Interpreting Transformer Attention Weights in 2D information Compound–Protein Interaction Models

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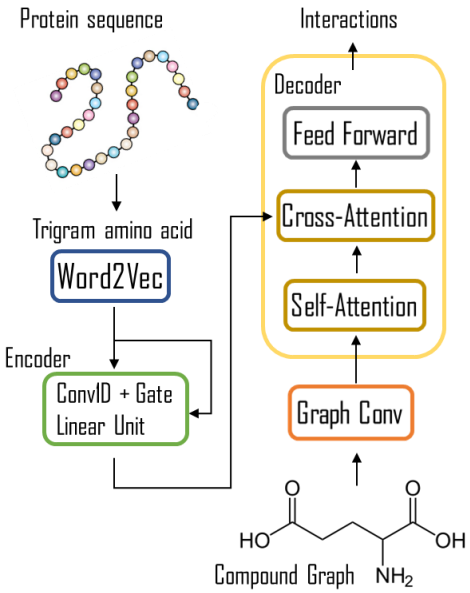
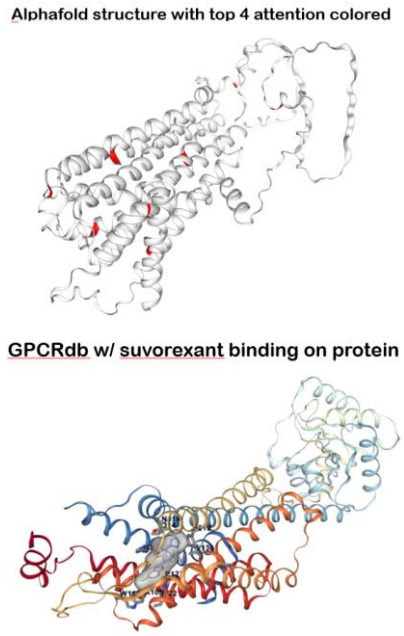
We investigate attention weight interpretation in Transformer-based compound–protein interaction models to enhance predictive accuracy using 2D representations. Building on TransformerCPI[1], we trained three variants—bn_gcn, bn_gcn_cls, and TylorCE_cls (using a TaylorSoftmax-based loss[2]). We extracted tri-gram level attention weights and combined them with solvent accessible surface area (SASA) data, including a variant focusing on α-helical regions, to probe their role in binding site prediction. While high attention did not always correlate with high SASA, certain moderately exposed regions exhibited strong attention, suggesting a multifactorial influence on model focus. Classical ML models (Random Forest and Linear Regression) applied to these features revealed that Random Forests generally provided better predictive performance, emphasizing the non-linear relationships in the data. Our findings highlight the dual role of attention weights as both predictive features and interpretable signals in CPI modeling.





References

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2. Feng, L.; Shu, S.; Lin, Z.; Lv, F.; Li, L.; An, B. Proceedings of the Twenty-Ninth International Joint Conference on Artificial Intelligence, **2020**, 29, 2206–2212