Inter-chain contact map prediction for protein complex based on graph attention network and triangular multiplication update

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***Abstract*—Residue-residue interactions between individual subunits of protein complexes are critical for predicting complex structures and can serve as distance constraints to guide complex structure modeling. Some recent studies have made some progress in predicting protein inter-chain contact maps based on multiple sequence alignments and deep learning models. Here we develop a new model based on graph attention network and triangular multiplication update to predict inter-chain contact maps for homologous protein complexes, named PGT (P is Protein, G is Graph attention network and T is Triangular multiplication update). Different from other methods which need to perform multiple sequence alignment processes and extract complicated manual features, PGT extracts embeddings of residues through the protein language model. Besides, we introduce structural information through the graph attention network to learn the spatial information of subunits from the complex structure and utilize the triangular multiplication module to capture triangular constraints between residues. To demonstrate the effectiveness of our method, we compare PGT with previous works such as DeepHomo, DRCon and Glinter on two independent test sets. The results show that PGT substantially outperforms these methods. Furthermore, we also perform two ablation experiments to demonstrate the necessity of introducing graph attention network and triangular multiplication update. In all, our framework presents new modules to accurately predict inter-chain contact maps in homologous protein complexes and it's also useful to analyze interactions in other type of protein complexes.**

Keywords—inter-chain contact, graph attention network, triangular multiplication update, homologous protein complex

I. INTRODUCTION

Protein is one of the main participants in life activities. Understanding the function of protein is very important to understand life activities. The function of protein is often determined by its structure, so it is particularly important to obtain the spatial structure of protein by experimental or computational methods. Recently, Alphafold2[1], developed by DeepMind, excelled in the CASP14 competition, achieving high precision prediction of protein monomer structure. Alphafold-multimer[2], an improved protein complex prediction algorithm based on Alphafold2, can also predict protein complexes, but its prediction accuracy is far from the experimental measurement accuracy. However, proteins often perform their biological functions by interacting with other biological macromolecules. Predicting the three-dimensional structure of protein-protein complexes is still a major challenge and has great research value. Therefore, due to the importance of residue-residue interactions between individual subunits of protein complexes, some works focus on the inter-chain contact prediction to help predict protein complex structure.

Some recent works have made some progress by exploiting multiple sequence alignment (MSA) information and deep learning-based methods to achieve inter-chain contact prediction. In order to avoid the generation of joint MSA, DeepHomo[3] and DRCon[4] only predict inter-chain contact maps for homodimers. Some works also put forward new ideas for solving the problem of MSA coupling between different species. According to the MSA of monomers, GLINTER[5] joints the MSA of heterodimers through the protocol proposed by ComplexContact[6], and CDPred[7] paires the two MSAs according to the biological classification ID of the sequence. Both methods feed MSA into a pretrained language model MSA Transformer[8] to generate attention maps, which imply coevolutionary information between residues. It is worth noting that, in addition to using

informations of MSA, these methods also extract the information of structure as features. For example, DeepHomo and CDPred introduce the structure information of the monomer through distance map, DRCon additionally extracts the intra-chain contact map of the protein monomer structure, and GLINTER obtains the three-dimensional structural information of two protein subunits through graph convolution. This suggests that the efficient introduction of monomer structural information plays an important role in inter-chain contact prediction. Of course, it is also feasible to predict the interaction between proteins only through monomer structure informations of proteins without using coevolution information. For example, MaSIf[9] use geometric deep learning to capture protein surface fingerprints, and PDII[10] try to learn inter-chain contact maps for protein complexes only from intra-chain contact maps by image inpainting.

Protein pre-training models can obtain protein sequence information, skipping the process of multiple sequence alignment and template search without losing the prediction accuracy. Its feasibility has been verified in the field of monomer structure prediction, such as OmegaFold[11], ESMFold[12], trRosettaX-Single[13] and so on. In addition to this, there are several studies predicting intra-chain contact maps for proteins with poor MSA, such as SPOT-Contact-Single[14] and Contact-Distil.[15]

Learning protein spatial structure information through graph attention networks has achieved good results on some protein prediction related tasks, for example, TAGPPI[16] for protein-protein interaction prediction and GAT-GO[17] for protein function prediction. These two methods input the structural contact map and the protein sequence embedding obtained by the language model into the graph attention network in order to learn the structural information of the protein. Besides, in order to better capture the residue-residue interaction information, Alphafold2 innovatively designs the triangular multiplication and the triangular attention modules to learn triangular constraints between residues. Subsequently, TANKBind[18] also designs a similar module to update the residue-residue interaction embedding for protein molecular docking.

Based on previous research, we develop PGT based on graph attention network and triangular multiplication update to predict the inter-chain contact maps of homodimers, starting from a single sequence without the process of multiple sequence alignment, and introducing structural information from subunits of protein complexes. To demonstrate the effectiveness of our method PGT, we follow DeepHomo's dataset to test the performance of PGT on two independent test sets.

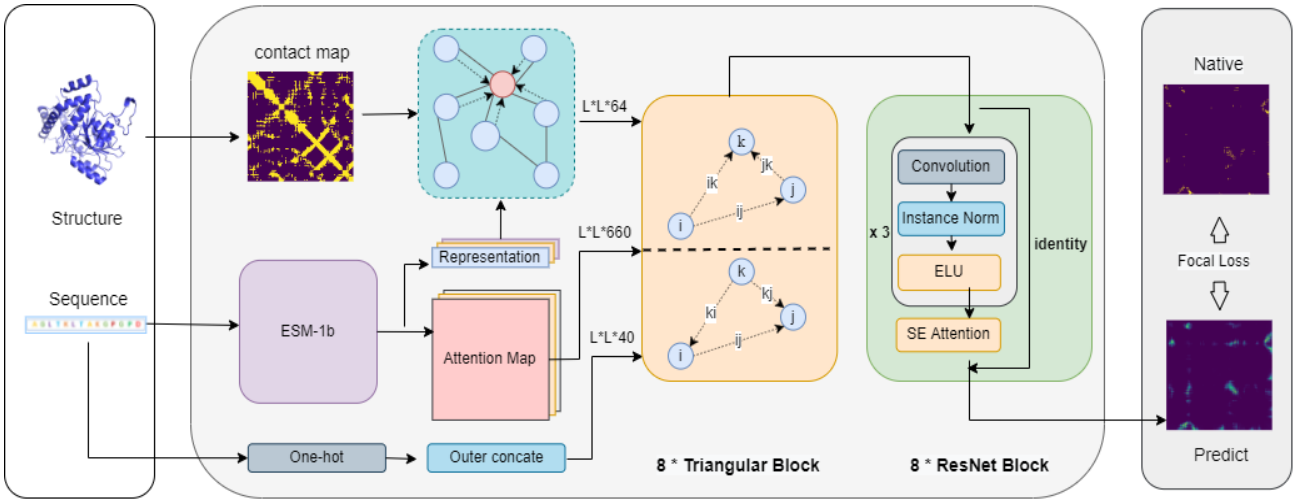

Fig. 1. The architecture of PGT. The complete network structure consists of two stages: 1) Features are obtained by ESM-1b and graph attention network 2) Interaction stage including 8 triangular multiplication blocks and 8 SE-ResNet blocks.

II. MATERIAL AND METHODS

A. Datasets

a) DeepHomo datasets: We trained PGT model using the homodimer datasets collected in DeepHomo, which only includes C2-symmetric homodimeric complex structures that have less than 30% sequence identity. Our train dataset includes 3532 structures and 300 structures are used as the valid set and 300 structures as the test set.

b) CASP-CAPRI datasets: This dataset include 28 homodimers from targets with experimental structures in the recent CASP-CAPRI competition. To analyze the impact of monomer structure quality, monomer structure predicted by Alphafold2 is also used as input to PGT model during evaluation.

B. Data preprocessing and Input features

a) Sequence-based features

Since the sequences of two chains of the homodimer are the same, we generate features from the monomer sequence, the single sequence is fed into the pretrained language model ESM-1b[19] to get the representation of the sequence, and we extract the attention maps from 20 attention heads in each layer (33 layers in total), which are symmetric and average product correction (APC) processed. In addition, the one-hot encoding based on the protein sequence is converted into a two-dimensional representation by outer concatenation, which is also used as part of the features.

b) Structure-based Features

In addition to sequence-based features, we also use the contact map of the monomer, where the contact map is

defined as the minimum distance between the heavy atoms of the residue pair is less than a cutoff, such as 8 Å .

C. Network architecture

The pipeline of PGT is shown in Figure 1. It include several parts: the encoding and features of the input protein, the graph attention network module that updates the sequence representation, the triangular multiplication modules and ResNet modules that learn the triangular relationship and interaction relationship between residues.

a) Details of Graph Attention Network

We describe the protein with a graph $G(V,E)$, each node $v_i \in V$ represents an amino acid, the node feature $h_i \in R^{1280}$ is the representation of each residue extracted by ESM-1b, E represents the adjacency matrix, defined by the contact map of the monomer structure, describing the relative positions between residues. We apply the graph attention network (GAT)[20] to update the representation of the residue. We hope that the GAT captures the spatial structure information of protein monomer structure. The node features, the residue embeddings extracted by the ESM-1b model, are used as the initial input of the graph attention network. Each node feature ${h^{l-1}}_i$ is updated by the *l-th* graph attention layer, and the output ${h^l}_i$ is calculated by using M-head attention

$$h^l{}_i = \Big\|_{m=1}^{M} \sigma\Big(\sum_{v_j \in N(v_i)} {\alpha_{ij}}^m W^m h_j \Big) \tag{1}$$

In the above equation, the GAT aggregate the information of neighbor nodes through the aggregation coefficient α_{ij},

$$\alpha_{ij} = \frac{\exp(Leaky\,\mathrm{Re}\,LU(w^T[Wh_i \,||\, Wh_j]))}{\sum_{v_k \in N(v_i)} \exp(Leaky\,\mathrm{Re}\,LU(w^T[Wh_i \,||\, Wh_k]))} \tag{2}$$

which is the normalized attention coefficient, N represents the number of neighbors v_k of node v_i, and $||$ represents concatenation operation, W represents learnable weight matrix. PGT applies two graph attention layers, each layer includes M = 4 attention heads, and the hidden layer is set to 128. Therefore, each node feature updated by the two graph attention layers is $h_i \in R^{128*4}$.

After the node features are updated by the graph attention network, a fully connected layer is used to reduce the number of 1D channels from $h_i \in R^{128*4}$ to $h_i \in R^{64}$. Then we use the residue representation to compute the symmetric 2D feature z_{ij},

$$diff_{ij} = \left| h_i - h_j \right| \tag{3}$$

$$mul_{ij} = \left| h_i \odot h_j \right| \tag{4}$$

$$z_{ij} = \mathrm{Re}\,LU(Instance[diff_{ij}, mul_{ij}]W + b) \tag{5}$$

This symmetrical feature $z_{ij} \in R^{64}$, which captures direct interactions between residues, was previously used by Bonnie Berger et al.[21] to predict protein-protein interactions. Where $\odot$ indicates the Hadamard product and $-$ indicates the element-wise difference, and W and b are learnable weights and biases. Instance and ReLU represent instance normalization and activation function, respectively.

b) Details of the triangular multiplication update

Here we represent the relationship between residues with three features, the symmetric feature $z_{ij} \in R^{64}$ obtained above, the attention maps $z_{ij} \in R^{660}$ extracted by the ESM-1b model, and the two-dimensional feature $z_{ij} \in R^{40}$, which is obtained by performing the outer concatenation operation on the one-hot encoding of sequence. The pair representation $z_{ij} \in R^{764}$ is obtained by concatenating these three features, and we regard z_{ij} as interaction between residues. Then followed by a block to reduce the number of channels from $z_{ij} \in R^{764}$ to $z_{ij} \in R^{64}$, the block includes 1*1 convolutional layer, instance normalization and Exponential Linear Unit (Elu) activation function.

To learn the triangular constraint relationship between residues on the graph, we update the pair representation z_{ij} through the triangular multiplication module which is essential for structure module of AlphaFold2[1]. In the triangular multiplication module, the representation z_{ij} of each edge is updated by receiving informations from all the other two edges that form a triangle with it. The update ways includes two forms of 'incoming' (formula 6) and 'outgoing'(formula 7), which have the advantages of symmetry and cheapness. In *l-th* layer $\forall(i,j)$, $\tilde{z}_{ij}{}^{(l)}$ is the update result of the pair representation $z_{ij}{}^{(l)}$:

$$\tilde{z}_{ij}{}^{(l)} = \Phi\Big(\sum_{k=1}^{n} a_{ki}{}^{(l)} \odot b_{kj}{}^{(l)}\Big) \odot g(z_{ij}{}^{(l)}) \tag{6}$$

$$\tilde{z}_{ij}{}^{(l)} = \Phi\Big(\sum_{k=1}^{n} a_{ik}{}^{(l)} \odot b_{jk}{}^{(l)}\Big) \odot g(z_{ij}{}^{(l)}) \tag{7}$$

where Φ consists of a layer norm function and a linear transformation. In the 'incoming' way (formula 6), a_{ki} and b_{kj} are calculated by z_{ki} and z_{kj} respectively represent the information of ki and kj edges on graph, the two edges with the ij edge form a triangle (as shown in Figure 1, the Triangular block). For the 'outcoming' way, the same is true. And $a_{ij}{}^{(l)}$ and $b_{ij}{}^{(l)}$ are both the gated linear transformations of $z_{ij}{}^{(l)}$,

$$a_{ij}{}^{(l)} = Linear(z_{ij}{}^{(l)}) \odot g(z_{ij}{}^{(l)}), a_{ij}{}^{(l)} \in R^{L*L*s} \tag{8}$$

$$g(z_{ij}{}^{(l)}) = sigmoid(Linear(z_{ij}{}^{(l)})) \tag{9}$$

Where L is the length of the protein monomer sequence, that is, the number of residues, s is the embedding size, which is set to 32. To capture the triangular constraints between residues on graph, we use 8 triangular multiplication bolcks, each block include two update ways of 'incoming' and 'outgoing'.

c) SE-ResNet module

Previous research work has shown that ResNet [3, 5, 22]can capture the interaction information between residues well, the triangular multiplication blocks are followed by 8 residual blocks to learn the interactions between residues. In addition to the regular convolutional layers, instance normalization, and Exponential Linear Unit (Elu) activation function included in each block, in order to capture the importance between different channels, we also add a channel attention squeeze-and-excitation block[23] after each block. Finally, the SE-ResNet module is followed by a 1*1 convolutional layer and a sigmoid layer for contact probability prediction.

D. Implementation and Training Details

The network was implemented in Pytorch, PGT was trained on DeepHomo's training dataset. Since our dataset is unbalanced, which means the number of non-interacting residue pairs are much larger than interacting residue pairs, so we chose focal loss[24] as the loss function, and α is set as 0.25 and γ is set to 1.5. Due to GPU limitations, we limit the sequence length of the protein fed into the network to 400, if it exceeds 400, we crop the first 400 residues and if it is less than 400, we will padding with 0. And batchsize is set to 1. After we trained our network for 20 epochs , the model converged to a stable solution. Finally, we selected the best model in the validation set according to the precision of the top L/30 inter-chain contact predictions.

III. RESULTS

A. Evaluation criteria

a) Top N precision

Since residue pair constraints can help to guide protein-protein docking and filter decoys with correct binding types, here we use the percentage of true positive contacts among the top N predicted contacts to evaluate the results of our methods. In addition, we also evaluate the accuracy of $top\ L/k$ $(k = 1,2,5,10,20)$ where L is the length of one monomer of the homodimer.

B. Evaluation of inter-chain contact prediction

a) Contact precision on DeepHomo datasets

As shown in Table 1, we compare the precision of our model with DeepHomo on DeepHomo test dataset (contains 300 complex structures). Since DRcon only consider the evaluation results for 218 structures in the test dataset, we also show our comparations with DRCon model on this subset which are shown in Table 2. The input of all three methods are the monomer structures, which are provided by DeepHomo dataset. To explore the effect of inter-chain contact distance thresholds on performance, here we use 6Å or 8Å ('D8' and 'D6' in TABLE I-II) as a cutoff to define residue-residue contacts.

TABLE I. PRECISION ON THE DEEPHOMO TEST SET(300)

Pred	methods			
	DeepHomo		***PGT***	
threshold	D8	D6	D8	D6
Top 10	55.6	47.9	68.96	60.03
L/30	57.2	49.9	69.3	61.24
L/20	54.9	46.9	68.58	59.61
L/10	52.1	42.2	67.33	56.8
L/5	47.8	35.7	64.71	52.41
L/2	39.4	25.9	60.29	43.3

TABLE II. PRECISION ON THE DEEPHOMO TEST SET(218)

Pred	methods			
	DRCon		***PGT***	
threshold	D8	D6	D8	D6
L/10	56.5	50.17	68.31	57.66
L/5	53.75	47.1	65.88	53.31
L	41.91	27.81	55.07	34.05

As shown in Table I, PGT achieve the precision of 64.71% for top L/5 inter-chain contact predictions, which is substantially higher than DeepHomo's 47.80%. Here our train dataset and test dataset are the same as DeepHomo, so this comparation shows that our model can learn inter-chain contact better. As shown in Table II, when test on a subset with 218 structures, PGT achieves the precision of 65.88% for top L/5 inter-chain contact predictions, which is also substantially higher than DRcon's 53.75%. And we find that the contact precision of PGT will degrade when a smaller threshold is used.

b) Contact precision on CASP-CAPRI datasets

We use 8Å as a distance threshold for residue-residue contacts and compare PGT with DeepHomo, Glinter on the CASP-CAPRI dataset of 28 complex structures. When compare with DeepHomo and Glinter, the results are evaluated on monomer structures based on AlphaFold2's predicted although only native structures are used in training pipeline. Besides, here we also show the results with unbound monomer structures are used as the initial monomer structure. As shown in Table III, 'AF2' means that the monomer structure is predicted by Alphafold2, and 'native' means the monomer structure is extracted from the complex structure. We use the monomer structure predicted by Alphafold2 as input for the Deephomo server to obtain the inter-chain contact prediction, the prediction results of the Deephomo server only contains the upper triangle of the inter-chain contact map, which is converted to a diagonally symmetric full contact map, table III shows the results of our evaluation. And the evaluation results of Glinter from the literature[7]. PGT achieve substantially higher precision than DeepHomo

and Glinter. Besides, we find that the results based on AlphaFold2's predicted structures perform very close to results when native structures are used, which means our method is not very sensitive to monomer structure quality.

TABLE III. PRECISION ON THE CASP-CAPRI DATASETS

Pred	methods			
	DeepHomo(AF2)	*Glinter(AF2)*	*PGT (AF2)*	*PGT (native)*
Top 10	54.28	54.07	59.28	62.5
L/30	51.27	#	60.44	62.76
L/20	49.82	#	59.21	62.06
L/10	46.98	50.54	54.56	58.15
L/5	44.11	48.09	49.48	55.65
L/2	36.95	41.9	42.55	49.88

For example, when the monomer structure predicted by Alphafold2 is used as input of PGT, the top L/10 inter-chain contact precision of PGT is 54.56%, which is substantially higher than 46.98% of DeepHomo and 50.54% of Glinter.

C. Ablation study

To investigate the impact of network modules such as graph attention network and triangular multiplication update on the performance of our model, we implement two ablation experiments. The first one is 'no_GAT' where we remove the graph attention network, which is equivalent to the whole model lacks the structural information of protein monomers. The second one is 'no_ triangular ' which means we replaced the 8 triangular multiplication blocks in the model with 8 blocks of SE-Resnet. We retrained these two models, and Table IV shows the evaluation results on the CASP-CAPRI dataset.

TABLE IV. ABLATION STUDY COMPARISON

Pred	methods		
	no_GAT	*no_ triangular*	*PGT*
Top 10	45.35	43.92	59.28
L/30	45.25	45.33	60.44
L/20	44.76	42.01	59.21
L/10	42.98	40.84	54.56
L/5	40.55	37.15	49.48
L/2	36.06	30.52	42.55

The ablation results show that if we remove triangular multiplication update or graph attention network, the performance of our model decreased by about 30% almost for all evaluation metric. Both triangular blocks and GAT are important for inter-chain contacts prediction.

D. Case study

As shown in Figure 2, taking two targets(T0805, T0843 from CASP-CAPRI) as examples, we show the comparison between the predicted contact map and the real contact map on different models, where 'PGT' represents our final model, 'no_triangular' means that we replace the 8 triangular multiplication blocks in the 'PGT' model with 8 SE-ResNet blocks, and 'DeepHomo' comes from the result obtained by sending the target to the DeepHomo server, they are all predicted inter-chain residues contact probability. 'Groundtruth' is the contact map obtained according to the experimental structure, with a distance threshold of 8 Å.

The first row in Figure 2 shows the evaluation results of target T0805, where we compare the contact probability matrix predicted by 'PGT', 'no_triangular' and the real contact map. We find that the inter-chain contact map predicted by 'PGT' is more similar to the real contact map than 'no_triangular', and 'no_triangular' tends to predict many non-interacting residue pairs as interacting, indicating more false positives, which also demonstrates the importance of triangular multiplication module for the model.

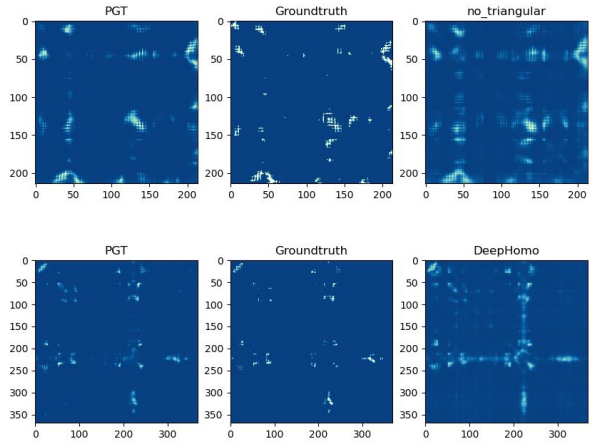

Fig. 2. Model-predicted contact probability matrices and ground-truth contact maps for T0805 and T0843

IV. DISSCUSION

When the input features are taken into consideration, firstly we don't use multiple sequence alignment (MSA) which is important for contact map prediction as reported by DeepHomo. Instead, our model is based on single sequence, here we use embeddings and attention maps extracted by the self-supervised language model. Besides, we discard many hand-crafted features, such as secondary structure features, hydrophobic features, PSSM matrix extracted by DeepHomo and co-evolution information used in DRCon from CCPred output.

In addition, we introduce some useful modules like GAT and triangular multiplication update. Following DeepHomo and DRCon, we regard contact map or distance matrix of the monomer structure as one type input feature. We interpret the contact map of the tertiary structure as the adjacency matrix to build the graph model, and specially design the graph attention network to learn structural information. Besides, we find that triangular multiplication modules are very useful for contact map prediction, which was firstly introduced by AlphaFold2. The model with triangular multiplication update can learn the triangular constraints that are difficult to be captured by ResNet. We know that the triangular attention module is also useful for contact map prediction problem, which is also a key module of AlphaFold2. Here our network

is lightweight and in the future work we will consider how to add triangular attention block to our model.

V. CONCLUSION

We propose a new method combined with protein language model, graph attention network, and the triangular multiplication update for predicting inter-chain contact maps specifically for C2-type homodimers, which does not require multiple sequence alignments and only single sequence and intra-chain contact map are included. Evaluating on two independent test sets, the results show that PGT outperforms existing methods such as DeepHomo, DRCon and Glinter. Besides, the results of our ablation experiments show that both the graph attention network and the triangular multiplication update are essential in our model, which is capable of capturing some spatial information or triangular informations. In conclusion, our model can be effectively used for homologous complex inter-chain contact prediction.

The ultimate goal of our inter-chain prediction is to improve the accuracy of protein docking algorithms by distinguishing near-native conformations from a large number of decoys. In this paper, our method can effectively learn the interaction informations of residue pairs between chains. Next, we hope to continue to study the topic of protein-protein docking on this basis. We are interested in protein-protein docking algorithms based on SE(3) equivariance[25]. In future research, we hope to combine the PGT with SE(3) equivariance to predict the structure of protein complex structures end-to-end.

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REFERENCES

[1] J. Jumper et al., "Highly accurate protein structure prediction with AlphaFold," Nature, vol. 596, no. 7873, pp. 583-589, 2021/08/01 2021, doi: 10.1038/s41586-021-03819-2.

[2] R. Evans et al., "Protein complex prediction with AlphaFold-Multimer," bioRxiv, p. 2021.10.04.463034, 2022, doi: 10.1101/2021.10.04.463034.

[3] Y. Yan and S.-Y. Huang, "Accurate prediction of inter-protein residue-residue contacts for homo-oligomeric protein complexes," Briefings in Bioinformatics, vol. 22, no. 5, Sep 2021, Art no. bbab038, doi: 10.1093/bib/bbab038.

[4] R. S. Roy, F. Quadir, E. Soltanikazemi, and J. Cheng, "A deep dilated convolutional residual network for predicting interchain contacts of protein homodimers," Bioinformatics, vol. 38, no. 7, pp. 1904-1910, Mar 28 2022, doi: 10.1093/bioinformatics/btac063.

[5] Z. Xie and J. Xu, "Deep graph learning of inter-protein contacts," Bioinformatics, vol. 38, no. 4, pp. 947-953, Feb 15 2022, doi: 10.1093/bioinformatics/btab761.

[6] H. Zeng et al., "ComplexContact: a web server for inter-protein contact prediction using deep learning," (in eng), Nucleic Acids Res, vol. 46, no. W1, pp. W432-w437, Jul 2 2018, doi: 10.1093/nar/gky420.

[7] Z. Guo, J. Liu, J. Skolnick, and J. Cheng, "Prediction of inter-chain distance maps of protein complexes with 2D attention-based deep neural networks," bioRxiv, p. 2022.06.19.496734, 2022, doi: 10.1101/2022.06.19.496734.

[8] R. Rao et al., "MSA Transformer," bioRxiv, p. 2021.02.12.430858, 2021, doi: 10.1101/2021.02.12.430858.

[9] P. Gainza et al., "Deciphering interaction fingerprints from protein molecular surfaces using geometric deep learning," Nature Methods, vol. 17, no. 2, pp. 184-+, Feb 2020, doi: 10.1038/s41592-019-0666-6.

[10] H. Huang, C. Zeng, and X. Gong, "Inter-protein contact map generated only from intra-monomer by image inpainting," in 2021 IEEE International Conference on Bioinformatics and Biomedicine (BIBM), 9-12 Dec. 2021 2021, pp. 131-136, doi: 10.1109/BIBM52615.2021.9669709.

[11] R. Wu et al., "High-resolution de novo structure prediction from primary sequence," ed: bioRxiv, 2022.

[12] Z. Lin et al., "Language models of protein sequences at the scale of evolution enable accurate structure prediction," 2022.

[13] W. Wang, Z. Peng, and J. Yang, "Single-sequence protein structure prediction using supervised transformer protein language models," bioRxiv, 2022.

[14] J. Singh, T. Litfin, J. Singh, K. Paliwal, and Y. Zhou, "SPOT-Contact-LM: improving single-sequence-based prediction of protein contact map using a transformer language model," Bioinformatics, vol. 38, no. 7, pp. 1888-1894, Mar 28 2022, doi: 10.1093/bioinformatics/btac053.

[15] Q. Wang et al., "Contact-Distil: Boosting Low Homologous Protein Contact Map Prediction by Self-Supervised Distillation," Proceedings of the AAAI Conference on Artificial Intelligence, vol. 36, pp. 4620-4627, 06/28 2022, doi: 10.1609/aaai.v36i4.20386.

[16] B. Song, X. Luo, X. Luo, Y. Liu, Z. Niu, and X. Zeng, "Learning spatial structures of proteins improves protein-protein interaction prediction," Briefings in Bioinformatics, vol. 23, no. 2, Mar 10 2022, Art no. bbab558, doi: 10.1093/bib/bbab558.

[17] B. Lai and J. Xu, "Accurate protein function prediction via graph attention networks with predicted structure information," Briefings in Bioinformatics, vol. 23, no. 1, Jan 17 2022, Art no. bbab502, doi: 10.1093/bib/bbab502.

[18] W. Lu, Q. Wu, J. Zhang, J. Rao, C. Li, and S. Zheng, "TANKBind: Trigonometry-Aware Neural NetworKs for Drug-Protein Binding Structure Prediction," bioRxiv, 2022.

[19] A. Rives et al., "Biological structure and function emerge from scaling unsupervised learning to 250 million protein sequences," Proceedings of the National Academy of Sciences of the United States of America, vol. 118, no. 15, Apr 13 2021, Art no. e2016239118, doi: 10.1073/pnas.2016239118.

[20] P. Velickovic, G. Cucurull, A. Casanova, A. Romero, P. Lio', and Y. Bengio, "Graph Attention Networks," ArXiv, vol. abs/1710.10903, 2018.

[21] S. Sledzieski, R. Singh, L. Cowen, and B. Berger, "D-SCRIPT translates genome to phenome with sequence-based, structure-aware, genome-scale predictions of protein-protein interactions," Cell Systems, vol. 12, no. 10, pp. 969-+, Oct 20 2021, doi: 10.1016/j.cels.2021.08.010.

[22] K. He, X. Zhang, S. Ren, and J. Sun, "Deep Residual Learning for Image Recognition," in 2016 IEEE Conference on Computer Vision and Pattern Recognition (CVPR), 27-30 June 2016 2016, pp. 770-778, doi: 10.1109/CVPR.2016.90.

[23] J. Hu, L. Shen, and G. Sun, "Squeeze-and-Excitation Networks," in 2018 IEEE/CVF Conference on Computer Vision and Pattern Recognition, 18-23 June 2018 2018, pp. 7132-7141, doi: 10.1109/CVPR.2018.00745.

[24] T. Y. Lin, P. Goyal, R. Girshick, K. He, and P. Dollar, "Focal Loss for Dense Object Detection," (in eng), IEEE Trans Pattern Anal Mach Intell, vol. 42, no. 2, pp. 318-327, Feb 2020, doi: 10.1109/tpami.2018.2858826.

[25] O. Ganea et al., Independent SE(3)-Equivariant Models for End-to-End Rigid Protein Docking. 2021.