Docking a ligand from a SMILES input

Docking a ligand file from a smiles file input is the real need for medicine chemist, as often time, 3-D sdf files for specific ligands are not available. Orbital's proprietary smiles to 3-D ligand generator function makes docking from a smiles file possible for the first time.

1. **Open** Orbital from the desktop. In the **File** dropdown menu, select **Open PDB ID** (Ctrl+P).

2. In the Open PDB ID popup window, enter the PDB ID **2HYY** and select OK in order to open the Human Abl kinase domain in complex with imatinib (STI571, Glivec)

3.

4.
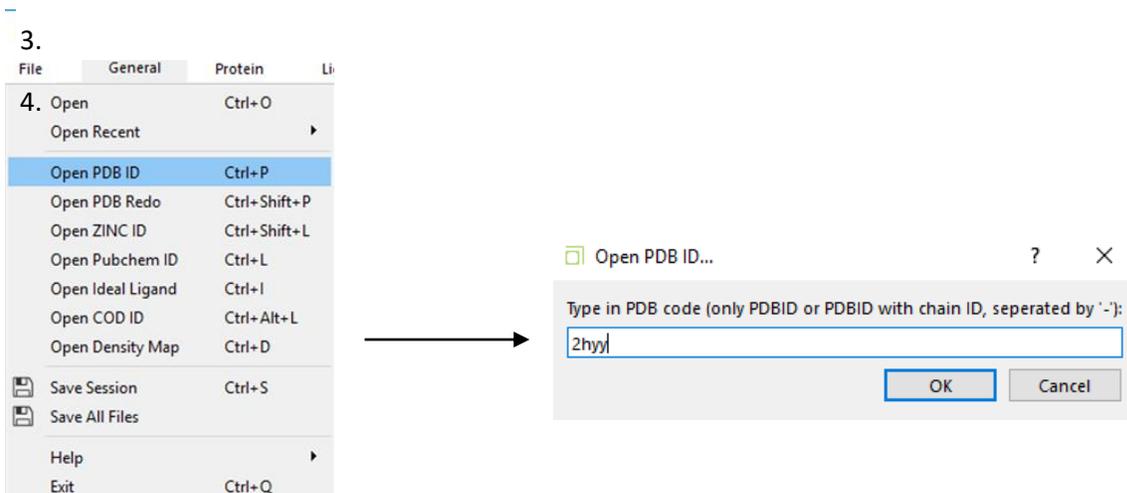
5. Under the **General** tab select the **Cartoon** setting in the **Display** panel in order show the protein in its cartoon structure.
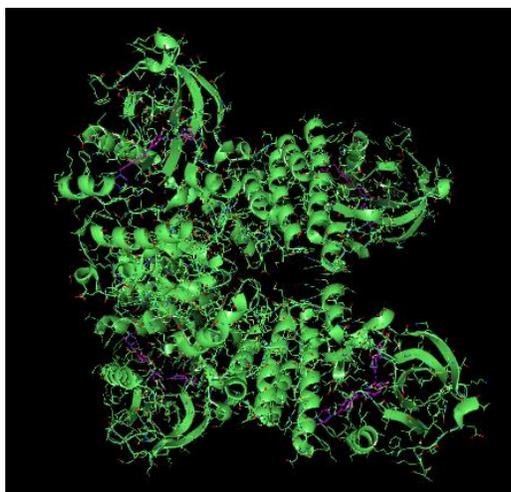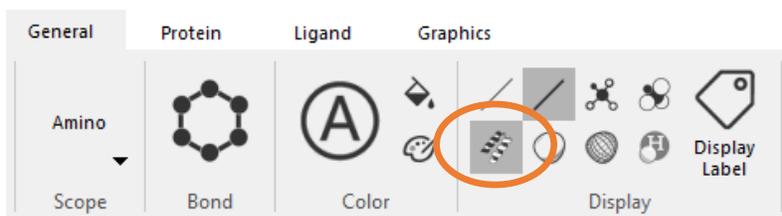
6. Next, open the dropdown menu for **2hyy** in the **Object Manager** by selecting the downward facing caret next to the name.

7. Select the ligand tab and right click **A 600 STI** and select **Extract Ligand** (E).
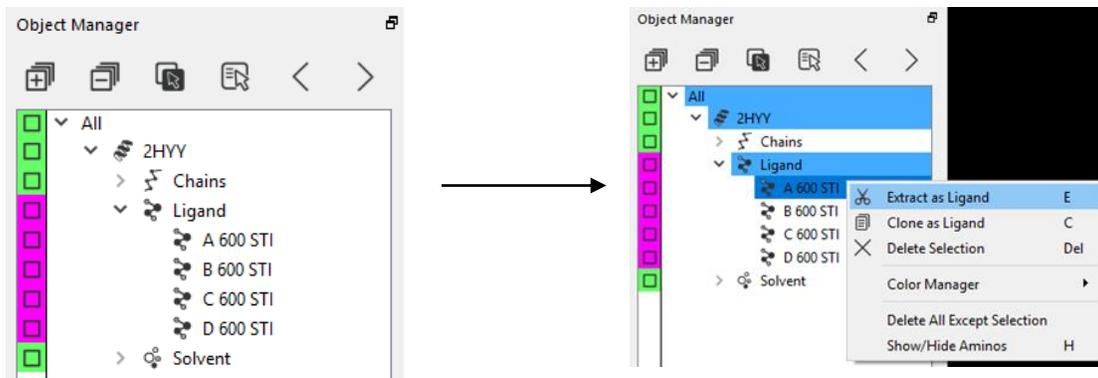
8. In the **Protein** tab select **Show Pockets** under the **Pocket** panel (circled in orange below). Orbital will then assign pockets to the protein surface.
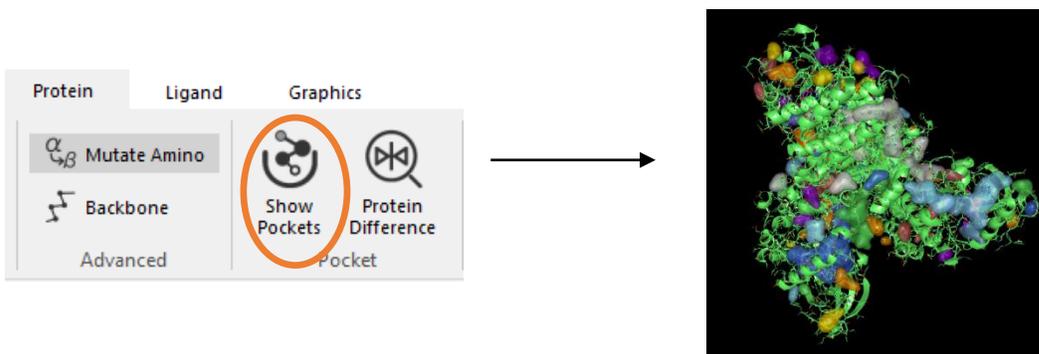
9. In the **Object Manager** click on the STI ligand using the scroll mouse button. This will zoom and center the ligand in the viewport.
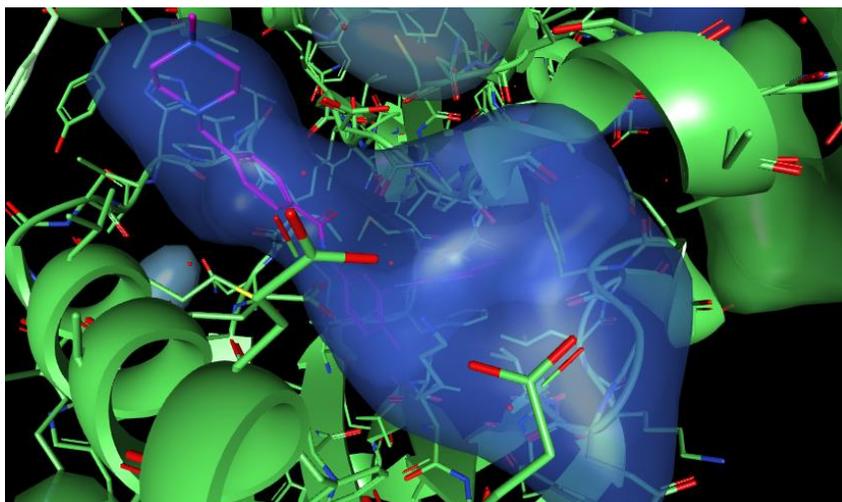
10. Next, in the **Object Manager** select the square next to 2HYY_pockets object in order to hide all pockets in the viewport. Select the black square next to 2HYY_pockets_3 in order to make only that pocket visible. In addition, hide the ligand STI by clicking the box next to its name.

11. In the **Ligand** tab select **Dock Wizard**. The wizard will open a panel on the right side of the screen. Delete STI that is already in the ligand input and select the button Switch to SMILES input. Identify the isomeric SMILES name for the STI ligand (https://www4.rcsb.org/ligand/STI) and insert this name into the Ligand input in the Dock Wizard. In the **Advanced Options** select Flexible within ring structure and click **Dock Begin**. In the **Object Manager**, right click on the SMILE dock object and change the color to yellow by opening the dropdown menu for the Color Manager (see below).Then, hide all pockets by selecting the square next to 2HYY as well as all docked ligands except for dock0.
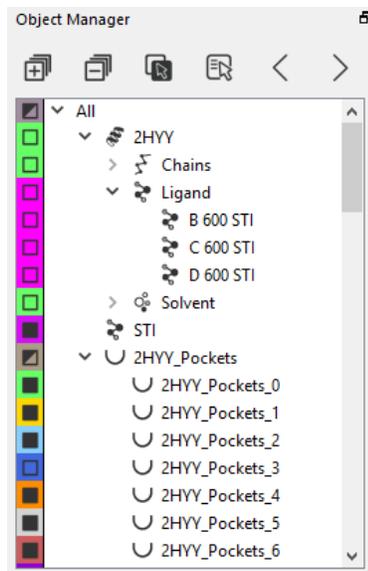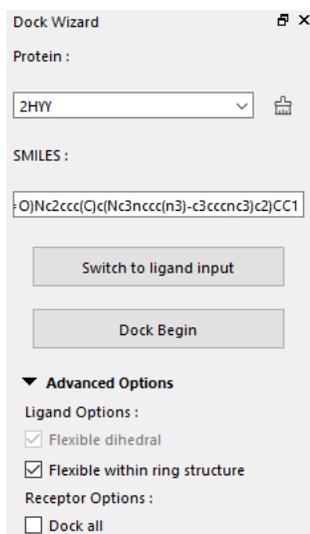
12. In the Object Manager, select the black box to the left of the name of the original STI ligand in order to display it in the screen (in purple below).
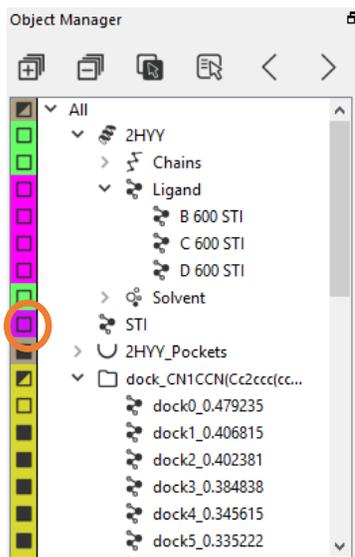
13. Select both the first docked ligand and the original ligand STI. In the **Ligand** tab select **RMSD**. The RMSD will be displayed in the Orbital logger window at the bottom left of the screen.
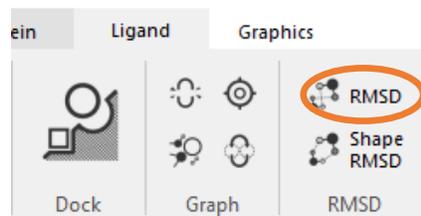
14. The RMSD of each atom between the structures will also be displayed on the screen.

Orbital Logger

Matched RMSD between STI and
dock0_0.479235 : 1.38201