Protein - Ligand Complex

I. Problem Statement

Download a PDB file corresponding to protein-ligand complex of your choice and represent the protein in the cartoon representation and identify different secondary structure elements

II. Introduction

In the following project we are going to download a pdb file corresponding to a protein and find its secondaries.

III. Construction

Go to rscb.org website and download a protein of your choice. After downloading it, open it in vmd software. In it, there, go to Graphics and select Representations then select NewCartoon in Drawing Style.

For viewing different secondary structures, select them under select tab. The secondary structures are as follows :

Helix : π , α , 3_{10}
β Sheets : Extended , Bridge
Turn
Coil

IV. Results

The protein looks like this : Different secondary structures of the protein :

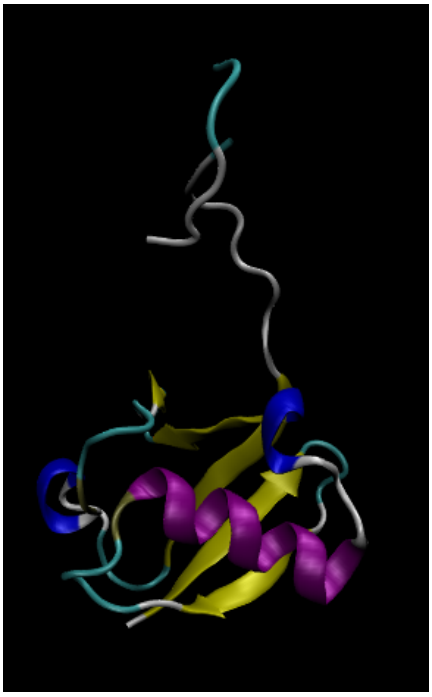

Fig. 1. Protein with ligand

- Helix
  - α

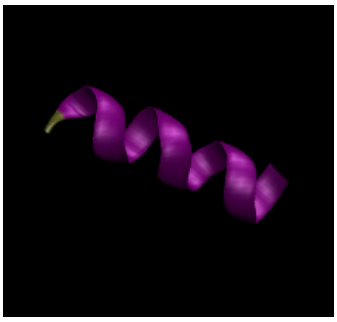

Fig. 2. α Helix

  - 3_{10}

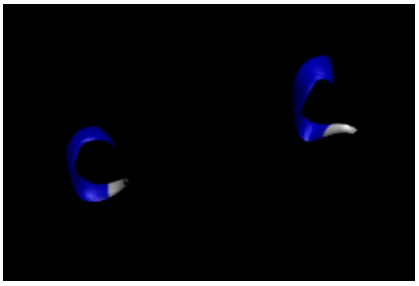

Fig. 3. 3_{10} Helix

- β Sheets
  - Extended

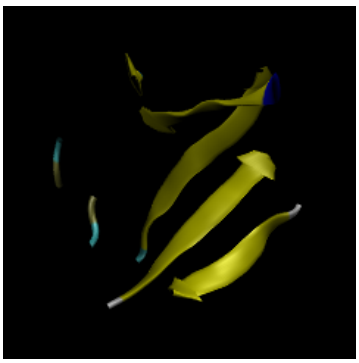

Fig. 4. Extended

– Bridge

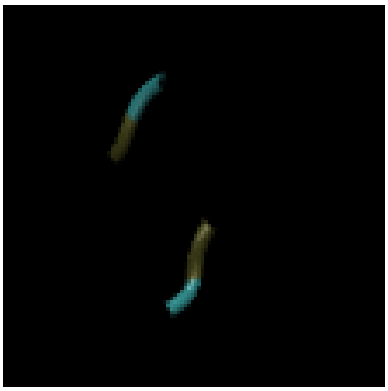

Fig. 5. Bridge

- Turn

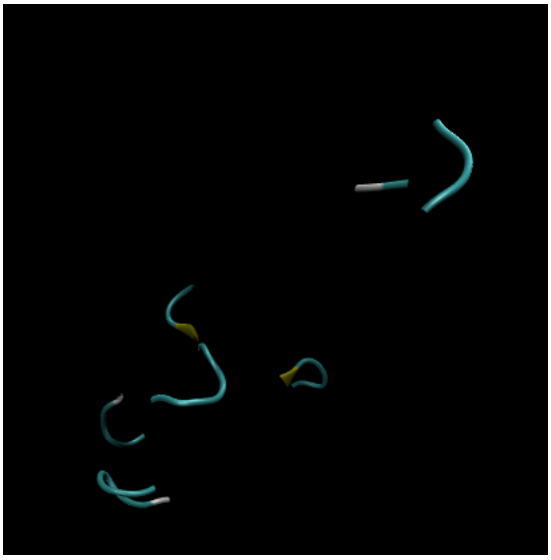

Fig. 6. Turn

- Coil

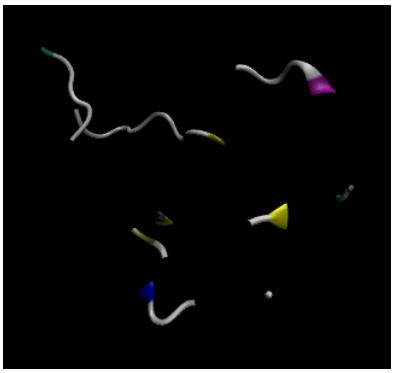

Fig. 7. Coil

V. Conclusion

A protein consists of multiple secondary structures which are formed by different residues (Amino acids) and have different folding which characterizes them.

Protein - Ligand Complex

I. Problem Statement

Download a PDB file corresponding to protein-ligand complex of your choice and identify the residues that are actively binding the ligand and also find the non bonded interactions.

II. Introduction

In the following project we are going to download a pdb file corresponding to a protein and find the residues that bind the ligand and its non bonded interactions.

III. Construction

After getting the protein, the first step is to find the ligands and then finding the residues it binds itself to. For finding the ligands, go to rscb.org from where you downloaded it and search for the properties of the molecule which is available on the website. There look for the ligand properties and then find the residues binding to it.

IV. Results

The ligands in the following molecule are :

- Ligand A

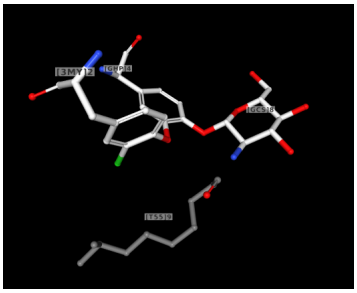

Fig. 1. Protein with ligand

The residues actively binding to it are :
3MY
GCS
GMP

None of the residues have any non bonded interactions with the ligand.

- Ligand B

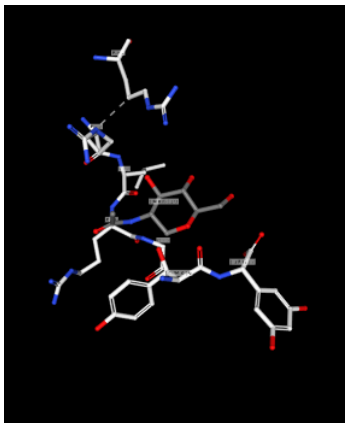

Fig. 2. Protein with ligand

The residues actively binding to it are :
3FG
OMX
GLY
LEU
ARG

ARG has a Hydrophobic contact with the molecule.

- Ligand C

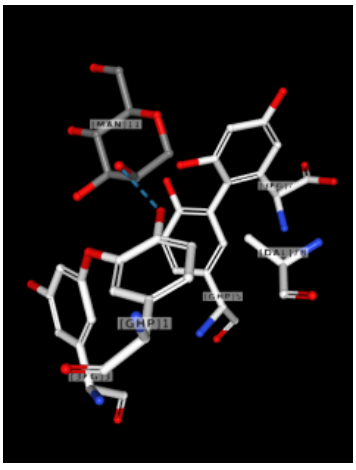

Fig. 3. Protein with ligand

The residues actively binding to it are :
DAL
3FG
GHP
GHP

GHP has a H bond with the ligand with it having a bond length of 2.63 Angstorm.

V. Conclusion

A ligand binds to a protein only when its residues bind to it directly or indirectly. In this experiment we saw the ligands that were actively binding to it and also the non bonded interactions it.

VI. Appendix

The key geometric criterias for having an H bond are :

The maximum donor to acceptor distance is generally 3.5 and 4.1 for bonding with sulfur atoms. Angles are checked according to the following guidelines:

Maximum 45 degree deviation from optimal (90 degree) acceptor angle (AA-A-D)
Maximum 45 degree deviation from optimal (90 for sp2, 60 for sp3) donor angle (DA-D-A)
Maximum 90 degree deviation from optimal (0 degree) acceptor plane angle (A-D to A-AA-AA or AAA instead of AA)
Maximum 30 degree deviation from optimal (0 degree) donor plane angle (D-A to D-DA-DA or DAA instead of DA)

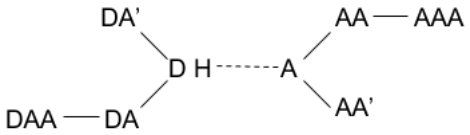

Fig. 4. H Bond

For Contact Bonds :

Hydrophobic contacts are calculated according to the following parameters: Contacts are made between carbons that are connected only to carbon or hydrogen, the default maximum hydrophobic distance is 4.0 , for atoms that interact with several atoms in the same residue, only the one with the closest distance is kept, and hydrophobic contacts between pi-stacked aromatic rings are removed.

Ramachandran Plot

I. Problem Statement

Download a PDB file corresponding to protein-ligand complex of your choice plot a ramachandran plot labeling important secondary structures and finding the residues present int he forbidden region.

II. Introduction

In the following project we are going to find the ramachandran plot of the molecules

III. Construction

After getting the protein, the first step is to find the ramachandran plot which can be found in VMD after loading the molecule.

IV. Results

The plot for the protein is: There are many residues

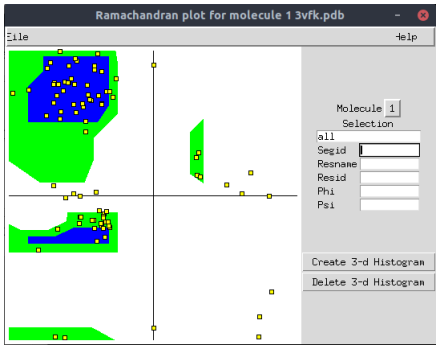

Fig. 1. Protein with ligand

present in the forbidden region. The ramachandran plot for the secondary structures are :

- Helix

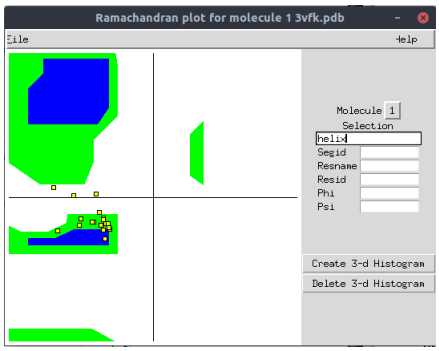

Fig. 2. Protein with ligand

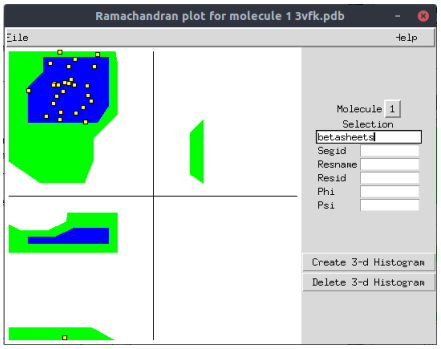

Fig. 3. Protein with ligand

- β Sheets
- Coil

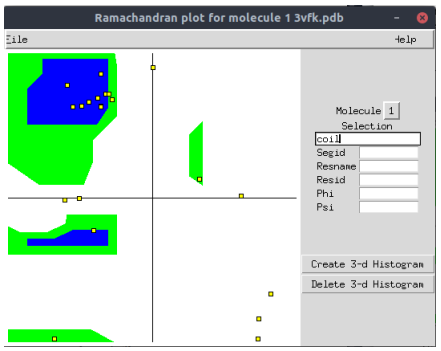

Fig. 4. Protein with ligand

- Turn

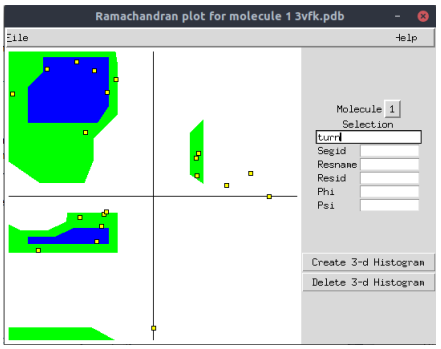

Fig. 5. Protein with ligand

V. Analysis

Analyzing the ramachandran plot, it is clear that most of the residues in the forbidden region are part of the secondary

structures turn and coil with helix and sheets having very less residues in the forbidden region.

The residues in the forbidden region are :

MET
3MY
GLY : II
DAL : II
GHP : III
GLN
CCS
TYR
3FG
ASP

From this is seen that GHP occurs the most followed by GLY residues.

VI. Conclusion

From this it is concluded that the most amount of residues in the forbidden region are in the secondary turn and coil.

VII. Appendix

The ramachandran plot is:

Ramachandran Plot is a way to visualize dihedral angles ψ against ϕ of amino acid residues in protein structure. Ramachandran recognized that many combinations of angles in a polypeptide chain are forbidden because of steric collisions between atoms.

Due to variour factors where the steric reasons do not remain the major factor for having a specific angle many molecules fall in the forbidden region.

Usually Glysine and Proline are in the forbidden region. Glycine as it has H as its chain which has the least steric and Proline as it has to have a specific configuration as it is a cyclic circle.

Butane Conformer Analysis

I. Problem Statement

Perform a simulation on butane molecule in the presence and absence of water, compare the probability distributions of the dihedral angle corresponding to the rotation about the central single bond and compare the differences in the rates of transition between anti and gauche conformers using the trajectory.

II. Introduction

In the following project we are going to model the butane molecule and run a configuration on it from namd with and without water.

III. Construction

Make a PDB file using the information provided in the rscb website. Make a butane molecule without the Hydrogens and open the molecule in VMD. Then create an Autopsf of the molecule thus generating a .psf file and also adds Hydrogen to it. Also go to tk console and generate a solvate box.

After solvating the molecule run it under a namd minimization and equilibration. After that run it under a namd production configuration.

The following rate of a reaction can be found out using the equation :

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

$$\Delta G_o = e^{-k_c/RT}$$

IV. Results

The Dihedral distribution for Water Solvated Molecule is :

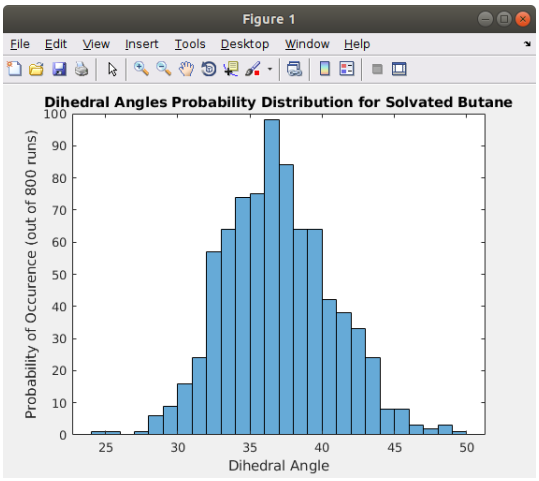

Fig. 1. Solvated

The Dihedral distribution for Unsolvated Molecule is :

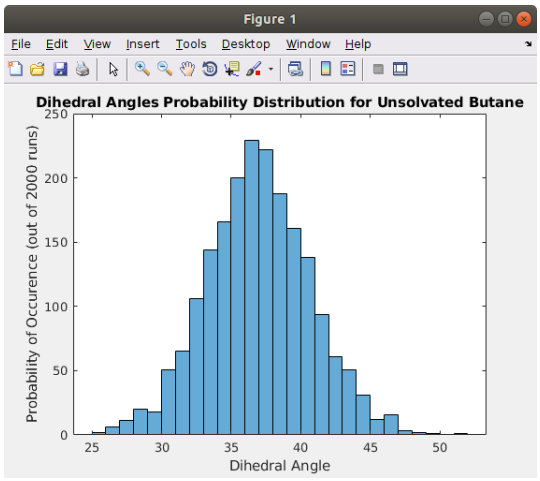

Fig. 2. Non Solvated

V. Analysis

It can be seen that at a particular range of angle, the probability of the conformer is the greatest whereas other conformers are not that high. It is due to the fact that some conformers are exceptionally stable.

In water, the distribution is less balanced as the water molecule has steric effect on butane thus making all the conformers a less stable than they generally are.

From the above equation, it can be seen that the equilibrium constant depends directly on the amount of reactant and inversely to the amount of products.

Hence it can be concluded that the rate of transfer of Anti to Gauche is less than rate of transfer of Gauche to Anti as ΔG_o is more for the Anti conformer and less for Gauche conformer.

VI. Conclusion

From the following experiment, it can be seen that in water all the conformers are less stable than in vaccuum when the Anti conformer is the most stable and has a lot less probability than the others. Analyzing the data, it can be seen that the following effect is created due to steric hindrance.

It can also be seen that Gauche to Anti occurs faster than Anti to Gauche.