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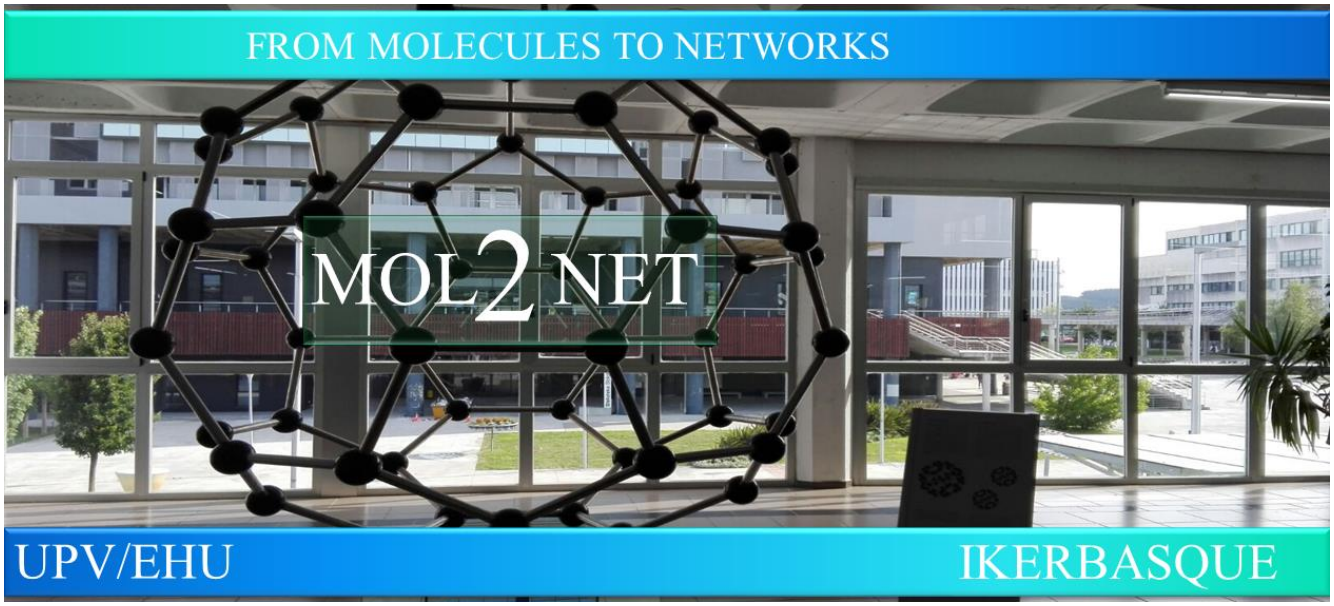

Application of Discrete Molecular Descriptors As Filters to Select Theoretical Antibacterial Compounds

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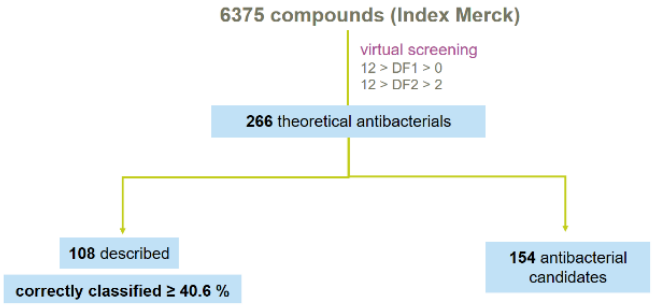
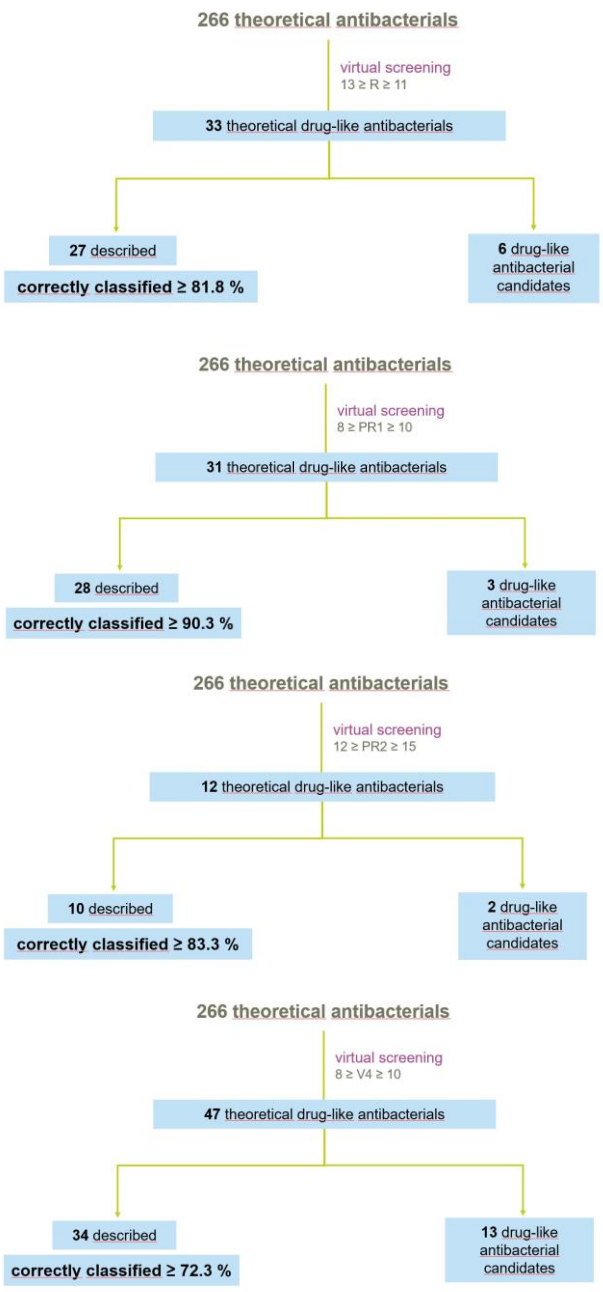
Graphical Abstract



Abstract.

Virtual screening has been the basis for the design of new molecules with a wide variety of pharmacological activities. The great advantage of QSAR (Quantitative Structure-Activity Relationship) methods is that they are a low cost solution which allows the identification of molecules that are likely to present a specific activity.

Currently, the development of antibiotic resistance by microorganisms is one of the most important problems that have appeared in



recent years in the treatment of infectious diseases. This increased resistance is associated with increased morbidity and mortality from infections, as well as an increase in healthcare costs.

QSAR methods appear as an increasing popular tool in the search of new treatment options against bacteria. In this paper, a tree-based classification method using Linear Discriminant Analysis (LDA) and discrete indices was used to create a QSAR model to predict antibacterial activity.

The model consists on a hierarchical decision tree in which, in a first step, a combination of discriminant functions capable of predicting antibacterial activity (FD1 and FD2) is applied to a database with 6375 commercial compounds, where 266 compounds were selected as candidates, from which 40.6% have this activity according to bibliography. The second step consists in the application of a discrete index, which is used to divide compounds into groups according to their values for said index in order to construct probability space.

The topological discrete indices R, PR1, PR2 and V4 have proven to have the ability to group active compounds effectively, considerably increasing the bibliographic success activity rate (up to 81.8%, 90.3%, 83.3% and 72.3%, respectively) which suggests a close relationship between them and the antibacterial activity of commercial compounds.

This methodology has proven to be a viable alternative to the traditional methods and its application provides interesting new drug candidates to be studied as repurposed antibacterial treatments.

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