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Advanced Computational Drug Repositioning with Attention-guided Random Walks on Refined Heterogeneous Network

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Drug repositioning offers a cost-effective and time-saving strategy to uncover new therapeutic indications for approved drugs and clinically safe compounds whose efficacy has not been fully established. The accuracy of computational drug repositioning critically depends on both the quality of the underlying network and the ability to capture informative structural patterns. We proposed a novel framework that integrates network refinement and attention-guided random walks for robust drug–disease association prediction. First, drug and disease similarity networks are enhanced using reduced-rank singular value decomposition to remove noise and improve network purity. A heterogeneous network is then constructed, and a subgraph surrounding each target drug–disease pair is extracted to focus on local topology. To avoid overfitting, two graphs are generated based on the subgraph, where one contains the association between the target drug-disease pair and the other does not. Subsequently, graph neural networks are employed to learn structural representations of nodes, followed by attention-guided random walks to compute transition probabilities and capture salient connectivity patterns. Finally, a multi-layer perceptron classifies the subgraph as positive or negative, indicating the presence of the association. Experiments on multiple benchmark datasets demonstrated superior performance compared to state-of-the-art methods, as well as consistent performance across additional datasets, confirming the generalizability and robustness of the approach.