

Searching Fragment Spaces with Feature Trees

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Virtual combinatorial chemistry easily produces billions of compounds, which can not be screened in a conventional manner even with the fastest methods available. An efficient solution for such a scenario is the generation of Fragment Spaces which encode huge numbers of virtual compounds by their fragments/reagents and rules of how to combine them. Fragment Spaces can be screened with so-called Fragment Space searches.

Rarey and Stahl [1] published a method for such searches based on the Feature Tree descriptor [2]. The Feature Tree descriptor is frequently used for virtual screening and has a potential for scaffold hopping [e.g. 3]. The Fragment Space searches are performed without ever fully enumerating all virtual products.

In this presentation we show the preparation of Fragment Spaces based on combinatorial chemistry and share our experiences with Fragment Space searches based on the Feature Tree descriptor in a possible workflow to use this methodology in a pharmaceutical setup.

1. Rarey, M.; Stahl, M. Similarity searching in large combinatorial chemistry spaces. *J. Comp.-Aided Molecular Design* **2001**, 15, 497-520.
2. Rarey, M.; Dixon, J.S. Feature trees: A new similarity measure based on tree matching. *J. Comp.-Aided Molecular Design* **1998**, 12, 471-490.
3. Good, A.C.; Hermsmeier, M.A.; Hindle, S.A. Measuring CAMD technique performance: A virtual screening case study in the design of validation experiments. *J. Comp.-Aided Molecular Design* **2004**, 18, 529-536.