IMPACT OF PRODUCT AND RECYCLE TIMES IN MCSGP POLISHING ON CHARGE VARIANT SEPARATION

Sebastian Vogg, Institute for Chemical and Bioengineering, ETH Zürich
sebastian.vogg@chem.ethz.ch
Nicole Ulmer, Institute for Chemical and Bioengineering, ETH Zürich
Fabian Steinebach, Institute for Chemical and Bioengineering, ETH Zürich
Massimo Morbidelli, Institute for Chemical and Bioengineering, ETH Zürich

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In recent years, there has been an increased research interest in continuous processing of biopharmaceuticals. This is not only due to technological advancements and better economics, but can also be attributed to enhanced quality control, for example facilitated by reduction or elimination of intermediate storage. Thus, these processes allow to improve both the product's profitability and the patient's safety. In case of downstream processing, multi-column counter-current processes have emerged both for capture (e.g. CaptureSMB, 3C-PCC) and polishing applications (e.g. SMB, MCSGP) enabling these advantages. With the exception of the well-established AEX flow-through, polishing steps are typically carried out in bind-elute mode. This is also true for the continuous processes such as SMB or MCSGP. In the latter case, the part of the eluate with high enough purity is obtained as final product, while on either side of it impure sections containing significant amounts of product are recycled onto the second column. This allows to meet purity requirements while not sacrificing yield when high resolutions are hard to achieve. An example of such a situation is the separation of charge variants of antibodies, which have been shown to have different immunogenicity and efficacy [1, 2]. While tuning the charge variant profile for a novel active pharmaceutical ingredient is currently not relevant from a regulatory point of view, it becomes very important with regards to biosimilars, where there is a target profile to be met. Industrial and academic interest in this kind of biopharmaceutical has increased over the past years due to the expiration of patents of blockbuster drugs and the necessity for processes to meet the originator's properties. In this study, we show how selection of product and recycle window of the MCSGP process impact the charge variant profile of an industrial mAb and therefore the capability of the process to tune the profile while conserving high yields.

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