Neuricular: An Online Platform for Integrated CNS Drug Candidate Screening

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The blood-brain barrier (BBB) is a crucial protective membrane that prevents toxins and pathogens from entering the brain but also represents a major obstacle for central nervous system (CNS) drug development [1]. Experimental evaluation of BBB permeability and clinical toxicity is costly and low throughput [2,3], making early computational screening highly valuable. Hereby is presented Neuricular, a free online platform for integrated CNS drug candidate evaluation combining machine learning prediction of BBB permeability and toxicity with CNS MPO scoring [4], automated Tanimoto similarity to nearly 90 approved CNS drugs, Lipinski [5] and Veber [6] rule assessment and dynamic compound-specific explanations.

The models are Random Forest classifiers trained on DeepChem's MoleculeNet datasets (BBBP [7] and ClinTox [8]). Molecules were encoded using 2048-bit Morgan fingerprints (ECFP4) combined with eight physicochemical descriptors (MW, logP, logD, TPSA, HBD, HBA, rotatable bonds, QED), computed via RDKit. Stratified 80/20 splits and balanced class weighting address dataset imbalance, with isotonic calibration applied only to the BBB model. The BBB model showed great performance (AUC = 0.952, F1 = 0.937), while the toxicity model showed moderate (AUC = 0.831) with low recall due to severe class imbalance (1:12). Additionally, validation on ten CNS drugs showed correct classifications for all but levodopa, a LAT1 transporter substrate, highlighting limitations of structure-based models. All in all, Neuricular enables quick and accessible early-stage CNS drug screening, supporting experimental validation without replacing it, and provides a solid ground for further development of the machine learning models through more nuanced datasets and hyperparameter tuning.

Neuricular: https://neuricular.streamlit.app/

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