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Computational analysis to predict the impact of non-synonymous mutations in a protein: an example with the Odorant Receptor 49b

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Non-synonymous mutations lead to amino acid substitutions within proteins, potentially affecting protein structure and function. While some mutations have a minimal impact on protein structure and function, others can alter their stability, conformation, and biological activity. Therefore, predicting how mutations affect proteins is important when uncovering the genetic basis of honey bee response to selective pressures.

In a recent whole-genome scan for signatures of selection in *Apis mellifera syriaca*, we found a non-synonymous mutation under selection in the Odorant Receptor 49b (Or49b) gene. According to the literature, this gene plays a role in honeybee foraging, communication, and environmental adaptation. In an attempt to understand the biological impact at the molecular level of the discovered mutation, we assembled a pipeline that integrates bioinformatics and protein modelling techniques to evaluate the structural and functional consequences of a mutation in a protein. Protein structures were generated from a FASTA file using AlphaFold3, converted from mmCIF to PDB format, and visualized in PyMOL, where mutations were introduced. Functional site predictions were performed using Proteins Plus, and molecular dynamics simulations were conducted in YASARA to assess stability and conformational changes.

Our findings suggest that the mutation under selection in the OR49b gene, which replaces tyrosine with histidine, alters protein dynamics by modifying its energy landscape and stability. At the end of the molecular dynamics simulation, the total potential energy of the wild-type protein was calculated as -384,675 kcal/mol. In contrast, this value increased to -287,075 kcal/mol for the mutant protein. This difference suggests that the mutation may affect the OR49b conformation, flexibility, and eventually its biological function. Whether this change affects honey bee olfactory perception remains uncertain. However, given that the mutation is under selection, it is plausible that the alternative amino acid variants confer an adaptive advantage in different environments. From a practical perspective, understanding how mutations affect biological function can ultimately assist honey bee breeders in selecting colonies for breeding programs, enhancing resilience and adaptability.