Contribution ID : **201** Type : **Poster Presentation**

# Quantifying molecular chiral properties in solution using Ensemble Steric and Electrostatic Chirality (ESEC) descriptors

Enantiomers of chiral molecules behave differently in chiral environments. This is typically due to interactions with a chiral host system, such as a chiral reagent or catalyst in a synthetic context, a target protein in the context of drug discovery or a chiral stationary phase in chiral chromatography. The most obvious route for studying these interactions in solution phase is through MD simulations that include both the aforementioned host system and the (chiral) guest molecule of interest. However, doing so is laborious and computationally intensive, and in many cases poorly eligible for automation. For such purposes, it would be more convenient if generic chiral properties of the molecule of interest could be calculated and correlated with differences in behavior between its enantiomers.

While considerable effort has been invested into developing chiral molecular descriptors,[1][2] existing chiral descriptors are hard to interpret and often yield acceptable results only when applied to highly congeneric molecules. Therefore, we developed universal chiral descriptors based on a molecule's asymmetric microscopic properties using the 2 distinct approaches in figure 1: (A) scalar triple products of molecular vector properties, and (B) descriptors that attempt to quantify the amount of twist in the overall molecular shape. Because both approaches give rise to conformation dependence, descriptor values were averaged over a conformational ensemble obtained by Molecular Dynamics. In addition, a method is introduced that attempts to quantify the asymmetry of the distribution of the descriptor values over the conformational ensemble. As a proof-of-concept, the resulting "Ensemble Steric and Electrostatic Chirality (ESEC) descriptors" were applied to construct Quantitative Structure-Enantioselectivity Relationships (QSER) for chiral High-Performance Liquid Chromatography (HPLC) on a set of known chiral pharmaceuticals.

[1] R.I.J. Amos, P.R. Haddad, R. Szucs, J.W. Dolan, C.A. Pohl. *Trends. Anal. Chem.* **2018**, *105*, 352-359. [2] P. De Gauquier, K. Vanommeslaeghe, Y. Vander Heyden, D. Mangelings, *Anal. Chim. Acta* **2022**, *1198*, 338861.

**Primary author(s) :** PEETERS, Jordy; DE GAUQUIER, Pieter

**Co-author(s) :** AMELI, Fardine; VANDER HEYDEN, Yvan; MANGELINGS, Debby; Prof. VANOMMESLAEGHE, Kenno

**Presenter(s) :** Prof. VANOMMESLAEGHE, Kenno