

A Perspective on the Prospective Use of AI in Protein Structure Prediction

Description

This article examines the impact and limitations of AlphaFold2 (AF2) and RoseTTaFold (RF) as highly reliable and effective methods for predicting protein structure. Emphasis is placed on their integration into experimental pipelines and their application to different classes of proteins, including membrane proteins, intrinsically disordered proteins (IDPs) and oligomers. Due to difficulties in capturing conformational ensembles and interactions with the membrane, predicting the structure of membrane proteins remains challenging for both AF2 and RF. Improvements in the incorporation of membrane-specific features and the prediction of the structural effects of mutations are crucial. For intrinsically disordered proteins, AF2's confidence score serves as a competitive disorder predictor. However, integrative approaches with molecular dynamics simulations or hydrophobic cluster analyses are advocated for an accurate representation of the dynamics. AF2 and RF show promising results for oligomeric models, outperforming traditional docking methods, with Alpha Fold-Multimer showing improved performance. However, some caveats remain in particular for membrane proteins. AF2 and RF show promising results for oligomeric models, outperforming traditional docking methods. AlphaFold-Multimer shows improved performance. However, some caveats remain, particularly for membrane proteins. Combining AF2 models with molecular dynamics simulations can be used complementarily.

The authors propose a “wish list” for improving deep learning-based protein folding prediction models, including using experimental data as constraints and modifying models with binding partners or post-translational modifications. In addition, a meta-tool for ranking and suggesting composite models is proposed to drive future progress in this rapidly evolving field.

Category

1. News