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Computational comparative modeling and visualization for HIV1 and HIV2 proteins via the software SYBYL-X 2.0

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***Abstract*-** Human immunodeficiency virus is a lentivirus (slowly replicating virus) that causes "Acquired immuno deficiency syndrome "(AIDS). HIV attached to the human CD4 receptor and leads to the infection. Protein modelling is type of structure prediction from its sequence with an accuracy that is comparable from different softwares .Computational protein modelling is a method designed for the most probable 3D structure from a sequence given its alignments with related structure .In this topic we discuss about the 3D structure of HIV1and HIV2 protein from different softwares and their variations in core value, hydrophobicity, residues and intermolecular forces

Index Terms- *protein modeling; core value; software's; HIV1; HIV2*

I. INTRODUCTION

Acquired immunodeficiency syndrome (AIDS) was first reported by the us centre of disease (CDC),a few years later it was found that's a retrovirus called human immune deficiency virus (HIV) and is causative agent in AIDS. The study of HIV protease is one of the most important approaches for the therapeutic intervention in HIV infection and their development is regarded as major success of design[1]HIV type I (HIV-1) and type 2 (HIV-2) are very closely related but differ in pathogenicity, natural history and therapy. HIV-1 is more easily transmitted and consequently accounts for the vast majority of global HIV infections. The less transmissible HIV-2 was thought to be largely confined to West Africa(where it is thought to have originated).[2-3] but has spread to parts of Europe and India.[4-5] When compared to HIV-1, HIV-2 infected individuals have a much longer asymptomatic stage, slower progression to AIDS6-8, slower decline in CD4 count[7-10] lower mortality lower rate of vertical transmission and smaller gains in CD4 count in response to antiretroviral treatment (ART)Serologic reactivity to HIV-1 and HIV-2 (HIV-1/2) has also increased in HIV-2 endemic areas over the past decade. In terms of antiretroviral drug regimens, HIV-2 is intrinsically resistant to non nucleoside reverse transcriptase inhibitors (NNRTI) such as nevirapine and efavirenz and not all the protease inhibitors (PIs) provide good viral suppression.[11-12]

B. About SYBYL-X 2.0 (software)

The SYBYL-X Suite has everything you need for drug design and other molecular discovery projects, from HTS follow-up through late Lead Optimization. Project needs may change, but you'll have all the tools available and easily be able to move from identifying potential lead candidates, to lead optimization projects, or to building a homology model for a target of interest. All of the components for life science research are included as standard with the SYBYL-X suite. [13]

C. About HIV 1 and HIV 2 proteins

HIV-1 protease is a retroviral aspartyl protease (retropepsin) that is essential for the life-cycle of HIV, the retrovirus that causes AIDS.[14-15] HIV protease cleaves newly synthesized polyproteins at the appropriate places to create the mature protein components of an infectious HIV virion. Without effective HIV protease, HIV virions remain uninfectious. The human immunodeficiency virus integrase (HIV IN) protein cleaves two nucleotides off the 3′ end of viral DNA and subsequently integrates the viral DNA into target DNA. IN exposes a specific phosphodiester bond near the viral DNA end to nucleophilic attack by water or other nucleophiles, such as glycerol or the 3′ hydroxyl group of the viral DNA molecule itself. [16-17]

II. MATERIAL AND METHODS

For this analysis we use different type on online and offline tools for suitable scientific analysis and for protein sequence of HIV1protease and HIV2 integrase retrieves from NCBI and model prediction via the online software and servers like ,GENO3D , , RaptorX ,phyre .were use to find out potential 3D structure of proteins basis on their statical values , and validate the potential models via the SAVES SERVER and the structure visualise via **Discovery studio**, ***SYBYL-X 2.0*** with analysed potential parameters for comparative modelling between two different proteins

III. RESULTS

Analysis of computational comparative modeling and visualization for HIV1and HIV2 proteins contains a two different type of protein like protease for HIV1 and integrase for HIV 2

A. ***Analysis of HIV1 protease with the help of different type of tables*****Table 1: 3D models with annotated name**

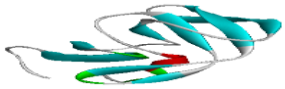
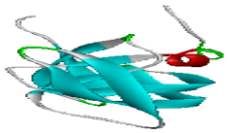
S.No	Software Used	Annotated Model Name	Structures predict via the discovery studio	Validation of models via SAVES server (Core)	(Verify 3D)	(Errat)
2.	GENO3D	>Geno3D_Pro_Model8		87.3%	75%	97.468
3.	RaptorX	>RaptorX_Protease		98.7%	98.96%	65.116
4.	Phyre 2	>Phyre_Pro_Model3		92.4%	100.00%	79.762

Table 1 explains: 3D model generated via the different type of software and validates the model via the SAVES server with avourablef statical value. Green color shows the best models with best score validation.

Table 2:Query of model with ramchandran plot and hydrophobicity plot

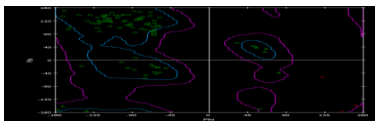
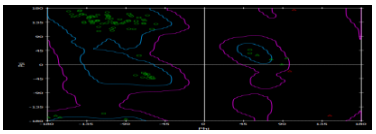
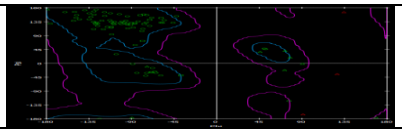
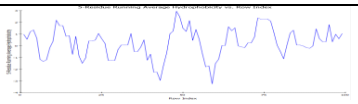
S.no.	Software Used	Annotated Model Name	Ramachandran plot via the discovery studio	Hydrophobicity plot via the discovery studio
2.	GENO3D	>Geno3D_Pro_Model8		
3.	RaptorX	>RaptorX_Protease		
4.	Phyre 2	>Phyre_Pro_Model3		

Table 2 explains: Ramchandran plot for analysis of residue and hydrophobiciy plot for hydrogen atom analysis and Ramachandran plot shows the phi and psi torision angles for all residues in structure.phi value on x-axis and psi value on y axis. the darkest area (in green colour) corresponds to the core. Hydrophobicity plot is the physical property of a molecule repelled from the mass of water.

Table 3: 3D model visualization via the *SYBYL-X 2.0*

S.No.	Software Used	Annotated Model Name	Model add with Hydrogen Molecule	Model add with Residue	Model predicted in cavity form

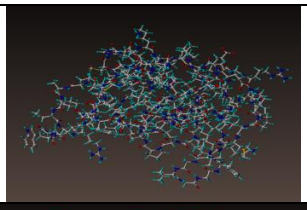
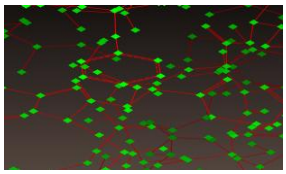
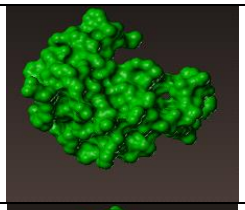
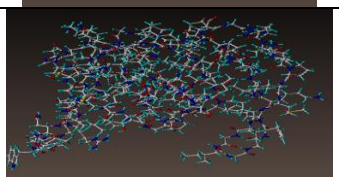
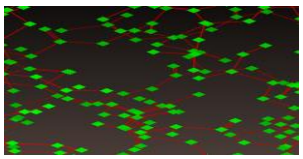
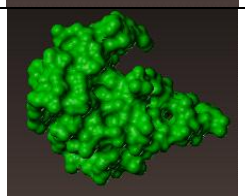
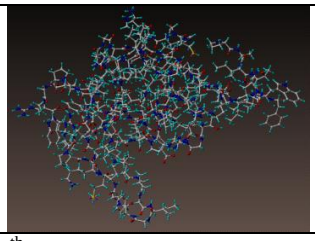
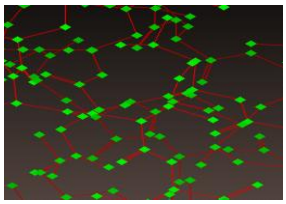
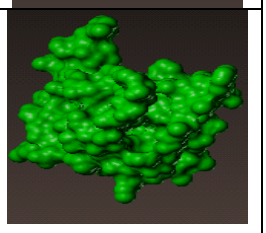
2.	GENO3D	>Geno3D_Pro_Model8			
3.	RaptorX	>RaptorX_Protease			
4.	Phyre 2	>Phyre_Pro_Model3			

Table 3 explains : In this table column no.4th figure shows Carbon (white in color) , Nitrogen (dark blue in color), Oxygen (red in color), Hydrogen(blue in color).Column no. 5th shows residues (green in color),Peptide bonds(red in color).Column no.6th shows the structure in cavity form.

Table 4: Structure with ball stick and C-C interaction

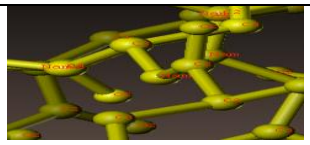
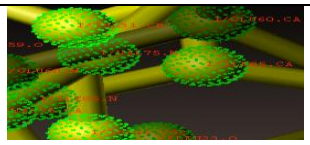
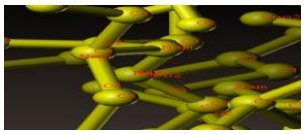
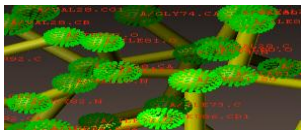
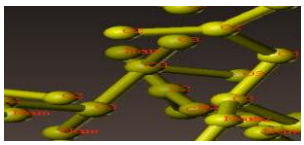
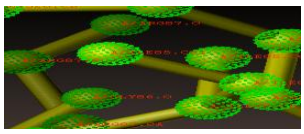
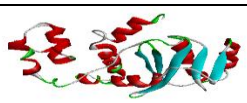
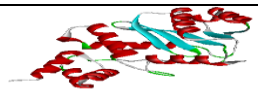
S.No.	Software Used	Annotated Model Name	Model label with tripose	Model with full name with intermolecule
2.	GENO3D	>Geno3D_Pro_Model8		
3.	RaptorX	>RaptorX_Pro		
4.	Phyre 2	>Phyre_Pro_Model3		

Table 4 explains: Binding between C-C, C-N and intramolecule analysis with green ball like structure with name of protein.

B. **Analysis of HIV2 integrase with the help of different type of tables**

Table 5: 3D models with annotated name

S.No	Software Used	Annotated Model Name	Structures predict via the discovery studio	Validation of models via SAVES server (Core)	(Verify3D)	(Errat)
1.	GENO3D	>GENO3D_IN_model3		81.2%	61.95%	93.878
2.	RaptorX	>RaptorX_IN		93.%	91.00%	82.178

3.	Phyre 2	>Phyre2_IN_model1		93.4%	81.64%	91.667

Table 5 explains: 3D model generated via the different type of software and validate the model via the SAVES server with favorable statical value.

Table 6:Query of model with ramchandran plot and hydrophobicity plot

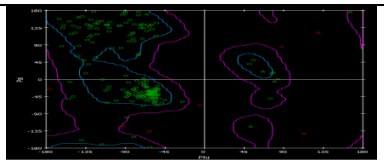
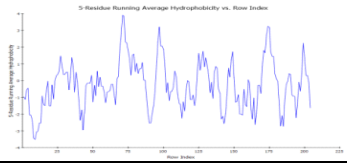
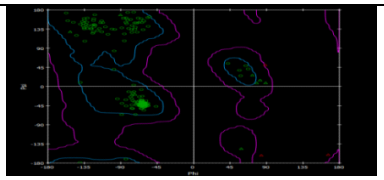
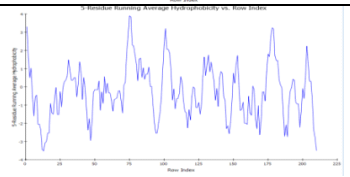
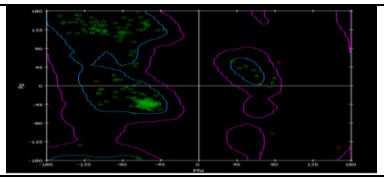
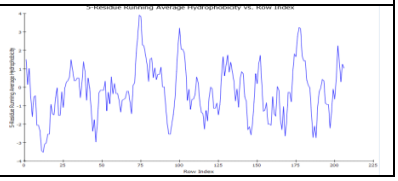
S.no.	Software Used	Annotated Model Name	Ramachandran plot via the discovery studio	Hydrophobicity plot via the discovery studio
1.	GENO3D	>GENO3D_IN_model3		
2.	RaptorX	>RaptorX_IN		
3.	Phyre 2	>Phyre2_IN_model1		

Table 6 explains: Ramchandran plot for analysis of residue and hydrophobiciy plot for hydrogen atom analysis and Ramachandran plot shows the phi and psi torision angles for all residues in structure.phi value on x-axis and psi value on y axis. the darkest area (in green colour) corresponds to the core. Hydrophobicity plot is the physical property of a molecule repelled from the mass of water.

Table: 7. 3D model visualization via the *SYBYL-X 2.0*

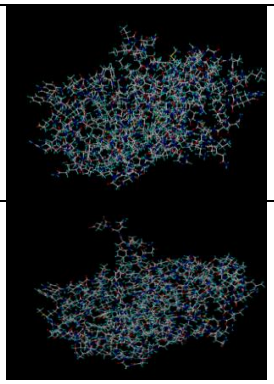
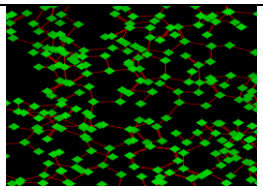
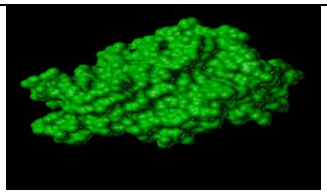
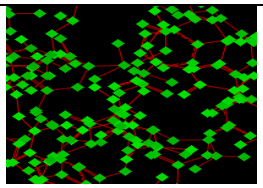
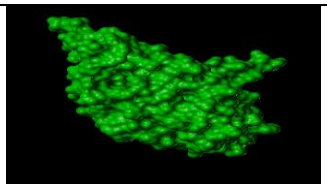
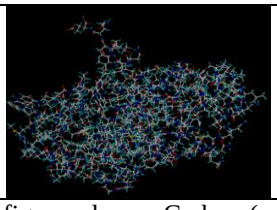
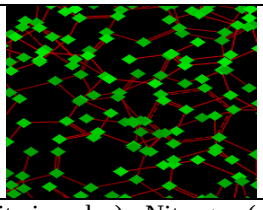
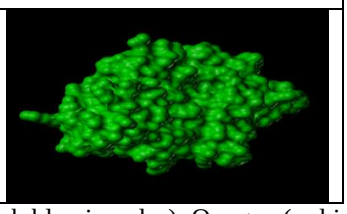
S.No.	Software Used	Annotated Model Name	Model add with Hydrogen Molecule	Model add with Residue	Model predicted in cavity form
1.	GENO3D	>GENO3D_IN_model3			
2.	RaptorX	>RaptorX_IN			
3.	Phyre 2	>Phyre2_IN_model1			

Table 7 explains : In this table column no.4th figure shows Carbon (white in color) , Nitrogen (dark blue in color), Oxygen (red in color), Hydrogen(blue in color).Column no. 5th shows residues (green in color),Peptide bonds(red in color).Column no.6th shows the structure in cavity form.

Table 8: structure with ball stick and C-C interaction

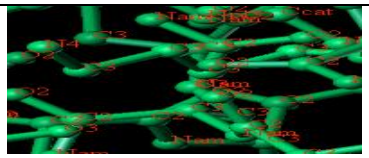
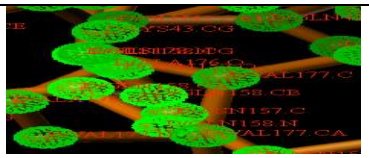
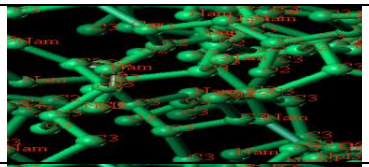
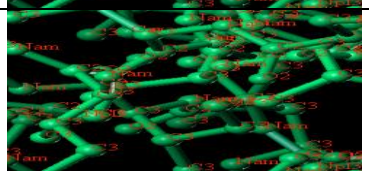
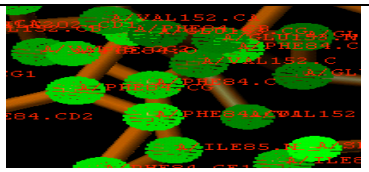
S.No.	Software Used	Annotated Model Name	Model label with tripos	Model with full name with intramolecule
1.	GENO3D	>GENO3D_IN_model3		
2.	RaptorX	>RaptorX_IN		
3.	Phyre 2	>Phyre2_IN_model1		

Table 8 explains: Binding between C-C, C-N and intramolecule analysis with green ball like structure with name of protein.

IV DISCUSSION

In this topic we discuss about comparative modeling of HIV1protease and HIV2 integrase protein for best model prediction and we analyzed very important potential parameters for this comparative prediction and such a very difference between two different structure basis on their statical values and basis on their models with different amino acid positions (residues) Comparative modeling of HIV1and HIV2 proteins of best model prediction we analyze ,the core value ,verify 3Dand errat
value of model. Errat value is the statistics of non bonding interaction ,verify 3D determines the compatibility of atomic model .for analyzing best model higher value of verfy3D will be the best model .in output section of verify 3D ,if the results come in gteen box that's mean without error and higher value it will be the best model and if results comes in an error states (>75%) then box will be red such a very major difference between two protein only in human immunodeficiency virus .

V CONCLUSION

In HIV1 protease protein modeling the best results come from phyre2 (>Phyre_Pro_Model3) because the verify 3D value is higher (100%) in comparison to GENO3D and raptorx in HIV2 integrase , protein modeling the best results come from RaptorX (>RaptorX_IN) because the verify 3D a value is higher (91%) in comparison to GENO3D and Phyre 2 so we analyzed in this topic .comparative protein modeling highest value verify 3D will be the best for given structural model

REFERENCES

[1] Alka Dwivedi and Vijay Laxmi Saxena, "In Silico Drug Designing of Protease Inhibitors to Find the Potential Drug Candidate for HIV1"*Computational Biology and Bioinformatics*,2013, Vol. 1, No. 3, pp. 10-14,

[2] PJ. Kanki , KU.Travers , S.Mboup , CC.Hsieh , RG.Marlink , Guèye-Ndiaye A, "Slower heterosexual spread of HIV-2 than HIV-1",*Lancet* ,1994; *343:* 943-6.

[3] CR.Horsburg ,SD. Holmbreg , "The global distribution of human 2. Immunodeficiency virus type 2 (HIV-2) infections"*Transfusion*, 1988; *343* : 943-6.

[4] Rübsamen-Waigmann, H. Maniar ,S. Gerte ,HD. Brede , Dietrich, "High proportion of HIV-2 and HIV-1/2 double-reactive sera in two Indian states Maharashtra and Goa: first appearance of an HIV-2 epidemic along with an HIV-1 epidemic outside of Africa", *Zentralbl Bakteriol* ,1994; *280* : 398-402.

[5] S. Kulkarni, M. Thakar , J. Rodrigues ,K. Bannered, "HIV-2 antibodies in serum samples from Maharashtra state"*Indian J Med Res,*1992; *95:* 213-5.

[6] PG.Babu , NK.Saraswathi , F.Devapriya ,TJ. John . "The detection 5. of HIV-2 infection in southern India". *Indian J Med Res,*1993; *97* : 49-52.

[7] H.Whittle , J.Morris , J.Todd , T.Corrah ,S. Sabally ,J. Bangali, "HIV-2-infected patients survive longer than HIV-1 infected patients. *AIDS," IJB,*1994; *8* : 1617-20.

[8] Marlink R, Kanki P, Thior I, Travers K, Eisen G, Siby T, " Reduced rate of disease development after HIV-2 infection as compared to HIV-1"*Science,*1994; *265* : 1587-90.

[9] S.Jaffar , A.Wilkins , PT.Ngom , Sabally ,S. Corrah ,T Bangali , "Rate of decline of percentage CD4+ cells is faster in HIV-1 than in HIV-2 infection"*J Acquir Immune Defic Syndr Hum Retrovirol* 1997; *16* : 327-2.

[10] M.Schim van der Loeff , S.Jaffar , A.Aveika ,S, Sabally , Corrah 10. T, Harding E, "Mortality of HIV-1, HIV-2 and HIV-1/HIV-2 dually infected patients in a clinic-based cohort in the Gambia". *AIDS,*2002; *16* : 1775-83
,

[11] WK.Ampofo , Y.Koyanagi , J.Brandful , K.Ishikawa , "Seroreactivity clarification and viral load quantification in HIV-1 and HIV-2 infections in Ghana"*J Med Dent Sci,*1999; *46* : 53-62.

[12] PJ.Weidle , S.Malamba , R.Mwebaze , C.Sozi, G.Rukundu.,"Assessment of a pilot antiretroviral drug therapy programme in Uganda: patients response survival and drug resistance" *Lancet,*2002; *360* : 34-40

[13] http://www.certara.com/products/molmod/sybyl-x

[14] DR. Davie,"The structure and function of the aspartic proteinases". *Annu Rev Biophys Biophys Chem* ,1990,**19** (1): 189–215.

[15] **A.**Brik , CH.Wong, "HIV-1 protease: mechanism and drug discovery". *Org. Biomol. Chem, 2013,* **1** (1): 5–14.

[16] HG.Kräusslich , RH.Ingraham , MT.Skoog, WE.immer , PV.Pallai , CA.Carter ,"Activity of purified biosynthetic proteinase of human immunodeficiency virus on natural substrates and synthetic peptides, *Proc. Natl. Acad:. Sci. U.S.A*, 1989,**86** (3): 807–11.

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