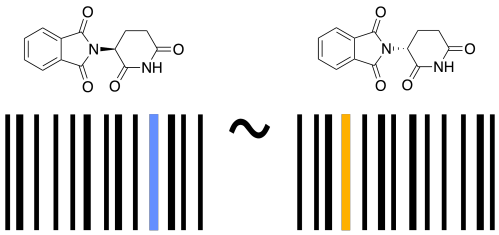
Encoding Stereochemistry in Molecular Fingerprints

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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.



[1] Peter Willet, *Drug Discov. Today* **2006**, *11* (23–24), 1046–1053.

[2] Alice Capecchi, Mahendra Awale, Daniel Probst, Jean-Louis Reymond, *Mol. Inform.* **2019**, *38* (5), 1900016.

[3] Raymond E. Carhart, Dennis H. Smith, Rengachari Venkataraghavan,*J. Chem. Inf. Comput. Sci.* **1985**, *25* (2), 64–73.

[4] Alice Capecchi, Daniel Probst, Jean-Louis Reymond, *J. Cheminformatics* **2020**, *12* (1), 43.

[5] David Rogers, Mathew Hahn, *J. Chem. Inf. Model.* **2010**, *50* (5), 742–754.

[6] Daniel Probst, Jean-Louis Reymond, *J. Cheminformatics* **2018**, *10* (1), 66.