



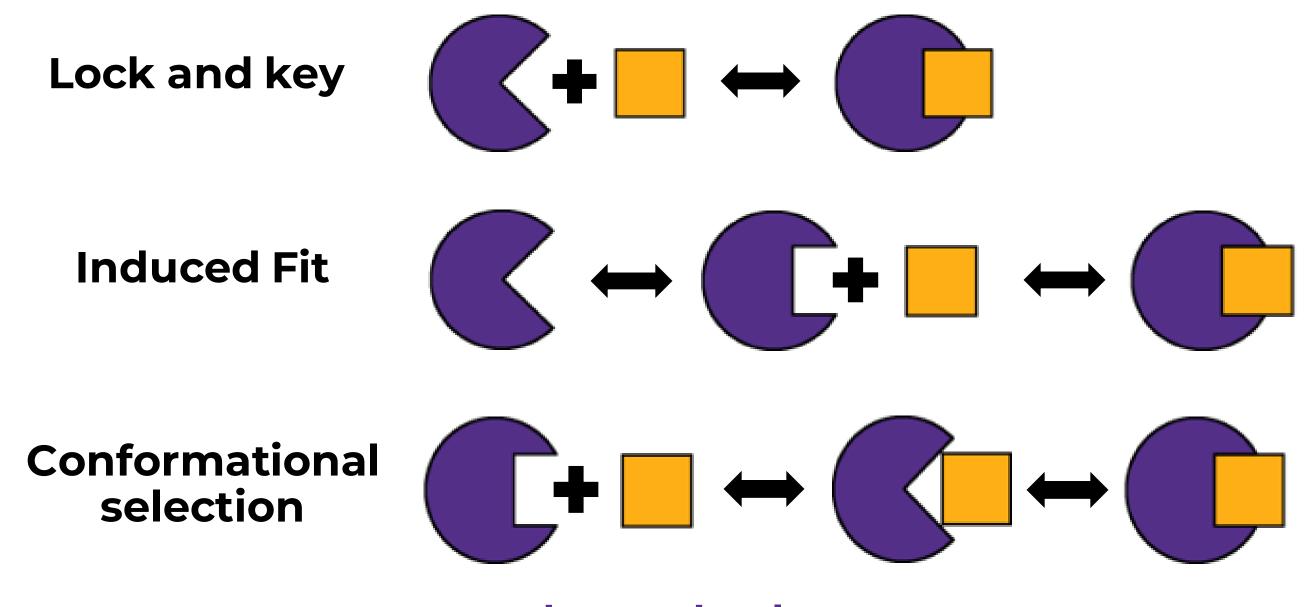
N=16; Score=0.52

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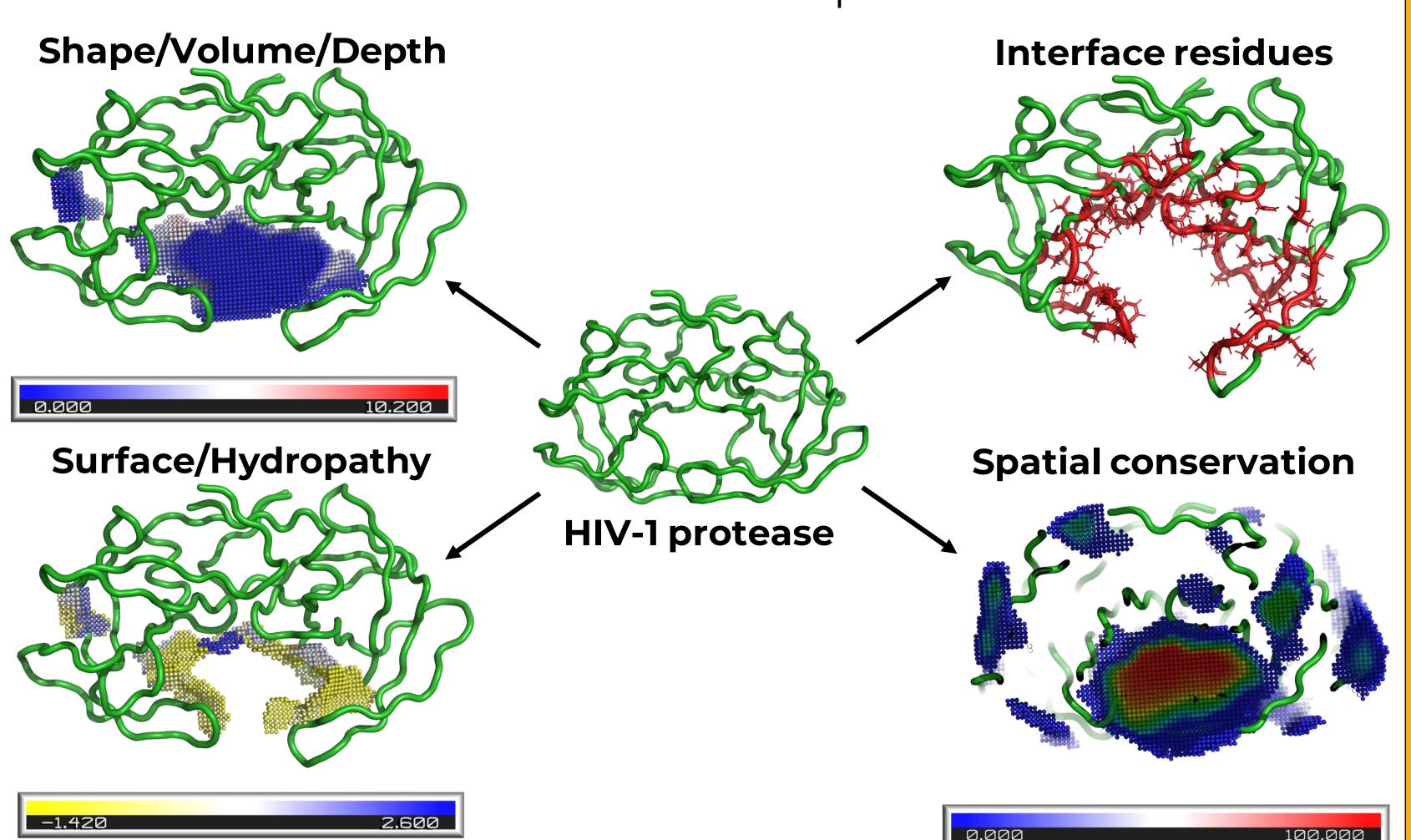
Background

Biomolecular interactions dictate many biological processes, which mainly occur by receptors interacting with other molecules. These ligands usually interact in specific binding sites formed by cavities. The protein-protein and protein-ligand interactions rely on the intrinsic dynamics of the target receptor, in which the classical lock and key model fails, and more recent binding models, e.g., conformational selection and induced-fit, thrive [1]. Thus, molecular dynamics (MD) is applied to understand the biomolecular function.

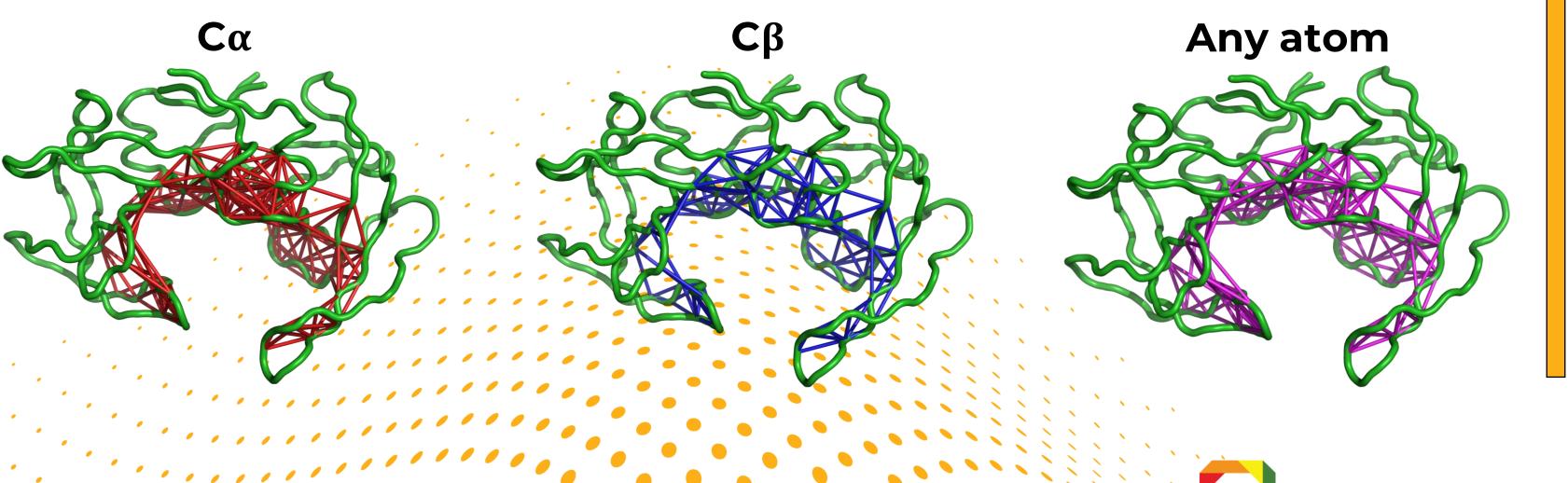


Methodology

Using pyKVFinder, recently developed by our group, as a building block, we developed <u>KVFinder</u> for <u>Molecular Dynamics</u> analysis (KVFinderMD), to explore binding site dynamics in biomolecular structures of interest. Since the intrinsic MD may change characteristics over time, KVFinderMD describe cavities in respect to:



Besides that, we also implemented a graph-based algorithm that considers distances from $C\alpha$, $C\beta$ or any atom to topologically describe the binding site.



Results & Discussion

As case studies, we applied KVFinderMD with important therapeutic targets, i.e., HIV-1 protease [3] and ALDH1/2 [4].

Case study I: HIV-1 protease

3D grid alignment

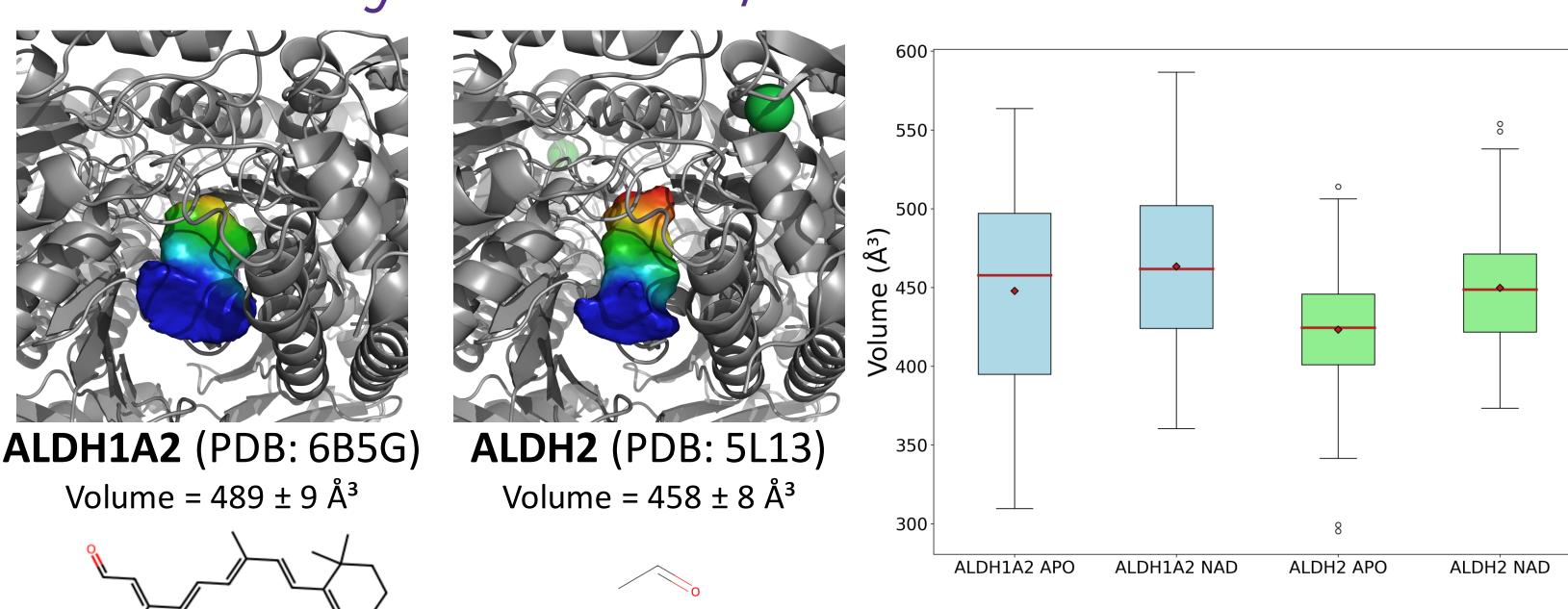
N=10; Score=0.41

Distance alignment

N=15; Score=0.54

Contact alignment

Case study II: ALDH 1/2



Conclusion

We successfully developed a useful tool to describe the molecular dynamics of binding sites in biomolecular structures of relevant therapeutic targets, e.g., HIV-1 protease and ALDH 1/2.

References

- [1] Holyoak, T. Molecular Recognition: Lock-and-Key, Induced Fit, and Conformational Selection. Encyclopedia of Biophysics 1584–1588 (2013)
- [2] Guerra, J. V. da S. et al. pyKVFinder: an efficient and integrable Python package for biomolecular cavity detection and characterization in data science. BMC Bioinformatics vol. 22 (2021).
- [3] Guerra, J. V. da S. et al. ParKVFinder: A thread-level parallel approach in biomolecular cavity detection. SoftwareX vol. 12 100606 (2020).
- [4] Sobreira, T. J. P. et al. Structural shifts of aldehyde dehydrogenase enzymes were instrumental for the early evolution of retinoid-dependent axial patterning in metazoans. PNAS. vol. 108 226–231 (2010).

Acknowledgments

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