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**Beneficial Aspects of Multicolumn Countercurrent Solvent Gradient Purification (MCSGP) in Difficult Center Cut Separations**

The rapid growth of the biopharmaceutical market is accompanied by stringent regulatory requirements in terms of purity and clinical safety. To comply with these more and more stringent regulations, the pharmaceutical companies are required to develop robust and reliable downstream processes capable to adapt to the different productions and to the various biomolecules that will populate the market. Chromatography, due to its sensitivity and high efficiency, is typically the technique of choice for reaching the required purity standards. However, it is often necessary to purify the product from impurities with very similar physico-chemical properties. Under this circumstance, the product elutes in the middle of and partially overlaps with slightly more weakly adsorbed and more strongly adsorbed impurities. When handling these separations with single-column processes, the result is a severe purity-yield tradeoff. The purity of the product pool can, in fact, be increased only by narrowing the collection window, which inevitably reduces the yield, and vice versa.

A valuable alternative is represented by the Multicolumn Countercurrent Solvent Gradient Purification (MCSGP). This continuous process relies on the fully automated internal recycling of the product-containing side-fractions fractions, which leads simultaneously to high purity and high product recovery. The advantages of MCSGP are particularly evident in challenging separations, where only a rather small product pool reaches the specified purity. Two particularly relevant case studies, related to the purification of a PEGylated protein and a 20mer single stranded DNA, will be presented to demonstrate the superior performances of the MCSGP in ensuring high product recovery and purity compared to a traditional single-column operation. In addition, other important advantages of the MCSGP in the framework of the downstream processing cadence will be discussed.

**Biography**

Mattia Sponchioni graduated in Chemical Engineering (M.Sc.) in 2015 with a grade of 110/110 *cum laude* at Politecnico di Milano. In 2018, he got his PhD *cum laude* in Industrial Chemistry and Chemical Engineering also at Politecnico di Milano, with a thesis focused on the development of thermo-responsive polymers for controlled drug delivery and tissue engineering under the supervision of Prof. D. Moscatelli. After the PhD, Mattia spent 10 months at ETH Zürich as a Postdoc in the laboratory of Prof. M. Morbidelli, where he maturated his interest for biopharmaceutical processes. Back to Politecnico di Milano, Mattia got a position as Assistant Professor (RTDa) in Applied Physical Chemistry in March 2022. The current research interests of Mattia Sponchioni include the synthesis of controlled and advanced polymeric materials for biomedical applications and the development of integrated and continuous processes for the manufacturing of biopharmaceuticals. Mattia is now leading the Biomanufacturing group at Politecnico di Milano, whose ambition is to demonstrate the benefits of converting the traditional manufacturing of biopharmaceuticals, mainly relying on discontinuous operations, into continuous and integrated processes. In the vision of the group, this would be the way to streamline the drug development stage, reduce the time-to-market and increase the consistency, and hence safety, of these therapeutics.