

## Finding Characteristic Ligand Substructures to Dopamine Receptors

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A data mining system using the cascade model and linear fragment descriptors is developed to discriminate characteristic substructures for a group of bioactive molecules. Results are shown by a set of rules, each of which shows the change in the activity distributions before and after the application of a condition. The condition is denoted by the presence/absence of a linear fragment. When distributions of other fragments also change sharply by this condition, they are also added as collateral correlations. The length of a linear fragment was limited by 10, and its expression includes two terminal atoms from both ends and all bond symbols. The system was applied to agonists and antagonists of dopamine receptors, and a set of valuable knowledge was obtained. For example, the active site of D1 agonists was identified to be a catechol moiety, and the binding site was characterized by ethylamine substituent at meta and para positions to the catechol. Some compounds possessing a longer chain with secondary amine were also shown to have D1 agonist activity. These sorts of knowledge were compiled to characterize D1, D2 and Dauto agonists as well as D1-D4 antagonists.