Predictions of Protein Adsorption and Desorption in Liquid-Solid Circulating Fluidized Bed Ion Exchange System

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Introduction

The interest in recovery of various functional proteins from large volume of industrial broths and biological wastewater streams has increased in recent years, due to the advancement in genetic engineering, and concerns about recycling limited resources and environmental protection (Lan, 2001). Ion exchange adsorption and chromatography have long been used for downstream processing in the biotechnology industry because of its high binding capacity, high resolving power, and relatively inexpensive (Chang and Chase, 1996). As the protein concentration in the feedstock is fairly low, large volumes must be treated to recover proteins in an industrial scale. Therefore, a highly efficient continuous ion exchange process is necessary for the industrial scale protein purification.

Lan et al. (2002) had developed a Liquid-Solid Circulating Fluidized bed (LSCFB) ion-exchange system for the continuous recovery of protein from unclarified broth. LSCFB ion-exchange system is used as an integrated reactor and regenerator system; two different operations (adsorption and desorption) are carried out simultaneously in two separate columns (downcomer and riser respectively) in continuous mode (with continuous circulation of ion exchange particles between two columns). Again, with the shift into the circulating fluidization regime from convention fluidization, liquid and solid phase dispersion is significantly reduced. Moreover, LSCFB has some obvious advantages in addition to the advantages of conventional fluidized bed such as high liquid-solid contact efficiency, higher throughput and enhanced mass transfer due to higher velocity, reduced back mixing of phases and uniform flow pattern (Zhu et al., 2000).

Detailed modeling of the hydrodynamics, mass transfer and kinetics of adsorption and desorption of protein in the LSCFB ion-exchange system is fundamental and crucial for better understanding of the adsorption and desorption behaviors, the design and scale up of the LSCFB system, and optimization of the operating parameters. A number of models have been developed to describe the protein adsorption behaviors in packed bed, expanded bed and fluidized beds considering various types and degrees of approximation to physical reality. Several steps are involved in the process of adsorption of proteins onto the adsorbents: convective and diffusion mass transfer from liquid phase to adsorbent surface, diffusion through the pore of the ion exchange resins and the surface reactions. The surface adsorption process is sufficiently rapid compared to the former two

steps and is not considered as a limiting step. Lan et al. (2000) developed a model for continuous protein recovery in LSCFB ion-exchange system assuming the process is surface reaction limited.

In this work, we present a model to predict the continuous adsorption and desorption of BSA protein onto and from anion exchange resin (Diaion HPA25®) in the LSCFB ion-exchange system taking into account the fluidization behaviors in the LSCFB, overall mass transfer for adsorption process and surface desorption kinetics. The model was validated by comparing the predicted results with experimental data reported by Lan et al. (2000; 2002).

LSCFB Ion Exchange System and Continuous Protein Recovery

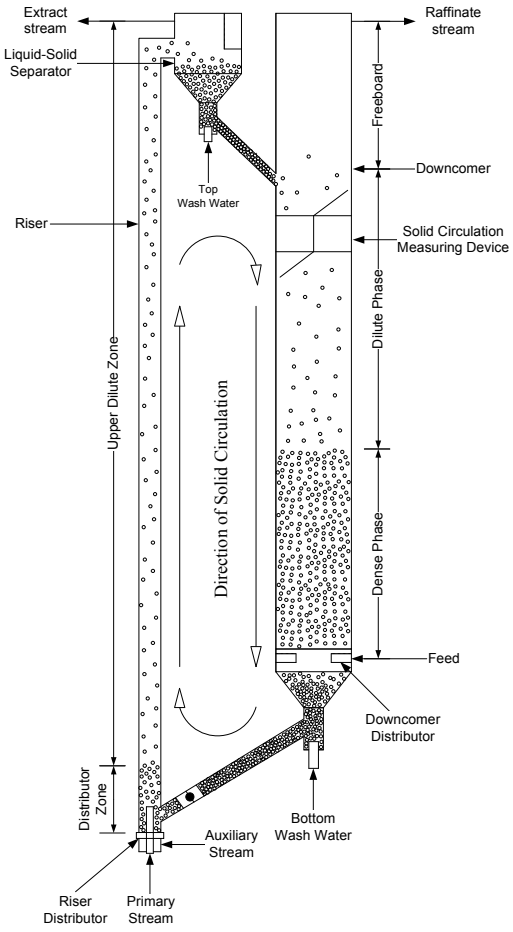

Figure 1: Schematic diagram of the Liquid-solid Circulating Fluidized bed (LSCFB) ion exchange system (Lan et al., 2002).

LSCFB is composed of two interconnected columns namely: a riser and a downcomer. Lan et al. (2002) used LSCFB for simultaneous adsorption and desorption of BSA protein using anion exchange resins Diaion HPA25® in the two separate columns of the LSCFB. *Figure 1* shows a schematic diagram of the LSCFB ion-exchange system developed by Lan et al. (2002). Adsorption of protein from the BSA solution was carried out in the downcomer of the system and the adsorbed protein were extracted from the ion exchange resins in the riser. The configurations of the LSCFB ion exchange system and continuous protein recovery in the LSCFB unit were described by Lan et al. (2002).

Hydrodynamic Modeling

Fluidization in the Downcomer:

The liquid and solids contact counter-currently in the downcomer of the liquid solid circulating fluidized bed: the liquid moves upward and the solids downward. Lan et al. (2002) observed three different operating zones in the downcomer which differ in solids holdup: the dense phase zone, the dilute phase zone and the freeboard zone. The section from the top to the solids entrance of the downcomer is the freeboard region which is necessary to prevent the loss of ion exchange resins through the raffinate stream. The dilute phase is in between the freeboard and the dense phase. The protein concentration is very low in the dilute phase and the freeboard zone. Solids holdup in the dense phase zone is much higher than that of the other zones and contains most of the ion-exchange particles. Hence, the dense phase zone is the most important zone for protein adsorption in the downcomer (Lan et al., 2002). The dense-phase zone operates as a conventional fluidized moving bed (Kwauk, 1992). Ricardson-Zaki equation is modified for the counter current arrangement to calculate the bed-voidage in the dense-phase zone:

$$U_{ld} + U_{sd}\frac{\varepsilon_d}{1-\varepsilon_d} = U_i \varepsilon_d{}^n \tag{1}$$

The bed expansion index (n) can be determined from the following correlation:

$$n = (4.4 + 18\frac{d_p}{D_c})\,\mathrm{Re}_t{}^{-0.01} \tag{2}$$

$$\text{where, } \mathrm{Re}_t = \frac{U_t d_p \rho}{\mu} \tag{3}$$

U_i, the superficial liquid velocity at $\varepsilon = 1$, which can be determined using following empirical equation (Khan and Richardson, 1989):

$$\frac{U_i}{U_t} = 1 - 1.15(\frac{d_p}{D_c})^{0.6} \tag{4}$$

Hence, ε_d can be calculated from Eq.1 for a given U_{ld} and U_{sd} and determining n and U_i from Eq. 5 and Eq. 7 respectably.

Fluidization in the Riser:

The riser of the LSCFB ion-exchange system is operated in circulating fluidization regime: liquid velocity in the riser is greater than the terminal settling velocity of the solid particles. As discussed earlier, the riser distributor separates the liquid flow into two portions: primary liquid flow and auxiliary liquid flow. Because of the arrangement of the riser distributor, two distinct zones, namely a distributor zone and a upper dilute zone, are observed along the riser based on their solids holdup. Solids holdup in the distributor zone is much higher than the upper dilute zone and the distributor zone can be considered to be operated as conventional fluidization. Therefore, the voidage in the distributor section can be approximated using the correlations for homogeneous conventional fluidization. The modified Richardson–Zaki equation for the distributor zone of the co-current up flow riser can be written as:

$$U_{lr} - U_{sr}\frac{\varepsilon_{r1}}{1-\varepsilon_{r1}} = U_i \varepsilon_{r1}{}^{n} \tag{5}$$

The bed expansion index (n) and the superficial liquid velocity (U_i) at ε = 1 in the distributor zone of the riser can be calculated using Eqs. (2)-(4).

The upper dilute zone is operated in circulating fluidization regime and solids holdup in this zone is nearly uniform. Solids holdup in the riser is function of both the liquid velocity in the riser and solids circulation rate. Lan et al. (2002) had reported data for the solids holdup in upper dilute phase of the riser (ε_{sr2}) as a function of liquid velocity and solids circulation rate. Based on these data a correlation has been developed:

$$\varepsilon_{sr2} = 2.64\times10^{-14} U_{lr}{}^{-5.343} + 2.57\times10^{-5} G_s U_{lr}{}^{-1.578} \tag{6}$$

where, U_{lr} is the superficial liquid velocity in the riser in m/s and G_s is the solids circulation rate in kg/m^{2}s.

Modeling of LSCFB Ion Exchange System

Design equation for the downcomer:

$$\mathrm{U_{ld}}\frac{\partial \mathrm{C_d}}{\partial \mathrm{Z_d}} + \psi k_f a(C_d - C_s)(1-\varepsilon_d) = 0 \tag{7}$$

where, C_d is the protein concentration in the bulk liquid phase of the downcomer; U_{ld} is the superficial liquid velocity in the downcomer; Z_d is the axial distance from the bottom of the downcomer; ε_d is the voidage in the downcomer dense phase; ψ is a constant factor

which includes the effects of intra-particle diffusion and liquid phase axial dispersion; a is the specific surface area of the ion-exchange resins. C_s is the equilibrium liquid phase protein concentration at liquid-solid interface predicted using the Langmuir isotherm:

$$C_s = \frac{K_d q_d}{q_m - q_d} \tag{8}$$

where, q_m is the maximum adsorption capacity of the ion-exchange particles, K_d is the dissociation constant, q_d is the solids phase protein concentration in the downcomer.

$$q_d = \frac{U_{ld}}{U_{sd}}(C_d - C_{ed}) + q_{od} \tag{9}$$

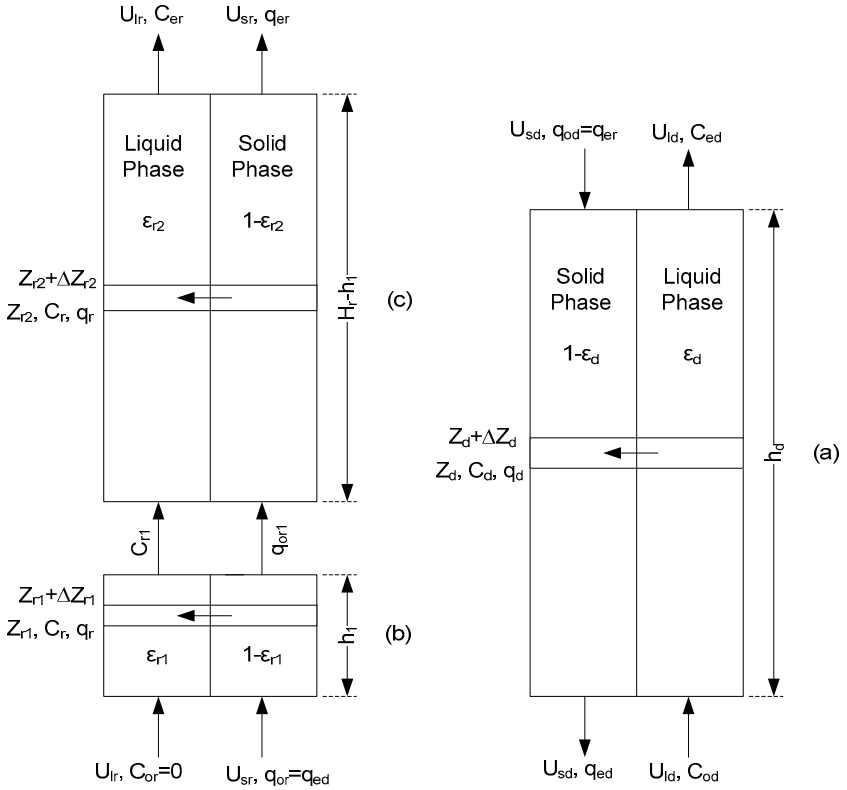

Figure 2: Flow patterns in (a) the downcomer, and (b) distributor zone and (c) upper dilute zone of the riser.

k_f is the film mass transfer co-efficient (k_f) in the downcomer dense phase calculated as a function of solids holdup (ε_{sd}) and particles Reynolds number (Re_p) using the correlation reported by Fan et al. (1960):

$$k_f = \frac{D_m}{d_p}(2 + 1.03(\varepsilon_{sd}\,\mathrm{Re}_p)^{1/2}(Sc)^{1/3} \quad (10)$$

where, $\mathrm{Re}_p = \frac{d_p U_{slip}\rho}{\mu}$; $Sc = \frac{\mu}{\rho D_m}$; $u_{slip} = \frac{U_{ld}}{\varepsilon_d} + \frac{U_{sd}}{1-\varepsilon_d}$ (11)

The value of D_m for BSA solution was estimated using the following correlation reported by Young et al. (1980):

$$D_m = 8.34 \times 10^{-8}\left(\frac{T}{\mu M^{1/3}}\right) \quad (12)$$

Design equation for the riser:

Distributor zone of the riser, $U_{sr}\frac{\partial q_r}{\partial Z_{r1}} + k_{r1} q_r \varepsilon_{sr1} = 0$ (13)

Boundary Conditions:

At $Z_{r1} = 0$ $C_r = 0$; $q_r = q_{or}$ (14a)

At $Z_{r1} = h_1$ $C_r = C_{r1}$; $q_r = q_{or1}$ (14b)

Upper dilute zone of the riser, $U_{sr}\frac{\partial q_r}{\partial Z_{r2}} + k_{r2} q_r \varepsilon_{sr2} = 0$ (15)

Boundary Conditions:

At $Z_{r2} = h_1$ $C_r = C_{r1}$; $q_r = q_{or1}$ (16a)

At $Z_{r2} = 3$ $C_r = C_{er}$; $q_r = q_{er} = q_{od}$ (16b)

where, k_{r1} and k_{r2} are desorption rate constants in the distributor zone and the upper dilute zone respectively.

Simulation

The design equations for the downcomer, the distributor zone and upper dilute zone of the riser were solved in succession using FORTRAN (IMSL subroutine). Non-linear algebraic equations and ordinary differential equations were solved using NEQNF and IVPAG (Gear's BDF method) subroutines of the IMSL library respectively. The computation flowchart for the simulation of the LSCFB ion-exchange system is outlined in *Figure 3*.

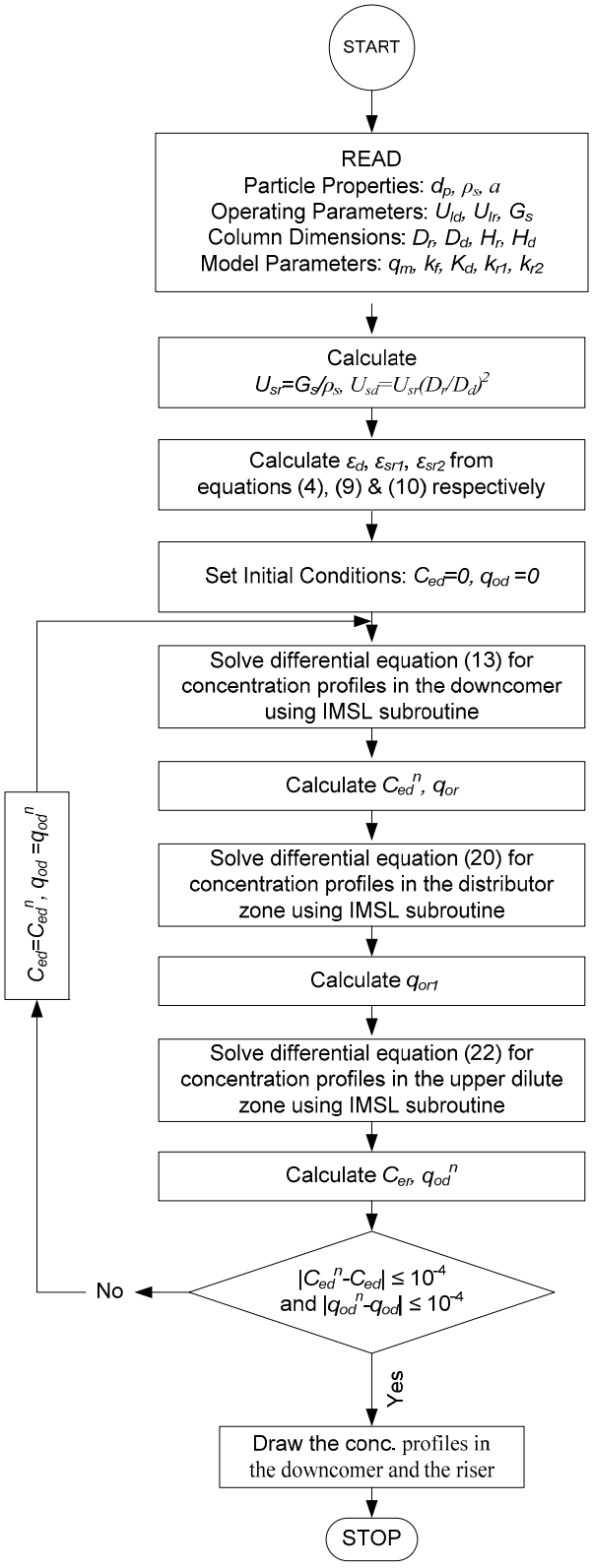

Figure 3: Algorithm for simulation of the LSCFB ion-exchange system.

Parameter Estimation and Model Validation

As the values of some of the parameters for this particular system are not available in the literature, these parameters were tuned by fitting the model predicted results with the experimental results (Lan et al., 2001). The downcomer and the riser are coupled by the circulation of the ion-exchange resins and change in any parameters affect both the adsorption and the desorption process. Hence, predicted results for both the variation of liquid phase concentration profile in the downcomer and the variation of liquid phase concentration profile in the riser with operating conditions were fitted with the experimental data simultaneously.

Predicted results for the liquid phase protein concentration profile in the downcomer under different solid circulation rate and the liquid phase protein concentration profile in the riser under different superficial liquid velocity were fitted with the experimental data simultaneously as shown in *Figure 4* and *Figure 5* respectively. Estimated values of dissociation constant (K_d), constant lumped parameter related to diffusion and dispersion (ψ), desorption rate constant at the distributor zone (k_{r1}) and desorption rate constant at the upper dilute zone of the riser, (k_{r2}), are listed in *Table I*.

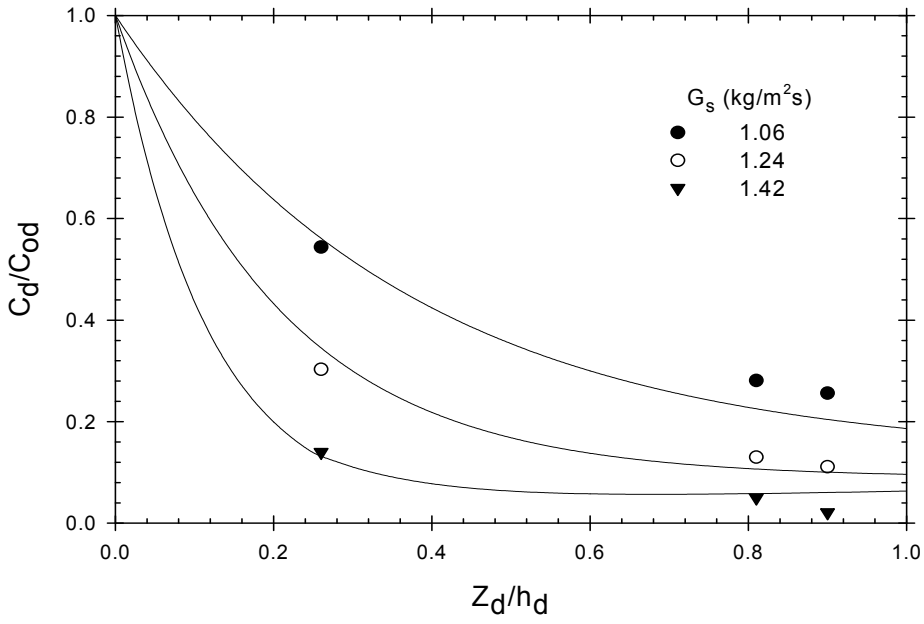

Figure 4: Liquid phase protein concentration profile in the downcomer under different solids circulation rate G_s (experimental data from Lan et al. (2000) and solid lines: model predicted results using the values of the parameters as listed in Table IV, C_{od} = 2 kg/m^3, U_{ld} = 0.6 cm/s, U_{lr} = 11.3 cm/s, 3 kg dry resins).

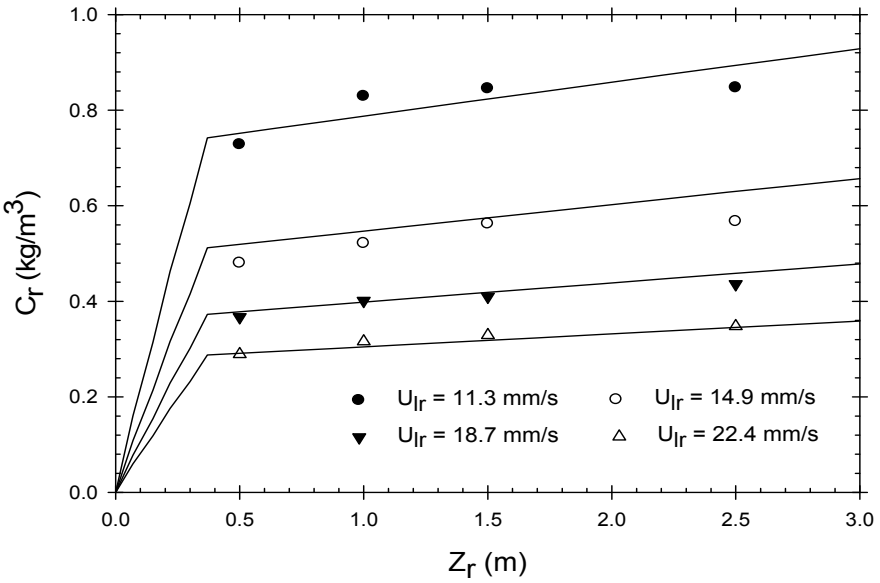

Figure 5: Liquid phase protein concentration profile in the riser under different superficial liquid velocity in the riser U_{lr} (experimental data from Lan et al. (2000) and solid lines: model predicted results using the values of the parameters as listed in Table IV, C_{od} = 2 kg/m^3, G_s = 1.24 kg/m^{2}s, U_{ld} = 0.6 cm/s, 3 kg dry resins).

Table I: Tuned parameters obtained based on the experimental data using NSGA II

K_d (kg/m^3)	K_{r1} (1/s)	K_{r2} (1/s)	ψ
0.25	0.005253	0.0006	0.68

To validate the model and the values of estimated model parameters, the predicted results for the liquid phase protein concentration profile under different superficial liquid velocity in the downcomer are compared with the experimental data (Lan et al. 2000; 2002) as shown in *Figure 6*. It is seen that the model resulted in quite good prediction of the variation of adsorption capacity of the downcomer with the change in superficial liquid velocity.

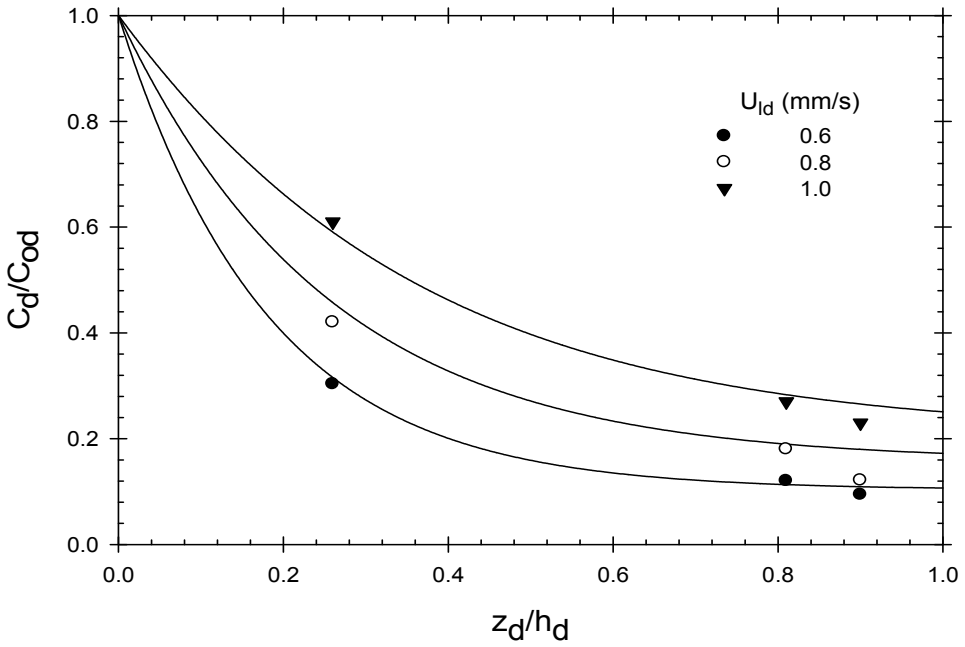

Figure 6: Liquid phase protein concentration profile in the downcomer under different superficial liquid velocity in the downcomer U_{ld} (experimental data from Lan et al. (2000; 2002) and solid lines: model predicted results using the values of the parameters as listed in Table IV, C_{od} = 2 kg/m^3, G_s = 1.24 kg/m^{2}s, U_{lr} = 11.3 cm/s, 3 kg dry resins).

Conclusions

The interaction between the hydrodynamics and the kinetics makes the adsorption and desorption behavior in the liquid-solid circulating fluidized bed quite complex. The change in the operating conditions in one column influences the performance of another column of the LSCFB. A experimentally verified model was developed to predict adsorption and the desorption performance of the LSCFB ion-exchange system and the model showed good agreement with the experimental data available. As LSCFB is being applied in an ever increasing number of new applications, this model can be used as a tool for predicting the performance of LSCFB for many more applications.

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