

ABSTRACT

The rising demand for biopharmaceutical products has driven the need for greater operational speed and efficiency for bio-manufacturing. Existing downstream process technologies have struggled to achieve these metrics, but recently new solutions have become commercially available. Natrix Separations is working to provide a fully disposable, single-use (per batch) toolset for biomolecule purification that offers superior throughput and flexibility with no compromise on quality. The currently available tools employ well-known ion exchange binding modalities, but others (including affinity), are under development. Natrix HD membranes feature a high density of highly accessible binding sites that enable high productivity capture, intermediate purification and/or polishing operations for monoclonal antibody, recombinant proteins and vaccines GMP manufacturing. The results presented here demonstrate the performance of Natrix HD membranes for mAb purification.

INTRODUCTION

High titers in upstream processes, needs for small and local productions, and fierce competition requiring short development times are all imposing challenges on traditional purification platforms. Natrix Separations is proud to present a fully disposable toolset, paving the way to implementation of flexible and continuous purification processing of biotherapeutics to meet the needs of markets like monoclonal antibodies (mAbs), recombinant proteins and vaccines.

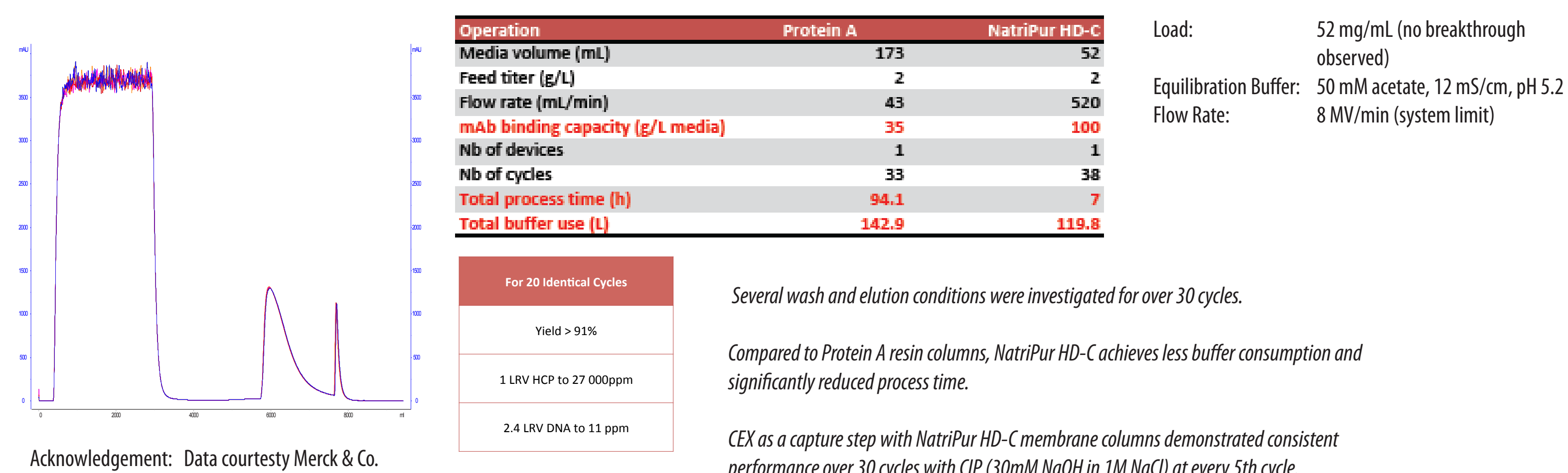
This study highlights some of the results generated with HD-C, HD-Sb and HD-Q, which are all High Density membranes based on Natrix Separations proprietary hydrogel technology.

Designed for capture and intermediate purification operations, **Natrix HD-C (weak cation exchanger)** and **Natrix HD-Sb (strong cation exchanger with hydrophobic modality)** enable fast flow rates with high binding capacity as well as multi-cycle capability to optimize process economics. Designed for flow-through operation, **NatriFlo HD-Q (strong anion exchanger)** is able to process very high loads at fast flow rate and maintains exceptional impurity reduction over a wide range of operating conditions at every operating scale.

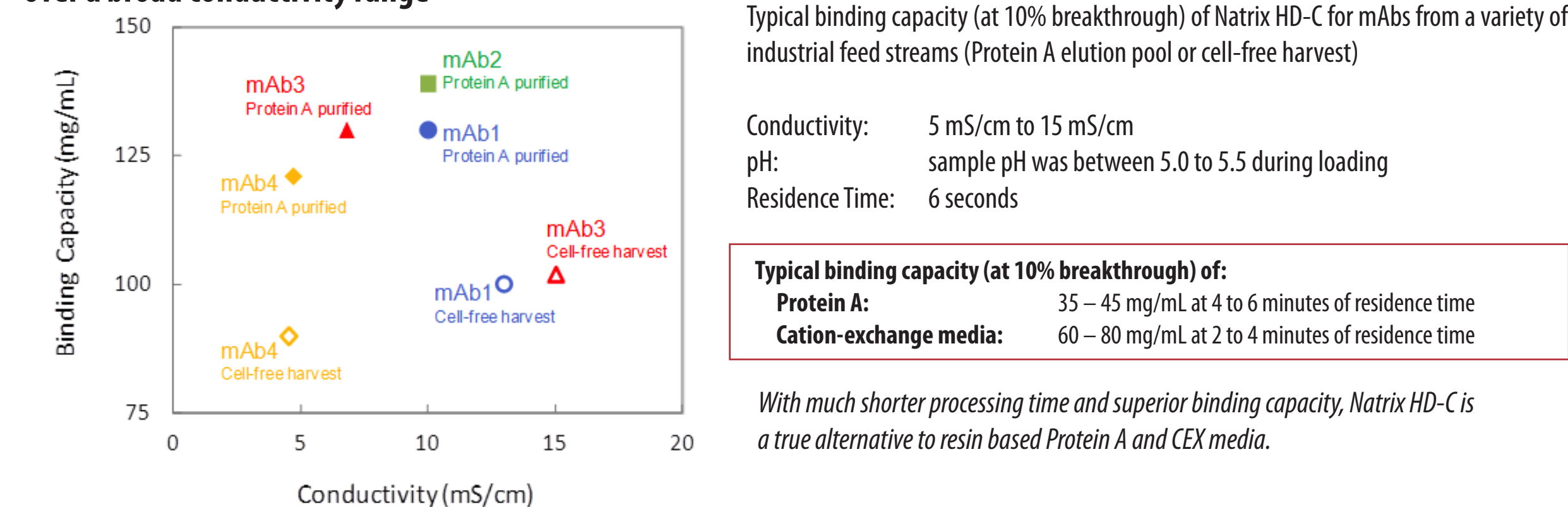
Natrix HD-C

- Weak cation exchange (CEX) membrane adsorber
- Polycrylate hydrogel with carboxylate groups (C chemistry)
- High dynamic binding capacity
- Binding and elution conditions can be fine-tuned to optimize process design
- High salt tolerance minimizes need for costly dilution steps
- Low salt elution enables easier next step
- mAb purification
- Intermediate purification
- Protein A primary capture alternative

Multi-cycle, single-use per batch performance



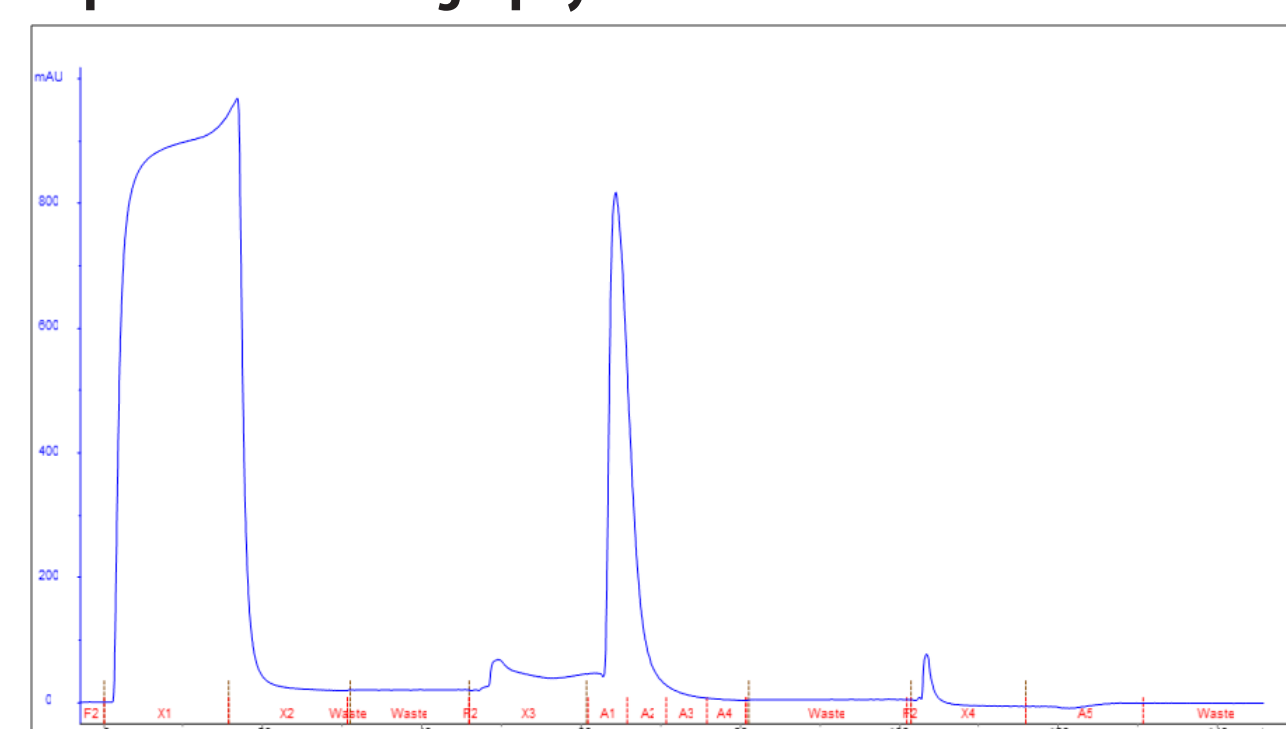
High binding capacity at 6 seconds residence time over a broad conductivity range



Natrix HD-Sb

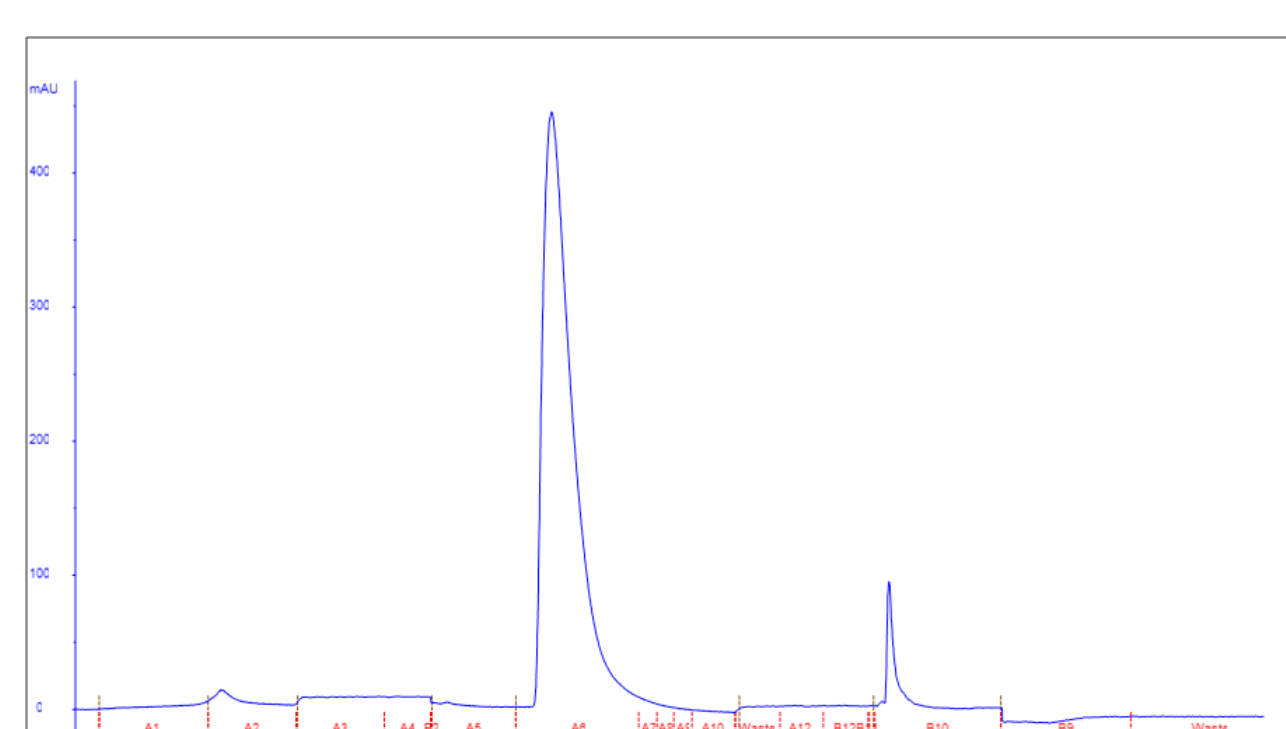
- Mixed mode membrane formulations
- Strong cation exchange (CEX) → sulfonic acid
- Hydrophobic interaction chromatography (HIC) → t-butyl
- mAb purification application: capture or intermediate polish
- High capacity
- Good impurity clearance (HCP, aggregates)
- Suitable/flexible binding & elution conditions

Capture Chromatography



The HD-Sb membrane can be used to rapidly and efficiently remove impurities at high yields, making it a viable alternative to Protein A capture in monoclonal antibody production.

Intermediate Purification of mAb



Excellent clearance of aggregates and HCP along with high product yield also makes the HD-Sb membrane a great option for the intermediate purification of mAbs.

Performance Summary

mAb load	58 mg/mL
Yield	96%
Aggregate clearance	>8% to 2.6%
HCP clearance (ppm)	350,813 to 12,727
HCP clearance (LRV)	1.4

Equilibration Buffer: 45 mM NaOAc + 130 mM NaCl, pH 4.5, 16 mS/cm
Elution Buffer: 20 mM Phosphate, pH 6.3, 10 mS/cm

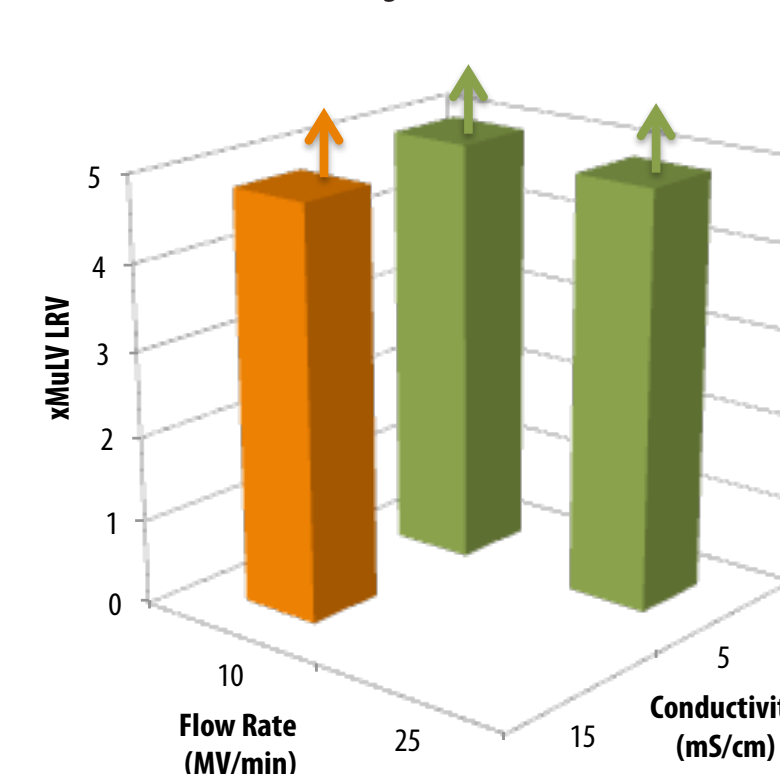
Performance Summary

mAb load	65 mg/mL
Yield	99%
Aggregate reduction	1.8% to 0%
HCP clearance (ppm)	140 to 2.8
HCP clearance (LRV)	1.7

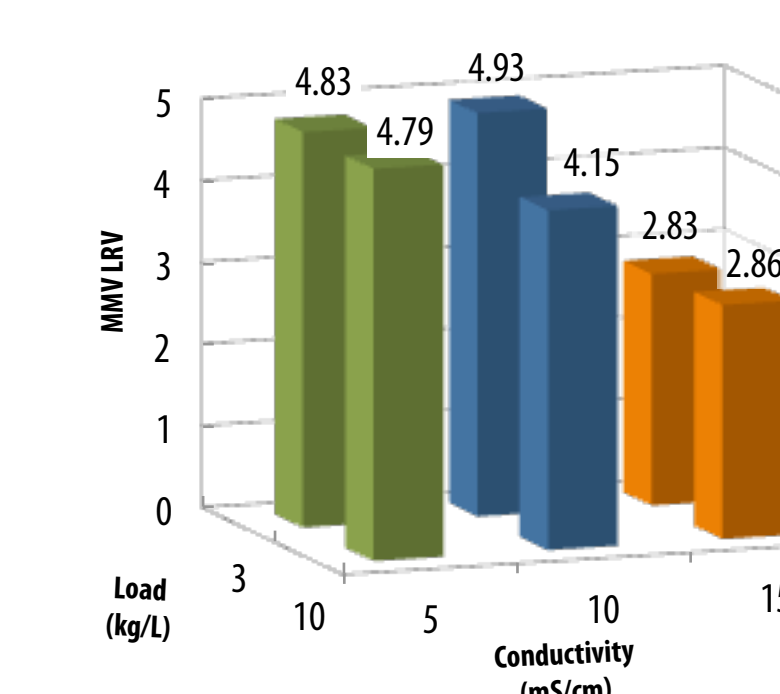
Equilibration Buffer: 45 mM NaOAc + 130 mM NaCl, pH 4.5, 16 mS/cm
Elution Buffer: 20 mM Phosphate, pH 6.3, 6.6 mS/cm

Natrix HD-Q

xMuLV clearance at 10 kg/L load



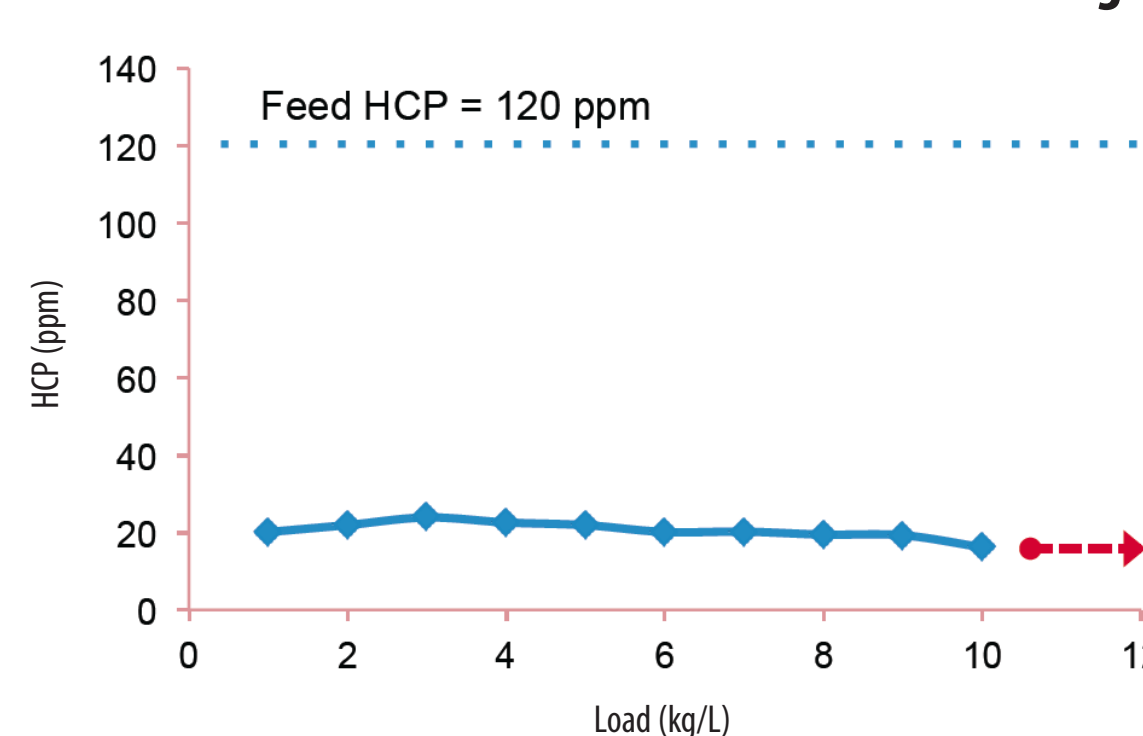
MMV clearance at 10 MV/min flow rate



Natrix HD-Q Overview

- Strong anion exchange (AEX) membrane adsorber
- Polycrylamide hydrogel with positively charged quaternary amine groups (Q chemistry)
- Available in 4 process scales
- Recon Mini, Recon, Pilot, and Process
- High salt tolerance and great performance in phosphate and acetate buffers
- Excellent for polishing applications

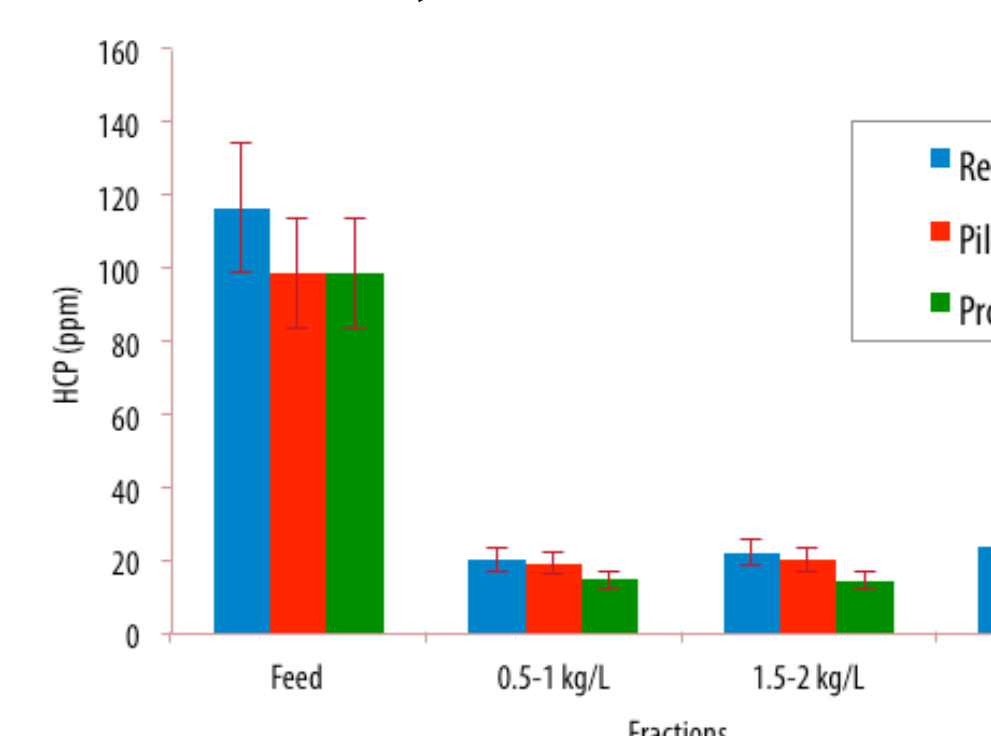
HCP Reduction Performance at Lab Scale for 10 kg/L Load



Scalability of the DNA Clearance



Linear Scalability



ABOUT NATRIX SEPARATIONS

Natrix Separations is the developer and manufacturer of Natrix HD membrane technology, an advanced chromatography material that enables significant speed and capacity improvements for the capture and purification of biologics. Natrix products utilize established industry-standard chemistries in a single-use format to provide a low cost manufacturing advantage for drug developers. The Natrix team is comprised of industry leaders in downstream processing, as well as engineering, design, quality and manufacturing. Natrix is privately-held and based in Burlington, Ontario, Canada.

About Natrix Technology

Natrix HD Membranes offer a breakthrough in membrane architecture that will change downstream purification. With a three-dimensional macroporous hydrogel structure that provides a High Density of binding sites and rapid mass transfer, Natrix HD Membranes deliver binding capacity that exceeds resin-based columns with the fast flow rates typical of membrane adsorbers. Additionally, Natrix HD Membrane technology is highly versatile, and can be deployed in flow-through or bind-elute mode, with nearly any ion exchange, affinity or customized chemistry.

CONCLUSION

Many purification teams have been seeking a leap forward in the downstream technology to address their DSP bottleneck. Their current processes require upgrades to promote higher throughput, efficiency and flexibility.

Natrix Separations has developed an innovative toolset to tackle this challenge: HD membranes are designed to function at fast flow rates typical of membrane adsorbers while exhibiting high binding capacities comparable to resin columns. Natrix HD-C and HD-Sb provide high productivity alternatives to Protein A and cation exchange resins for capture and intermediate purification. NatriFlo HD-Q products have proven robustness with unparalleled purification performance even in challenging conditions.

Pre-packaged in an economical single-use, plug-and-play format, Natrix HD products facilitate disposable, continuous processing and remove the hassle of column packing, QC validation, cleaning between batches, and storage. With three different binding modalities (and more in the pipeline), Natrix offers a variety of products at several process scales that can be incorporated individually into a process or together in a platform approach, making them excellent tools for flexible monoclonal antibody and vaccine purification processing.