MolKGNN: Interpretable Chirality-Aware Graph Neural Network for Drug Discovery

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ABSTRACT

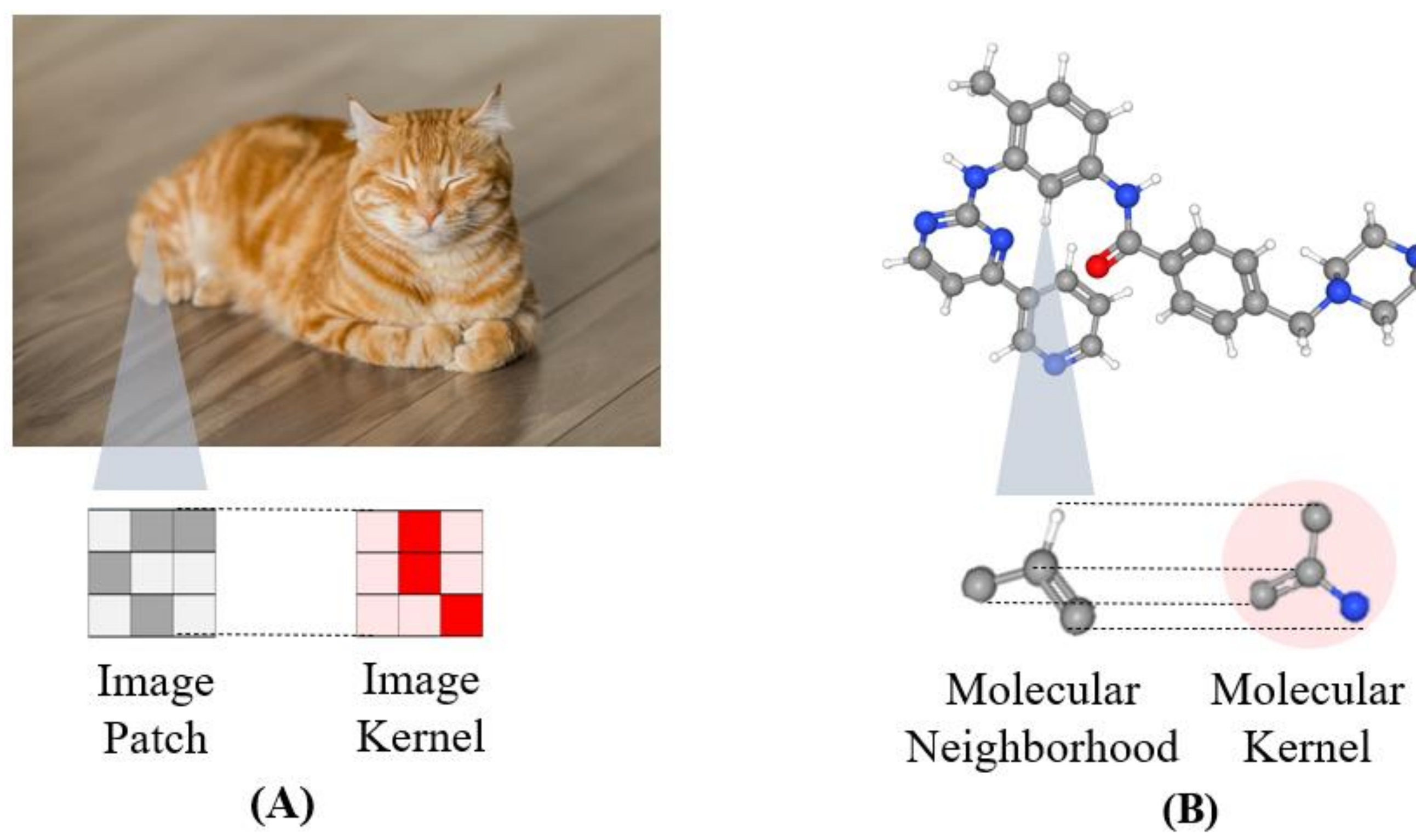


Fig. 1 MolKGNN extends convolution specifically for drug discovery

BACKGROUND AND SIGNIFICANCE

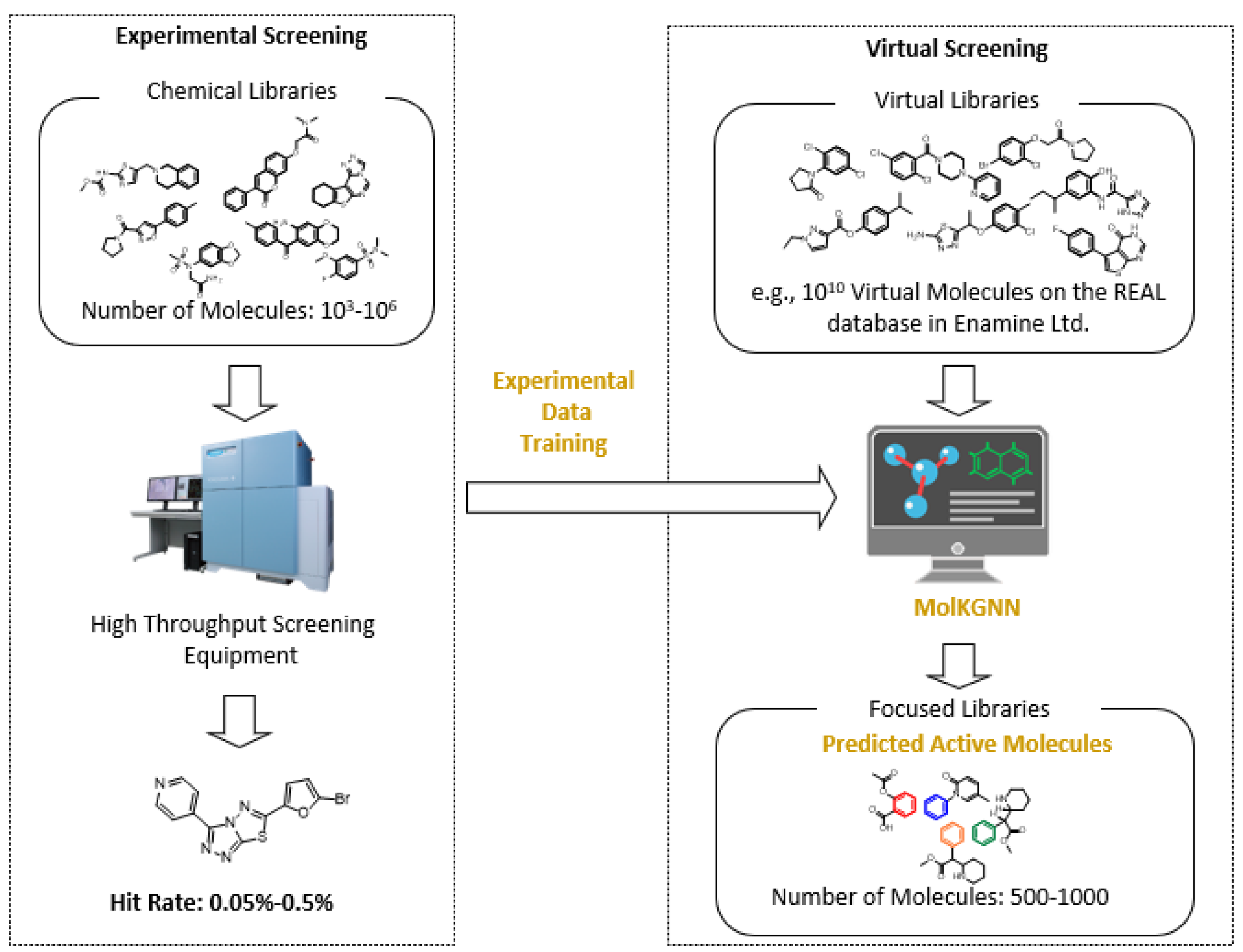


Fig. 2 MolKGNN could enable a larger exploration of the chemical space

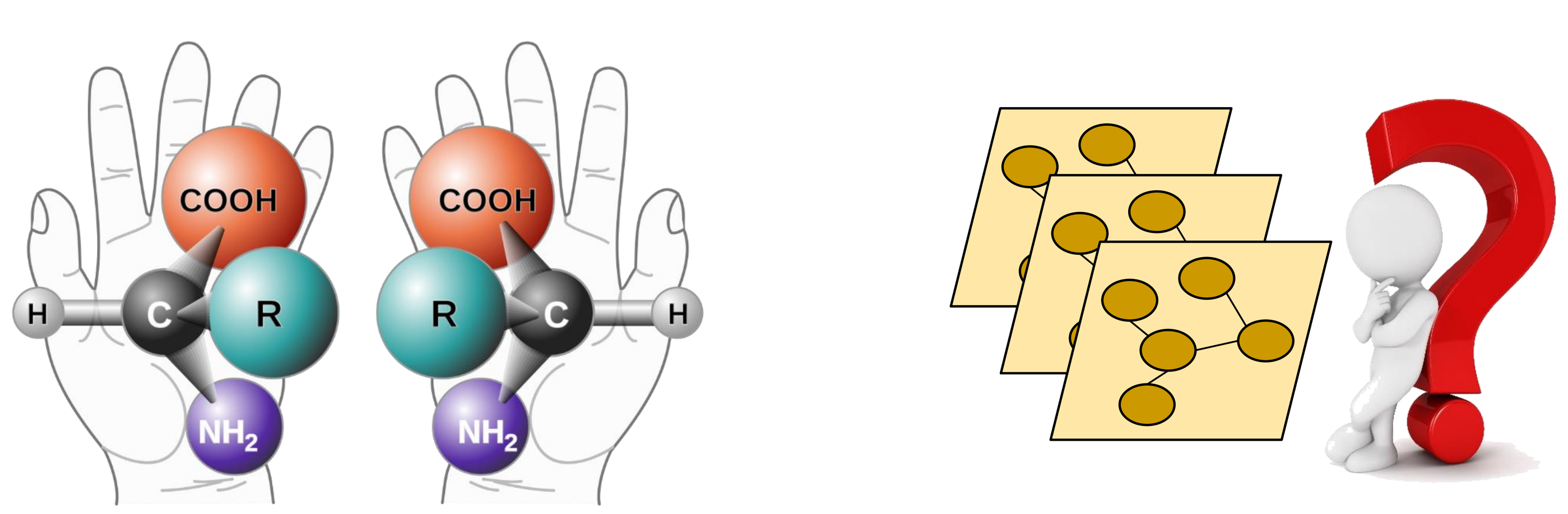


Fig. 3 Challenges: chirality and interpretability

METHOD

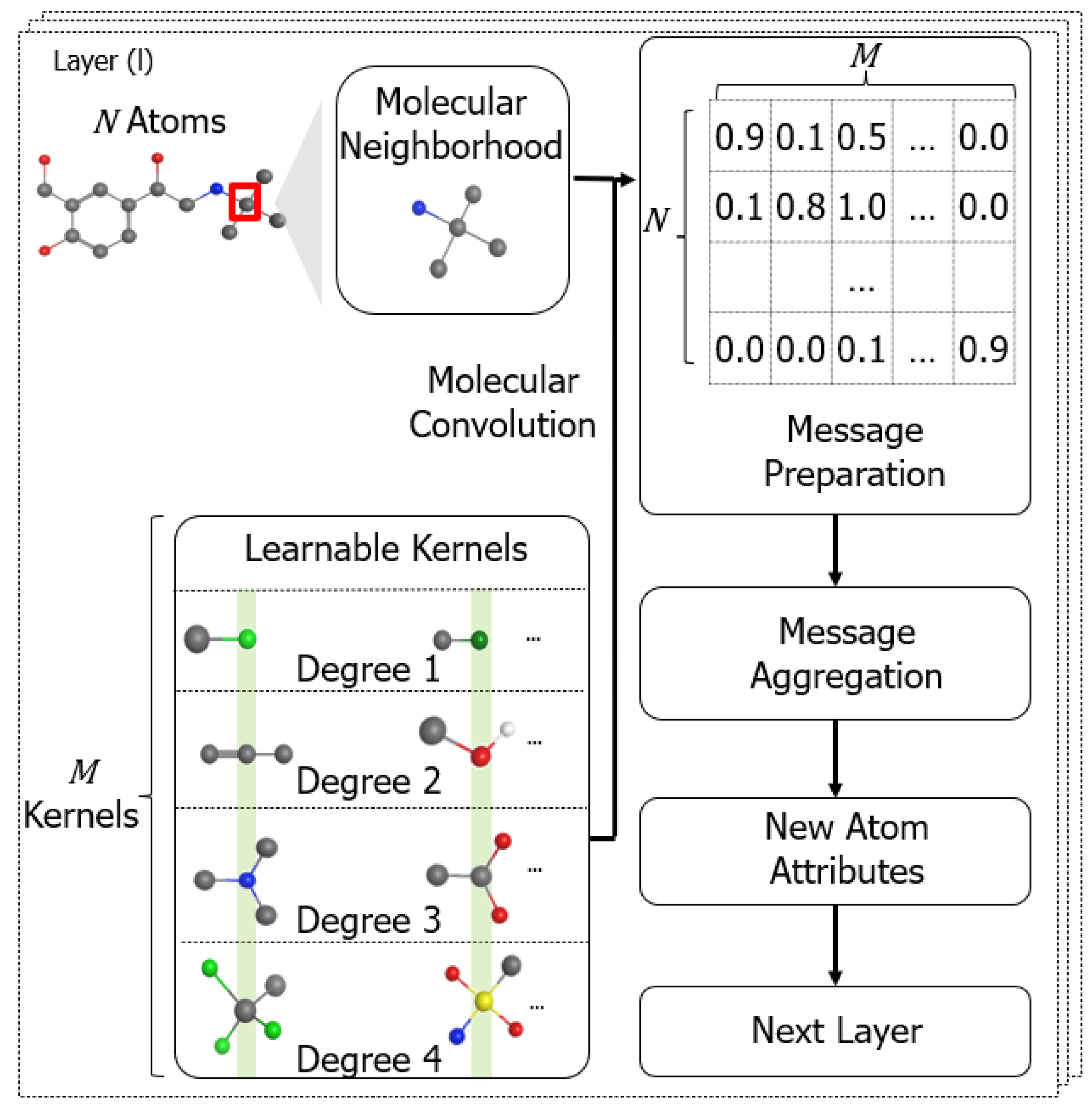


Fig. 4 Method overview

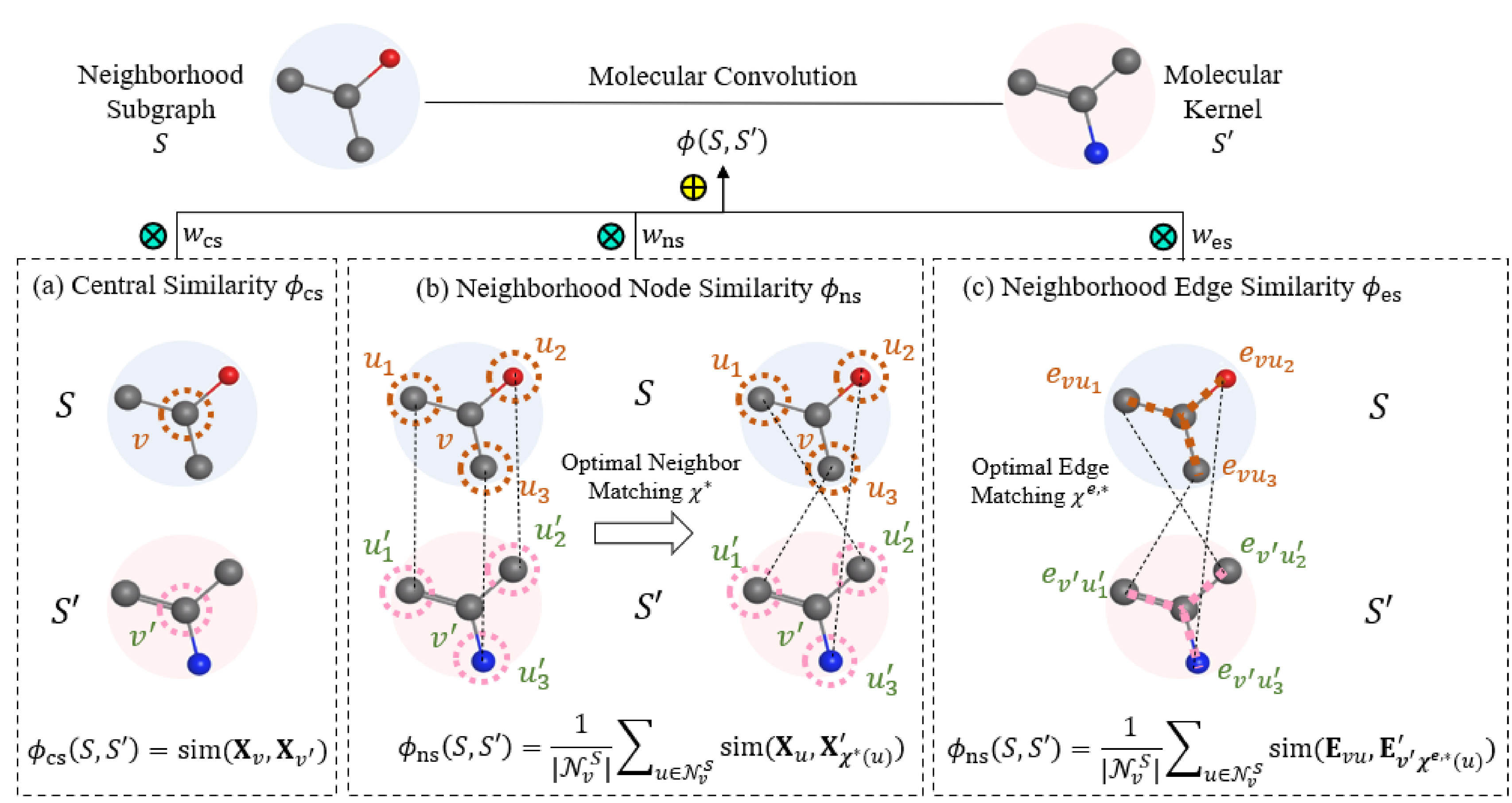
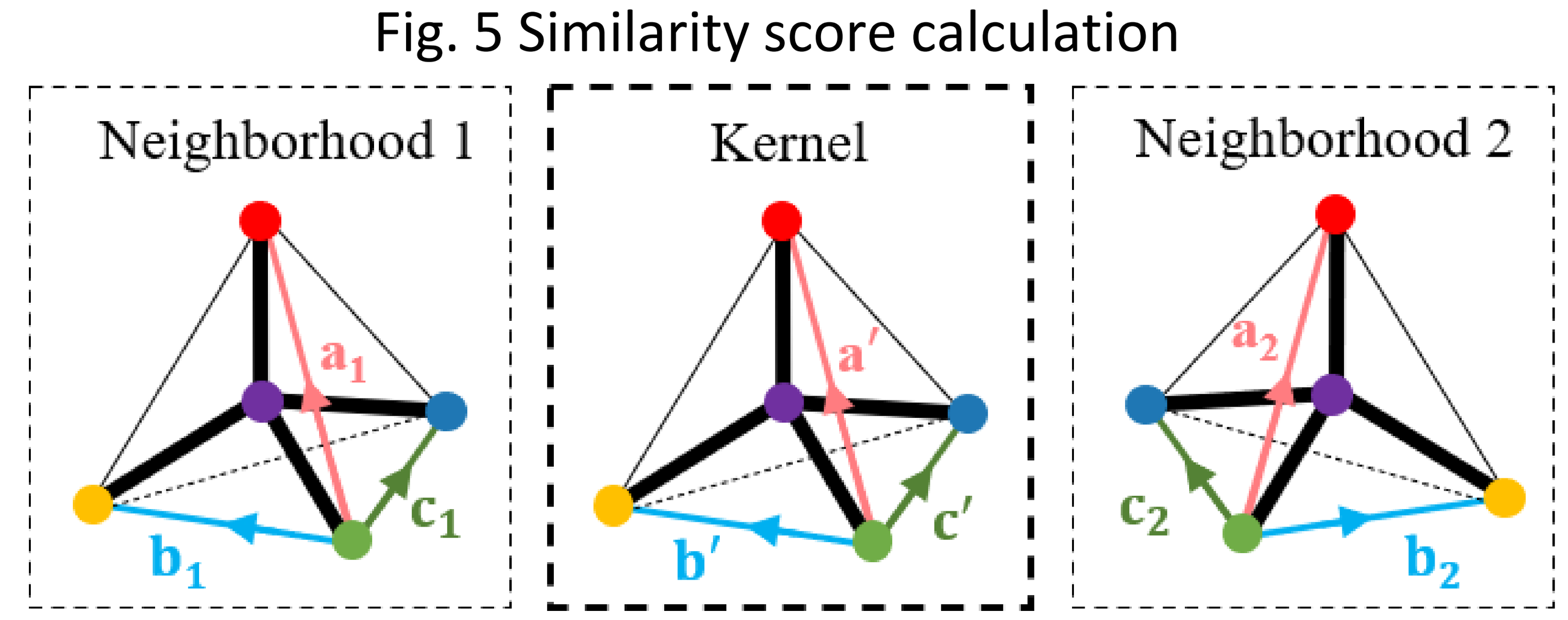


Fig. 5 Similarity score calculation



$$Sgn(a_1 \times b_1 \bullet c_1) = Sgn(a' \times b' \bullet c') \neq Sgn(a_2 \times b_2 \bullet c_2)$$

Fig. 6 Chirality Calculation

DOMAIN-RELEVANT METRIC

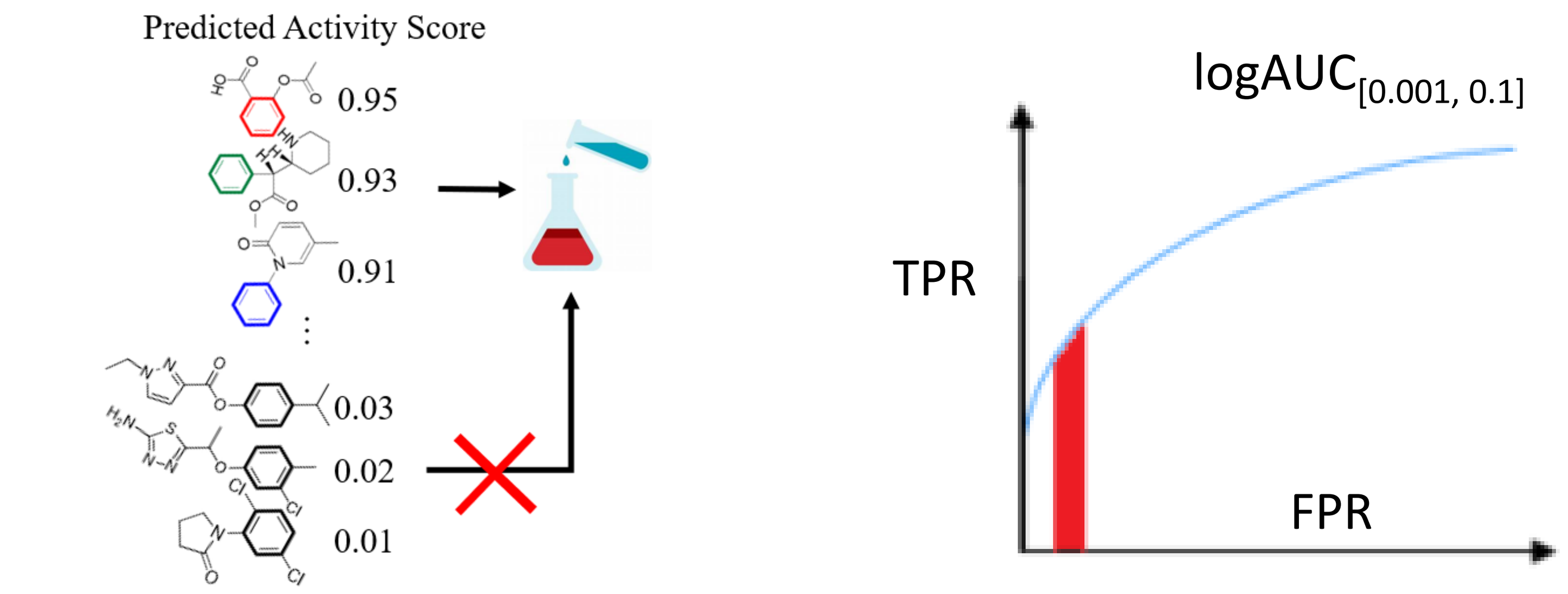


Fig. 7 Only top-ranked predictions are being experimentally validated due to the cost. $\log AUC_{[0.001, 0.1]}$ is used to bias toward the performance on these top-ranked predictions

REPRESENTATIVE RESULT

Tab. 1 $\log AUC_{[0.001, 0.1]}$ Performance (↑)

Dataset[1]	MolKGNN	KerGNN[1]	ChIRo[2]	SphereNet[3]
435008	0.25±0.01	0.15±0.01	0.17±0.02	0.22±0.02
1798	0.17±0.03	0.08±0.04	0.17±0.04	0.20±0.04
435034	0.23±0.02	0.18±0.05	0.21±0.02	0.23±0.03
1843	0.36±0.03	0.29±0.03	0.33±0.01	0.26±0.05
2258	0.30±0.03	0.19±0.02	0.25±0.01	0.38±0.04
463087	0.39±0.06	0.15±0.01	0.26±0.02	0.40±0.01
488997	0.30±0.03	0.08±0.02	0.19±0.03	0.31±0.03
2689	0.42±0.02	0.26±0.02	0.35±0.05	0.40±0.02
485290	0.50±0.01	0.22±0.03	0.29±0.07	0.45±0.04

Fig. 8 Intepretability Example

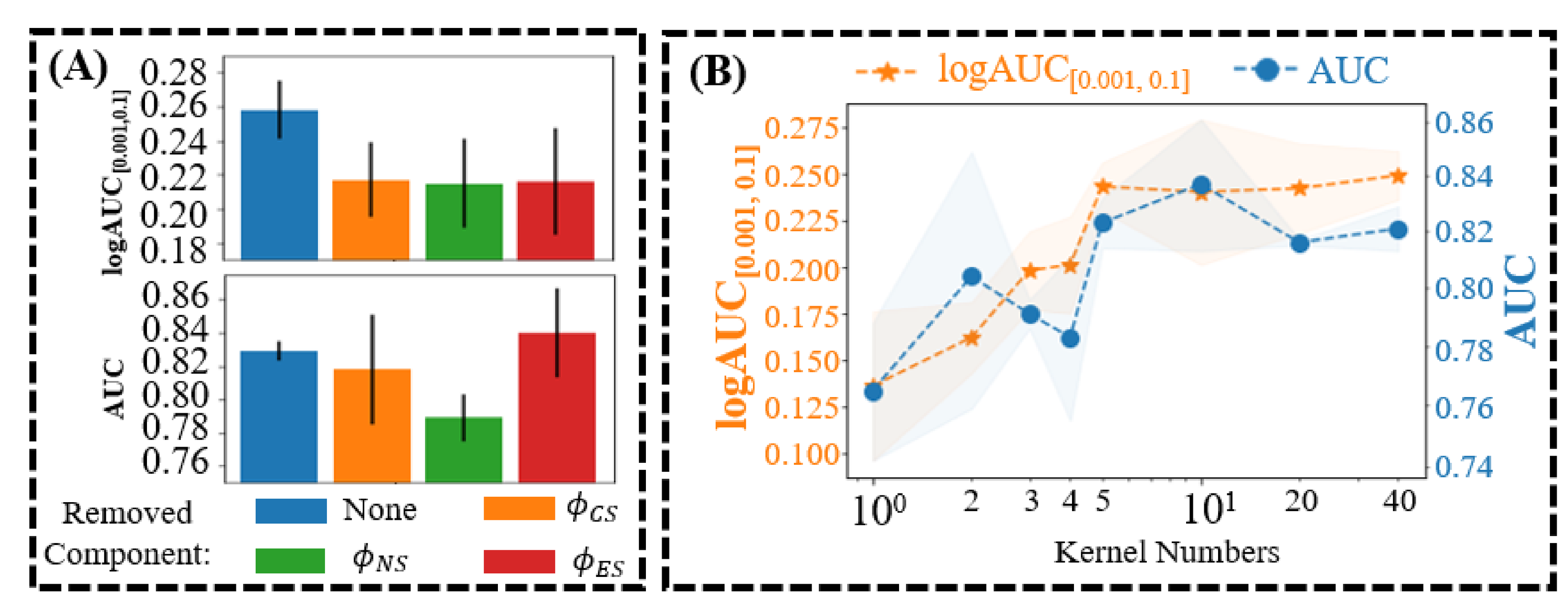


Fig. 9 Ablation Study

References

1. Butkiewicz, M., et al. (2017). High-Throughput Screening Assay Datasets from the PubChem Database
2. Feng, A., et al. (2022). KerGNNs: Interpretable Graph Neural Networks with Graph Kernels
3. Adams, K., et al. (2021). Learning 3D Representations of Molecular Chirality with Invariance to Bond Rotations
4. Coors, B., et al. (2018) Spherenet: Learning spherical representations for detection and classification in omnidirectional images.