

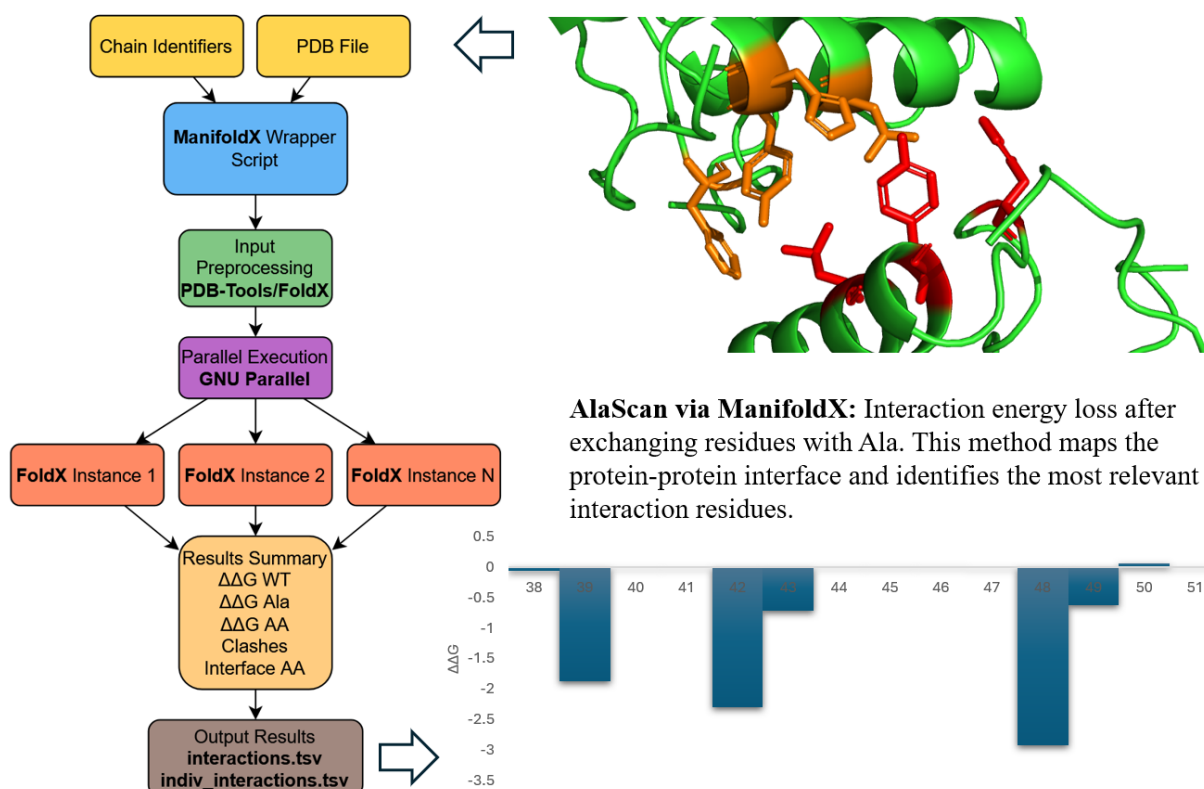
ManifoldX: A Parallel Wrapper for FoldX with Integrated Structure Preprocessing

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We introduce **ManifoldX**¹, a pipeline that wraps the FoldX² software to enhance its performance and usability. ManifoldX supports FoldX workflows such as *in silico* alanine (Ala) scanning³ and comprehensive 20 amino acid (20AA) substitution scans, facilitating free energy ($\Delta\Delta G$) interaction mapping and stability analysis for static protein-protein complexes. By providing FoldX with a scalable wrapper suitable for high-performance computing (HPC) and incorporating quality control (QC) features, ManifoldX substantially improves processing speed and simplifies workflows.

ManifoldX enables parallel computing through multithreading, significantly accelerating large-scale protein stability and interaction analyses. Additionally, it features integrated input file preprocessing, automating the preparation and formatting of input data to ensure compatibility with FoldX to minimise manual intervention. Results are summarized as automated reports to minimise raw output data postprocessing. FoldX is freely available as academic⁴ license, and we provide ManifoldX on GitHub¹ under a MIT open-source license.



[1] <https://github.com/Simon-K-Schaefer/ManifoldX>

[2] J. Schymkowitz, J. Borg, F. Stricher, R. Nys, F. Rousseau, L. Serrano. The FoldX web server: an online force field. *Nucleic acids research* **2005**, *33*, W382-8. DOI: 10.1093/nar/gki387.

[3] L. Weißenborn, E. Richel, H. Hüseman, J. Welzer, S. Beck, S. Schäfer, H. Sticht, K. Überla, J. Eichler. Smaller, Stronger, More Stable: Peptide Variants of a SARS-CoV-2 Neutralizing Mini-protein. *Int J Mol Sci.* **2022** Jun 4;23(11):6309. doi:10.3390/ijms23116309

[4] <https://foldxsuite.org/academic-license-info>