Electrochemical Elution Reduces Aggregation of pH-Sensitive Monoclonal Antibodies in Digital Membrane Chromatography

Voltage-driven elution enables antibody purification without low-pH exposure.

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AVOID LOW-pH STRESS

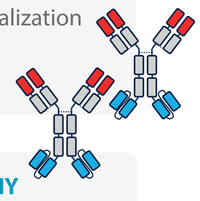
Electrochemical elution reduces aggregation and improves recovery of pH-sensitive monoclonal antibodies.

DMC ELECTROCHEMICAL

Load → Wash → Voltage
Neutral pH
Aggregation ↓ Monomer ↑

TRADITIONAL PROTEIN A

Load → Wash → Low pH → Neutralization
pH 3 - 3.5 !
Aggregation ↑ Monomer ↓



INTRODUCTION

Protein A chromatography is widely used for monoclonal antibody purification. Traditional workflows rely on low-pH elution (pH 3–3.5) to release antibodies from the affinity ligand.
For pH-sensitive antibodies, transient acid exposure can cause:

- Aggregation
- Reduced monomer purity
- Reduced stability
- Increased downstream polishing burden.

Digital Membrane Chromatography (DMC) enables voltage-driven electrochemical elution, reducing reliance on acidic buffers

PLATFORM OVERVIEW: DIGITAL MEMBRANE CHROMATOGRAPHY

ELECTROCHEMICAL ELUTION

The DMC Protein A system enables antibody release through voltage-controlled electrochemical elution, intended to reduce dependence on acidic elution buffers.
Key characteristics:

- Voltage-driven elution (example runs used 2.0 V for ~2–2.5 min)
- Reduced reliance on low-pH exposure
- Controlled elution environment
- Optional in-line neutralization (histidine used in some runs)

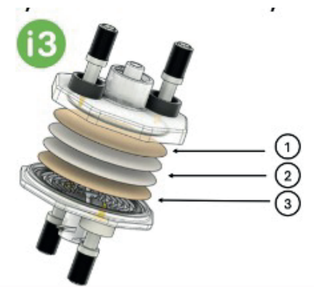


Fig. 1: Schematic illustration of DMC^{PrA} Membrane Adsorber in exploded view. (1) Gold-coated membrane electrode (upper side); (2) Regenerated cellulose membrane functionalized with Protein A; (3) Gold-coated membrane electrode (lower side).

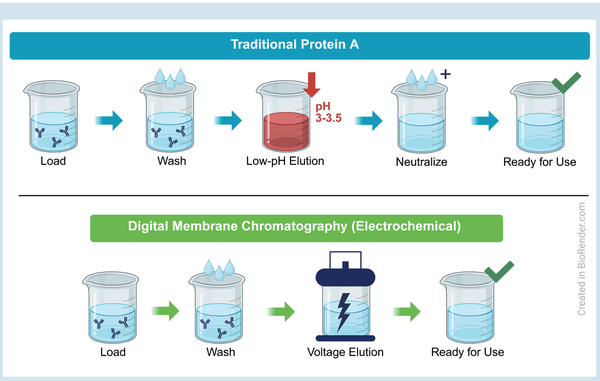
PROBLEM

Standard low-pH Protein A elution conditions can promote aggregation and product heterogeneity in acid-labile antibodies, reducing recovery of intact monomer and impacting overall process robustness.

OBJECTIVE

Evaluate electrochemical elution using Digital Membrane Chromatography (DMC) as an alternative to conventional low-pH Protein A elution to:

- Reduce aggregation of pH-sensitive antibodies
- Maintain or improve monomer recovery
- Improve overall recovery/yield and process consistency



DMC vs PROTEIN A WORKFLOW

EXPERIMENTAL OVERVIEW DMC ELECTROCHEMICAL ELUTION

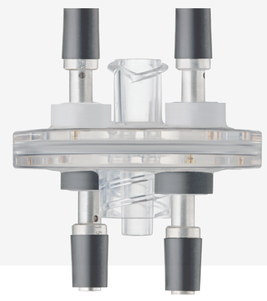
- 0.1 mL DMC Protein A unit
- Voltage elution: 2.0 V
- Optional neutralization: 20% 100 mM histidine (pH 5.8)

Conventional Comparison

- 1 mL HiTrap MabSelect SuRe 70 column*
- Standard low-pH Protein A elution
- Bio-Rad NGC chromatography system*

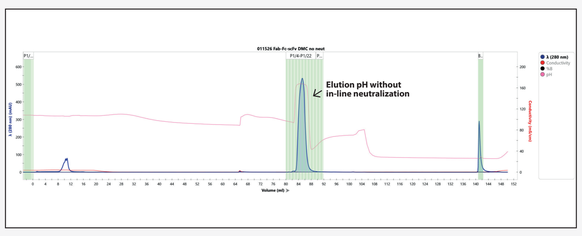
Analytics

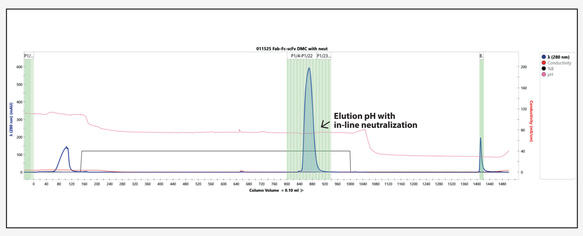
- Analytical SEC (aSEC)
- UV chromatogram analysis
- pH trace analysis
- Yield and recovery calculation



CHROMATOGRAPHY BEHAVIOUR

Chromatograms showing voltage elution peak comparing no neutralization and in line neutralization with pH trace.



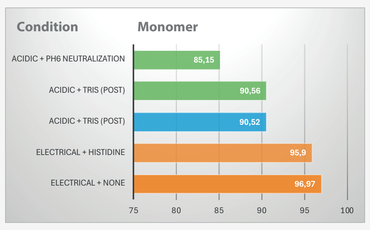


KEY OBSERVATIONS:

- Distinct voltage elution peaks
- Reduced acidic exposure profile
- Consistent elution behavior with optional neutralisation

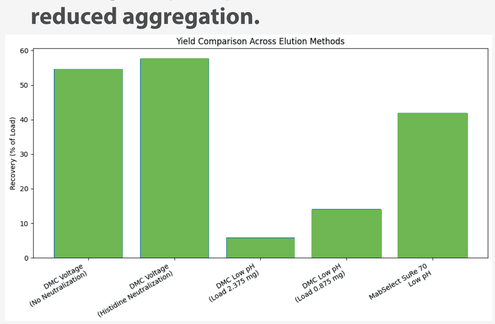
MONOMER PURITY

Electrochemical elution produced higher monomer purity.
Avoiding low-pH exposure is consistent with reduced aggregation.



YIELD

Electrochemical elution produced higher yield monomer purity.
Avoiding low-pH exposure is consistent with **reduced aggregation.**



CONCLUSION

Electrochemical elution using Digital Membrane Chromatography (DMC) is a **alternative** to traditional low-pH Protein A elution for pH-sensitive mono-clonal antibodies, demonstrating:

- **Reduced aggregation** (higher monomer purity)
- **Higher recovery**/yield relative to low-pH elution in the DMC unit comparisons
- **Elution with low-pH exposure** that can stress acid-labile antibodies
- **Potential to simplify downstream** processing by reducing aggregate burden.

REFERENCES

HiTrap™ MabSelect SuRe™ 70 columns are trademarks of Cytiva*
NGC Medium-Pressure Chromatography Systems is a trademark of Bio-Rad*

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