Analysis of Drug Design for a Selection of G Protein-Coupled Neuro-Receptors Using Neural Network Techniques - DTU Orbit (08/11/2017)

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A study is presented on how well possible drug-molecules can be predicted with respect to their function and binding to a selection of neuro-receptors by the use of artificial neural networks. The ligands investigated in this study are chosen to be corresponding to the G protein-coupled receptors mu-opioid, serotonin 2B (5-HT_{2B}) and metabotropic glutamate D5. They are selected due to the availability of pharmacological drug-molecule binding data for these receptors. Feedback and deep belief artificial neural network architectures (NNs) were chosen to perform the task of aiding drug-design. This is done by training on structural features, selected using a "minimum redundancy, maximum relevance"-test, and testing for successful prediction of categorized binding strength. An extensive comparison of the neural network performances was made in order to select the optimal architecture. Deep belief networks, trained with greedy learning algorithms, showed superior performance in prediction over the simple feedback NNs. The best networks obtained scores of more than 90 % accuracy in predicting the degree of binding drug molecules to the mentioned receptors and with a maximal Matthew's coefficient of 0.925. The performance of 8 category networks (8 output classes for binding strength) obtained a prediction accuracy of above 60 %. After training the networks, tests were done on how well the systems could be used as an aid in designing candidate drug molecules. Specifically, it was shown how a selection of chemical characteristics could give the lowest observed IC50 values, meaning largest bio-effect pr. nM substance, around 0.03-0.06 nM. These ligand characteristics could be total number of atoms, their types etc. In conclusion, deep belief networks trained on drug-molecule structures were demonstrated as powerful computational tools, able to aid in drug-design in a fast and cheap fashion, compared to conventional pharmacological techniques.

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