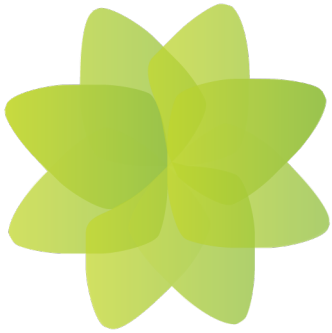


OpenDiscovery

www.opendiscovery.org.uk

Version: 1.0a

Contacts: gareth.price@warwick.ac.uk; a.marsh@warwick.ac.uk

Example 1: Statin + HMG-CoA Reductase

You can follow along with this example by downloading the initial PDB from here. Before starting, watch the video tutorial provided by the authors of AutoDock Vina, here.

Preparing the files

We first need to split the crystal structure of the complex into separate receptor and ligand files. Open up the file 1T02.pdb in your favourite text editor and look at the file. The first section are REMARKS about the structure:

```
HEADER    OXIDOREDUCTASE                          07-APR-04   1T02
TITLE     CRYSTAL STRUCTURE OF A STATIN BOUND TO CLASS II HMG-COA
TITLE    2 REDUCTASE
COMPND    MOL_ID: 1;
COMPND   2 MOLECULE: 3-HYDROXY-3-METHYLGLUTARYL-COENZYME A REDUCTASE;
COMPND   3 CHAIN: A, B;
COMPND   4 SYNONYM: HMG-COA REDUCTASE;
COMPND   5 EC: 1.1.1.88;
COMPND   6 ENGINEERED: YES
SOURCE    MOL_ID: 1;
SOURCE   2 ORGANISM_SCIENTIFIC: PSEUDOMONAS MEVALONII;
SOURCE   3 ORGANISM_TAXID: 32044;
SOURCE   4 GENE: MVAA;
SOURCE   5 EXPRESSION_SYSTEM: ESCHERICHIA COLI BL21(DE3);
SOURCE   6 EXPRESSION_SYSTEM_TAXID: 469008;
SOURCE   7 EXPRESSION_SYSTEM_STRAIN: BL21(DE3);
SOURCE   8 EXPRESSION_SYSTEM_VECTOR_TYPE: PLASMID;
SOURCE   9 EXPRESSION_SYSTEM_PLASMID: PKK177-3
KEYWDS    STATIN, HMG-COA REDUCTASE, COMPLEX, OXIDOREDUCTASE
EXPDTA    X-RAY DIFFRACTION
AUTHOR    L.TABERNERO,V.W.RODWELL,C.STAUFFACHER
REVDAT   2   24-FEB-09 1T02    1       VERSN
REVDAT   1   03-AUG-04 1T02    0
JRNL        AUTH   L.TABERNERO,V.W.RODWELL,C.V.STAUFFACHER
JRNL        TITL   CRYSTAL STRUCTURE OF A STATIN BOUND TO A CLASS II
JRNL        TITL 2 HYDROXYMETHYLGLUTARYL-COA REDUCTASE.
JRNL        REF    J.BIOL.CHEM.                  V. 278 19933 2003
JRNL        REFN                   ISSN 0021-9258
JRNL        PMID   12621048
JRNL        DOI    10.1074/JBC.M213006200
REMARK   1
REMARK   2
REMARK   2 RESOLUTION.    2.60 ANGSTROMS.
```

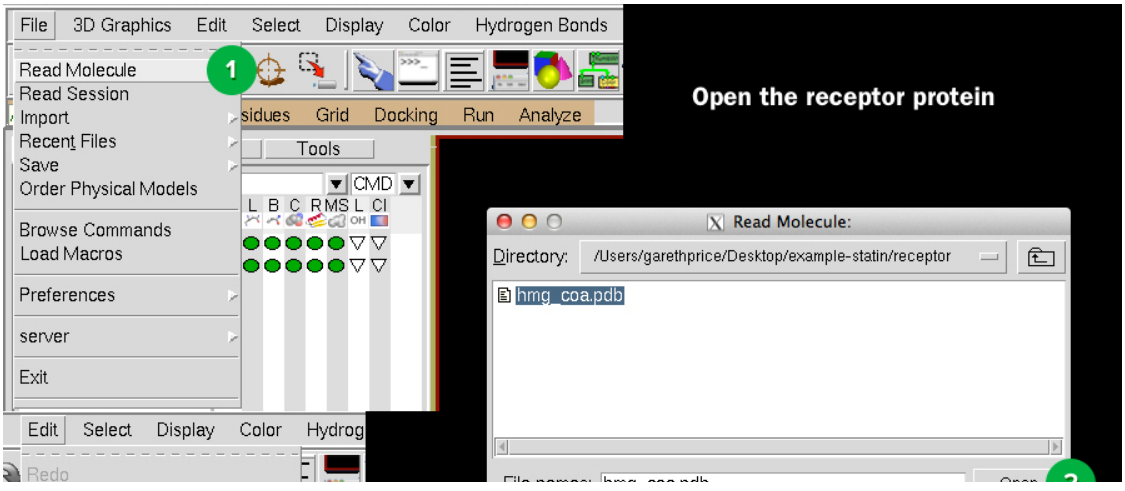
Delete all the header lines, up to line 765 which is the first atom of the structure.

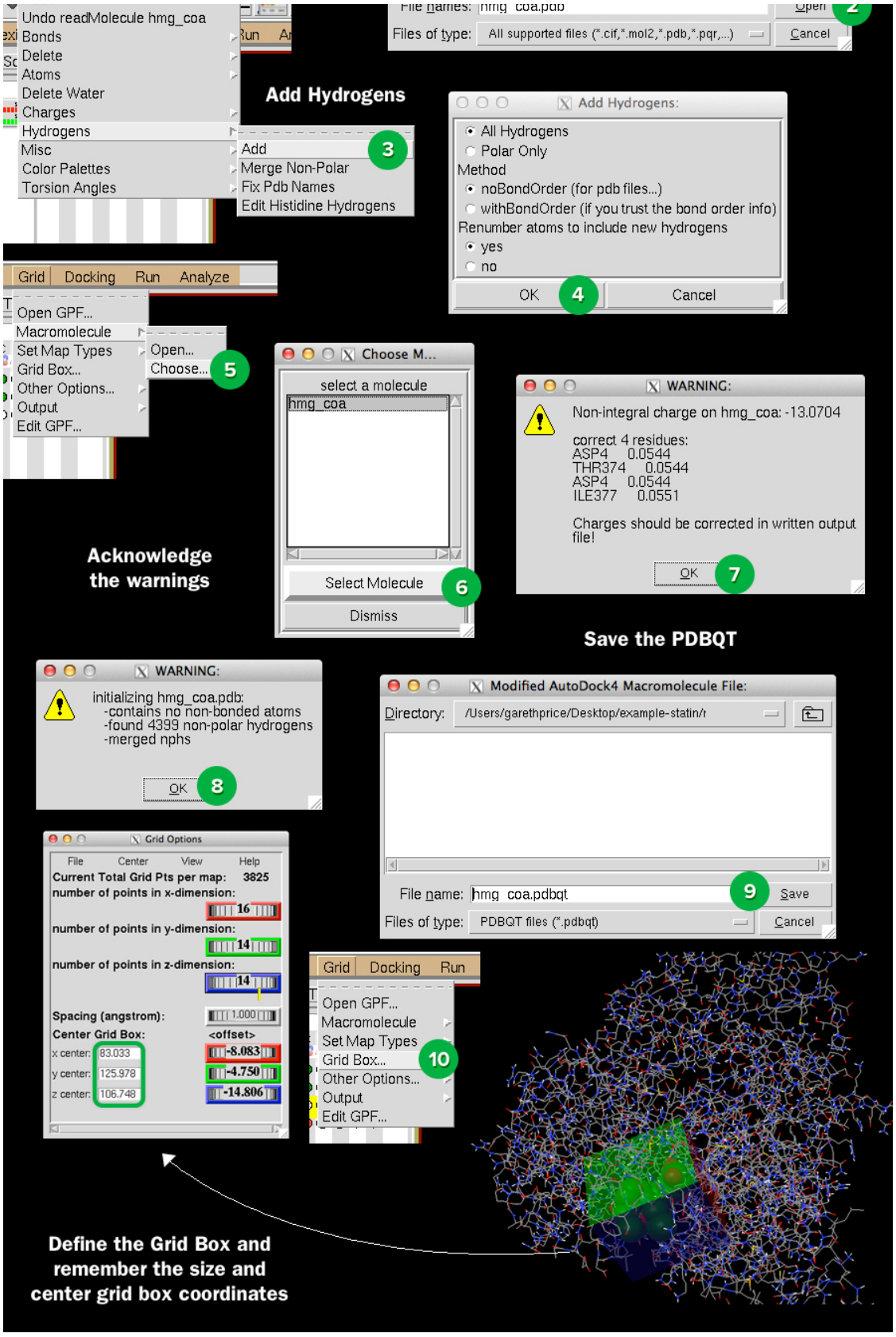
Copy all lines with ATOM at the start into its own file, named `hmg_coa.pdb`. Include the TER statement in line 5529. Then, copy the subsequent lines starting with HETATM and LVA in the the fourth column into its own file, `LVA.pdb`:

```
HETATM 5530  O1  LVA A 429      86.909 124.095 109.838  1.00 29.33           O
HETATM 5531  O2  LVA A 429      86.507 128.170 108.114  1.00 20.16           O
HETATM 5532  O3  LVA A 429      86.864 123.804 107.707  1.00 27.05           O
HETATM 5533  O8  LVA A 429      84.788 129.227 110.408  1.00 11.88           O
HETATM 5534  O4  LVA A 429      80.841 127.668 105.566  1.00 36.01           O
HETATM 5535  C5  LVA A 429      79.054 124.995 108.378  1.00 19.62           C
HETATM 5536  C6  LVA A 429      78.856 126.160 107.545  1.00 22.90           C
HETATM 5537  C7  LVA A 429      84.257 128.194 109.522  1.00 17.04           C
HETATM 5538  C8  LVA A 429      79.875 124.940 109.429  1.00 20.40           C
HETATM 5539  C9  LVA A 429      79.632 127.431 107.958  1.00 24.43           C
HETATM 5540  C10 LVA A 429      86.967 124.566 108.590  1.00 23.47           C
HETATM 5541  C11 LVA A 429      80.677 126.143 109.812  1.00 18.97           C
HETATM 5542  C12 LVA A 429      80.962 127.009 108.579  1.00 20.64           C
HETATM 5543  C13 LVA A 429      85.938 126.854 108.348  1.00 18.19           C
HETATM 5544  C14 LVA A 429      78.029 126.156 106.515  1.00 22.58           C
HETATM 5545  C15 LVA A 429      79.964 128.209 106.624  1.00 29.33           C
HETATM 5546  C16 LVA A 429      82.827 127.987 109.966  1.00 16.97           C
HETATM 5547  C17 LVA A 429      85.118 126.936 109.609  1.00 16.96           C
HETATM 5548  C18 LVA A 429      81.826 128.257 108.857  1.00 19.74           C
HETATM 5549  C19 LVA A 429      78.612 128.587 106.018  1.00 28.96           C
HETATM 5550  C20 LVA A 429      79.918 126.866 110.908  1.00 18.11           C
HETATM 5551  C21 LVA A 429      87.077 125.953 108.412  1.00 19.54           C
HETATM 5552  C22 LVA A 429      77.823 127.339 105.609  1.00 27.45           C
HETATM 5553  C23 LVA A 429      78.144 126.939 104.114  1.00 27.49           C
HETATM 5554  C24 LVA A 429      81.879 128.353 105.045  1.00 36.32           C
HETATM 5555  C25 LVA A 429      82.754 127.503 104.174  1.00 33.59           C
HETATM 5556  O26 LVA A 429      82.059 129.532 105.295  1.00 40.47           O
HETATM 5557  C27 LVA A 429      82.364 127.528 102.717  1.00 32.10           C
HETATM 5558  C28 LVA A 429      82.665 126.087 104.739  1.00 35.43           C
HETATM 5559  C29 LVA A 429      83.114 126.580 101.841  1.00 28.07           C
```

Now, put `hmg_coa.pdb` into a 'receptor' folder and `LVA.pdb` into a 'pdb' folder. Next, we need to prepare the receptor protein (`hmg_coa.pdb`).

Open up AutoDockTools, and follow the steps in the image below. Make sure to remember the coordinates and dimensions. Make sure Spacing (Angstrom) is set to 1.000.



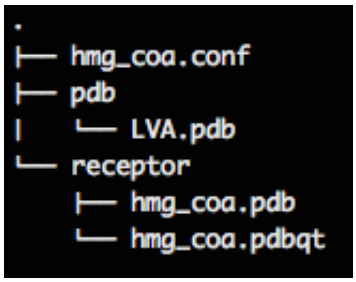


Open a new file and enter the box coordinates and dimensions such as:

```
center_x = 83.033
center_y = 125.978
center_z = 106.748

size_x = 16
size_y = 14
size_z = 14
```

Save it as `hmg_coa.conf`.

You should have a folder that looks like:



Running ODScreen

We can now run the screening. First, let's check that everything is installed properly. In terminal, `cd` to the Protocol Folder (i.e. the folder with `odscreen.py`, `odparam.py` etc.) and run `python odcheck.py`. Check that there are no failures, and follow the installation guides if there are. You can ignore the warnings. Now, we can run the screening protocol. Navigate to the folder where hmg_coa.conf is located (from before). Now we can run `odscreen.py`. Make sure you use the correct path to the `odscreen.py` file.

`python /protocolfolder/odscreen.py -d . -r hmg_coa -i pdb -c hmg_coa.conf`

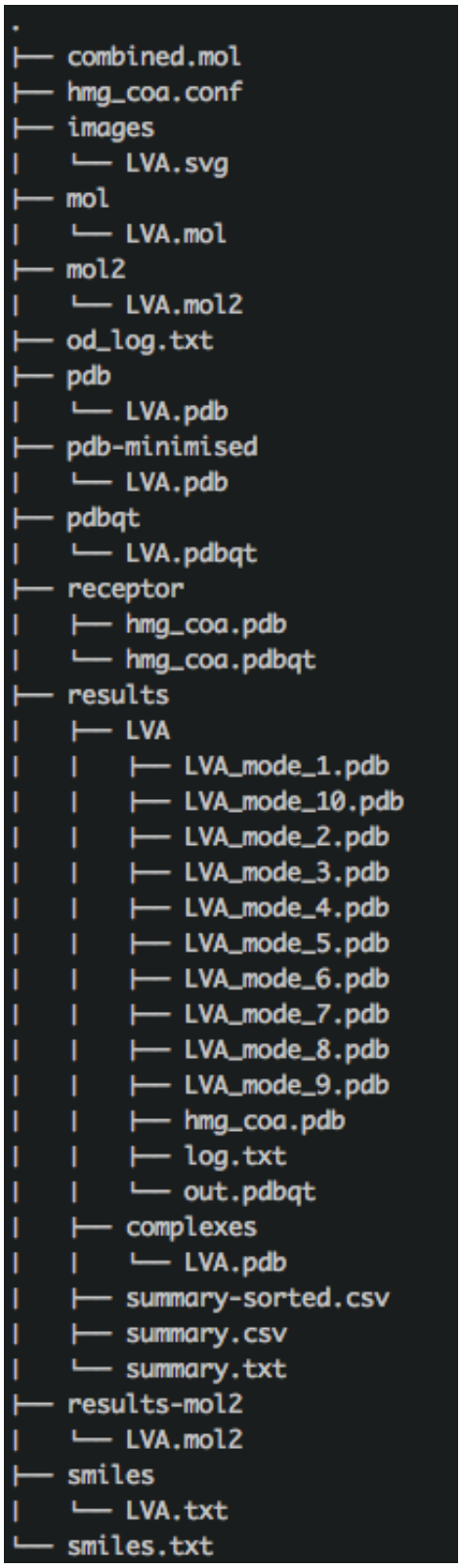
This is the result:

```
# ---------------------------------------- #
#              OPEN DISCOVERY              #
#             Screening Module             #
# ---------------------------------------- #
# Version:  1.0                            #
# URL:      www.opendiscovery.org.uk       #
# Contacts: gareth.price@warwick.ac.uk     #
#           a.marsh@warwick.ac.uk          #
# ---------------------------------------- #
# LigDir: /Desktop/example-statin          #
```

```
#           Receptor Name: hmg_coa          #
#              Input Type: pdb              #
#             Conf: hmg_coa.conf            #
#             Exhaustivness: 20             #
# ------------------------------------------ #
#  Time Started: Mon, 22 Jul 2013 00:15:20  #
# ------------------------------------------ #


               PDB -> SMILES
            Writing smiles/LVA.txt


                    IMAGES
            Writing images/LVA.svg


                     MOL
             Writing mol/LVA.mol


                     MOL2
            Writing mol2/LVA.mol2


                 MINIMISATION
                Minimising LVA


               PDBQT PREPARATION
              Writing LVA.pdbqt


                   SCREENING
                Processing LVA


                  EXTRACTING
           Processing results/LVA/


                  PDB -> MOL2
        Writing results-mol2/LVA.mol2
```

```
                   SUMMARISING
                Summarising LVA


                MAKING COMPLEXES
                  Writing LVA


# ---------------------------------------- #
#                   FINSHED                #
#         Time Taken: 231.40 seconds       #
# ---------------------------------------- #
```

The resulting files are:



From this point on you can analyse the results. A starting point is to look at the binding energies, sorted and summarised in the `summary-sorted.csv` file. This should open in any text editor or programs like Excel.