Title

Decoding Mutation Effects on Protein Structure Using AlphaFold

Authors

Yoshitha Evuri[1], Enrique Garcia[1], Jonathon E Mohl[2]

[1]Bioinformatics Program, [2]Department of Mathematical Science, The University of Texas at El Paso, El Paso, TX

Abstract

The overall goal of this study is to compare and analyze the structural effects of mutations in proteins by generating and evaluating 3D models of both wild-type and mutant sequences. Mutations in protein sequences can alter folding, stability, and function, which may contribute to disease mechanisms or modified biological activity. Understanding these differences provides valuable insights into the functional consequences of mutations and their broader biomedical significance.

The process starts with the preparation of input FASTA sequences, one of which contains the desired mutation and the other of which represents the wild-type protein. AlphaFold, a cutting-edge deep learning-based structure prediction tool, processes both sequences with uniform parameters, reference databases, and template cutoffs. To find variations in global folding, secondary structures, and functional regions that might be impacted by the mutation, AlphaFold creates high-confidence structural models in Protein Data Bank (PDB) format.

Python is primarily used to organize and process AlphaFold outputs, while molecular visualization tools such as PyMOL, ChimeraX are employed to highlight structural deviations between the wild-type and mutant proteins. Quantitative metrics such as root mean square deviation (RMSD) are calculated to evaluate the degree of structural change. Results are then interpreted in relation to protein stability and potential impacts on function.

This project aims to demonstrate the utility of AlphaFold in mutation analysis and emphasizes how computational approaches can connect sequence variation to structural and functional understanding.