Millipore®
Preparation, Separation,
Filtration & Monitoring Products

Natrix® Q Chromatography Membrane Best Practices Guide

Table of Contents

MERCK

1. Product Information

With an innovative macroporous hydrogel structure that provides a high density of binding sites and rapid mass transfer, Natrix® Q anion exchange (AEX) chromatography membranes deliver higher binding capacities than resin-based columns at fast flow rates typical of traditional membrane adsorbers. Exceptional impurity reduction is maintained over a wide range of operating conditions for improved process design flexibility and robustness. Natrix® Q products are easily scalable from laboratory to clinical and commercial manufacturing scale and are designed to work with existing chromatography systems. Featuring a disposable, plug-and-play device format, Natrix® Q enables highly productive and flexible solutions for purification of biologics.

1.1. Technical Characteristics

	Recon Mini	Pilot	Process 150	Process 600
Component Material				
Membrane	Polyacrylamide hydrogel reinforced with polypropylene mesh			
Functional chemistry	Quaternary amine			
Housing	Polypropylene			
Internal core/guard	N/A	Polypropylene		
Inlet/Outlet flange	N/A	Polypropylene		
Product Characteristics				
Nominal membrane volume (mL)	0.2	15	115	460
Membrane configuration	Flat sheet	Pleated sheet		
Membrane bed thickness (mm)	0.5			
Minimum BSA binding capacity (g)[1]	0.04	3	23	92
Typical mAb polishing capacity (g)[2]	2	150	1150	4600
Flow rate (MV[3]/min)	5–25			
Flow rate (mL/min)	1–5	75–375	600–3000	2300–11500
Maximum operating pressure (psi/bar)	75/5	75/5	90/6	90/6
Connections				
Inlet/Outlet	Female luer	¾" Sanitary (TC)	1" Sanitary (TC)	
Vent	N/A	Luer with cap	Sanitary vent	
Drain	N/A	Luer with cap	¼" Sanitary drain	

[1] 10% breakthrough dynamic binding capacity of Bovine Serum Albumin at 10MV/min in 25mM Tris buffer, pH 8.1

[2] Based on typical process stream and loading to 10kg mAb per L membrane volume. Loading capacity is not limited to 10kg/L and depends on the total impurity content.

[3] Membrane volume (MV): the quantity of membrane available for binding within the device. MV is also used in this document to describe both fluid volumes and flow rates (in MV/min). The use of MV is analogous to the use of column volume (CV) in resin chromatography.

1.2. Chemical Compatibility

The table below shows the compatibility of the Natrix® Q chromatography membrane with a number of chemicals frequently used in biomolecule purification processes. Membrane samples were exposed to each chemical for 4 hours at room temperature. Subsequent to the chemical exposure, membrane performance was characterized by determining water flux through the membrane at 100 kPa applied pressure and BSA dynamic binding capacity (measured at 10% breakthrough). Natrix® Q membrane is compatible with most buffers and solvents commonly used in chromatographic biomolecule purification processes, but incompatible with hypochlorite (1%) and SDS (1%).

This information should be used as a guide only, as chemical compatibility can be influenced by a number of conditions, including exposure time, temperature and chemical concentration.

Chemical	Score
Acids	
1M HCl	Excellent
0.1M HCl	Excellent
Bases	
1M NaOH	Fair
0.1M NaOH	Good
1M NaOH + 2M NaCl	Excellent
0.5M NaOH + 2M NaCl	Excellent
Alcohols	
Isopropanol	Excellent
Methanol	Good
70% Ethanol	Excellent
50% Glycerol	Excellent
Ketones	
Acetone	Fair
Nitrogen-containing solutions	
Acetonitrile	Excellent
6M Guanidine	Excellent
8M Urea	Excellent
Oxidative solutions	
2 wt% hydrogen peroxide	Excellent
1% hypochlorite	Not recommended
Surfactants	
1% SDS	Not recommended

2. Device Installation and Setup

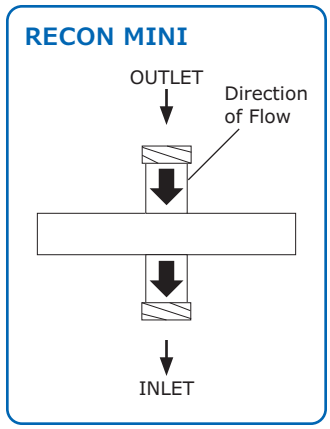
Personal protective equipment should be worn when handling the device or during operation in accordance with any applicable safety protocols and standard operating procedures.

2.1. Storage Prior to Use

Natrix® Q chromatography membrane products are supplied dry and should be stored in original packaging in a clean, dry location at room temperature and away from direct sunlight.

2.2. Natrix® Q Recon Mini

Natrix® Q Recon Mini has two ports: inlet and outlet, manufactured with female luer connections on all ports. Adapters may be required to connect the device to the intended chromatography system which can be configured with M6 or 10-32 threaded connectors. An example is the IDEX® P-656 connector which will adapt Natrix® Q Recon Mini luer connections to 10-32 threaded connections.



A visual inspection of the product before use is recommended to ensure that no damage has occurred during shipment. The fluid flow direction is indicated by an arrow molded into each port. Follow the steps below to connect and prime Natrix® Q Recon Mini.

1. Remove luer caps from the inlet and outlet ports.
2. Connect the inlet and outlet of the device to the chromatography system using the appropriate connector or adapter.
3. Flow equilibration buffer at 10 MV/min with the outlet facing up. Gently tap or shake to dislodge trapped air. Once primed, orient the device so that the outlet is facing down.
4. A system backpressure of at least 20 psi is required for optimum Recon Mini performance. Use of a flow restrictor is recommended when operating at low flow rates (ex. 10 MV/min = 2 mL/min)

2.3. Natrix® Q Pilot, Process 150, and Process 600

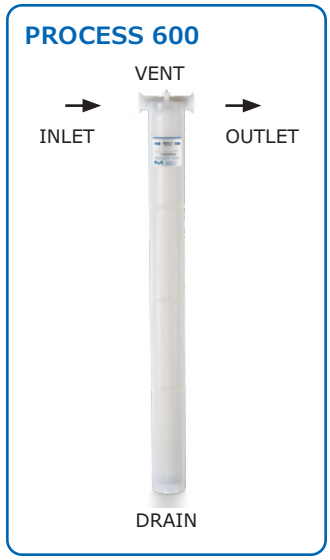
A visual inspection of the adsorber before use is recommended to ensure that no damage has occurred during shipment.

2.3.1. Connect and Prime Natrix® Q Pilot

1. Process flow direction is indicated by an arrow on the housing and the product label.
2. Install the device in an upright position with inlet at the bottom and the outlet at the top.
3. Connect the outlet and inlet of the device to the skid or pump with sanitary connectors and gaskets.
4. Open the vent on the outlet side of the device.
5. Flush the device with equilibration buffer at 10 MV/min. Close the vent when liquid is coming out. Note: operator may have to tilt the device to remove the air in the inlet and outlet.
6. Continue filling until no air can be seen coming out of the outlet and pH and conductivity signals are stable.
7. In case of visible air bubbles, gently tap or shake the device to dislodge trapped air.

2.3.2. Connect and Prime Natrix® Q Process 150 or Process 600

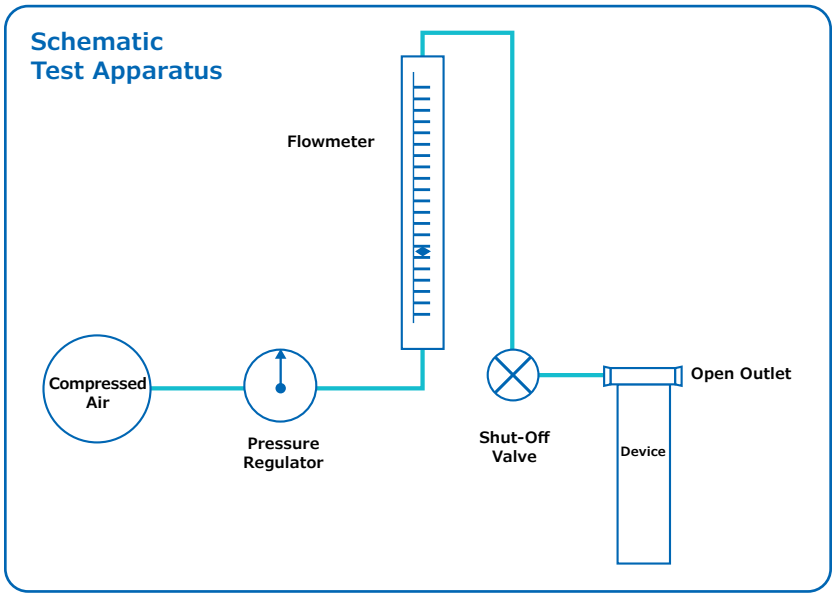
1. Process flow direction is indicated by an arrow on the housing and the product label.
2. Connect the outlet and inlet of the device to the skid or pump with sanitary connectors and gaskets while keeping the device in the upright position.
3. Open the vent on the top of the device.
4. Flush the device with equilibration buffer at 10 MV/min for approximately 5 minutes or until pH and conductivity signals are stable.
5. Close the vent when liquid is coming out. Note: operator may have to tilt the device to remove the air in the inlet and outlet.
6. Continue filling until no air can be seen coming out of the outlet.
7. If air bubbles are visible at the outlet of the device, gently tap or shake to dislodge trapped air.



2.3.3. Structural Integrity Test

A structural integrity test can be performed for Natrix® Q Pilot, Process 150, and Process 600 devices to detect any gross defects in the membrane and/or the housing prior to use.

1. As described in Section 3, install and prime the device by filling with the equilibration buffer of choice at room temperature.
2. Allow to soak for 5 minutes and then drain. Open the drain plug and allow fluid to flow out of both the inlet and the outlet. Drain thoroughly.
3. The figure below shows a schematic representation of the test apparatus.
   - Prior to testing the device, check that the test system is air-tight to avoid false results. With the outlet capped, there should be no flow under pressure.
   - The shut-off valve is used to protect the flow meter from liquid that may be drawn back through the system. The valve must be closed before connecting the device and before decreasing the pressure at the end of the test.
   - Automated test equipment that can process the required test parameters can also be used.



4. With the apparatus assembled and the device connected, open the compressed air source. Set the regulator to apply a pressure of 2.0 ± 0.1 psi.
5. Open the shut-off valve. Allow the system to stabilize for 3 minutes and then record the air flow rate.
6. The maximum air flow rate for any device under 2.0 psi pressure should not exceed 100 mL/min.
   - This specification represents an upper limit for diffusive flow across the membrane.
   - Above this limit, bulk flow may be occurring, which is indicative of a possible defect in the membrane and/or device housing that could cause immediate bypass and loss of function.
7. The table below lists other factors that could cause test failure, which should be checked and ruled out before concluding that the product is defective.

Cause	Remedy
Membrane incorrectly hydrated	Use correct priming medium (equilibration buffer)
Membrane not sufficiently hydrated	5 minutes soak required
System not sealed	Check all fittings, joints etc. and ensure vents are shut
System not sufficiently stabilized	3 minutes stabilization required
Incorrect test pressure used	2.0 ± 0.1 psi required
Different test gas used	Method has been developed for air
Test not performed at suitable temperature	Method has been developed for room temperature conditions (22 ± 2°C)

2.4. Sanitization Prior to Use (Optional)

1. The recommended sanitizing solution is 1 M NaOH containing 2 M NaCl. The use of NaOH alone can contribute to osmotic forces between the polyacrylamide hydrogel and mobile phase solution which may result in membrane expansion[i]. Include 2 M NaCl in the NaOH sanitization buffer to prevent membrane expansion.

   Note: Please use sanitization agents and conditions that are suitable for the process requirements. Sanitization agents must comply with applicable local regulations.
2. To sanitize the adsorber, first complete the priming procedure with equilibration buffer.
3. Flush the adsorber with sanitizing solution for 5 minutes at 10 MV/min, followed by a static soak for up to 60 minutes.
4. Flush the adsorber with equilibration buffer at the desired flow rate for at least 50 MV, or until pH and conductivity return to the specified range. The use of a higher concentration buffer can reduce the buffer flush volume required after sanitization.

3. Disconnection and Disposal

Ensure that all system pressure has been relieved prior to disconnecting the device. Natrix® Q Pilot and Process devices are equipped with a drain port at the bottom to drain all fluid if required.

4. Process Development with Natrix® Q

4.1. Know the Molecule's Isoelectric Point (pI)

The pI is the pH at which the molecule of interest has a net zero charge. Knowing this property, one can determine initial screening conditions based on the desired mode of operation for the ion exchange chromatography step, i.e. bind and elute mode or flow through mode. At a pH below the molecule's pI, the molecule of interest will have a net positive charge and flow through the positively charged AEX chromatography media. At a pH above the molecule's pI, the molecule of interest will have a net negative charge and bind to AEX chromatography media. The pI of a molecule can be determined by isoelectric focusing or through bioinformatic methods.

4.2. Flow Through Mode Chromatography

Flow through mode chromatography, as the name implies, is where the target molecule does not interact with the functional group and flows directly through the chromatography media. A typical flow through AEX application is monoclonal antibody (mAb) polishing. Most mAbs feature a basic pI in the range of 7.5–9.0, therefore at neutral pH the positively charged mAb will not interact with the functional group and flow through the media during sample loading. Impurities with acidic pI's (ex. virus, DNA, some HCP) are negatively charged at neutral pH and will bind to the membrane's functional group. Selecting an initial pH condition one pH unit below the pI of the target molecule is a good initial screening condition. Further pH screening over a wide range will help to optimize the balance between impurity clearance, product yield, and loading capacity. Normally, higher pH helps to improve impurity clearance, although yield and loading capacity may decrease at a pH near or above the product pI.

4.3. Bind and Elute Mode Chromatography

Bind and elute mode, as the name implies, is where the negatively charged target molecule binds to the functional group during loading and is later eluted with increased purity. Some examples of bind and elute AEX chromatography include purification of plasmid DNA, virus, and acidic recombinant proteins. Purification is achieved when positively charged impurities flow through the media during sample loading, while bound negatively charged impurities are removed during intermediate wash and selective elution. Adjusting the feed pH to at least one pH unit above the pI of the target molecule is a good initial screening condition for product binding capacity assessment. As a rule of thumb, the membrane's binding capacity tends to increase with reduced conductivity and increased pH. Further screening over a wide range of pH and conductivity conditions will help to determine the optimal balance between flow through impurity clearance and product binding capacity.

Elution conditions for optimal purity and yield can subsequently be determined by linear conductivity gradient at Recon Mini scale, for example up to 500 mM NaCl over 500 MV. The conductivity at the point of product elution can then be used to formulate an isocratic step elution buffer for use at Pilot and Process scale. In order to maximize elution pool purity, it may be beneficial to wash the membrane with intermediate conductivity buffer for selective removal of weakly bound impurities prior to product elution. Confirm step elution conditions at Pilot or Process scale to ensure acceptable purity and yield.

4.4. General Process Development Considerations

Optimization of process parameters such as conductivity, buffer species, and flow rate are important to maximize the performance of any AEX media. The effect of these parameters on loading capacity, impurity clearance, and yield should be studied through screening experiments. It is also important to consider the holistic purification process during development. For example, select a Natrix® Q buffer species and operating conductivity which is compatible with neighboring unit operations to avoid excessive dilution or buffer exchange between steps. These holistic process considerations are especially important for linked or continuous manufacturing applications.

The following sections discuss some of these key optimization parameters and provide example binding capacity data using bovine serum albumin (BSA) as a model protein. This data should be considered only as directional information for screening or experiment design and may not translate to capacity or purification performance of other biomolecules. For application data related to specific biomolecules, please refer to Natrix® Q chromatography membrane performance guide and application notes.

4.4.1. Conductivity

Although Natrix® Q chromatography membrane has been developed for salt tolerance, higher conductivity can result in lower binding capacity. When using Natrix® Q, concentrations of up to 150mM NaCl will provide capacities greater than many alternative Q-chemistry based chromatographic resin or membrane based systems (**Figure 1**); however, lower conductivity of the process feed will result in both increased capacity and allow for consideration of tonicity of end-state formulation.

4.4.2. Buffer Selection

For Q-chemistry based chromatography media, cationic buffer systems are generally recommended as they have no competitive binding to functional groups. Zwitterionic and anionic buffer systems can interact with positively charged chromatography media and interfere with binding of biomolecules, resulting in low capacity. In some cases, however, zwitterionic or anionic buffers can be useful to enhance product elution or selectivity for an AEX media[ii]. All buffers and process feed streams should have enough buffering capacity to maintain pH during operation; common buffer strengths are in the range of 20–50 mM. The combination of buffer species, concentration, pH, and conductivity should be evaluated to ensure optimal binding capacity and purification.

Tris(hydroxymethyl)aminomethane (Tris) based Buffers

Tris-based buffer systems are optimal for Q-chemistry based chromatographic systems in general. As a cationic buffer salt, Tris contains no anionic species within the range of pH 7.0–9.0 and will not competitively inhibit binding sites. Although pH and conductivity still have an impact on the performance, Tris generally works well for a wide range of conditions (**Figure 2**). Bis-Tris may be used as an alternative to extend range of buffer capacity (pH 6.0–7.0).

Phosphate Buffers

Phosphate is a multivalent anionic buffer salt that can interact with AEX media; however Natrix® Q features increased phosphate tolerance relative to other resin-based or membrane-based systems (**Figure 3**). The impact of conductivity and pH can be elevated in presence of phosphate, therefore reducing conductivity and/or increasing pH can help to improve performance (**Figure 4**).

Acetate Buffers

Acetate is an anionic buffer salt that that can interact with Q-chemistry based chromatography media. Like phosphate, the impact of conductivity and pH can be elevated in presence of acetate, therefore reducing conductivity and/or increasing pH can help to improve performance (**Figure 5**). Note that pI of model protein BSA is 4.7 which explains the low binding capacity at pH below 5.5 in **Figure 5** data.

In mAb purification, acetate buffers are commonly used for elution of Protein A or cation exchange chromatography steps, which may be followed by AEX polishing after pH adjustment (ex. with Tris) to target AEX loading condition. In such cases, the combined Acetate-Tris buffer system may show different outcome than the single buffer system at a given pH and conductivity (**Figure 6**).

Citrate Buffers

Multivalent anionic citrate buffers are not generally recommended due to very strong competitive binding to Q-chemistry based chromatography media. A diafiltration buffer exchange may be required to remove citrate ions from the feed prior to loading Natrix® Q.

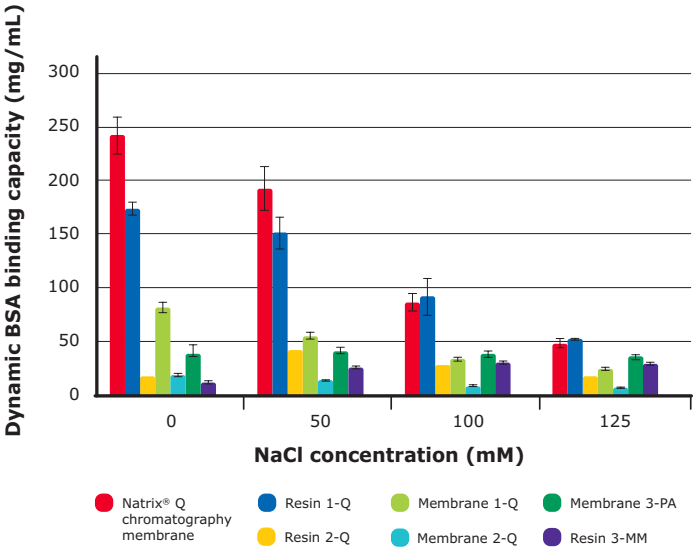


Figure 1: Effect of NaCl concentration on BSA binding capacity (10% breakthrough). Membrane adsorbers were operated at 6-second residence time, and resins were operated at 1-minute residence time. Feed: 1 g/L BSA in 25 mM Tris + NaCl buffer, pH 8.0.

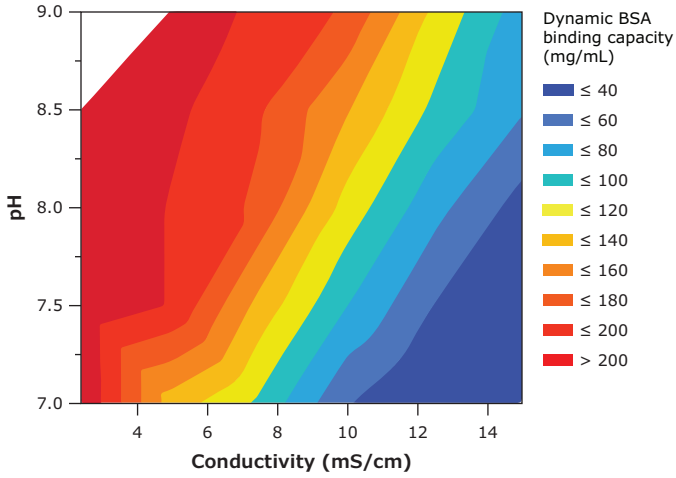


Figure 2: Effect of pH and NaCl concentration on BSA binding capacity (10% breakthrough) in 25mM Tris buffer. Residence time: 6 seconds. Feed: 2 g/L BSA in 25 mM Tris + NaCl buffer at various pH.

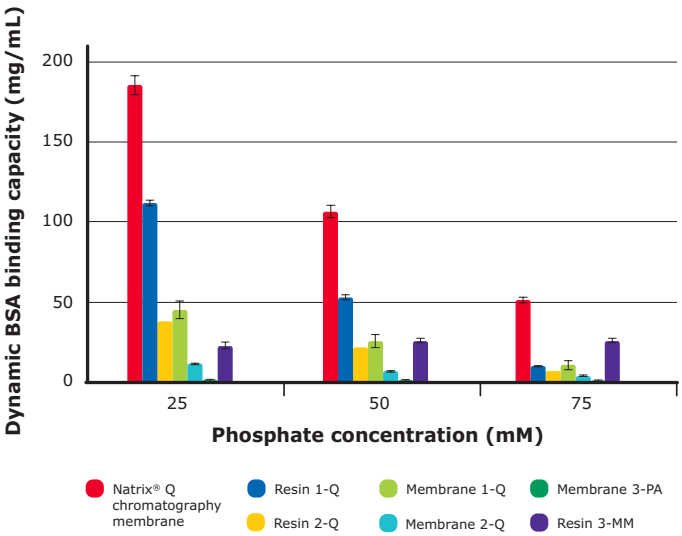


Figure 3: Effect of phosphate concentration on BSA binding capacity (10% breakthrough). Membrane adsorbers were operated at a 6-second residence time, and resins were operated at a 1-minute residence time. Feed: 1 g/L BSA in phosphate buffer, pH 8.0.

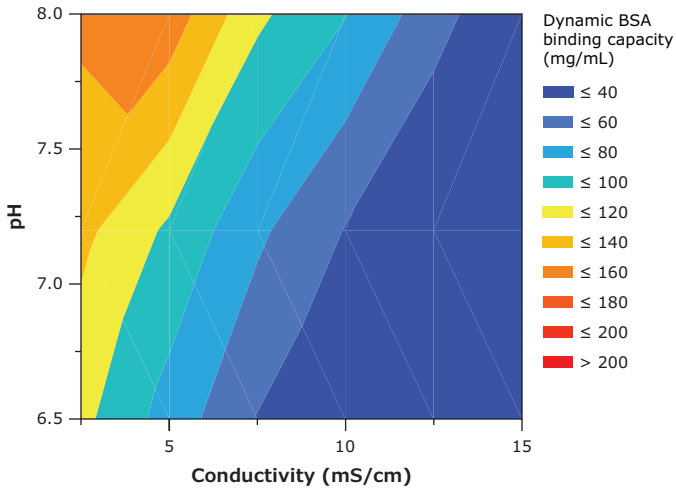


Figure 4: Effect of pH and NaCl concentration on BSA binding capacity (10% breakthrough) in 20mM phosphate buffer. Residence time: 6 secondes. Feed: 2 g/L BSA in 20 mM phosphate + NaCl buffer at various pH.

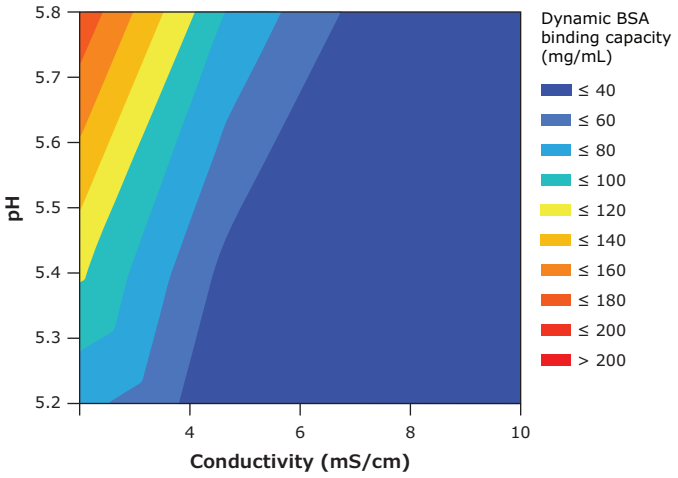


Figure 5: Effect of pH and NaCl concentration on BSA binding capacity (10% breakthrough) in 25mM acetate buffer. Residence time: 6 seconds. Feed: 2 g/L BSA in 20 mM acetate + NaCl buffer at various pH.

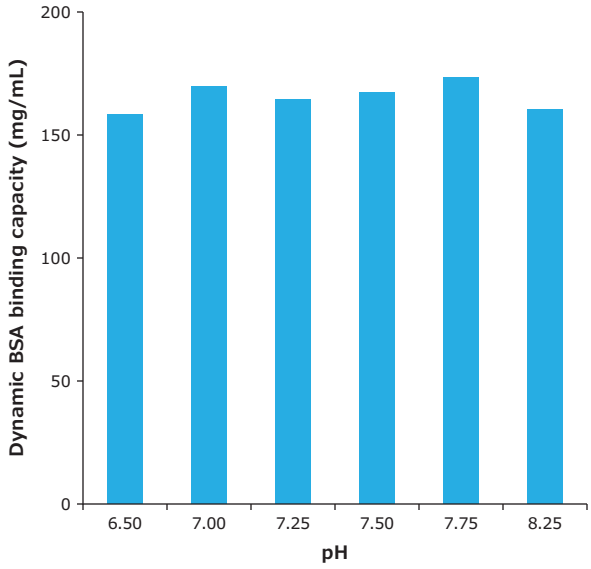


Figure 6: BSA binding capacity (10% breakthrough) in Acetate-Tris buffer system. Residence time: 6 seconds. Feed: 2 g/L BSA in 50mM acetic acid adjusted to various pH with 1M Tris.

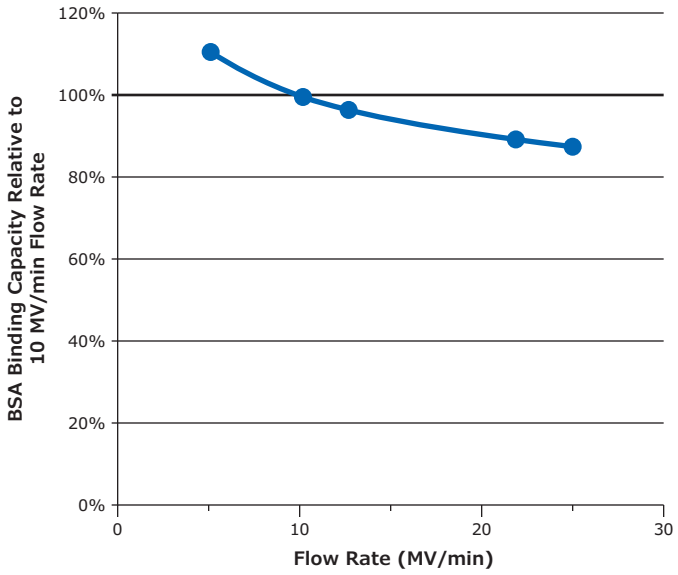


Figure 7: Effect of flow rate on BSA binding capacity (10% breakthrough). Feed: 2 g/L BSA in 25 mM Tris, pH 8.1.

4.4.3. Flow Rate

Since the Natrix® Q binding sites exist within the convective fluid flow path, the membrane maintains very good binding capacity over a wide flow rate range and can be operated as high as 25 MV/min without significant loss in binding capacity (**Figure 7**). The membrane's high flow rate capability improves process productivity and flexibility relative to traditional resin-based technologies which are limited by diffusive fluid flow. A typical flow rate for Natrix® Q is 10 MV/min, which results in a residence time of 6 seconds.

4.4.4. Feed Purity

The quality of the Natrix® Q feed stream may help identify the optimal buffer system and conditions. For example, a product flow through mAb polishing application with feed HCP concentration greater than 1,000 ppm should utilize a low conductivity buffer system in order to maximize HCP binding capacity.

4.5. Sample Preparation

The pH and conductivity of the feed sample should be appropriately adjusted before loading. The conductivity of the sample can be lowered through dilution in most cases. However, diafiltration may be necessary in some cases to remove specific interfering ions, such as citrate. It is recommended to microfilter the process stream (i.e. 0.22 µm or 0.45 µm membrane) before loading.

5. Implementation Strategies: Single-Cycle and Multi-Cycle Processing

The Natrix® Q chromatography membrane is designed for disposable processing within a single batch or continuous campaign, making it possible to eliminate cleaning buffer, storage buffer, and the associated validation, operation, and cross-contamination risk. While single-cycle implementation is economically feasible, it is also possible to re-use a single device for multiple cycles within a batch or continuous campaign. Considerations for single-cycle and multi-cycle implementation are described below.

	Single-Cycle Implementation	Multi-Cycle Implementation
Process Time	+++ No time needed for post-use cleaning.	++ Membrane cleaning takes time, although performed at a rapid 10 MV/min flow rate.
Buffer Consumption	+++ No post-use cleaning buffer. No storage buffer.	+ Additional cleaning buffer volumes and tanks required. No storage buffer.
Validation	+++ No re-use cleaning or carryover validation. No storage validation.	+ Re-use cleaning and carryover validation required. No storage validation.
Lifetime Device Load Capacity	+ Limited to the amount of product loaded in a single cycle.	+++ Each additional cycle increases the device's lifetime product load capacity.

5.1. Single-Cycle Implementation

Natrix® Q is a cost-effective solution for single-cycle implementation[iii]. Using Natrix® Q for just one cycle prior to disposal eliminates the need for cleaning buffers and tanks, effectively shrinking facility footprint for the AEX step. Additionally, this approach eliminates all testing and documentation related to cleaning validation, simplifying implementation. Employing Natrix® Q as a single-cycle device enables rapid processing with fast turnover times, increased flexibility, and reduced cross-contamination risk.

5.2. Membrane Cleaning for Multi-Cycle Implementation

In some scenarios, it may be beneficial to clean a single Natrix® Q device to process a batch or continuous campaign over consecutive re-use cycles. In these cases, it is recommended to utilize the re-use procedure listed below for initial testing. In the case of highly fouling feeds, alternative cleaning strategies may be required. All cleaning steps can be performed at the rapid flowrates enabled by Natrix® Q (i.e. 10 MV/min). It is recommended to perform the post-caustic pH equilibration at high salt.

Step	Buffer	# MV
Load	Product feedstream	N/A
Wash	pH and conductivity similar to product feedsteam. Example: 50 mM Tris + 10 mM NaCl, pH 7	25–50
High Salt Strip	pH similar to product feedstream + 2M NaCl Example: 50 mM Tris + 2M NaCl, pH 7	25–50
Caustic pH Sanitization	0.5M–1M NaOH + 2M NaCl	25–50
High Salt pH Equilibration	pH similar to product feedstream + 2M NaCl Example: 50 mM Tris + 2M NaCl, pH 7	25–50
Low Salt Equilibration	pH and conductivity similar to product feedsteam. Example: 50 mM Tris + 10 mM NaCl, pH 7	25–50

In one flowthrough mAb polishing application using this cleaning procedure, a single Natrix® Q device was re-used for 5 consecutive processing cycles (loaded to 10 kg mAb/L membrane in each cycle) with consistent product yield, HCP impurity clearance, XMuLV clearance, and device backpressure (**Figure 8**). It is important to note that the number of re-use cycles is heavily dependent on process specific parameters such as feed quality and mass loading.

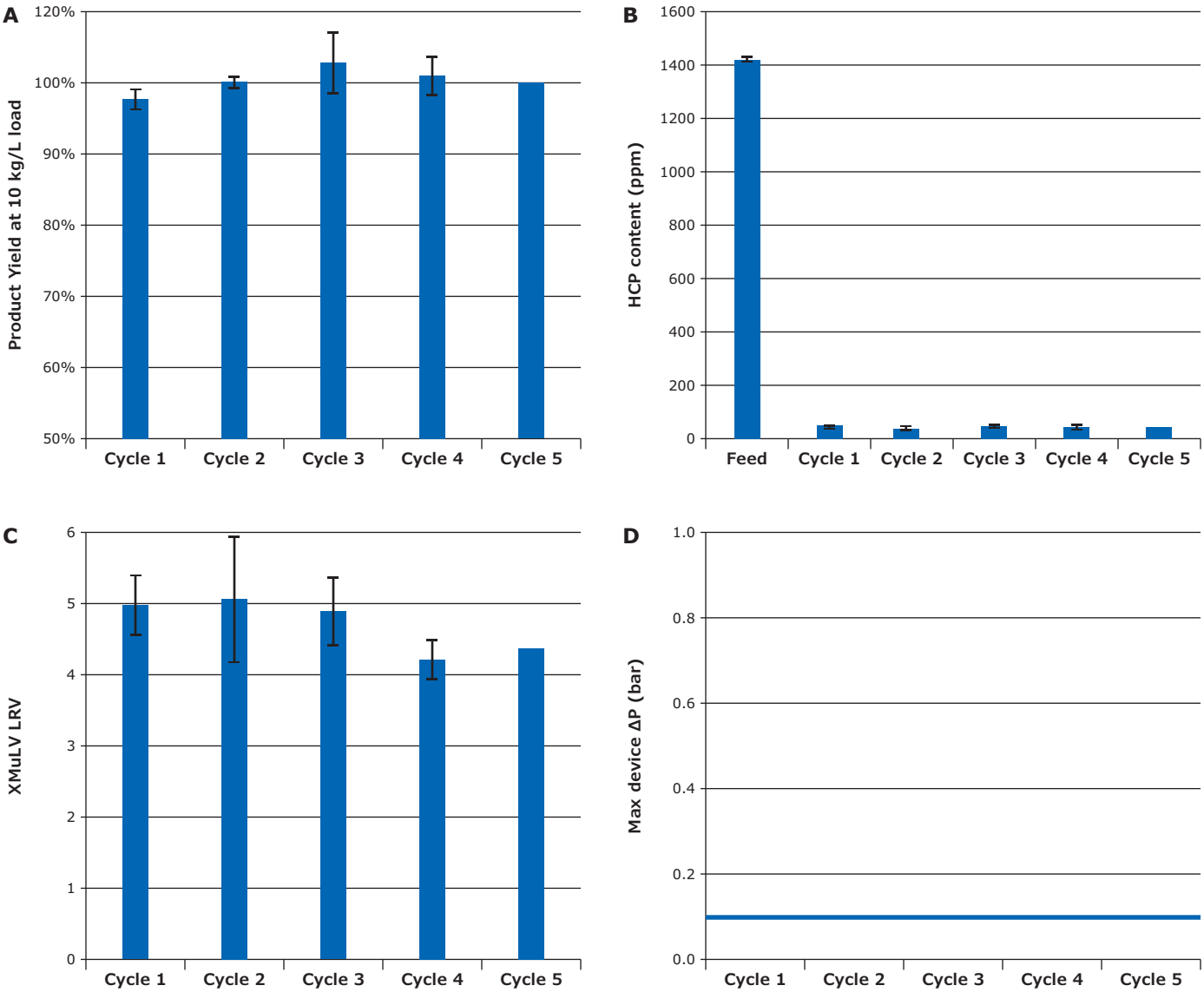


Figure 8: Product yield, HCP, XMuLV, and pressure data for a product flowthrough purification performed with a Natrix® Q Recon Mini device re-used for 5 consecutive processing cycles. Mass loading was 10 kg mAb/mL membrane in each cycle. Error bars represent standard deviation of replicate tests.

Membrane cleaning and lifetime should be characterized during development studies and properly validated prior to implementation. Note that it is recommended to implement Natrix® Q re-use in the context of consecutive processing cycles. This strategy is consistent with a “single-use per batch” approach, in which the device is discarded after the batch or continuous campaign is complete. Storage of previously used Natrix® Q devices is not recommended.

6. Scale Up Strategy

6.1. Scale Up Calculation for Single Device

Since Natrix® Q capacities are linearly scalable through all device sizes, scale-up parameters are determined based on the membrane volume. Parameters that are independent of scale are the membrane's loading capacity (kg/L-media) and the residence time, which determines the flow rate in MV/min. Parameters that vary with membrane volume are the volumetric flow rate (mL/min) and volumetric or mass load (L or kg of feed). An example mAb flow through polishing scale-up scenario is shown in the table below. This approach results in consistent purity and yield with scale-up (**Figure 9**).

	Recon Mini	Pilot	Process 150
Membrane Volume (mL)	0.2	15	115
Loading Capacity (kg/L-media)	20	20	20
Load per Device (g)	4	300	2300
Mab Titer (g/L)	10	10	10
Loading Volume (L)	0.4	30	230
Flow Rate (MV/min)	10	10	10
Flow Rate (mL/min)	2	150	1150
Process Time (min)	200	200	200

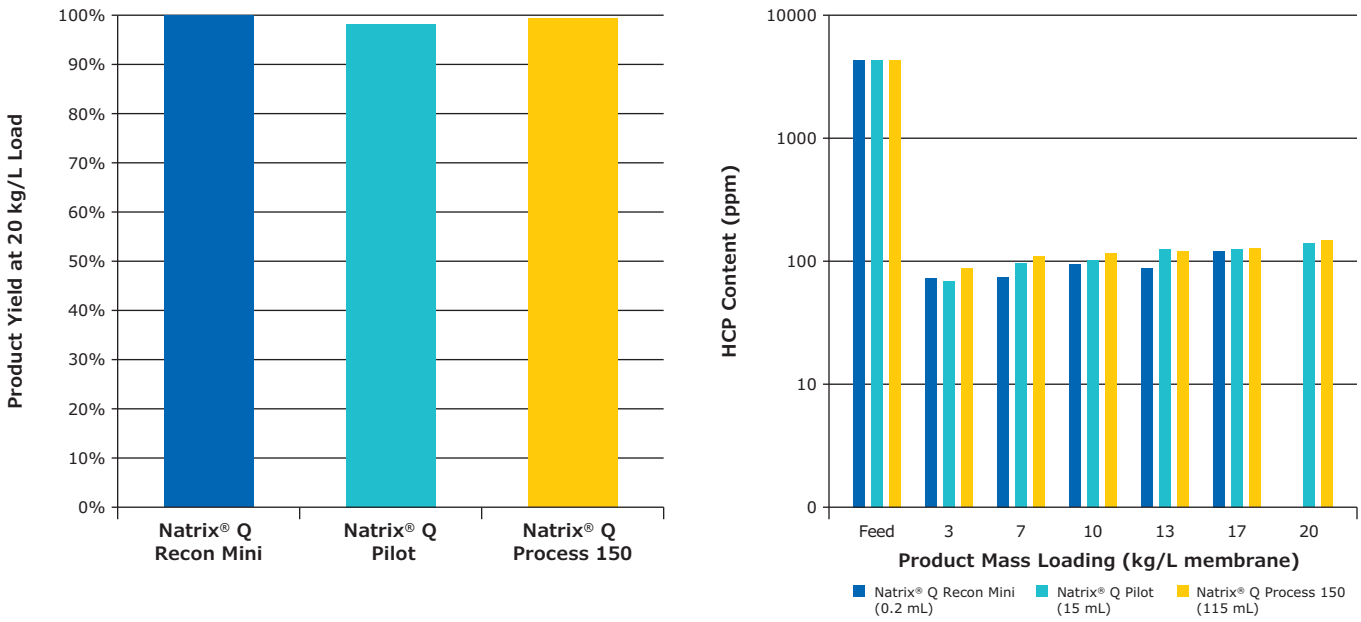


Figure 9: Yield and HCP clearance data for a mAb flowthrough purification conducted on three different Natrix® Q device scales.

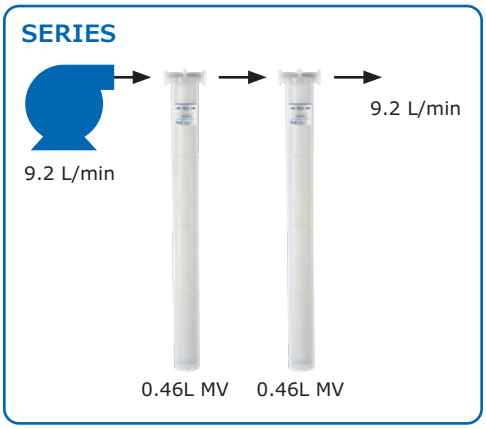
When scaling up, note that pipe and system volumes in different sized chromatography systems can vary significantly and should be considered when determining fluid volumes. Minimize tubing size and length in chromatography systems to reduce buffer consumption.

6.2. Manifold Considerations

For very large-scale applications, multiple Natrix® Q Process 600 devices (0.46 L MV) can be manifolded in series, parallel, or a combined arrangement of series and parallel devices. For example, a manifold arrangement of four Process 600 devices may consist of two parallel flow paths which each contain two devices in series. Considerations for series and parallel manifold strategies are detailed below.

6.2.1. Connecting Multiple Devices in Series

When connecting multiple devices in series, volumetric flow rate should be calculated based on the total media volume of serial devices in order to maintain consistent process time across scales. Confirm purification performance of serial devices at small scale by testing Recon Mini devices manifolded in series. Also perform any validation work with Recon Mini devices connected in series in order to mimic the large-scale configuration.



Natrix® Q Process 600 Serial Manifolding Example	
Total Membrane Volume:	2 x 0.46 L = 0.92 L
Flow Rate at 10 MV/min:	= 9.2 L/min
Key Considerations:	Ensure system and pump can accommodate increased pressure drop of serial devices.

Note that while serial manifolding will increase the total pressure drop of the Natrix® Q step, the membrane's open pore structure maintains a manageable pressure drop for serial devices (**Figure 10**). For feeds with water-like viscosity, serial devices can be operated with just 0.5–1.0 bar pressure drop. It is recommended to evaluate and confirm that pressure drop across a serial device manifold is within acceptable limits for the device and system.

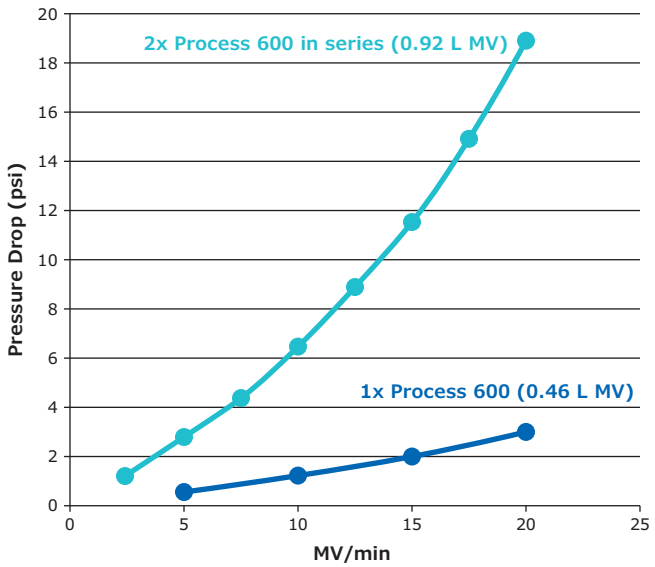
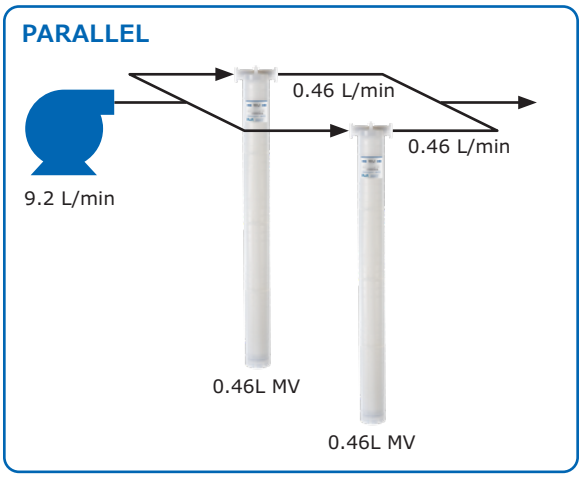


Figure 10: Pressure drop for single and serial Natrix® Q Process 600 devices at various flowrates. Mobile phase: 25 mM Tris + 50 mM NaCl, pH 8.1.

6.2.2. Connecting Multiple Devices in Parallel

When connecting multiple devices in parallel, volumetric flow rate should be calculated based on the total media volume in order to maintain the same process time. Since each parallel flow path is exposed to a single device, process development and validation can be conducted with a single Recon Mini device. In this configuration, it is critical to ensure equivalent flow distribution to each parallel flow path. Factors that could potentially create different flow resistance include tubing I.D., tubing length, fittings, and instrumentation. Pressure gauges, flow controllers, and valving can help to monitor and control the flow resistance in each parallel flow path.



Natrix® Q Process 600 Parallel Manifolding Example	
Total Membrane Volume:	2 x 0.46 L = 0.92 L
Flow Rate at 10 MV/min:	= 9.2 L/min
Key Considerations:	For equivalent flow to each device, flow resistance of piping and instrumentation must be equivalent in each parallel flow path. Pressure gauges, flow controllers, and valving help to monitor and control flow resistance.

7. Ordering Information

Product Code	Product Name	Nominal Membrane Volume (mL)	Quantity per Pack
NXF-01	Natrix® Q Recon Mini	0.2	10
NXF-10	Natrix® Q Pilot	15	1
NXF-20	Natrix® Q Process 150	115	1
NXF-50	Natrix® Q Process 600	460	1

References

i Bhadani R. and Mitra U.K. Macromolecular Symposia, 2016.

ii Santry et al., BMC Biotechnology, 2020.

iii Jacquemart R., and Stout J. BioProcess International, 2017.

Merck KGaA
Frankfurter Strasse 250
64293 Darmstadt, Germany

To place an order or receive technical assistance

Please visit:
MerckMillipore.com/contactPS

For additional information, please visit:
MerckMillipore.com

MK_PG7333EN Ver. 0.0
34662
03/2021