



OpenDiscovery

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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.TABERNEIRO,V.W.RODWELL,C.STAUFFACHER
REVDAT      2 24-FEB-09 1T02 1 VERSN
REVDAT      1 03-AUG-04 1T02 0
JRNL        AUTH L.TABERNEIRO,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.

```

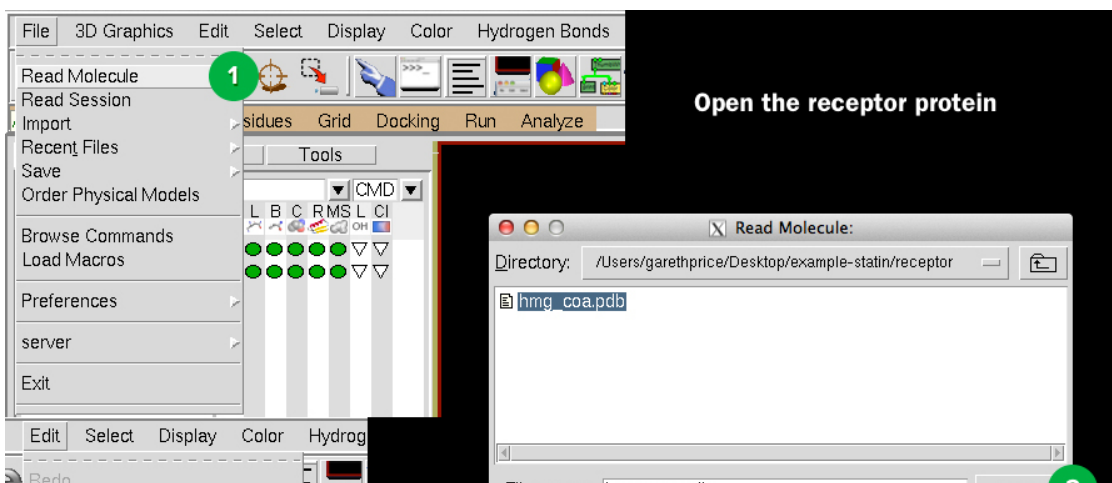
Delete all the header lines, up to line 765 which is the first atom of the structure.

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.



2 File names: hmg_coa.pdb
Files of type: All supported files (*.cif,*.mol2,*.pdb,*.pqr,...)

3 Add Hydrogens

4 Add Hydrogens:

- ☒ All Hydrogens
- ☐ Polar Only

Method

- ☒ noBondOrder (for pdb files...)
- ☐ withBondOrder (if you trust the bond order info)

Renumber atoms to include new hydrogens

- ☒ yes
- ☐ no

OK Cancel

5 Choose M...

select a molecule

hmg_coa

Select Molecule Dismiss

6 WARNING:

Non-integral charge on hmg_coa: -13.0704

correct 4 residues:
ASP4 0.0544
THR374 0.0544
ASP4 0.0544
ILE377 0.0551

Charges should be corrected in written output file!

OK

7 Save the PDBQT

WARNING:

initializing hmg_coa.pdb:
-contains no non-bonded atoms
-found 4399 non-polar hydrogens
-merged nphs

OK

8 Grid Options

File Center View Help

Current Total Grid Pts per map: 3825

number of points in x-dimension: 16

number of points in y-dimension: 14

number of points in z-dimension: 14

Spacing (angstrom): 1.000

Center Grid Box:

x center: 83.033

y center: 125.978

z center: 106.748

offset: -8.083, -4.750, -14.806

9 Modified AutoDock4 Macromolecule File:

Directory: /Users/garethprice/Desktop/example-statin/t

File name: hmg_coa.pdbqt

Files of type: PDBQT files (*.pdbqt)

Save Cancel

10 Grid Docking Run

Open GPF...
Macromolecule
Set Map Types
Grid Box...
Other Options...
Output
Edit GPF...

Define the Grid Box and remember the size and center grid box coordinates

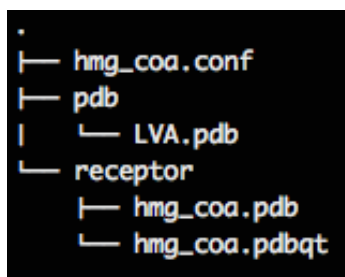
Open a new file and enter the box coordinates and dimensions such as:

```
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

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

The resulting files are:

```

.
├─ combined.mol
├─ hmg_coa.conf
├─ images
│   └─ LVA.svg
├─ mol
│   └─ LVA.mol
├─ mol2
│   └─ LVA.mol2
├─ od_log.txt
├─ pdb
│   └─ LVA.pdb
├─ pdb-minimised
│   └─ LVA.pdb
├─ pdbqt
│   └─ LVA.pdbqt
├─ receptor
│   ├── hmg_coa.pdb
│   └─ hmg_coa.pdbqt
├─ results
│   ├── LVA
│   │   ├── LVA_mode_1.pdb
│   │   ├── LVA_mode_10.pdb
│   │   ├── LVA_mode_2.pdb
│   │   ├── LVA_mode_3.pdb
│   │   ├── LVA_mode_4.pdb
│   │   ├── LVA_mode_5.pdb
│   │   ├── LVA_mode_6.pdb
│   │   ├── LVA_mode_7.pdb
│   │   ├── LVA_mode_8.pdb
│   │   ├── LVA_mode_9.pdb
│   │   ├── hmg_coa.pdb
│   │   ├── log.txt
│   │   └─ out.pdbqt
│   ├── complexes
│   │   └─ LVA.pdb
│   ├── summary-sorted.csv
│   ├── summary.csv
│   └─ summary.txt
├─ results-mol2
│   └─ LVA.mol2
├─ smiles
│   └─ LVA.txt
└─ smiles.txt

```

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.

