

KINARI-Web Case Study of 1HVR

How a Ligand Affects Protein Rigidity

Filip Jagodzinski

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KINARI-Web can be used to determine how a ligand affects a protein's rigidity. To demonstrate this feature, rigidity analysis of HIV-1 Protease PDB structure 1HVR was performed with and without the inhibitor XK2. HIV-1 Protease has two molecular “flaps” that move as the protease performs its function. When rigidity analysis is performed with the ligand present, the flaps are part of a large rigid cluster composed of 1,713 atoms, Fig. 1(a). When the ligand is excised, Fig. 1(b), the largest rigid body contains 1,371 atoms, and the flaps are found to be rigid. These results are consistent with previous studies that have shown that the inclusion of a ligand greatly affects the rigidity of the flaps and protease [2, 1].

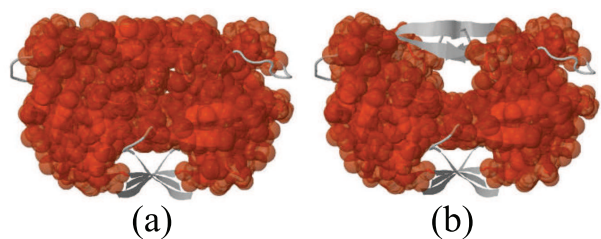


Figure 1: (a) HIV-1 Protease 1HVR analyzed with a ligand, and (b) without it. Only largest rigid cluster is shown. In (b), the protease's flaps (gray color ribbons at the top of the protease) are found to be flexible and are not part of a large rigid body.

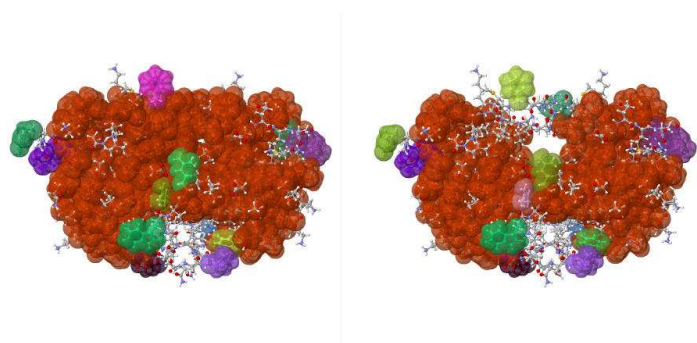


Figure 2: (a) HIV-1 Protease 1HVR analyzed with a ligand, and (b) without it. All clusters larger than 10 atoms in size are shown.

References

- [1] J. W. Heal, S. A. Wells, J. E. Jimenez-Roldan, R. F. Freedman, and R. A. Roemer. Rigidity analysis of hiv-1 protease. In *Proceedings for 10th Biennial Conference on High Resolution X-Ray Diffraction and Imaging*, 2010.
- [2] D. J. Jacobs, A. J. Rader, L. A. Kuhn, and M. F. Thorpe. Protein flexibility predictions using graph theory. *Proteins*, 44:150–165, Aug 2001. [PubMed:11391777].

Curation & Modeling Paramters

Curation Options		Rigidity Analysis Modeling	
Curation Version	v0.02	Rigidity Version	v0.01-146-g0574d22
Chains Retained	A & B (all)	Cluster Representation	KINARI
Waters Retained	None	Single Covalent Bonds	Hinges
Hydrogne Atoms Added	Using Reduce	Double Covalent Bonds	6 Bars
Retain LINK Records	No	Disulfide Bonds	Hinges
Retain CONECT Records	No	Hydrogen Bonds	Hinges
Hydrogen Bonds	Using Hbplus	Resonance Bonds	6 Bars
Interactions Removed	None	Hydrophobic Interaction	2 Bars
Ligands Retained	XK2, CSO, Fig 1(a) None, Fig 1(b)		

Website & Notes

Website	http://kinari.linkage.cs.umass.edu
Date Performed	25 April 2011