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SIBAR Descriptors and Support Vector Machine for ABCB1 Substrate Prediction

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As part of the ATP-binding cassette transporter superfamily ABCB1 (P-gp) exports a multitude of xenobiotics and is strongly connected to multi-drug resistance (MDR). With the decreasing number of new drugs entering the market prediction of possible side effects in new lead structures gains increasing importance. In silico methods hereby have become highly significant. As crystal structures of membrane proteins are difficult to produce and a structure of ABCB1 has yet to be published, ligand based approaches are still the method of choice. The aim of this study is to compare two approaches widely used for substrate prediction.

In this study we present a classification model using the SIBAR (Similarity Based Relationship) [1] approach. Based on 2D descriptors, VSA descriptors and 3D Autocorrelation descriptors and a reference set SIBAR descriptors are calculated and further used for classification. 2D desciptors comprise for example hydrogen bond acceptors and donors, lipophilicity, etc. VSA descriptors describe features based on surface area for logP, molar refractivity and partial charge properties whereas Autocorrelation descriptors are topological descriptors encoding the level of correlation between two objects in terms of their specific structural or physicochemical properties. Using the support vector machine (SVM) function implemented in WEKA we generated a model based on a dataset of highly complex natural products [2].

We additionally compared the performance of the RBF (Radial Basis Function) Kernel and the Polykernel in the SVM. Validation of our model was achieved via ten-fold-cross validation and on an external test set. The RBF Kernel showed slightly better results. Prediction of the external test set gave an overall accuracy for the RBF Kernel of 77% opposed to nearly 73% with the Polykernel approach.

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