DRUG DESIGN PROJECT

QUANTUM COMPUTATION, MOLECULAR DOCKING

4/19/2021

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Section 1:

Quantum Computation

My Selected Drug was **Cycloserine**

1. **I Drew Assigned Drug's structure in WebMo server and performed optimization, frequency, and molecular orbital calculations in gas phase.**

   Geometry Optimization: HF/STO-31G (Minimal)

   Vibrational frequency: HF/STO-31G (Minimal)

   Molecular Orbitals (MOs): HF/6-31G (d)

   I followed All of those

2. **I Collected good image of your drug after optimization and frequency calculation. I did not find any imaginary frequency**

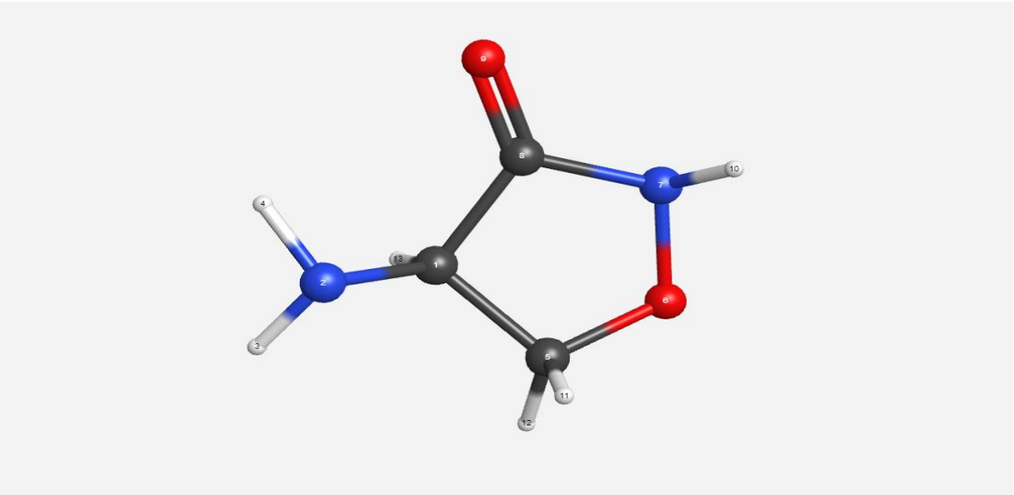

Figure : Cycloserine Drug's Optimize Picture(NO Imaginary Frequency)

3. I Found Cycloserine's bond distance [3 distances] and angle [3 angles] drug in gas phase.

And draw a table bellow:

Two Bond Distance	Distance Value	Three Angle	Angle's value
B1 (1,2)	1.4545	A1 (2,1,5)	112.1406
B2 (1,5)	1.5436	A2 (2,1,8)	111.8383
B3 (1,8)	1.5138	A3 (2,1,13)	111.5253

Table-01: Bond Distance & Bond angle

In this Table B1 (1,2) indicate the bond distance among 1&2 position in the Cycloserine's drug
B2 (1,5) is another bond distance , B3(1,8) is also indicate bond distance among 1&8
A1 (2,1,5) indicate the angle between 2,1&5 position in the Cycloserine's Drug.
A2 (2,1,8) is another angle , A3 (2,1,3) is also indicate angle distance between selected position.

4. **Table for HOMO, HOMO-1. HOMO-2, LUMO, LUMO+1 and LUMO+2, homo lumo gap of Cycloserine drug**

Types	Orbital	Value
HOMO	27	-0.408
HOMO-1	26	-0.430
HOMO-2	25	-0.434
LUMO	28	0.141
LUMO+1	29	0.205
LUMO+2	30	0.226
HOMO LUMO Gap	28-27	0.549

➤ **Table-02: HOMO, LOMO Calculation**

5. Table for the electronic energy (E), enthalpy (H), Gibbs free energy (G) and dipole moment (Debye) of Cycloserine drug .

Electronic (RHF)Energy(E)	-370.720992021 Hartree
Enthalpy(H)	-370.598137 Hartree
Free Energy(G)	-370.632798 Hartree
Dipole Moment	2.4890 Debye

➤ **Table-03: Electronic (RHF)Energy(E), Enthalpy(H), Free Energy(G), Dipole Moment Data**

5. I made image for HOMO and LUMO orbital of Cycloserine drug.

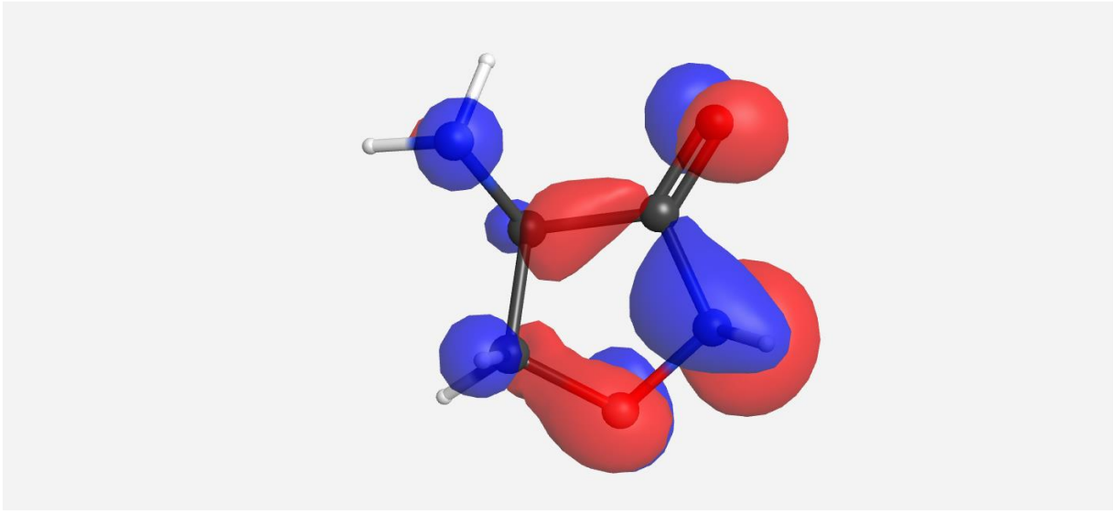

Figure: HOMO Picture of Cycloserine drug

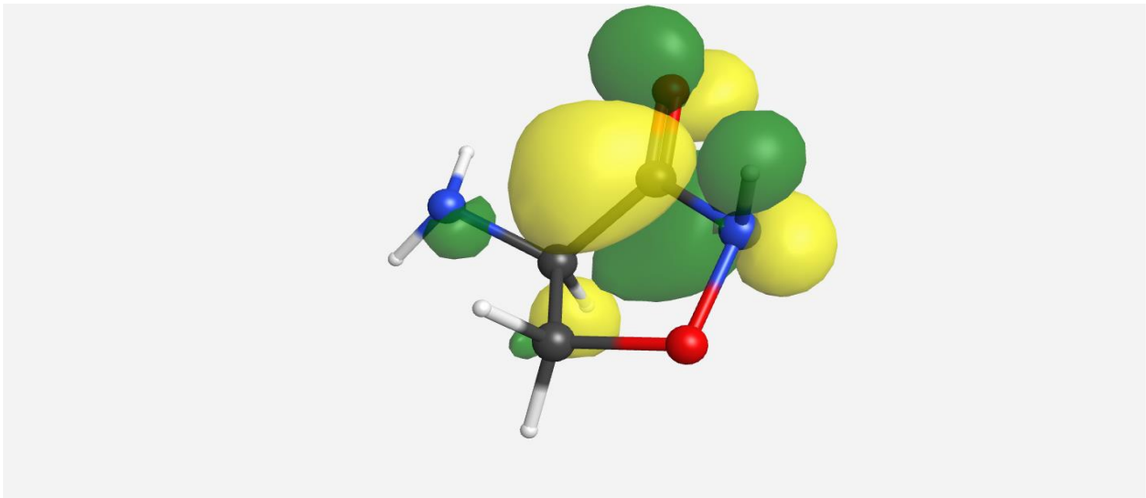

Figure: LUMO Picture of Cycloserine drug

Section 2

Molecular Docking

My Selected Drug was Fenticonazole

1. I drew my assigned drug's 3D structure in WebMo server and performed optimization in gas phase using PM3 level of theory and save the Fenticonazole drug molecule in PDB format.

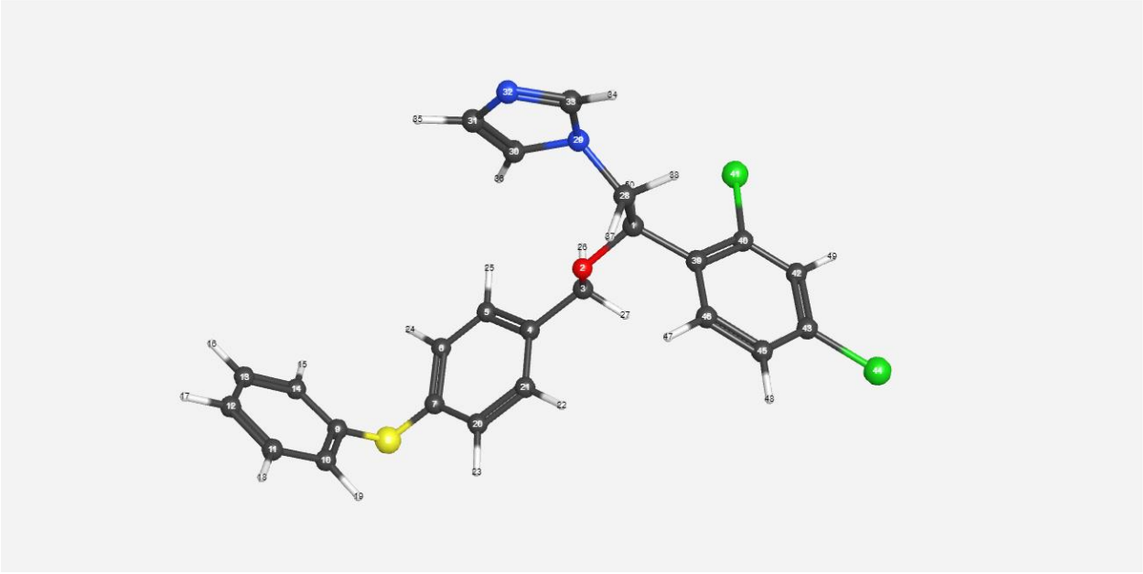

Figure: Fenticonazole drug's optimize Picture

2. I Prepared My protein [PDB id: 3ibd] in pymol and optimized it with SwissPDB viewer .

3.Performed molecular docking between My selected **Fenticonazole** drug and the receptor protein(3IBD) by Autodock Vina and reported grid box size

Vina Search Space

Center X: 20.2575 Y:11.0403 Z: 24.3480

Dimensions (Angstrom) X:60.1667 Y:65.2751 Z:66.7326

And The binding energy table listed Bellow:

Ligand	Binding Affinity	rmsd/ub	rmsd/lb
3ibdem_Fenticonazole	-8.9	0	0
3ibdem_Fenticonazole	-8.4	8.876	4.638
3ibdem_Fenticonazole	-7.9	9.261	6.453
3ibdem_Fenticonazole	-7.7	7.657	5.576
3ibdem_Fenticonazole	-7.5	7.697	4.769
3ibdem_Fenticonazole	-7.5	26.097	23.903
3ibdem_Fenticonazole	-7.4	26.309	24.309
3ibdem_Fenticonazole	-7.2	26.88	24.777
3ibdem_Fenticonazole	-7.1	26.391	24.029

Table-04: The binding energy table

When the binding affinity value is more negative, it will be consider as the best binding. For this reason here the best binding affinity is **-8.9.**

3. I Collected 5 non-bonding interactions (in a table) of drug with amino acids and took a picture by discovery studio shown bellow:

Name	Distance	Category	Types
:UNK1:S A:PHE297	5.38066	Other	Pi-Sulfur
A:CYS436:SG - :UNK1	3.56853	Other	Pi-Sulfur
:UNK1 - A:PHE297	5.63583	Hydrophobic	Pi-Pi T-shaped
:UNK1:Cl - A:CYS436	4.27733	Hydrophobic	Alkyl
:UNK1:Cl - A:LEU363	4.79925	Hydrophobic	Alkyl

Table-05: non-bonding interactions from discovery studio.

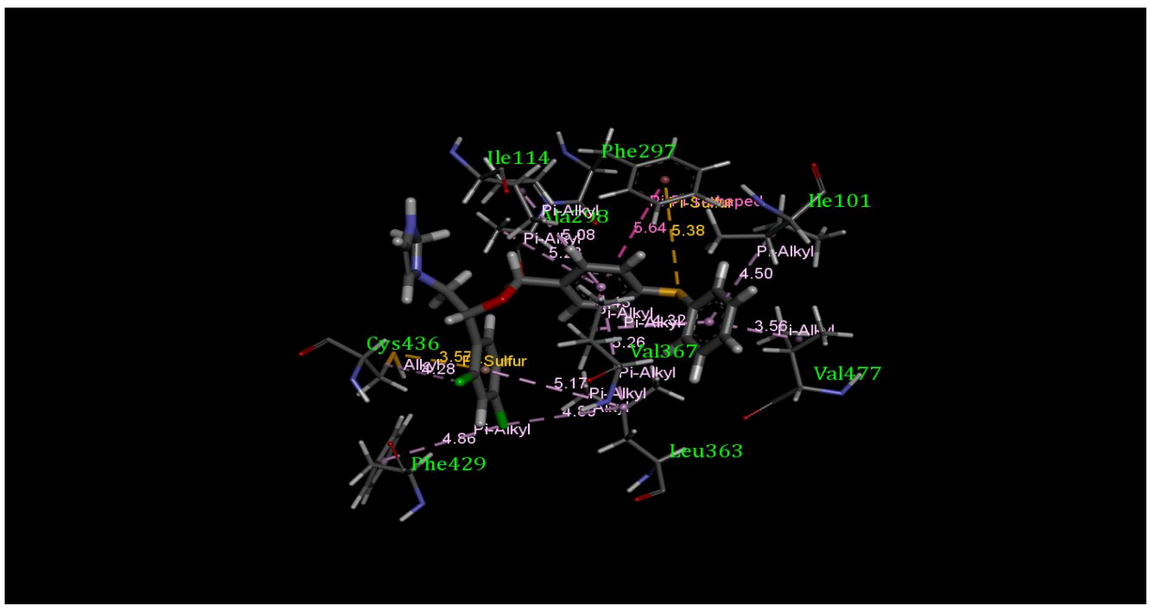

Figure: Non-bonding interactions of drug with amino acids

4.Aurein 1.2 peptide (Sequence: GLFDIIKKIAESF) is an antifungal peptide. I have Designed five structure of this peptide by PEP-FOLD3.5 then docked against 3IBD protein in patchdock.

Compared (in a table) the Score, Area and ACE of five model peptides shown bellow:

Solution	Name	Score	Area	ACE
1	Model1	7964	1148.4	-90.46
2	Model2	7148	859.70	387.17
3	Model3	7878	1102	-31.61
4	Model4	7418	996.90	411.46
5	Model5	8208	1093.20	-117.72

Table-06: Comparisoon of the Score, Area and ACE of five model peptids

I have collected nonbonding interaction image of 5 peptides model with the protein by discovery studio. Listed Bellow

Image1:

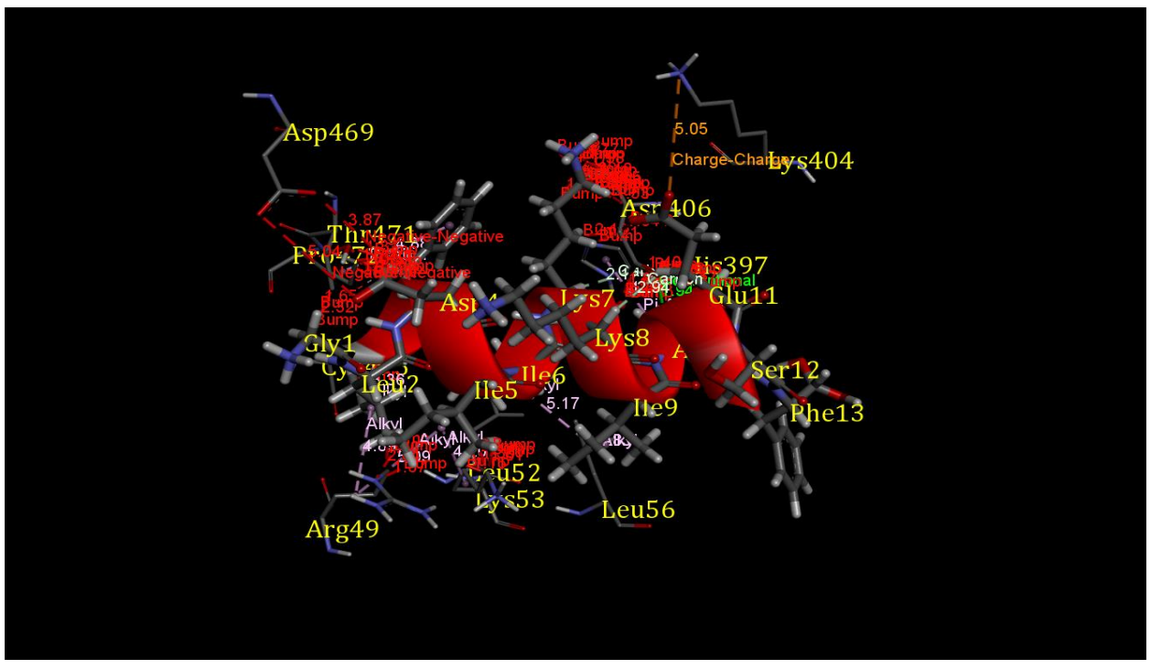

Figure: Non-Bonding interaction image of peptide model1 with 3IBD protein

Image2:

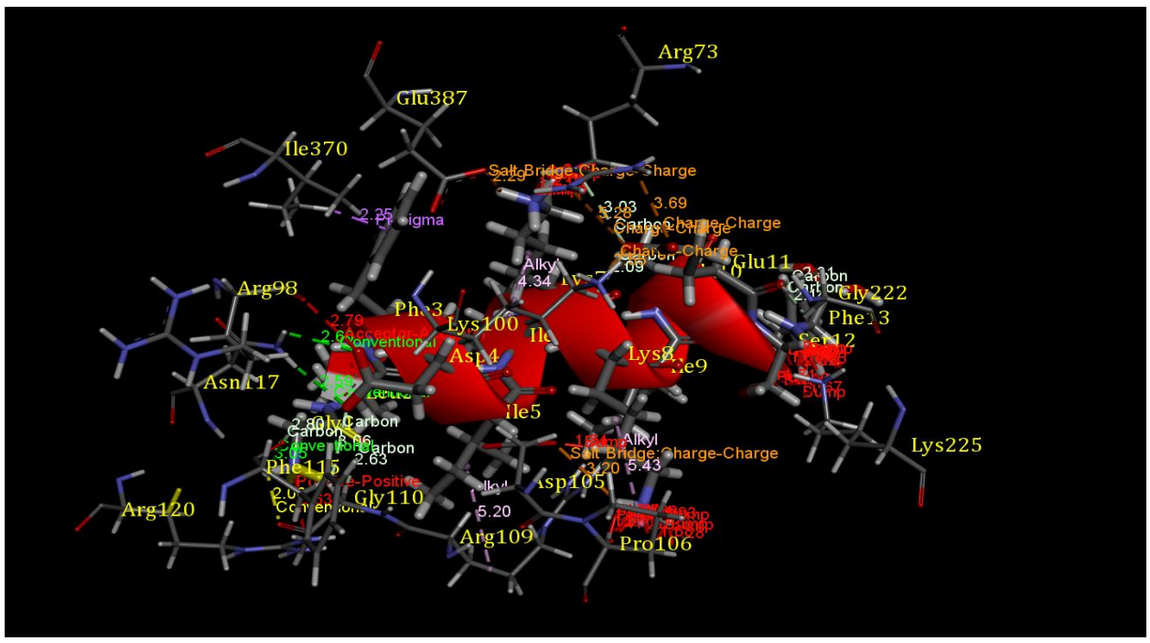

Figure: Non-Bonding interaction image of peptide model2 with 3IBD protein

Image3:

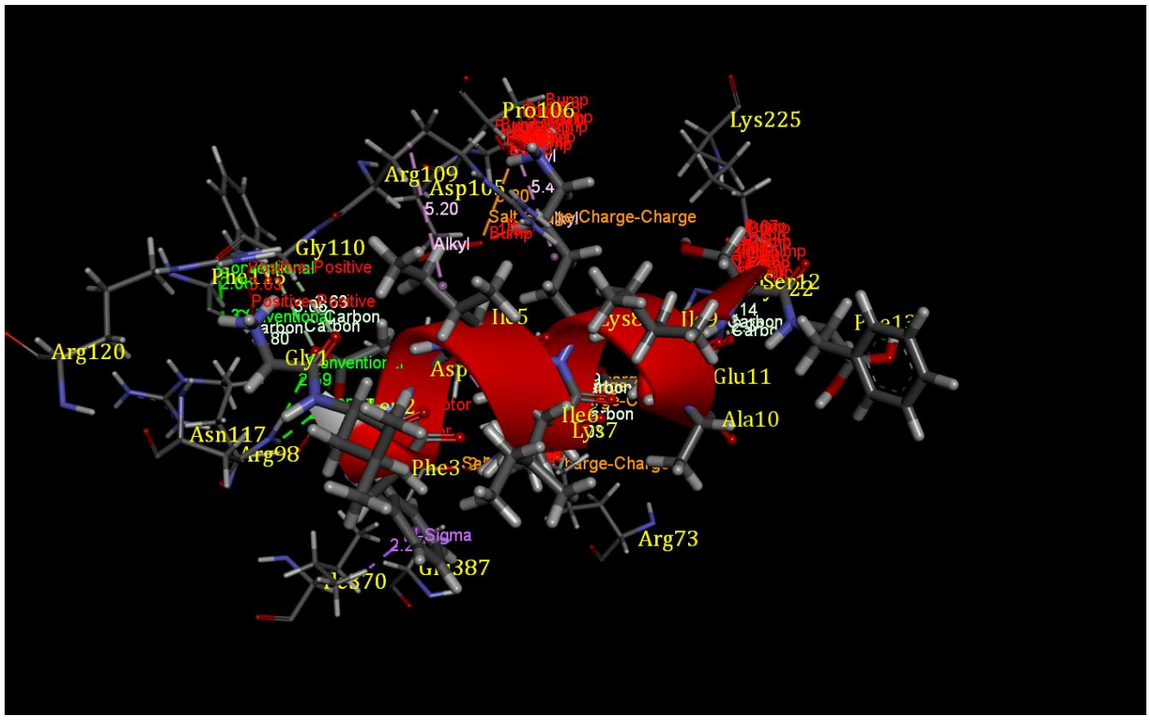

Figure: Non-Bonding interaction image of peptide model3 with 3IBD protein

Image4:

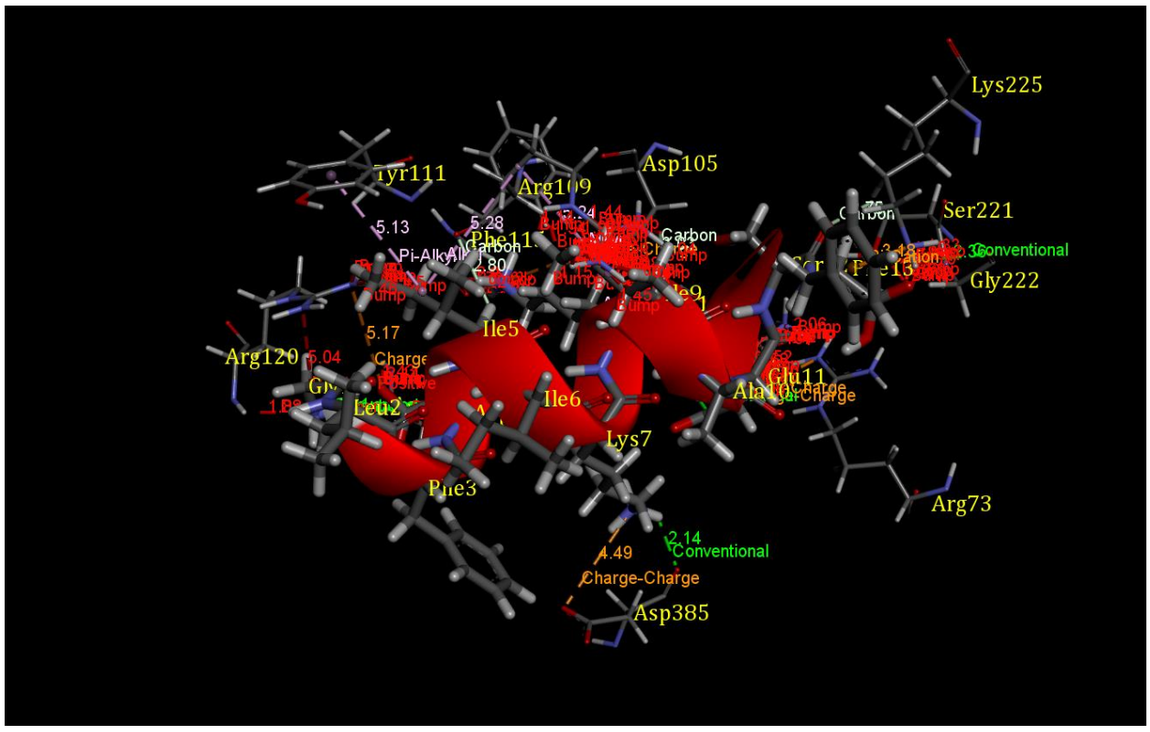

Figure: Non-Bonding interaction image of peptide model4 with 3IBD protein

Image5:

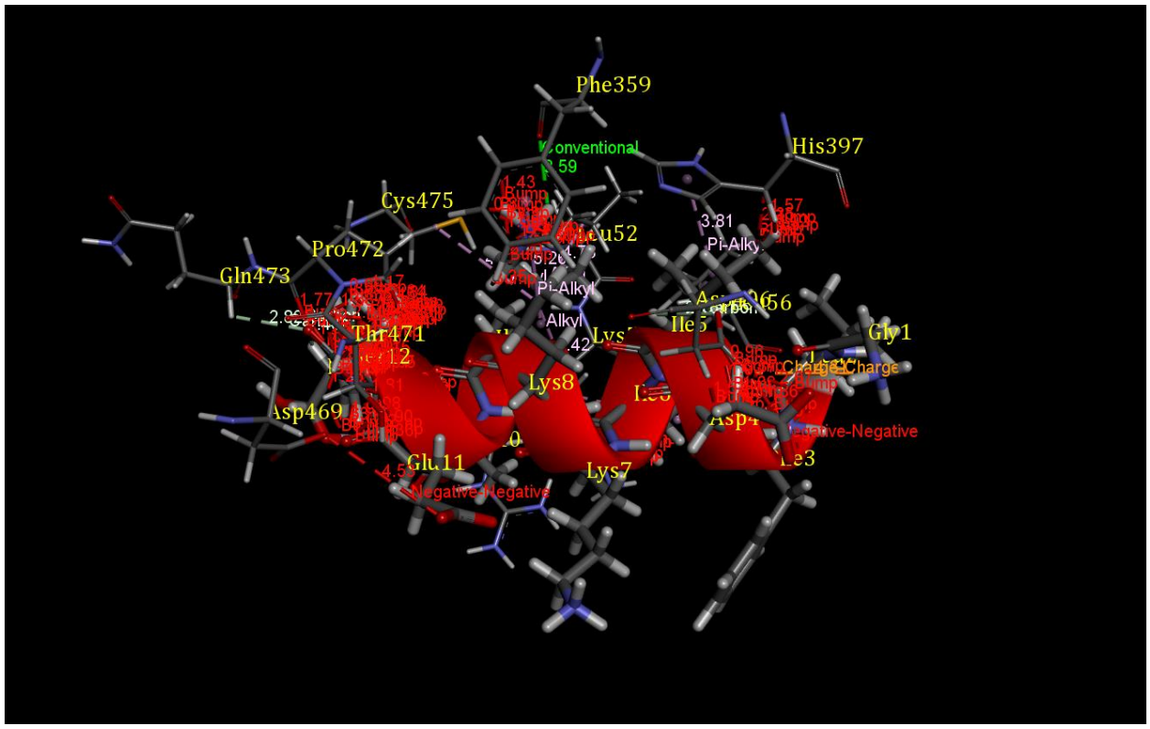

Figure: Non-Bonding interaction image of peptide model5 with 3IBD protein

End