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Scale-up and predicting flux-pressure relationships of tangential flow filtration (TFF) using a combined computational fluid dynamics (CFD) and ultra-scale-down (USD) techniques: Method and application

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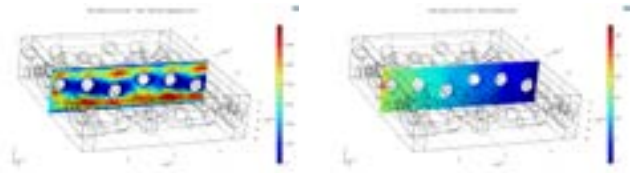
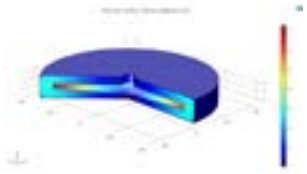
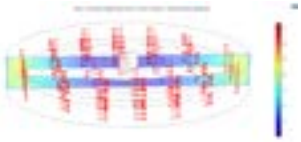
Ultra scale-down tools have demonstrated the huge benefit for rapid process development with reduced material requirement and better solutions. One of the key issues in USD techniques is its prediction accuracy of large scale performance. A new method is reported to predict the flux and transmembrane pressure relationships of a diafiltration and concentration applications for a tangential flow filtration (TFF) process, based on data generated using a novel Ultra Scale-Down (USD) membrane filtration device that uses simplistic dead-end mode of operation to mimic TFF. The system resistance, a combination of channel and applied system resistances, is constant for a given system configuration and can be easily determined by water tests. Flux-pressure drops relationships for TFF can be predicted by combining the characterised system resistances and USD model inputs. CFD studies, validated by experimental data, were carried out for TFF screened channel and the USD device, to develop correlations for averaged wall shear rates, which was used as the scale-up parameter. A flux prediction protocol was developed to predict TFF performance at scale using CFD techniques and USD data. *Escherichia coli* homogenate and *Saccharomyces cerevisiae* was used as feed material for clarification/recovery of a 46 kDa antibody fragment and primary recovery case studies respectively. Scale-up was successfully carried out for the two applications, scaling up from 13.2 cm^2 flat sheet disc (USD device) to 0.1 m^2 V-screen cassette (TFF). Predicted and experimental flux-transmembrane pressure drop and transmission data showed good agreement, which achieved the improvement on the prediction accuracy.



3D slice plots of CFD study modelling fluid flow and pressure drops in screened TFF channel (Pellicon 2 V-screen cassettes). Simulation feed flux of 5 LMM and viscosity of 0.001 Pa. s was used. Fluid flow is from left to right.



3D revolution plot of 2D axi-symmetrical model of the USD membrane filtration device



Arrow volume plot of 3D model of the USD membrane filtration device

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