[P39]Screening Explorer – An interactive tool for the analysis of screening results

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Virtual screening of compound collections has become extensively used in drug discovery programs to reduce the number of compounds going into high throughput screening procedures. However, scoring functions are still imperfect and their performances can vary largely depending on the conditions of the experiment (i.e. for structure-based experiments: the preparation of the binding site, the addition of water molecules to the pocket and the parameters of the conformational search algorithm; or more generally: the characteristics of the molecular dataset and the parameters of the scoring function) [1].

Additionally, consensus scoring methods aim at combining the results of different scoring functions to improve the final enrichments and diminish the importance of the choice of a particular scoring function. However, if the majority of published work reports great enrichments compared to the use of single scoring functions, it appears that each of the combined scoring function must yield reasonable results; a blind combination of some arbitrarily chosen scoring functions will not necessarily lead to better results [2].

While a number of programs and R packages are available for the analysis of virtual screening results, their usage requires to generate metrics separately, calculate partial metrics repeatedly for each fractional threshold of interest, and there exists no handy tool that regroup all usual metrics. Therefore, we developed a web-based interactive application that covers all aspects of the analysis of the results and allows to calculate partial metrics on the fly for specific fractions of the datasets: Screening Explorer (http://stats.drugdesign.fr). We also focused on rendering the application user-friendly and suitable for educational purposes.

Our primary interest in developing this program is to provide an intuitive tool to facilitate the apprehension of the results of both individual scoring functions and consensus scoring methods; which should support the development of scoring functions and help in the process of selecting active compounds in drug discovery programs. The study of consensus scoring coupled to the assessment of each scoring function performances allow to evaluate the reproducibility of the results of consensus scoring methods from benchmarking to prospective assays. Although this program was initially designed for the analysis of the results of target-based and ligand-based virtual screenings, it can be used equally for the analysis of HTS data which include validation assays.

References:

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[2] Feher M. Drug Discov Today 11 (2006) 421–428.