FoldScript: a new webserver for interpreting artificial intelligence in structural biology

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Abstract

3D modeling programs based on artificial intelligence (AI) have revolutionized structural biology, often predicting protein structures with an unprecedented level of confidence.

However, these structures remain models, and it is always interesting to compare the results of different predictors (AlphaFold3, RoseTTAFold, ESMFold...), not to limit one's choice to the model generated with the highest confidence score, and to introduce experimental data such as known intermolecular contact regions in the selection of the best model.

We have created a web server, named "FoldScript", to address these issues. It can be used to synthesize in 1D, 2D and 3D the multi-model information generated by the AI. We have tested this web software on different protein complexes of therapeutic targets studied by our team, for which low or high confidence scores had been obtained. We show that, while AI can provide relevant answers, a critical look remains crucial. Indeed, the "top score" solution proposed by the AI is not always the "best".

FoldScript therefore enables a wide community, whether specialized in structural biology or not, to easily analyze any AI-generated 3D model, especially macromolecular assemblies, and offers a rational aid to decision-making. This new tool complements our ESPript (https://espript.ibcp.fr) and ENDscript (https://endscript.ibcp.fr) web servers to enable exhaustive analysis of experimental or predicted protein structures.