

Supplementary Files

A Preliminary Experiments

Before this work begins, we’ve performed some preliminary experiments to evaluate the feasibility. Our initial hypothesis is that the node information within the graph network constructed by ProteinMPNN can significantly enhance model performance when enriched with prior knowledge derived from sequences corresponding to homologous structures. In ProteinMPNN, these node features are originally initialized to zero, leaving substantial room for improvement by incorporating more informative priors. Theoretically, augmenting this initialization with sequence context from homologous structures should effectively improve the model’s accuracy by providing a richer representation of the underlying protein features.

On the CATH dataset, we initialized a certain proportion of the ProteinMPNN node features with the native protein sequences, while another certain proportion was initialized with incorrect sequences. This setup aimed to simulate the characteristics of amino acids in homologous structural pairings, where some regions share identical sequences while others contain mismatches. The purpose of this approach was to better mimic real-world scenarios where structural alignments provide partial but imperfect sequence information. The preliminary experimental results are shown in **Table S1**. When the wrong initialization rate is fixed, increasing the correct initialization rate improves recovery. For example, with 0% wrong rate, recovery rises from 49.87% (0% correct) to 54.57% (10%) and 61.39% (30%). At a fixed correct rate, higher wrong initialization lowers recovery. With 10% correct, recovery drops from 53.42% (20% wrong) to 51.82% (40%); with 20% correct, it drops from 58.67% (10%) to 52.61% (60%). Both correct and wrong initialization rates markedly affect recovery, underscoring the importance of template quality. This is consistent with the analysis in *Section 4.3*.

Table S1: Sequence perplexity and recovery rate under different initializing ratio in preliminary experiments.

Init ratio			Perplexity↓	Recovery rate↑
Correct	Wrong	Zeros		
0%	0%	100%	5.41	49.87%
10%	0%	90%	4.09	54.57%
10%	20%	70%	4.12	53.42%
10%	40%	50%	4.73	51.82%
20%	10%	70%	4.53	58.67%
20%	60%	20%	4.62	52.61%
30%	0%	70%	3.77	61.39%
30%	20%	50%	3.85	60.01%
40%	40%	20%	3.57	62.11%

B Cases of Protein Templates in Five TM-score Intervals

Protein templates are divided into five intervals: $[0, 0.3)$, $[0.3, 0.5)$, $[0.5, 0.7)$, $[0.7, 0.9)$, $[0.9, 0.99]$. There are some cases of query-template proteins down below (**Fig. S1**), each presents a combined view of sequence and structural alignment between a query protein and a template protein, typically used to assess homology modeling or structural similarity. On the left, the sequence alignments highlight the correspondence between residues in the query and template, with matched or similar residues indicated by colored symbols, where exact matches often shown as aligned letters, and conservative substitutions marked with symbols such as plus signs. Gaps introduced to optimize alignment are represented by dashes. The sequence alignments are annotated with residue indices to indicate positional context. On the right, ribbon diagrams overlay the 3D structures of the two proteins—commonly using distinct colors (blue for the query and orange for the template) to visually demonstrate structural conservation. Quantitative metrics such as TM-score, RMSD, aligned length, and matched length are usually provided to objectively evaluate the quality of the alignment, with higher TM-scores and lower RMSD values indicating greater structural similarity.

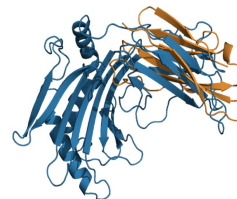
These template cases illustrate the structure and sequence similarities between proteins across different TM-score intervals. When the TM-score is below 0.5, the alignment tends to be short, and the type of aligned amino acid shows low similarity. In contrast, when the TM-score exceeds 0.5, the alignment length increases, and the residue-level correspondence improves significantly. These examples support the findings presented in *Section 4.3* of the experiments, further highlighting the critical role of template quality in influencing the accuracy of sequence recovery by the model.

Query: 3IT8.D Template: 6DDV.C

TM-score=0.27, RMSD=2.65, Aligned length=91, Matched length=21

Q 182 TPTVKTGNELEDGNMTECTVNSFYPPDVITKWIESEHFKEGYKYNVGRYPPEWGRKSNYEPGEGFPWNIKKDKDAN 261
P V VT +E +GN+T+ C +SFYP ++I W +
T 2 VPVMNVTRSEAGNITVTCTASSFYPRNIILTWQRD-----GVSLSHDTQQWGDVLPDGNG 59

Q 262 TYSLTDLVRTSKMSSQPVCFVFDHLEAQVY 294
TY R + + C + H + +
T 60 TYQTWVATRISRGEERFTCYMEH-SGNHSTH 92

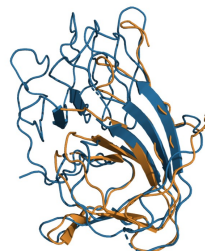


Query: 3MYX.A Template: 3BCW.A

TM-score=0.43, RMSD=2.13, Aligned length=111, Matched length=32

Q 117 PDKSGITALDRLLALLTSPSPDPSPS-IISPLPQCRSNNLFEDTASTLRIGVWDSTPYERISRPHK--IHENLIEGRVVL 193
DKS + +D ++ P PS I+ R+ FE + GVW+ST I ++IEG L
T 1 HDKSLRVRIDTGPMPINP-VAGKPSRPIAGDASFRITVAFEGGQKVESGVWESTSGSF-QSNTTGYIEYCHIEGEARLV 78

Q 194 LENGSSLTIVNTGDTVFVAQAPCKWTSTGYVRKFYAVT 231
+G+ V GD + +G +W +V+K Y VT
T 79 DPDGTVHAVKAGDAPIMPEGYTGRWEVDHRHVKKIYFVT 115

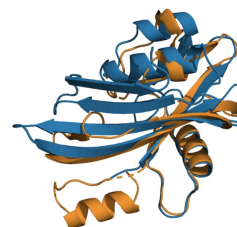


Query: 3FK9.A Template: 3SMD.A

TM-score=0.63, RMSD=2.19, Aligned length=108, Matched length=38

Q 2 QRVTNCIVVDH-DQVLLQKPRRGWVAPGGKMEAGESILETVKREYWEETG--ITVKNPELKGFISM---VIFDEGKI 74
++ + ++L+ Q P +W P+G +E GE+ E V RE WEETG + VK KG+F + G
T 19 MSPVAIVIRNEQGEELLF-QYP---YWSLPAGAIEPGETPEEAVIREVWEETGLKGVKK--QKGVFGGKEFRYYANGDK 92

Q 75 VSEWMLFTFKATEHEGEMLKQSPGKLEWKKKDE--VLELPMAGDKWIF 122
V E+++ F+ G++ K L++ E L LP DK IF
T 93 V-EYIVVVFCEITSGKLK-----LQYFSFSEKPLALPYP--DK-IF 132

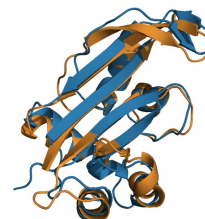


Query: 2WNY.A Template: 2OGK.B

TM-score=0.81, RMSD=2.17, Aligned length=134, Matched length=45

Q 5 IHNISYCLMVGYTEDEEKVIEALRNVPGA-TPERESAEGYHGNPITVLRGRLLRRALREFMEKFTEV----FRGRMDE 79
I + +V+ TED EKV EA+ + P A+G++GNP+ L L + +++F + + E+ +
T 2 IEWVRVSADVHSTEDREKVGAEISTLFPFEFEIAYSKAKGHYGNPMEYLEVELTKSSEIKKFWNKLLLELQGEAEILST 81

Q 80 LEDRFDENGLFLRLDKQKALEGVWEPVRHGDALHLKIKVEAYPAKREVAVENIRKIL 137
LEDR DE+ L +R+DKQKA G GD I +K+++ YP+KRE +E R++
T 82 LEDRIDEQNVLHIRIDKQKAYLGEVSLTSGGDPIAVKLRLVTPSKREKRVIEFARELC 139



Query: 1UAS.A Template: 4NZJ.A

TM-score=0.95, RMSD=1.77, Aligned length=359, Matched length=154

Q 3 NGLGRTPQMGSWNHFCYGINEQIIRETADALVNTGLAKLGYQVYNIDDCWAEYSRDSQGNFVPNRQTFFSGIKALADY 82
L TP MGWNSWN F + E+++ +TADA++ G+ LGY Y+NIDD W R + G++ ++ FP GIK +ADY
T 91 DELLTPPMGSWNWTFGGHLEELVLQTADAMITNGMRDLGYSYINIDDFWQLPERGADGHLQIDKTKFFRGIKYVADY 170

Q 83 VHAKGLKLIYSDAGSQTCSNKMPSGLDHEEQDVKTFASWGVDYLKYDNCNDAGRSV--MERYTRMSNAMKTYGKNIFFS 160
H +G+KLGIYSDA+ +TC + GS +EE D K FASWGDV LKYD CN V MERY +M A++ ++I +S
T 171 LHERGFKLGIYSDAAECTG-GVCGSYGYEETDAKDFASWGDVLLKYDYCNAPVDRVEAMERYAKMGRALRATNRSIVYS 249

Q 161 LCEWGKENPATWAGR-MGNSWRTTGDIDN---G-----SMTSRADENDQWAAAYAGPGGWNDPDMLEVGN---G 224
CEWG+ P WA + G+ WR +GDI+D W G + + + N + YAGP GWNDPDM VG +G G
T 250 VCEWQREPWKWAKQVGGHLWRVSGDIGDIWYRDGNRVGGHLGILNILEINAPLSEYAGPSGWNDPDMLVVGDGKSMG 329

Q 225 MSEAEYRSHFSIWALAKAPLIGCDVRMSQTKNILSNSEVIANVQDSLGVQKVKVQSDNGLEVWAGPLSNRKAIVLV 304
++ +Y+SHFS+W + +PLL G DVR+M+ T IL + ++IA+NQD LG Q+++ + ++W PL++ RKAV +
T 330 CTQEQYKSHFSLWCMMSAPLLSGNDVRNMNDSTLKLDPDLIAINQDVLGRQAERSIRSDHYDIWVKPLADGRKAVACF 409

Q 305 NRQSYQATITAHWSNIGLAGSVAVTARDLWHSFSAAG----QISASVAPHDCMKMYVL 359
NR S T+ + + I+ L H + G ++ +AP+ CK+Y++
T 410 NRASSPQTVILNENTIADLSF--EQIYCLDNHLT--KSGSDSKELIVKLAPYQCKVYIF 464

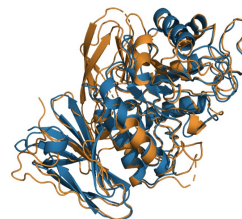


Figure S1: Five cases of protein templates across different TM-score intervals. The query-template pairs with higher structural TM-scores tend to exhibit more similar sequence alignments.