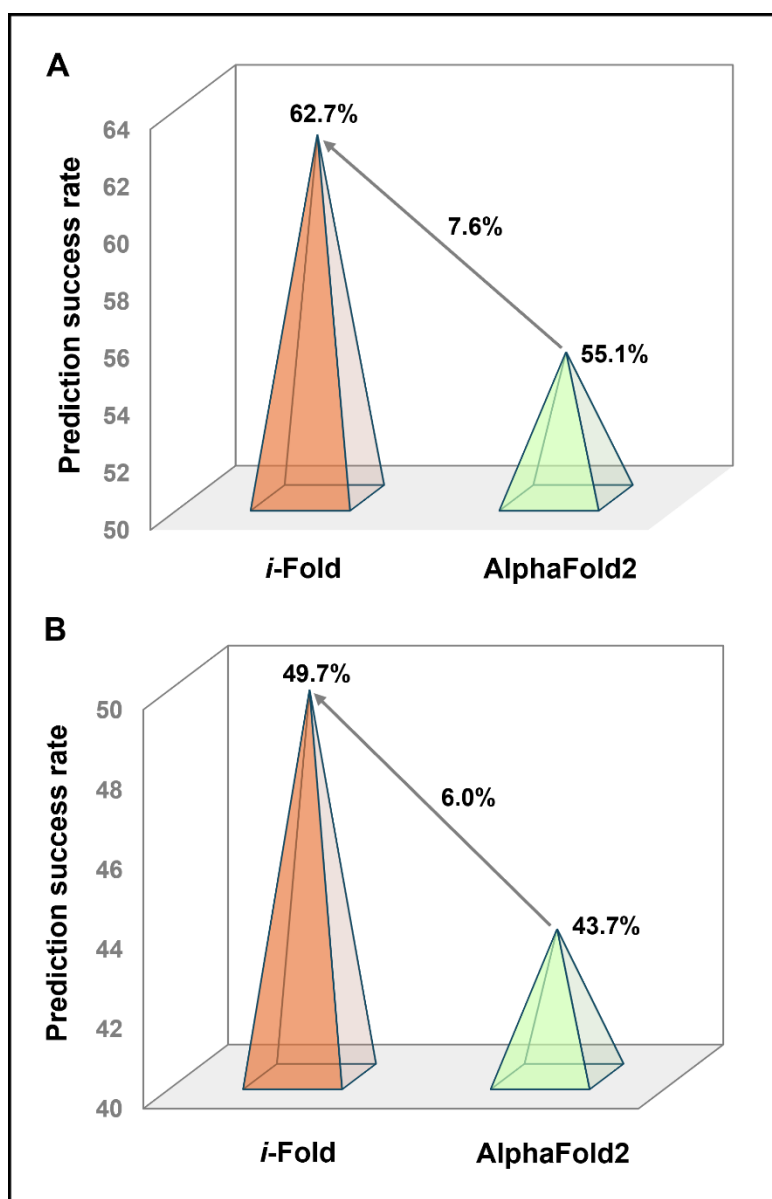


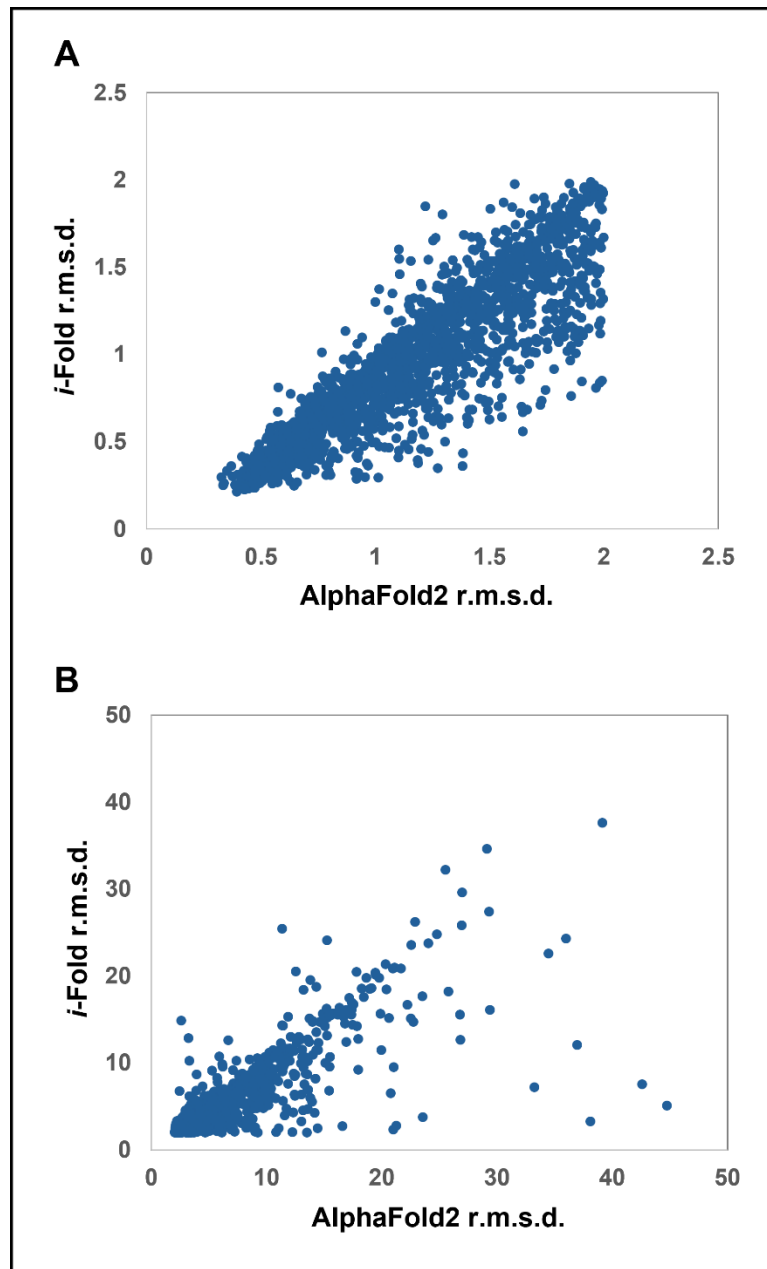
Supplementary Information



Supplementary Figure 1. *i*-Fold showed improved prediction success rate on different test sets.

(A) The prediction success rates of *i*-Fold and AlphaFold2 on the test set containing 3599 protein structures.

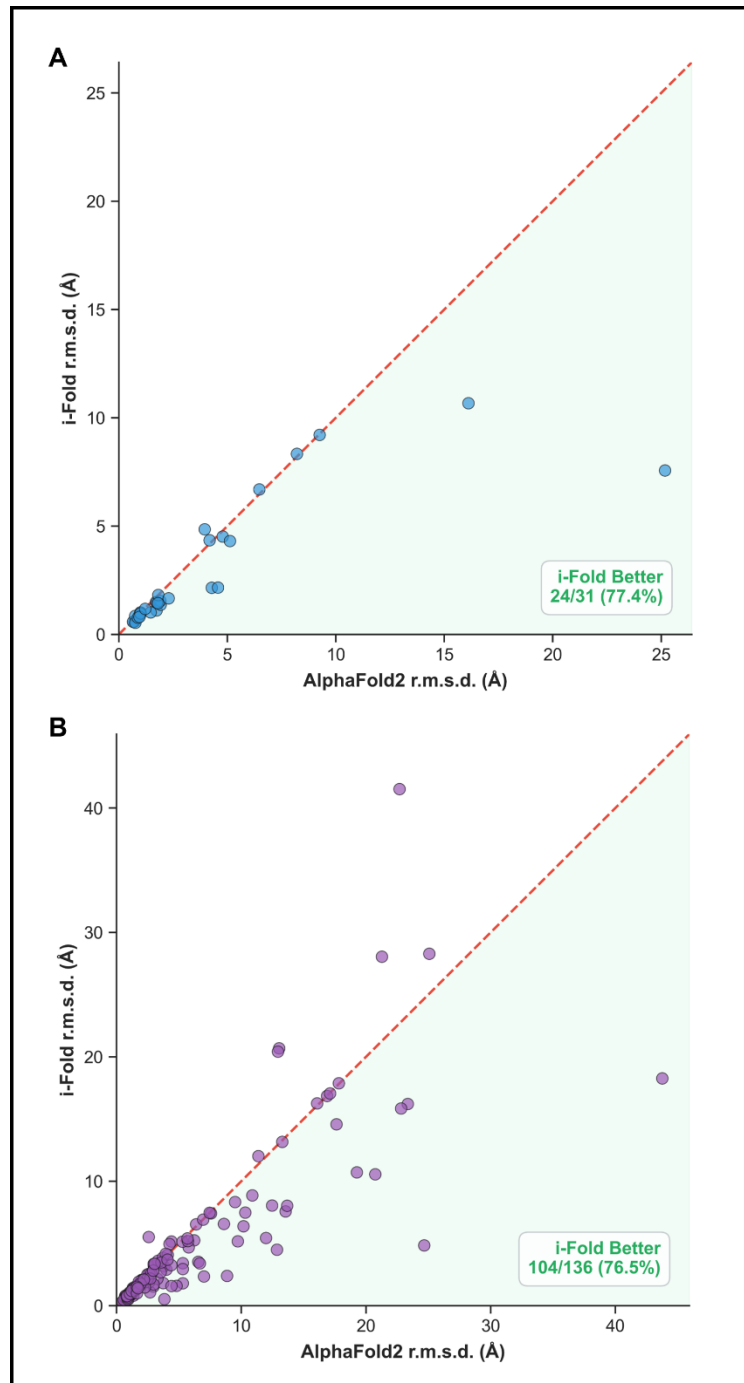
(B) The prediction success rates of *i*-Fold and AlphaFold2 on the independent test set containing 167 novel protein structures.



Supplementary Figure 2. *i*-Fold showed consistent performance improvement across protein sets with different prediction difficulties.

(A) Comparison of prediction performance between *i*-Fold and AlphaFold2 for protein structures that were successfully predicted by both.

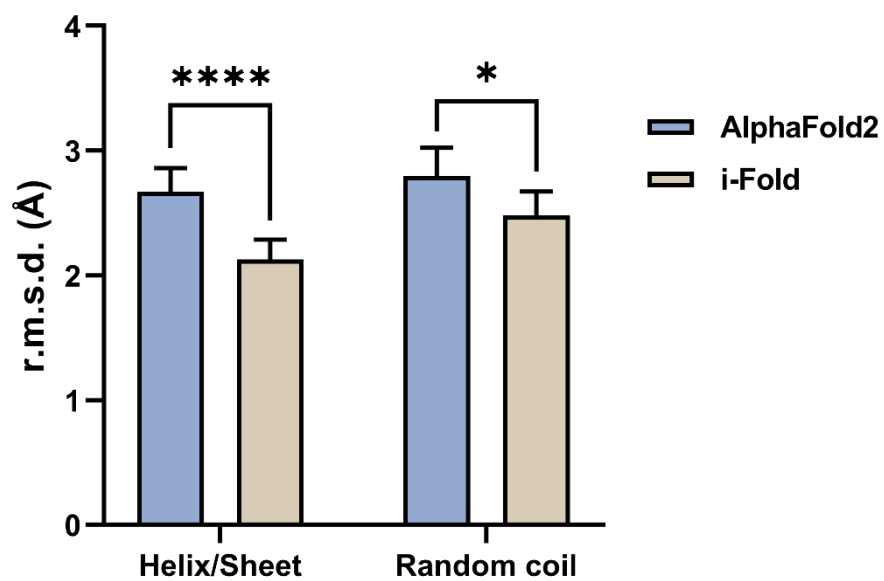
(B) Comparison of prediction performance between *i*-Fold and AlphaFold2 for protein structures that both failed to predict.



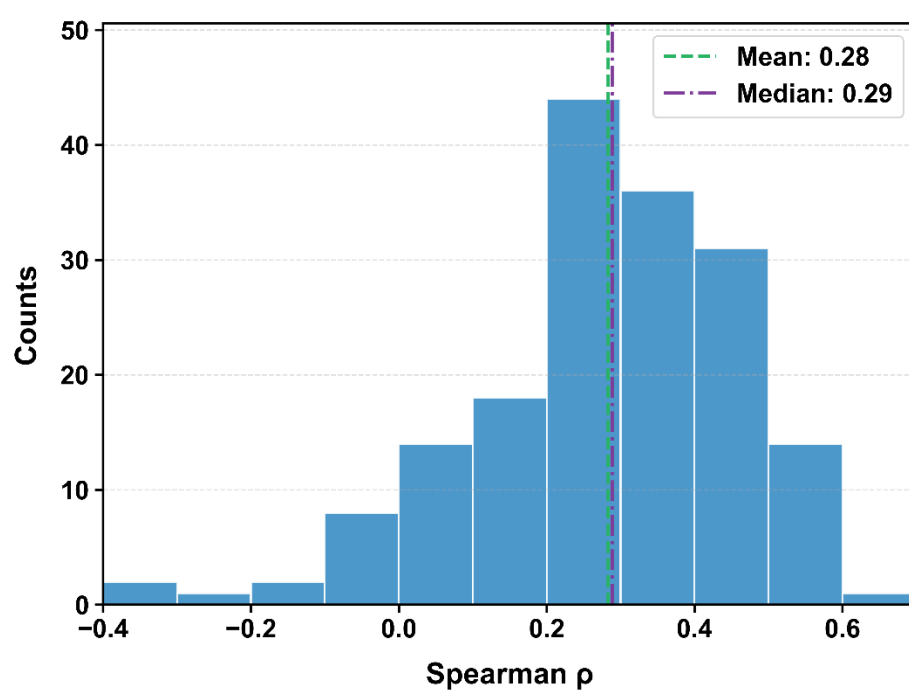
Supplementary Figure 3. *i*-Fold demonstrates consistent performance improvement across protein datasets with different homology levels.

(A) Comparison of prediction performance between *i*-Fold and AlphaFold2 on low-homology protein datasets with $MSA \leq 1000$.

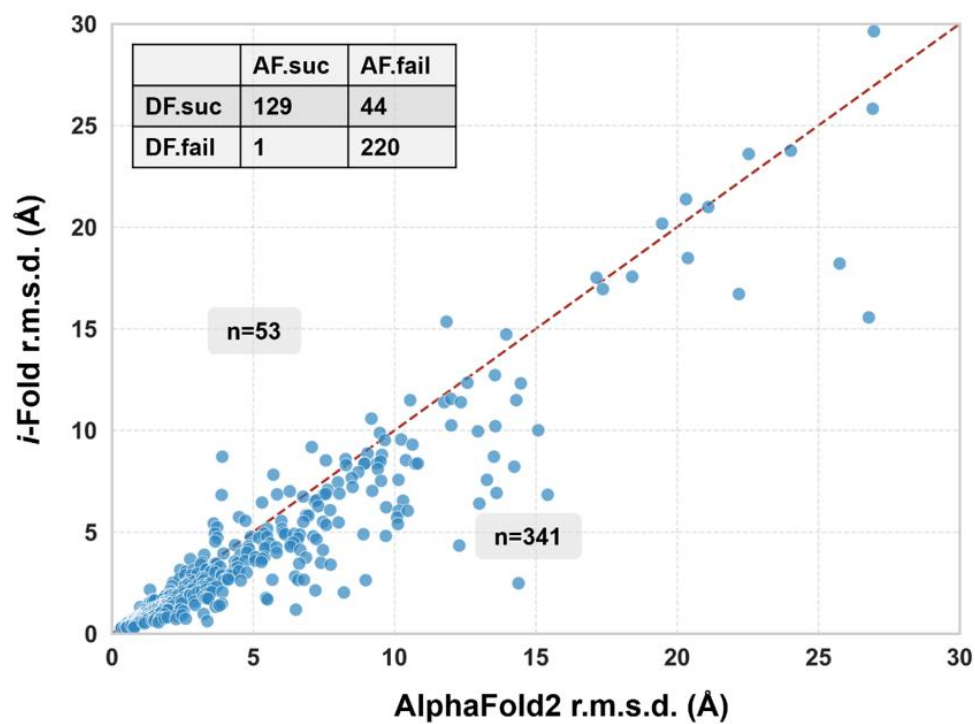
(B) Comparison of prediction performance between *i*-Fold and AlphaFold2 on high-homology protein datasets with $MSA > 1000$.



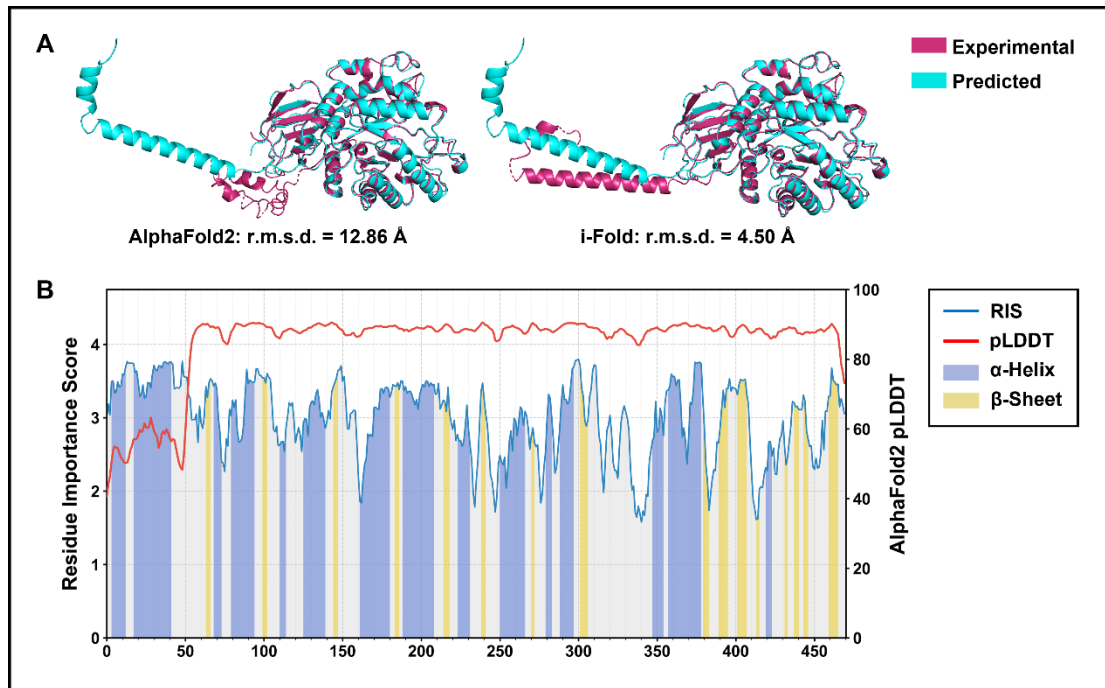
Supplementary Figure 4. *i*-Fold exhibits a global accuracy improvement. Error bars indicate standard error; **** $p < 0.0001$, * $p < 0.05$.



Supplementary Figure 5. Distribution histogram of the Spearman's correlation between pLDDT and RIS weights for each protein in the independent test set.



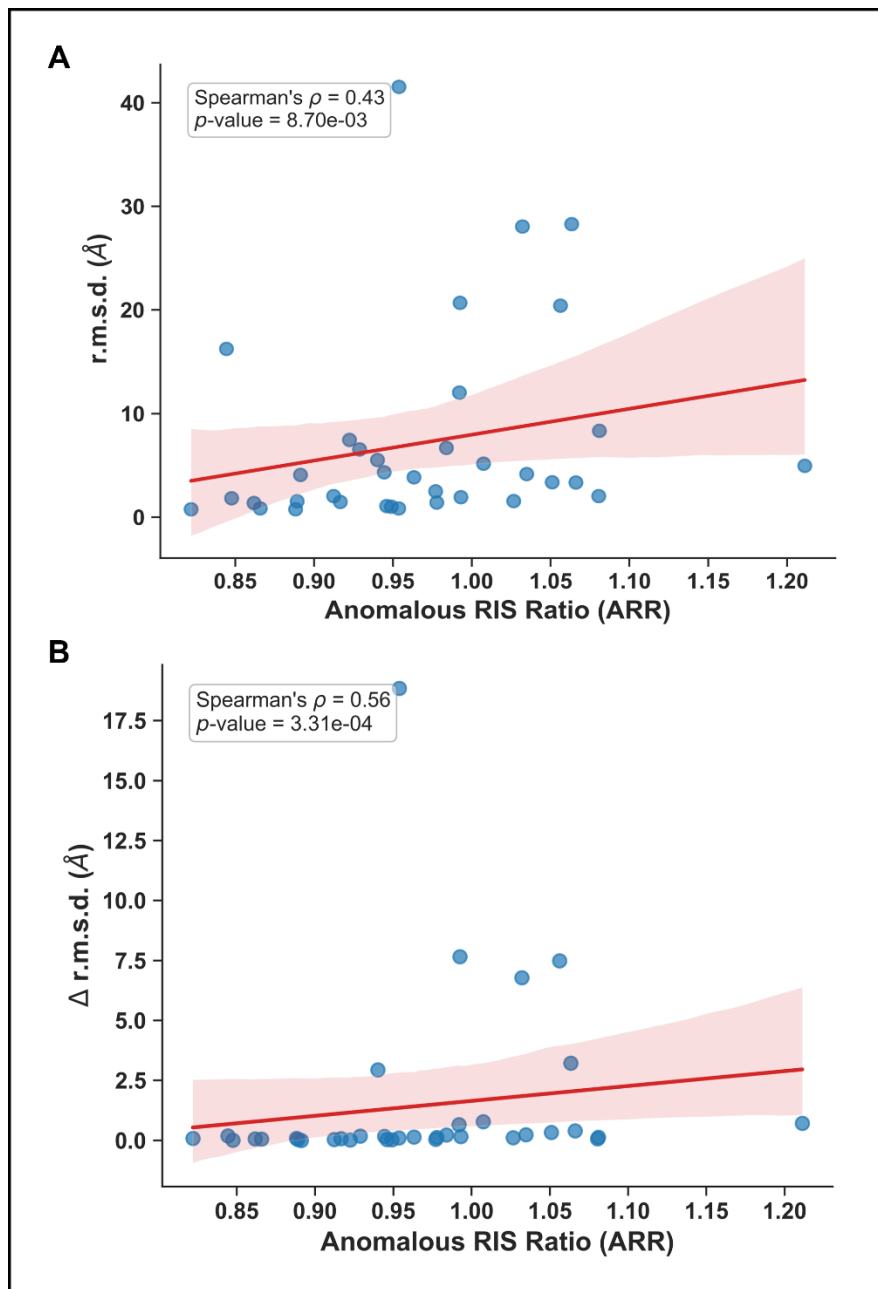
Supplementary Figure 6. Comparison of the prediction performance between AlphaFold2 and *i*-Fold on low-homology proteins ($n = 400$) with fewer than 500 effective MSA hits.



Supplementary Figure 7. RIS can emphasize and correct regions that AlphaFold2 predicts with low confidence.

(A) Predicted structures of protein 8ida generated by AlphaFold2 and *i*-Fold.

(B) RIS, pLDDT and corresponding secondary structure elements along the full-length sequence of 8ida.



Supplementary Figure 8. Performance of *i*-Fold depends on the appropriate RIS weighting.

(A) Correlation between the Anomalous RIS Ratio (ARR) and the absolute error of the *i*-Fold prediction.

(B) Correlation between the Anomalous RIS Ratio (ARR) and *i*-Fold predicted r.m.s.d. increment compared with AlphaFold2.