What are the benefits of continuous chromatography?

Continuous chromatography using multiple columns and a counter-current principle can improve downstream process economics in many different ways. It can increase the productivity by 10 fold; reduce the buffer demand by 50-80% and/or increase yield and purity by 50% in average. Thus, the same production output requires less installed total column volume and smaller tanks than in batch chromatography and the equipment footprint is smaller. The operational expenditures are significantly lower since less stationary phase and buffers are consumed in order to produce the same amount of material. The MIT has published together with Sandoz a study that they can save 8.5 Mio USD OPEX per year by replacing a single batch chromatography step for a single biologic by MCSGP. In addition to cost savings, continuous chromatography can also be an enabling technology in discovery, process development and manufacturing.

Continuous chromatography is a scalable engineering solution to the challenges in purification, as it employs at least two chromatography columns instead of a single column and as it fully relies on existing hardware and stationary phases with a validated supply chain.
How “continuous” is continuous chromatography?
It is important to emphasize, that in order to exploit the advantages of continuous, counter-current chromatographic processes, these do not need to be operated for a long time period. The transit time can be kept the same as with the conventional unit operations, e.g. 48hrs for a chromatographic polishing step. This also improves the regulatory compliance since the batch definition is in this way virtually the same for continuous and conventional batch chromatography.

What are the main applications of continuous chromatography?
Two different types of continuous chromatography processes are relevant for purification of biologics. The first process type is used for capture of biologics, namely monoclonal antibodies by Protein A affinity chromatography. Processes like BioSc®, BioSMB® and CaptureSMB™ fall into this category. The second type of process (MCSGP) is used mainly in all the polishing steps of biologics downstream processing where difficult separation challenges have to be solved but also in product development and discovery. Continuous chromatography has proven to be a powerful tool to purify peptides and proteins.

How has continuous chromatography evolved during the last years?
Continuous chromatography for biologics has moved away from classical processes like SMB that are limited to the separation of two components towards processes with gradient and ternary separation capabilities. The number of columns is being decreased to reduce hardware demand and complexity. As in single column chromatography, disposable columns and equipment parts are increasingly used.

In your opinion, what is to be expected from continuous chromatography in the future?
With increasing biologics manufacturing cost pressure due to legislation and competition, downstream processes will be re-assessed for cost savings. With its advantages over conventional batch chromatography, continuous chromatography will make a decisive difference in more and more cases. We will also see continuous chromatography as a key process step to enable the production of certain compounds, which are currently not accessible due to production challenges.
Continuous Chromatography recommended reading

1. Aumann L, Morbidelli M. WO/2006/116886


