Encoding Stereochemistry in Molecular Fingerprints

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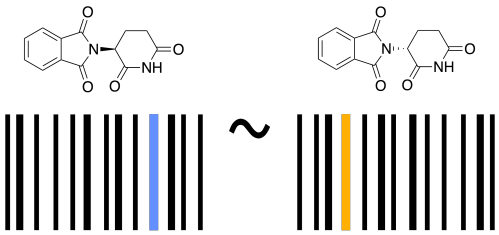
Molecular fingerprints are important tools enabling fast similarity comparisons between molecules[1]. These fingerprints encode different molecular properties, such as pharmacophores[2], atom distances[3,4] and substructures[4–6], and are particularly useful in the context of virtual screening, where one carries out millions of comparisons to detect potential hits. However, a serious limitation of the most well-known fingerprints is their inability to account for chirality in a chemically meaningful manner. Specifically, the challenge lies in encoding chirality to distinguish enantiomers and diastereomers as highly similar yet distinct entities. In this study, we introduce MHFP6* and MAP4*, enhanced versions of our MHFP6[6] and MAP4[4] fingerprints, which correctly encode CIP chirality in a chemically meaningful manner. Both fingerprints demonstrate the capability to correctly differentiate isomers, thereby overcoming the previously mentioned limitations.



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