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Abstract Book

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PREDICTION OF LIGAND BINDING BY MACHINE LEARNING ANALYSIS OF MOLECULAR DYNAMICS TRAJECTORIES

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The affinity of the ligand-target binding plays a critical role in the design and screening of potential drugs. Traditionally the most stringent approaches to affinity prediction have been based on time-consuming analysis of relatively long molecular dynamics trajectories of their complexes. However, their accuracy is still limited. In this work, we propose to build machine learning QSAR models capable of predicting the ligand binding constants with rather high accuracy from the molecular dynamics simulation data. The structural data and binding constants were obtained from the PDBbind-CN database (version 2017). The Gromacs 2018 software package was used to produce short (2 ns) molecular dynamics trajectories for the ligand-protein complexes. For each frame of the trajectory, the RMSD values and the van der Waals and electrostatic interaction energies were calculated. The resulting vector-valued time series were used as descriptors characterizing the ligand-protein binding. The classification and regression models were derived using various machine learning methods such as recurrent neural networks of different architecture (GRU, LSTM), Fourier networks (FNN, ND), and classical methods like Random Forest and Support Vector Machines. It was shown that the modern neural network architectures in combination with the data describing the dynamics of the complexes allow one to achieve high quality affinity ranking of compounds with small computational cost.