LIGAND-PROTEIN BINDING SITE ANNOTATION USING GRAPH NEURAL NETWORKS
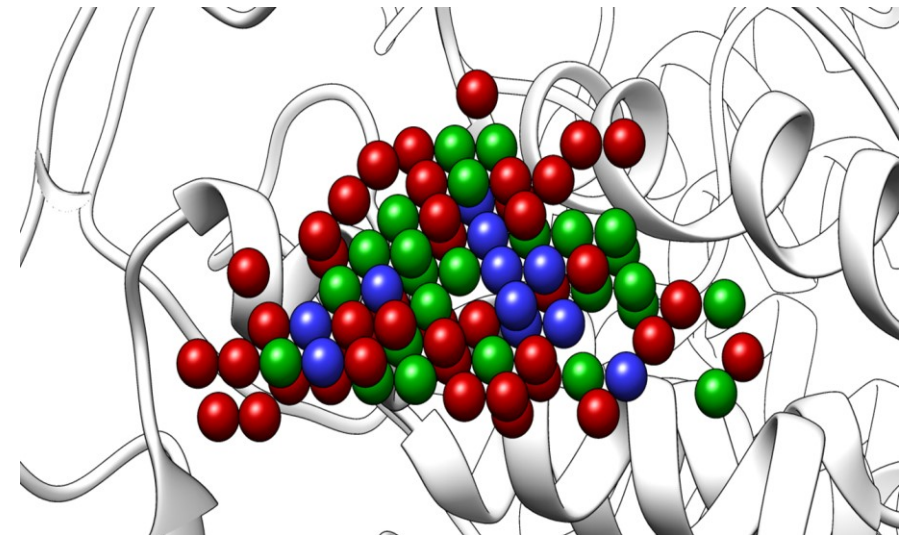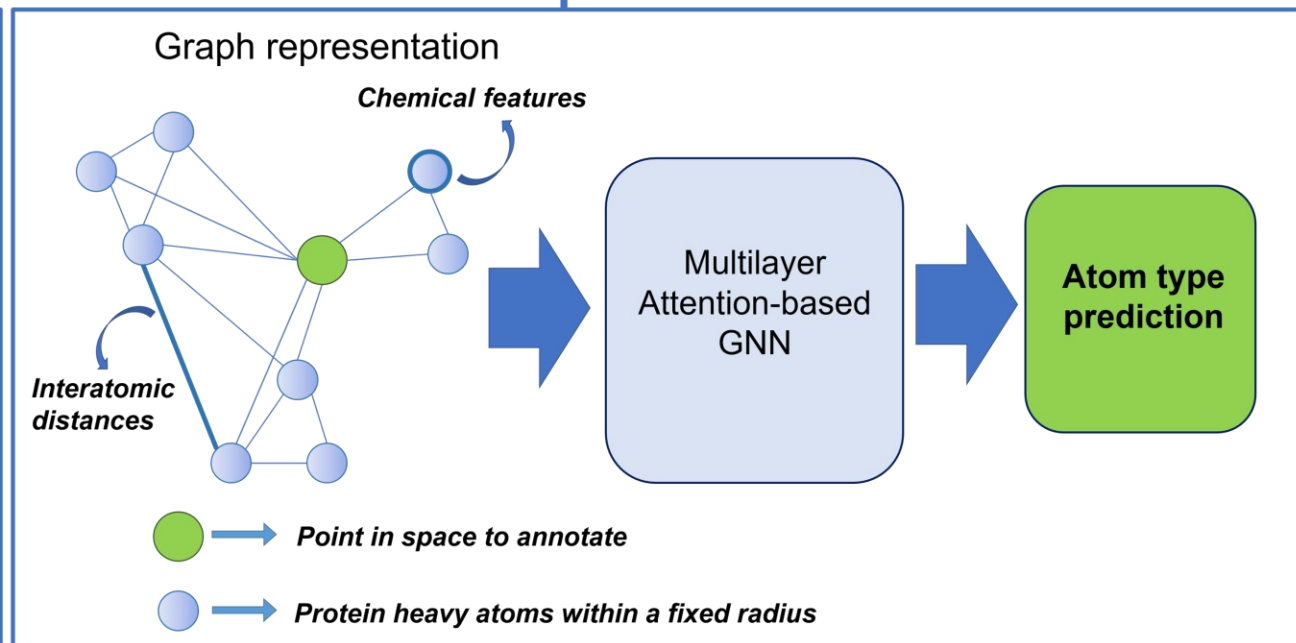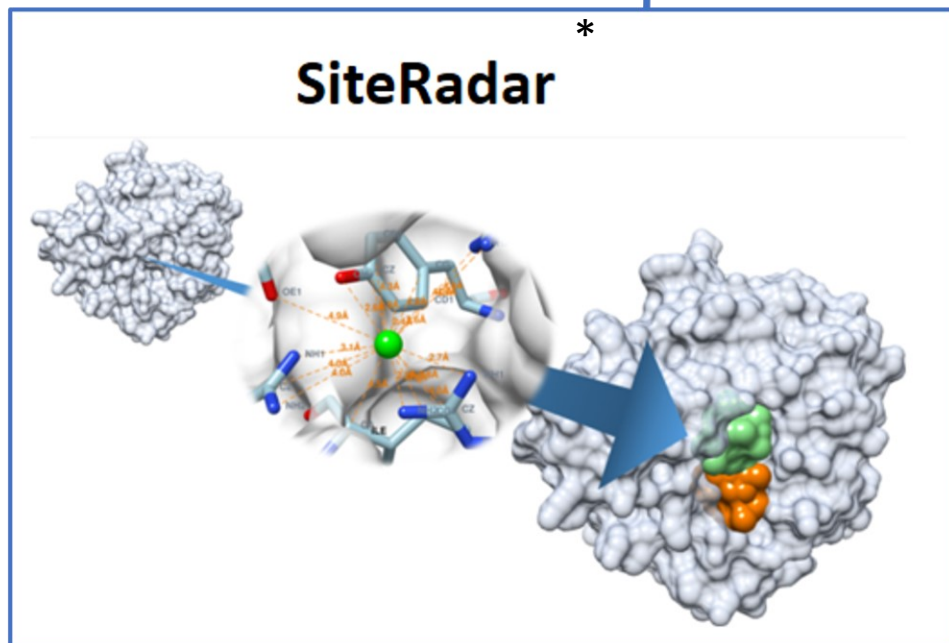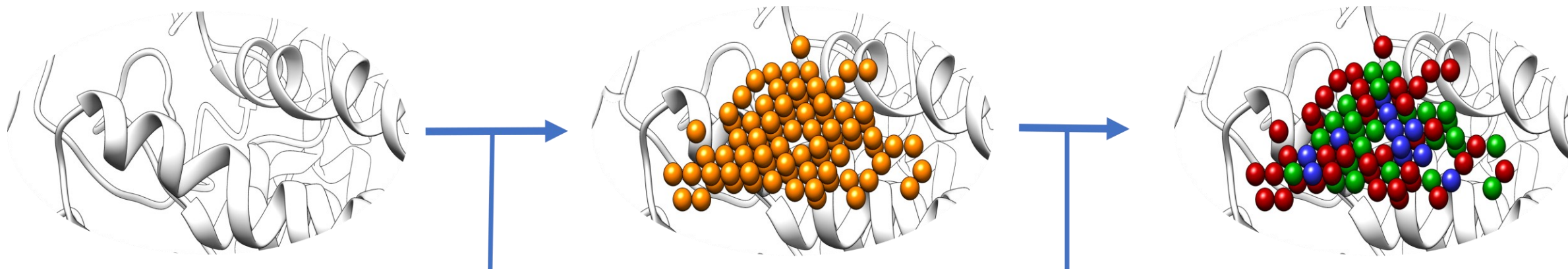
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Purpose of the study

➢ Develop an AI-based method for binding site annotation

➢ Evaluate its effectiveness

➢ Evaluate its application for solving practical tasks:
  ➢ ligand-protein binding sites classification
  ➢ ligand-protein affinity prediction

Binding site annotation Model

SiteRadar *

Graph representation

Chemical features

Interatomic distances

Multilayer Attention-based GNN

Atom type prediction

→ Point in space to annotate

→ Protein heavy atoms within a fixed radius

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Binding site annotation Results

- Two energy based methods were selected for evaluation

- Our predicted classes were grouped in the broader categories of HD, HA and HC

- Developed approach showed better or comparable results

| MODEL	FRACTION OF CORRECTLY IDENTIFIED ATOMS		
	HD	HA	HC
Our model	0.644	0.792	0.925
AutoSite*	0.657	0.686	0.908
AutoLigand**	0.201	0.447	0.717

Binding site classification Model
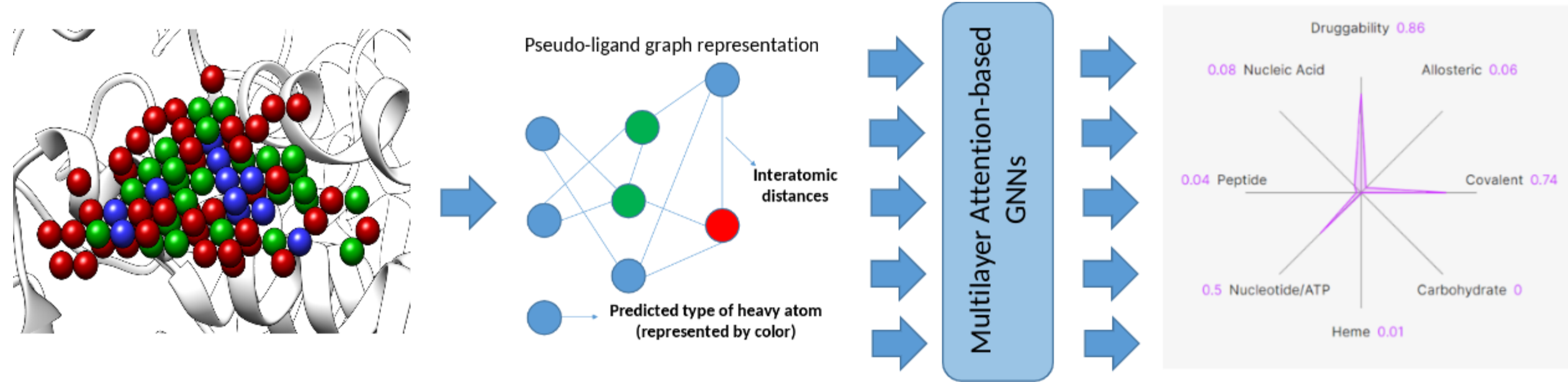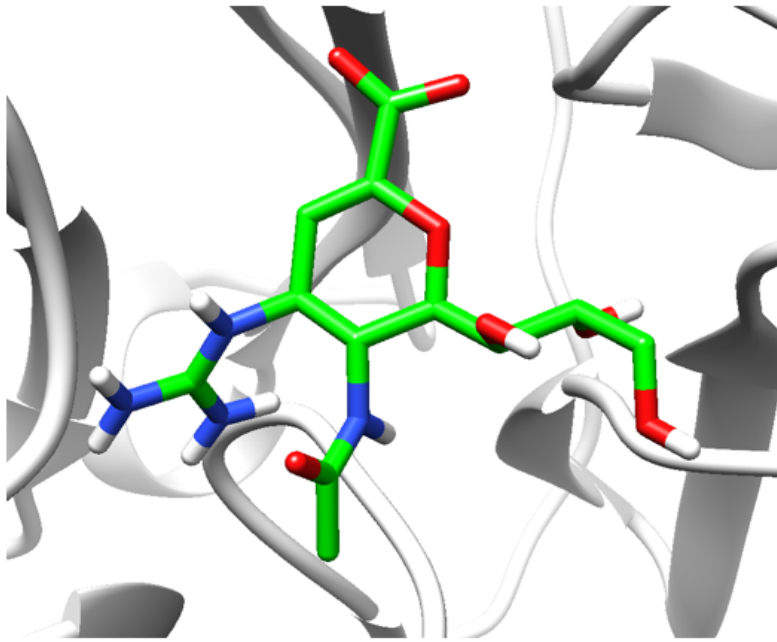
Binding site classification Results

➢Classification accuracy was measured on an independent test

➢The example illustrates prediction of properties for BTK active site (PDB ID 8UD2)
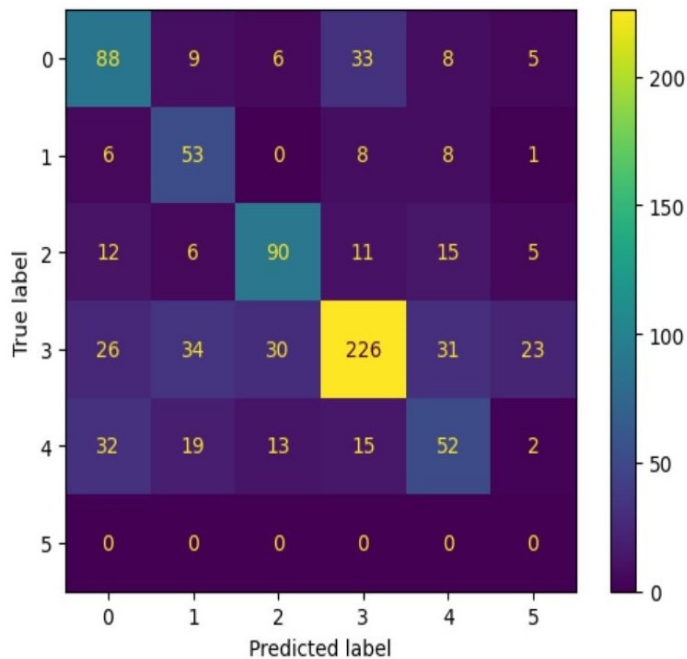
Classes:
0 - Nucleic acid
1 - Carbohydrate
2 - Heme
3 - Nucleotide
4 - Peptide
5 - the values of all five classes are less than the threshold
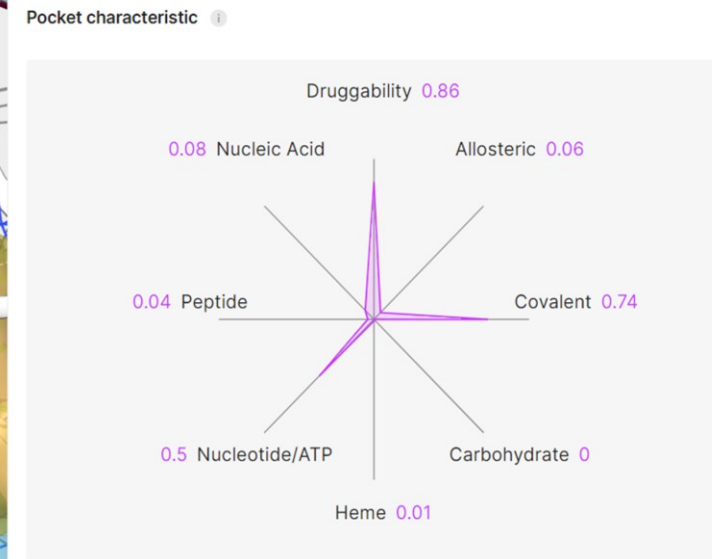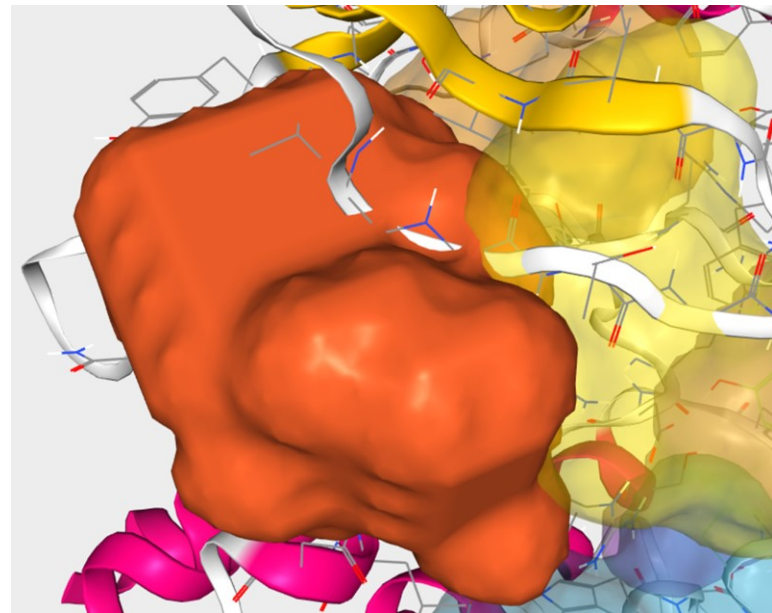
Ligand-protein affinity prediction Model
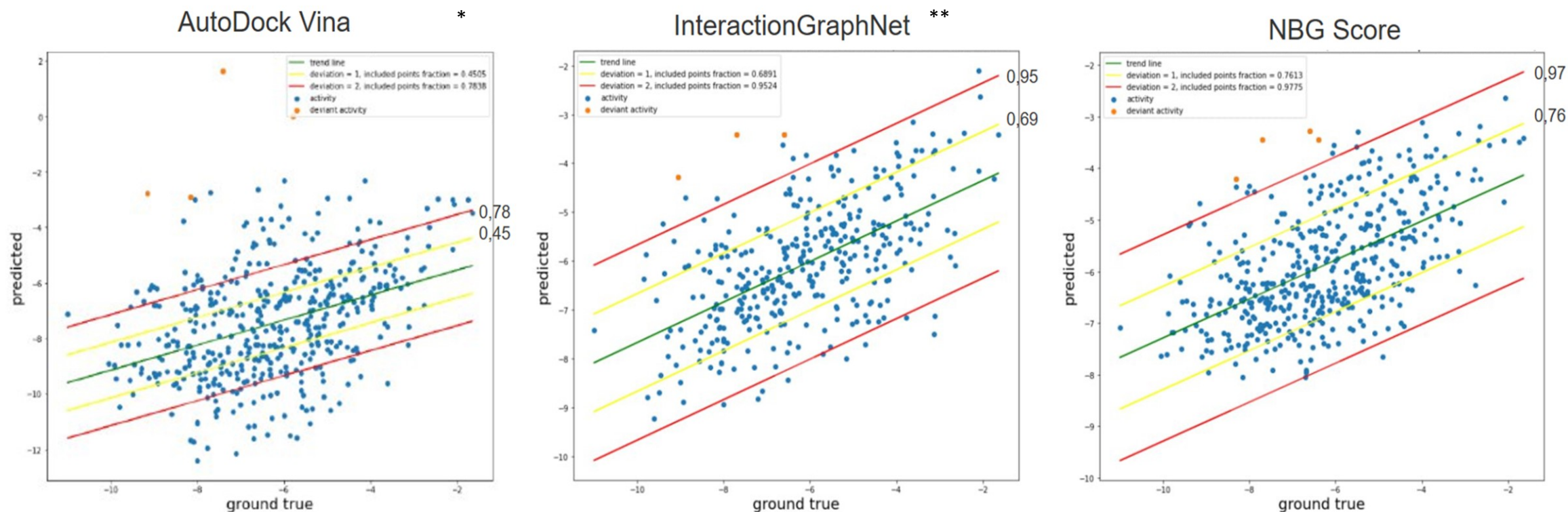

Ligand graph with node features

Multilayer Attention-based GNN

Predicted pK_d

Ligand-protein affinity prediction Results

Developed model showed comparable results with modern GNN approach InteractionGraphNet and significantly outperformed AutoDock Vina

Conclusion

➢New approach was developed for binding site annotation

➢The developed method was utilized to train models for:

  ➢binding site classification

  ➢small molecule affinity prediction

➢Developed solutions demonstrated performance on par with modern solutions