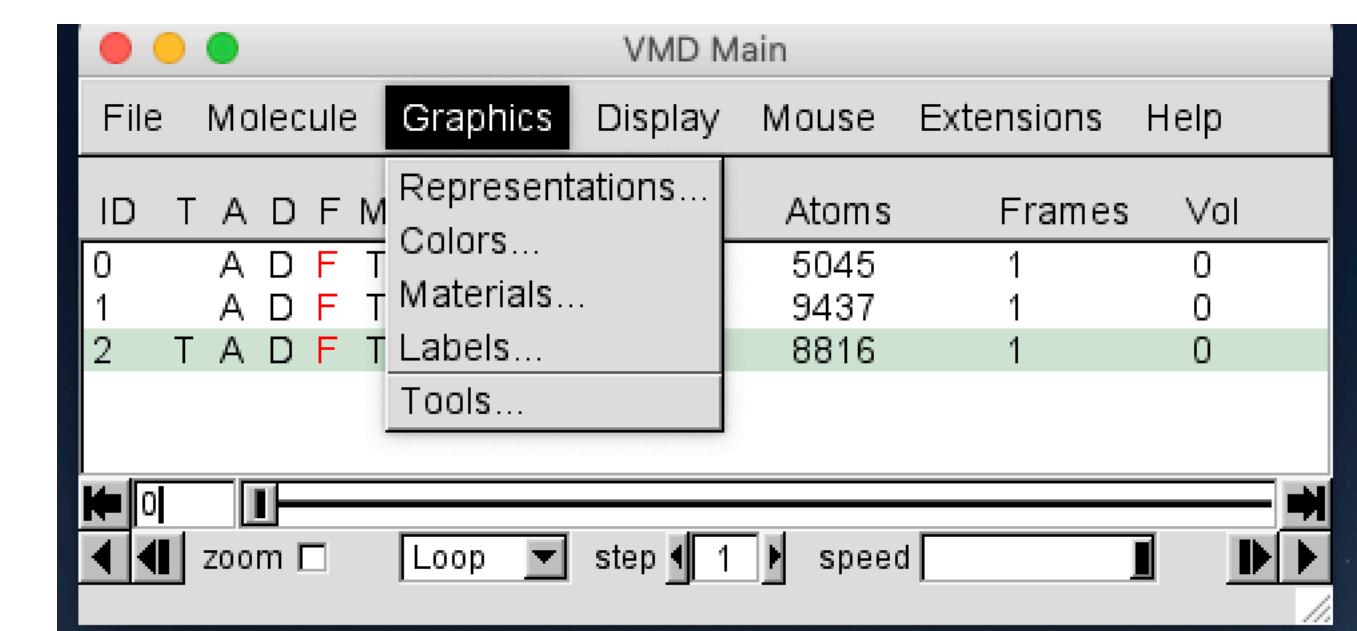
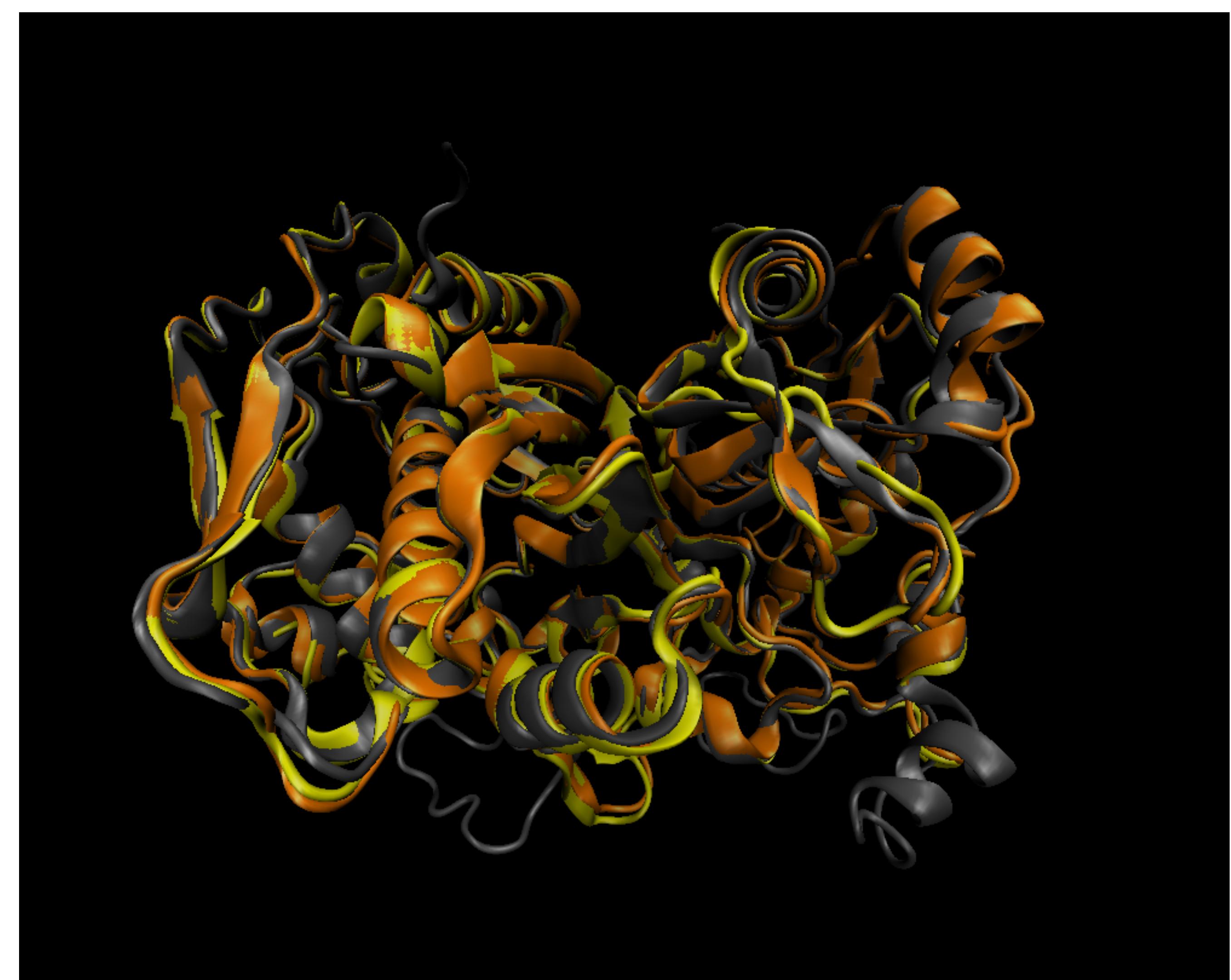
- Load the models of TS from human, E. coli, and W.g.b.
- Use the “NewCartoon” representation and color human gray (2), E. coli orange (3), and W.g.b. yellow (4)
- Your display should look something like the image to the right
- Which of the enzymes is least like the others?
- In the human structure, a short helix is extended and a coil added. A sheet is replaced by an extended loop.



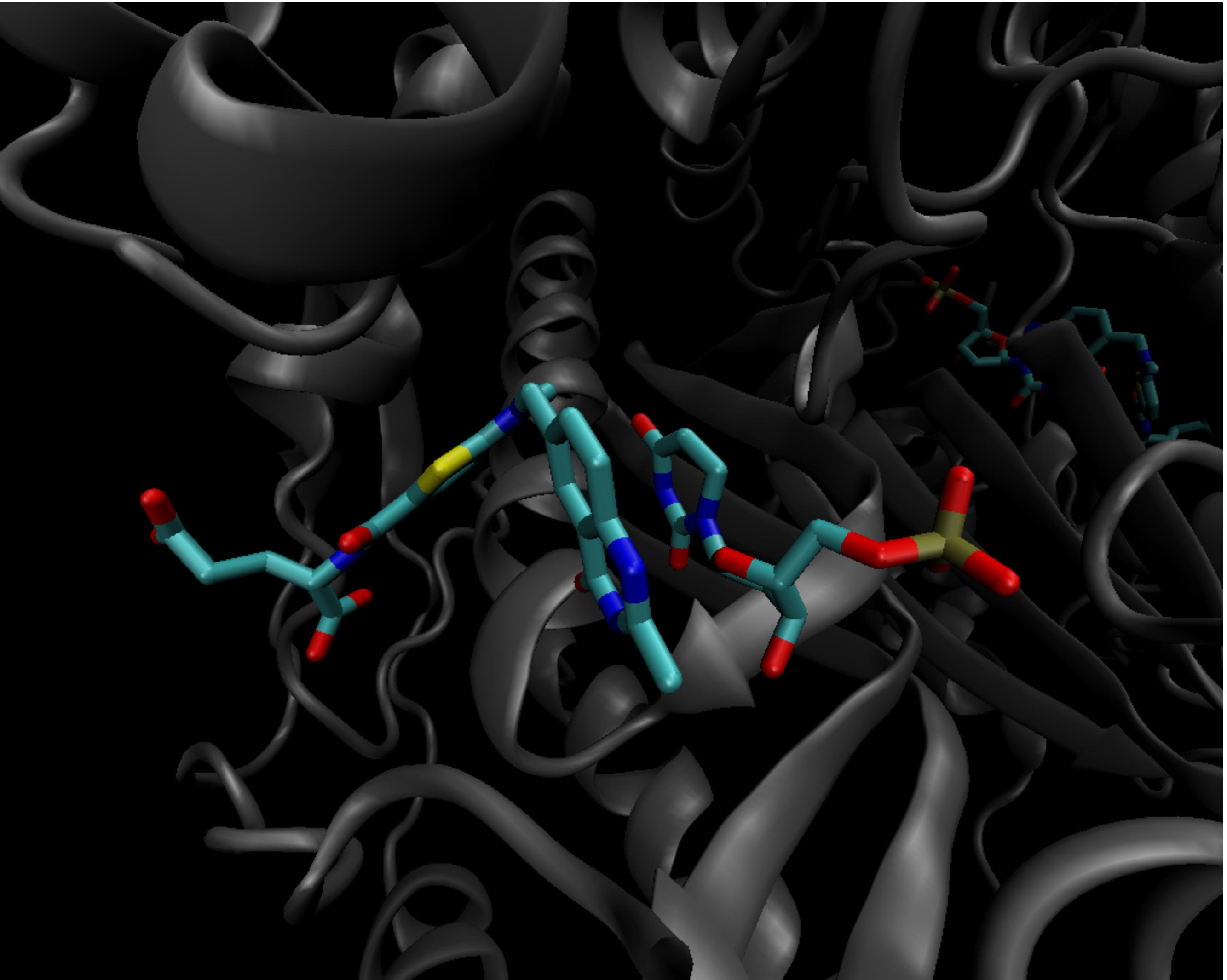
- Press 1 and then click to label specific atoms. Where (what residue numbers) are the unique parts of the human structure?



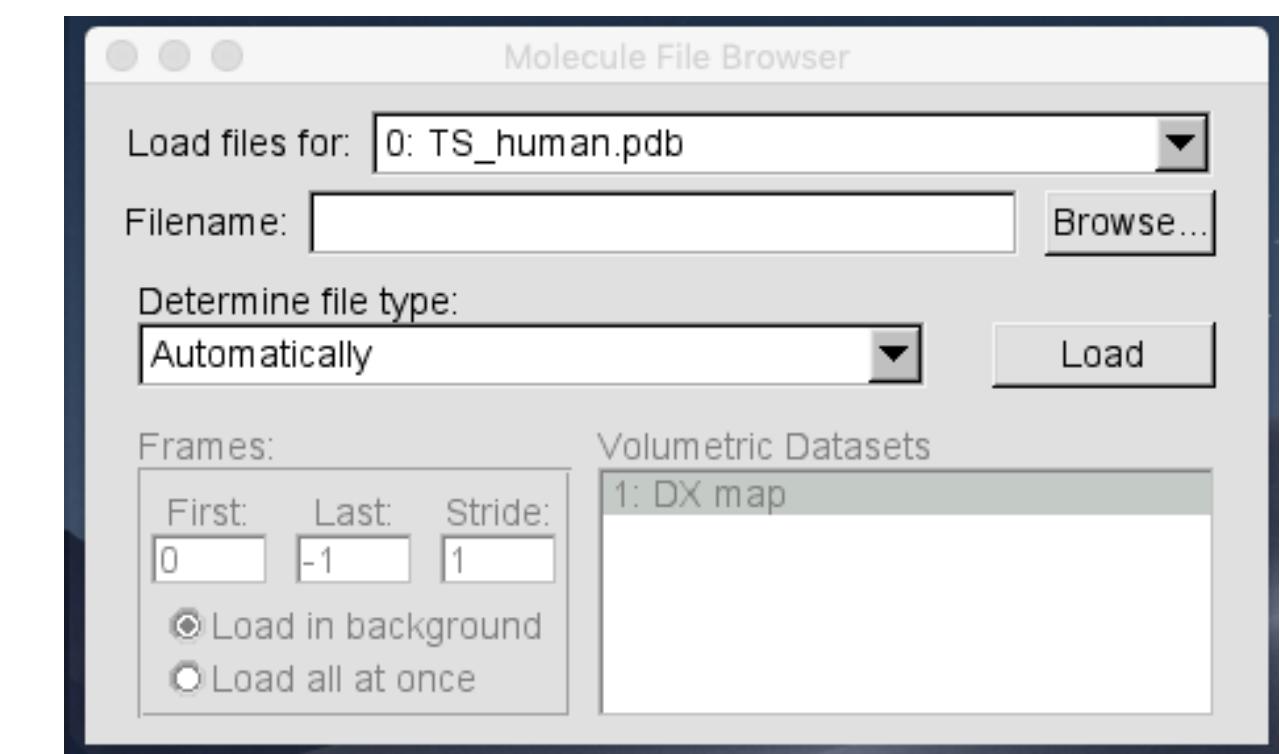
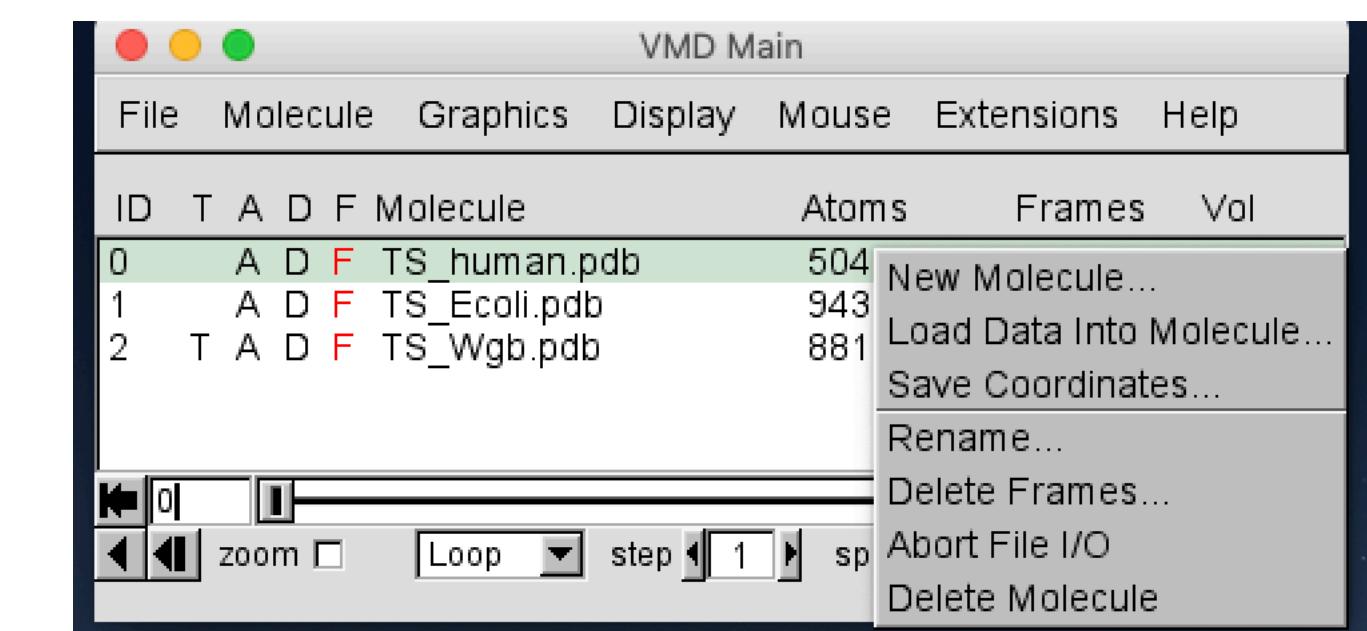
- Press 1 and then click to label specific atoms. Where (what residue numbers) are the unique parts of the human structure?
 - 114 to 125
 - 142 to 157
- You can remove the labels by going to the “Graphics” menu under “Labels”, selecting labels, and deleting them.



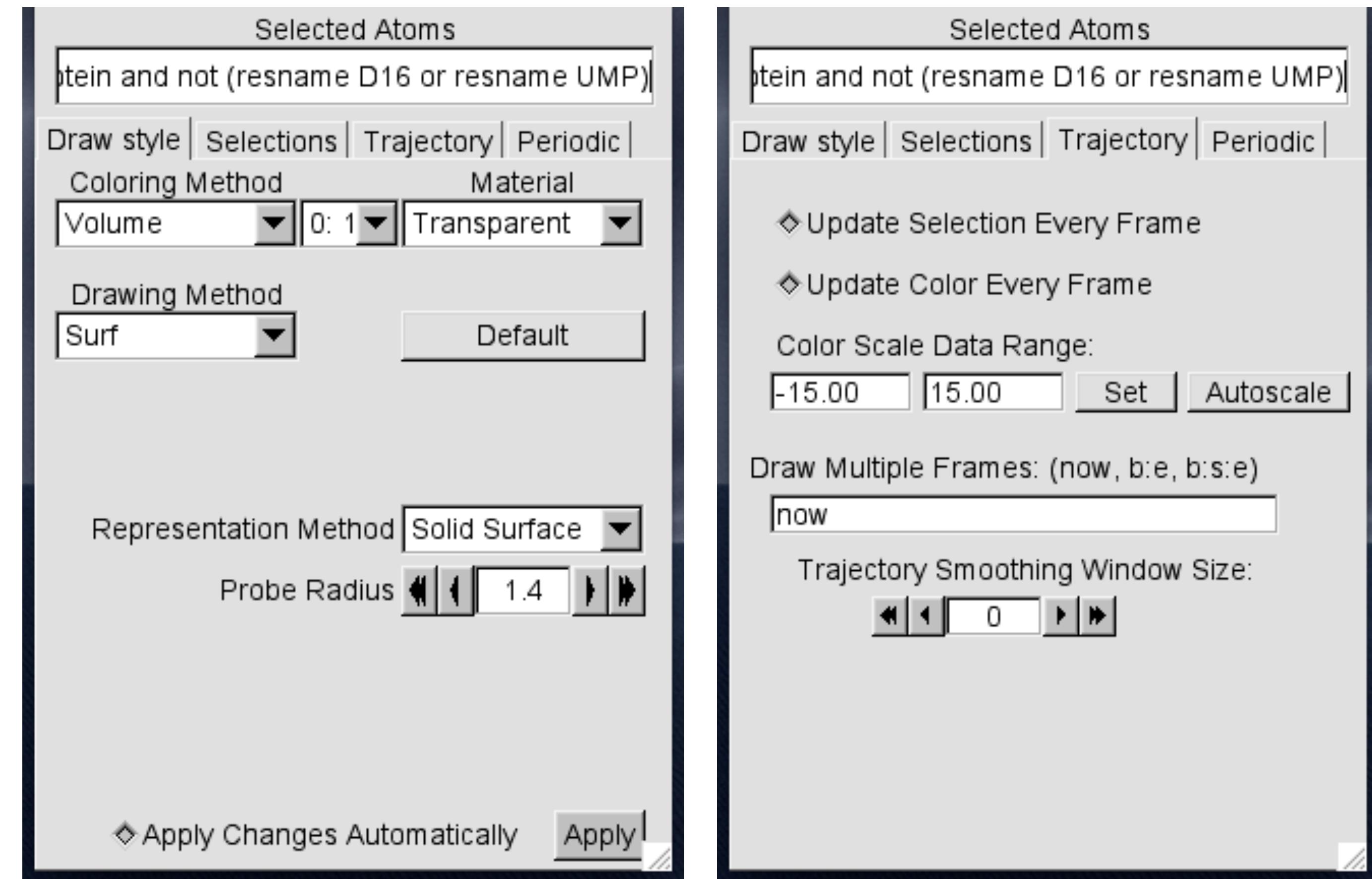
- The location of the active site is a lot more evident if you create a representation with Selected Atoms as “resname D16 or resname UMP”, Color Method “Element”, and Drawing Method “Licorice”



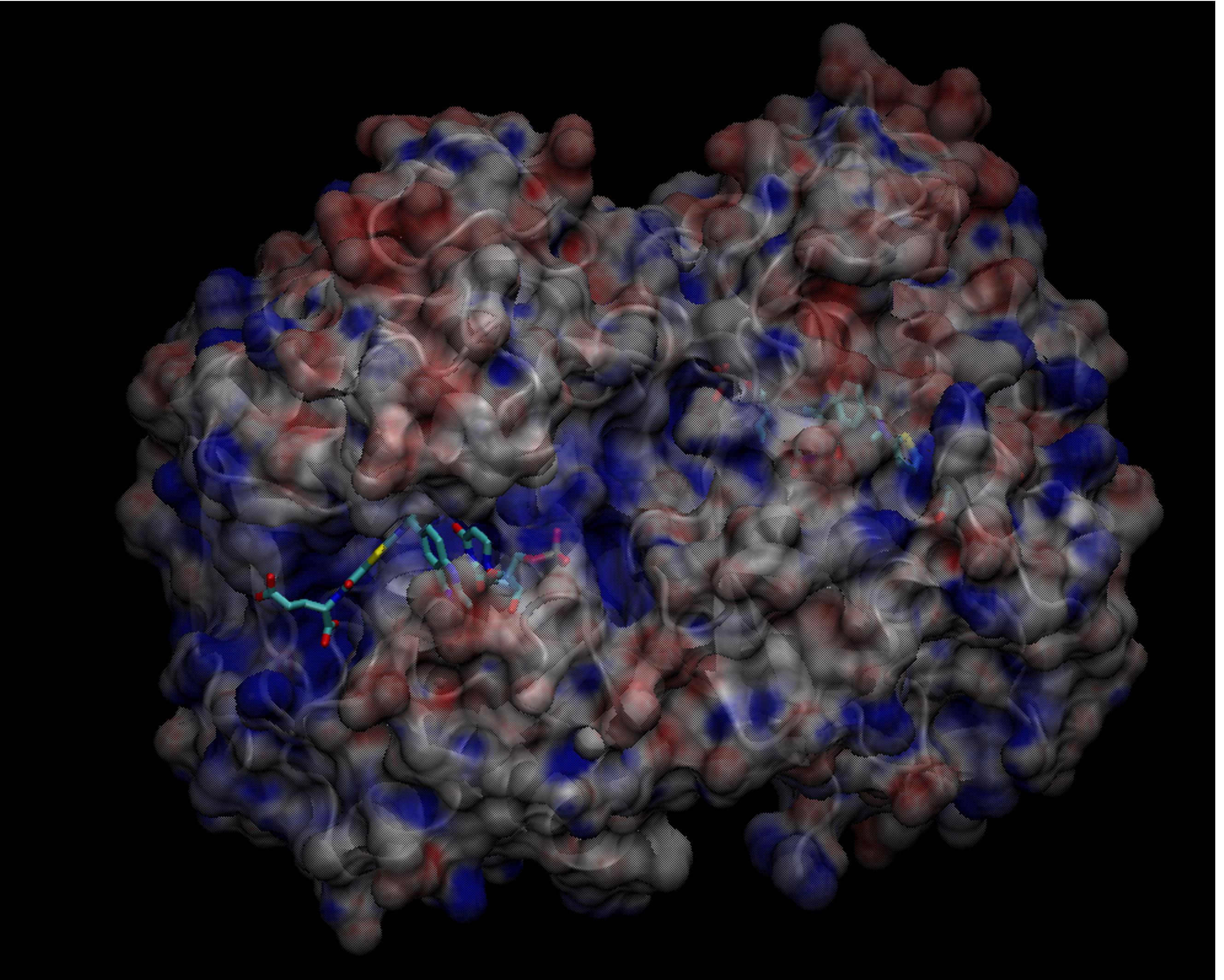
- Now let's actually load the electrostatic potential
- In the “VMD Main” window, right click on a molecule and select “Load Data Into Molecule”
- Browse to the .dx file in the same directory as the molecule of interest and load it
- It won't look like anything has happened except there will be a line under “Volumetric Datasets”
- Let's focus on human and hide the other structures by double-clicking on D in the VMD Main window



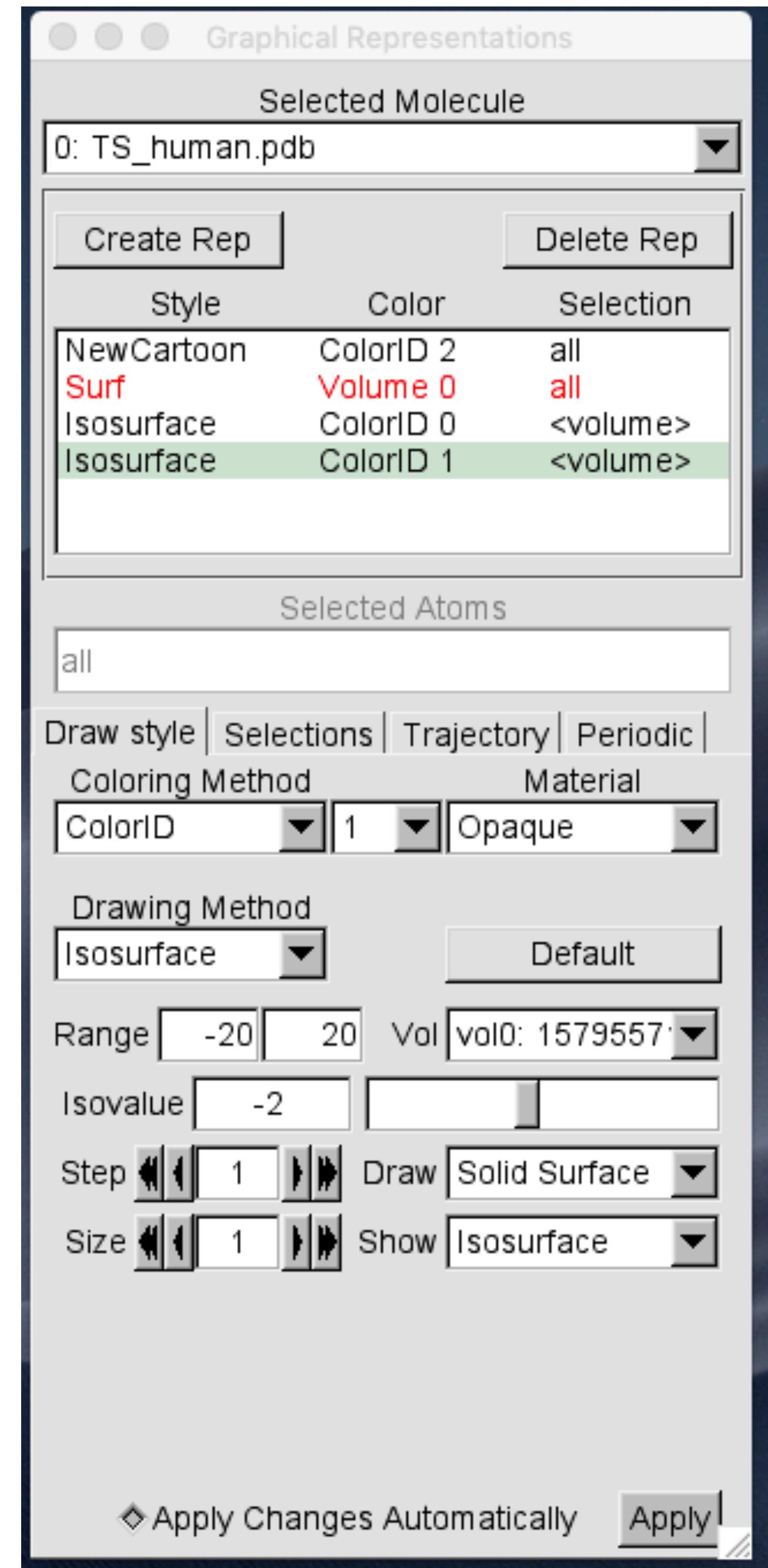
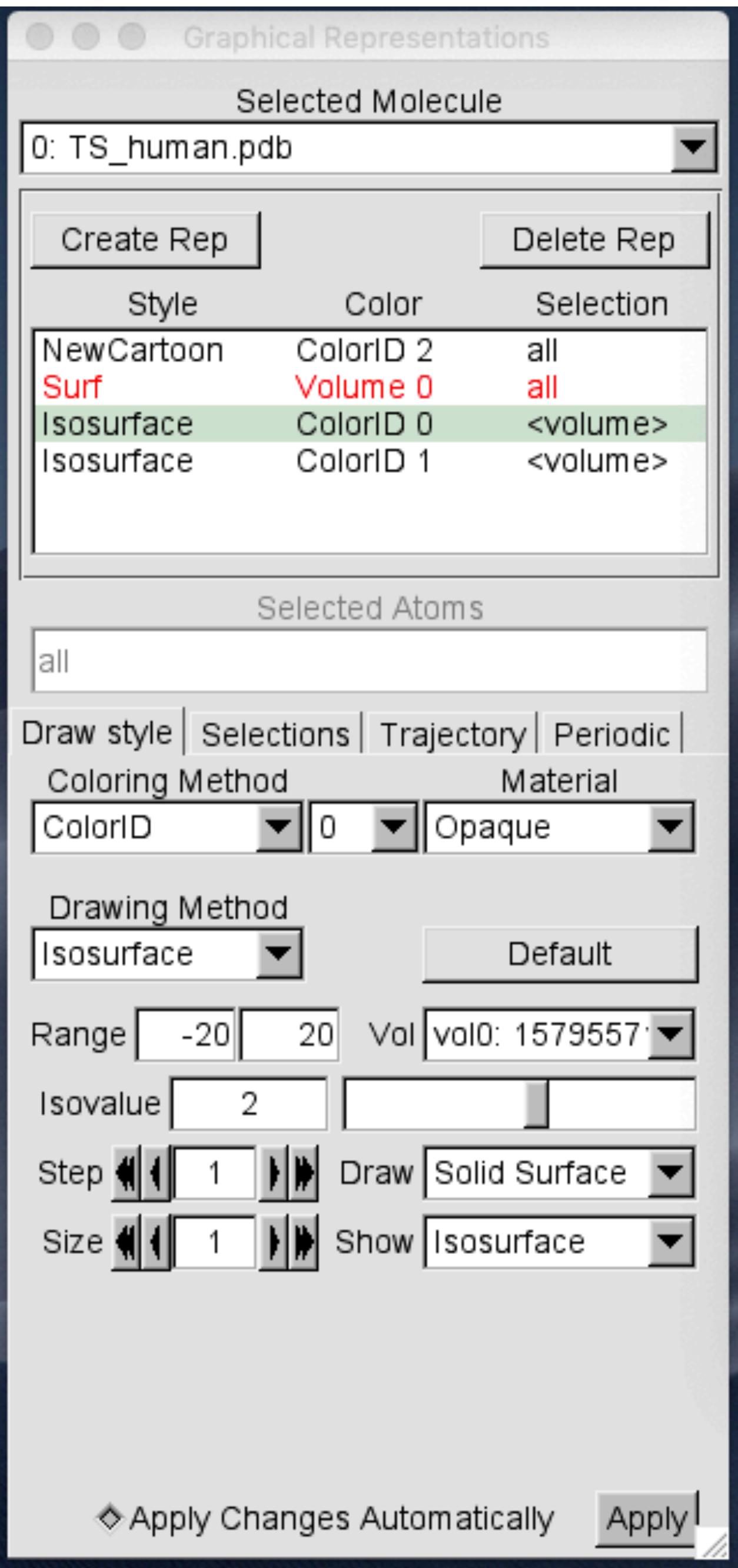
- In VMD, volumetric data can be displayed
 - by Isosurface, VolumeSlice, or FieldLines representations
 - Using the “Volume Coloring Method”
 - To color a surface based on the electrostatic potential, create a new representation selecting “protein and not (resname D16 or rename UMP)”, set the Drawing Method to “Surf”, Coloring Method to “Volume”, and Material to “Transparent”
 - Also click on the “Trajectory” tab and set Color Scale Data Range from -15 to 15. Otherwise everything will look white.



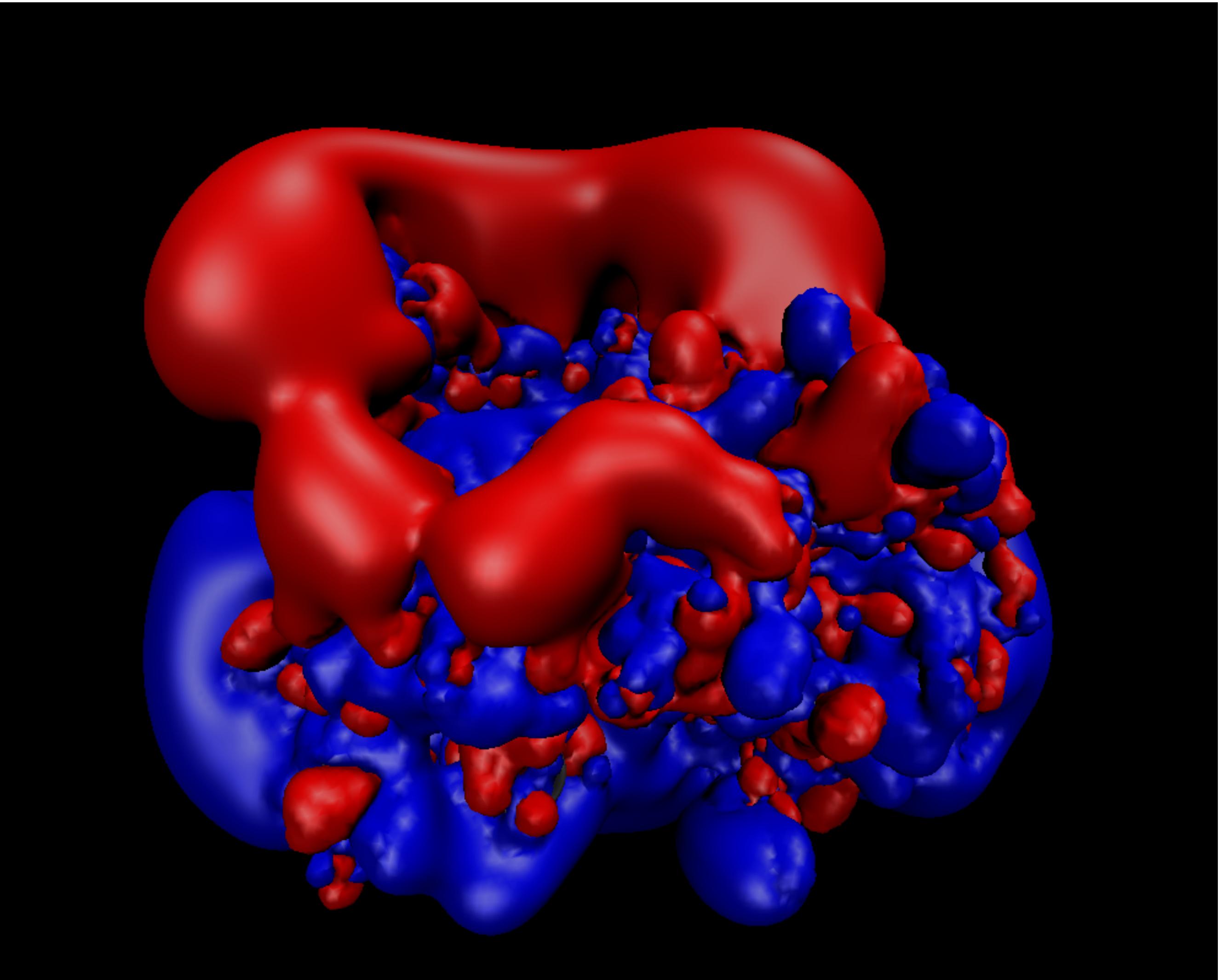
- On the surface, positive is blue and negative is red.
- Notice that there is a positive charge in the entire binding site cleft



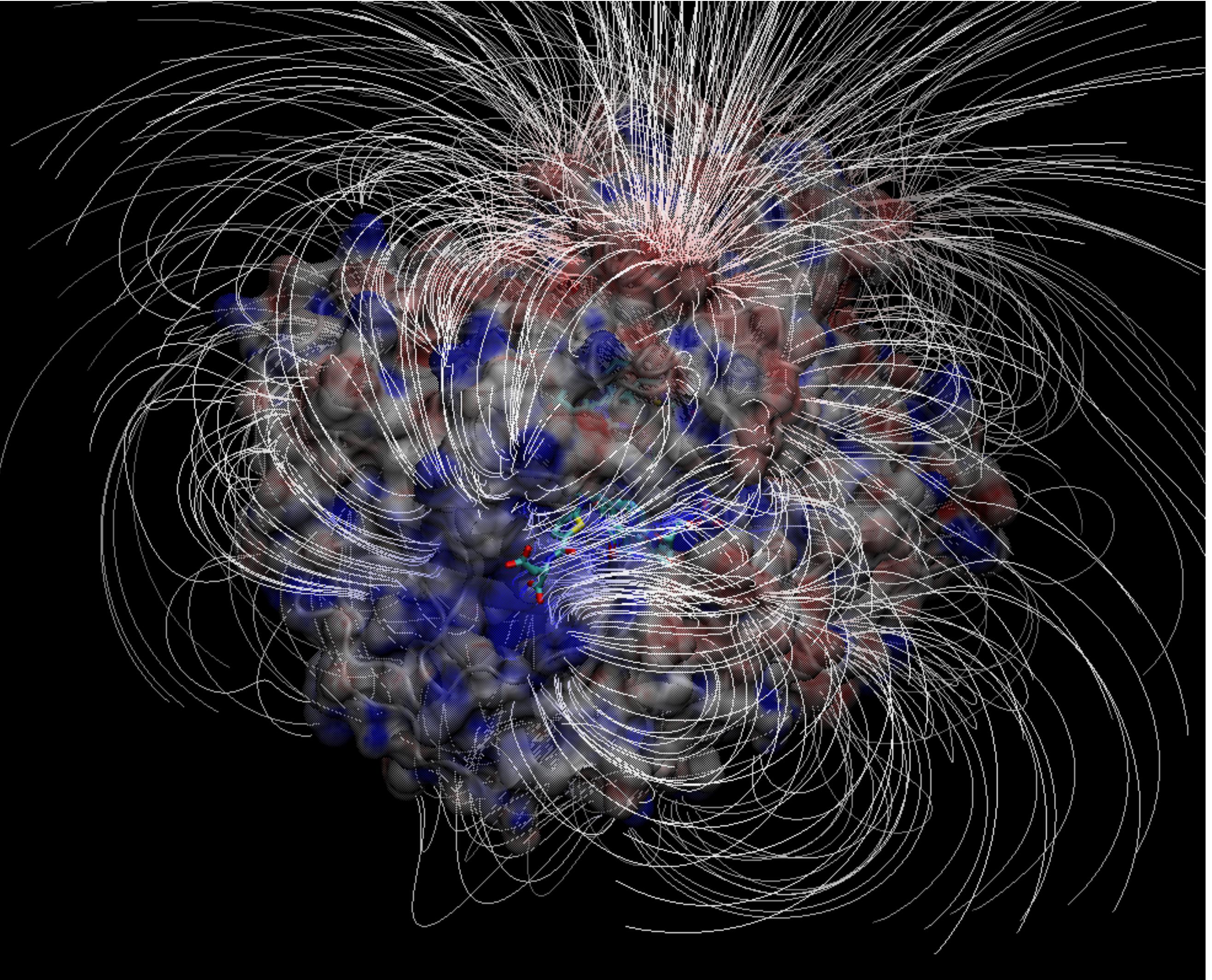
- Now let's try the isosurface representation. In this representation all points along the surface have the same electrostatic potential.
- Create two isosurfaces
 - a blue isosurface with isovalue 2
 - a red isosurface with isovalue -2
- Hide the solvent-accessible surface by double-clicking on "Surf"



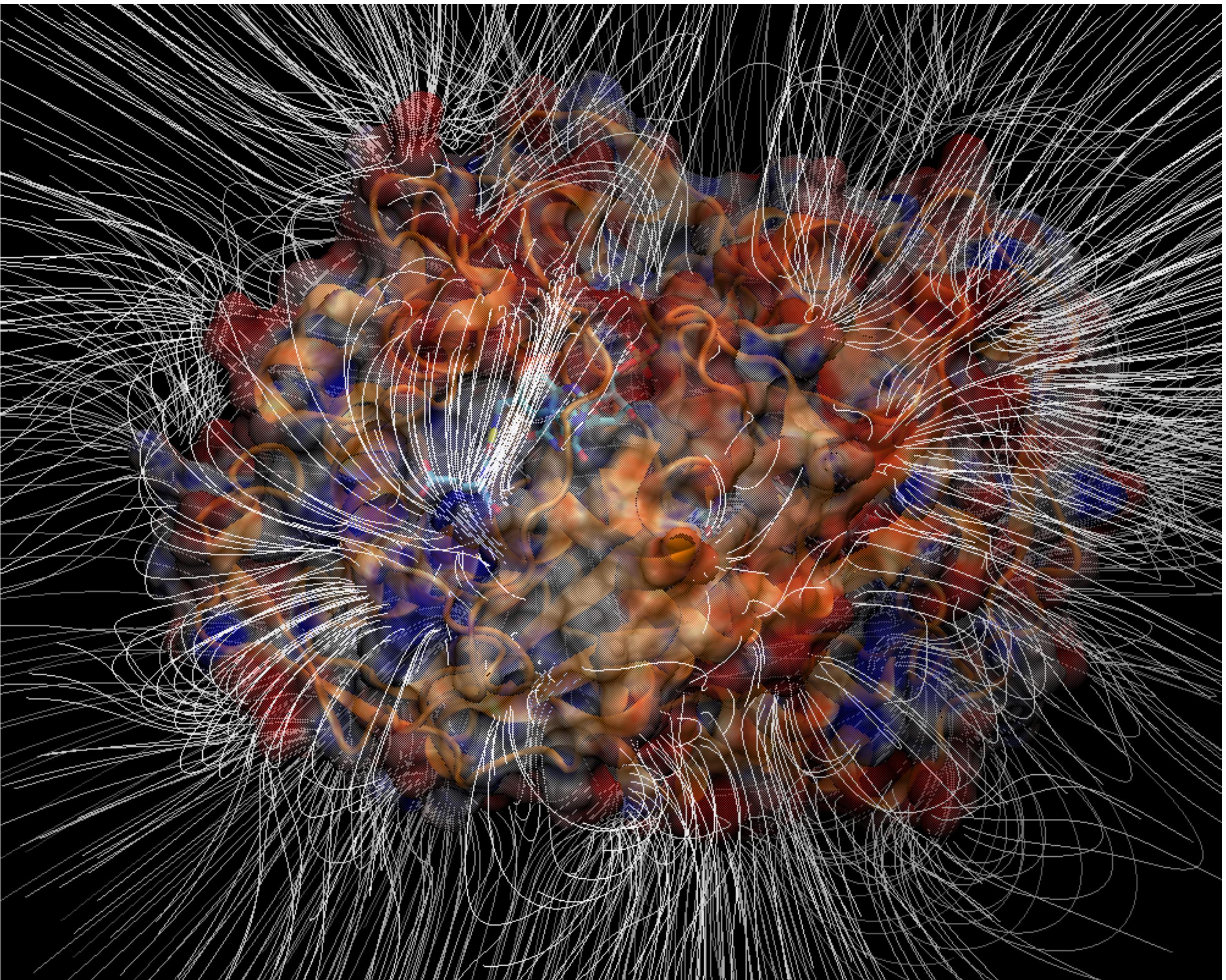
- The isosurfaces are a reasonable reproduction of Fig.1 from Garg *et al.* (2015).
- However, the charges here seem to have a larger magnitude than in the paper. This may be because of charge assignment or including the ligands in the PQR file.



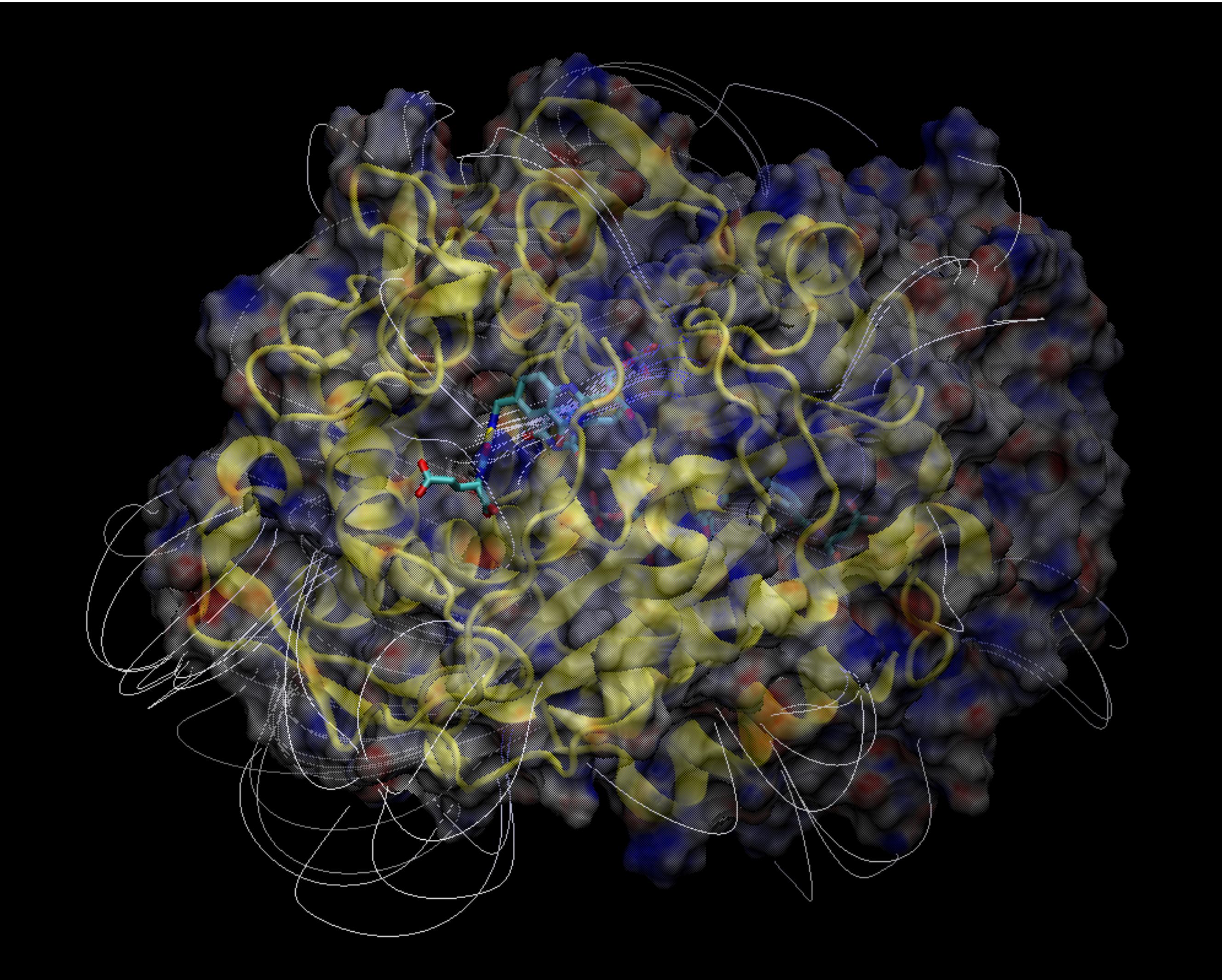
- Electric field lines show the path that a massless positive charge would take. The density of lines shows the intensity of the electric field.
- There is clearly a major electrostatic sink pulling negative ligands into the active site.



- The E. Coli enzyme has a similar positive patch and sink



- As a validation of Garg et. al. (2015), the W.g.b. electrostatic potential is much less pronounced.



References

- Garg, D.; Skouloubris, S.; Briffotaux, J.; Myllykallio, H.; Wade, R. C. Conservation and Role of Electrostatics in Thymidylate Synthase. *Sci Rep* 2015, 5 (1), 17356. <https://doi.org/10.1038/srep17356>, adapted under the CC BY 4.0 license.