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General applications of modified Stokes expression for modeling and scale-up of expanded beds

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Abstract−The modeling of the behavior of expanded beds using Richardson-Zaki correlation in combination with the modified Stokes expression developed by Chae et al. [1] was successfully applied to the cases of small expanded beds (1 cm in column diameter) containing two different polydisperse particles used for ion-exchange operations, Chelating excellose (70-210 μm in diameter, 1.21 g/cm^3 in density) and Streamline DEAE (100-300 μm in diameter, 1.20 g/cm^3 in density). Empirical parameters determined for the modeling of the expansion of these small-beds (1 cm diameter) were found to have values similar to those for the case of larger expanded beds (2.5 cm in diameter) containing the same particles. This indicates that the modeling method can be utilized for the scale-up purposes of the expanded beds with various feed solutions.

Key words: Expanded Bed, Modeling, Scale-up, Stokes Expression

INTRODUCTION

Traditional recovery of extra-cellular proteins from fermentation broths or intra-cellular proteins from cell homogenates starts with the clarification steps; protein solutions containing solid particles should be treated with centrifugation or filtration steps to remove cells or cell debris followed by dialysis and concentration steps to remove untargeted small molecules and decrease solution volume [2-4]. Those preliminary steps for protein recovery are the main causes for low yields, prolonged process time, and high operational costs. These problems become more serious as the scale of protein recovery process increases.

Expanded bed adsorption (EBA) technology, in which a feed stream containing both targeted proteins and cells or cell debris is applied from the bottom of the column containing proper resins for protein adsorption at a flow rate enough to maintain the resins well expanded but with low back-mixing, enables the simultaneous achievement of clarification, concentration, and selective separation [5-7]. Solid particles such as cells or cell debris contained in the feed stream can pass freely through the expanded bed; therefore, the clarification steps become unnecessary. EBA technology, however, lacks such thorough understanding about its hydrodynamic behavior as has been available for the conventional packed-column technology [8]. Therefore, in order to utilize EBA technology for industrial-scale protein purification processes, a method to describe the behavior of the expanded bed incorporating the properties of resins and feed streams should be provided. This model will be utilized to design the equipment and to preset the optimal values of operating parameters. The Richardson-Zaki correlation, which has been used to describe the expansion of beds, predicts a linear relation between logarithms of the superficial fluid velocity (v_o) and the void fraction of the bed ($1-\phi_s$) for fluidized beds by Eq. (1):

$$\log v_o = n \log (1-\phi_s) + \log v_t \quad (1)$$

where ϕ_s and v_t are the solid fraction of the expanded bed and the Stokes terminal settling velocity of the particle at infinite dilution ($\phi_s=0$), respectively [9]. The superficial velocity (v_o) is obtained by dividing the volumetric flow rate of the feed stream by the cross-sectional area of the column. The solid fraction, ϕ_s, of the expanded bed at a bed-height H can be obtained by

$$\phi_s = \phi_{so} H_o / H \quad (2)$$

where ϕ_{so} and H_o are the solid fraction and the height of the sedimented bed at zero flow rate of the feed stream, respectively. H/H_o represents the degree of bed expansion. Since the terminal settling velocity theoretically depends on the properties of feed solutions and the particles based on the Stokes equation, the Richardson-Zaki correlation cannot be utilized alone as a unified equation to describe behavior of the expanded beds.

We previously developed a modified Stokes expression as represented in Eq. (3) and Eq. (4) as a linealized form incorporating two empirical parameters, the effective particle diameter, d_{pe}, and an exponent of non unity, a, to model the behavior of expanded beds (2.54 cm in column diameter containing a polydisperse ion exchange resin, Chelating excellose) in combination with Richardson-Zaki equation [1].

$$v_t = g d_{pe}^2 [(\rho_p - \rho)/\mu]^a / 18 \quad (3)$$

$$\log v_t = \log [g d_{pe}^2 / 18] + a \log (\rho_p - \rho)/\mu \quad (4)$$

where g is the gravitational acceleration, ρ_p and ρ are the mean particle density of the ion exchange resin and solution, respectively, and μ the solution viscosity. Our modeling method was also successfully applied to the cases of expanded beds (2.54 cm in column diameter) containing another weak ion exchange resin, Streamline Red, with an *E-coli* homogenate as a feed stream [10]. In this study, we applied the method developed by Chae et al. [1] to small expanded beds (1 cm in column diameter) to examine the feasibility

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of the method for the scale-up purposes of expanded beds.

EXPERIMENTAL

Chelating excellose (70-210 μm in diameter, 1.21 g/cm^3 in mean particle density), which has Ni^{2+} ions enabling the selective binding of histidine-tagged proteins, was purchased from Bioprogen (Korea). Streamline DEAE (100-300 μm in diameter, 1.20 g/cm^3 in mean particle density) and a column of an internal diameter of 1.0 cm were purchased from Pharmacia (U.S.A). The column was first packed with acid-washed glass beads (425-600 μm in diameter, from Sigma) to a height of 2 cm; then the ion exchange resin was packed above the glass beads to a height of approximately 5 cm. This method of packing the resins ensures even flow distribution to minimize the channeling inside the bed. In order to vary the solution properties such as density and viscosity, aqueous buffers (50 mM NaH_2PO_4, 300 mM NaCl, 10 mM imidazole, pH 7) containing different concentrations of glycerol were used as feed streams. The viscosity of each glycerol-aqueous buffer mixture was estimated by interpolating the data provided by Poker and Janjic [11].

The solid fraction of the sedimented bed, ϕ_{so}, for the resins was measured as follows. In the column, the resin was settled in distilled water. The water contained inside the void fraction of the sedimented bed was drained off by slightly pressurizing the column from above with N_2 gas. The volume of the drained water was measured and divided by that of the total sedimented bed to determine the void fraction, ε, of the bed. Finally, ϕ_{so} value was determined by $1-\varepsilon$ and was 0.848 for Chelating excellose and 0.898 for Streamline DEAE.

RESULTS AND DISCUSSION

The effects of superficial velocity (v_o) of the feed stream containing different contents of glycerol on the bed-expansion (H/H_o) were measured and shown in Fig. 1. The bed-expansion was limited below 3 as recommended by Reichert et al. [12] for proper performance of expanded beds. The bed-expansions for the two ion exchange resins became greater as the solution viscosity increased at a fixed flow rate of the feed stream. Though the particle densities of the two ion exchange resins are similar to each other, the bed-expansions were quite different; to reach the same bed-expansion, Streamline DEAE requires approximately five times higher super-

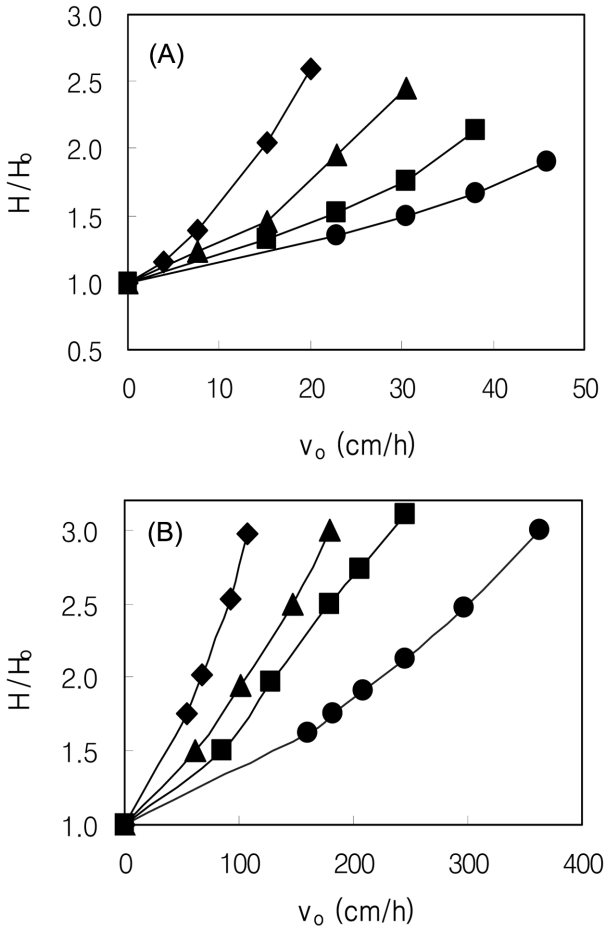

Fig. 1. Effects of the superficial velocity of feed streams on the bed-expansion of expanded beds packed with Chelating excellose (A) or Streamline DEAE (B). The concentrations of glycerol (v/v) in the feed streams are 0% (●), 10% (■), 20% (▲), and 30% (◆).

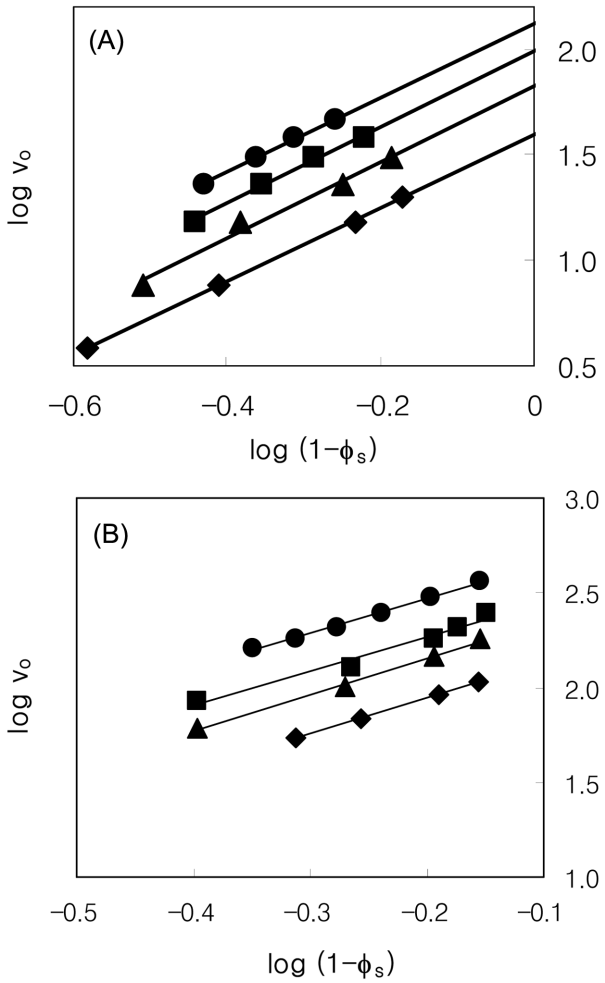

Fig. 2. Richardson-Zaki plots of the bed-expansion for Chelating excellose (A) and Streamline DEAE (B). The same symbols as in Fig. 1 are used for glycerol-aqueous buffer mixtures.

Table 1. Physical properties of glycerol-aqueous buffer mixtures and the parameter values of Richardson-Zaki correlation

Feed stream			Ion exchange resins			
			Chelating excellose		Streamline DEAE	
Glycerol (v/v %)	Density (g/cm^3)[a]	Viscosity (cp)[b]	n[c]	v_t (cm/h)[d]	n[c]	v_t (cm/h)[d]
0	1.01	0.89	1.76	132	1.84	685
10	1.04	1.25	1.80	97.6	1.79	418
20	1.06	1.67	1.80	66.4	1.92	348
30	1.11	2.50	1.74	39.4	1.90	212

[a]Density values were directly measured.
[b]Viscosity for each solution was estimated by interpolating viscosity data for glycerol-water mixtures provided by Poker and Janjic [11].
[c]Slope of the Richardson-Zaki plot.
[d]The Stokes terminal settling velocity.

ficial velocity of feed stream than that for Chelating excellose. For example, with 100% water as a feed stream, bed-expansion of 2 is obtained at 46 cm/h for Chelating excellose and at 250 cm/h for Streamline DEAE. Product instruction for Streamline DEAE supplied by the manufacturer also indicates that bed-expansion of 2-3 is obtained at 300 cm/h of feed stream. Therefore, higher flow rate of a feed stream can be applied to expanded beds containing Stream DEAE than Chelating excellose.

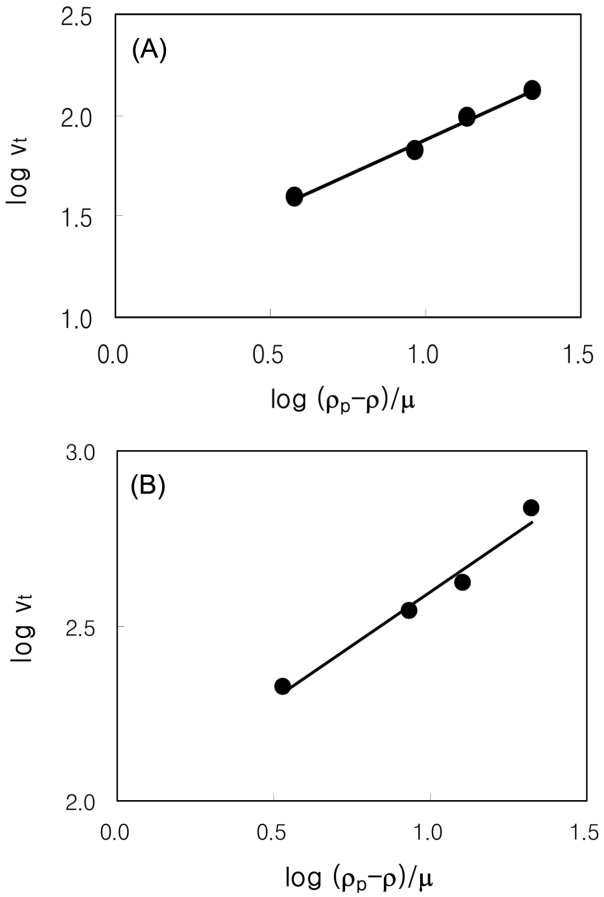

Fig. 3. Linear correlation between log v_t values determined from Richardson-Zaki plots with log $(\rho_p-\rho)/\mu$ values for the bed-expansion for Chelating excellose (A) and Streamline DEAE (B).

Fig. 2 shows the Richardson-Zaki plots for the experimental data in Fig. 1. In glycerol-aqueous buffer mixtures, expansions of the beds containing either Chelating excellose (Fig. 2(A)) or Streamline DEAE (Fig. 2(B)) follow the Richardson-Zaki relation very satisfactorily. All the linear lines in Fig. 2(A) and Fig. 2(B) have approximately the same slope (n) values with different intercepts for each resin. For both of the expanded beds, as the content of glycerol in the feed stream increases, the slope, n, changes little while the intercept, log v_t, decreases significantly. The average value of the slopes, n_{av}, was 1.78 for Chelating excellose and 1.86 for Streamline DEAE. Table 1 lists the values of n and v_t for expanded beds containing either Chelating excellose or Streamline DEAE with feed streams of glycerol-aqueous buffer mixtures along with their density and viscosity values.

Figs. 3 shows the linear dependence of log v_t values on the log $(\rho_p-\rho)/\mu$ values, which incorporate the properties of feed streams (density and viscosity) and the density of resins (ρ_p). The linear correlations in Figs. 3 can be represented by Eq. (5) and Eq. (6) for the expanded beds with Chelating excellose and Streamline DEAE, respectively.

$$\log v_t = 1.18 + 0.70 \log (\rho_p-\rho)/\mu \quad (5)$$

$$\log v_t = 1.97 + 0.63 \log (\rho_p-\rho)/\mu \quad (6)$$

Comparing Eq. (5) and Eq. (6) to Eq. (4) enables us to calculate the values of the two empirical parameters, the effective particle diameter, d_{pe}, and the exponent, a, for each expanded bed as listed in Table 2. For the expanded bed containing the same resin, Chelating excellose, the empirically determined values of the three param-

Table 2. Values of experimental parameters determined for Richardson-Zaki correlation (n_{av}) and the modified Stokes expression (a and d_{pe})

Resins Column ID[a]	Chelating excellose 2.54 cm[b]	Chelating excellose 1 cm	Streamline DEAE 1 cm
n_{av}	1.71	1.78	1.86
a	0.74	0.70	0.63
d_{pe} (μm)	80	88	220

[a]Inside diameter.
[b]Data taken from Chae et al. [1].

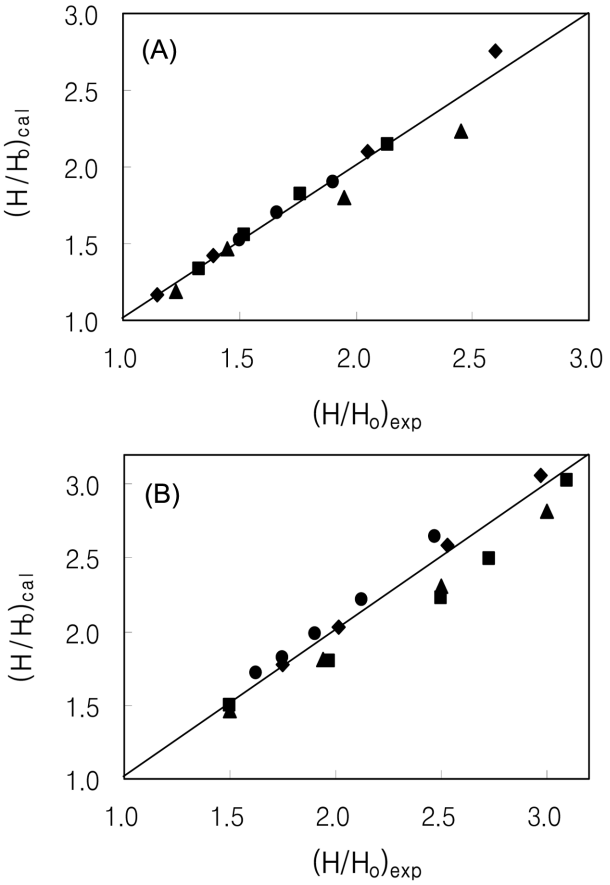

Fig. 4. Comparison of the bed-expansions calculated by using the modified Stokes expression, $(H/H_o)_{cal}$, with those of experimentally determined value, $(H/H_o)_{exp}$ for Chelating excellose (A) and Streamline DEAE (B). The same symbols as in Fig. 1 are used for glycerol-aqueous buffer mixtures.

eters (n_{av}, a, and d_{pe}) are almost the same for both columns of different diameters indicating that Richardson-Zaki correlation in combination with the modified Stokes equation can be useful in scale-up of the expanded beds with various types of feed streams. The values of the three empirical parameters determined for a small expanded bed can be used to predict the expansion behavior of larger beds containing the same resin with a variety of feed streams of known density and viscosity. The physical importance of the d_{pe} value, however, should not be emphasized due to the dimensional inconsistency of Eq. (3) when the exponent, a, is not equal to unity. In other words, the experimentally determined value of d_{pe} should only be used as an empirical parameter.

Combining Eq. (1) and Eq. (2) results in an explicit representation of the bed-expansion by

$$H/H_o=(\phi_s)_o/[1-(v_o/v_t)^{1/n}] \quad (7)$$

By replacing n in Eq. (7) with n_{av}, the bed-expansion can be calculated at a superficial velocity of feed stream by Eq. (7) with v_t value determined by Eq. (3). Fig. 4 demonstrates that the calculated bed expansions, $(H/H_o)_{cal}$ are in good agreement with experimentally measured values of bed expansion, $(H/H_o)_{exp}$ for all glycerol-aqueous buffer mixtures.

CONCLUSIONS

Conclusively, the Richardson-Zaki correlation in combination with modified Stocks expression for the terminal settling velocity of ion exchange particles can be successfully utilized to scale up the behavior of expanded beds with a variety of feed streams. This study also demonstrates that the same method can be applied to model the expansion of beds containing different types of polydisperse particles as ion exchange resins.

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