RESIDENCE TIME DISTRIBUTION OF CONTINUOUS PROTEIN A CHROMATOGRAPHY

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Establishing a continuous process is highly desired by both the biopharmaceutical industry and regulatory authorities. According to FDA guidelines on continuous manufacturing, the material flow should be characterized in a continuous process, and using residence time distribution (RTD) was suggested for this purpose. Residence time distribution shows how the material moves through the process, RTD can be determined for individual unit operation and the integrated process. Residence time distribution can be measured experimentally by injecting an inert tracer into the process and tracing it in the outlet.

Recombinant antibody production is rapidly increasing because of growing demand. Changing from batch processing to continuous processing is currently trending in the biopharmaceutical industry as it leads to higher quality, lower cost and lower environmental impact. The conventional antibody purification consists of filtration, protein A capture chromatography, virus inactivation, polishing chromatography and ultrafiltration and diafiltration.

For recombinant antibody production purification in continuous mode, periodic counter-current chromatography (PCC) is the most popular continuous capture chromatography. A three-column PCC was used in this work for monoclonal antibody (MAb) purification. Fluorescently labelled MAb was used as an inert tracer and injected into the inlet for determining the RTD. Then the Fluorescently labelled MAb was traced in the loading phase and elution phase.
The focus was to show how one part of loaded material distributes through the elution peak. We successfully showed that in the elution peaks, one portion of inlet material distributes equally through elution peaks. However, in the loading phase, we observed an unexpected constant equilibration between the MAb in the stationary phase and the MAb in the liquid phase.

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