Task-Specific Refinement of a Multitask AI Model for Blood–Brain Barrier Prediction

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Abstract text

ADMET (absorption, distribution, metabolism, excretion and toxicity) issues remain one of the main reasons why otherwise promising small molecules fail late in the pipeline. Being able to screen these liabilities early, directly from structure, is therefore a practical way to de-risk discovery. In this work we take an existing ADMET-AI multitask graph neural network as a baseline and develop a variant specifically strengthened for blood–brain barrier (BBB) permeability prediction. The original ADMET-AI model, trained on 41 ADMET datasets from the Therapeutics Data Commons and RDKit descriptors, already delivers broad ADMET coverage, but its performance on BBB was limited by the size and heterogeneity of the BBB data. We therefore integrated additional BBB datasets from the literature and retrained/fine-tuned the model on this expanded BBB subset. On two external BBB benchmarks, DeePred and Zhuang, the adapted model increased correct classifications from 87% to 95% and from 92% to 98%, respectively, with AUC values >0.90 in both cases, indicating more reliable separation of BBB-permeable versus non-permeable compounds. Because inference remains fast and deployable locally, the approach preserves the practicality of the original model while delivering a targeted improvement on a CNS-critical ADMET endpoint.