CNS Assignment 5

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1 Analysis of 2BAW Protein-Ligand Complex

1.1 Identification of Secondary Structures

The Protein-Ligand Complex 2BAW was analysed using the its pdb file obtained from RCSB through VMD.

A protein–ligand complex is a complex of a protein bound with a ligand, where a ligand is a substance that forms a complex with a biomolecule such as a protein to serve a biological purpose.

Any protein is made of several secondary structures which are formed by different residues i.e. amino acids.

Secondary structure refers to the local folded structures that form within a polypeptide due to interactions between atoms of the backbone.

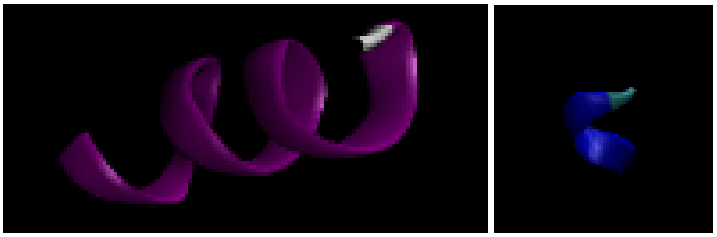
There are four major classes of Secondary structures:

- Helices
  - α helices (Purple)
  - 3_{10} helices (Blue)
  - π helices (Red)
- β Sheets
  - Extended β Sheets (Yellow)
  - β bridges (Tan)
- Turn (Cyan)
- Coil (White)

Colors written in brackets are color coding used in VMD

Figure 1: 2BAW

Helices in the Protein-Ligand Complex:

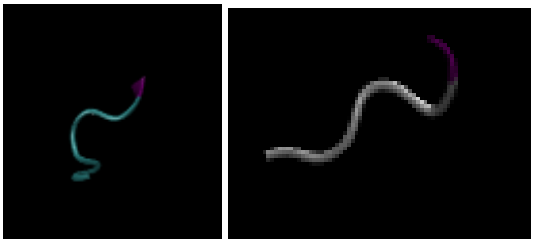


(a) α Helix (b) 3_{10}

β Sheets in the Protein-Ligand Complex:

(a) Extended Beta-sheet

Other secondary structures in the Protein-Ligand Complex:



(a) Turn (b) Coil

1.2 Identification of the residues that are actively binding the ligand

There are four ligands present in the complex :

- B7G - Ligand A1
- B7G - Ligand A2
- VCA - Ligand B1
- VCA - Ligand B2

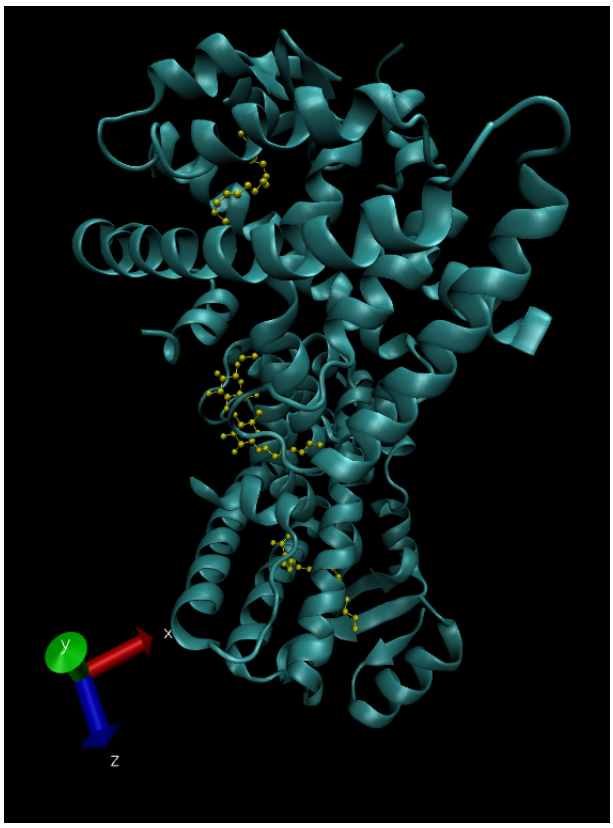
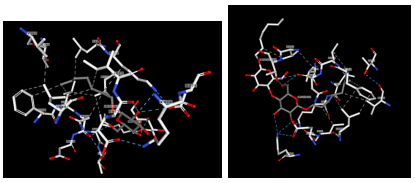
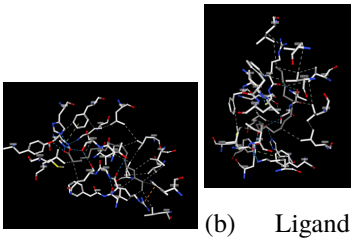


Figure 5: Ligands present in the protein



(a) Ligand A1 (b) Ligand A2



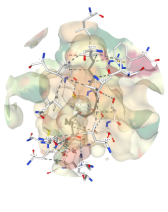
(a) Ligand B1 (b) Ligand B2

The residues that are actively binding the ligand :

- For ligand A1
  - Leucine
  - Asparagine
  - Valine
  - B7G

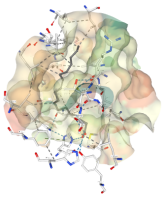
  - Lysine
  - Glutamine
  - Lysine
  - Aspartic Acid
- For ligand A2
  - Lysine
  - Glutamine
  - Lysine
  - Threonine
  - B7G
  - Phenyl Alanine
  - Leucine
  - Asparagine
  - Threonine
- For ligand B1
  - Leucine
  - Cytosine
  - Threonine
  - Histidine
  - Valine
  - Leucine
  - Valine
  - Histidine
- For ligand B2
  - Cytosine
  - Threonine
  - Histidine
  - ILE
  - Histidine
  - Methionine
  - Leucine
  - Tyrosine

Active binding sites:

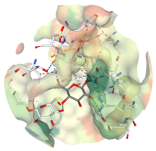


(a) Ligand B1

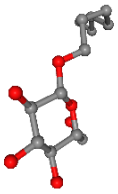
(b) VCA



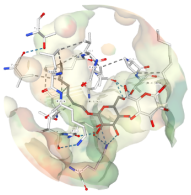
(c) Ligand B2



(a) Ligand A1



(b) B7G



(c) Ligand A2

1.3 Nature of non-bonded interactions

There are several type of non-bonded interactions:

- Hydrogen Bonds
- Halogen Bonds
- Hydrophobic Contacts
- Pi Interactions (Pi Stacking)
- Cation-Pi Interactions
- Metal Interactions

There exist only Hydrogen Bonds and Hydrophobic Contacts in the considered complex.
Some Hydrogen Bonds exist between - Hydrogen Bond: 2.0 to 3.5 Angstrom:

- B7G [O] - LYS [N] (3.24 A)
- B7G [O] - ASP [O] (3.5 A)
- VCA [O] - HIS [N] (2.53 A)
- VCA [O] - TYR [O] (2.67 A)

Some Hydrophobic Contacts exist between - Hydrophobic Contact: 3.5 to 4.0 Angstrom:

- B7G [C] - ILE [C] (3.75 A)
- B7G [C] - LEU [C] (3.65 A)
- VCA [C] - LEU [C] (3.94 A)
- VCA [C] - GLY [C] (3.96 A)

2 Ramachandran Plot and its Analysis

2.1 Graphs for Secondary Structures

The Ramachandran Plot of the complex is:

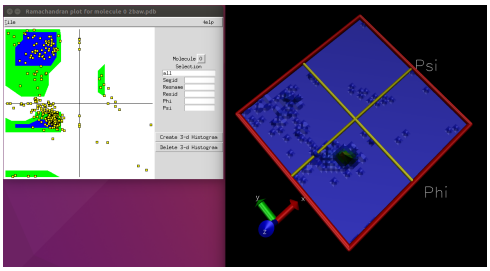
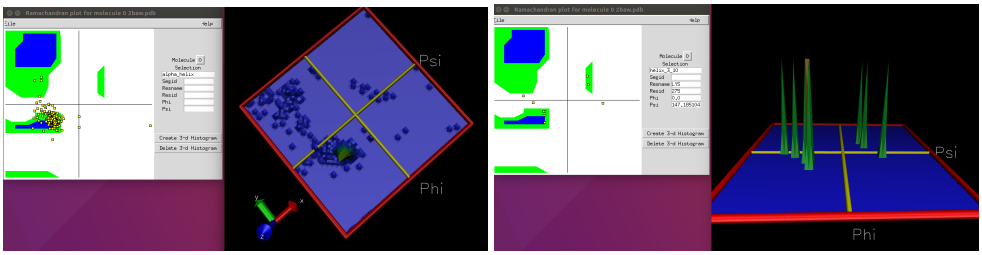


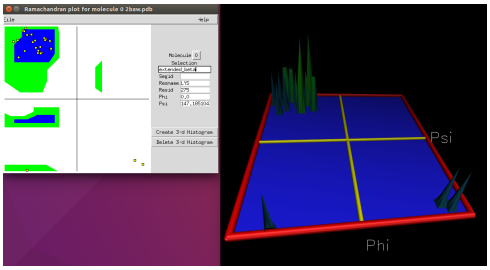
Figure 10: 2BAW

Graphs of Helices in the Protein-Ligand Complex:



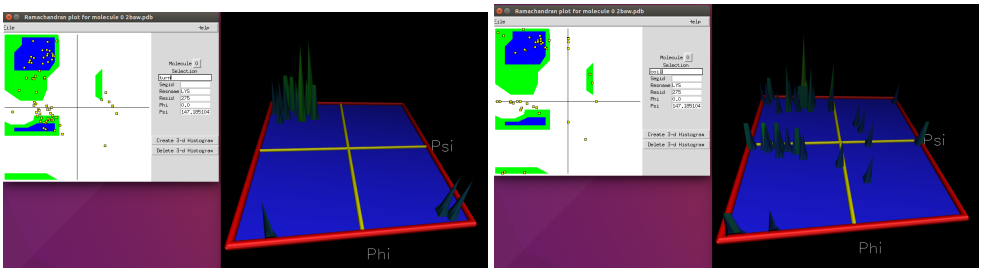
(a) α Helix (b) 3_{10}

Graphs of β Sheets in the Protein-Ligand Complex:



(a) Extended β-sheet

Graphs of other secondary structures in the Protein-Ligand Complex:



(a) Turn (b) Coil

Majority of the residues in the Ramachandran Plot that are in the forbidden region are under the

secondary structures turn and coil, while rest of the residue lie in the first quadrant (β Sheets) and fourth quadrant (α Helix)

2.2 Forbidden region and Residues present in it

The residues in the forbidden region are :

- LYS
- ILE
- GLU
- TYR
- SER
- LEU
- GLY
- ASN
- GLN
- ALA
- ASP
- THR
- PRO
- TRP
- HIS
- VAL

GLY residues occur the most in forbidden region followed by LYS and LEU. (GLY because the stearic hinderence is the least).

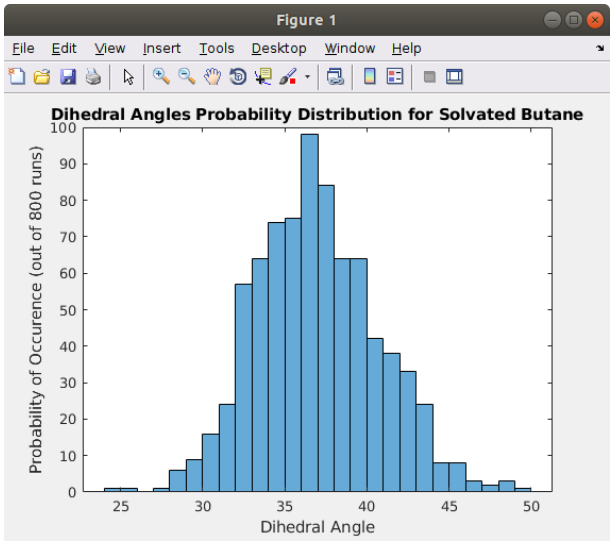
3 Simulation on Butane molecule in the presence and absence of water

3.1 Introduction

The pdb file of the molecule is created, which combined with the topology file generates the psf file. On solvation for the solvated butane we get the solvated psf and pdb file. Then, there are two NAMD simulations run: Minimization-Equilibration and Production.

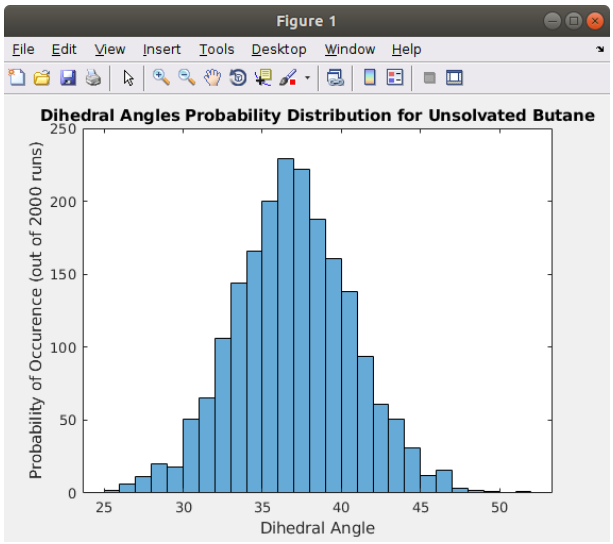
3.2 The probability distributions of the dihedral angle corresponding to the rotation about the central single bond

Probability distributions of the dihedral angle in water:



(a) Solvated Butane

Probability distributions of the dihedral angle without water:



(a) Unsolvated Butane

There are some conformers whose occurance is much more than those of the others which implies that there are conformers which are much more stable than the others. The probability distribution in water is unbalanced because there is steric effect on butane due to water which causes all the conformers to be less stable.

3.3 Compare the differences in the rates of transition between anti and gauche conformers

- mean = 36.9816 - Unsolvated

- mean = 36.9544 - [C] Solvated

The relative abundace of the products we compare the relative energies,
The rate of the reaction can be obtained from the equilibirium constant:
The equilibrium constant is :

$$k_c \propto [Reactants]/[Products]$$

And for Anti Gauche, ratio of the bin values gives the equilibirium constant. The relative energies are obtained from the

$$k = e^{-\frac{dG}{RT}}$$

Therefore, the free energy difference between the Gauche and Anti Conformers.

Rate of a reaction is directly dependant on the amount of reactant and inversely to the amount of products. The rate of transfer of Anti to Gauche is less than rate of transfer of Gauche to Anti. Also it can be seen that the amount of Gauche relative to the amount of Anti is more in the solvated one than the unsolvated one. Thus the rate of Gauche to Anti is even more in the unsolvated one than in the solvated one.