Rationalizing Molecular Promiscuity through Data Analysis and Explainable Machine Learning

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Multi-target activity of small molecules, also termed promiscuity, leads to desired and undesired effects in drug discovery. Exploring the ability of small molecules to form pseudospecific interactions with different targets is of interest to better understand molecular recognition phenomena and devise multi-target drug design strategies. In addition to proteomics or target profiling, compound promiscuity can also be investigated computationally, for example, through systematic analysis of structural and activity data and diagnostic machine learning for hypothesis testing. These studies confirm the presence of structural features that distinguish multi- and single-target compounds. Explaining machine learning predictions reveals structural characteristics of promiscuous compounds.