

Drug-like Property Prediction for Small Molecules: Comparing the Performance of Physics-based, Data-driven, and Quantum-inspired Machine Learning Models



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Developing disease-modifying drugs for various neurodegenerative diseases and infectious diseases is a major challenge in the healthcare sectors of developed and developing countries. [1,2] The traditional trial and error-based experimental high-throughput screening is enormously expensive and time-demanding [3,4], and so it is pragmatic to use rational computational approaches to facilitate the design of drugs. In general, the drug-discovery is a multi-variate optimization problem where the binding affinity, binding specificity, and various pharmacokinetic and pharmacodynamic properties of the lead compounds need to be optimized. Physics-based and data-driven models have been developed to compute these drug-like properties. The machine learning and deep learning models utilize the available chemical and biological databases to build the relationship between the chemical structure and bio-activities/drug-like properties. [4-6] The errors in the complete representation of molecules through descriptors, fingerprints, and molecular graphs can limit the performance of ML/DL approaches in drug-like property prediction. In physics-based approaches, these properties are computed as the free energy differences of small molecules in different environments (solvent, crystalline or biomolecular). In this presentation, the applications of various physics-based and data-driven (machine learning and deep learning) approaches for predicting different drug-like properties such as binding affinity, binding specificity, BBB permeability, partition coefficient, and solubility will be discussed [7]. Case studies involving the prediction of selected drug-like properties of small molecules, such as binding affinity, partition coefficient, and permeability, using different computational approaches, will be discussed in some detail [7].

References

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