Predicting Flux And Pressure Relationships of Large Scale Filtration with USD Model Inputs: Method and application

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Abstract

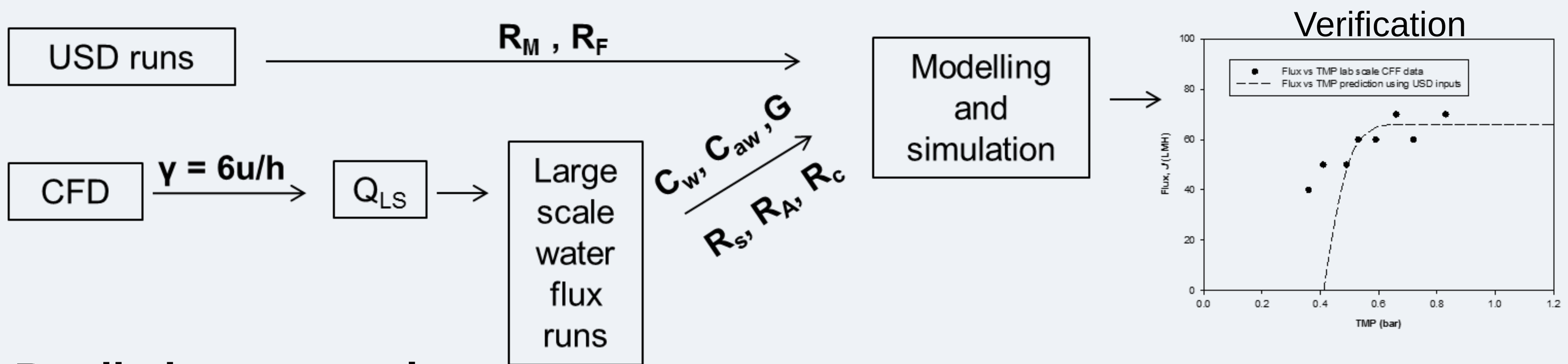
Ultra Scale-Down tools have demonstrated the huge benefit for rapid process development with reduced material requirement and better solutions. In this poster, a method was reported to predict the flux and transmembrane pressure relationships of a diafiltration application for a crossflow filtration (CFF) process, based on data generated using an Ultra Scale-Down (USD) device that uses dead-end mode of operation to mimic CFF. A new flux prediction protocol was developed to accurately determine the system resistance of large scale crossflow filtration (CFF) systems, and, to predict CFF performance using USD data. Antibody fragment (Fab') is expressed in *E. coli* as an intracellular product and *E.coli* homogenate was used for scale-up studies and to validate the prediction results. Predicted and actual flux-pressure drop and transmission data showed good agreement.

Wall shear rate correlations have been established for both the lab scale cassette and the USD device, and a mimic has been developed by operating both scales at equivalent membrane averaged shear rates.

Key objectives

- Defining and determining 'system resistance' for CFF, at scale
- Successful mimic, scale-up and prediction of CFF using USD data

Methods



Prediction protocol

Step 1: Determine membrane and fouling resistances by tests on water and the processing material using the USD device

Step 2: Determine coefficient and exponent values for channel pressure drop and flow rate power relationship by water test at large scale

Step 3: Estimate the impact of viscosity on channel & applied pressure drop

Step 4: Determine system, channel and applied system resistances using water flux test at large scale

Step 5: Predict the flux and pressure drop relationships at large scale using values of variables determined earlier

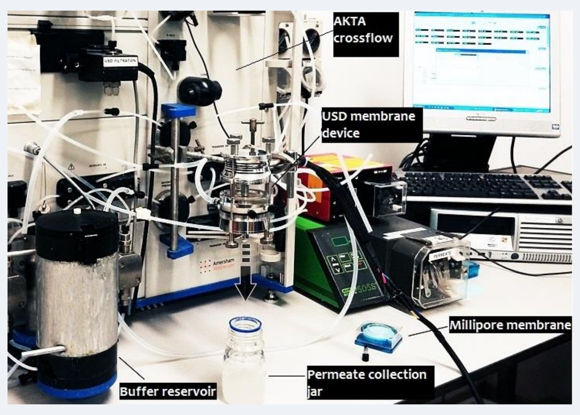


Figure 1. USD membrane filtration setup, with the AKTA Crossflow

Results: USD water and critical flux data

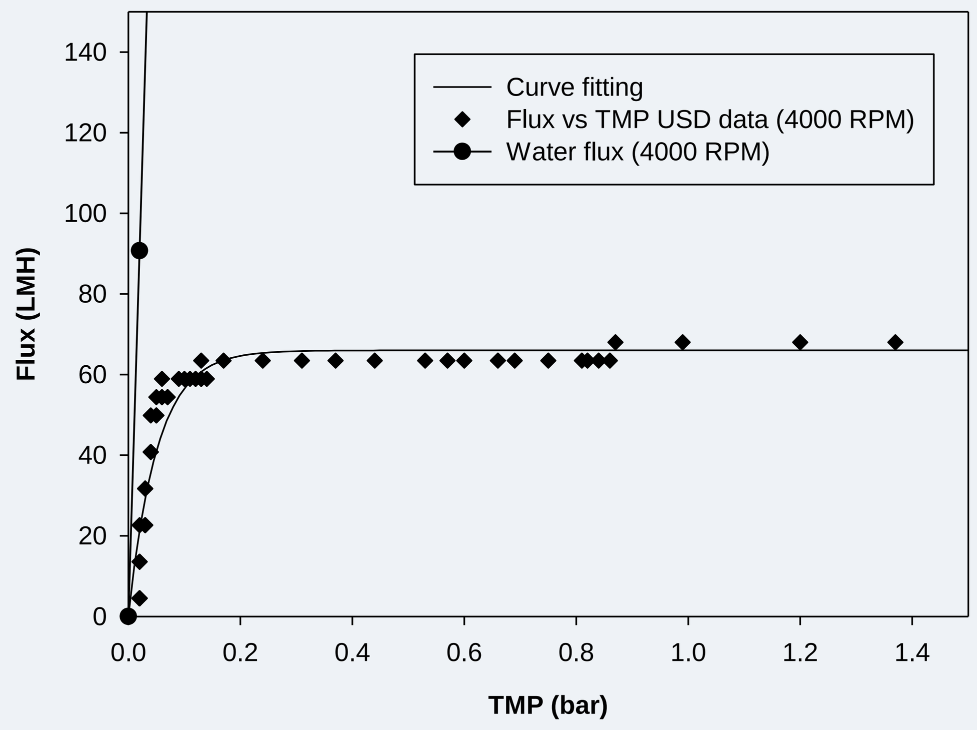


Figure 2. Flux-TMP curve for 25 g/L DCW *E. coli* homogenate, and water flux data for the USD membrane filtration device

Using USD data, parameters such as the intrinsic membrane resistance and the fouling resistance can be determined. Process scaled-up to TFF, at identical averaged wall shear rates and constant feed volume:membrane area.

Results: TFF system resistance and water flux

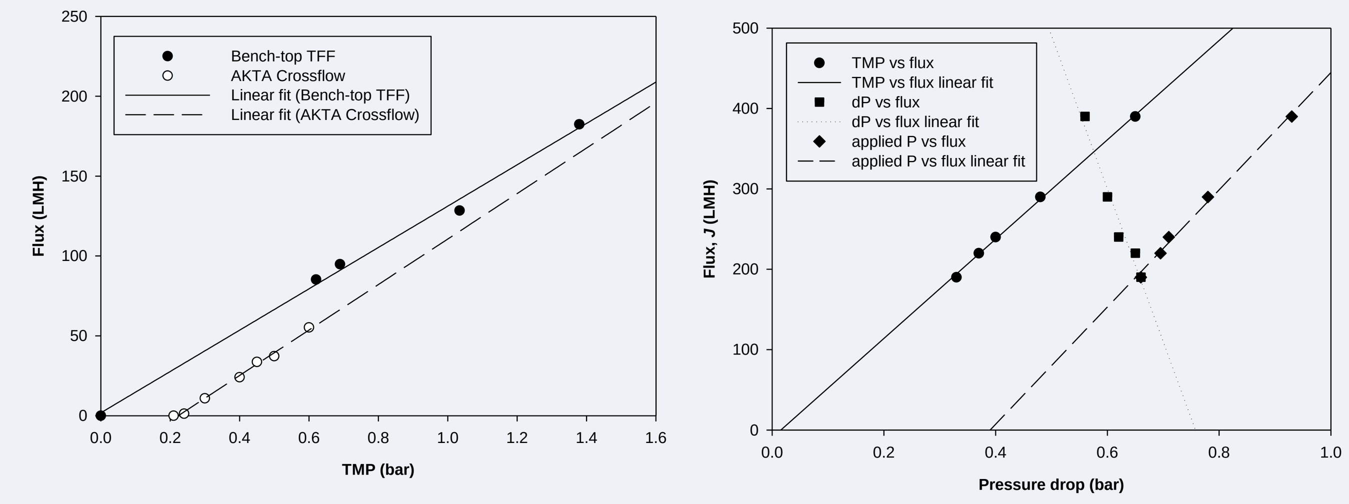


Figure 3. Left: Pure water flux data for the Pellicon XL® Ultracel 10 kDa 0.005 m^2 using the AKTA Crossflow and the TFF bench top system, at an inlet flow rate of 16.4 mL/min, at 20 ° C; Right: Water flux test for using Sartoflow Advanced, at an inlet flow rate of 110 L/hour.

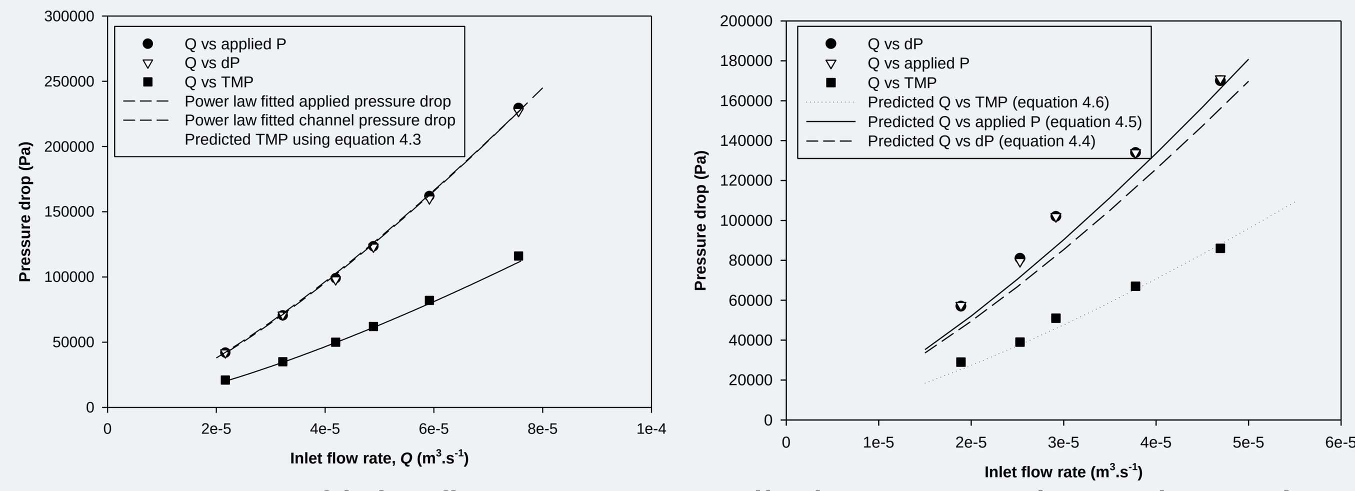


Figure 4. Impact of inlet flow rate on applied pressure drop, channel pressure drop and TMP for water (left) and *E. coli* homogenate (right)

Results: Large scale verification

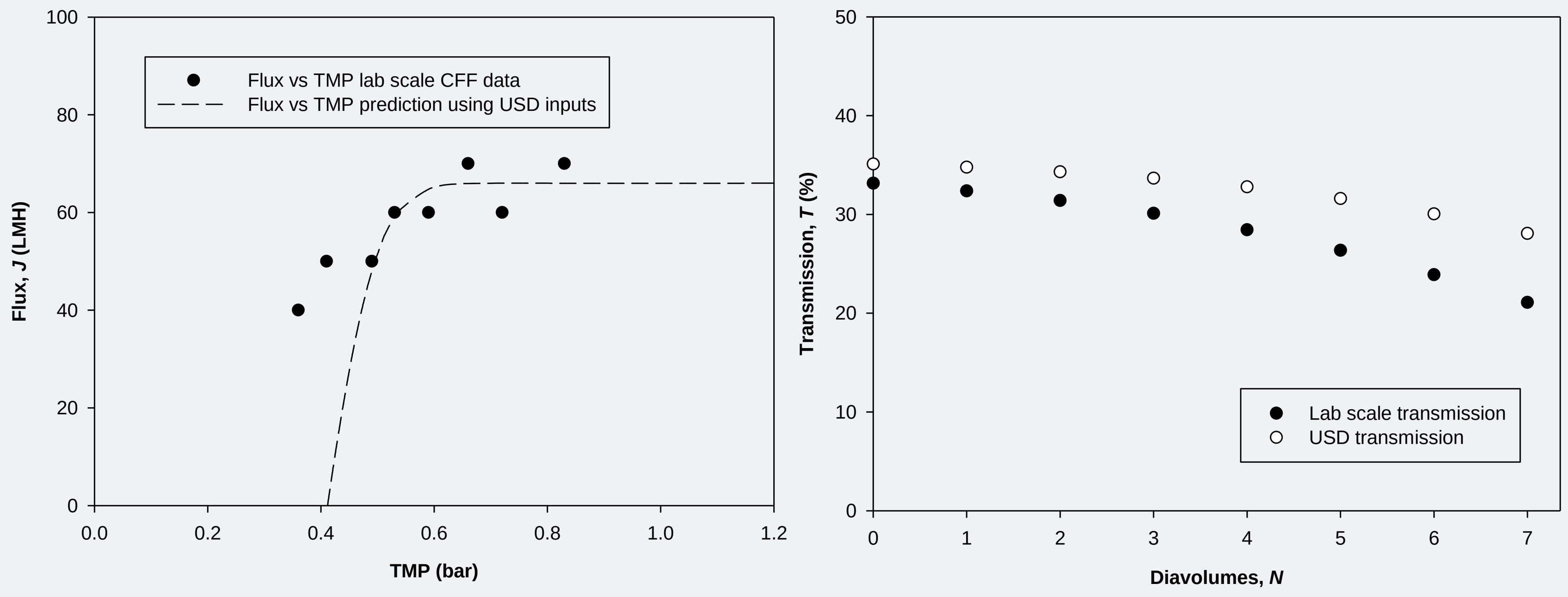


Figure 5. Pilot-scale critical flux and transmission (7 diavolumes), experimental and predicted data, for 25 g/L DCW *E. coli* homogenate at an inlet flow rate of 110 L/hr. Limiting flux was ~67 LMH, critical flux of ~60 LMH.

Conclusions and Future work

Conclusions

- System resistance of CFF systems was defined and a method to characterise them was presented, allowing prediction of CFF performance at scale
- Issue of accurately predicting TMP in large scale TFF; based on Figure 5, limiting flux and TMP values were not a perfect match

Future work

- Repeat runs with data logging system, run at constant recirculation flow rate and using CFD to develop wall shear rate correlations for both scales
- Potential of CFD, and optimising design for USD membrane filtration device
- Look into concentration applications, and using the USD device to carry out fouling studies

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