

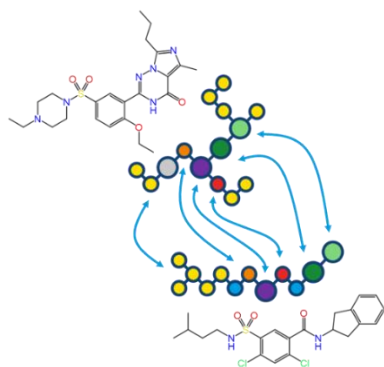


Search and navigate in Chemical Spaces and find new scaffolds in a flash based on fuzzy pharmacophore features. FTrees represents an excellent orthogonal method to molecular fingerprints.

How does FTrees work?

FTrees utilizes a tree structure to represent molecules. This tree consists of nodes that represent functional groups, interconnected to depict the overall molecular topology. Each node encompasses a profile that captures the physico-chemical properties of the corresponding substructure. The following attributes are encompassed within this profile:

- ◆ Spatial volume
- ◆ Ring or not
- ◆ Pharmacophore profile (donor, acceptor, amide-like, aromatic, hydrophobic/hydrophilic)



Two trees are then aligned with each other, similar to a sequence alignment. The alignment provides a mapping of corresponding nodes on either tree (as illustrated by the same coloring of corresponding substructures). Mapped nodes are compared based on their property profiles resulting in a "Local Similarity". The "Global Similarity" is essentially an overall average, it can be used to categorize multiple molecules as to how similar they are, where 0 is dissimilar, and 1 is identical.

The coloring of the substructures helps the user to identify which substructure of the query is matched onto which one of the hit molecule. The alignment (or mapping) found by FTrees is among all the one with the highest "Global Similarity".

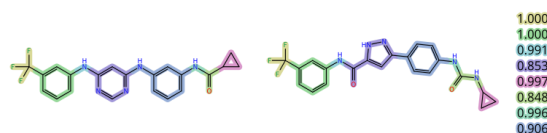
Advantages

- ◆ Understand similarity: Alignment of the molecules and an intuitive color code visualizes similarity
- ◆ Literally billions of molecules can be searched in 5 minutes

Scaffold hopping

The primary use case for FTrees is: "Find me a molecule with similar properties, but a different scaffold". For this purpose, large libraries are virtually screened, and the top-x compounds taken to be looked at. As you go down

such a hit-list, molecules appear with less and less structural similarity. Typically, in the range between 0.7 to 0.9 you will find the most interesting results — similar enough in terms of pharmacophore properties but highly enriched with scaffold hops.



Orthogonality

FTrees has demonstrated its orthogonality to other 2D descriptors. This implies that FTrees is capable of detecting molecular features that other methods might overlook, and vice versa. Instead of solely focusing on the structural aspects, FTrees takes a more holistic and "fuzzy" approach by perceiving molecules as targets with pharmacophore features arranged in specific topologies. Other approaches, like Tanimoto fingerprint similarity, often fail to capture the relevant chemistry that FTrees can easily recognize.

Accessible results

FTrees excels in screening vast Chemical Spaces that encompass an immense number of molecules, ranging from billions to trillions or even more. It effectively navigates through this vast chemical landscape and retrieves compounds that are not only relevant but also synthetically accessible. To enhance the breadth and diversity of Chemical Spaces available, we engage in collaborations with trusted partners. These collaborations result in the Chemical Spaces that contain commercially available, make-on-demand molecules, further expanding the range of compounds that can be explored and utilized in drug discovery and design.

Literature

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Several presentations held during the NIH Workshop on Ultra-Large Chemical Spaces featuring the FTrees technology can be found [here](#).