FLOW-VELOCITY PROGRAMMED CHROMATOGRAPHY AS AN ALTERNATIVE METHOD FOR INCREASING THE EFFICIENCY OF CONTINUOUS- OR INTEGRATED-CHROMATOGRAPHY PROCESSES

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Solvent (mobile phase) programming is most commonly employed for controlling adsorption/desorption in chromatography (linear gradient elution or stepwise elution). For gas separation, temperature- or pressure-swing adsorption is frequently used. Although flow-velocity is another important parameter, which affects both the dynamic adsorption capacity (DBC) and the resolution, it is seldom used as a programmed operating variable. The one exception is the standard 4-zone simulated moving bed (SMB) chromatography, in which the flow-velocities of the 4-zones are different. Several researchers have already shown that DBC can be increased by using two different flow velocities. However, a rational method for determining the optimum flow velocity program has not been established. Moreover, application of this method to periodic counter-current (PCC) chromatography or connected flow-through chromatography (FTC) has not been attempted yet. In this study, we have developed a flow-velocity gradient method for analyzing the breakthrough curves of proteins in ion-exchange or protein A chromatography (Figure 1). The data were obtained at various different gradient slopes. The obtained curves were analyzed based on a model considering mass transfer (pore diffusion) and non-linear isotherm. Then, numerical simulations were carried out in order to find the optimum flow-velocity program for improving the efficiency. This method was further applied to PCC and FTC (Figure 2). The effect of flow programming on productivity and cost reduction has also been examined in both batch and continuous configuration in capture chromatography of mAbs by simulation of the process models. Experimental verification was also carried out using monoclonal antibody samples in the filtered cell culture liquid.

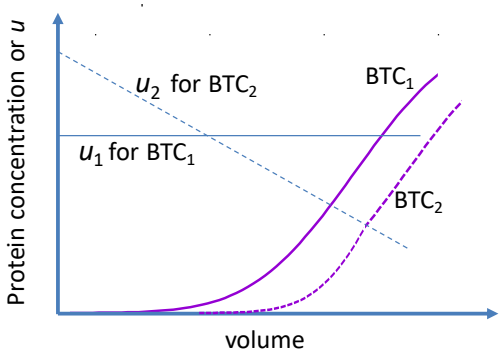

Figure 1 - Breakthrough curves at constant flow velocity (BTC_1) and at programmed flow velocity gradient (BTC_2)

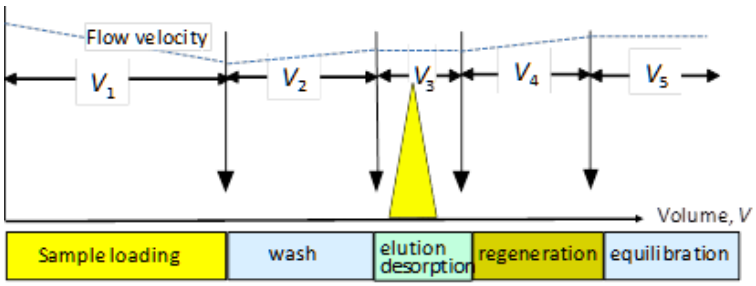

Figure 2 - Typical capture chromatography operations with flow-programming.