

# One- and two-dimensional LC methods for separating very complex samples

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Liquid chromatography is the most prolific techniques for the separation of complex mixtures of non-volatile analytes. There is a great range of columns and separation mechanisms and the separation power has increased significantly in recent years, thanks to better instrumentation (ultra-high-performance LC), new types of columns (smaller or solid-core particles, monoliths) and higher operating pressures. Nevertheless, one-dimensional LC separations do not suffice to separate the very complex samples encountered in many fields of science.

Comprehensive two-dimensional liquid chromatography (LC $\times$ LC) provides greater separation power in a shorter time. A peak capacity of 10,000 can be reached within a few hours. Two very different (“orthogonal”) separation mechanisms can be combined, to greatly increase the separation selectivity. The enhanced separation power may result in better quantitation or less need for laborious sample-preparation procedures.

Obstacles to the proliferation of LC $\times$ LC include the incompatibility of different mobile and stationary phases. For example, reversed-phase and normal-phase LC methods cannot easily be combined. Also, the detection sensitivity is affected by sequential dilutions. These two obstacles can be addressed by active modulation [1]. A final obstacle is the complexity of developing LC $\times$ LC methods. New software tools [2] promise to alleviate this problem.

The various aspects of LC $\times$ LC will be illustrated in this lecture using examples from life science, food science and material science.

## Acknowledgements and/or References

- [1] A.F.G. Gargano, M. Duffin, P. Navarro, P.J. Schoenmakers, Reducing Dilution and Analysis Time in Online Comprehensive Two-Dimensional Liquid Chromatography by Active Modulation., *Anal. Chem.* 88 (2016) 1785–1793. doi:10.1021/acs.analchem.5b04051.
- [2] B.W.J. Pirok, S. Pous-Torres, C. Ortiz-Bolsico, G. Vivó-Truyols, P.J. Schoenmakers, Program for the interpretive optimization of two-dimensional resolution., *J. Chromatogr. A.* 1450 (2016) 29–37. doi:10.1016/j.chroma.2016.04.061.