

Visualization of proteins

Tutorial by Dr. René Staritzbichler

<http://proteinformatics.org> -> Teaching -> Download course material

Course 3.8.2020

Visualization tools

Local:

- PyMol: structure <https://www.pymol.org>
- VMD: dynamics <http://www.ks.uiuc.edu>
- Chimera dynamics <https://www.cgl.ucsf.edu/chimera/>

All are powerful analysis and modeling tools.

Web-sharing / developed at the Hildebrand lab:

- NGL: structure <http://nglviewer.org>
- MDSrv: dynamics <http://proteinformatics.org>

Focus system: 3sn6.pdb

- β 2-Adrenergic receptor
 - Receptor for (nor)adrenalin
 - Drug target for high blood pressure and asthma
- First 3D structure of activated GPCR
 - GPCRs are the largest and most important single class of receptor
 - Human: 800 different (smell, taste, vision, ...)
 - 30% of drugs bind to GPCR
 - Undergo large conformational change upon activation
- Nobel price for Brian Kobilka 2012
- We work with Kobilka on understanding the signaling process

1. Exercise: say hello to 3sn6.pdb

- http://proteinformatics.uni-leipzig.de/mdsrv.html?load=file://_course/3sn6/session.js
- On the right side is a list of three opened proteins
- Click on the eye symbol right of the last two proteins
 - 6e67-crystal
 - 3sn6-crystal
- Now, you only see 3sn6
 - In the first section 'sim' below the '3sn6', click the play symbol
 - The first round takes a little because of loading

Resources for proteins

- Protein structures: protein data bank (PDB): <http://rcsb.org>
- Orientation of proteins in membranes (OPM): <https://opm.phar.umich.edu>
- Biological background: <https://www.uniprot.org>

- **Tasks:** find 3sn6 in each
 - Look at information provided from servers
 - Download pdb from OPM
 - Download sequence (fasta) from PDB
 - Download wildtype sequence from UNIPROT

Visualization using VMD

- Open VMD
- Open 3sn6.pdb
 - What do you see?
- In main window, go to ,Graphics‘ and then ,Representation‘
 - Coloring method: ,Chain‘
 - Drawing method: ,NewCartoon‘
- Create replicate
 - Click second line in window below ‘Create Rep‘ button.
 - Selected Atoms: sidechain or type CA
 - Drawing method: Licorice
 - Coloring method: Type

Whenever you want to change atom selection, drawing or coloring method, make sure to click on the correct replica in the list below the ‘Create Rep‘ button. The one highlighted is the one where changes will have effect.

Exercises 1/2

- Identify key units. Use two replica, one in 'Lines' drawing method and 'all' atom selection, the second with 'Licorice' representation and the following selections:
 - GPCR ('chain R')
 - G-protein ('not chain R')
 - ligand ('resname P0G')
- Find transmembrane region by biochemical properties
 - Membrane exposed residues should not be charged (acidic,basic) or polar
 - Use 'NewCartoon' representation
 - Use Drawing method 'ResType'
 - Color scheme: basic:blue; acidic:red; polar:green; non-polar:white
 - consider buried versus exposed
- Study the binding of the G-protein to the receptor
 - what part interacts with which counterpart?

Exercises 2/2

- Measure manually some distances of near neighbors between GPCR and G-protein.
 - Type '2' and then click with mouse on two atoms.
 - A dotted line will connect the selected atoms together with the distance.
 - Note the additional information printed in the shell.
- Systematic contact analysis of GPCR and G-protein
 - Main VMD window → Extensions → Analysis → Contact Map
 - Atom selection molecule A: 'chain R'
 - Atom selection molecule B: 'not chain R'
- Analyzing salt bridges
 - Main VMD window → Extensions → Analysis → Salt Bridges
 - Bridges are written to terminal in which you started VMD
 - To visualize them:
 - Main VMD window → Extensions → Analysis → Sequence Viewer
 - Shift-click on residues of interest: see graphical window (yellow highlight)

Scripting in VMD “power to the people”

- Visualization tools become most powerful by providing scripting language
- This allows to do whatever you want...within the capabilities of a visualization software
- In VMD the scripting language is tcl/tk (a little old fashioned)
- To use this: VMD Main => Extensions => Tk Console
- Enter the block of code from the next page

Defining functions

```
proc geom_center {selection} {  
    # set the geometrical center to 0  
    set gc [veczero]  
    # [$selection get {x y z}] returns a list of {x y z}  
    # values (one per atoms) so get each term one by one  
    foreach coord [$selection get {x y z}] {  
        # sum up the coordinates  
        set gc [vecadd $gc $coord]  
    }  
    # and scale by the inverse of the number of atoms  
    return [vecscale [expr 1.0 /[$selection num]] $gc]  
}
```

```
proc gyr_radius {sel} {  
    # make sure this is a proper selection and has atoms  
    if {[$sel num] <= 0} {  
        error "gyr_radius: must have at least one atom in selection"  
    }  
    # gyration is  $\sqrt{\text{sum}((r(i) - r(\text{geometric-center}))^2) / N}$   
    set com [geom_center $sel]  
    set sum 0  
    foreach coord [$sel get {x y z}] {  
        set sum [vecadd $sum [veclength2 [vecsub $coord $com]]]  
    }  
    return [expr sqrt($sum / ([$sel num] + 0.0))]  
}
```

Using defined functions

In order to calculate the geometric center of the receptor type:

```
set sel [atomselect top "chain R"]
```

The variable \$sel contains all selected atoms.

With this you can now calculate the geometric center of the molecule by typing:

```
geom_center $sel
```

this may return the following output (NOTE: your output will be different!):

```
0.912778 4.61792 2.78021
```

Next, we calculate the radius of gyration:

```
gyr_radius $sel
```

Let's say the output is:

```
5.45443
```

Now, we can visualize this point by placing a sphere at this position:

```
graphics top sphere {0.91 4.62 2.78} radius 5.4 resolution 21
```