

Assessing Protein Structural Changes Caused by Missense Variants via Molecular Dynamics Simulations

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INTRODUCTION & AIM

SNPS CAN ALTER PROTEIN STABILITY AND DYNAMICS, WHICH WE ASSESS USING MOLECULAR MODELING AND DYNAMICS OF XP_62482 IN *APIS MELLIFERA*.

GOALS:

BENCHMARKING DEEP-LEARNING AND HOMOLOGY-BASED PROTEIN STRUCTURE PREDICTION METHODS

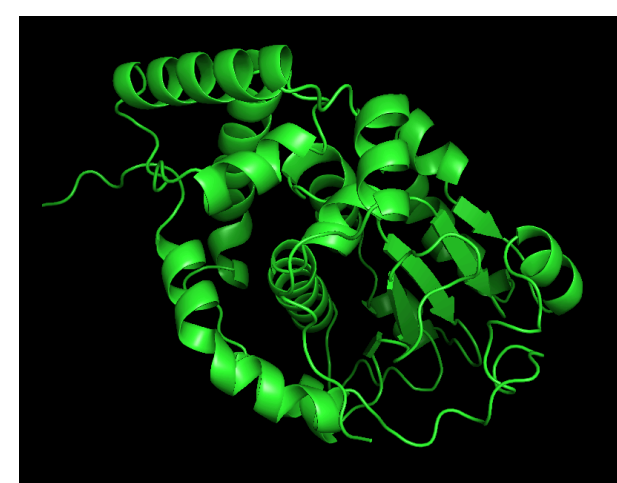
MODELING SNP-INDUCED STRUCTURAL AND DYNAMIC PROTEIN CHANGES VIA MOLECULAR DYNAMICS

EVALUATING ALPHAFOLD ROBUSTNESS FOR POPULATION-SCALE FUNCTIONAL GENOMICS

METHOD

Protein structure prediction

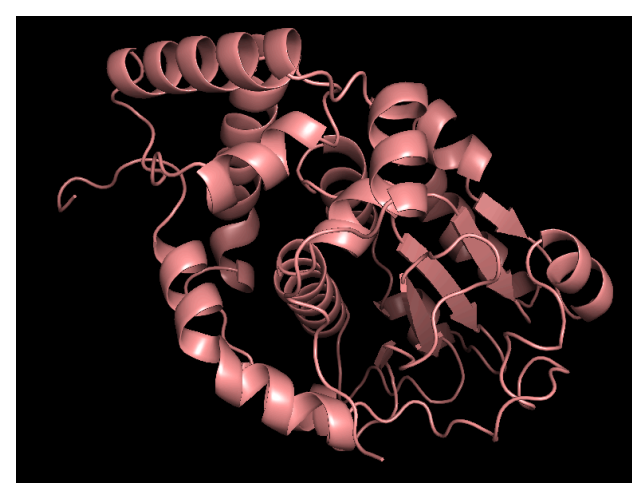
Wild-type protein structures were predicted using:



AlphaFold2



AlphaFold Protein Structure Database (AFD)



SWISS-MODEL

Mutant protein structures were predicted using:



AlphaFold2



MODELLER of AFD

Model evaluation metrics:

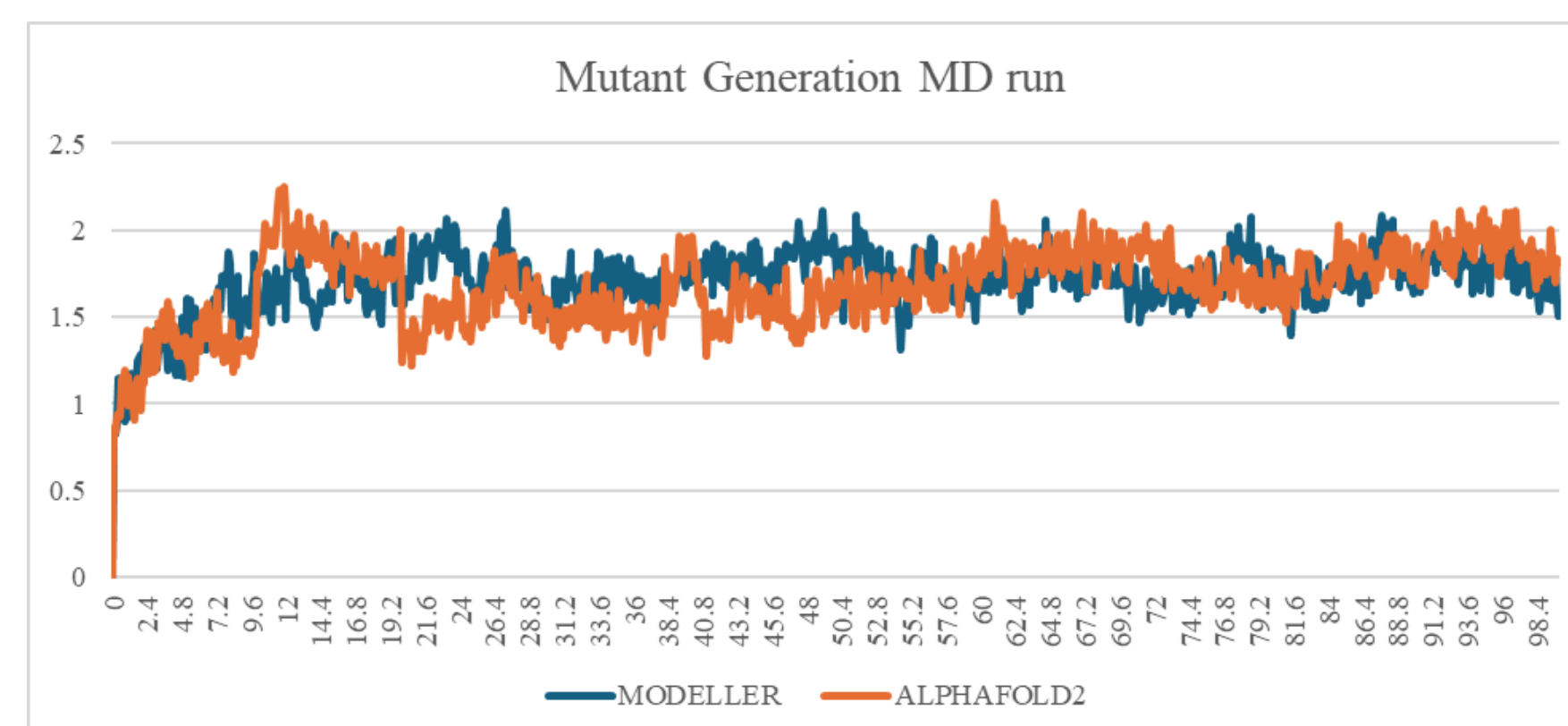
- pLDDT (per-residue confidence)
- DOPE score
- TM-score (structural similarity)

Molecular dynamics simulations (AMBER25/100 ns)

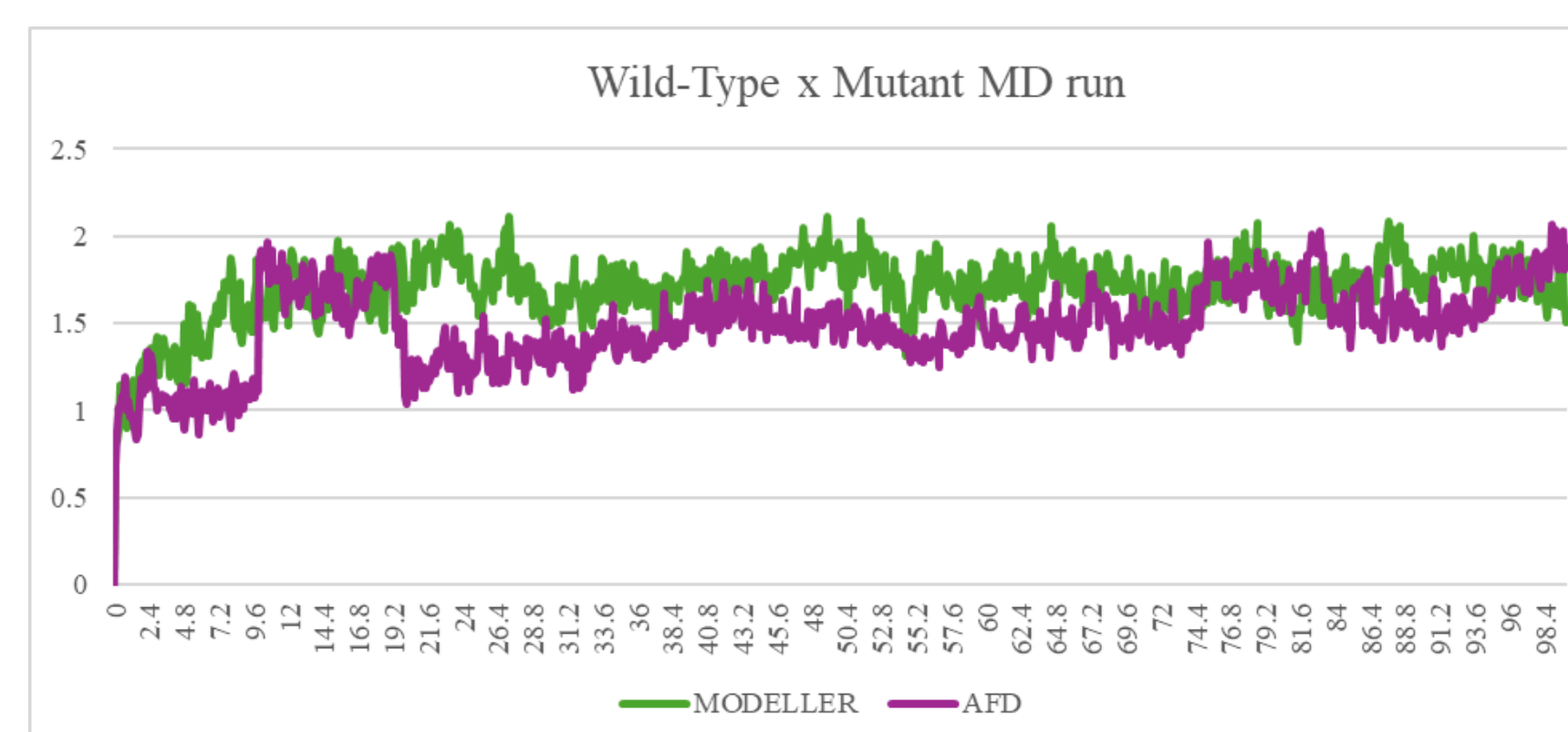
Trajectory analyses included:

- Root Mean Square Deviation (RMSD)
- Root Mean Square Fluctuation (RMSF)
- Radius of Gyration (Rg)
- Solvent-Accessible Surface Area (SASA)
- Hydrogen bonds
- Backbone dihedral angles (φ / ψ)

RESULTS & DISCUSSION



- AlphaFold2 and AlphaFold DB wild-type models combined with MODELLER showed greater sensitivity to SNP perturbations.
- Mutant structures retained high congruence with mutation-aware prediction



CONCLUSION

- ALPHAFOLD-DERIVED MODELS ARE ROBUST AND SENSITIVE FOR SNP EFFECT MODELING.
- SNPS INDUCE SUBTLE BUT MEASURABLE CHANGES IN PROTEIN STABILITY, FLEXIBILITY, AND SOLVENT EXPOSURE.
- THE APPROACH ENABLES FUNCTIONAL INTERPRETATION OF GENOMIC VARIATION AT POPULATION SCALE.