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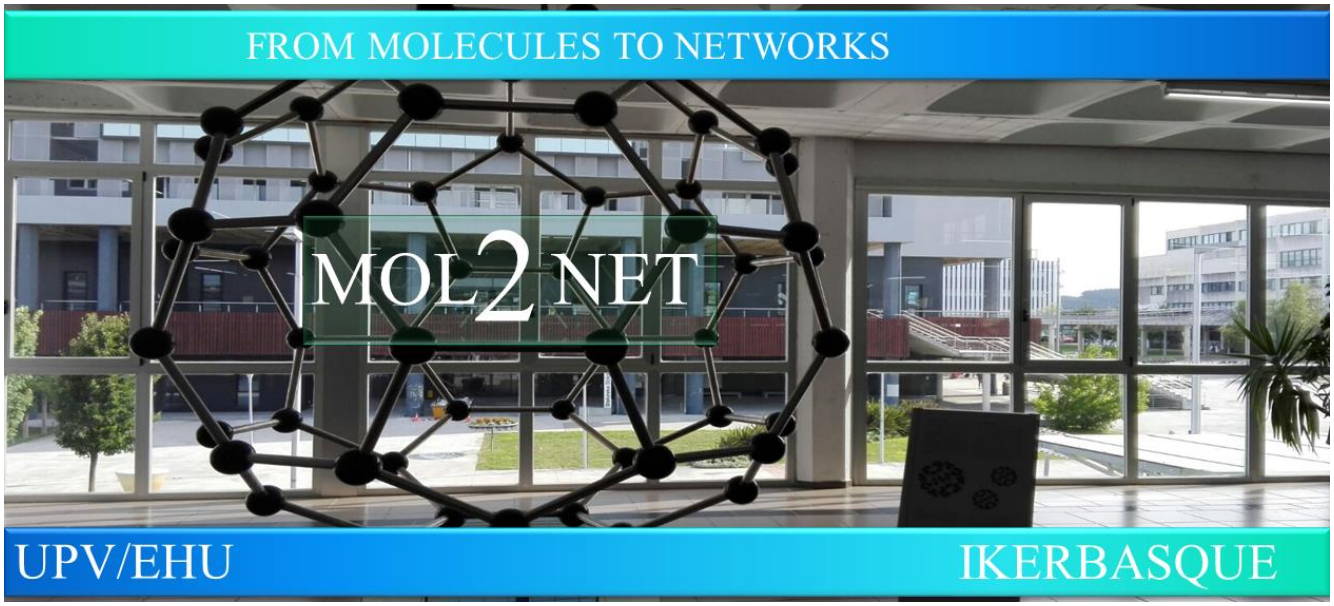

Identification of New Potential acetylcholinesterase inhibitors for Alzheimer's disease treatment using machine learning

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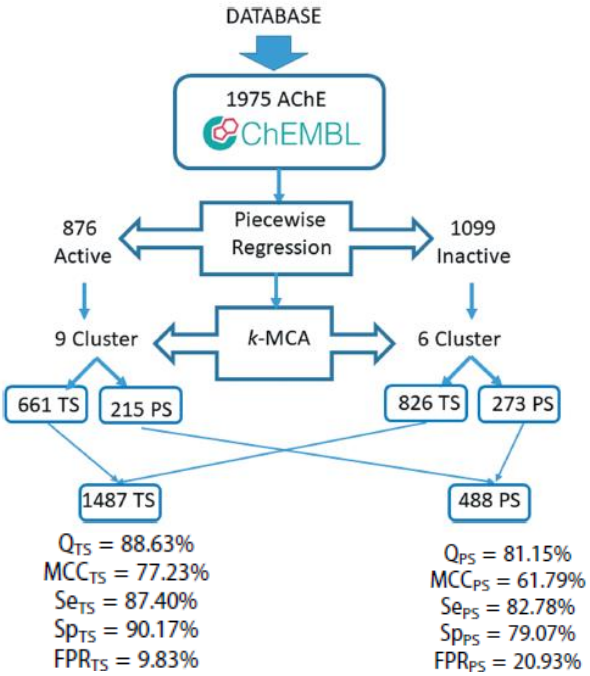
Graphical Abstract



Abstract.

The enzyme acetylcholinesterase (AChE) is currently a therapeutic target for the treatment of neurodegenerative diseases. These diseases have highly variable causes but irreversible evolutions. Although the treatments are palliative, they help relieve symptoms and allow a better quality of life, so the search for new therapeutic alternatives is the focus of many scientists worldwide. In this study, we use a freely available dataset downloaded from the ChEMBL site composed of 1975 compounds of great structural diversity and with reported IC_{50} enzyme inhibition against AChE. Using the MATLAB numerical computation system and the molecular descriptors implemented in the Dragon software, a QSAR-SVM classification model was developed; the obtained parameters are adequate for its adjustment (Q_{TS} = 88.63%), and the validation exercises verify that it is stable (Q_{CV} = 81.13%), with good predictive power (Q_{PS} = 81.15%) and is not the product of a casual correlation. In addition, its application domain was determined to guarantee the reliability of the predictions. Finally, the model was used to predict ACh inhibition by a group of quinazolinones and benzothiadiazine 1,1-dioxides obtained by chemical synthesis, resulting in 14 drug candidates with in silico activity comparable to acetylcholine.

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