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Compatibility of Hollow Fiber Modules With Sartoflow® Single-Use (SU) Tangential Flow Filtration (TFF) Systems

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Abstract

Sartorius manufactures single-use (SU), humectant-free hollow fiber tangential flow filtration (TFF) modules for lab-, pilot- and production-scale separation operations. We have now integrated our hollow fiber modules into the Sartoflow® 1000 and Sartoflow® 4500 single-use tangential flow filtration (SU TFF) systems via an add-on. This integration provides end users with a cGMP-compliant filtration strategy while retaining convertibility to flat-sheet filtration.

This application note covers the addition of Sartorius' Hollow Fiber TFF Modules | Single-Use Line to the Sartoflow® 1000 and Sartoflow® 4500 systems.

Introduction

Hollow fiber tangential flow filtration is a competitive filtration method experiencing rapid uptake throughout the biomanufacturing industry thanks to its small footprint, closed self-contained modules, flexibility in process volumes, and high surface area-to-volume ratio compared to traditional tangential flow filtration methods.

Sartoflow® SU TFF systems offer a combination of hardware, control system, and single-use flow kits designed to work together seamlessly. The smart system design ensures ease of use when running fully-automated TFF process sequences, with plug-and-play SU flow kits incorporating all critical sensor and instrumentation technologies.

Sartorius has now integrated hollow fiber modules via an add-on to the Sartoflow® 1000 (pilot scale) and Sartoflow® 4500 (commercial scale) SU TFF systems. This integration provides end users with an efficient, cGMP, 21 CFR Part 11-compliant process and maximizes flexibility to meet individual requirements. The standard TFF system flow kit requires no modifications to enable hollow fiber filtration; users benefit from connectivity to both hollow fiber and flat-sheet filters.

Sartoflow® 1000 and Sartoflow® 4500 SU TFF systems can be adapted to enable the operation of hollow fiber TFF modules rapidly and with little training, dramatically reducing installation time and time-to-market. A variety of surface areas, retention rates, lengths, and sample volumes means there is a module fit for every process step. These hollow fiber tangential flow filtration offerings provide an ideal SU filtration solution for batch volumes from 10 mL to 2,500 L. On the Sartoflow® 1000 and Sartoflow® 4500, a range of modules suitable from 5 L up to 500 L can be operated.

The setup described in this application note is designed for ultrafiltration and diafiltration applications. To perform microfiltration, an auxiliary permeate flow control must be added.

Figure 1: *Sartoflow®1000 (pilot scale) and Sartoflow®4500 (commercial scale)*

System Compatability

Sartorius' hollow fiber modules are designed for linear scale-up, offering consistency in design elements such as materials of construction, fiber configuration, and fiber length. Additional product attributes include low fouling, minimal hold-up volume, a self-contained design, and the absence of glycerin and other humectants. This application note demonstrates the feasibility of performing hollow fiber tangential flow filtration with Sartoflow® TFF systems.

Sartoflow® 1000 Compatibility

The hollow fiber TFF modules compatible with Sartoflow® 1000 are:

- Investigator 12-inch, 24-inch, and 41-inch | Single-use Line
- Mini Bioproducer 12-inch, 24-inch, and 41-inch | Single-Use Line

Table 1 specifies the calculated flow rates based on different shear rates, for the different HF modules in combination with the Sartoflow® 1000.

Table 1: *Calculated Feed Flow Rates and Their Related Shear Rates for Hollow Fiber Modules at the Sartoflow® 1000 Scale*

	Hollow Fiber Module	**Investigator**			**mini-BioProducer**		
	Hollow fiber length [inch]	12	24	41	12	24	41
	Surface area [m²]	0.13	0.27	0.5	0.63	1.3	2.5
	Batch volume [L]	1 to 25			5 to 250		
Shear [sec-1]	**Lumen ID [mm]**	**Feed Flow [L/hr]**			**Feed Flow [L/hr]**		
2000	0.5	-			150		
	1	120			570		
	2	480			-		
3000	0.5	45			225		
	1	180			855		
	2	720			-		
4000	0.5	60			300		
	1	240			-		
	2	-			-		
5000	0.5	75			375		
	1	300			-		
	2	-			-		
6000	0.5	90			450		
	1	360			-		
	2	-			-		
7000	0.5	105			525		
	1	420			-		
	2	-			-		
8000	0.5	120			600		
	1	480			-		
	2	-			-		
9000	0.5	135			675		
	1	540			-		
	2	-			-		
10000	0.5	150			750		
	1	600			-		
	2	-			-		

Sartoflow® 4500 Compatibility

The hollow fiber TFF modules compatible with Sartoflow® 4500 are:

- Bioproducer 24-inch | Single-Use Line with a surface area of 2.7 m²
- Bioproducer 41-inch | Single-Use Line with a surface area of 5 m².

Both systems can be operated in both 0.5 mm and 1.0 mm fiber IDs. When installing a Bioproducer 24-inch or 41-inch in 0.5 mm, a shear rate of 10,000 sec^{-1} can be achieved (1,500 L/h feed flow). When operating a Bioproducer 24-inch or 41-inch in 1.0 mm, a shear rate of 6,000 sec^{-1} can be achieved (3,420 L/h feed flow) (Table 2).

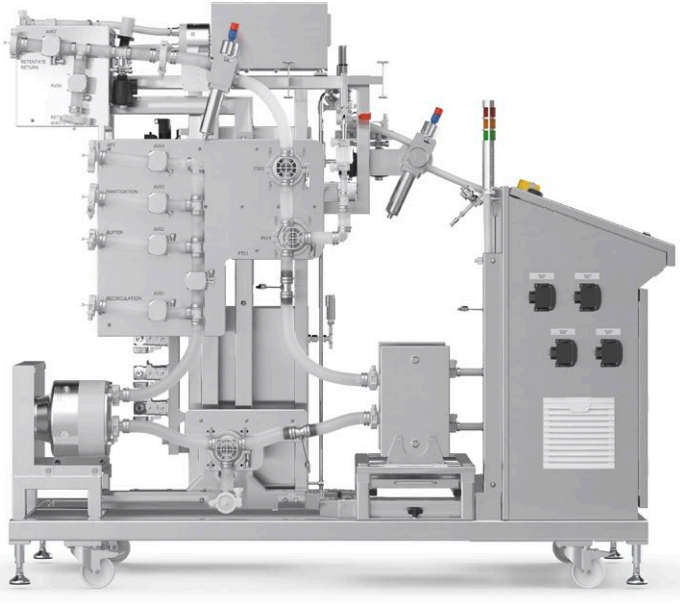

Table 2: *Calculated Feed Flow Rates and Their Related Shear Rates for Hollow Fiber Modules at the Sartoflow® 4500 Scale*

	Hollow Fiber Module	**BioProducer**	
	Hollow fiber length [inch]	24	41
	Surface area [m²]	2.7	5
	Batch volume [L]	25 – 500	
Shear [sec-1]	**Lumen ID [mm]**	**Feed Flow [L/hr]**	
2000	0.5	300	
	1	1,140	
	2	-	
3000	0.5	450	
	1	1,710	
	2	-	
4000	0.5	600	
	1	2,280	
	2	-	
5000	0.5	750	
	1	2,850	
	2	-	
6000	0.5	900	
	1	3,420	
	2	-	
7000	0.5	1,050	
	1	-	
	2	-	
8000	0.5	1,200	
	1	-	
	2	-	
9000	0.5	1,350	
	1	-	
	2	-	
10000	0.5	1,500	
	1	-	
	2	-	

Materials and Methods

To establish hollow fiber functionality within Sartoflow® 1000 and Sartoflow® 4500 systems, tests were conducted using three modules: Investigator 12-inch, Bioproducer 24-inch, and Bioproducer 41-inch (Table 3). All tests were conducted using non-purified facility water, and environmental variables were assumed to be standard temperature and pressure.

Table 3: *Scope of Testing*

Module	Sartoflow® 1000	Sartoflow ® 4500	Surface Area [m²]	Recommended Batch Size [L]	MWCO [kDa]	Lumen ID [mm]	Hold Up Volume [L]
Investigator 24-inch | Single-Use Line	■	-	0.28	1 – 25	300	1.0	0.249
Bioproducer 24-inch | Single-Use Line	-	■	2.7	25 – 500	750	1.0	2.386
Bioproducer 41-inch | Single-Use Line	-	■	5.0	25 – 500	300	1.0	4.241

Assembly & Disassembly

A minimally invasive mounting bracket (Figure 2) enables rapid and straightforward addition and removal of hollow fiber tangential flow filtration functionality. Assembly and disassembly should require no more than two people and around ten minutes to mount or remove the hollow fiber module and bracketry. The hollow fiber brackets do not need to be removed from the system when exchanging used modules of the same dimension. When swapping modules of different dimensions, bracket arms may need to be adjusted, removed, or added. The additional flexibility enables users to adapt quickly and increase system utilisation and efficiency.

Please note that depending on geographical location, a different mounting bracket model may be required for compatibility with the system's frame. Please reach out to Sartorius application specialists.

Figure 2: *CAD Drawing of the Hollow Fiber Mounting Brackets*

Module Preparation

The Single-Use Line offers a ready-to-use hollow fiber TFF module, with no cleaning required. Therefore, no cleaning regimen or cleaning validation documentation is provided.

Modules are delivered packaged, validated, and ready to deploy thanks to a gamma-irradiation regimen adherent to rigorous industry standards. Each single hollow fiber module is integrity tested to guarantee desired out-of-box performance. New hollow fiber modules are packaged in two separate, sealed polyethylene bags.

Module feed, retentate, and permeate ports are double-capped to retain moisture and prevent contamination from external sources.

Short preparation time is required to begin using the module. However, all residual air from the filter must be vented out before process deployment, and equilibration must be performed with purified water or buffer. Flow kit ventilation can be achieved by running the feed pump at 35% output until the absence of air bubbles is visually confirmed.

Results and Discussion

The exceptional uniformity of Sartorius single-use hollow fiber TFF membranes and the precision of module assembly means the modules perform consistently and show high lot-to-lot similarity. As a result, hollow fiber module performance is scalable, with results for a given module closely corresponding to other module sizes. Therefore, the testing scope was limited to the modules in Table 1.

The scope of testing included filling of retentate and permeate lines, maximum achievable crossflow flux (CFF), transmembrane pressure (TMP) control, hold-up and recoverable volumes, and minimum TMP. The recorded data are shown in Tables 4 and 5.

Table 4: *Process Data for Standard Sartoflow® 1000 and Sartoflow® 4500 with Associated Hollow Fiber Modules*

System	Module	Pump Output [%]	CFF***** [LMM****]	Shear Rate [s^{-1}]	Retentate Valve [%]	Retentate Pressure [psi | barg***]		Permeate Pressure [psi | barg***]		TMP* [psi | barg***]	
Sartoflow® 1000	Investigator 24"	25	16.31	4,856		5.88	0.41	0.25	0.02	3.03	0.21
		50	29.85	8,872		16.45	1.13	0.28	0.02	10.19	0.70
		70**	40	11,900		27.5	1.90	0.33	0.02	17.85	1.23
Sartoflow® 4500	Bioproducer 24"	25	9.24	2,641		3.60	0.25	0.77	0.05	1.79	0.12
		50	17.27	4,935	100	9.43	0.65	3.75	0.26	3.75	0.26
		100	31.7	9,060		20.50	1.41	9.86	0.68	7.15	0.49
	Bioproducer 41"	25	4.40	2,338		5.0	0.35	2.10	0.14	2.0	0.14
		50	8.45	4,489		11.75	0.81	4.75	0.33	5.0	0.34
		100	16	8,500		23.20	1.60	11.0	0.76	8.70	0.60

Note. Shear rate was calculated using Sartorius Shear Rate Calculator (https://watersep.net/calculator-shear-calculator/)

Table 5 displays the hold-up volume of the Investigator 24" and Bioproducer 41" hollow fiber modules for functionality transparency. The results further demonstrate the use of hollow fiber modules on Sartoflow® SU TFF systems does not alter the hold-up volume of standard flow kits.

Table 5: *Hold-Up and Recoverable Volumes*

	Hollow Fiber Module	Trial 1 [L]	Trial 2 [L]	Trial 3 [L]	Average	Standard Deviation
Flow Kit Hold-Up Volume (Incl. Module)	Investigator 24"	0.60	0.54	0.51	0.55	0.05
	Bioproducer 41"	6.25	6.40	6.80	6.48	0.28
Flow Kit Hold-Up Volume (Excl. Module)	Sartoflow® 1000	0.35	0.29	0.26	0.30	0.045
	Sartoflow® 4500	2.01	2.16	2.56	2.24	0.28

* There exists an inherent minimum back pressure even when CV-01 is opened to 100%
** Not possible to reach 100% pump output as feed pressure maximum is reached beforehand. Therefore, the highest achievable output (70%) was recorded
*** All measurements were taken in psi. Conversion to barg was rounded to the nearest hundredth.
**** LMM = liter/minute/m^2
***** CFF = Cross flow flux

Conclusion

Sartoflow® 1000 and Sartoflow® 4500 production-scale TFF systems can now be configured to add a mounting bracket that enables hollow fiber TFF functionality without compromising the structure of the sytem. This integration provides users with a cGMP, single-use, 21 CFR Part 11-compliant filtration solution that requires no special configuration.

Adding hollow fiber TFF functional support to the Sartoflow 1000 and Sartoflow 4500 supports a small facility footprint, flexibility in process volumes, and a high surface area-to-volume ratio compared to traditional tangential flow filtration methods. Furthermore, hollow fiber brackets and modules were designed with a focus on speed and ease of use, enabling significant reductions in total time to market.

References

1. Sartorius. (2021). Green Line Single-Use Hollow Fiber Modules. Retrieved from https://shop.sartorius.com/fr/p/single-use-line/M_Green_Line

For more information about Hollow Fiber TFF Modules, visit
www.sartorius.com/en/products/process-filtration/tangential-flow-filtration/hollow-fiber-tff

For more information about the Sartoflow 1000 Single-use TFF System, visit
www.sartorius.com/en/products/process-filtration/tangential-flow-filtration/tff-systems/sartoflow-1000

For more information about the Sartoflow 4500 Single-use TFF System, visit
www.sartorius.com/en/products/process-filtration/tangential-flow-filtration/tff-systems/sartoflow-4500

Figure 3: *Sartorius Hollow Fiber TFF modules (Single-use Line, Steamer Line, Re-use Line)*

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