

## Introduction

In recent years, social norms and global environmental challenges have focused more on finding sustainable solutions for designing and building pharmaceutical manufacturing facilities. Significant challenges are a possible “carryover” effect of equipment fouling from previous production runs and the potential cross-contamination between manufacturing processes from the remaining cleaning-in-place (CIP) cleaning agent.

The aim of this study is to increase the fundamental knowledge of ultrafiltration (UF) membrane fouling and cleaning kinetics and estimate parameters to control fouling and cleaning. The replicability of the cleaning process was investigated. The cleaning efficiency of a UF membrane was characterized in terms of fouling and cleaning time, pure water flux recovery rate (permeate flux), and cleansing effect of used chemical agents (base and acid).

## Methods

Polyethersulfone (PES), a flat sheet ultrafiltration membrane fouled by a 1,5 wt% whey protein concentrate solution, was cleaned using sodium hydroxide. Chemical cleanliness was evaluated by UV-Vis spectroscopy and conductivity measurements of the amount of residual proteins passed through the membrane following cleaning.

The laboratory setup used for fouling and CIP is shown in Figure 1. It consists of UF cross-flow membrane module (Vibro-Lab35P, SANI Membrane A/S, Farum, Denmark), a peristaltic feed and retentate pumps, permeate and retentate outlets.

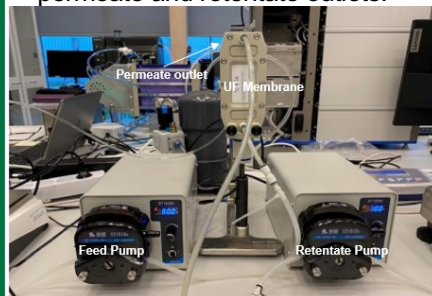


Figure 1. Vibro Lab35P laboratory set-up (SANI Membranes)

## Outcome

Cleaning of PES membranes, after ultrafiltration alkaline first step followed by a nitric acid step mode, provided satisfactory results regarding permeate flux recovery. Comparison of PES UF membranes with molecular weight cut-off (MWCO) of 10 and 30 kDa is shown below.

Exp. design	Membr. type (kDa)	TMP (bar)	Feed conc. (g/l)	No. of exp.	WF (min.)	Fouling (h)	FWF (ml.)	Alkaline wash (min.)	SWF (min.)	Acid wash (min.)	TWF (min.)	FinWF (min.)
1	10	3	150	4	40	4	40	20	40	35	40	40
2	30	3	150	4	40	4	40	20	40	35	40	40

Table 1. Two experimental design: 1- 10 kDa membrane and 2- 30 kDa membrane (abbreviations: WF- water flush before fouling step; FWF- first water flush; SWF- second water flush; TWF- third water flush; FinWF- final water flush)

Exp. design	WF 1 (l/h/m <sup>2</sup> )	Fouling 1 (l/h/m <sup>2</sup> )	FWF 1 (l/h/m <sup>2</sup> )	Alkaline 1 (l/h/m <sup>2</sup> )	SWF 1 (l/h/m <sup>2</sup> )	Acid 1 (l/h/m <sup>2</sup> )	TWF 1 (l/h/m <sup>2</sup> )	Fin WF 1 (l/h/m <sup>2</sup> )
1	19	0.02	19	82	25	36	15	19
2	16	3	11	25	15	19	15	19

Table 2. Change in permeate flux of 10 kDa (exp. design 1) and 30 kDa (exp. design 2)

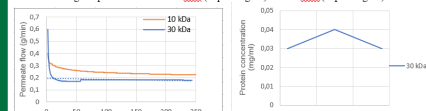


Figure 2. Typical fouling curve, 10 and 30 kDa

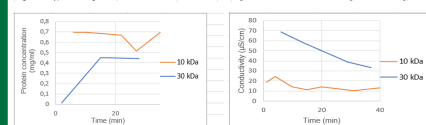


Figure 3. UV-Vis measurement during alkaline cleaning, 10 and 30 kDa

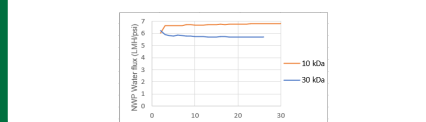


Figure 4. UV-Vis measurement during acid cleaning, 10 and 30 kDa

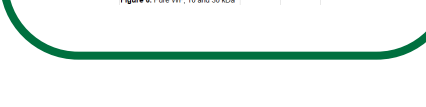


Figure 5. Conductivity of FinWF, 10 and 30 kDa



Figure 6. Pure WF, 10 and 30 kDa

## Perspectives

The study “Kinetics and parameter control of membrane CIP” is one of a kind and has never been done by the NNE. We are the pioneers in characterizing the process parameters and tapping into the cleaning kinetics.

I am grateful for the opportunity to be the initiator of future work on CIP cleaning of the membrane. I hope prospective students and their mentors will continue to build upon my work and further improve its use in the industry.

Through my fellowship at the Helix Lab, I was able to experience the academic environment while networking with industry professionals. All this can lead to a better future career opportunity, ideally in the Kalundborg industry.