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PhAST: pharmacophore alignment search tool

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We developed the Pharmacophore Alignment Search Tool (PhAST), a text-based technique for rapid hit and lead structure searching in large compound databases. For each molecule, a two-dimensional graph of potential pharmacophoric points (PPPs) is created, which has an identical topology as the original molecule with implicit hydrogen atoms. Each vertex is coloured by a symbol representing the corresponding PPP. The vertices of the graph are canonically labelled [1]. The symbols associated with the vertices are combined to a so-called *PhAST-Sequence* beginning with the vertex with the lowest canonical label. Due to the canonical labelling the created PhAST-Sequence is characteristic for each molecule.

For similarity assessment, PhAST-Sequences are compared using the sequence identity in their global pairwise alignment [2]. The alignment score lies between 0 (no similarity) and 1 (identical PhAST-Sequences). In order to use global pairwise sequence alignment, a score matrix for pharmacophoric symbols was developed and gap penalties were optimized. PhAST performed comparably and sometimes superior to other similarity search tools (CATS2D [3], MOE pharmacophore quadruples [4]) in retrospective virtual screenings using the COBRA [5] collection of drugs and lead structures. Most importantly, the PhAST alignment technique allows for the computation of significance estimates that help prioritize a virtual hit list.

References

1. Weininger D, *et al.*: *J Chem Inf Comput Sci* 1989, **29:**97.
2. Needleman S, Wunsch C: *J Mol Biol* 1970, **48:**443.
3. Schneider G, *et al.*: *Angew Chem Int Ed* 1999, **38:**2894.
4. Sheridan RP, *et al.*: *J Chem Inf Comput Sci* 1996, **36:**128.
5. Schneider P, Schneider G: *QSAR Comb Sci* 2003, **22:**713.