

FOULING MITIGATION IN MEMBRANE BASED PERFUSION SYSTEMS BY OSCILLATING TANGENTIAL FLOW

Maria Weinberger, Chair for Food and Bioprocess Engineering, Technical University of Munich, Germany

maria.weinberger@tum.de

Ulrich Kulozik, Technical University of Munich, Germany

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Good scalability and robust handling have promoted the application of membrane based cell retention devices. A physical barrier, i.e. a filter, retains cells and cell debris. One major drawback of these devices is their tendency to foul and clog. One form of fouling is deposit layer formation on the filter surface, consisting of cells, cell debris and other fermentation broth constituents. This leads to the build-up of a secondary membrane, which can alter the permeation profile. Furthermore, deposit layers lead to an increased filtration resistance and thus negatively affect permeate flux, filtration efficiency and process robustness. In tangential flow filtration, the tangential flow velocity is increased in order to enhance shear forces that can promote deposit layer removal. A new approach to mitigate fouling is oscillation, i.e. pulsation or alternation of the tangential flow. Alternating tangential flow filtration (also known as ATF) is already used as a cell retention device. Thereby, the alternating flow is triggered by a pressurized air driven diaphragm pump, which is placed at the retentate side of a hollow fiber module (HFM). If vacuum is applied, the diaphragm moves down and fermentation broth is pulled into the HFM. The exhaust phase is followed by a pressure phase. Pressurized air moves the diaphragm up, thus expelling the broth from the HFM back to the bioreactor [1]. Although this alternating stress mitigates deposit layer formation, long residence times in the HFM can lead to nutrient shortage and negatively affect cell viability. With a customized test filtration plant we aim at reaching comparable deposit layer mitigation, while drastically reducing mean residence time in the HFM and, compared to common tangential flow filtration, at reduced tangential flow velocities. To reach this goal, not only alternating, but also pulsating tangential flow is examined. This poster will report on the methodology established in order to understand the mechanisms of deposit layer removal in both ATF and oscillating mode. First results from a systematic study on the influence of frequency and amplitude of the oscillation will also be reported.

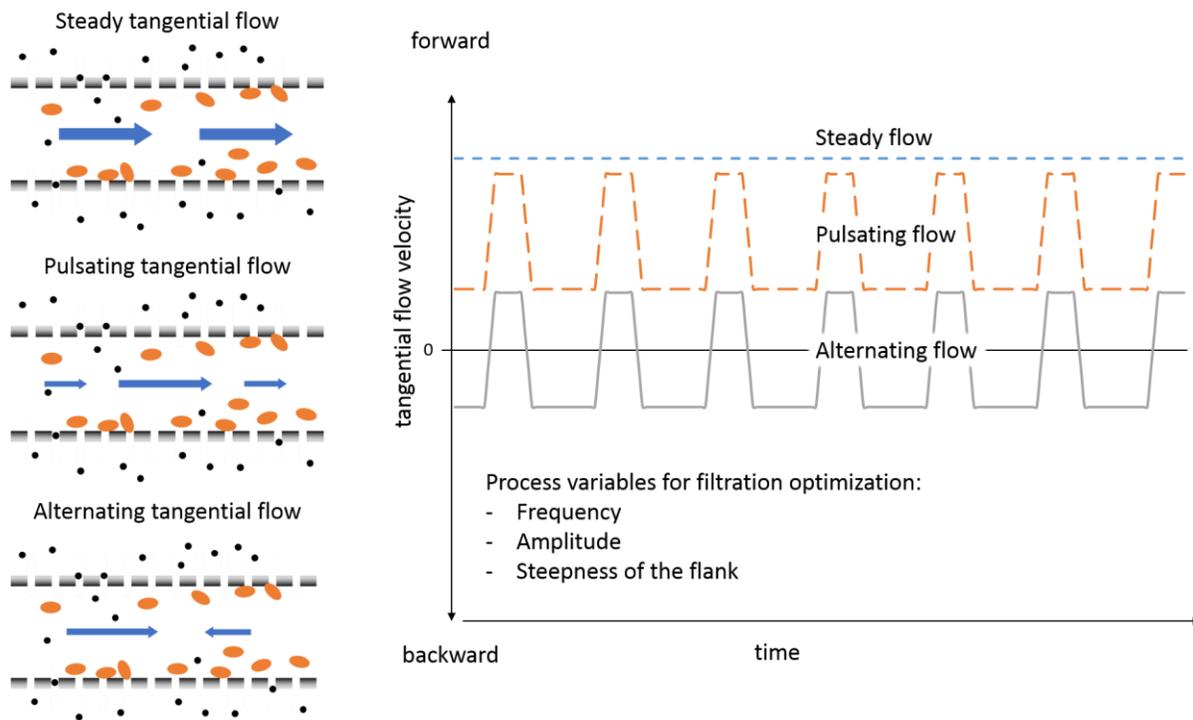


Fig. 1: Comparison of flow modes

[1] J. Furey. (2002) Scale-up of a cell culture perfusion process. Genetic engineering news. 62.