

Multi-dimensional liquid chromatography: from small molecules to large particles and from method development to data analysis

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In the MANIAC project, completely different and (seemingly) incompatible separation mechanisms are compared into a single highly efficient and extensively optimized instrument. Hence the name “Making Analytically Incompatible Approaches Compatible”. In MANIAC, various chemical, physical and microbial processes are integrated with (multi-dimensional) separation systems. Amongst the investigated applications is the characterization of complex polymeric nanoparticles encountered in coating formulations and drug-delivery systems. These complex samples feature a multitude of sample dimensions, such as the particle-size distribution, the surface composition and charge, and the molecular weight and chemical composition of the constituting molecules including its active-ingredient if applicable. A successful technique for the separation of complex mixtures is comprehensive two-dimensional liquid chromatography (LC×LC).

We recently demonstrated a proof-of-principle system, which combined a separation of particles in aqueous hydrodynamic chromatography with a fast separation of the constituting polymers by organic size-exclusion chromatography. The developed method featured a novel implementation of intermediate sample transformation and now has been expanded to allow even hydrophilic and charged particles to be modulated. In addition, we focus on the use of capillary and chip-based microreactors to improve the applicability and flexibility of the overall potential of LC×LC separations towards drug-delivery particles.

In this presentation, these and other developed methods for large and small molecules will be shown. Moreover, the development and application of method-development and data-analysis tools will be demonstrated.