Bench top continuous chromatography: an enabling platform for bioprocess development

Robert Mieweerd, Alla Ziberman, Bruce Thalay, and Anthony Gralinski
Sembla Biosciences, Inc., 505 South Rose Road, Madison, WI 53719 USA. www.semblabio.com

Abstract

Simulated moving bed chromatography (SMBC) and its variant multicomponent continuous chromatography (MCC) have the potential to elevate the industrial chromatographic platform by conversion of conventional batch processes to more efficient continuous processes. The high productivity, recovery and purity achieved by SMBC on an industrial scale for small molecules hold promise for an enabling platform to perform SMB/MCC on the research scale.

The Octave System developed by Sembla Biosciences is a line of laboratory instruments capable of performing SMB/MCC protocols on scales from 10 ml to 500 ml. This unique system provides the opportunity to rapidly test materials and develop methods in continuous operating modes that correspond to large-scale operations. Flexibility in programming column and flow configurations enables optimization of purity, yield, and adsorbent utilization for various separation chemistries and overall process variability between targets, and sterility and regulatory requirements. In our experiments we purified a humanized IgG1 monoclonal antibody from CHO culture fluid using the Octave system in a continuous Protein A capture (PAC) process and an AKTA System in an standard batch PAC process. We compared the performance of three commercial Protein A adsorbents in SMB and single-column (SC) modes.

For this study we purified a humanized IgG1 monoclonal antibody from CHO culture fluid using the Octave system in a continuous Protein A capture (PAC) process and an AKTA System in a standard batch PAC process. We compared the performance of three commercial Protein A adsorbents in SMB and single-column (SC) modes.

Materials & Methods

 RESULTS & DISCUSSION

Figure 3. Representative chromatograms from continuous PAC runs.

Figure 4. Predicted PAC productivities of SC and SMB processes with increasing mAb-titer.

Table 1. Results of SC and SMB runs.

Table 2. Observed vs. predicted PAC productivities.

Conclusions & Future Directions

This study has shown that the SMBC produced from a continuous PAC process performed on the Octave platform is equivalent in quality to that produced by the analogous batch process. Productivity and recovery will be optimized in future studies using higher titer mAb preparations.

As mAb-titer increases, productivity is predicted to dramatically increase with SMB vs. SC processes (see Fig. 4). This is because unlike SC, SMB is primarily a volume-driven process. As titer increases, intra-column distribution of species increases, which leads to increased elution efficiency. The productivities were in the range expected at the mAb concentration (2.37 g/L) used in our experiments. Figure 4 shows a comparison of productivity predicted for SMB and SC methods at increasing antibody titer, assuming 100% yield. Calculations are based on the process parameters and binding capacities of the adsorbent used in this study. This trend is expected for MabSelect SuRe and Toyopearl SuSan and Toyopearl reagents reflect the points at which maximum linear flow rates recommended by the manufacturer are reached.

Future studies will also investigate alternative adsorbents, column configurations, and protocols.

In addition to the 5-step protocol employed in these studies, the Octave System has been configured to perform on other PAC protocols including many as low as 5 mmol using 7 pumps (data not shown). Future studies will also investigate alternative adsorbents, column configurations, and protocols.

Materials & Methods

Materials & Methods

Table 2 shows the productivity data obtained from the SC-PAC vs. SMB-PAC performed with loading columns to 80% of their measured static binding capacities. Productivities of the SMB vs. SC process with MabSelect SuRe and POROS MabCapture A were within 3% of the predicted values, whereas SMB productivity was 21% less than that predicted for the Toyopearl AF-rProtein A resin. We believe that this shortfall in productivity was most likely due to the significant difference in yield between SC and SMB processes for this resin.

Further experiments are needed to determine the practical limits of residence time on the productivity of SMB-PAC.

Table 2. Observed vs. predicted PAC productivities.

Bench top continuous chromatography: an enabling platform for bioprocess development

Robert Mieweerd, Alla Ziberman, Bruce Thalay, and Anthony Gralinski
Sembla Biosciences, Inc., 505 South Rose Road, Madison, WI 53719 USA. www.semblabio.com

Abstract

Simulated moving bed chromatography (SMBC) and its variant multicomponent continuous chromatography (MCC) have the potential to elevate the industrial chromatographic platform by conversion of conventional batch processes to more efficient continuous processes. The high productivity, recovery and purity achieved by SMBC on an industrial scale for small molecules hold promise for an enabling platform to perform SMB/MCC on the research scale.

The Octave System developed by Sembla Biosciences is a line of laboratory instruments capable of performing SMB/MCC protocols on scales from 10 ml to 500 ml. This unique system provides the opportunity to rapidly test materials and develop methods in continuous operating modes that correspond to large-scale operations. Flexibility in programming column and flow configurations enables optimization of purity, yield, and adsorbent utilization for various separation chemistries and overall process variability between targets, and sterility and regulatory requirements. In our experiments we purified a humanized IgG1 monoclonal antibody from CHO culture fluid using the Octave system in a continuous Protein A capture (PAC) process and an AKTA System in a standard batch PAC process. We compared the performance of three commercial Protein A adsorbents in SMB and single-column (SC) modes.

For this study we purified a humanized IgG1 monoclonal antibody from CHO culture fluid using the Octave system in a continuous Protein A capture (PAC) process and an AKTA System in a standard batch PAC process. We compared the performance of three commercial Protein A adsorbents in SMB and single-column (SC) modes.

Materials & Methods

 RESULTS & DISCUSSION

Figure 3. Representative chromatograms from continuous PAC runs.

Figure 4. Predicted PAC productivities of SC and SMB processes with increasing mAb-titer.

Table 1. Results of SC and SMB runs.

Table 2. Observed vs. predicted PAC productivities.

Conclusions & Future Directions

This study has shown that the SMBC produced from a continuous PAC process performed on the Octave platform is equivalent in quality to that produced by the analogous batch process. Productivity and recovery will be optimized in future studies using higher titer mAb preparations.

As mAb-titer increases, productivity is predicted to dramatically increase with SMB vs. SC processes (see Fig. 4). This is because unlike SC, SMB is primarily a volume-driven process. As titer increases, intra-column distribution of species increases, which leads to increased elution efficiency. The productivities were in the range expected at the mAb concentration (2.37 g/L) used in our experiments. Figure 4 shows a comparison of productivity predicted for SMB and SC methods at increasing antibody titer, assuming 100% yield. Calculations are based on the process parameters and binding capacities of the adsorbent used in this study. This trend is expected for MabSelect SuRe and Toyopearl AF-rProtein A reagents. We believe that this shortfall in productivity was most likely due to the significant difference in yield between SC and SMB processes for this resin.

Further experiments are needed to determine the practical limits of residence time on the productivity of SMB-PAC.

In addition to the 5-step protocol employed in these studies, the Octave System has been configured to perform on other PAC protocols including many as low as 5 mmol using 7 pumps (data not shown). Future studies will also investigate alternative adsorbents, column configurations, and protocols.

Materials & Methods

Table 2 shows the productivity data obtained from the SC-PAC vs. SMB-PAC performed with loading columns to 80% of their measured static binding capacities. Productivities of the SMB vs. SC process with MabSelect SuRe and POROS MabCapture A were within 3% of the predicted values, whereas SMB productivity was 21% less than that predicted for the Toyopearl AF-rProtein A resin. We believe that this shortfall in productivity was most likely due to the significant difference in yield between SC and SMB processes for this resin.

Further experiments are needed to determine the practical limits of residence time on the productivity of SMB-PAC.

In addition to the 5-step protocol employed in these studies, the Octave System has been configured to perform on other PAC protocols including many as low as 5 mmol using 7 pumps (data not shown). Future studies will also investigate alternative adsorbents, column configurations, and protocols.