Model-based Experimental Analysis for the Determination of Nonlinear Adsorption Isotherms

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Abstract: The new challenge for simulated moving bed (SMB) technology is its application to the separation and purification of biomolecules. For this purpose, ion-exchange SMB can be enhanced implementing a solvent-gradient. Here, the underlying mechanism for protein separation can be described by nonlinear competitive adsorption equilibrium. For the explicit consideration of non-isocratic operation Brooks & Cramer, 1992 developed a steric mass (SMA) ion-exchange equilibrium formalism, which explicitly accounts for the steric hindrance of salt counterions upon protein binding in multicomponent equilibria. In this work, we discuss a systematic determination of all 7 relevant SMA-parameters. For this target-setting, batch experiments were conducted, where given volumes of adsorbent are equilibrated in a solution with known initial concentrations. Thus, the adjustable variables are the initial protein concentrations, the salt concentration and the amount of adsorbent (anion exchanger Source 30Q, GE-Healthcare). However, optimal decisions for the experimental design are not obvious. This is especially due to the lack of a direct measurement of the adsorbed protein amount and the reduction from the dissolved initial protein concentration to the equilibrium concentration. To overcome this problem, a systematic approach based on optimal experimental design has been developed.

In this contribution, the comparison of preliminary theoretical design studies with the finally conducted experiments shows that these restrictions can degrade the information content of the experiments. At first glance, a parallel design of experiments seems to be natural since it corresponds to the standard procedure in a lab. This approach is also mandatory for the first number of experiments to be planned in order to ensure for identifiability of the SMA-parameters. Nevertheless, in this work, we will demonstrate that due to various uncertainties, a sequential-parallel experimental design approach exhibits more advantages than the parallel one. These uncertainties are both the unknown model parameters and uncertainties which arise from an imprecise implementation of the planned experiments. The developed sequential estimation procedure allows for an iterative refinement of the experiments to be planned. In doing so, it can be demonstrated that the significant loss of information content due to uncertainties can be partially compensated. Moreover, the results of intuitive and optimal planned experiments and the statistical analysis of the corresponding estimated parameters as well as a cross validation with additional experimental data will be presented.

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