Introduction to Molecular Interaction Fields (MIFs) in RDKit

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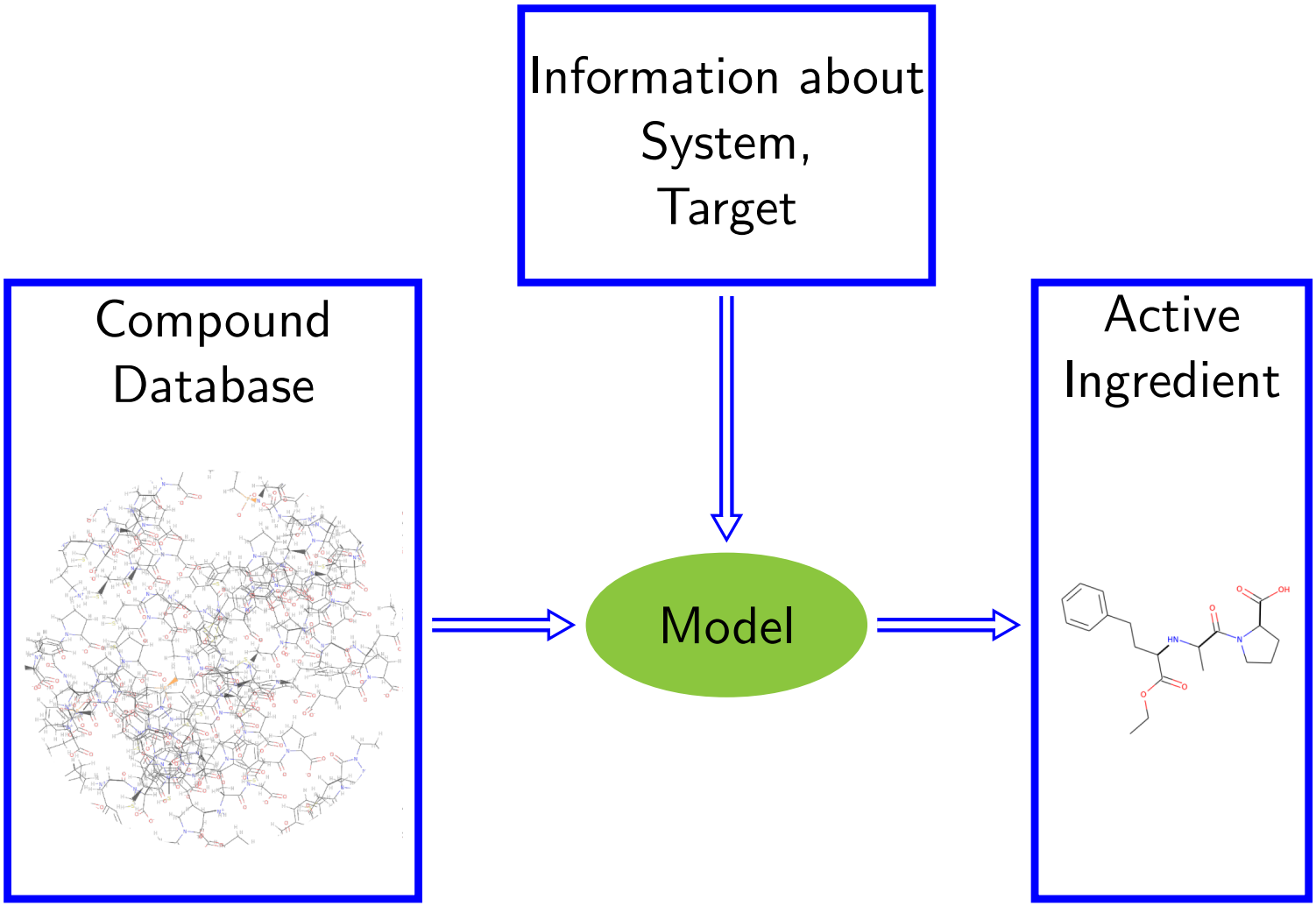
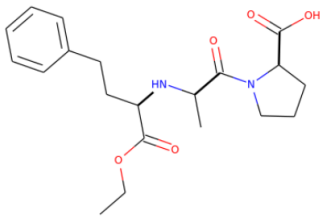
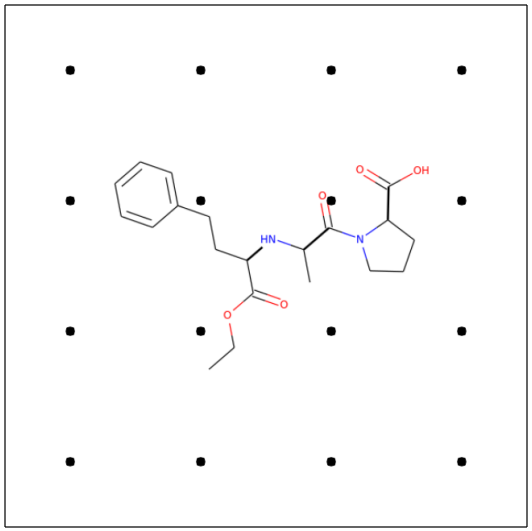
Overview

Aim: Find active ingredient in silico.



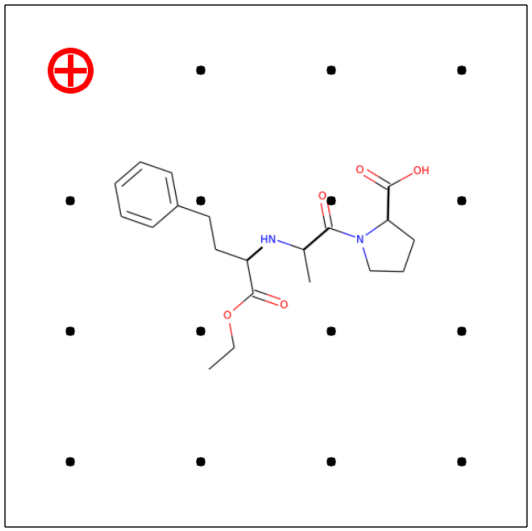
Procedure
Place grid around molecule





Procedure
Defining probe and type of interaction

- Type of interaction:
  - electrostatic interaction
  - van der Waals interaction
  - hydrogen bonding interaction
- Probe:
  - charge
  - atom (Lennard-Jones parameter)
  - hydrogen bond acceptor/donor



Implementation

- `UniformRealValueGrid3D` for storing and manipulating fields
- Several descriptor functors, which are constructed for specific molecules
- Function `calculateDescriptors(UniformRealValueGrid3D, Functor)` to efficently calculate MIF on the given `UniformRealValueGrid3D`
- PYTHON wrappers to C++ MIF library

Example code

In [1]:
```
import rdkit.Chem.AllChem as AllChem
from rdkit.Chem.Draw import IPythonConsole
import rdkit.Chem.rdMIF as Mif
```

Load structure from SDF file to mol.

In [2]:
```
mol = AllChem.SDMolSupplier('mif_rdkit_tutorial/enalapril.sdf',   removeHs=False)
mol = mol.next()
```

Construct grid around molecule (using default values for spacing and margin).

In [3]:
```
grd = Mif.ConstructGrid(mol)
```

Construct a van der Waals descriptor class, calculate descriptor values on the grid and save it to a CUBE file.

In [4]:
```
vdw = Mif.ConstructVdWaalsUFF(mol)
Mif.CalculateDescriptors(grd, vdw)
Mif.WriteToCubeFile(grd, mol, "mif_rdkit_tutorial/vdw.cube")
```

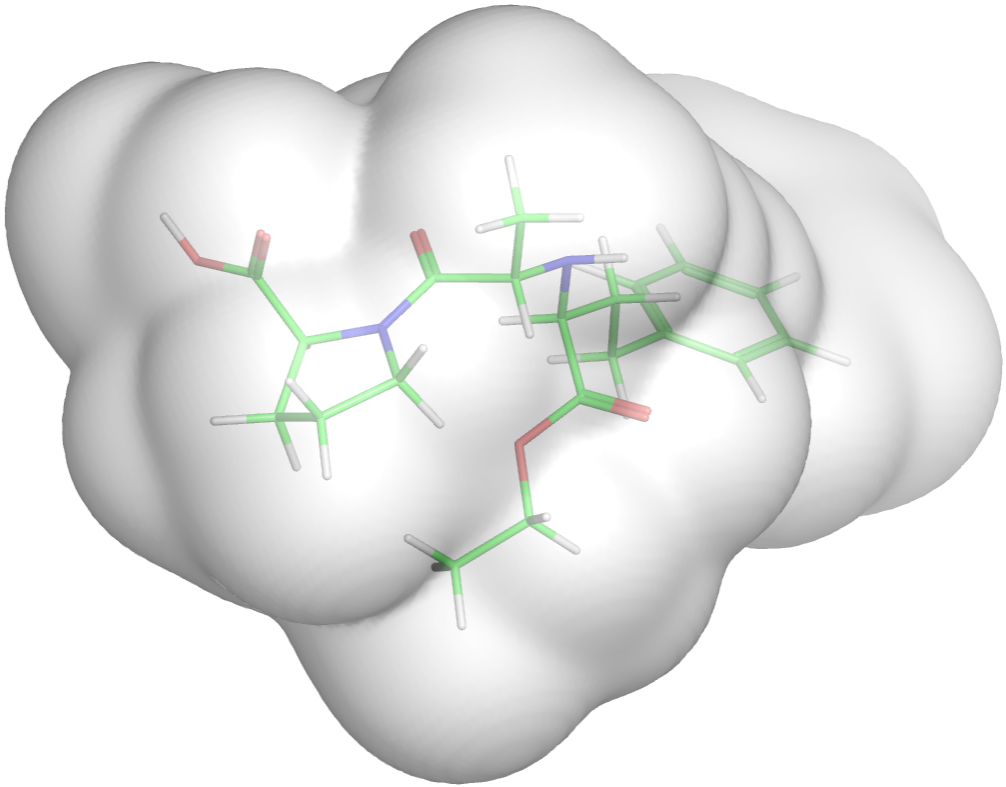
Visualize grid as an isosurface in PyMol. PyMol has to be running with the XML-RPC server active (-R argument to PyMol on launch).

In [5]:
```
from rdkit.Chem import PyMol
v = PyMol.MolViewer()
v.ShowMol(mol)
v.LoadFile("~/notebooks/mif_rdkit_tutorial/vdw.cube", "vdw")
v.server.do("isosurface surf, vdw, 0")
v.server.do('set transparency, 0.4, surf')
v.GetPNG(h=500)
```

Structure from: National Center for Biotechnology Information. PubChem Compound Database; CID=5388962, https://pubchem.ncbi.nlm.nih.gov/compound/5388962 (accessed Aug. 24, 2015).

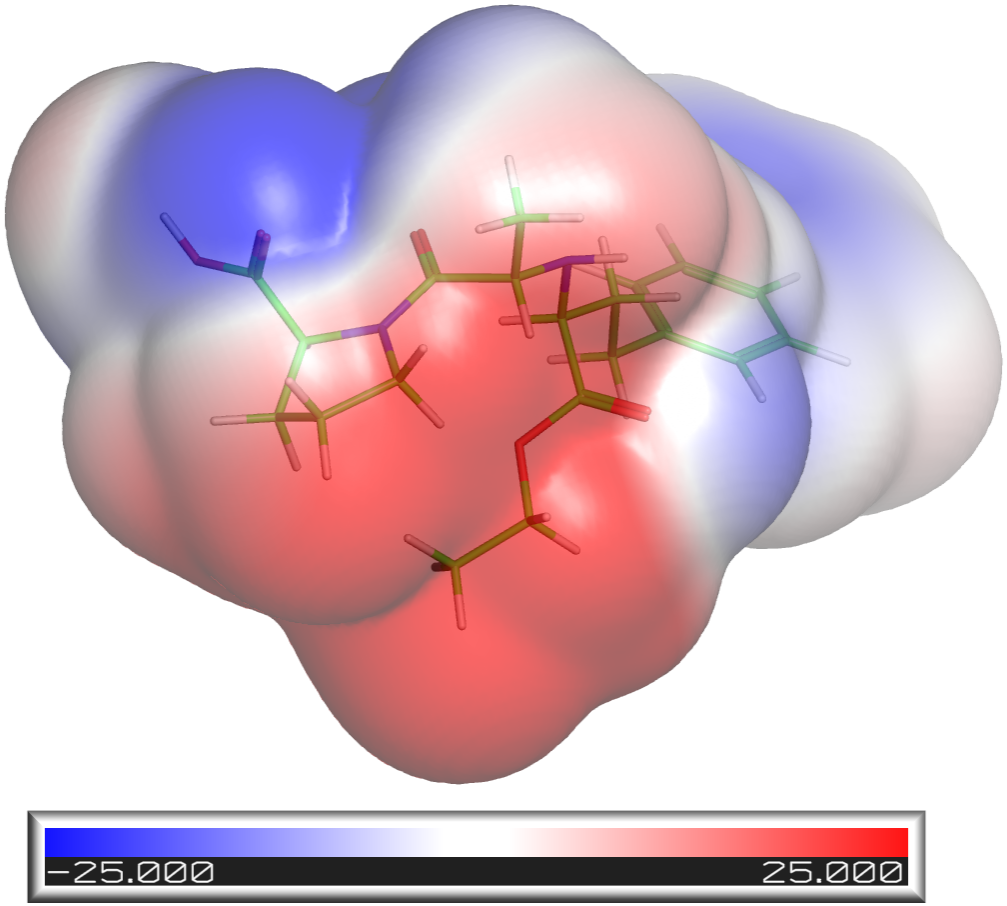
Van der Waals Field

Probe: sp^2 oxygen (e.g. in alcohol or ether) - Isosurface at 0.0 kJ mol^{-1}



Coulomb field

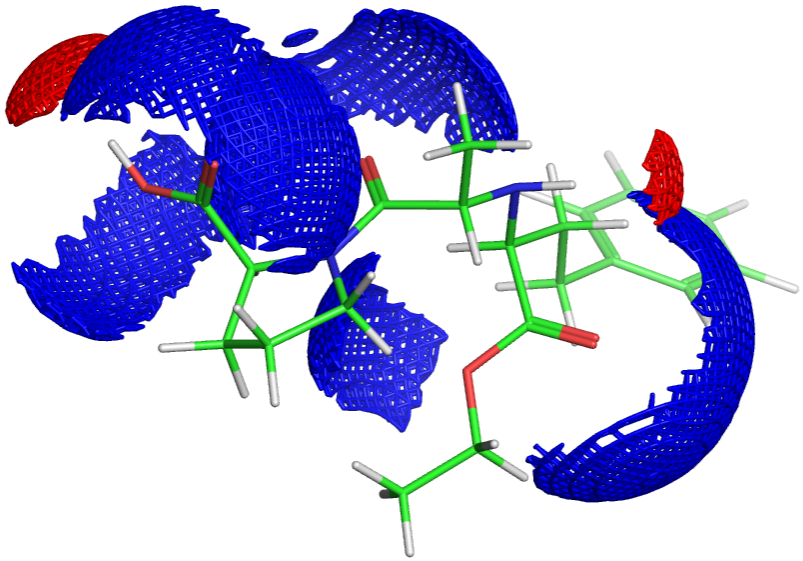
Probe: positive charge ($+1e$) - colormap ranging from -25.0 kJ mol^{-1} (blue) via 0.0 kJ mol^{-1} (white) to $+25.0$ kJ mol^{-1} (red)



Hydrogen bonding field

Probe: acceptor (C=O, red) - level -25.0 kJ mol^{-1}

Probe: donor (OH, blue) - level -20.0 kJ mol^{-1}



Conclusions & Outlook

The newly developed RDKit functionalities

- can compute different MIFs of different molecules.
- can be used in PYTHON.
- open new possibilities for 3D-QSAR studies in RDKit.

Further work

- Review and get code merged onto the master.
- Use them for 3D-QSAR studies.
- Implement descriptors based on MIFs, but independent of alignment.

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