Lezione 2

Bioinformatica

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Lezione 11: PDB format interpretation and visualization

- Introduction
- Information on biochemistry
- Chemical Component Dictionary

Drawing small molecules from PDB files

Simplified Molecular Input Line Entry Specification

- SMILES format
- From SMILES to chemical graph

Sommario

Worldwide Protein Data Bank (wwPDB)

The web site

consists of organizations that act as deposition, data processing and distribution centers for PDB data.
The founding members are

- RCSB PDB (USA)
- PDBe (Europe)
- and PDBj (Japan).
- The BMRB (USA) group joined the wwPDB in 2006.

Sommario

Information on biochemistry

Some resources

great resources about

- Bioinformatics
- Information on biochemistry
- Computational biology

can be found on web site biocheminfo.org, by Professor Toni Kazic, at Department of Computer Science, University of Missouri — Columbia

Sommario

Chemical Component Dictionary (CCD)

The CCD is as an external reference file describing all residue and small molecule components found in PDB entries

Search and browse the CCD using resources such as PDBeChem and Ligand Expo.

- contains detailed chemical descriptions for standard and modified amino acids / nucleotides, small molecule ligands, and solvent molecules
- includes stereochemical assignments, aromatic bond assignments, idealized coordinates, chemical descriptors (SMILES & InChI), and systematic chemical names.
- is organized by the 3-character alphanumeric code that PDB assigns to each chemical component
- is updated with each weekly PDB release.

The Protein Data Bank in Europe (PDBe)

Bringing Structure to Biology

PDBe is the European resource for the collection, organisation and dissemination of data on biological macromolecular structures.

The main objectives of the work at PDBe are:

- to provide an integrated resource of high-quality macromolecular structures and related data and make it available to the biomedical community via intuitive user interfaces.
- to maintain in-house expertise in all the major structure-determination techniques (X-ray, NMR and EM) and on issues of mutual interest (such as data representation, formats and standards, or validation of structural data).
- to provide high-quality deposition and annotation facilities for structural data.

European Bioinformatics Institute (EBI)

The European Bioinformatics Institute (EBI) is a non-profit academic organization that forms part of the European Molecular Biology Laboratory (EMBL)

The EBI is a centre for research and services in bioinformatics.

- The Institute manages databases of biological data including nucleic acid, protein sequences and macromolecular structures.

- For example: Ligands in PDB

European Bioinformatics Institute (EBI)

Macromolecular Structure Database

- The MSD (Macromolecular Structure Database) group has moved to http://www.ebi.ac.uk/pdbe/ and changed its name to the Protein Databank in Europe (PDBe).
- see Macromolecular Structure Database Group Overview
- A project is being undertaken to develop an Application Programming Interface (API) to the EBI-MSD database. This consists of a series of functions that will allow external 3rd party software to access the EBI-MSD database independently. This is based around a SOAP-XML based messaging system

European Bioinformatics Institute (EBI)

EMBL-EBI maintains the world's most comprehensive range of molecular databases

- Services include:
  - ENA (DNA and RNA sequences)
  - Ensembl (genomes)
  - ArrayExpress (microarray data)
  - UniProt (protein sequences)
  - PDBe (macromolecular structures)
  - IntAct (protein–protein interactions)
  - Reactome (pathways)
  - CiteXplore (EMBL portal to the scientific literature)
- The details of each database vary, but they all uphold the same principles of web service provision

Drawing small molecules from PDB files

Include the Bio.PDB module from Biopython (and read this tutorial :o)

```
from Bio.PDB import *

def myprint (string):
    print "\n" + string + " ->", eval(string)
```

The `myprint()` function is used to show both an expression and the value produced by its evaluation

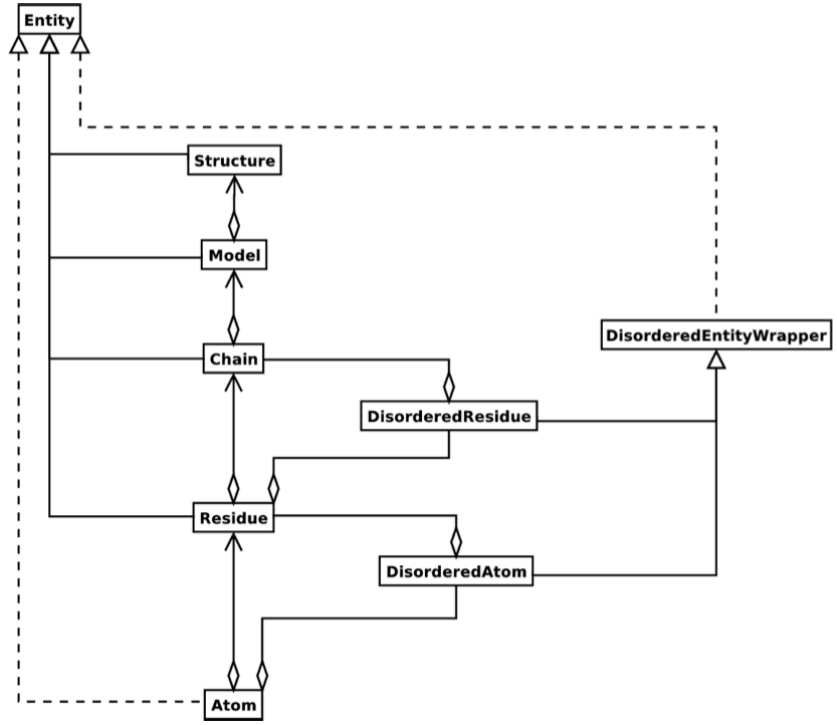
Complete source of the following programming example can be found in bio-pdb-example

Drawing small molecules from PDB files

The overall layout of a Structure object

The Bio.PDB package follows the Structure/Model/Chain/Residue/Atom architecture

- A structure consists of models
- A model consists of chains
- A chain consists of residues
- A residue consists of atoms



UML diagram of SMCRA architecture of the Structure object. Full lines with diamonds denote aggregation, full lines with arrows denote composition, full lines with triangles denote inheritance and dashed lines with triangles denote interface realization

Get the input PDB file

One (of many) possible path ...

Search and browse the Chemical Component Dictionary (CCD) using resources such as PDBeChem

- Ligand Dictionary
- Ligand Expo

1. look at the short Tutorial
2. and
   - 2.1 search
   - 2.2 browse
   - 2.3 download

The input file BTC.pdb

```
HEADER    NONAME 22-Aug-09
TITLE     Produced by PDBeChem
COMPND    BTC
AUTHOR    EBI-PDBe Generated
REVDAT   1  22-Aug-09     0
ATOM      1  N   BTC     0       1.585   0.483  -0.081  1.00 20.00           N+0
ATOM      2  CA  BTC     0       0.141   0.450   0.186  1.00 20.00           C+0
ATOM      3  CB  BTC     0      -0.533  -0.530  -0.774  1.00 20.00           C+0
ATOM      4  SG  BTC     0      -0.247   0.004  -2.484  1.00 20.00           S+0
ATOM      5  C   BTC     0      -0.095   0.006   1.606  1.00 20.00           C+0
ATOM      6  O   BTC     0       0.685  -0.742   2.143  1.00 20.00           O+0
ATOM      7  OXT BTC     0      -1.174   0.443   2.275  1.00 20.00           O+0
ATOM      8  H   BTC     0       1.693   0.682  -1.065  1.00 20.00           H+0
ATOM      9  H2  BTC     0       1.928  -0.454   0.063  1.00 20.00           H+0
ATOM     10  HA  BTC     0      -0.277   1.446   0.042  1.00 20.00           H+0
ATOM     11  HB2 BTC     0      -0.114  -1.526  -0.630  1.00 20.00           H+0
ATOM     12  HB3 BTC     0      -1.604  -0.554  -0.575  1.00 20.00           H+0
ATOM     13  HG  BTC     0      -0.904  -0.965  -3.145  1.00 20.00           H+0
ATOM     14  HXT BTC     0      -1.326   0.158   3.186  1.00 20.00           H+0
CONECT    1    2    8    9
CONECT    2    5    3   10    1
CONECT    3    2   11   12    4
CONECT    4    3   13
CONECT    5    2    6    7
CONECT    6    5
CONECT    7    5   14
CONECT    8    1
CONECT    9    1
CONECT   10    2
CONECT   11    3
CONECT   12    3
CONECT   13    4
CONECT   14    7
END
```

Drawing small molecules from PDB files

BTC (cysteine) is a small molecule, with only 1 model, 1 “chain”, 1 “residue”

`chain = model[' ']`, since there is an empty field for chain code in the file `BTC.pdb`

```
parser=PDBParser()
structure=parser.get_structure('cysteine', 'BTC.pdb')
myprint("structure")

model = structure[0]
myprint("model")

chain = model[' ']
myprint("chain")

residue = chain[0]
myprint("residue")
```

```
structure -> <Structure id=cysteine>

model -> <Model id=0>

chain -> <Chain id= >

residue -> <Residue BTC het=  resseq=0 icode= >
```

Drawing small molecules from PDB files

Get the ordered list of atom names in structure

```
for atom in residue:
        print atom.get_serial_number(), atom.get_coord()

myprint("[atom.get_name() for atom in residue]")
```

equivalently:

```
myprint("[atom.get_name() for atom in structure[0][' '][0]]")
```

```
[atom.get_name() for atom in residue] -> ['N', 'CA', 'CB', 'SG', 'C', 'O', 'OXT
', 'H', 'H2', 'HA', 'HB2', 'HB3', 'HG', 'HXT']
```

Drawing small molecules from PDB files

`CONECT` records are not parsed by `Bio.PDB` module — we go doing :o)

```
def getPdbConnect (filename):
    myfile = open(filename,'r')
    for record in myfile:
        terms = record.split()
        if terms[0] == "CONECT": print terms
    myfile.close()

## units = Angstrom: 1 x 10^(-10)


myprint("getPdbConnect('BTC.pdb')")
```

```
getPdbConnect('BTC.pdb') -> ['CONECT', '1', '2', '8', '9']
['CONECT', '2', '5', '3', '10', '1']
['CONECT', '3', '2', '11', '12', '4']
['CONECT', '4', '3', '13']
['CONECT', '5', '2', '6', '7']
['CONECT', '6', '5']
['CONECT', '7', '5', '14']
['CONECT', '8', '1']
['CONECT', '9', '1']
['CONECT', '10', '2']
['CONECT', '11', '3']
['CONECT', '12', '3']
['CONECT', '13', '4']
['CONECT', '14', '7']
None
```

Drawing small molecules from PDB files

Select the useful information

```
from pyplasm import *
def getPdbConnect (filename):
    myfile = open(filename,'r')
    for record in myfile:
        terms = record.split()
        if terms[0] == "CONECT":
            terms = AA(eval)(terms[1:])
            print terms
    myfile.close()

myprint("getPdbConnect('BTC.pdb')")
```

```
getPdbConnect('BTC.pdb') -> [1, 2, 8, 9]
[2, 5, 3, 10, 1]
[3, 2, 11, 12, 4]
[4, 3, 13]
[5, 2, 6, 7]
[6, 5]
[7, 5, 14]
[8, 1]
[9, 1]
[10, 2]
[11, 3]
[12, 3]
[13, 4]
[14, 7]
None
```

Drawing small molecules from PDB files

Compute the list of adjacent nodes (`terms`) to each `node`

```
from pyplasm import *
def getPdbConnect (filename):
    myfile = open(filename,'r')
    for record in myfile:
        terms = record.split()
        if terms[0] == "CONECT":
            node,terms = eval(terms[1]),AA(eval)(terms[2:])
            print node,terms
    myfile.close()

myprint("getPdbConnect('BTC.pdb')")
```

```
getPdbConnect('BTC.pdb') -> 1 [2, 8, 9]
2 [5, 3, 10, 1]
3 [2, 11, 12, 4]
4 [3, 13]
5 [2, 6, 7]
6 [5]
7 [5, 14]
8 [1]
9 [1]
10 [2]
11 [3]
12 [3]
13 [4]
14 [7]
None
```

Drawing small molecules from PDB files

Compute the directed arcs outgoing from each node

```
from pyplasm import *
def getPdbConnect (filename):
    myfile = open(filename,'r')
    for record in myfile:
        terms = record.split()
        if terms[0] == "CONECT":
            arcs = DISTL([ eval(terms[1]),AA(eval)(terms[2:]) ])
            print arcs
    myfile.close()

myprint("getPdbConnect('BTC.pdb')")
```

```
getPdbConnect('BTC.pdb') -> [[1, 2], [1, 8], [1, 9]]
[[2, 5], [2, 3], [2, 10], [2, 1]]
[[3, 2], [3, 11], [3, 12], [3, 4]]
[[4, 3], [4, 13]]
[[5, 2], [5, 6], [5, 7]]
[[6, 5]]
[[7, 5], [7, 14]]
[[8, 1]]
[[9, 1]]
[[10, 2]]
[[11, 3]]
[[12, 3]]
[[13, 4]]
[[14, 7]]
None
```

Drawing small molecules from PDB files

Compute the undirected arcs

```
from pyplasm import *
def getPdbConnect (filename):
    myfile = open(filename,'r')
    for record in myfile:
        terms = record.split()
        if terms[0] == "CONECT":
            arcs = DISTL([ eval(terms[1]),AA(eval)(terms[2:]) ])
            arcs = [arc for arc in arcs if arc[0] < arc[1]]
            print arcs
    myfile.close()

myprint("getPdbConnect('BTC.pdb')")
```

```
getPdbConnect('BTC.pdb') -> [[1, 2], [1, 8], [1, 9]]
[[2, 5], [2, 3], [2, 10]]
[[3, 11], [3, 12], [3, 4]]
[[4, 13]]
[[5, 6], [5, 7]]
[]
[[7, 14]]
[]
[]
[]
[]
[]
[]
[]
None
```

Drawing small molecules from PDB files

Finally returns the list of undirected arcs

```
from pyplasm import *
def getPDBconnect (filename):
    myfile = open(filename,'r')
    arcs = []
    for record in myfile:
        terms = record.split()
        if terms[0] == "CONECT":
            pairs = DISTL([ eval(terms[1]), AA(eval)(terms[2:]) ])
            arcs += [arc for arc in pairs if arc[0] < arc[1]]
    myfile.close()
    return arcs

myprint("getPDBconnect('BTC.pdb')")
```

```
getPDBconnect('BTC.pdb') -> [[1, 2], [1, 8], [1, 9], [2, 5], [2, 3], [2, 10], [
3, 11], [3, 12], [3, 4], [4, 13], [5, 6], [5, 7], [7, 14]]
```

Drawing small molecules from PDB files

Extraction of atom coordinates (3D points), as a list of array

```
myprint("[atom.get_coord() for atom in residue]")
```

```
[atom.get_coord() for atom in residue] -> [array([ 1.58500004,  0.48300001, -0.
081     ], dtype=float32), array([ 0.141     ,  0.44999999,  0.186     ], dtype
=float32), array([-0.53299999, -0.52999997, -0.77399999], dtype=float32), array
([-0.24699999,  0.004     , -2.48399997], dtype=float32), array([-0.095     ,
0.006     ,  1.60599995], dtype=float32), array([ 0.685     , -0.74199998,  2.1
4299989], dtype=float32), array([-1.17400002,  0.44299999,  2.2750001 ], dtype=
float32), array([ 1.69299996,  0.68199998, -1.06500006], dtype=float32), array(
[ 1.92799997, -0.454     ,  0.063     ], dtype=float32), array([-0.27700001,  1
.44599998,  0.042     ], dtype=float32), array([-0.114     , -1.52600002, -0.63
     ], dtype=float32), array([-1.60399997, -0.55400002, -0.57499999], dtype=fl
oat32), array([-0.90399998, -0.96499997, -3.14499998], dtype=float32), array([-
1.32599998,  0.15800001,  3.18600011], dtype=float32)]
```

Drawing small molecules from PDB files

Extraction of atom coordinates (3D points), as a list of lists

```
myprint("[atom.get_coord().tolist() for atom in residue]")
```

```
[atom.get_coord().tolist() for atom in residue] -> [[1.5850000381469727, 0.4830
000102519989, -0.081000000238418579], [0.14100000262260437, 0.44999998807907104
, 0.18600000441074371], [-0.53299999237060547, -0.52999997138977051, -0.7739999
8903274536], [-0.24699999392032623, 0.0040000001899898052, -2.4839999675750732]
, [-0.094999998807907104, 0.0060000000521540642, 1.6059999465942383], [0.685000
00238418579, -0.74199998378753662, 2.1429998874664307], [-1.1740000247955322, 0
.44299998879432678, 2.2750000953674316], [1.6929999589920044, 0.681999981403350
83, -1.065000057220459], [1.9279999732971191, -0.45399999618530273, 0.063000001
013278961], [-0.27700001001358032, 1.4459999799728394, 0.041999999433755875], [
-0.11400000005960464, -1.5260000228881836, -0.62999999523162842], [-1.603999972
3434448, -0.55400002002716064, -0.57499998807907104], [-0.90399998426437378, -0
.9649999737739563, -3.1449999809265137], [-1.3259999752044678, 0.15800000727176
666, 3.1860001087188721]]
```

Drawing small molecules from PDB files

Prepare the graph data

```
def graph (filename):
    parser=PDBParser()
    structure=parser.get_structure('molecule', filename)
    model = structure[0]
    chain = model[' ']
    residue = chain[0]

    nodes = [atom.get_coord().tolist() for atom in residue]
    edges = getPDBconnect('BTC.pdb')
    return nodes,edges

myprint("graph('BTC.pdb')")
```

```
graph('BTC.pdb') -> ([[1.5850000381469727, 0.4830000102519989, -0.0810000002384
18579], [0.14100000262260437, 0.44999998807907104, 0.18600000441074371], [-0.53
299999237060547, -0.52999997138977051, -0.77399998903274536], [-0.2469999939203
2623, 0.0040000001899898052, -2.4839999675750732], [-0.094999998807907104, 0.00
60000000521540642, 1.6059999465942383], [0.68500000238418579, -0.74199998378753
662, 2.1429998874664307], [-1.1740000247955322, 0.442999988879432678, 2.27500009
53674316], [1.6929999589920044, 0.68199998140335083, -1.065000057220459], [1.92
79999732971191, -0.45399999618530273, 0.063000001013278961], [-0.27700001001358
032, 1.4459999799728394, 0.041999999433755875], [-0.11400000005960464, -1.52600
00228881836, -0.62999999523162842], [-1.6039999723434448, -0.55400002002716064,
-0.574999988807907104], [-0.903999998426437378, -0.9649999737739563, -3.144999980
9265137], [-1.3259999752044678, 0.158000000727176666, 3.1860001087188721]], [[1,
2], [1, 8], [1, 9], [2, 5], [2, 3], [2, 10], [3, 11], [3, 12], [3, 4], [4, 13],
[5, 6], [5, 7], [7, 14]])
```

Drawing small molecules from PDB files

Return a geometric value — i.e. a `<pyplasm.xge.xgepy.Hpc>` object

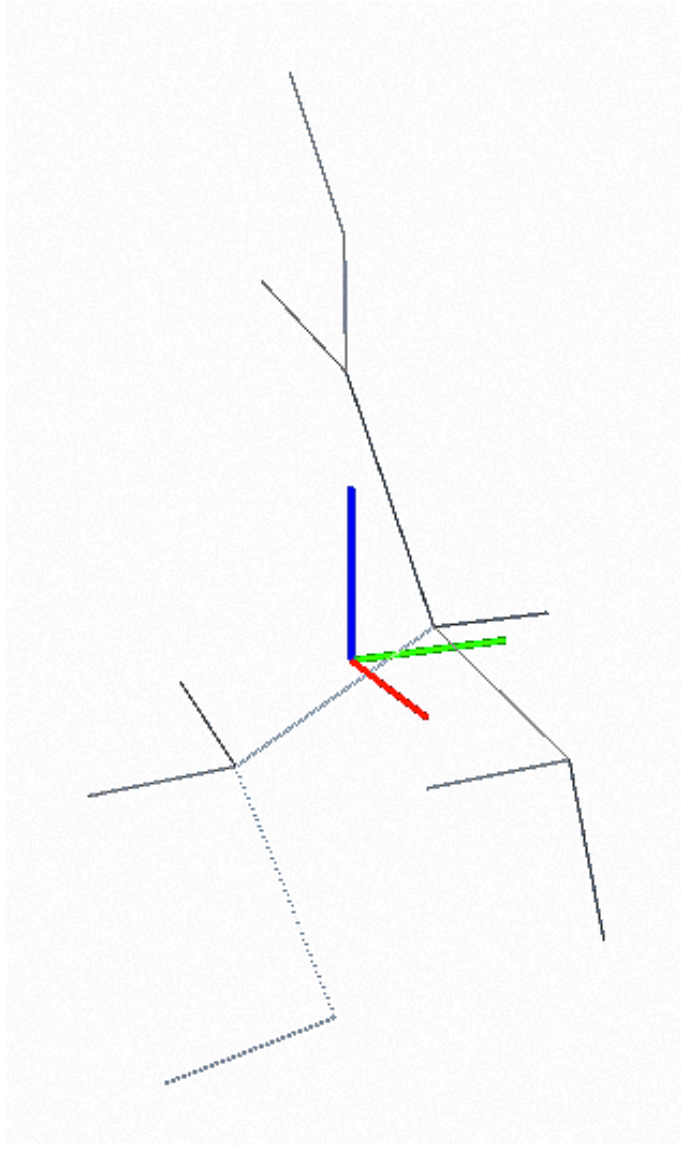
```
def graph (filename):
    parser=PDBParser()
    structure=parser.get_structure('molecule', filename)
    model = structure[0]
    chain = model[' ']
    residue = chain[0]

    nodes = [atom.get_coord().tolist() for atom in residue]
    edges = getPDBconnect('BTC.pdb')
    return MKPOL([nodes,edges,None])

myprint("graph('BTC.pdb')")
```

```
graph('BTC.pdb') -> <pyplasm.xge.xgepy.Hpc; proxy of <Swig Object of type 'std:
:tr1::shared_ptr< Hpc > *' at 0x326c50> >
```

Drawing small molecules from PDB files

View the 1-complex — embedded in 3D — of the molecule from `BTC.pdb`

```
VIEW(graph('BTC.pdb'))
```



Drawing small molecules from PDB files

Get the atomic radiuses from `atomic_radius.py`

```
## http://en.wikipedia.org/wiki/Atomic_radius#Calculated_atomic_radii
## http://en.wikipedia.org/wiki/Atomic_radius#Empirically_measured_atomic_radius
## http://en.wikipedia.org/wiki/Van_der_Waals_radius
## http://en.wikipedia.org/wiki/Covalent_radius

## 0 => No data available
## units = picometers: 1.0 x 10^(-12)

RADIUS_TYPE = 3 # van der Waals

## symbol:(name, empirical, Calculated, van der Waals, covalent)
atomic_radius = {
     "H":("hydrogen",35,53,120,38),
     "He":("helium",0,31,140,32),
     "Li":("lithium",145,167,182,134),
     "Be":("beryllium",105,112,153,90),
     "B":("boron",85,87,192,82),
     "C":("carbon",70,67,170,77),
     "N":("nitrogen",65,56,155,75),
     "O":("oxygen",60,48,152,73),
     "F":("fluorine",50,42,147,71),
     "Ne":("neon",0,38,154,69),
     "Na":("sodium",180,190,227,154),
     "Mg":("magnesium",150,145,173,130),
     "Al":("aluminium",125,118,184,118),
     "Si":("silicon",110,111,210,111),
     "P":("phosphorus",100,98,180,106),
     "S":("sulfur",100,88,180,102),
     "Cl":("chlorine",100,79,175,99),
```

Drawing small molecules from PDB files

Extract atom data (radiuses and type)

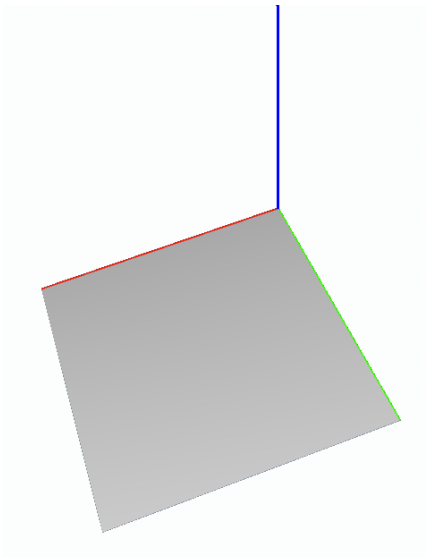
```
from atomic_radius import *


myprint("atomic_radius['Mg']")
myprint("atomic_radius['O'][0:2]")



myprint("[atom.get_id() for atom in residue]")
myprint("[atom.get_id()[0] for atom in residue]")
myprint("set([atom.get_id()[0] for atom in residue])")
myprint("list(set([atom.get_id()[0] for atom in residue]))")
```

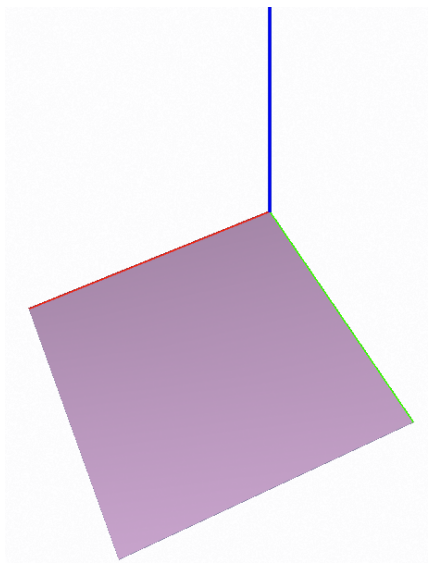
```
atomic_radius['Mg'] -> ('magnesium', 150, 145, 173, 130)

atomic_radius['O'][0:2] -> ('oxygen', 60)

[atom.get_id() for atom in residue] -> ['N', 'CA', 'CB', 'SG', 'C', 'O', 'OXT',
'H', 'H2', 'HA', 'HB2', 'HB3', 'HG', 'HXT']

[atom.get_id()[0] for atom in residue] -> ['N', 'C', 'C', 'S', 'C', 'O', 'O', '
H', 'H', 'H', 'H', 'H', 'H', 'H']

set([atom.get_id()[0] for atom in residue]) -> set(['H', 'C', 'S', 'O', 'N'])

list(set([atom.get_id()[0] for atom in residue])) -> ['H', 'C', 'S', 'O', 'N']
```

Drawing small molecules from PDB files

Atom color definition, according to practice (for biomolecules)

```
atom_color = {
     'H': Color4f([0.8, 0.8, 0.8, 1.0]), # ligth gray
     'C': Color4f([0.3, 0.3, 0.3, 1.0]), # dark gray (quite black)
     'N': BLUE,
     'O': RED,
     'F': Color4f([0.0, 0.75, 1.0, 1.0]), # ligth blue
     'P': ORANGE,
     'S': YELLOW,
     'Cl': GREEN,
     'K': Color4f([200./255, 162./255, 200./255, 1.0]) # lilac
}

myprint("VIEW(COLOR(atom_color['H'])(CUBOID([1,1])))")
myprint("VIEW(COLOR(atom_color['K'])(CUBOID([1,1])))")
```

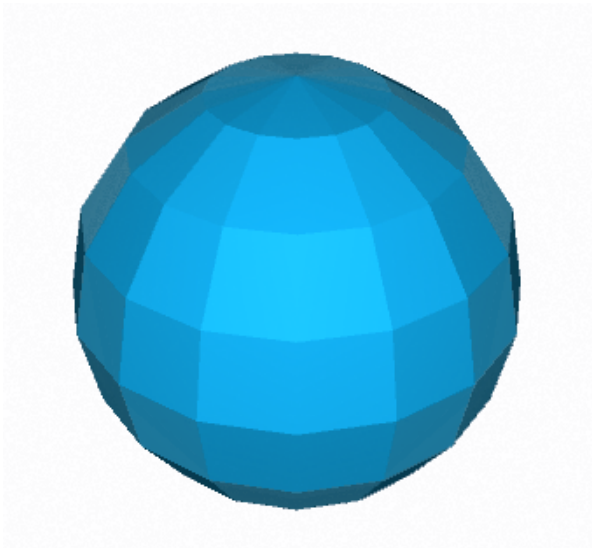


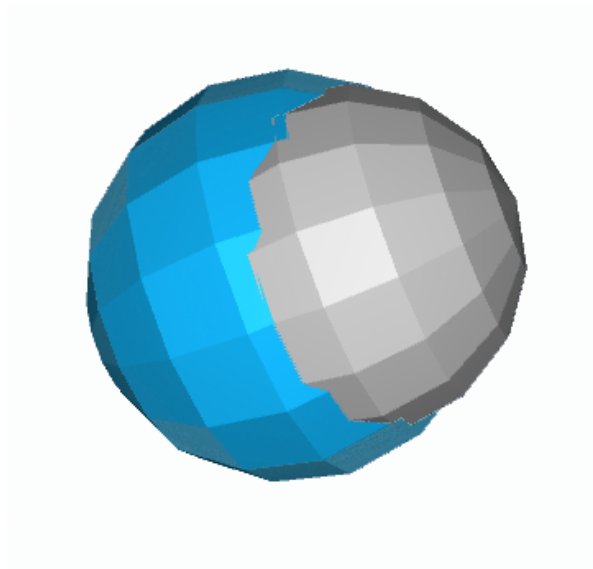


Drawing small molecules from PDB files

Drawing colored spheres — notice the conversion: picometers → Angstrom

```
def sphere(atom_code):
    return COLOR(atom_color[atom_code])(
        SPHERE(atomic_radius[atom_code][RADIUS_TYPE]/100.)([8,16]))

myprint("VIEW(sphere('F'))")


VIEW(STRUCT([ sphere('F'), T([1,2,3])([0.,.3,.5]), sphere('H') ]))
```

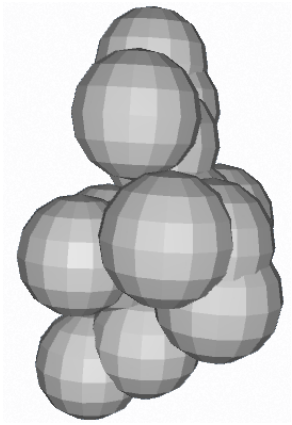


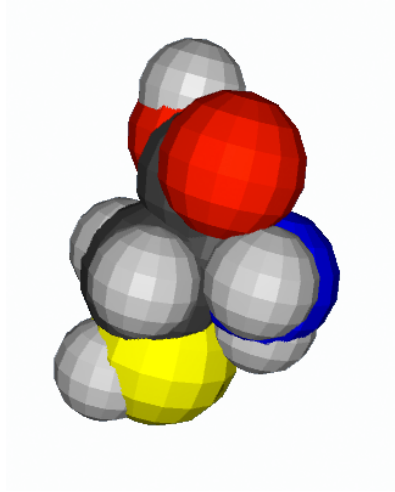


Drawing small molecules from PDB files

aaaaaaaa

```
def graph2 (filename):
    parser=PDBParser()
    structure=parser.get_structure('molecule', filename)
    model = structure[0]
    chain = model[' ']
    residue = chain[0]

    nodes = [atom.get_coord().tolist() for atom in residue]
    transls = AA(T([1,2,3]))(nodes)
    return STRUCT(CONS(transls)(sphere('H')))

myprint("graph2('BTC.pdb')")

VIEW(STRUCT([ graph('BTC.pdb'), graph2('BTC.pdb') ]))
```





Drawing small molecules from PDB files

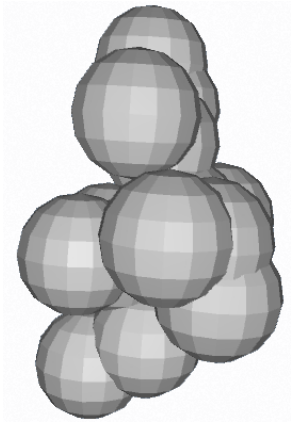
aaaaaaaa

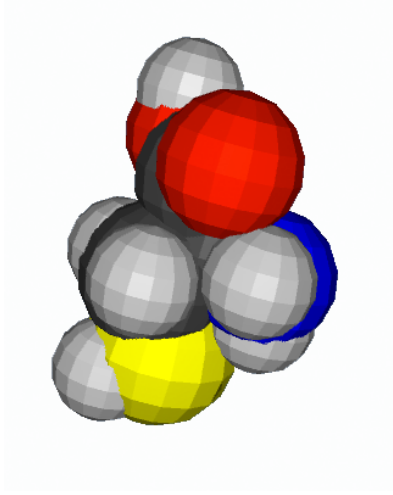
```
atom_types = [atom.get_id()[0] for atom in residue]
myprint("atom_types")

AA(sphere)(atom_types)
```

Drawing small molecules from PDB files

aaaaaaaa

```
def graph3 (filename):
    parser = PDBParser()
    structure = parser.get_structure('molecule', filename)
    residue = structure[0][' '][0]
    nodes = [atom.get_coord().tolist() for atom in residue]
    transls = AA(T([1,2,3]))(nodes)
    atom_types = [atom.get_id()[0] for atom in residue]
    atoms = AA(sphere)(atom_types)
    return STRUCT(AA(STRUCT)(TRANS([transls,atoms])))

VIEW(graph3('BTC.pdb'))
VIEW(STRUCT([ graph('BTC.pdb'), graph3('BTC.pdb') ]))
```

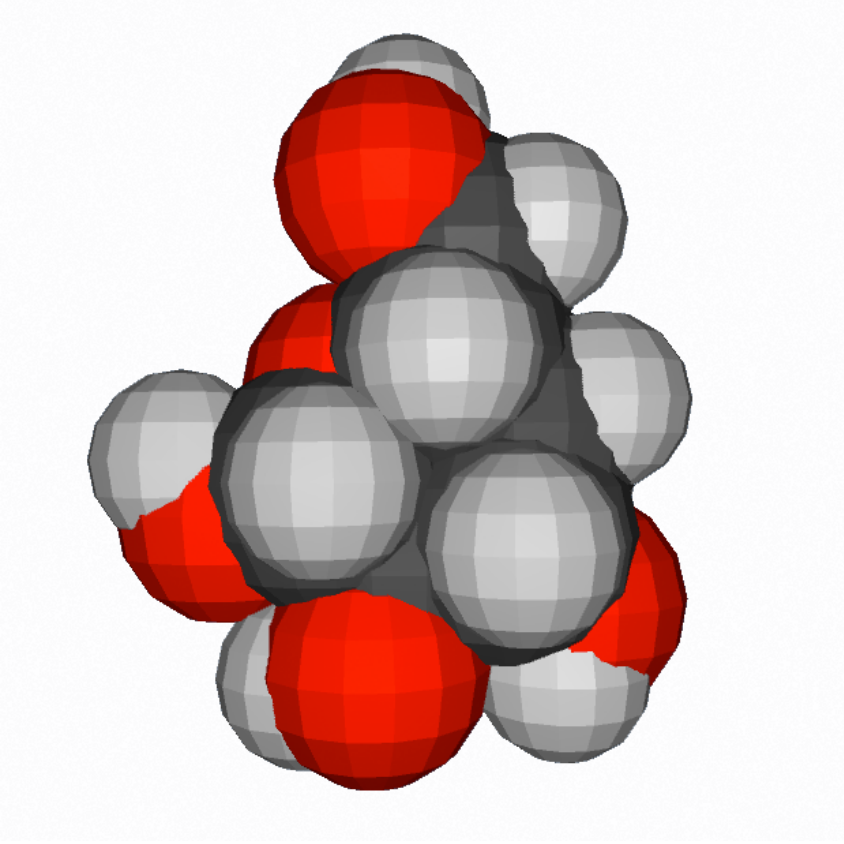




Drawing small molecules from PDB files

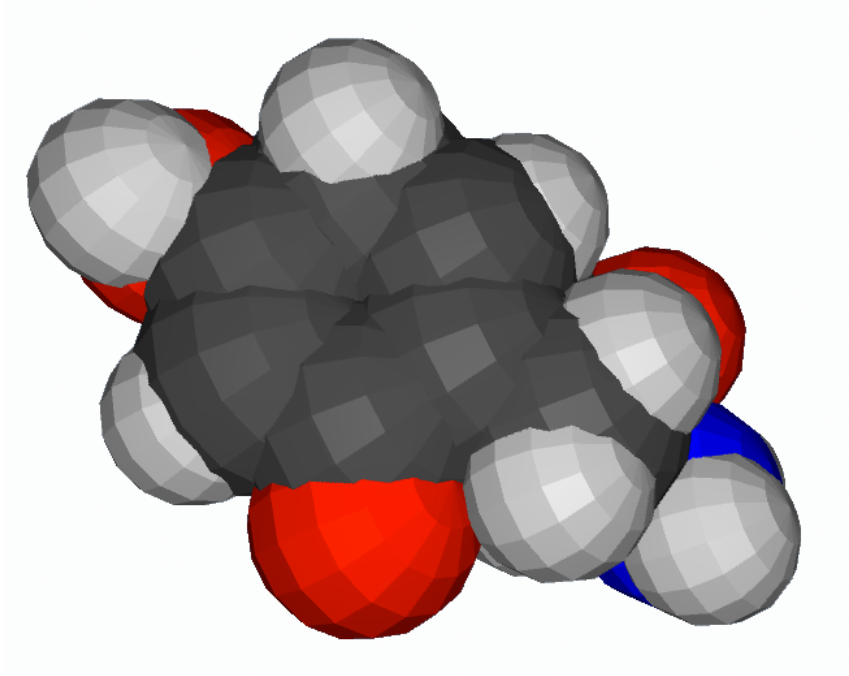
Other examples

BETA-D-GALACTOSE



```
VIEW(graph3('GAL.pdb'))
```

2-AMINO-3-(4-HYDROXY-6-OXOCYCLOHEXA-1,4-DIENYL)PROPANOIC ACID



```
VIEW(graph3('OTY.pdb'))
```

Sommario

aaaaaaaa

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- aaaaaaa
- aaaaaaa

Sommario

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- aaaaaaa
- aaaaaaa
- aaaaaaa