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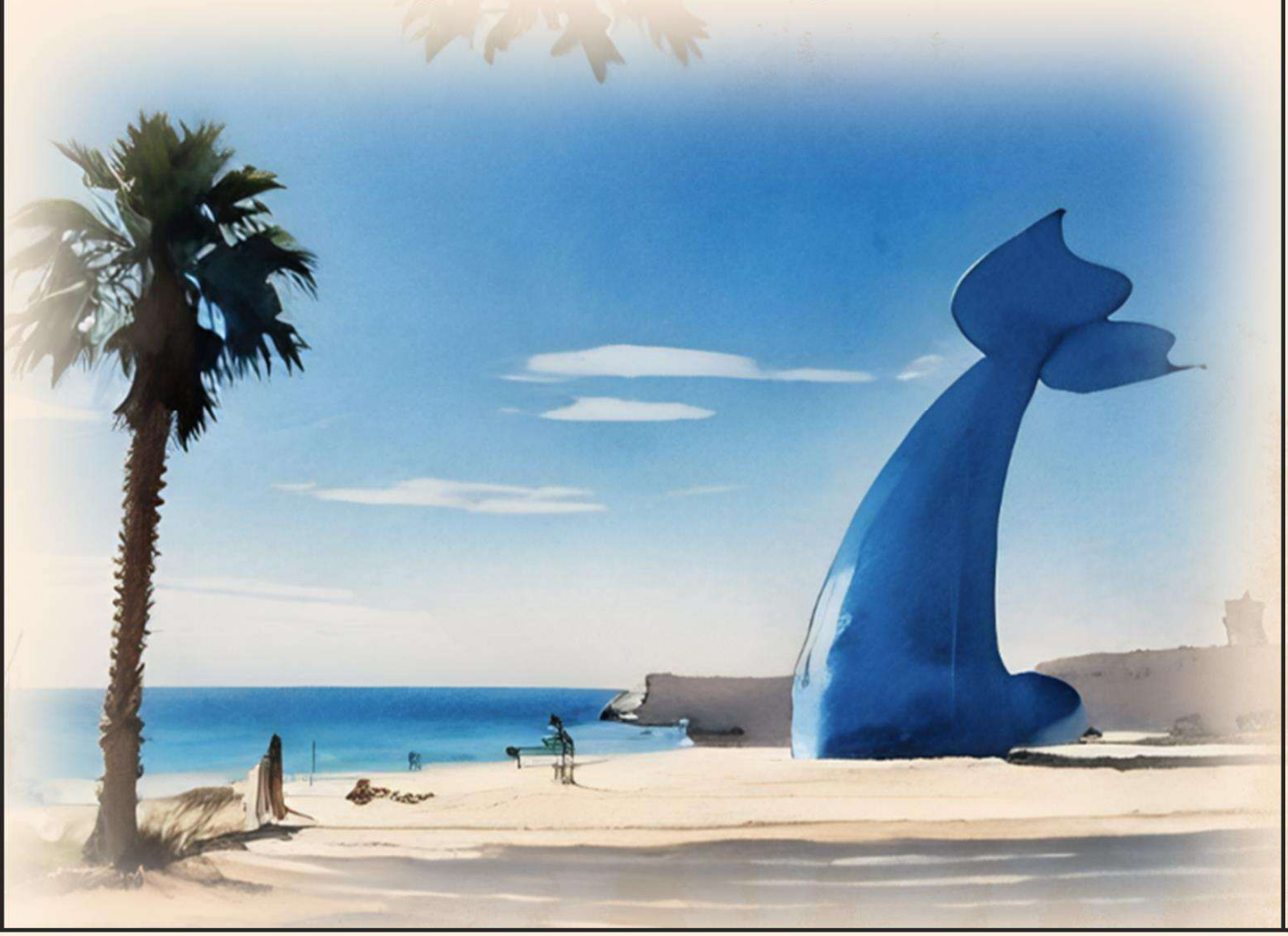

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A Computational Approach to Study Non-Synonymous Mutations

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Non-synonymous SNPs (Single Nucleotide Polymorphisms) result in amino acid substitutions within proteins. While some may have minimal impact on protein structure and function, others can significantly alter stability, conformation, and biological activity. Therefore, it is crucial to predict how SNP-induced changes affect protein structure and function. Here, we developed a novel pipeline that integrates bioinformatics and molecular modeling techniques to evaluate the structural and functional consequences of a non-synonymous SNP in a protein. Initially, Protein Plus was used to predict the potential active sites, which will help to determine whether a mutation is located within the functional binding regions. Identification of active sites is necessary to prioritize mutations that may alter protein structure and function. PolyPhen-2 and I-Mutant were used to evaluate the functional impact of mutations and the thermodynamic stability of the proteins. Next, to visualize the structural changes, AlphaFold3 was used to generate high-confidence 3D models for wild and mutant proteins. Finally, molecular dynamics (MD) simulations were conducted using YASARA to explore the dynamic behavior and stability of both mutant and wild-type proteins. MD simulations provide valuable insight into structural flexibility, potential conformational shifts, and the overall impact of the mutation on protein function. This computational pipeline provides a detailed framework to evaluate the structural and energetic consequences of non-synonymous mutations.