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Contents:
INTRODUCTION TO MOLECULAR GRAPHICS AND VMD

For background on using VMD, look at [Hsin2008] and the VMD tutorial. Basics of protein structure are illustrated in [BrandenTooze].

1.1 Learning Objectives

- basic understanding of protein structure
- familiarize with a molecular graphics program (VMD)
- loading of static structures and dynamics trajectories
- viewing a molecule (mouse, view modes)
- representations
- selections
- making images
- basic analysis
- use of RMSFitting tools

1.2 Protein structure

See also illustrations in slides and [BrandenTooze].

Introduction to protein structure

- polypeptides, amino acids
  - chemical structure of the 20 aa
  - natural aa: L-form (note: look down H-Ca and read CORN == L, otherwise D)
  - peptide bond
  - repeating unit: residue, same backbone, differing sidechain R
  - sequence, primary structure
- hydrogen bonds: donor-H...acceptor
Protein Structure and Visualization Documentation, Release 1.0

• secondary structure
  – alpha-helix (n..n+4 H-bonds of main chain, ~3.6 res per turn)
    * peptide units: phi, psi angles: flexible, omega (peptide bond) fixed (cis/trans)
    * must be right handed (otherwise clashes; only very short helices are left-handed)
  – beta sheet (extended), parallel/anti-parallel
  – (coiled coil)
  – 3-10 helix (n..n+3, 10 atoms between donor and acceptor, 3 res per turn)
  – pi helix (n..n+5)
• tertiary structure: - helices - sheets - hairpins, loops - coiled-coil
• quaternary structure

1.3 Practical excercise

For background on using VMD, look at [Hsin2008] and the VMD tutorial.

1.3.1 Topology and secondary structure

• settings in VMD:
  – Display -> Orthographic
  – Display -> Rendermode: GLSL
  – Graphics -> Color: Display: Background: White
• select protein
• new cartoon representation, color by secondary structure

Identify secondary structure and topology

Sketch a topology diagram on paper (use open structure for analysis):
• number helices H1 - H8 (ignore short < 4 res, count all helices as helix, alpha, pi, 3-10)
• sheets A, B, C, number strands SA1-SA5, SB1-3, SC1-2
• start with central b-sheet
• locate N-terminus (resid 1 and name CA, color blue, VDW) and C terminus

Note: You can do ranges: resid 1 to 5 or multiple ranges: resid 1 to 5 20 to 50.
You can use boolean operators and, or, not. See selections in the user manual for details.

• draw connections between secondary elements in your topology diagram and label secondary structure elements.
Identify domains (tertiary structure)

• compare to closed conformation
  – load adk_closed.pdb
  – select protein
  – new cartoon, color differently from the open structure
  – superimpose: Extensions -> Analysis -> RMSD tool: protein

\[
\text{RMSD} = \sqrt{\frac{1}{N} \sum_{i=1}^{N} (x_{a,i} - x_{b,i})^2}
\]

What is the RMSD after superposition?

– Investigate how the conformation of the molecule changes.
  * Which regions (domains) “move”?
  * Identify two moving domains (called “NMP” and “LID”) and one constant region (“CORE”):
    · give residue ranges (tip: use Extensions -> Analysis -> Sequence Viewer)
    · color regions differently and also mark them in your topology diagram
  – align on CORE domain only

What is the final RMSD when aligned on CORE only, i.e. how similar are the CORE regions in the two structures?

What is the overall protein RMSD, assuming that the two structures are superimposed on CORE?

Publication-quality images

To make an image with AO (ambient occlusion lighting) and depth cueing:

• Settings
  – Display -> Rendermode -> GLSL
  – Display -> Display Settings:
    * Shadows On,
    * Amb Occl On
    * Cue Mode: Linear
    * Cue start: 1.75
    * Cue end: 3.0
  – white bg: Graphics -> Colors: Display : White
• rendering: File -> Render
  – snapshot
    * glossy material looks nice
  – tachyon (internal): ray tracer (takes a while due to AO)
    * change materials to special AO materials (e.g. AOChalky)

1.3. Practical exercise
1.3.2 Dynamics

Analyze a trajectory of the closed-to-open transition of AdK [Beckstein2009]:

- load `adk.psf` with `adk_dims.dcd` (use `load all at once`, this is faster in general)
- color domains and show as new cartoon
  - resid 30 to 59: blue
  - resid 122 to 159: yellow
  - not (resid 30 to 59 122 to 159) (or resid 1 to 29 60 to 121 160 to 214): gray
- play (loop: rock)
- RMSD change over the trajectory: Extensions/Analysis/RMSD Trajectory Tool
- measure distance:
  - ‘2’ (or Mouse -> Label -> Bonds)
  - click tip of LID and tip of NMP
  - run : label changes
  - Graphics -> Labels: Bonds - select - Graph (preview) - Graph...
  - try different distances between residues (use the CA) and plot together: which change, which don’t?
    - What would be good distances to report on conformational changes, e.g. for FRET?
    - Look at I52-K145, A55-V169, A127-A194

1.3.3 Ligands

- Download 1AKE from the PDB
- show protein chain A
- show the co-crystallized ligand Ap5 (“resname AP5”)
  - rename AP5, licorice, color: name
- show charged residues within 5 Å of the ligand
  - same residue as (charged and within 5 of resname AP5)
  - use representation licorice, color: name for the residues, make ligand VDW.
  - Which side chains make contact with the ligand?
  - What have they got in common? (Tip: try out color: restype)
- water
  - show crystal water oxygens as VDW or licorice (small spheres)

1.4 References
BIBLIOGRAPHY

