KVFinderMD: a Python package to detect and describe binding sites in molecular dynamics trajectories

IV CEC
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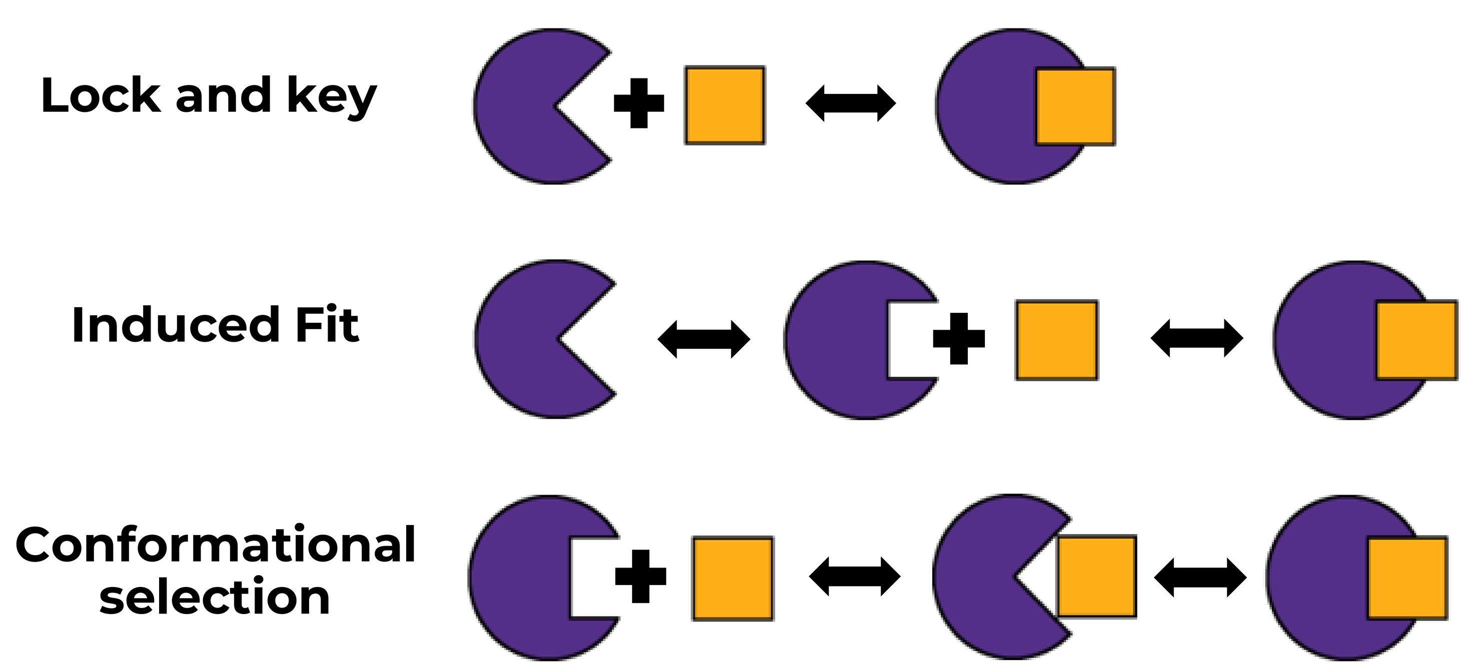
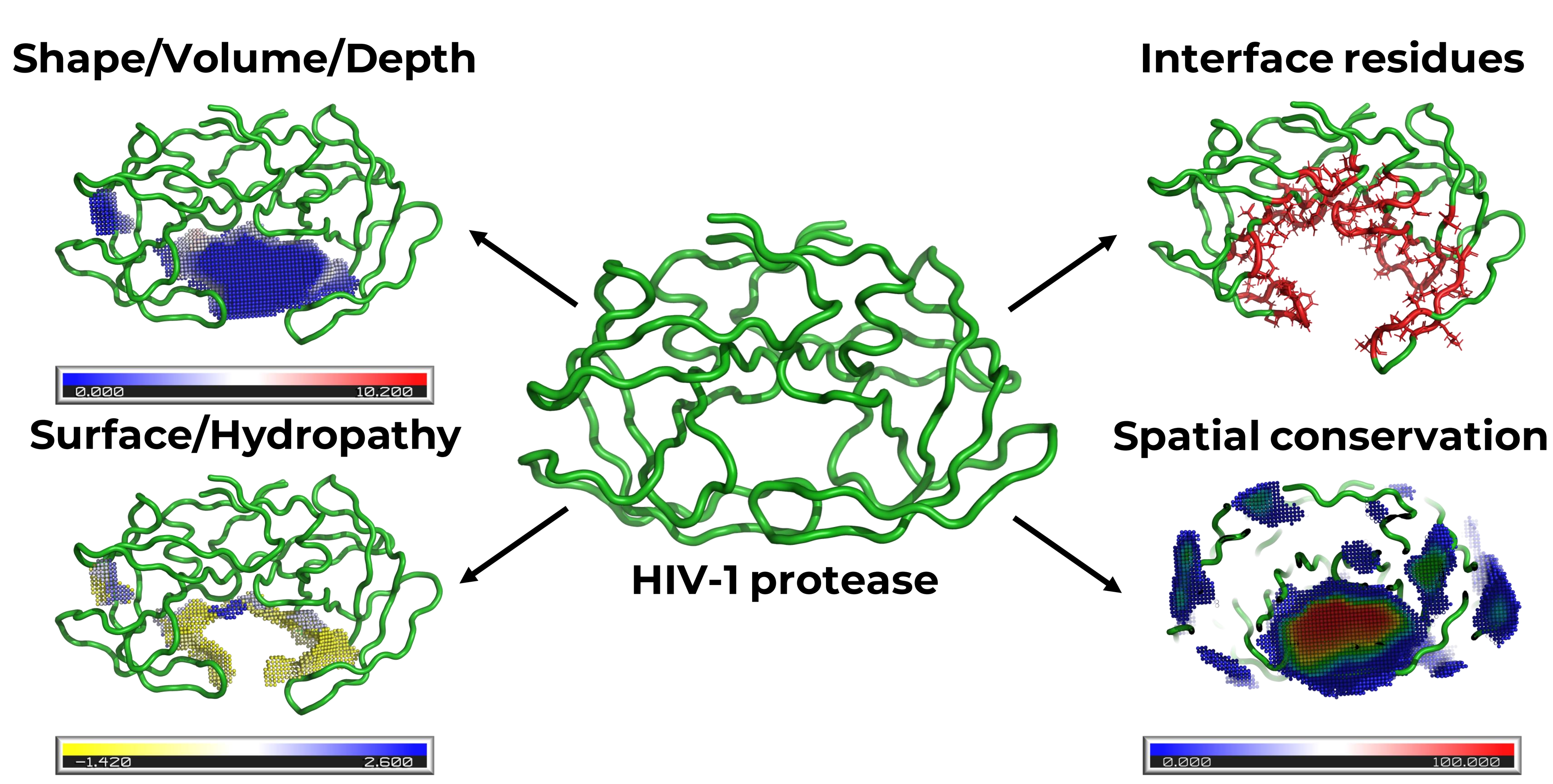
Background

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 (PPI) and protein-ligand (PLI) 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., induced-fit and conformational selection, thrive [1]. Thus, molecular dynamics (MD) is applied to understand the biomolecular function.

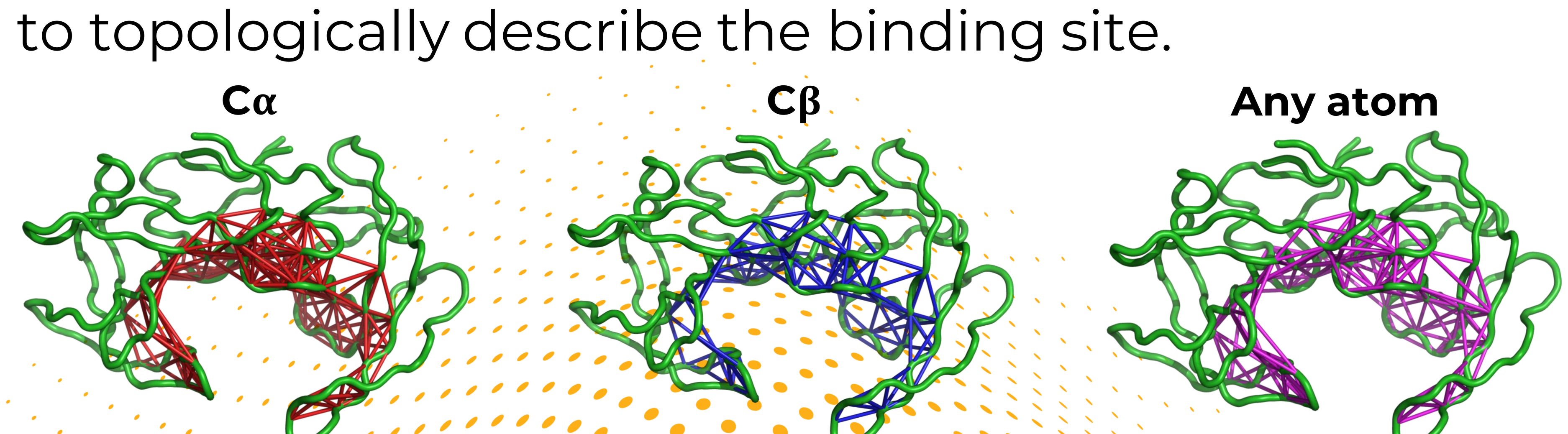


Methodology

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



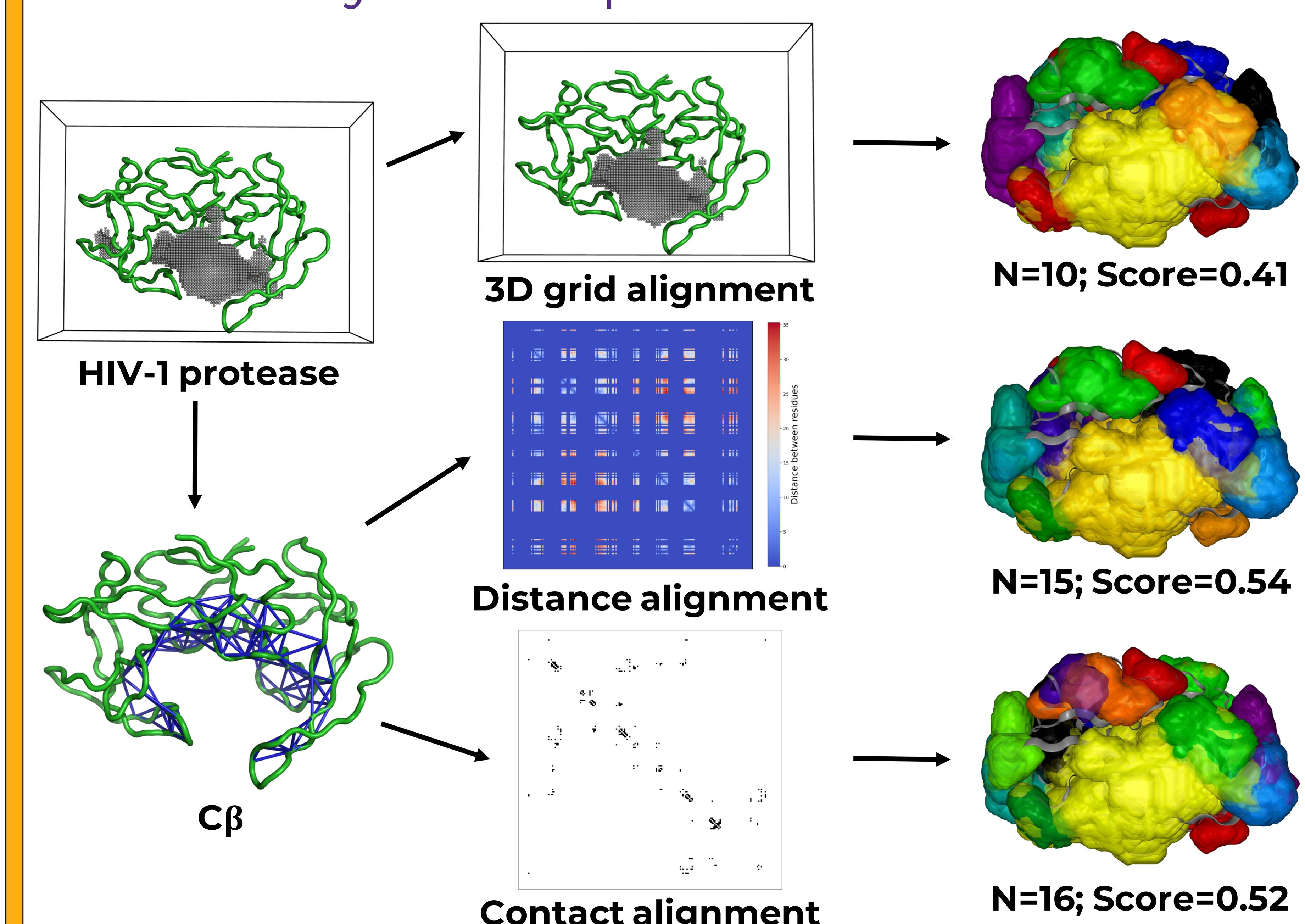
Besides that, we also implemented a graph-based algorithm, that consider Cα, Cβ or any atom distances to topologically describe the binding site.



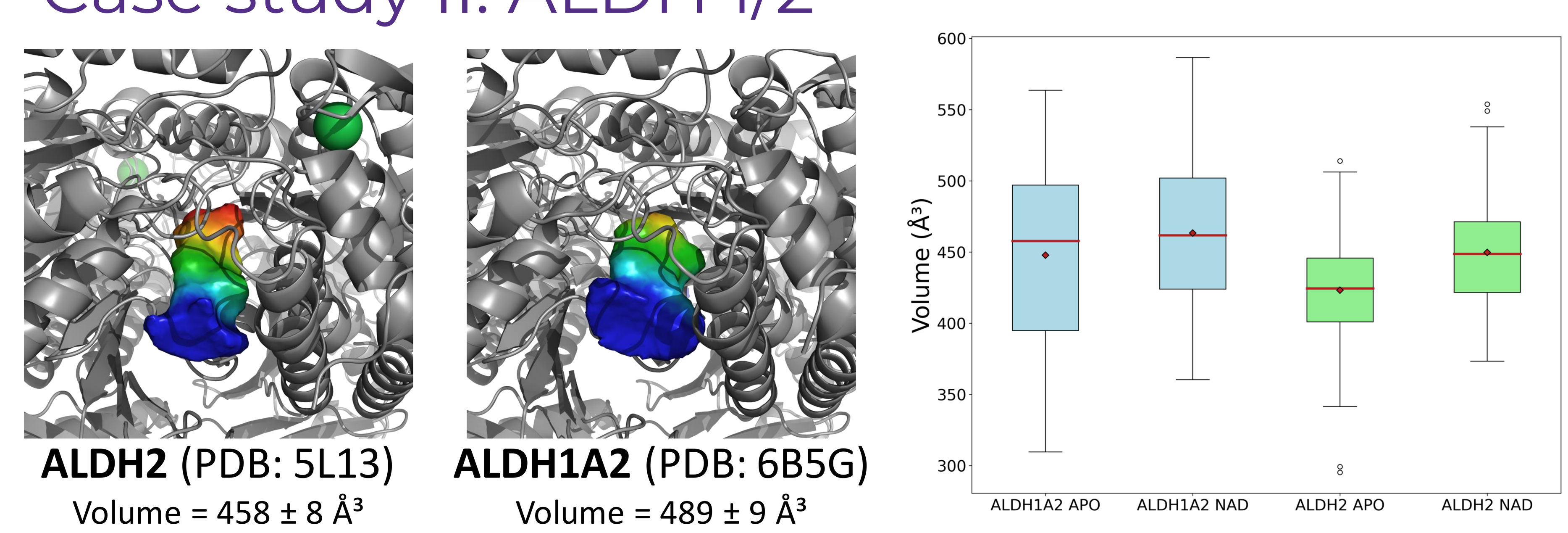
Results & Discussion

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

Case study I: HIV-1 protease



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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