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Development of multimodal membrane adsorbers for antibody purification using atom transfer radical polymerization

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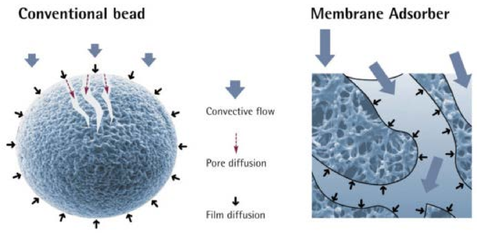
Introduction

- Demand for biopharmaceutical drugs has increased over the past decades. Estimated that in 2016, eight of top 10 US drugs will be biologics[1]
- 50-90% of the total cost for biologics production is associated with the downstream recovery and purification

Cell removal/ clarification → Product capture → Intermediate purification → Polishing

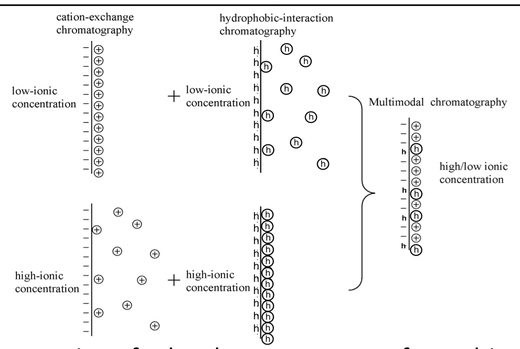
- High-productivity membranes with wide operating range should play a larger role in future biomanufacturing[2]



Objectives

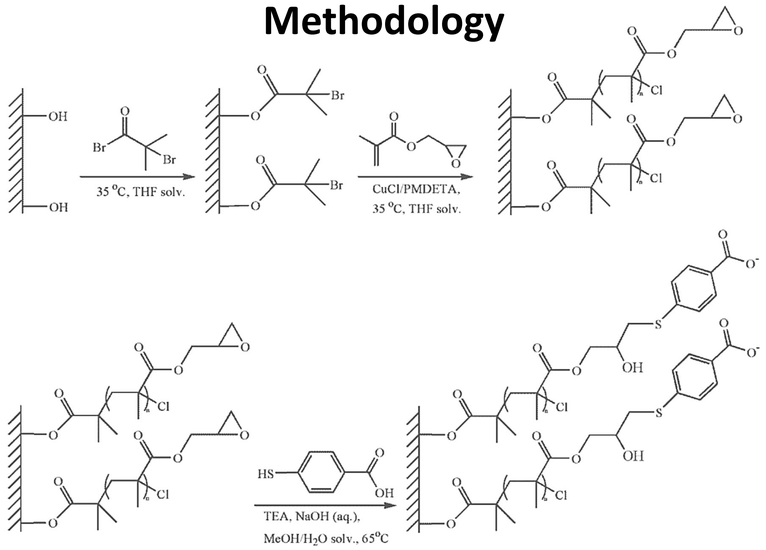
- Prepare a new class of multimodal membrane adsorbers with high binding capacities, salt-tolerance, and throughput for purification of biologics

Chromatography	Interaction types	Operation range	Selectivity
Ion-exchange	Coulombic	narrow	low for like-charged species
Multimodal	Coulombic/hydrophobic/ hydrogen bonding	broad	improved

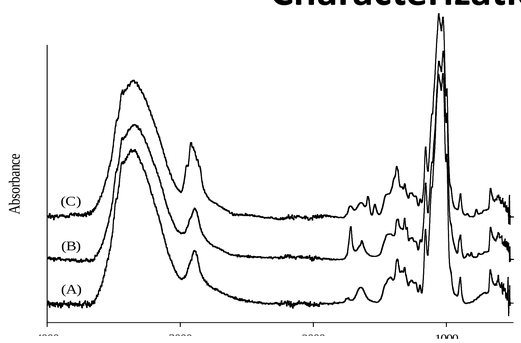


Demonstration of salt-tolerance property for multimodal chromatography media

Methodology



Characterization

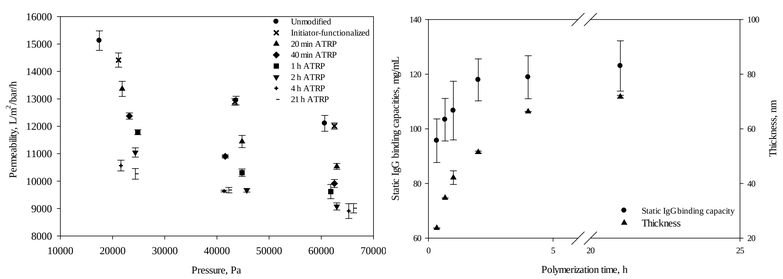


ATR-FTIR spectra for

(A) unmodified regenerated cellulose membrane,

(B) PGMA modified membranes,

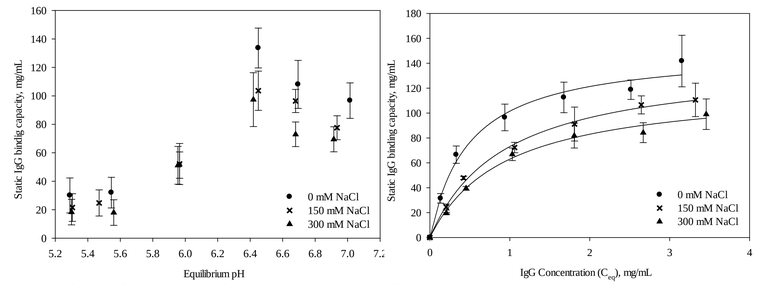
(C) Multimodal membranes.



(Left) Permeability measurements for unmodified membranes, initiator-activated membranes, and multimodal membranes. (Right) Dependence of static IgG binding capacities/ PGMA thickness on surface-initiated ATRP time for the multimodal membranes.

Performance Evaluation

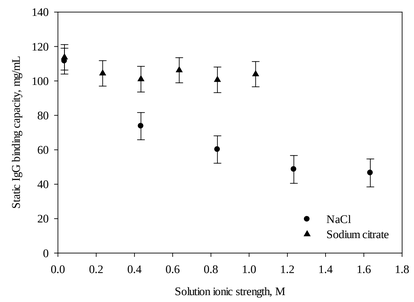
- The effects of pH and load concentration



(Left) Influence of pH on static IgG binding capacity for multimodal membranes (Right) Adsorption isotherms for IgG at 22°C and three sodium chloride concentrations (0, 150 and 300 mM). The Langmuir adsorption model parameters are shown in the table below.

Salt concentration (mM)	Association Coefficient (mL/mg)	Maximum Binding Capacity (mg/mL)
0	2.06±0.47	150.7±9.2
150	1.07±0.10	141.2±4.7
300	1.07±0.16	121.8±6.5

- Influence of ionic strength on static IgG binding capacities. Different types of salts were investigated. NaCl-neutral salt, NaCitrate-kosmotropic salt.



Summary

- A novel weak cation-exchange multimodal membrane adsorbers was developed for protein purifications.
- Polymerization time can be used to achieve high binding capacity while maintaining adequate permeability.
- Coulombic and hydrophobic interactions take place between the protein and the membrane, which contributes to the extraordinary salt tolerance property of the MMM.
- To further study the MMM, it will be necessary to develop effective elution strategy and to quantify dynamic binding capacity and selectivity.

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References: [1]Coker, V. *BioPharm Int.* March (2012), s20-s23. [2] Film Diffusion, Sartorius-Stedim Biotech SA. http://microsite.sartorius.com/index.php?id=14362&q=Film+Diffusion Accessed on March 3, 2014