Does Inter-Protein Contact Prediction Benefit from Multi-Modal Data and Auxiliary Tasks?

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Hypotheses

Proteins are essential biomolecules of life. Proteins are represented by 1D sequences folding into 3D structures (**multi-modality**) and interact to form assemblies to function (**multi-scale functionality**). Unlike protein structure prediction, protein complex/assembly structure prediction has yet seen as successful technology breakthroughs. We hypothesize improvements might root from two perspectives:

- incorporating **multi-modal features** for inputs, and
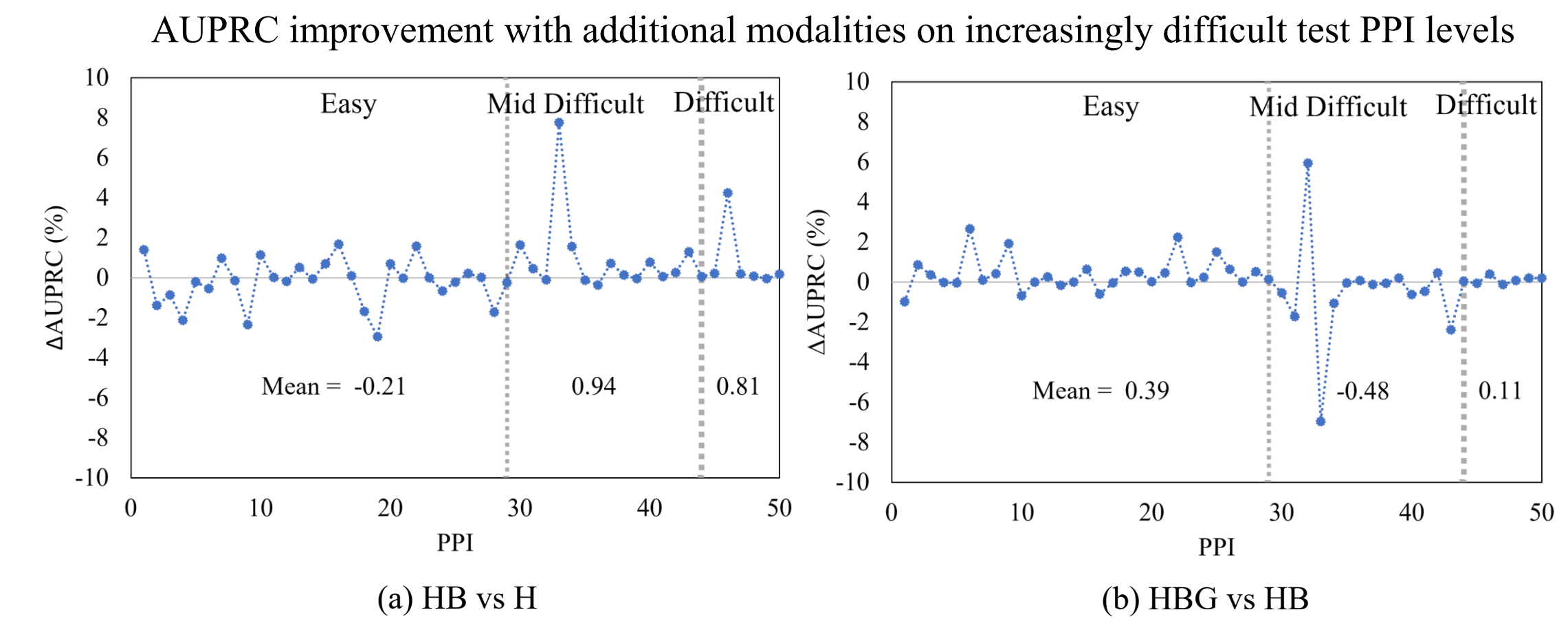- Synergizing contact predictions with **auxiliary predictive tasks**.
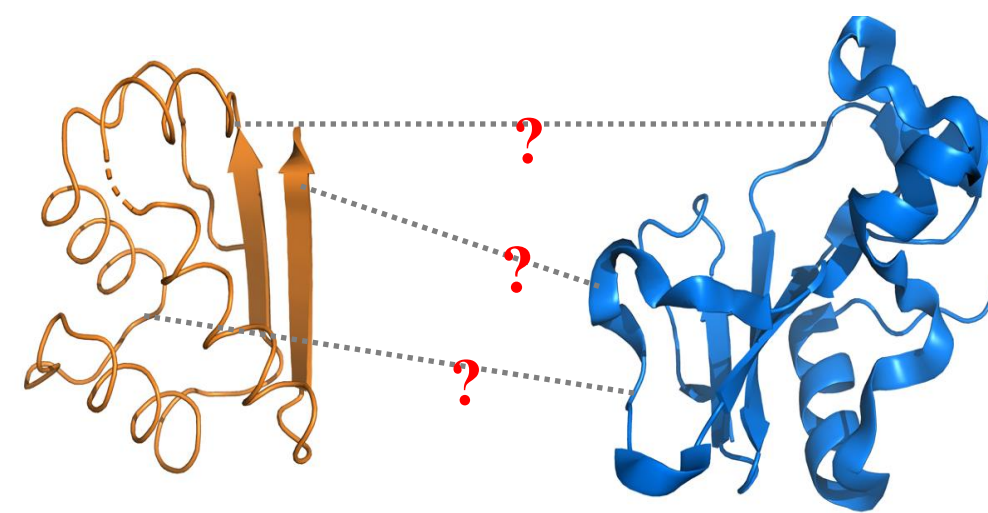
## Model Architectures in Experiments
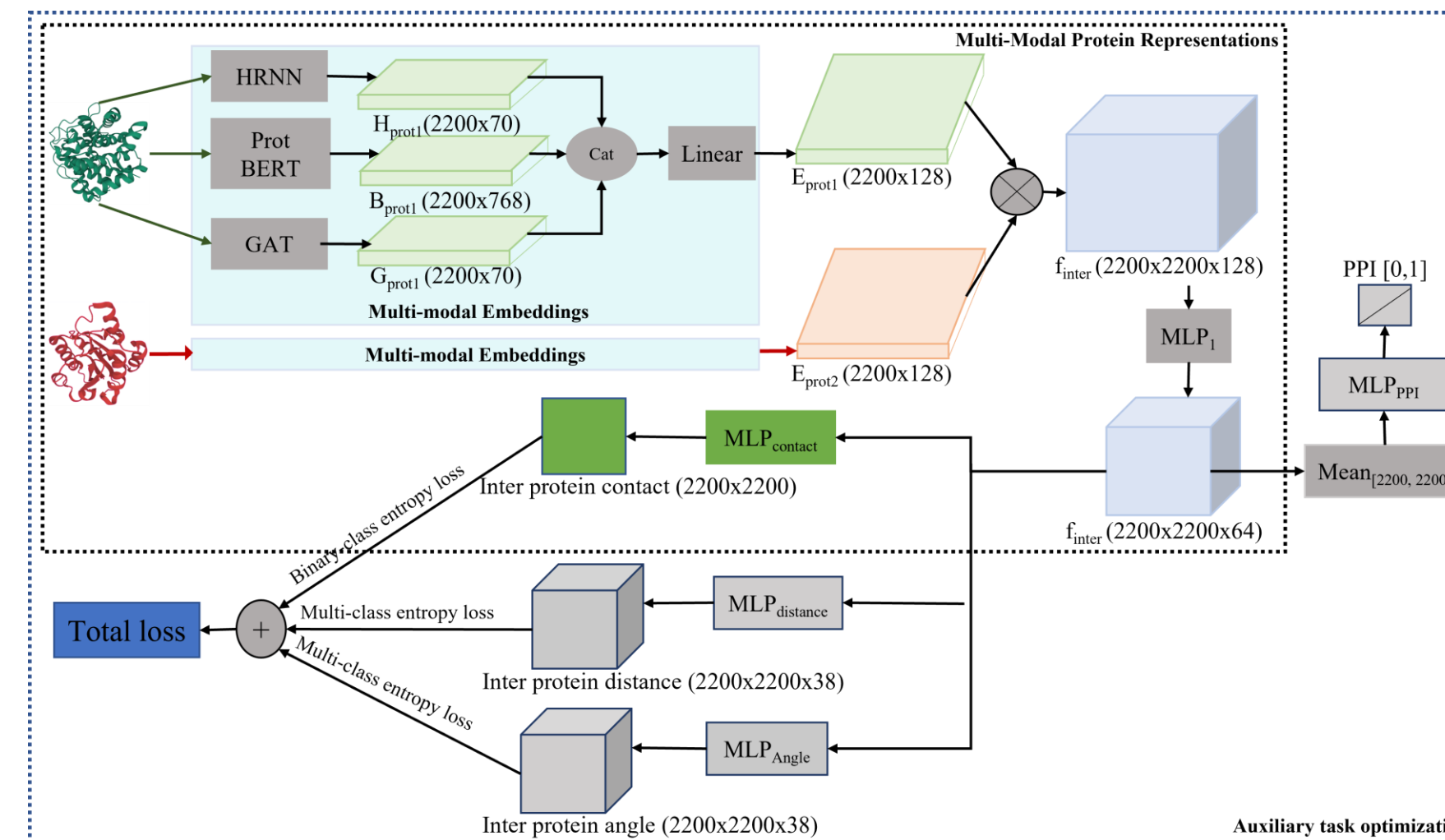
A general framework of model architecture using encoders, common and task-specific MLP layers.

Results: Multi-Modal Features

AUPRC improvement with additional modalities on increasingly difficult test PPI levels

(a) HB vs H

(b) HBG vs HB

- **83.3% of difficult, 73.3% of mid difficult and 41.4% of rigid** PPI samples have improved AUPRC with HB
- HBG in comparison to HB results in **66.6% of difficult, 33.3% of mid difficult and 69% of rigid PPI samples** AUPRC improvement

Assay Pipeline
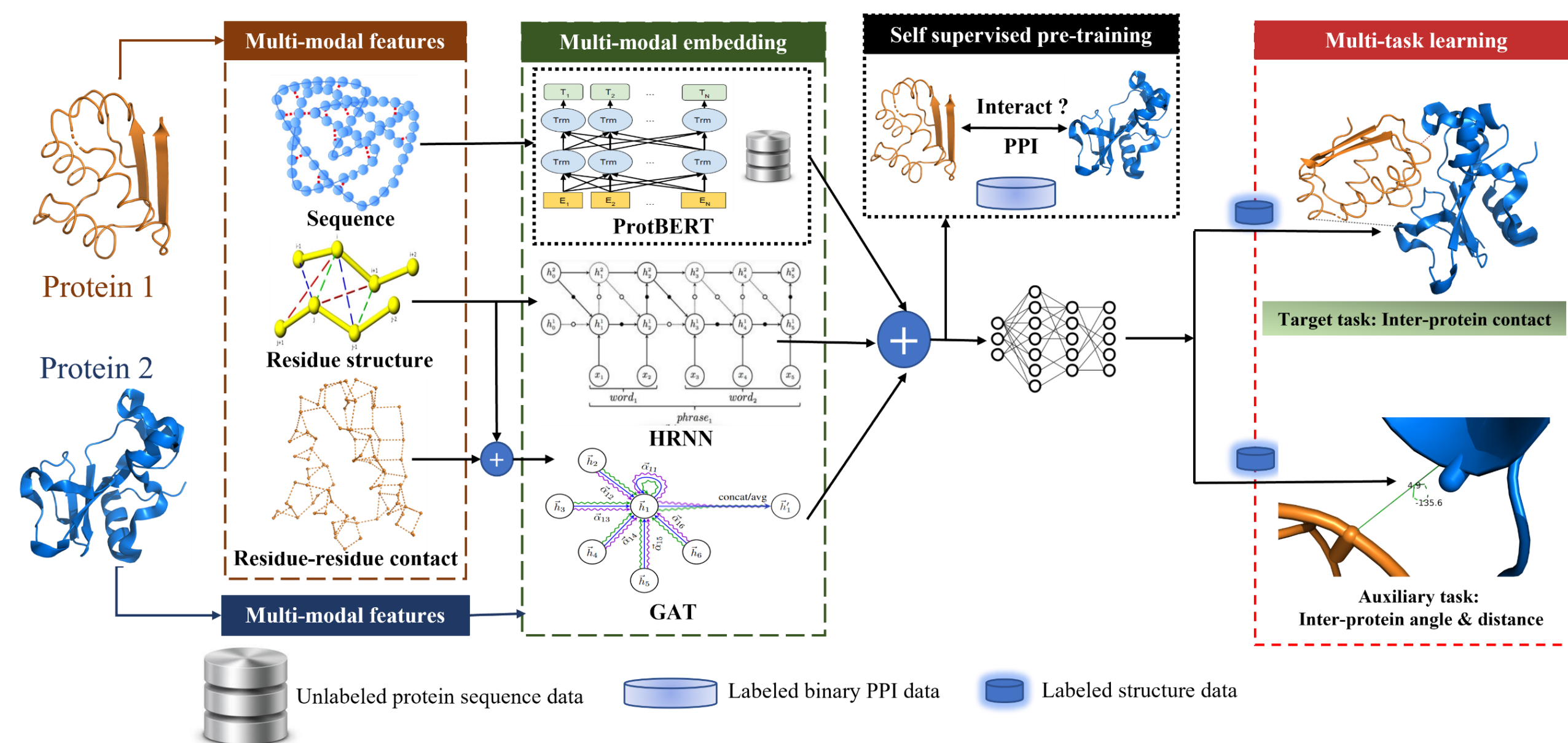
Given two proteins, we extract three of their modalities as features:

- protein sequences (encoded with HRNN) [1], evolutionary (with ProtBERT) [2] and structural information (with GAT) [3]
- For optimization objectives, we use multiple auxiliary tasks (distances and angles)
- Knowledge of binary protein-protein interaction (PPI) is introduced via pre-training.

Results: Multi-Modal Features

Multi-modal impact on AUPRC (%) distribution of test set.
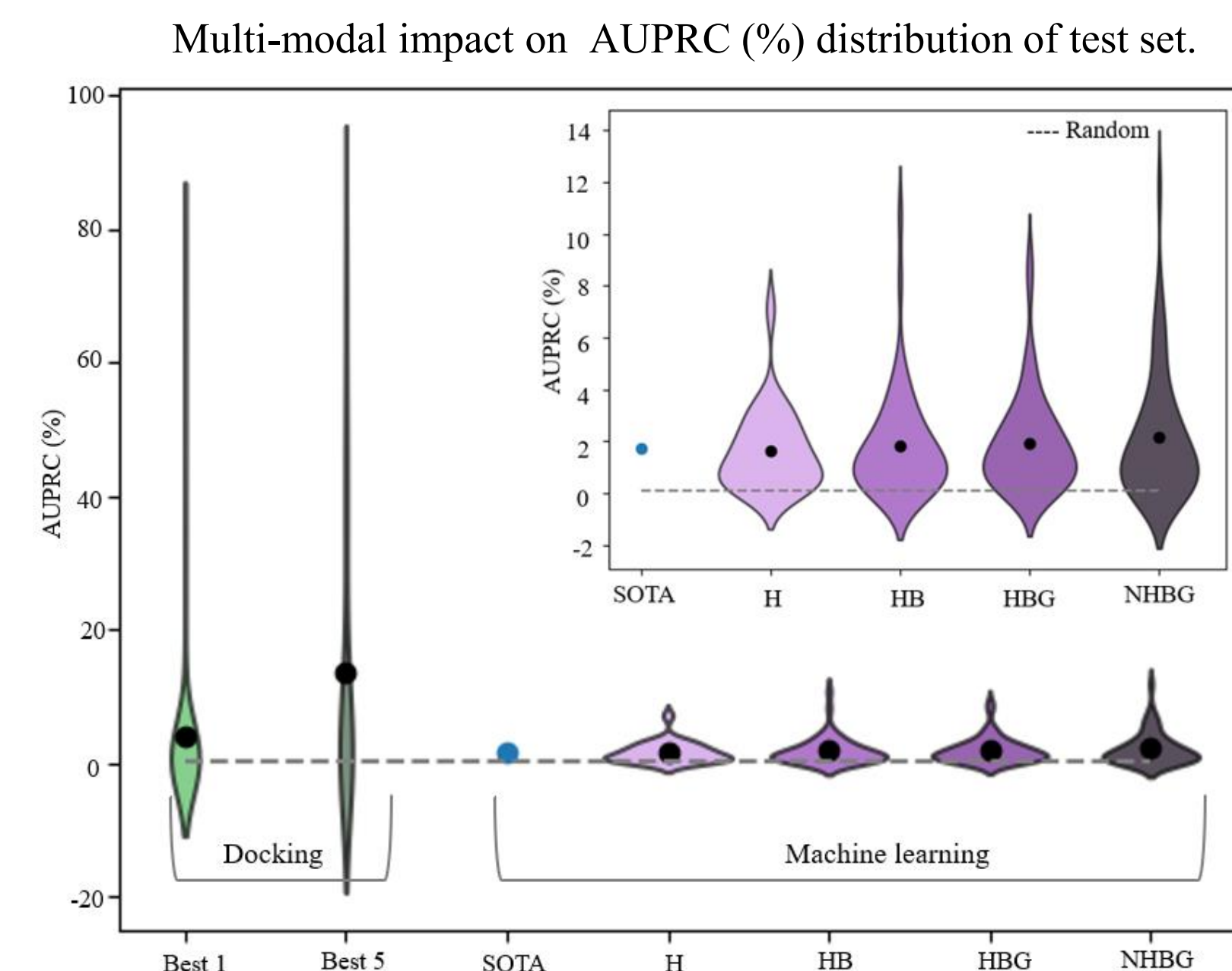
- Multi-modal incorporating model (NHBG) **improved 18.75%** compared to single modality (H)
- Best performing model (NHBG) **improved 34.38%** compared to single modality (H)
- Best test AUPRC also **surpasses SOTA score by 26.47%**

Results: Auxiliary Tasks

Auxiliary task learning
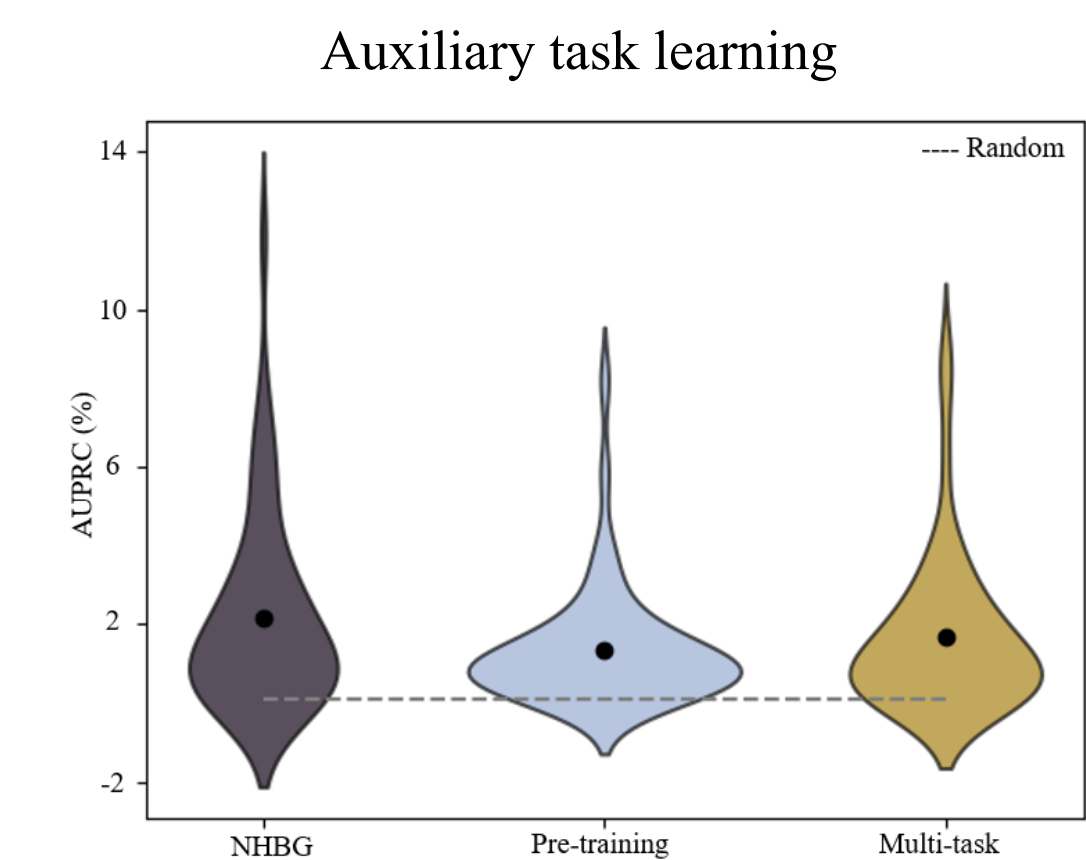
We do not observe the performance gains from any auxiliary tasks.

- Fine-grained distances and angles prediction might enforce more complicated (pseudo) predictions hurting generalizability
- Binary PPI outcome is overly simplified to indicate inter-contact maps

References

[1] Salah Hihi and Yoshua Bengio. Hierarchical recurrent neural networks for long-term dependen-cies. Advances in neural information processing systems, 8, 1995.

[2] Ahmed Elnaggar et al. Prottrans: towards cracking the language of lifes code through self-supervised deep learning and high performance computing. IEEE transactions on pattern analysis and machine intelligence, 2021

[3] Petar Veli`ckovi´c, Guillem Cucurull, Arantxa Casanova, Adriana Romero, Pietro Lio, and Yoshua Bengio. Graph attention networks. arXiv preprint arXiv:1710.10903, 2017..