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Combining biomimetic chromatography and the quantitative structure-(chromatographic) retention relationships approach using machine learning

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It is essential to include screening physicochemical properties as a crucial step in the drug discovery pipeline. Although for the evaluation of the physicochemical properties of molecules, both experimental and computational methods are available; still, experimental ones are preferred.

Biomimetic chromatography is a highly effective experimental method that can simulate the interactions between molecules and the biological environment. It provides more accurate data on the behavior of molecules in living organisms than classical physicochemical assessment methods. The main concept of biomimetic chromatography is the application of high-performance liquid chromatography (HPLC) with stationary phases containing proteins and phospholipids.

Biomimetic chromatography allows for linking the befits of HPLC, like low cost of analysis, short time, or need only a small amount of substances that do not need to be absolutely pure since their impurities are readily separated during the chromatographic process. The chromatographic methods are also repeatable, robust, and fully automated. Additionally, they can be integrated with more biomimetic settings than *n*-octanol used in the classical shake-flask method used for lipophilicity assessment.

The relationship between retention and the chemical structure of analytes has attracted attention from the beginning of chromatographic research. Generally, the Quantitative Structure-(Chromatographic) Retention Relationships (QSRR) methodology introduced by Kaliszan linked the relationship between retention and analyte structures mathematically. The QSRR models can illustrate which physicochemical parameters govern the retention in certain chromatographic systems and present the nature of the interactions among solutes, stationary phases, and mobile phases. In the case of biomimetic chromatography, the obtained models provide information about molecular properties that determine lipophilicity, phospholipids, and plasma protein affinity.

Inspired by recent advancements in machine learning (ML) and computational chemistry, we proposed integrating the bio-chromatographic approach and ML to build a tool for accelerating drug discovery. A summary of a single research facility in efforts and experiences on this topic will be presented.

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