P17-Refinement of a ligand activity and representation of topological pharmacophores in a colored network

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Structure-Activity Relationships is a critical aspect of drug design. It enables us to examine ligand interactions and performances towards specific targets, then to design effective drugs for treating diseases or improving existing medical therapies. In this context, we specifically study the activity of ligands towards kinases using the BCR-ABL dataset. The work is dedicated to introduce a refinement method for the activity of molecules. Instead of considering affinity as a binary activity, a molecule being either active or inactive, the compounds were partitioned into 4 classes according to their activity: very active, moderately active, slightly active, inactive. This activity is later used to evaluate molecular descriptors called topological pharmacophores [1]. These pharmacophores provide essential information by representing the key structural features of a molecule. Their quality is determined by measuring their "growth-rate" which corresponds to the ratio of active molecules over inactive ones, among the molecules supported by the pharmacophore. In our work, the calculation of the growth-rate is based on the classes of activity that we have created. Consequently, we will obtain three measurements of the growth rate, each one being related to a class of activity. In addition, we proposed to convert the new information of the quality of the pharmacophores into a visual representation called "The Pharmacophore Network" [2]. The latter is a graph whose nodes represent the pharmacophores and edges represent a graph-edit distance that separates them. Our goal was to structure more finely the pharmacophore space and to be able to detect visually interesting areas that can be explored. For this purpose, we integrated colors in this Pharmacophore Network, where each color refers to a class of activity.

References

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