PTools tutorial

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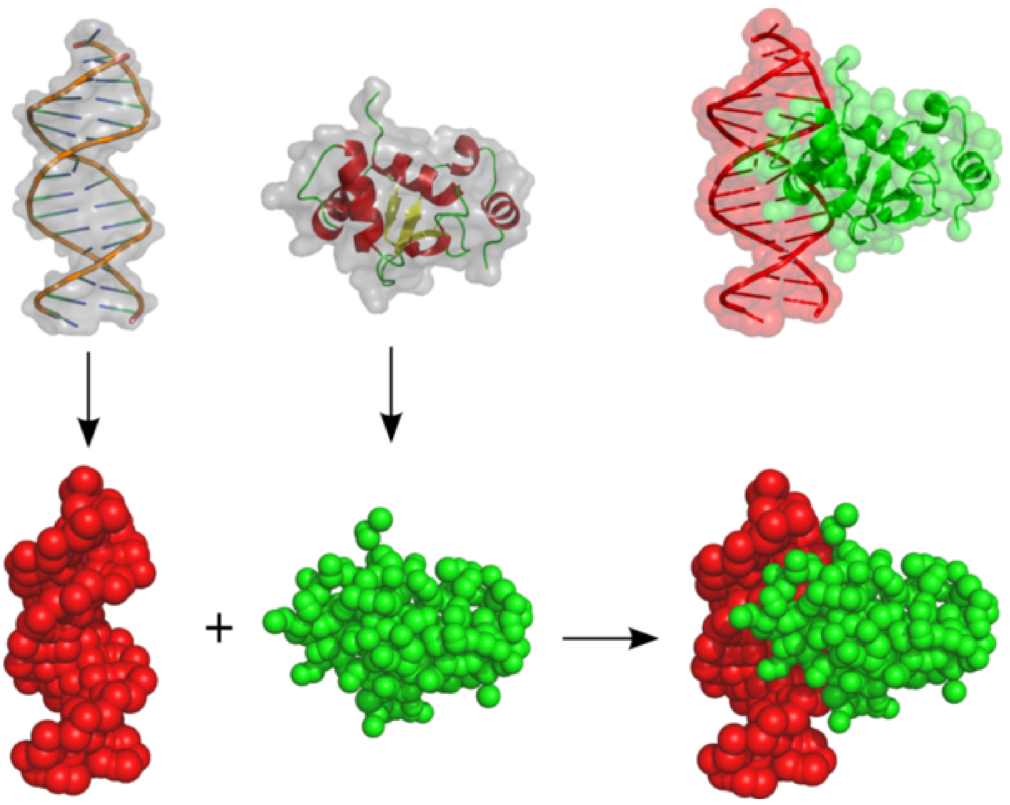

This tutorial presents the PTools library features and its docking application ATTRACT.

Contents

1 Set up, compilation and installation

1.1 Set up: Dell D420 laptop, Debian Lenny, 32-bit

This example installation has been performed on a Dell D420 laptop (Intel Core Duo 1.2 GHz, Debian Lenny, linux kernel 2.6.22-2-686).

The basic requirements are:

- Python 2.4 or 2.5 and its development library (python2.4-dev or python2.5-dev)
- gcc (4.x)
- gfortran (4.x)

SCons (make substitute): `apt-get install scons`
(1.34.1-11 version installed)

Boost C++ Libraries `apt-get install libboost-dev`
(1.34.1-11 version installed)

Boost Python Library: `apt-get install libboost-python`
(1.34.1-11 version installed)

libboost Python dev: `apt-get install libboost-python-dev`
(1.34.1-11 version installed)

Subversion: `apt-get install subversion subversion-tools`
(1.4.6dfsg1-2 version installed)

gccxml: `apt-get install gccxml`
(0.9.0+cvs20071228-2 version installed)

Some Ubuntu linux distribution have an incompatible gccxml 0.7 version that crashes when parsing headers files. The solution is to install gccxml from the official CVS repository (`http://www.gccxml.org/HTML/Download.html`)

Pyplusplus and Pygccxml: The homepage of `pyplusplus` and `pygccxml` projects is `http://www.language-binding.net/pyplusplus/pyplusplus.html`. From the download section [1], get the files `pygccxml-0.9.5.zip` and `Py++-0.9.5.zip`.

```
unzip pygccxml-0.9.5.zip
cd pygccxml-0.9.5/
python setup.py build
python setup.py install --prefix=$HOME/soft

unzip Py++-0.9.5.zip
cd Py++-0.9.5/
python setup.py build
python setup.py install --prefix=$HOME/soft
```

In your `$HOME/.bashrc` file, then add:

[1] `https://sourceforge.net/project/showfiles.php?group_id=118209`

```
export PATH=PATH:$HOME/soft/bin/
export PYTHONPATH=$HOME/soft/lib/python2.4/site-packages/
```

In a Python shell (obtained with the `python` command), test the installation of PyPlus-Plus:

```
>>> import pyplusplus
```

1.2 Set up: Dell Precision T7400, Linux Fedora Core 9, 64-bit

This example installation has been performed on a Dell Precision T7400 (Intel Xeon quad-core 2.3 GHz, Linux Fedora Core 9, linux kernel 2.6.25.6-55.FC9.x86_64).
The basic requirements are:

- Python 2.5 and its development library python2.5-dev
- gcc (4.x)
- gfortran (4.x)

SCons (make substitute): The scons package provided by Fedora is not up-to-date enough to link Fortran and C++ together and then rise an error. The last version of scons is obtained at the homepage of the project (`http://www.scons.org/`). From the download section [2], get the stable file `scons-0.98.5-1.noarch.rpm`.

```
 rpm -ivh scons-0.98.5-1.noarch.rpm
```

Boost C++ Libraries: `yum install boost boost-devel`
(1.34.1-13 version installed)

Python dev: `yum install python-devel`
(2.5.1-26 version installed)

Subversion: `yum install subversion`
(1.4.6-7 version installed)

gccxml: The homepage of `gccxml` project is `http://www.gccxml.org`. To install gccxml from the official CVS repository [3].

```
cvs -d :pserver:anoncvs@www.gccxml.org:/cvsroot/GCC_XML login
```

(just press enter when prompted for a password)
Follow this command by checking out the source code:

```
cvs -d :pserver:anoncvs@www.gccxml.org:/cvsroot/GCC_XML co gccxml
mkdir gccxml-build
cd gccxml-build
cmake ../gccxml -DCMAKE_INSTALL_PREFIX:PATH=/installation/path
make
make install
```

The "-DC_MAKE_INSTALL_PREFIX" option can be left off if you want to use "/usr/local" as the installation prefix.

[2] `http://sourceforge.net/project/showfiles.php?group_id=30337`
[3] `http://www.gccxml.org/HTML/Download.html`

Pyplusplus and Pygccxml: The homepage of `pyplusplus` and `pygccxml` projects is `http://www.language-binding.net/pyplusplus/pyplusplus.html`. From the download section [4], get the files `pygccxml-0.9.5.zip` and `Py++-0.9.5.zip`.

```
unzip pygccxml-0.9.5.zip
cd pygccxml-0.9.5/
python setup.py build
python setup.py install --prefix=$HOME/soft

unzip Py++-0.9.5.zip
cd Py++-0.9.5/
python setup.py build
python setup.py install --prefix=$HOME/soft
```

In your `$HOME/.bashrc` file, then add:

```
export PATH=PATH:$HOME/soft/bin/:/usr/lib/gcc/x86_64-redhat-linux/3.4.6/
export PYTHONPATH=$HOME/soft/lib/python2.4/site-packages/
```

In a Python shell (obtained with the `python` command), test the installation of PyPlus-Plus:

```
>>> import pyplusplus
```

1.3 Set up: Dell Precision 690, Linux Fedora Core 7, 64-bit

This example installation has been performed on a Dell Precision 690 (Intel Xeon bi-quad core 1.9 GHz, Linux Fedora Core 7, linux kernel 2.6.23.17-88.fc7).

The basic requirements are:

- Python 2.5 and its development library python2.5-dev
- gcc (4.x)
- gfortran (4.x)

SCons (make substitute): The scons package provided by Fedora is not up-to-date enough to link Fortran and C++ together and then rise an error. The last version of scons is obtained at the homepage of the project (`http://www.scons.org/`). From the download section [5], get the stable file `scons-0.98.5-1.noarch.rpm`.

```
 rpm -ivh scons-0.98.5-1.noarch.rpm
```

Boost C++ Libraries: `yum install boost boost-devel`
(1.33.1-15.fc7 version installed)

Python dev: `yum install python-devel`
(2.5-15.fc7 version installed)

Subversion: `yum install subversion`
(1.4.4-1.fc7 version installed)

[4]`https://sourceforge.net/project/showfiles.php?group_id=118209`
[5]`http://sourceforge.net/project/showfiles.php?group_id=30337`

gccxml: The homepage of gccxml project is http://www.gccxml.org. To install gccxml from the official CVS repository [6].

```
yum install cvs
```

1.11.22-9.1.fc7 version installed

```
yum install cmake
```

2.4.8-1.fc7 version installed

```
cvs -d :pserver:anoncvs@www.gccxml.org:/cvsroot/GCC_XML login
```

(just press enter when prompted for a password)
Follow this command by checking out the source code:

```
cvs -d :pserver:anoncvs@www.gccxml.org:/cvsroot/GCC_XML co gccxml
mkdir gccxml-build
cd gccxml-build
cmake ../gccxml -DCMAKE_INSTALL_PREFIX:PATH=/installation/path
make
make install
```

The "-DC_MAKE_INSTALL_PREFIX" option can be left off if you want to use "/usr/local" as the installation prefix.

Pyplusplus and Pygccxml: The homepage of pyplusplus and pygccxml projects is http://www.language-binding.net/pyplusplus/pyplusplus.html. From the download section [7], get the files pygccxml-0.9.5.zip and Py++-0.9.5.zip.

```
unzip pygccxml-0.9.5.zip
cd pygccxml-0.9.5/
python setup.py build
python setup.py install --prefix=$HOME/soft

unzip Py++-0.9.5.zip
cd Py++-0.9.5/
python setup.py build
python setup.py install --prefix=$HOME/soft
```

In your $HOME/.bashrc file, then add:

```
export PATH=PATH:$HOME/soft/bin/:/usr/lib/gcc/x86_64-redhat-linux/3.4.6/
export PYTHONPATH=$HOME/soft/lib/python2.4/site-packages/
```

In a Python shell (obtained with the python command), test the installation of PyPlus-Plus:

```
>>> import pyplusplus
```

[6] http://www.gccxml.org/HTML/Download.html
[7] https://sourceforge.net/project/showfiles.php?group_id=118209

g2c library:

```
yum install g2clib-devel
```

1.0.5-3.fc7 version installed

1.4 Source download with subversion

From the local `$HOME/soft/` directory, download the full PTools sources with subversion (use the *checkout* option):

```
svn co http://svn-lbt.ibpc.fr/svn/PTools/ptools ptools
```

- for the first use, press *Enter* and then indicate your login and password
- both login and password are stored (without encryption) in the `$HOME/.subversion` directory

PTools source updates are then obtained by:

```
svn update
```

from the `ptools/` or `ptools/trunk` directories.

1.5 Compilation

From the main directory (`trunk`) of the PTools project, create the Python/C++ interface:

```
python interface.py
```

Compile then the library:

```
scons
```

Note that `scons -j2` compiles with two processors in parallel.
If scons complains about the g2c library, you may do (as root):

```
ln -s /usr/lib64/libg2c.so.0 /usr/lib64/libg2c.so
```

1.6 Final test and further documentation

In the `Test` directory, one can test the compilation worked:

```
python unittest1.py
```

The expected output is:

```
.......
----------------------------------------------------------------------
Ran 7 tests in 0.813s

OK
```

Further document may be obtained from the Trac server `http://svn-lbt.ibpc.fr/PTools/wiki`. The server access is controled by the same login/password of the subversion server. The `Timeline` and `Browse Source` sections are usually very usefull.

A `README` file is also available on line [8] or locally [9].

[8] `http://svn-lbt.ibpc.fr/PTools/browser/ptools/trunk/Tutorial/README`

[9] `$HOME/soft/ptools/trunk/Tutorial/README`

2 PTools library usages and capabilities

2.1 Directly from C++

2.2 From Python through the C++ binding

Explain here the different level of objects between rigidbody, selection, atom and points

From the Python interpreter or in a Python script, first load the PTools library:

```
from ptools import *
```

2.2.1 Rigidbody objects

Load PDB file into a rigidbody object.

```
pdb = Rigidbody("1BTA.pdb")
```

Number of atoms.

```
pdb.Size()
```

Maximum distance from geometric center in Å.

```
pdb.Radius()
```

Radius of gyration in Å.

```
pdb.RadiusGyration()
```

Structure translation. First create a translation vector as a Coord3D object (for instance 5, 0, 1):

```
trans = Coord3D(5, 0, 1)
```

Then, apply the translation vector:

```
pdb.Translate(trans)
```

Center structure to origin.

```
pdb.CenterToOrigin()
```

Save structure as PDB file.

```
WritePDB(pdb, "1BTA_centered.pdb")
```

2.2.2 Selection objects

Selection of CA atoms.

```
sel_ca = pdb.CA()
```

Selection of backbone atoms.

```
sel_bkbn = pdb.Backbone()
```

Selection by chain.

```
sel_chainA = pdb.SelectChainId("A")
sel_chainB = pdb.SelectChainId("B")
```

Selection of a range of residues.

```
sel_res = pdb.SelectResRange(10, 20)
```

Selection number of atoms.

```
sel_res.Size()
```

Selection reunion.

```
sel_chainAB = sel_chainA | sel_chainB
```

or directly

```
sel_chainAB = pdb.SelectChainId("A") | pdb.SelectChainId("B")
```

Selection to rigidbody conversion.

```
ca_trace = sel_ca.CreateRigid()
```

3 Docking with PTools: ATTRACT

This part is illustrated by the docking of the protein and DNA found in the 1DNJ complex.

3.1 Extraction of the docking partners and coarse grain reduction

Before docking, one has to separate both partners. This is possible with visualisation software such as Pymol [10] or VMD [11], and also directly with the PTools library.

[10]http://pymol.sourceforge.net/
[11]http://www.ks.uiuc.edu/Research/vmd/

3.1.1 Partner preparation

Within the Python interpreter, first load the PTools library:

```
from ptools import *
```

Read the PDB file 2NJ.pdb:

```
pdb=Rigidbody("2DNJ.pdb")
```

The chain selection allows the separation between the protein (chain A) and the DNA (chains B and C).

```
selectA=pdb.SelectChainId("A")
selectB=pdb.SelectChainId("B")
selectC=pdb.SelectChainId("C")
```

Reunion of both DNA strands:

```
selectBC=selectB | selectC
```

Creation of the protein as a rigid body and file saving as a PDB:

```
prot=selectA.CreateRigid()
WritePDB(prot,"2DNJ_prot.pdb")
```

Creation of the DNA as a rigid body and file saving as a PDB:

```
DNA=selectBC.CreateRigid()
WritePDB(DNA,"2DNJ_dna.pdb")
```

Once both partners are isolated in separe files, close the Python interpreter.
To check DNA atom names are compatible with the one used is the reduced model, use the `parse.pl` script:

```
parse.pl 2DNJ_dna.pdb >2DNJ_dnaf.pdb
```

3.1.2 Protein coarse grain reduction

```
reduce.py 2DNJ_prot.pdb 2DNJ_prot.cg.z.pdb
```

Parameters:

- an all-atom protein pdb file (`2DNJ_prot.pdb`)
- a reduced output pdb file (`2DNJ_prot.cg.z.pdb`)

Visualise both to check that the reduction worked properly.

3.1.3 DNA coarse grain reduction

DNA is reduced using two scripts: `reduceDna.py` and `convertPdb2Zacharias.py`. The first one perform the proper reduction.

```
reduceDna.py atom2cgDna.dat 2DNJ_dnaf.pdb 2DNJ_dna.cg.pdb
```

Parameters are the following:

- the correspondance between atoms and beads (`atom2cgDna.dat`)
- an input all-atom pdb file (`2DNJ_dnaf.pdb`)
- an output coarse grain pdb file (`2DNJ_dna.cg.pdb`)

The second program converts the output DNA reduced pdb file into a pdb-like file compatible with ATTRACT. Its usage is:

```
convertPdb2Zacharias.py ffParamDna.dat 2DNJ_dna.cg.pdb 2DNJ_dna.cg.z.pdb
```

with the parameters:

- the parameters of the coarse grain force field (bead type and charge) (`ffParamDna.dat`)
- an input coarse grain pdb file (`2DNJ_dna.cg.pdb`)
- an output coarse grain pdb file compatible with ATTRACT (`2DNJ_dna.cg.z.pdb`)

As for protein reduction, a visual inspection with any visualisation software is preferable.

3.2 Docking simulation

3.2.1 Initial ligand positions

The systematic docking simulation uses starting points placed around the receptor. The Python script `translate.py` employs a slightly modified Shrake and Rupley [1] method to define starting positions from receptor surface. The surface generation fonctions are implemented in the PTools library. The script first reads the coarse grain (reduced) receptor and ligand files, then generates a grid of points at the certain distance from the receptor and outputs the grid with a given density.

Remarks:

- `translate.py` reads the `aminon.par` parameter file. This file must be in the directory of the receptor and ligand files.
- the density option (`-d`) controls the minimum distance between starting points (in Å^2). The default value is 100.0 (Å^2).
- the `-h` options, shows the help message and exit.

In the case of the 1DNK complex, it gives:

```
translate.py 2DNJ_prot.cg.z.pdb 2DNJ_dna.cg.z.pdb > translat.dat
```

The visualisation of the starting points may be viewed with any visualisation software by renaming `translat.dat` in `translat.pdb`.

3.2.2 ATTRACT parameters

ATTRACT parameters are found in the file `attract.inp`. A typical configuration file is:

```
 6 0 0
-34.32940 38.75490 -3.66956 0.00050
 30  2 1 1 0 0 0 0 1 2000.00
 30  2 1 1 0 0 0 0 1 1000.00
 50  2 1 1 0 0 0 0 0  500.00
 50  2 1 1 0 0 0 0 0   50.00
 100 2 1 1 0 0 0 0 0   50.00
 500 2 1 1 0 0 0 0 0   50.00
```

The first line indicates the number of minimisations performed by ATTRACT for each starting position. The last six lines are the caracteristics of each minimisation. The first column is the number of steps before the minimisation stops. The last column is the square of the cutoff distance for the calculation of the interaction energy between both partners.

Remarques: Columns with zeros or ones should not be modfied, as well as the second line.

3.2.3 Initial docking simulation

A docking simulation with ATTRACT requires:

- a receptor (fixed partner) file (`2DNJ_prot.cg.z.pdb`)
- a ligand (mobile partner) file (`2DNJ_dna.cg.z.pdb`)
- the ATTRACT program (here for protein–DNA docking, `Attract_dna.py`)
- the coarse grain parameters (`aminon.dna.par`)
- rotations performed for each translational starting point (`rotation.dat`)
- translational starting points (`translat.dat`)
- docking parameters (`attract.inp`)

ATTRACT can be used with different options:

- -s, performs one single serie of minimisations with the ligand in its initial position.
- -ref=, provides a ligand pdb file as a reference. After each docking, the RMSD is calculated between this reference structure and the simulated ligand.

A single ATTRACT simulation may thus be obtained by:

```
Attract_dna.py 2DNJ_prot.cg.z.pdb 2DNJ_dna.cg.z.pdb
-s -ref=2DNJ_dna.cg.z.pdb > 2DNJ_single.att
```

The first pdb file provided must be the receptor file (and the second the ligand).
For a full systematic docking in the translational and rotational space:

```
Attract_dna.py 2DNJ_prot.cg.z.pdb 2DNJ_dna.cg.z.pdb
-ref=2DNJ_dna.cg.z.pdb > 2DNJ_dock.att
```

The output file `2DNJ_dock.att` contains all informations on the docking simulation.

3.3 Docking output analysis

Any simulated ligand structure can be extracted with the script `Extract.py`:

```
Extract.py 2DNJ_dock.att 2DNJ_dna.cg.z.pdb 101 153 > 2DNJ_dock.pdb
```

with the parameters:

- an ouput of the docking simulation (`2DNJ_dock.att`)
- the inital ligand file (`2DNJ_dna.cg.z.pdb`)
- a translation index (`101`)
- a rotation index (`153`)
- an output ligand structure file (`2DNJ_dock.pdb`)

4 Misc. tips and tricks

References

[1] A. Shrake, and J.A. Rupley, *Environment and exposure to solvent of protein atoms. Lysozyme and isulin*, Journal of Molecular Biology, **79**:351-364, 1973.