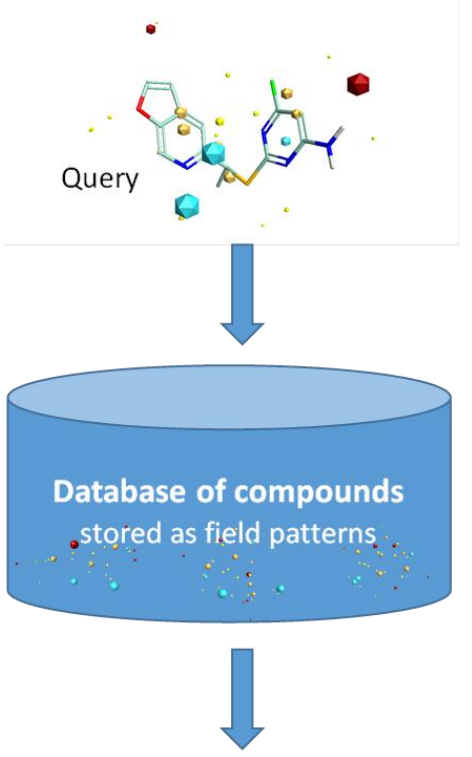
Virtual Screening with Blaze

Virtual screening is the process of computationally assessing large databases of molecules for the propensity to bind to a biological target of interest. In the context of a ligand alignment and scoring method this entails taking one or more ligands that are known to be active at the target of interest (the reference molecule(s)) and comparing these to each molecule in the database, returning a molecular similarity score. The Cresset™ Blaze virtual screening system approaches this task from the viewpoint of molecular interaction fields: two molecules are similar if they have the same shape, electrostatic potentials, and patterns of hydrophobicity.

The great advantage of the Blaze metric is that two molecules can be highly similar in terms of their field properties even if their 2D structures are very different. This allows Blaze to find active molecules that are in completely different chemical series to the query, which is usually the most desirable outcome of a virtual screen. Blaze has been extensively used by Cresset™ in its service offerings (more than 150 virtual screening projects, with a › 80% success rate). A full description of the Blaze methodology has been published (1,2), and published applications include steroid, kinase and GPCR targets (3,4,5).



The normal Blaze method requires access to both the molecular structure and the calculated molecular interaction fields and their extrema (called 'field points'). For the OIDD project, Cresset™ has developed a variant system that does not directly compare the molecule's structure to the reference ligand. Instead only the field point information is required, which although derived from the molecular structure, reveals no structural information. This breakthrough allows the Blaze method to be applied to the OIDD database, giving accurate 3D shape and electrostatic scoring while maintaining the internal OIDD information firewall.

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