# Cheat Sheet of the "Manual Fitting" Workflow

1) Select the receptor (and reference ligand, can be from the same PDB entry)
2) Start PyMOL
3) Download the specific chain(s) from the RCSB PDB (e.g. via PyMOL)
4) Check for any missing/mutated residues within the interested region
   a) PDB headers
   b) Visualize in 3D
   c) Corresponding journal article
5) Prepare receptor with the pdb2pqr server
6) Restore essential cofactors to the protonated receptor
7) Reference complex preparation
   a) Extract the reference ligand from co-crystal
   b) Protonate the reference ligand from co-crystal
   c) (optional) re-combine the receptor-ligand complex to remove steric clashes of the protonated receptor/ligand
      i) Combine the protonated ligand with the protonated receptor
      ii) In "builder" fix receptor coordinates
      iii) Sculpt to remove steric clashes due to the new hydrogens
      (Note the inaccuracies in ligand geometry!)
      iv) Extract the ligand again for geometry optimization
   d) Optimize the geometry of protonated reference ligand
   e) Combine the processed receptor and ligand to make the reference complex
   f) Save the reference pdb to "complex" folder
8) Preparing a model of the "new" complex
   a) Copy the reference complex to a new object (copy 1)
   b) Fix receptor coordinates
   c) Modify the ligand
   d) Use the sculpting tool to fit the new ligand by hand
   e) Extract the new ligand
   f) Optimize the geometry of the new ligand
   g) Make another copy of the reference complex (copy 2) and give it a name
   h) Delete the ligand in copy 2 of the reference complex
   i) Copy the optimized new ligand to the unliganded copy 2 of reference complex
   j) Save the complex as pdb in the "complex" folder
9) From the provided "scripts/PLATFORM/box-local" folder copy the scripts to the directory containing "complex" folder
   *a)* Quick minimization only: "min-autolist.sh" *(+ "minimize-auto-win.bat" for windows)*
   *b)* Quick minimization with flexible receptor: "min-flex-autolist.sh" *(+ "minimize-flex-auto-win.bat" for windows)*
   *c)* Docking with the gridbox defined by ligand: "dock-autolist.sh" *(+ "dock-auto-win.bat" for windows)*
10) check the directory structure
**11) Make sure there is no space in all the filename!!!**
*12) (**Windows only**, option: using double-click scripts):*
   *a) Edit the path to conda environment in the .bat scripts*
   *b) Edit the smina variable in the .sh scripts*
   *c) double-click "XXX-auto-win.bat" and follow the instructions*
13) (Non-windows users or command-line option for windows):
   a) open a terminal
   b) activate the conda environment with smina installed
   c) cd to the directory with the scripts, then type:

```
bash xxx-autolist.sh #where xxx is min, dock, min-flex etc depends on the method you are using
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14) Open the results for visualization and analysis