Hessisches Kompetenzzentrum
für Hochleistungsrechnen

CompuGene Student Lab Protein Engineering



Project Manager
Kai Kabuth

Researchers
Nadja Eisenbruch

Principal Investigator
Prof. Dr. Heinz Koeppl

Project Term
2023 - 2024

Clusters
Lichtenberg II Cluster Darmstadt

Software
GROMACS

Additional Software
RosettaFold

Institute
Centre for Synthetic Biology

University
Technische Universität Darmstadt

Introduction

The field of protein engineering is a rapidly evolving area of research that holds great promise for numerous applications in both science and industry. By designing and optimizing enzymes—proteins that act as catalysts in various biochemical reactions—we can develop tailored solutions for a wide range of challenges, from improving industrial processes to advancing medical treatments. However, the complexity of protein structures and the vast number of possible modifications present significant challenges. This is where High-Performance Computing (HPC) becomes indispensable. The intricate calculations required to model protein structures and predict their behavior under different conditions would be impossible to perform in a reasonable time frame without the power of HPC. By utilizing sophisticated computational tools, we can explore the structural space of proteins more thoroughly, enabling us to design enzymes with enhanced stability, specificity, and activity.

Methods

To achieve our research objectives, we employed a combination of advanced computational tools specifically designed for protein modeling and simulation. The primary software used in this project was RosettaFold, a state-of-the-art tool for protein structure prediction. RosettaFold allows us to generate highly accurate models of protein structures by leveraging deep learning techniques. These models serve as the foundation for further modifications aimed at optimizing enzyme properties. In addition to RosettaFold, we utilized Gromacs, a versatile molecular dynamics simulation software, to evaluate the

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stability and dynamics of the designed proteins. Gromacs allowed us to simulate how the proteins would behave in a real-world environment, providing insights into their potential performance and identifying any weaknesses that might need to be addressed. Together, these tools enabled us to explore a wide range of possible protein modifications, ensuring that the most promising designs could be identified and refined.

Results

The project was divided into several phases, each focusing on different aspects of protein engineering. During the initial phase, we generated a variety of protein models using RosettaFold. These models were designed with specific modifications intended to enhance the proteins' catalytic activity, substrate specificity, and stability.
In the subsequent phase, we employed Gromacs to simulate the behavior of these models under various conditions. These simulations provided critical data on the stability of the proteins, allowing us to identify which designs were likely to be successful in real-world applications.
Despite the promising results from the simulations, the decision was made to halt the project before proceeding to the next phase. The simulations revealed that while some models showed improved stability and activity, the overall performance did not meet the stringent criteria required for further development. As a result, the project was not continued, although the data generated will be valuable for future research efforts.

Discussion

The results of this project highlight both the potential and the challenges of computational protein engineering. The use of HPC and advanced modeling software like RosettaFold and Gromacs allowed us to explore a wide range of protein designs in a relatively short time. This approach significantly reduces the time and cost associated with traditional experimental methods. However, the decision to pause the project underscores the difficulties inherent in enzyme design. Even with the power of HPC, predicting the behavior of modified proteins remains a complex task. The results we obtained, while promising, were not sufficient to justify further development at this stage.

Outlook

Looking forward, advances in computational algorithms and more powerful HPC systems will likely overcome some of the current limitations. As these technologies continue to evolve, they will enable even more precise and effective protein engineering, opening up new possibilities for customized enzymes tailored to specific applications.

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