“Fuzzy” pharmacophores for virtual database screening and library design

Gisbert Schneider

Institute of Organic Chemistry & Chemical Biology, Johann Wolfgang Goethe-University
Siesmayerstr. 70, D-60323 Frankfurt, Germany
Email: G.Schneider@chemie.uni-frankfurt.de

The degree of diversity of virtual hits obtained by a similarity searching technique is influenced by the molecular representation. Different hit lists are found at different level of abstraction from the atomic structure. A high degree of abstraction is thought to facilitate the identification of novel structures that exhibit a similar pharmacological profile as the query. We have developed molecular descriptors that allow for variable degrees of “fuzziness” of potential pharmacophore-points. The theoretical concept and several prospective applications will be presented. These include “scaffold-hopping” applications and the design of natural-product derived combinatorial libraries.