NOVEL CONCEPTS FOR EFFICIENT AND PREDICTABLE MEMBRANE SEPARATION IN CONTINUOUS CELL RETENTION AND DOWNSTREAM PROCESSING

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Membranes are applied in biotechnological operations for sterile filtration, cell retention during continuous operation, and cell separation as the first step after fermentation. Membranes are also in use in various steps during purification and isolation of certain target components. In all applications the retained substances, mainly biogenic material such as cells, protein or polysaccharides, form a deposited layer at the membrane surface. This layer acts as an often dominating secondary membrane, which affects the permeability of the whole system more than the membrane as such. Thus, predictability, efficiency and consistency of all affected processing steps are impaired, which might create issues especially in GMP processes. Therefore, a deeper understanding and a better control of deposit formation would be beneficial for biotechnological operations in general and membrane filtrations in continuous processes in particular.

This presentation reports on recent work on a better understanding of deposit formation on membrane surfaces. It was the aim to intensify processes by minimizing the effect of deposit formation and, in turn, increasing flux and permeation of target substances. Success factor in all related projects was a better control of deposit formation on membrane surfaces, which in particular was enabled by assessing deposit formation along the membrane flow path using special membrane module constructions. These modules allow for the measurement of flux, solutes permeation, structure and amount of deposited material as a function of position in an industrially sized membrane system. Ceramic and polymeric membrane materials as well as tubular and spiralwound module (SWM) configurations are compared.

Fig. 1 provides an impression of the intensity of deposit formation in an SWM. The darker the colour, the more protein material is deposited. The shape of the spacer net can clearly recognized through the more intense deposition of material in the areas of flow shadows behind the spacer filaments.

Processing modes including crossflow, oscillating and alternating flow (ATF), uniform transmembrane pressure (UTP) and gradient membranes (both latter ones yielding the same transmembrane pressure or flux along the membrane length) were investigated as a function of processing conditions. These systems and variations are shown to have a tremendous impact on filtration results and, thus, on the potential for improvement of membrane performance by application of novel processing and membrane concepts. Results on cell retention in longterm membrane operation and protein fractionation by microfiltration membranes are presented as examples.

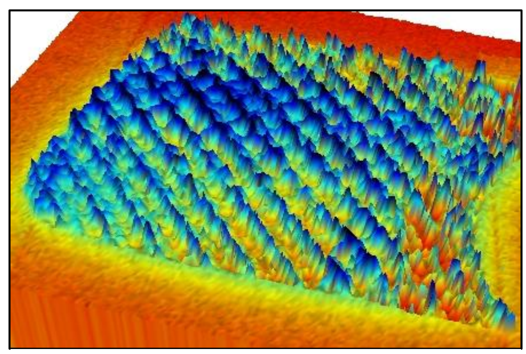

Fig. 1: Visualization of protein deposition on a UF SWM membrane using a staining method

Fig. 2 depicts flux performance for microfiltration in UTP mode of a complex biogenic fluid over 12 h filtration time. Qualitatively, the results also allow for conclusions related to optimization of membrane based processes in general from microfiltration to reverse osmosis, i.e. irrespective of pore size or nominal cut-off.

Based on the work presented, novel membrane concepts beyond ATF systems are proposed and/or optimal processing conditions avoiding or minimizing deposit formation can be selected. In conclusion, the new insights gained in this work are important for continuous operation of biological processes, where high performance in flux and a defined, stable permeation over long periods are key.

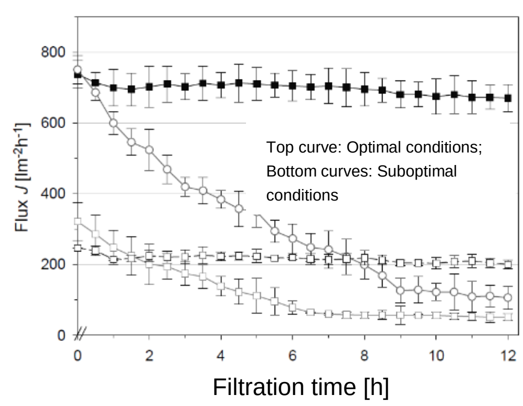

Fig. 2: Flux as a function of filtration time for MF under various conditions