

Development of continuous matrix-assisted protein refolding method

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This study successfully applied the batch chromatographic protein refolding approach to the SMB (simulated moving bed) chromatography. In spite of the advantages of recombinant IBs, difficulties in refolding were the bottleneck for research and industrial applications. The benefits of SEC (size exclusion chromatography) refolding are high yield and purity at high protein concentration (>1 mg/mL). In SMB protein refolding, much lower initial concentration (2 mg/mL) of denatured protein than batch SEC protein refolding (10 mg/mL) is applied in continuous mode, nevertheless the protein recovery and specific refolding yield were high and aggregation was reduced. The further advantages are the continuous and recycle operation resulting in low consumption of refolding buffer and high efficiency of medium.

Size exclusion factors and kinetic parameters for SMB operation were estimated from the best-fit values by comparing the simulation and experimental batch chromatography refolding results. Standing-wave analysis is used to obtain the SMB design for nonequilibrium system. The experimental SMB data are in close agreement with the theoretical predictions.