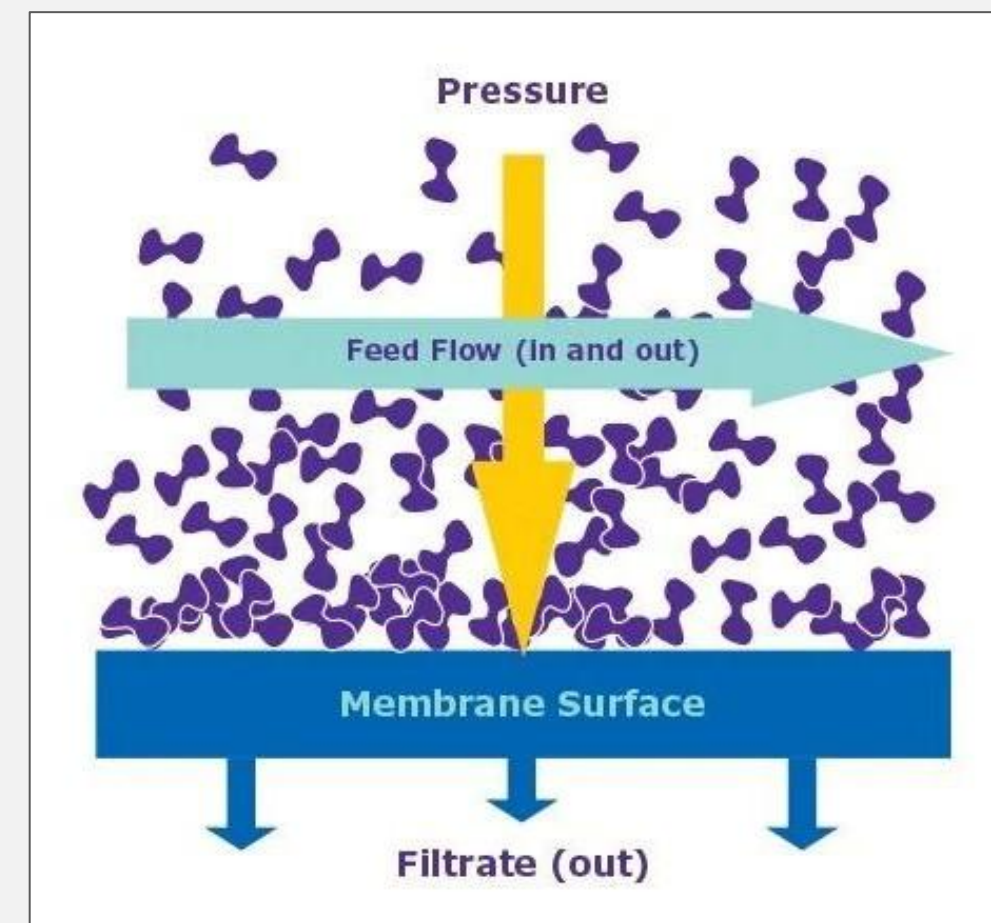


Productivity and Economic Comparisons of Single-Pass and Recirculating TFF in Manufacturing-Scale Processing

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Background

Ultrafiltration/diafiltration (UF/DF) is a membrane-based separation step used in most biopharmaceutical manufacturing processes. Ultrafiltration refers to the concentration and purification of the molecule of interest in a process. Diafiltration refers to the exchange of buffers.



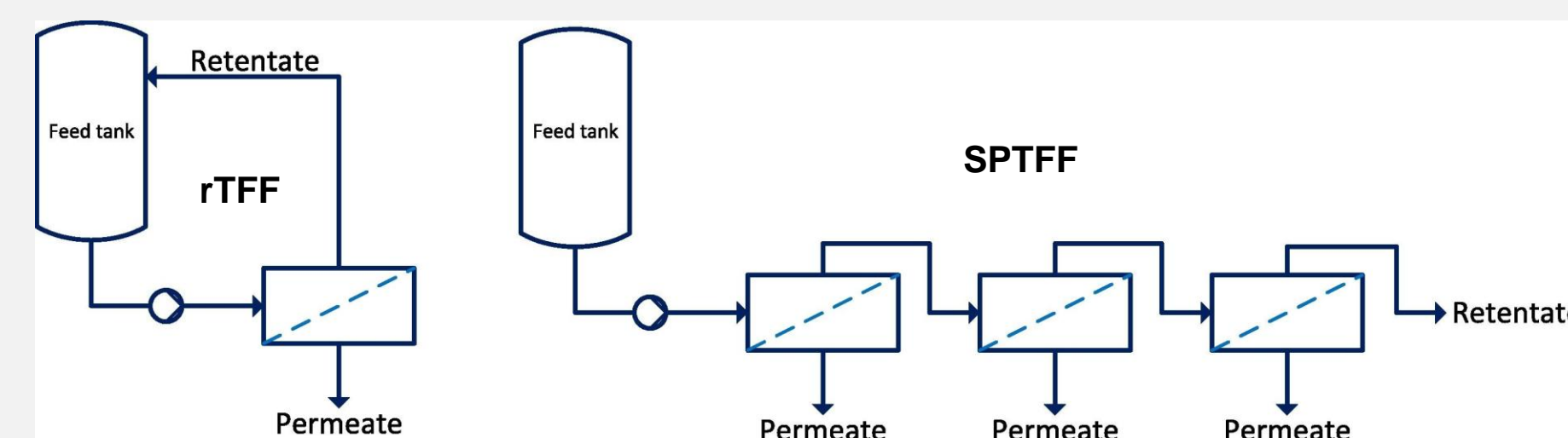
At KBI Biopharma, 3 UF/DF steps are used for a client's process. Each of the UF/DF steps uses tangential flow filtration (TFF) cassettes (above). When using TFF as your filtration method, there are two options:

1. Recirculating TFF (rTFF)

- A method that is established in the biopharmaceuticals industry
- Runs in multiple passes through the membrane, recirculating through the tank and filtration unit

2. Single-Pass TFF (SPTFF)

- A novel method that most companies are not familiar with, but offers many potential benefits
- Moves feed solution through a linear flow path, slower flow rates and increased membrane surface area eliminate the need for recirculation



Project Goal

The NCSU KBI Senior Design Team's goal was to determine if a switch to SPTFF technology for specific unit operations in KBI Biopharma's plant is beneficial.

Two factors were considered to determine if SPTFF is beneficial for the process:

1. Operational productivity (suite time)
2. Economic cost (equipment, buffers, and operations)

Methods/Results

rTFF

UF/DF 2 rTFF Process Parameters		Cassette + Accessory Pricing	
Load Volume	281.5 L	1.14 m ² cassette	\$18,822
Load Concentration	4 g/L	mixing bag	\$496
Load Factor	600 g/m ²	total	\$19,318
# of cassettes	2	Minimum area:	1.88 m ²
Mixing Bag	900 L		

rTFF Total Equip. Cost \$95,634 per process

UF/DF 2 rTFF Process Parameters		Time Calculation	
Permeate Flux	2.5 L/m ² /min	WFI Flush Time	36 min
Load Volume	281.501 L	Equilibration Time	4 min
Load Concentration	4 g/L	Concentration Step Time	30 min
Retentate Volume	111.475 L	Diafiltration Step Time	176 min
Retentate Concentration	10 g/L	Recovery Flush Time	0.2 min
Membrane Area	2.28 m ²	Dilution Time	0 min
Diavolumes	8	Total Time	246 min
WFI Flush	90 L/m ²		
Equilibration	10 L/m ²		
Recovery Flush	1 L		

Total Suite Time for rTFF 16.54 h

TFF Process				
Utilities	\$	/Units	Unit/day	Est. Cost/ 10 days
Electricity	\$0.070	\$/kWh	105.60 kW	\$73.92
Labor	\$30.000	\$/hr per person	16.54 hrs	\$9,924.53
Waste Disposal	\$0.036	\$/kg	8611.36 kg	\$3,100.09
Total Cost				\$13,201.86

UFDF 2			
Method Block	Buffer	Volume (L/m ²)	Volume (L)
WFI Flush	WFI		205.20
Equilibration	Buffer 7		10
Diafiltration	Buffer 7 in DVs		891.80
Recovery Flush	Buffer 7	Calculated to target final concentration	0.40
Dilution	Buffer 7	Optional step, dilution continues if target is not met post-recovery flush	0.00

rTFF Total Buffer Cost: \$92,238.09

SPTFF

UF/DF 2 SPTFF Process Parameters		SPTFF min. area:	
Load Volume	281.5 L	rTFF min. area:	1.86 m ²
Conc. Time	30 min		
Feed Flux Rate	1 LMM		
# of cassettes for concentration	9	Feed Bag	500 L
# of cassettes for diafiltration	2	Retentate Bag	200 L
		Mixing Bag	200 L
		Cassette + Accessory Pricing	
		1.14 m ² cassette	\$84,699
		1.14 m ² cassette	\$18,822
		Bags	\$3,765
		total	\$107,286

SPTFF Total Equip. Cost \$250,070 per process

UF/DF 2 SPTFF Process Parameters		Time Calculation	
Feed Flux	1 L/m ² /min	WFI Flush Time	36 min
Load Volume	281.5 L	Equilibration Time	4 min
Load Concentration	4 g/L	Concentration Step Time	30 min
Retentate Volume	111.5 L	Diafiltration Step Time	176 min
Retentate Concentration	10 g/L	Recovery Flush Time	0.2 min
SPTFF Membrane Area	10.26 m ²	Dilution Time	0 min
TFF Membrane Area	2.28 m ²	Total Time	246 min
Diavolumes	8		
WFI Flush	90 L/m ²		
Equilibration	10 L/m ²		
Recovery Flush	2.2 L		

Total Suite Time for SPTFF 16.57 h

SPTFF Process				
Utilities	\$	/Units	Unit/day	Est. Cost/ 10 days
Electricity	\$0.070	\$/kWh	52.80 kW	\$36.96
Labor	\$30.000	\$/hr per person	16.57 hrs	\$9,939.39
Waste Disposal	\$0.036	\$/kg	8398.39 kg	\$3,023.42
Total Cost				\$13,130.58

UFDF 2			
Method Block	Buffer	Volume (L/m ²)	Volume (L)
WFI Flush	WFI		90
Equilibration	Buffer 7		10
Diafiltration	Buffer 7 in DVs		891.80
Recovery Flush	Buffer 7	Calculated to target final concentration	2.20
Dilution	Buffer 7	Optional step, dilution continues if target is not met post-recovery flush	0.00

SPTFF Total Buffer Cost: \$90,863.54

Discussion

Equipment Costs:

- The in-line configuration of SPTFF steps greatly increases equipment costs as two sets of cassettes are needed

Suite Time:

- Both rTFF and SPTFF have nearly identical suite times across the three UF/DF steps in this process

Operational Costs:

- Operational costs are very similar between rTFF and SPTFF

Buffer Costs:

- SPTFF process buffer costs are slightly lower (~1-2%) than rTFF

Acknowledgements

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Conclusions

UF/DF step times are very similar between rTFF and SPTFF, but SPTFF has nearly double the expenses per process due to the equipment costs. For this reason, it is not yet feasible for KBI Biopharma to use SPTFF in this process.

Based on these findings and our research, we would recommend the use of SPTFF in continuous bioprocessing. It decreases hold-up volumes and can minimize product loss while decreasing downtime in the product stream.

References

Link to references →

