COMPUTATIONAL FLUID DYNAMICS (CFD) MODELLING AND EXPERIMENTAL CONFIRMATION OF HOLLOW FIBER TANGENTIAL FLOW FILTRATION (HFTFF) AND ALTERNATING TANGENTIAL FLOW FILTRATION (ATF) IN A PERFUSION BIOREACTOR

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Hollow fiber tangential flow filtration (HFTFF) and Alternating tangential flow filtration (HFATF) are technologies of choice in continuous (perfusion) bioreactor operations. A major drawback of these technologies is membrane fouling and associated reduction in membrane permeability. Membrane fouling leads to a gradual decline in trans-membrane flux and the sieving of the protein product. Additionally, experimental data suggests that under otherwise similar conditions protein sieving may be different in TFF vs. ATF, indicating that flow behavior patterns in the two technologies may be different.

Many models of fouling and protein sieving have been reported in the literature for HFTFF. In comparison, however, there is limited research work on HFATF, making it hard to compare mechanisms of fouling and product sieving between HFTFF and HFATF. Additionally, almost all mechanisms of fouling and predictive models make sweeping assumptions with regards to the complex flow patterns prevailing in HFTFF and HFATF. In this study, we provide experimental data and computational fluid dynamics (CFD) information to gain insight into factors that impact fouling and product sieving. Specifically, first we present the confirmation of CFD model outputs by comparing experimentally measured trans-membrane flux and pressure with model predictions. Next, we compare the CFD model predictions of pressure drop, shear rate profile and axial and radial fluid velocity distributions between HFTFF and HFATF. Subsequently, we investigate the shear effect on cell damage, using the concept of constant Camp number, defined as Gt = constant, where G is the prevailing shear rate and t is the exposure time. Our CFD model predicts that shear rate (G) and hence the resulting stress experienced by cells in HFATF has a distribution that is determined by the operation of the diaphragm pump. Finally, we use CFD to compare Gt profile generated by imposing different pump conditions.