Increased Productivity with Single-Use Membrane Chromatography

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Introduction

Membrane chromatography is a well-established technology in bioprocessing. It is routinely used in the capture of large particles such as viruses and viral vectors, as well as in polishing steps for the removal of DNA, HCPs and virus. It has a disruptive potential for solving the DSP bottleneck in intensified bioprocessing.

The most important benefits of membrane chromatography in bioprocessing are

Ready-to-use | **Single-batch use** | **Productivity**

The development of single-use membrane chromatography systems designed to fully support and exploit the potential of membrane adsorbers will deliver additional productivity increases for this technology.

Ready-to-use: membrane chromatography devices

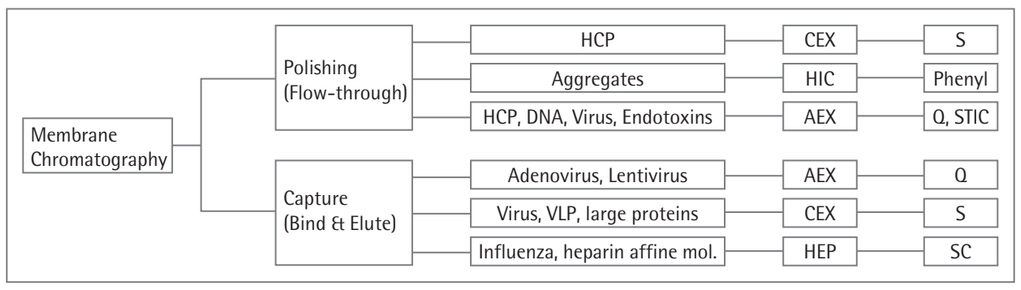

Fig. 1: Typical modes of operation and applications for membrane chromatography in the biopharmaceutical industry. Ligands: S = sulfonic acid for cation exchange (CEX), Phenyl for hydrophobic interaction chromatography ligand (HIC), Q = quaternary ammonium, STIC = STIC PA primary amine (salt tolerant) for anion exchange (AEX), SC = sulfated cellulose

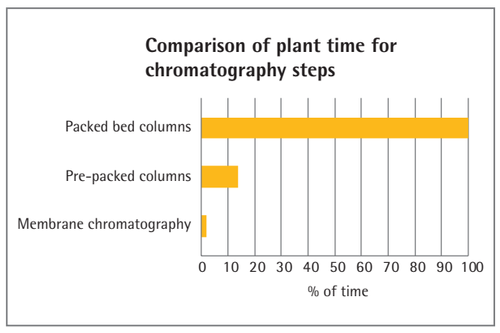

Fig. 2: Comparison of plant time for traditional chromatography (packed bed) versus prepacked columns and membrane chromatography.

Fig. 3: Gamma-irradiated Sartobind® Q cassettes are sterilized with ≥ 25 kGy without showing any performance difference to standard Q cassettes.

Ready-to-use membrane chromatography devices are available in a wide range of sizes suitable from process development to manufacturing. Different modalities come in either 4 mm or 8 mm membrane bed heights, for flow-through polishing and bind & elute applications, respectively (see fig. 1). Upfront investment for columns and large resin volumes is by-passed, and hands-on time for column packing and testing is eliminated. Using membrane chromatography reduces plant time up to 95%[1] (see fig. 2). Sterile membrane chromatography devices provide further benefits for bioburden control especially when the product cannot be sterile filtered due to large molecule size.

Single-batch use: lifetime usage within one batch

	Membrane chromatography	Conventional chromatography
Protein A	12 sec	4 – 6 min
CEX	12 sec	2 min
AEX	6 sec	2 min

Tab. 1: Comparison of standard residence times for membrane chromatography and conventional bead chromatography.

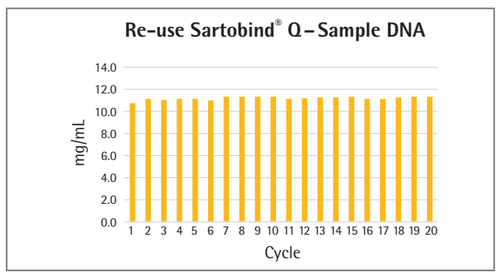

Fig. 4: DBC 10% for 1 mL Sartobind® Q (4 mm) was measured using Salmon Sperm DNA over 20 cycles with a flow rate of 10 MV/min resulting in constant DBC over 20 cycles (incl. CIP after each cycle).

Membrane chromatography is usually run at 20× higher flow rates compared to resins. Membrane design enables functional performance at convective flow rates with very short residence times, and thus with much shorter cycle times compared to resins (see tab. 1). Fig. 4 shows that re-use of membranes for at least 20 cycles does not affect binding capacity, thus allowing intra-batch re-use of membranes[2].

Productivity: comparing conventional & membrane chromatography

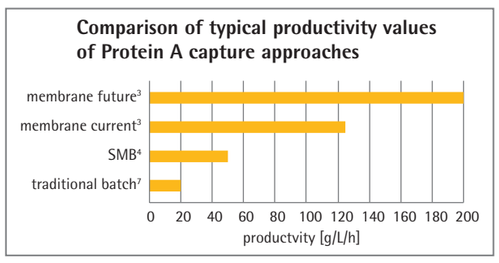

Fig. 5: Comparison of typical productivity values for traditional batch protein A capture, simulated moving bed (SMB), current membrane chromatography and potential of future protein A membranes.

	Membrane chromatography	Conventional chromatography
Capacity	>10.9 kg/L	50 – 100 g/L
Flow rate	450 – 600 cm/h	100 – 150 cm/h
Operation time	2 – 2.5 h	8 – 9 h
Buffer consumption	5%	100%
Cleaning validation	single-use	yes

Tab. 2: Comparison of Q membrane and conventional chromatography in flow-through contaminent removal applications[5].

The bottleneck in DSP is caused by the low productivity of traditional batch chromatography. This may be overcome by SMB approaches but membrane chromatography shows game-changing potential, especially when binding capacities are further improved[3] (see fig. 5). The challenge of throughput in flow-through polishing is also addressed by membrane chromatography, while avoiding oversizing and high buffer consumption[5] (see tab. 2).

Dedicated membrane chromatography system

Fig. 6: Membrane Chromatography skid based on the BioSC platform

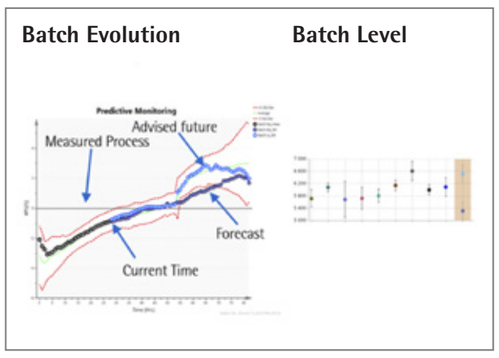

Fig. 7: SIMCA®-online for Multivariate Data Analytics

Novasep's established BioSC platform and Sartorius Stedim Biotech's single-use technology will form the basis for the development of innovative chromatography systems. Systems currently on the market are designed for resins, and do not take full advantage of membrane chromatography capabilities. Optimally run membrane chromatography processes will provide a more attractive alternative to batch and continuous resin-based chromatography – namely higher productivity, smaller scale operations and increased robustness (see fig. 6). Systems will incorporate SIMCA®-online. Delivering in-depth insights into process performance across the manufacturing network, managerial staff can take evidence-based proactive actions that will help achieve better, more timely decisions, ensuring superior manufacturing success. Umetrics® Suite has the potential to "auto-drive" the system within the boundaries of the Design Space or a golden batch (see fig. 7).

Summary

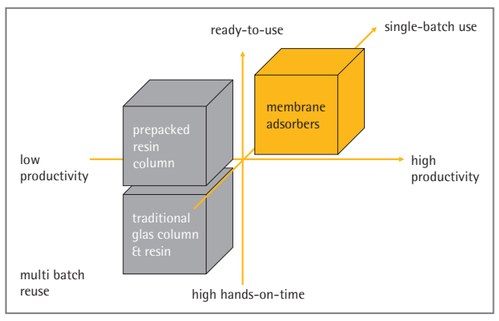

Fig. 8: Competitive landscape of different chromatography approaches in bioprocessing.

Fig. 9: Sartobind® capsules and cassettes are scalable from 3 mL to 100 L.

Membrane chromatography simultaneously provides three major benefits for bioprocessing – high productivity, ready-to-use devices and single-batch use (see fig. 8). Compared to conventional chromatography approaches, this dramatically reduces hands-on time, eliminates packing failures, obviates the need for cold room storage, reduces upfront investment and COGs, all while throughput is increased. The Sartobind® membrane chromatography portfolio provides easy scalability from 3 mL to 100 L[6] (see fig. 9).

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[2] Application Note Sartorius Stedim Biotech GmbH: Batch re-use with Membrane Chromatography [in progress]
[3] Mothes *et al.*, BioProcess International, 14(5), 2016
[4] Najera, M. Pharma's Almanac, 80-82, Q4 2016
[5] Zhou & Tressel, BioProcess International, 32-37, Sep. 2005
[6] Application Note Sartorius Stedim Biotech GmbH, Order No.: 85034-536-64, 2018
[7] Application Note GE Healthcare, KA2210051018AN, 2018