Benchmarking of GPCR AlphaFold models

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AlphaFold is a computational technique designed for predicting three-dimensional (3D) protein structures from their respective protein sequences [1]. Although AlphaFold has demonstrated remarkable accuracy near to experimental results in predicting the 3D structure of monomeric proteins, it typically represents a singular conformational state with minimal structural diversity [2].
However, in the context of G protein-coupled receptors (GPCRs), our focus lies in capturing an active state to discover how extracellular interactions translate into downstream cellular responses. One strategy to bias predictions towards a desired conformational state involves modulating GPCRs in conjunction with G-proteins. Consequently, in our work comparative analysis between the structures of monomeric and multimeric complexes has been conducted to evaluate the accuracy of AlphaFold models generated through various methods.

Bibliography :

[1] Jumper, J., Evans, R., Pritzel, A. et al. Highly accurate protein structure prediction with AlphaFold. Nature 596, 583–589 (2021). https://doi.org/10.1038/s41586-021-03819-2
[2] Sala, D., Engelberger, F., Meiler, J. et al. Modeling conformational states of proteins with AlphaFold. Current Opinion in Structural Biology 81, 102645 (2023). https://doi.org/10.1016/j.sbi.2023.102645