AI-Driven Graph Neural Networks for Dual-Target AChE and BACE1 Drug Repurposing in Alzheimer's Disease

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Drug repurposing involves identifying new therapeutic uses for existing drugs that have already been approved or tested for other diseases, offering a faster and lower-cost alternative to traditional drug development. In this project, I developed an artificial intelligence (AI)-driven model that applies graph neural networks (GNNs) to support multi-target drug repurposing. The model combines two complementary models: a message passing neural network (MPNN), which captures overall molecular structure, and a task-specific edge-attention graph neural network (TaskEdgeGAT), which identifies important local interactions within molecules. Predictions from both models are combined using an ensemble model to improve accuracy and stability. Alzheimer's disease (AD) is used to demonstrate the model. Using curated bioactivity data from the ChEMBL database, the models are trained to predict inhibitory activity against two key AD-related targets: acetylcholinesterase (AChE) and ß-secretase 1 (BACE1). The trained ensemble model is then applied to screen a library of approved drugs to identify candidate compounds with predicted dual-target inhibitory activity. The results show that this model can effectively identify potential dual AChE–BACE1 inhibitors while also providing insights into which parts of the molecule are important for each target. This project demonstrates how AI-based models can accelerate drug repurposing and support the discovery of new treatments for complex diseases such as Alzheimer's disease.

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