Rigorous Model for Ion Exchange Equilibria of Strong and Weak Electrolytes

Marcel L. Jansen, Adrie J. J. Straathof, Luuk A. M. van der Wielen, Karel Ch. A. M. Luyben, and Will J. J. van den Tweel
Dept. of Biochemical Engineering, Delft University of Technology, Julianalaan 67, 2628 BC Delft,
The Netherlands

A thermodynamics-based equilibrium model was developed to describe ion exchange equilibria of strong and weak electrolytes. It is applicable to binary and multicomponent systems, using selectivity coefficients for all ion pairs and distribution coefficients for all neutral species as parameters. The model was successfully tested for a strong-base anion exchange resin with the strong electrolyte NaCl and the weak electrolytes acetic acid and N-acetylmethionine in a wide concentration range. Compared to conventional models, this model is more advantageous because it takes into account the uptake of all species, counterions as well coions and neutral species, thus making it possible to calculate the intraparticle pH. Especially when weak electrolytes are involved and when electrolyte concentrations strongly exceed the resin capacity, it is superior to conventional ones, whereas for dilute systems it converges to the conventional stoichiometric displacement model.

Introduction

Conventional models for ion-exchange processes are based on a number of simplifying and therefore limiting assumptions (Helfferich, 1962; Vermeulen et al., 1984). A common assumption is that the maximum uptake of ions by an ion-exchange resin is constant and determined by the number of functional groups on the resin matrix. The usual second assumption is a strict stoichiometric coupling among different components involved in the ion-exchange process. This implies that each ion released from the resin phase has to be replaced by another component from the liquid phase with an equivalent charge. Furthermore, it is assumed that only counterions, with a charge opposite to that of the functional groups, can enter the resin phase. Coions are assumed to be excluded from the resin phase due to the strong repulsive forces between like charges. Thus, a cation is supposed not to enter an anion-exchange resin, and a cation-exchange resin is supposed to repel anions effectively (Saunders et al., 1989). The electroneutrality condition determines the quantity of counterions that will enter the resin; in any case, their total number of charge equivalents must equal the resin capacity.

These conventional models may be useful for the prediction of the ion-exchange behavior of simple, dilute strong electrolyte solutions. They, however exhibit a number of shortcomings when dealing with more complex systems, such as weak electrolyte solutions or solutions with high solute concentrations, exceeding the resin capacity:

- Despite the repulsive forces between functional groups of the resin and coions in the solution, the latter may enter the resin if the concentration in the bulk is sufficiently high (Kawakita and Matsuishi, 1991).
- The uptake of counterions may exceed the total capacity of the resin in case of high concentrations (Vermeulen et al., 1984).
- The uptake of neutral and zwitter-ionic species is often not taken into account (Jones and Carta, 1993), although it does occur (Peterson and Jeffers, 1952; Peterson and Gowen, 1953; Reichenberg and Wall, 1956).
- Because of the assumed exclusion of coions, conventional models are unable to give information on the intraparticle pH, which is a key variable when dealing with weak electrolytes, the stability of proteins in ion exchange chromatography, or the activity of enzymes immobilized on ion-exchange resins (Goldstein, 1976).

The objective of this study is to develop a more rigorous,

Correspondence concerning this article should be addressed to L. A. M. van der Wielen.

Present address of W. J. J. van den Tweel: DSM Andeno, P. O. Box 81, 5900 AB Venlo, The Netherlands.

comprehensive and predictive equilibrium model for ion-exchange processes, based on equilibrium thermodynamics and including the Donnan equilibrium (Donnan, 1925) and in which the above-mentioned assumptions are abandoned in order to circumvent the shortcomings of conventional models. In this article the model is developed and tested on the basis of ion-exchange experiments with single strong and weak electrolytes.

Theory

Conventional ion-exchange models

Before introducing the new Donnan ion-exchange (DIX) model the conventional ion-exchange model will be treated briefly. The selectivity of the exchange of two ions, i and j, is described quantitatively with a selectivity constant, $S_{i,j}$, which is usually expressed in terms of the ionic concentrations or fractions. The selectivity constant for a 1:1 electrolyte is defined as

$$S_{i,j}=\frac{y_i}{y_j}\cdot\frac{x_j}{x_i}. \tag{1}$$

Here x_i is the ionic fraction of ion i in the liquid phase and y_i is the ionic fraction of i in the resin phase. The sum of the counterion concentrations in the resin phase equals the resin capacity, Q, so y_i is defined as follows:

$$y_i=\frac{c_i^R}{Q}. \tag{2}$$

Index R denotes the resin phase and c is the concentration. The sum of the ionic fractions of i and j in either phase equals unity for a binary ion-exchange process. Equation 1 can then be written as

$$S_{i,j}=\frac{y_i}{1-y_i}\cdot\frac{1-x_i}{x_i}. \tag{3}$$

This is rearranged to

$$y_i=\frac{x_iS_{i,j}}{x_iS_{i,j}+1-x_i}. \tag{4}$$

A similar relation can be derived for multicomponent systems with n ions (Appendix A). Multiplication of the resin-phase ionic fraction by the capacity and of the liquid-phase ionic fraction by the total counterion concentration gives a general relation for the resin-phase concentration of component i:

$$c_i^R=Q\cdot\frac{c_i^LS_{i,j}}{\sum_{i=1}^{n}c_i^LS_{i,j}}. \tag{5}$$

Index L denotes the liquid phase. Obviously $S_{i,j}$ is equal to 1 for $i=j$. The electroneutrality condition imposes that the sum of the resin-phase counterion concentrations equals the resin capacity. This stoichiometric displacement (SD) model therefore does not predict uptake of ions beyond the resin capacity.

To explain higher uptake values, ion exchangers are often presented as heterogeneous particles consisting of a solid matrix and liquid-filled pores. The liquid in the pores of the resin is considered as being part of the mobile phase (Bellot and Condoret, 1991), and is hence supposed to have the same composition as the surrounding liquid. The total concentration of a component in the resin particle is then given by the sum of the ion-exchange contribution according to Eq. 5 and the quantity present in the liquid fraction, ϵ_L, of the resin:

$$c_i^R=Q\cdot\frac{S_{i,j}c_i^L}{\sum_{i=1}^{n}S_{i,j}\,c_i^L}+\epsilon_Lc_i^L. \tag{6}$$

According to this definition, the resin capacity, Q, is based on the total (hydrated) resin volume and not on the solid fraction only. The latter contribution in this nonstoichiometric sorption (NS) model only gives an apparent rise of the uptake capacity in equilibrium experiments, but since the liquid fraction is considered to be part of the mobile phase, the apparent rise of the capacity does not affect the chromatographic behavior.

Rigorous ion-exchange model

Ion-exchange resins are composed of flexible polymer chains with fixed functional groups that are to a certain extent free to move within the space occupied by the resin. The electrostatic interactions between fixed charges (functional groups) and mobile charges (ions) in the resin are long-range interactions covering distances much larger than molecular radii. Therefore in this study the resin phase is considered as a homogeneous phase instead of a heterogeneous phase. The solvent and solutes, if not size-excluded, distribute freely over the two phases, but the functional groups are covalently linked to the matrix and cannot leave the resin phase. The phase boundary is visualized as a semipermeable membrane, permeable to all species except the functional groups. With this concept in mind, the theory for ion-exchange equilibria presented here is based on the Donnan membrane equilibrium theory (Donnan, 1925). The presence of small pores may cause steric hindrance and create energetic inhomogeneities (Myers and Byington, 1986), but this is not expected for the small-sized solutes used in this study. Physical inhomogeneities may be caused by very large pores, of which the liquid should be regarded as being part of the liquid phase (Jansen et al., 1996).

At equilibrium the chemical potential (electrochemical potential in the case of electrolytes) of each component i, μ_i, is equal in both phases (Smith and Van Ness, 1975):

$$\mu_i^R=\mu_i^L. \tag{7}$$

Considering also osmotic effects, the electrochemical potential of a charged component i in the liquid phase is given by the following expression:

$$\mu_i^L(p,T,a,\phi)=\mu_i^{0,L}+RT\ln a_i^L+\int_{p^0}^{p^L}\bar{v}_idp+z_iF\phi^L. \tag{8}$$

Here index 0 denotes the standard state, R the gas constant, T the temperature, a the activity, p the pressure, $\bar{v}$ the partial molar volume assumed to be constant, z the valence, F the Faraday constant, and ϕ the electrical potential. A similar expression is set up for the resin phase (R). Substituting Eq. 8 into Eq. 7 leads to the following expression:

$$\Delta\mu_i^0 + RT\ln\frac{a_i^R}{a_i^L} + \bar{v}_i\pi + z_iF\Delta\phi = 0, \qquad (9)$$

where $\Delta\phi$ is the electrical potential difference between the resin and liquid phase (Donnan potential) and π is the pressure difference or osmotic pressure. The electrical potential term can be omitted for components with no net charge, like water and undissociated acetic acid. This equation is the basis for calculating the resin-phase composition from known liquid phase concentrations. It was set up for phase equilibria in general without limiting assumptions concerning partitioning of neutral species and exclusion of coions and therefore it applies to counter-ions as well as co-ions and neutral species.

For both phases the concentration of component i is related to its activity via the activity coefficient, γ_i:

$$a_i = \gamma_i c_i. \qquad (10)$$

The liquid-phase activity coefficients are defined using the conventional standard state of infinite dilution; for concentrations approaching zero, the activity coefficients approach unity. The standard state of the resin phase is defined as the resin in equilibrium with an infinitely dilute aqueous solution of ions, such that the activity coefficient approaches unity as the resin phase molar fraction of a component approaches unity. Because of the asymmetric convention, the values of the standard electrochemical potential of a component are not necessarily equal in both phases, so the values of $\Delta\mu_i^0$ will in general differ from zero. Electrostatic interactions and pressure effects, which usually contribute to nonideal behavior, are incorporated explicitly in Eq. 9. Other relevant energetic effects concern solute–matrix interactions (Van der Waals forces), ion–dipole interactions (polarization), and ion–solvent interactions (hydration) (Harland, 1994). Since these are much weaker than coulombic interactions between resin and ions, their contribution to nonideal behavior will be of minor importance and they are not taken into account here. Moreover, the definition of the standard states implies infinite dilution of solutes, so for low concentrations the deviation from ideal behavior will be small. The activity coefficients will thus be close to unity, and activities are replaced by concentrations.

Writing the terms for the electrical potential and osmotic pressure explicitly hence justifies the use of this model at higher concentrations than would be allowed with conventional models. At increasing solute concentration the departure from thermodynamically near-ideal behavior should be taken into account. Suitable models for activity coefficients are given by Zemaitis et al. (1986) for the liquid phase and by Vamos and Haas (1994) and Mehablia et al. (1994) for the resin phase.

Minimum Requirements for Determination of the Resin-Phase Composition. An ion-exchange process in which N ionic as well as molecular species are involved is characterized by N liquid-phase concentrations and N resin-phase concentrations. Supposing that the concentrations of all species in the liquid phase are known and that the equilibrium concentrations in the resin phase are to be determined, N independent relations between liquid phase and resin phase concentrations are required. The components in an aqueous electrolyte solution are water and its ionization products H^+ and OH^-, strong electrolyte cations (κ), strong electrolyte anions (α), weak amphoteric species (ζ), and other weak electrolytes (ω). Because the amphoteric components appear in three forms (neutral or zwitter-ionic, conjugate acid, and conjugate base) and monovalent weak acids or bases appear in two forms (neutral and conjugate acid or base) the general expression for N is

$$N = 3 + \kappa + \alpha + 3\zeta + 2\omega. \qquad (11)$$

A similar relation can be set up if multivalent weak electrolytes are present.

The number of unknown variables in the system is $N+2$, the concentrations of N species plus the osmotic pressure and the Donnan potential. For each of these species an equilibrium relation is given by Eq. 9. These N equations contain N parameters, $\Delta\mu_i^0$. If the parameter values are known, two additional independent relations would be sufficient to determine all resin phase concentrations plus π and $\Delta\phi$. However, the individual values of $\Delta\mu_i^0$ cannot readily be determined. By proper substitutions the set of equations must be rearranged to come to more useful parameters. And since we are interested especially in the resin phase concentrations, the set of equations can be reduced by elimination of π and $\Delta\phi$. This is detailed in Appendix B. Then N unknowns still need to be determined, requiring a total of N independent relations, parameters, and/or measurements.

Two valid relations are the electroneutrality condition and the water dissociation equilibrium relation. Furthermore, the water concentration in the resin phase can be measured quite easily. By elimination of π from Eq. 9 for neutral species, $(\omega + \zeta)$ relations between water and other neutral species are obtained. Through combination of Eq. 9 for all ions with the same equation for a reference ion, $\Delta\phi$ can be eliminated and $(\kappa + \alpha + \omega + 2\zeta)$ additional equations are obtained. The latter two sets of equations require distribution coefficients for the neutral species and selectivity coefficients between ion pairs, respectively. These parameters, if yet unknown, can be fitted from experimental results.

For example, an ion-exchange resin in equilibrium with an aqueous sodium chloride solution contains five species: H_2O, H^+, OH^-, Na^+, and Cl^-. Hence five independent relations are necessary to determine the resin-phase concentrations. The number of unknowns, and thus required relations, is reduced by one if the water concentration in the resin is measured. Besides the water dissociation constant and the electroneutrality condition, two relations are required. These are the relations between Cl^- and OH^- ions and between Na^+ and H^+ ions, with the corresponding selectivity coefficients as parameters. In case of a sodium acetate solution the total number of species is six, with undissociated acetic acid in addition to the acetate anion. This is schematically depicted in Figure 1. The occurrence of undissociated acetic acid re-

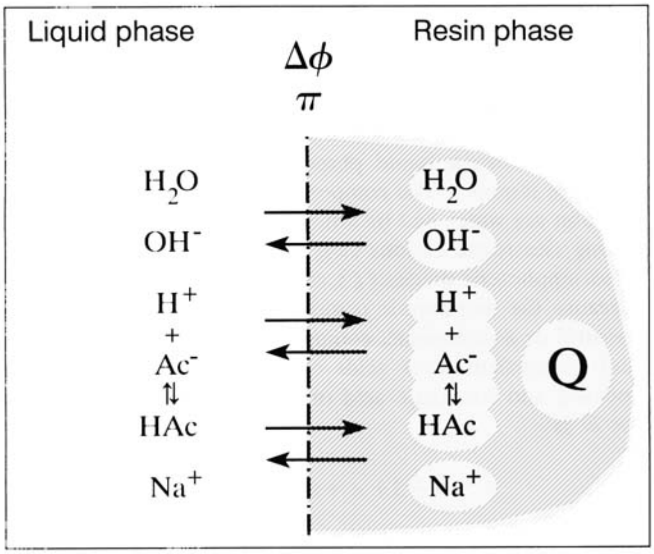

Figure 1. Species involved in the distribution of a sodium acetate solution over the liquid-phase and an ion-exchange resin: $\Delta\phi$—Donnan potential; π—osmotic pressure; Q—capacity.

quires one extra parameter, which is the distribution coefficient of the neutral species.

Calculation of Resin-Phase Concentrations. Starting from Eq. 9, a general relation between resin- and liquid-phase activities of anions and cations is obtained, from which the osmotic pressure and Donnan potential are eliminated (see Appendix B, Eq. B18). Assuming a thermodynamically ideal system gives:

$$\sum_c (c_c^R)^{1/z_c} \sum_a (c_a^R)^{-1/z_a} = \sum_c \left[(c_c^L)^{1/z_c} S_{c,\mathrm{H}^+}^{1/(z_c z_{\mathrm{H}^+})}\right] \times \sum_a \left[(c_a^L)^{-1/z_a} S_{a,\mathrm{OH}^-}^{1/(z_a z_{\mathrm{OH}^-})}\right]. \quad (12)$$

The indices c and a denote cations and anions, respectively. This equation was derived to circumvent the necessity of simultaneously solving a set of equations relating resin-phase and liquid-phase concentrations, and to provide a basis for calculating the resin-phase composition analytically. Equation 12 can be simplified further for monovalent ions:

$$\sum_c c_c^R \sum_a c_a^R = \sum_c c_c^L S_{c,\mathrm{H}^+} \sum_a c_a^L S_{a,\mathrm{OH}^-}. \quad (13)$$

Obviously the values for S_{a,OH^-} and S_{c,H^+} are equal to 1 for $a = \mathrm{OH}^-$ and $c = \mathrm{H}^+$. An equation similar to Eq. 13 was used by Kawakita and Matsuishi (1991), but these authors have neglected pressure effects and implicitly assumed equal standard chemical potentials in both phases. Therefore their model is not thermodynamically consistent since the underlying assumptions imply that the selectivities for all ion pairs are equal to 1.

For an anion exchange resin, the electroneutrality condition demands that

$$\sum_c z_c c_c^R + Q = \sum_a - z_a c_a^R. \quad (14)$$

The plus sign should be replaced by a minus sign in case of a cation exchanger. Substitution into Eq. 13 gives for a system with only monovalent ions:

$$\left(\sum_a c_a^R - Q\right) \sum_a c_a^R = \sum_c c_c^L S_{c,\mathrm{H}^+} \sum_a c_a^L S_{a,\mathrm{OH}^-}. \quad (15)$$

Now this equation can be expressed solely in terms of the resin-phase OH^- concentration, $c_{\mathrm{OH}^-}^R$, and known liquid-phase concentrations using the selectivity of any anion, a, over OH^-:

$$S_{a,\mathrm{OH}^-} = \frac{c_a^R}{c_a^L} \cdot \frac{c_{\mathrm{OH}^-}^L}{c_{\mathrm{OH}^-}^R}. \quad (16)$$

The anion concentration is written explicitly as

$$c_a^R = c_a^L S_{a,\mathrm{OH}^-} \frac{c_{\mathrm{OH}^-}^R}{c_{\mathrm{OH}^-}^L}. \quad (17)$$

Substitution of the anion concentration into Eq. 15 leads to the following expression:

$$\left[\frac{c_{\mathrm{OH}^-}^R}{c_{\mathrm{OH}^-}^L}\left(\sum_a c_a^L S_{a,\mathrm{OH}^-}\right) - Q\right] \cdot \frac{c_{\mathrm{OH}^-}^R}{c_{\mathrm{OH}^-}^L}\left(\sum_a c_a^L S_{a,\mathrm{OH}^-}\right) = \left(\sum_c c_c^L S_{c,\mathrm{H}^+}\right)\left(\sum_a c_a^L S_{a,\mathrm{OH}^-}\right). \quad (18)$$

This is a quadratic relation of the OH^- concentration in the resin phase. The solution of this equation is as follows:

$$c_{\mathrm{OH}^-}^R = c_{\mathrm{OH}^-}^L \cdot \frac{Q + \sqrt{Q^2 + 4AC}}{2A} \quad (19)$$

with

$$A = \left(\sum_a c_a^L S_{a,\mathrm{OH}^-}\right) \qquad C = \left(\sum_c c_c^L S_{c,\mathrm{H}^+}\right). \quad (20)$$

All other anion concentrations in the resin phase can now be calculated from Eq. 17. This leads to the following expression:

$$c_a^R = c_a^L S_{a,\mathrm{OH}^-} \cdot \frac{Q + \sqrt{Q^2 + 4AC}}{2A}. \quad (21)$$

The proton concentration is calculated using the water dissociation constant:

$$c_{\mathrm{H}^+}^R = \frac{K_w}{c_{\mathrm{OH}^-}^R}. \quad (22)$$

The other cation concentrations are then calculated using the corresponding cation selectivities:

$$c_c^R = c_c^L S_{c,\mathrm{H}^+} \cdot \frac{2A}{Q+\sqrt{Q^2+4AC}}. \tag{23}$$

For neutral compounds, like water, the electrical potential term cancels from Eq. 9 and the following equation is obtained for the osmotic pressure if nonidealities are neglected:

$$\pi = -\frac{\Delta\mu_w^0}{\bar{v}_w} - \frac{RT}{\bar{v}_w}\ln\frac{c_w^R}{c_w^L}. \tag{24}$$

A similar equation holds for any other neutral species i. The osmotic pressure can then be eliminated and the following relation is derived for the resin-phase concentration of i:

$$c_i^R = c_i^L K_i^{\mathrm{ov}}, \tag{25}$$

with an overall distribution coefficient, K_i^{ov}:

$$K_i^{\mathrm{ov}} = \left(\frac{c_w^R}{c_w^L}\right)^{\bar{v}_i/\bar{v}_w} \cdot \exp\left[\frac{\left(\Delta\mu_w^0 \dfrac{\bar{v}_i}{\bar{v}_w} - \Delta\mu_i^0\right)}{RT}\right]. \tag{26}$$

If the water concentration ratio and the partial molar volumes are constant, the overall distribution coefficient is constant. This is in agreement with a model by Helfferich (1990).

Once the values of the distribution constants of the neutral species and of the selectivity constants of ion pairs are known, only the water content of the resin has to be measured and the complete composition of the resin phase can be calculated from the liquid-phase concentrations.

Limiting Cases: Low and High Solute Concentrations. At very low solute concentrations, the auxiliary functions A and C, defined by Eq. 20, are negligible compared to the resin capacity Q. Then Eq. 21 simplifies to that for the SD model, Eq. 5. For dilute systems the term in Eq. 6 representing the liquid fraction of the resin is also negligible and the equation for the NS model reduces to Eq. 5. So where the counterions are concerned the models converge for low concentrations, but for the coion concentrations, including H^+ in the case of an anion-exchange resin, the models differ significantly. The SD model predicts total exclusion of H^+ so the pH cannot be defined, whereas the NS model assumes a pH equal to that of the liquid. The DIX model, on the other hand, does not exercise restraints on the coion concentration in the resin phase and thus the pH may have any value.

At very high solute concentrations A and C will become much larger than Q. The contribution of Q in Eq. 21 will be small and the uptake is no longer a function of the resin capacity. Thus Eq. 21 can be simplified to

$$c_a^R \approx c_a^L S_{a,\mathrm{OH}^-} \cdot \sqrt{\frac{\sum\limits_c c_c^L S_{c,\mathrm{H}^+}}{\sum\limits_a c_a^L S_{a,\mathrm{OH}^-}}}. \tag{27}$$

Furthermore, if the pH is not extremely low or high, that is, the concentrations of H^+ and OH^- are small compared to the concentration of the other ions, and if we consider a single 1:1 electrolyte solution, then it follows from the electroneutrality condition for the liquid phase that $c_c^L \approx c_a^L$. The preceding equation can now be simplified further, and it follows that the resin-phase concentration approaches a direct proportionality to the liquid-phase concentration:

$$c_a^R \approx c_a^L \sqrt{S_{c,\mathrm{H}^+} S_{a,\mathrm{OH}^-}}. \tag{28}$$

Materials and Methods

Chemicals

Acetic acid and sodium hydroxide (analytical grade) were obtained from Baker, Deventer, The Netherlands. *N*-acetyl-DL-methionine was obtained from Sigma, St. Louis, MO, USA. Hydrochloric acid (analytical grade), was obtained from Merck, Darmstadt, Germany. Macro-Prep Q ion exchange resin was obtained from Bio-Rad, Hercules, CA, USA. Macro-Prep Q is an acrylate-based, macroporous, hydrophilic, strong-base anion exchanger with quaternary ammonium functional groups.

Resin preparation

The resin, 1 L of approximately 50% v/v suspension in 20% ethanol in water, was filtered to remove the storage solution, equilibrated with 8 times 500-mL 1-M solution of sodium hydroxide, and subsequently washed with 8 times 500-mL demineralized water. The water was degassed under vacuum prior to use in order to remove dissolved $\mathrm{CO_2}$. Thus, 506 g of hydrated resin in the hydroxide form was obtained. The resin was stored at 4°C in a closed container to prevent dehydration.

Resin characterization

Water Content. The water content was calculated from the change of the mass when hydrated resin was dried to a constant mass in a microwave oven.

Resin Density. The hydrated resin density was determined from the slope of the cumulative mass against the volume when aliquots of hydrated resin were added repeatedly to a measuring cylinder with water while the volume and mass increase were registered.

Resin Capacity. A column packed with hydrated resin was equilibrated with a sodium hydroxide solution to bring the resin in the OH^- form and washed with demineralized water to remove excess OH^-. The column was then equilibrated with an HCl solution and washed. The resin capacity was determined by back-titration of the excess HCl in the effluent with a solution of NaOH.

Ion exchange experiments

Chloride/Hydroxide Exchange. Quantities of 1 to 2 g of hydrated resin were placed into 10-mL vials. To each vial 5 mL of a HCl or NaCl solution ranging from pH 2 to pH 12 was added. Initial chloride concentrations varied from 1.07 to 536 mmol/L. The suspensions were equilibrated for 24 h at 25 ± 2°C under repeated shaking. After equilibration the particles were allowed to settle and the supernatant was decanted. The pH and chloride concentration of the supernatant were determined. Experiments with chloride concentrations of 0.1 mol/L and higher were done with a resin containing 30.4% water instead of 27.5%; the resin capacity was corrected correspondingly in the calculations.

Acetate/Hydroxide and N-Acetylmethionine/Hydroxide Exchange. Quantities of about 1 g of hydrated resin were placed into 10-mL vials. To each of the vials 5 mL of an *N*-acetyl-DL-methionine solution or an acetic acid solution with concentrations between 1 and 500 mmol/L were added. Then the pH was adjusted by the addition of a known volume of a 0.1-M or 1.0-M NaOH solution. The suspensions were equilibrated under repeated shaking for 24 h at 25 ± 2°C. Then the particles were allowed to settle and the supernatant was decanted. The pH and total *N*-acetylmethionine or acetic acid concentration of the supernatant were determined.

A second series of experiments was done with acetate at initial concentrations between 1 and 1,000 mmol/L. Resin quantities were about 1 g and the liquid volumes were 5 mL; the initial pH was preset before the solution and resin were put together; no extra sodium hydroxide was added to adjust this value prior to equilibration.

Analyses

Acetic Acid and N-Acetylmethionine. Determination of acetic acid and *N*-acetylmethionine was done by HPLC on a Bio-Rad HPX-87H column of 30-cm × 7.8-mm internal diameter, operating at 60°C. The eluent was a 10-mM phosphoric acid solution of pH 2 at a flow rate of 0.6 mL/min. Acetic acid and *N*-acetylmethionine were detected by UV absorption at 210 nm.

Chloride. Chloride was determined by ion chromatography on a Waters IC-PAK A column of 5-cm × 4.6-mm internal diameter with a capacity of 30 ± 3 meq/mL, operating at 30°C. The buffer used was 1-mM potassium benzoate of pH 6 at a flow rate of 1 mL/min. A conductivity electrode was used for detection of chloride.

Parameter estimation and statistical analysis

Parameter estimates were obtained according to the following procedure. The resin-phase concentration of a component i was calculated from the measured liquid-phase composition using the model presented earlier with estimated values of the parameters. The total quantity of the component in the resin phase and in the liquid phase were added and compared to the quantity that was initially present in the liquid, prior to equilibration. The errors were squared and added for the total number of measurements, N_m:

$$SS_{\text{res}} = \sum_{i=1}^{N_m} \left(V_L c_i^L + V_R c_i^R - V_L c_{i,0}^L\right)^2, \tag{29}$$

where SS_{res} is the sum of squares of the residuals, V is the volume, and c_0 is the initial liquid phase concentration of the component. In the case of the chloride experiments the sum of squares of the relative errors compared to the initial amount was calculated. Subsequently, the sum of squares was minimized by adjusting the parameter estimates. In this study the nonlinear conjugate parameter optimization procedure of Borland's Quattro Pro (version 5.0) was used. The standard deviations of the estimated parameters were determined by analysis of the variance/covariance matrix (Himmelblau, 1970), using the value of SS_{res} to determine the variance.

Results and Discussion

Resin characterization

Characterization of the hydrated resin in the OH^- form, after removal of adhering water, gave the following results:

Resin density	1.0575 ± 0.0023 g/mL
Water fraction	0.7253 ± 0.0009 g/g $\triangleq$ 0.767 mL/mL
Resin capacity	0.2055 ± 0.0005 mmol/g $\triangleq$ 0.217 mol/L

Chloride/hydroxide ion exchange

The liquid-phase composition was determined by measuring the chloride concentration and the pH. The H^+ concentration follows from the pH, and the OH^- concentration was calculated using the water dissociation constant of 1.0×10^{-14} mol^2/L^2 at 25°C. The electroneutrality condition was used to calculate the Na^+ concentration. The water concentration was assumed to be constant, 55.56 mol/L.

The chloride concentration in the resin phase, $c^R_{Cl^-}$, was calculated from the mass balance over the resin and liquid phase:

$$c^R_{Cl^-} = V_L\left(c^{L,0}_{Cl^-} - c^L_{Cl^-}\right)\frac{\rho_R}{m_R}. \tag{30}$$

Here m_R is the amount of resin, ρ_R is the density of the resin, index 0 denotes the initial concentration prior to equilibration, and V_L is the volume of the chloride solution. This volume and the volume of the resin were assumed to remain constant because swelling or shrinking is of minor importance over a broad pH and concentration range for this specific resin (Bio-Rad, 1990).

The resin-phase chloride concentration was also calculated with the conventional models (Eqs. 5 and 6) and the DIX model (Eq. 21) using estimated values for the selectivity constants for Cl^-/OH^- and Na^+/H^+. The best estimates for the parameters were obtained with the least squares optimization procedure outlined in the Materials and Methods section. Data with $(1 - m_{Cl}/m^0_{Cl})^2 \geq 0.2$ were considered to be outliers and were not used.

The results of the parameter optimization procedure are presented in Table 1. The value of 0.241 for the selectivity of Cl^- over OH^- is not in agreement with common values for the selectivity of anions over OH^- that are greater than 1 (Harland, 1994). The value neither corresponds to the value of 22, that is given for a polystyrene-based strong anion-exchange resin by the manufacturer (Bio-Rad, 1994). Fitting the data with Eq. 6 for the NS model yields a value of 0.224, which is in good agreement with the value of 0.241. The slight difference may be the consequence of the conceptual differ-

Table 1. Estimated Parameter Values from Binary Ion-Exchange Equilibrium Experiments with the Ion Pairs Chloride/Hydroxide, Acetate/Hydroxide, and *N*-Acetylmethionine/Hydroxide

Parameter	Donnan Ion Exchange Model	Nonstoichiometric Sorption Model
S_{Cl^-,OH^-}	0.241 ± 0.0049*	0.224*
S_{Ac^-,OH^-}	0.0245 ± 0.0053**	0.0251**
	0.0253 ± 0.0004†	0.0280†
S_{AcM^-,OH^-}	0.0330 ± 0.0058‡	0.0516‡
S_{AcM^+,H^+}	0.565 ± 291	—
S_{Na^+,H^+}	3.41 ± 0.769*	—
	64.0 ± 18.3**	
	28.7 ± 4.40†	
	15.2 ± 3.78‡	
K_{HAc}	0.743 ± 0.063**	—
	0.876 ± 0.071†	
K_{AcM}	0.850 ± 0.318‡	—

*Chloride experiments.
**Acetate (Ac) experimental series 2.
†Acetate (Ac) experimental series 1.
‡*N*-acetylmethionine (AcM) experiments.

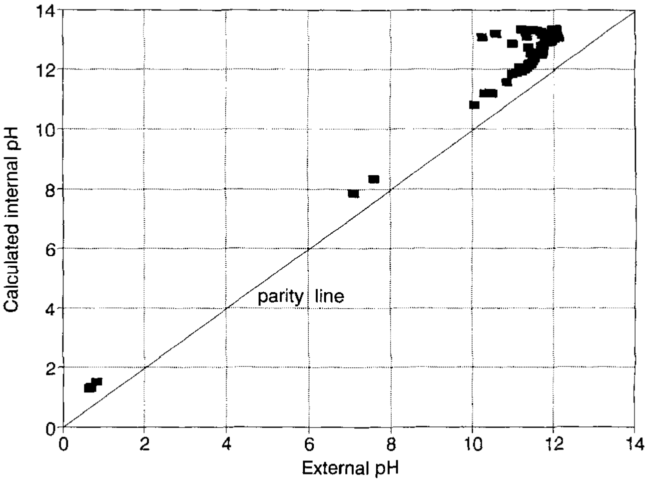

Figure 2. Calculated resin-phase pH vs. liquid-phase pH for the binary ion-exchange equilibrium of chloride and hydroxide.

ence between an ion-exchange resin as a homogeneous phase, the approach chosen in this study, or as a heterogeneous particle with a distinct solid matrix and water-filled pores.

According to the NS model, the liquid in the pores is the same as the surrounding liquid from which the ions, including OH^-, really bind to the functional groups. Then the pH "observed" in the resin is the same as the external pH. However, considering the resin as a homogeneous phase implies that the ions are more or less free to move within the resin and the observed concentration and hence the pH may differ from that in the surrounding liquid phase. According to Eq. 16 the value of the selectivity of an anion over OH^- is also determined by the concentration ratio of OH^- between resin and liquid phase. The excess of positive charges from the functional groups causes a partial exclusion of cations, including protons, leading to a higher pH inside than outside the resin phase. This pH difference may be as large as two pH units (Helfferich, 1962; Kierstan and Coughlan, 1991). Figure 2 shows the predicted pH difference between resin and liquid phase. This difference is not constant, but increases with decreasing solute concentration due to a more efficient ion exclusion at low solute concentrations. In general the data with the largest pH difference in the high pH region of Figure 2 refer to lower solute concentrations.

In Figure 3 the chloride uptake predicted by the model is plotted against the value that follows from the mass balance for chloride. For comparison, the predictions by the SD model and the NS model are shown as well. It appears that there is a good agreement between the measured chloride uptake the and the calculations with the DIX model except at resin-phase concentrations higher than 0.55 mol/L, which may be due to experimental or analytical errors. It is clearly demonstrated that for resin-phase concentrations exceeding the resin capacity the model gives a much better prediction than the SD model. The difference with the NS model is apparently small, but careful analysis of all data demonstrates that the prediction by the NS model is on average 10% higher than that of the DIX model. The variance of the deviations between model predictions and measurements is 17% higher and the Cl^-/OH^- selectivity constant is about 8% lower. As expected there is not a significant difference in the anion uptake predicted by the three models at low solute concentrations. For this strong electrolyte the major distinction is in the prediction of the intraparticle pH, as can be seen from Figure 2, and in the sodium concentration (not shown).

The measured chloride uptake is plotted against the liquid-phase concentration in Figure 4. Even for this simple binary exchange process of two strong electrolyte anions the experimental results show a considerable scatter instead of a smooth equilibrium isotherm. This is only partly the consequence of analytical errors. First, the scatter is a result of the large variation in the pH within a series of experiments with similar liquid-phase chloride concentration (Figure 2). At a constant chloride concentration the OH^- concentration varies over two decades. Especially in the high pH region this has a pronounced effect on the competition between OH^- and Cl^-, and thus on the uptake of Cl^- by the resin.

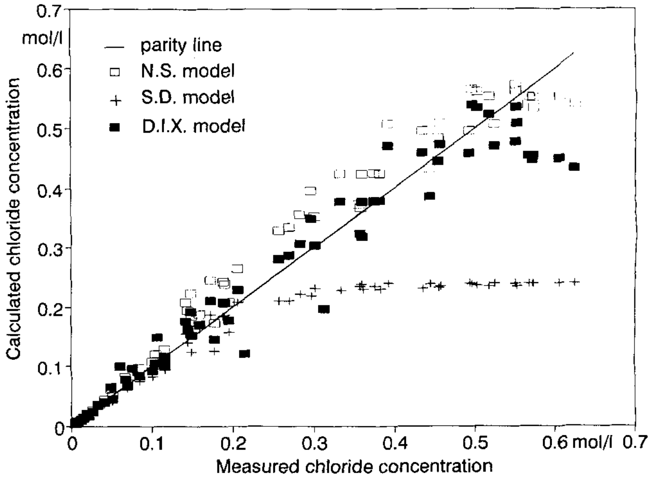

Figure 3. Parity of calculated and measured chloride uptake by the resin.

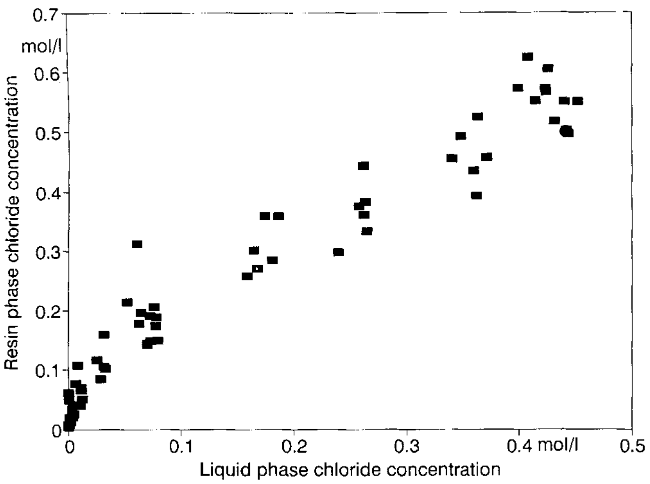

Figure 4. Measured equilibrium uptake of chloride as function of the chloride concentration in solution.

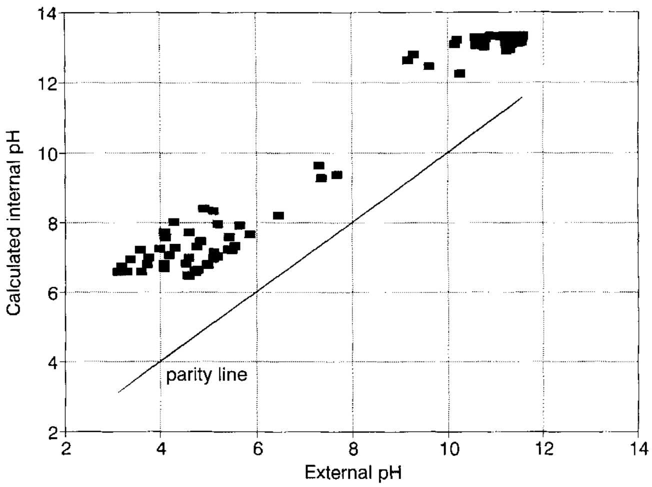

Figure 5. Calculated resin-phase pH vs. liquid-phase pH for the binary ion-exchange equilibrium of acetic acid/acetate and hydroxide.

Acetate/hydroxide ion exchange

The concentrations of undissociated acetic acid and of the acetate anion in the solution were calculated from the total acetate concentration using a pK value of 4.75 at 25°C. For the partial molar volume of acetic acid a value of 51.8×10^{-3} L/mol was used (Weast, 1986). The water concentration was assumed to be 55.56 mol/L, the OH^- concentration was calculated using the water dissociation constant, and the Na^+ concentration was determined from the electroneutrality equation.

The total acetate uptake by the resin (anion and neutral molecule) was determined via the mass balance for acetate. The acetate uptake was also calculated with the DIX model, using estimated values for the model parameters, and with the conventional models. The least squares estimates of the model parameters were obtained as described earlier. The best estimates are given in Table 1 for both series of experiments. The values obtained with the NS model are 0.0251 and 0.0280; the values obtained with the DIX model are 0.0245 and 0.0253, with an average standard deviation of about 12% of the parameter value. Again the value for the anion selectivity is two orders of magnitude lower than the value of 3.2, given by the resin manufacturer for a polystyrene-based resin (Bio-Rad, 1994). Using these binary data, a selectivity constant for Cl^- over Ac^- of 11.5 is calculated, whereas a value of 6.9 can be calculated from the data from Bio-Rad for a comparable anion exchange resin.

The determination of the value of the selectivity constant for Na^+ over H^+ is not very reproducible and the value also deviates strongly from the one obtained from the chloride experiments. For a more accurate estimation of this parameter, sufficient data must be available with H^+ concentrations high enough to "compete" efficiently with Na^+, which means that more experiments must be done at a pH below 3. The accuracy of the estimation of the distribution coefficient of acetic acid is good, but for an even better estimation dynamic column experiments can be used (Jansen et al., 1996), or more equilibrium experiments would be needed in a pH region where the undissociated form of acetic acid is dominant. These conditions are, however, not relevant for our application of this resin for the chromatographic separation of acetic acid and other weak electrolytes (Jansen et al., in preparation).

The low selectivity for Ac^- over OH^-, in combination with the exclusion of cations from the resin, favors the uptake of OH^-. Therefore the calculated difference between internal and external pH is even higher than in the case of Cl^- and OH^-, as can be seen from Figure 5. The data in the high pH region refer without exception to low acetate concentrations because the buffer capacity of these solutions is insufficient to capture the OH^- ions released by the resin during the equilibration. The data in the lower pH region refer to the higher acetate concentrations. Of those data those nearest to the parity line, representing the external pH, in general correspond to the highest concentrations, and the lower the concentration, the larger the pH difference. In the low pH-range, the calculated internal pH asymptotically approaches the value of 6.2, independent of the acetate concentration. A similar result was predicted for the calculated pH in a cation-exchange resin exchanging lysine and ammonium (Kawakita and Matsuishi, 1991).

The calculated acetate uptake is plotted in Figure 6 against the measured uptake for both conventional models and the DIX model. The latter model appears to give a good description except in the intermediate concentration range of 0.10–0.25 mol/L, were the model predicts too high values for the acetate uptake. This is possibly due to analytical errors, because similar deviations exist when using the SD model and the NS model, while they were absent in the other series of experiments that were done (results not shown). Apart from that, both series exhibited the same typical phenomena. The DIX model is much better in describing the ion-exchange process at higher concentrations than the SD model. The NS model gives a reasonable description, but seems to overestimate the acetate uptake in the entire concentration region studied. On average the predicted uptake is about 15% higher than that of the DIX model, while the variance of the deviations between model predictions and measurements is also higher for the NS model than for the DIX model, 20% for

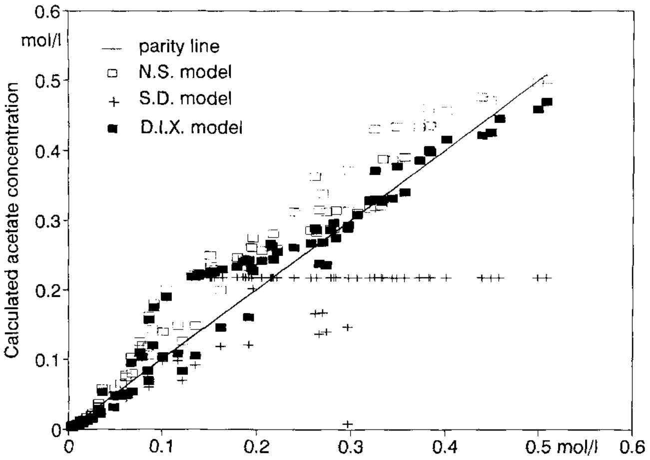

Figure 6. Parity of calculated and measured acetate uptake by the resin.

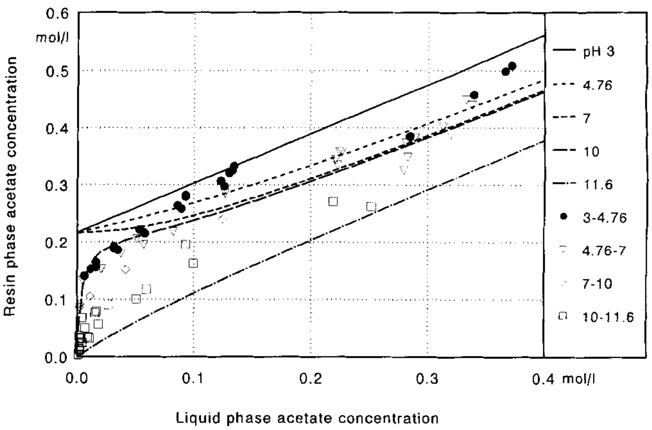

Figure 7. Measured equilibrium distribution and calculated equilibrium isotherms for acetate/hydroxide ion exchange at varying pH and concentration.

Lines represent model calculations; markers represent measurements.

the first series of experiments, and more than 100% for the other set.

For a weak electrolyte, like acetic acid, the pH plays a much more important role than for strong electrolytes because, depending on the pH, acetic acid is present as the neutral acid or as the acetate anion. The uptake of the acetate anion is governed by electrostatic interactions, whereas the uptake of the neutral molecule is less specific. At low pH competition by OH^- is virtually absent and the resin is entirely in the acetate form. Raising the pH increases the concentrations of sodium and the acetate anion at the expense of neutral acetic acid. The effect of the increase of the term $4AC$ in Eq. 21 is somewhat smaller than the influence of neutral acetic acid, which results in a net decrease of the total acetate concentration in the resin phase and in an apparent decrease of the capacity. This is illustrated in Figure 7, where the measured acetate uptake is plotted against the total acetate concentration in the liquid.

One smooth isotherm for all data is not found here. The pH in the different experiments varied between 3.1 and 11.6, so acetic acid may occur solely as the neutral molecule, as the acetate anion, or as a mixture of both. Therefore the experimental data are subdivided into four groups with different pH ranges: 3–4.76, 4.76–7, 7–10, and 10–11.6. In the first group acetate occurs predominantly in the neutral form, and in the second, in neutral as well as anionic form. In the third group, only the anion is present as in the fourth group; but, in the latter considerable differences in Na^+ concentrations occur, more importantly, competition with OH^- becomes significant. Using the estimated parameters from Table 1, the isotherms at these pH values were computed and compared to the experimental results. The experimental data with pH values between 10 and 11.6 lie almost without exception within the area enclosed by the corresponding isotherms. From these experiments and calculations the competition of OH^- is obvious: at low acetate concentrations only a limited part of the available capacity is occupied by acetate. For the other ranges the experimental uptake is generally in reasonable to good agreement with the calculated values, except in the low concentration region, at concentrations below 0.06 mol/L, where the model seems to overestimate the measured uptake. The reason for this is unclear since the functional groups should all be occupied by acetate. Most deviating points are, however, within the model's confidence region. Nevertheless, both model and experiments show the important role of the pH in the ion-exchange process of weak electrolytes, like acetic acid.

N-acetylmethionine/hydroxide ion exchange

Since *N*-acetylmethionine is an amphoteric compound, it may be present in the solution as cation, in the neutral form, and as anion, depending on the pH. To calculate the concentrations of different ionic forms the following values for the dissociation constants were used: $K_1 = 1 \times 10^{-2}$ mol/L (Jansen et al., 1996), $K_2 = 3.02 \times 10^{-4}$ mol/L (Wandrey and Flaschel, 1979; Jansen et al., 1996). Since no data were available, the partial molar volume of *N*-acetylmethionine in solution was estimated at 0.11 L/mol from the specific density of crystalline methionine (Weast, 1986). The precise value of this parameter is not really relevant because it only appears in the overall distribution coefficient for the neutral species (Eq. 25), which is estimated from the results. The water concentration in the liquid phase was assumed to be constant at 55.56 mol/L, the OH^- concentration was calculated from the pH, and the Na^+ concentration was calculated using the electroneutrality condition.

The model parameters were estimated using the least squares procedure outlined earlier. The results are presented in Table 1. The selectivity of the *N*-acetylmethionine anion over OH^- was found to be 0.033. This value substantially deviates from the value of 0.052, found by fitting the data with the NS model. The latter model furthermore predicts an uptake that is on average about 30% higher than that predicted by the DIX model, and the variance of the deviations between model predictions and measurements is almost three times as high. The selectivity of the *N*-acetylmethionine cation over H^+ could not be determined from these results. With the present set of experimental data the standard deviation is much larger than the parameter value itself due to the practi-

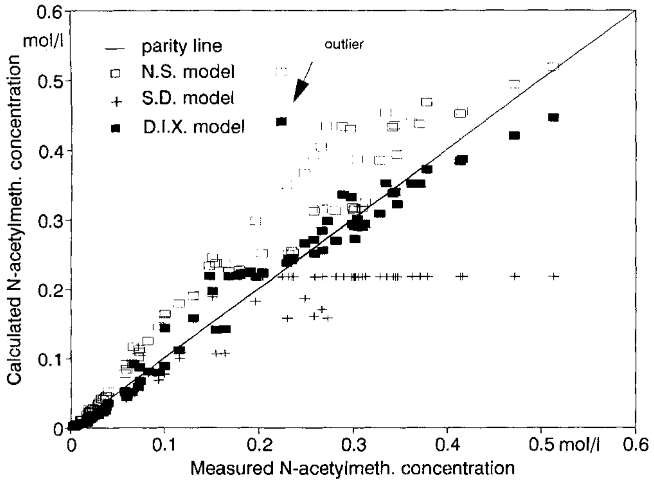

Figure 8. Parity of calculated and measured *N*-acetylmethionine uptake by the resin.

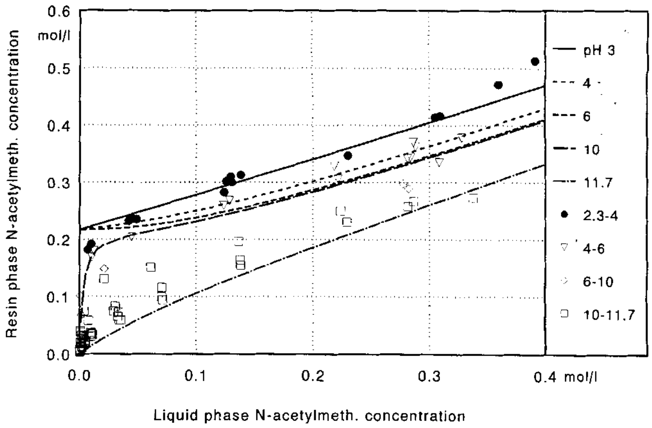

Figure 9. Measured equilibrium distribution and calculated equilibrium isotherms for *N*-acetylmethionine/hydroxide ion exchange at varying pH and concentration.

Lines represent model calculations; markers represent measurements.

cally zero *N*-acetylmethionine cation concentrations in most experiments. In the pH range of interest for practical application (Jansen et al., 1996) the model is insensitive to this parameter. The value found for the selectivity of Na^+ over H^+ is somewhere in between the values found for the chloride and acetate experiments. It can be concluded that this parameter cannot be determined sensitively from these results with the current experimental setup. Only the order of magnitude can be determined in this way. Due to the limited number of data with a sufficiently high concentration of the neutral molecule, the distribution coefficient of this species could be estimated with only a moderate accuracy. A more accurate estimation can be obtained from dynamic column experiments (Jansen et al., 1996).

N-Acetylmethionine is a stronger acid than acetic acid. At a similar concentration, the solution pH as well as the internal pH are lower, but the relation between the external and calculated internal pH appears to be very similar to that for acetate, which also has a difference of about two units (results not shown). In Figure 8 the predicted *N*-acetylmethionine uptake is plotted against the experimentally determined uptake. There is a good agreement between the measured resin-phase concentration and the prediction by the DIX model. As expected, the SD model fails at higher concentrations, whereas the correction for the pore volume in the NS model is apparently too large. This indicates that the assumption that the concentration of *N*-acetylmethionine in the pores is equal to that in the liquid phase is not justified.

The influence of the pH is made visible in Figure 9. The pH of the solutions varied between 2.3 and 11.7, so isotherms were computed for different values within this range: pH 3, 4, 6, 10 and 11.7. Below pH 4 the anion fraction is still small, between 4 and 6 it goes to unity, and above pH 10 competition with OH^- becomes important. It appears that for all pH ranges most experimental data lie between the corresponding isotherms. Just as with acetate, the maximum uptake is reached at a pH of 3, but with *N*-acetylmethionine the uptake decreases again at lower pH due to the formation of the cationic form of *N*-acetylmethionine. At increasing pH the fraction and thereby the uptake of neutral *N*-acetylmethionine decreases. This is only partly compensated by an increase of the anion uptake resulting in a slightly decreasing overall uptake.

Conclusions

The Donnan ion-exchange model derived from basic thermodynamic equations is well able to describe ion-exchange equilibria of both strong and weak electrolytes at a wide concentration and pH range. Because no assumptions concerning exclusion of certain species have been made, the model is more powerful since it takes more effects into account than conventional models. Taking the uptake of coions and neutral species into account brings about an increase in the required number of model parameters, and the larger number of parameters results in a greater flexibility than that of conventional models. At least as important is the fact that the DIX model has a more fundamentally sound structure. For dilute systems the model converges to the stoichiometric displacement model and nonstoichiometric sorption model as far as counterions are concerned. But analysis of all data in Figures 3, 6, and 8 demonstrates that the prediction by the NS model is up to 30% higher. Besides, the variance of the deviations between model predictions and measurements is always lower for the DIX model than for the NS model. However, the main difference is that the DIX model also describes the uptake of neutral species and coions. The latter enables calculation of the intraparticle pH, which is a key variable in ion-exchange chromatography of proteins and weak electrolytes, and especially in the immobilization of enzymes on ion-exchange resins. A survey of the most important characteristics of the three models discussed in this article is given in Table 2.

Parameter sensitivity analysis revealed that the confidence interval of estimated selectivities of anions over OH^- is usually small. On the other hand, the selectivity of cations over H^+ could not be determined with great accuracy. This is due to the fact that insufficient data were available in a pH and concentration range where these species could be found in

Table 2. Conventional Ion-Exchange Models vs. Donnan Ion-Exchange Model

Donnan Ion-Exchange Model	Nonstoichiometric Sorption Model (Bellot and Condoret, 1991)	Stoichiometric Displacement Model (Helfferich, 1962)
Resin structure treated as a homogeneous phase	Biphastic structure of resin matrix and accessible pores	Single homogeneous phase, not including pores
No restrictive assumptions concerning uptake of coions or neutral species	Uptake of coions and neutral species only in pore liquid, $c^R = \epsilon c^L$	Complete exclusion of coions and neutral species, $c^R = 0$
Relatively complex model, requiring parameters for counterions, coions, and neutral species	Simple model, requiring only counterion selectivities and resin pore fraction	Simple model, requiring only counterion selectivities
Suited for dilute as well as concentrated solutions	Applicable up to moderately concentrated solutions	Only useful for dilute solutions
Applicable to both strong and weak electrolytes	Mainly applicable to strong electrolytes	Only applicable to strong electrolytes
Intraparticle pH well-defined, in general different from liquid-phase pH	Intraparticle pH by definition equal to liquid-phase pH	Intraparticle pH cannot be defined
Not all parameters easy to determine, but greater flexibility because of more parameters	Parameters relatively simple to determine	Parameters relatively simple to determine

appropriate concentrations to affect the total uptake. For a more accurate estimation of the cation selectivity more experiments are necessary at conditions where the variable C and the term $4AC$ contribute significantly to the total uptake. The overall distribution coefficients could be estimated with moderate to good accuracy, but they can be estimated more accurately if more data are available at pH values where the neutral species dominates. The distribution coefficient of the neutral species can also be determined from dynamic column experiments (Jansen et al., 1996). Despite the sometimes moderate accuracy of the model parameters concerning coions and neutral species, incorporation of their contribution into the model already significantly improves the description of an ion-exchange process involving these species.

Values for the anion selectivities relative to OH^- are not in agreement with values generally found in literature, but the mutual selectivities between the anions used in this study are in better agreement. The conceptual difference between this model and conventional models also leads to the prediction of internal pH values that deviate from the external pH. This is most likely the cause of the discrepancy between published selectivities of counterions relative to OH^- and those found in this study. The difference of two orders of magnitude corresponds very well with the predicted pH difference of approximately two units.

A drawback of the model, as it is presented here, is that the convenient analytical solution is derived for systems containing only monovalent ions and neutral species. Nevertheless, for some more complex systems analytical solutions are also available. For systems containing divalent anions or cations, Eq. 18 becomes a cubic expression in $c^R_{OH^-}$. If both divalent cations and anions are present, a quartic expression in $c^R_{OH^-}$ results. For these situations analytical solutions are given by Spiegel (1968), but these are less simple than that for the quadratic expression. In the case of thermodynamically nonideal systems, and if ions with higher valences are present, a numerical solution of the set of equations is inevitable. These disadvantages, however, also apply to conventional ion-exchange models.

Acknowledgment

A part of the ion-exchange experiments was carried out by J. Houwers. Analyses were done by J. Knoll and C. Ras. Their contribution is gratefully acknowledged. The authors also wish to thank M. Gude for checking the thermodynamic consistency of the model, and J. C. Bellot for many discussions on ion-exchange models.

Literature Cited

Bellot, J. C., and J. S. Condoret, "Liquid Chromatography Modelling: A Review," *Process Biochem.*, **26**, 363 (1991).

Bio-Rad, "New Macro-Prep 50Q, S, and CM Ion Exchange Supports," Bulletin 1623, Bio-Rad, Richmond, CA (1990).

Bio-Rad, "Chromatographic Supports, Ion Exchange Chromatography," *Life Science Research Products*, Bio-Rad, Richmond, CA, p. 78 (1994).

Donnan, F. G., "The Theory of Membrane Equilibria," *Chem. Rev.*, **1**, 73 (1925).

Goldstein, L., "Kinetic Behavior of Immobilized Enzyme Systems," *Methods in Enzymology*, K. Mosbach, ed., Vol. 44, Academic Press, New York, p. 397 (1976).

Harland, C. E., *Ion Exchange. Theory and Practice*, 2nd ed., Chap. 5, Roy. Soc. of Chemistry, Cambridge, England (1994).

Helfferich, F. G., *Ion Exchange*, McGraw-Hill, New York, p. 95 (1962).

Helfferich, F. G., "Ion-Exchange Equilibria of Amino Acids on Strong-Acid Resins: Theory," *React. Poly.*, **12**, 95 (1990).

Himmelblau, D. M., *Process Analysis by Statistical Methods*, Wiley, New York, pp. 143, 176 (1970).

Jansen, M. L., G. W. Hofland, J. Houwers, A. J. J. Straathof, L. A. M. van der Wielen, K. Ch. A. M. Luyben, and W. J. J. van den Tweel, "Effect of pH and Concentration on Column Dynamics of Weak Electrolyte Ion Exchange Processes," *AIChE J.*, **42**, 1925 (1996).

Jones, I. L., and G. Carta, "Ion Exchange of Amino Acids and Dipeptides on Cation Resins with Varying Degree of Cross-linking: 1. Equilibrium," *Ind. Eng. Chem. Res.*, **32**, 107 (1993).

Kawakita, T., and T. Matsuishi, "Elution Kinetics of Lysine from a Strong Cation-Exchange Resin with Ammonia Water," *Sep. Sci. Technol.*, **26**(7), 991 (1991).

Kierstan, M. P. J., and M. P. Coughlan, "Immobilization of Proteins by Noncovalent Procedures: Principles and Applications," *Protein Immobilization: Fundamentals and Applications*, R. F. Taylor, ed., Marcel Dekker, New York, p. 13 (1991).

Mehablia, M. A., D. C. Shallcross, and G. W. Stevens, "Prediction of Multicomponent Ion Exchange Equilibria," *Chem. Eng. Sci.*, **49**(14), 2277 (1994).

Myers, A. L., and S. Byington, "Thermodynamics of Ion Exchange: Prediction of Multicomponent Equilibria from Binary Data," *Ion Exchange Technology*, A. E. Rodrigues, ed., Nijhoff, Dordrecht, The Netherlands, p. 119 (1986).

Peterson, S., and R. W. Jeffers, "Equilibria between Aliphatic Acids and a Strong Base Anion Exchanger," *J. Amer. Chem. Soc.*, **74**, 1605 (1952).

Peterson, S., and E. Gowen, "Equilibria between Aromatic Acids and Weak Base Anion Exchangers," *Ind. Eng. Chem.*, **45**(11), 2584 (1953).

Reichenberg, D., and W. F. Wall, "The Absorption of Unchanged Molecules by Ion-Exchange Resins," *J. Chem. Soc.*, **654**, 3364 (1956).

Saunders, M. S., J. S. Vierow, and G. Carta, "Uptake of Phenylalanine and Tyrosine by a Strong-Acid Cation Exchanger," *AIChE J.*, **35**(1), 53 (1989).

Smith, J. M., and H. C. van Ness, *Introduction to Chemical Engineering Thermodynamics*, 3rd ed., Chap. 8, McGraw-Hill, Singapore (1975).

Spiegel, M. R., *Schaum's Outline Series, Mathematical Handbook for Formulas and Tables*, McGraw-Hill, New York, p. 32 (1968).

Vamos, R. J., and C. N. Haas, "Reduction of Ion-Exchange Equilibrium Data Using an Error in Variables Approach," *AIChE J.*, **40**(3), 556 (1994).

Vermeulen, T., M. D. LeVan, N. K. Hiester, and G. Klein, "Adsorption and Ion Exchange," *Perry's Chemical Engineers' Handbook*, R. H. Perry and D. W. Green, eds., 6th ed., Chap. 16, McGraw-Hill, New York (1984).

Wandrey, C., and E. Flaschel, "Process Development and Economic Aspects in Enzyme Engineering. Acylase L-Methionine System," *Adv. Biochem. Eng.*, **12**, 147 (1979).

Weast, R. C., ed., *Handbook of Chemistry and Physics*, 67th ed., CRC Press, Boca Raton, FL, pp. D159, D221 FL, (1986).

Zemaitis, J. F., D. M. Clark, M. Rafal, and N. C. Scrivner, *Handbook of Aqueous Electrolyte Thermodynamics*, AIChE, New York (1986).

Appendix A: Conventional Ion-Exchange Model for Multicomponent Systems

For a ternary system of components, i, j, and k, the selectivity between k and j is defined according to Eq. 1, replacing index i by k. This equation is modified by elimination of the resin phase ionic fraction of k, y_k:

$$S_{k,j} = \frac{1 - y_i - y_j}{y_j} \cdot \frac{x_j}{x_k}. \tag{A1}$$

After some manipulations y_j can be written explicitly:

$$\frac{1}{y_j} = \frac{1}{1 - y_i}\left(S_{k,j}\frac{x_k}{x_j} + 1\right). \tag{A2}$$

Substitution of this equation into the selectivity equation for couple i,j, Eq. 1, results in the following expression:

$$S_{i,j} = \frac{y_i}{1 - y_i}\left(S_{k,j}\frac{x_k}{x_j} + 1\right)\frac{x_j}{x_i}. \tag{A3}$$

After some rearrangements this gives an expression for the resin phase ionic fraction of component i:

$$y_i = \frac{x_i S_{i,j}}{x_i S_{i,j} + x_k S_{k,j} + x_j}. \tag{A4}$$

Realizing that $S_{i,i} \equiv 1$, this equation can be generalized as follows for a multicomponent system with n monovalent ions:

$$y_i = \frac{x_i S_{i,j}}{\sum_{i=1}^{n} x_i S_{i,j}}. \tag{A5}$$

Appendix B: Derivation of a General Relation: Resin- and Liquid-Phase Composition

The osmotic pressure follows from Eq. 9 for neutral species since the electrical potential term is absent. For water (w):

$$\pi = p^R - p^L = -\left(\frac{\Delta \mu_w^0}{\bar{v}_w} + \frac{RT}{\bar{v}_w}\ln\frac{a_w^R}{a_w^L}\right). \tag{B1}$$

Starting from Eq. 9, the electrostatic potential difference between the phases, the Donnan potential $\Delta\phi$, can be written explicitly:

$$\Delta\phi = \phi^R - \phi^L = -\left(\frac{\Delta \mu_i^0}{z_i F} + \frac{RT}{z_i F}\ln\frac{a_i^R}{a_i^L} + \frac{\bar{v}_i \pi}{z_i F}\right). \tag{B2}$$

The osmotic pressure, which is a system property and thus equal for all species, can be eliminated by substitution of Eq. B1 into this equation, resulting in the following expression for $\Delta\phi$:

$$\Delta\phi = -\frac{\left(\Delta\mu_i^0 - \Delta\mu_w^0\frac{\bar{v}_i}{\bar{v}_w}\right)}{z_i F} - \frac{RT}{z_i F}\ln\left(\frac{a_i^R}{a_i^L}\right)\left(\frac{a_w^L}{a_W^R}\right)^{\bar{v}_i/\bar{v}_w}. \tag{B3}$$

The potential difference is also a system property and can be eliminated by combining Eq. B3 for two different ions, i and j:

$$\frac{\left(\Delta\mu_i^0 - \Delta\mu_w^0\frac{\bar{v}_i}{\bar{v}_w}\right)}{z_i F} + \frac{RT}{z_i F}\ln\left(\frac{a_i^R}{a_i^L}\right)\left(\frac{a_w^L}{a_w^R}\right)^{\bar{v}_i/\bar{v}_w}$$
$$= \frac{\left(\Delta\mu_j^0 - \Delta\mu_w^0\frac{\bar{v}_j}{\bar{v}_w}\right)}{z_j F} + \frac{RT}{z_j F}\ln\left(\frac{a_j^R}{a_j^L}\right)\left(\frac{a_w^L}{a_w^R}\right)^{\bar{v}_j/\bar{v}_w}. \tag{B4}$$

The following auxiliary function is defined for convenience:

$$f_i=\exp\left(\frac{\Delta\mu_i^0-\Delta\mu_w^0\dfrac{\bar{v}_i}{\bar{v}_w}}{z_iRT}\right). \tag{B5}$$

Eq. B4 can then be rearranged to

$$\left(\frac{a_i^R}{a_i^L}\right)^{1/z_i}\left(\frac{a_j^L}{a_j^R}\right)^{1/z_j}=\left(\frac{a_w^R}{a_w^L}\right)^{(\bar{v}_i/z_i\bar{v}_w)-(\bar{v}_j/z_j\bar{v}_w)}\cdot\frac{f_j}{f_i}. \tag{B6}$$

Let us now consider the exchange equilibrium as a chemical equilibrium reaction according to the mass action law, with the absolute values of the valences (in order to make the equation applicable to cations as well as anions) as stoichiometric coefficients:

$$|z_j|\,i^L+|z_i|\,j^R\rightleftharpoons|z_j|\,i^R+|z_i|\,j^L. \tag{B7}$$

The corresponding thermodynamic equilibrium constant, $K_{i,j}$, is given by the following relation:

$$\begin{aligned}-RT\ln K_{i,j}&=|z_j|\left(\mu_i^{0,R}-\mu_i^{0,L}\right)+|z_i|\left(\mu_j^{0,L}-\mu_j^{0,R}\right)\\&=|z_j|\,\Delta\mu_i^0-|z_i|\,\Delta\mu_j^0.\end{aligned} \tag{B8}$$

The separation factor or selectivity of the ion-exchange process, $S_{i,j}$, is defined as follows:

$$S_{i,j}=\left(\frac{a_i^R}{a_i^L}\right)^{|z_j|}\left(\frac{a_j^L}{a_j^R}\right)^{|z_i|}. \tag{B9}$$

Substitution of the latter two equations into Eq. B6 leads after some manipulation to the following equation:

$$\begin{aligned}S_{i,j}^{1/(|z_i||z_j|)}&=K_{i,j}^{1/(|z_i||z_j|)}\left(\frac{a_w^R}{a_w^L}\right)^{(\bar{v}_i/z_i\,|\,\bar{v}_w)-(\bar{v}_j/z_j\,|\,\bar{v}_w)}\\&\quad\cdot\exp\left[-\frac{\Delta\mu_w^0}{RT}\left(\frac{\bar{v}_i}{|z_i|\,\bar{v}_w}-\frac{\bar{v}_j}{|z_j|\,\bar{v}_w}\right)\right].\end{aligned} \tag{B10}$$

The selectivity proves to be directly proportional to the thermodynamic equilibrium constant and for those conditions where the ratio of water activity in the resin and in the liquid is approximately constant, that is, dilute systems, the selectivity is indeed constant.

For calculation of the resin-phase composition the resin-phase and liquid-phase activities in Eq. B6 are separated:

$$(a_i^R)^{1/z_i}\left(a_j^R\right)^{-1/z_j}=(a_i^L)^{1/z_i}\left(a_j^L\right)^{-1/z_j}\left(\frac{a_w^R}{a_w^L}\right)^{(\bar{v}_i/z_i\bar{v}_w)-(\bar{v}_j/z_j\bar{v}_w)}\cdot\frac{f_j}{f_i}. \tag{B11}$$

This equation is valid for any pair of ions i and j, so it is also valid for an anion/cation pair. The equation may be summed up over all anions (index a) and cations (index c), and then the following result is obtained:

$$\begin{aligned}\sum_c(a_c^R)^{1/z_c}\sum_a(a_a^R)^{-1/z_a}&=\sum_c(a_c^L)^{1/z_c}\left(\frac{a_w^R}{a_w^L}\right)^{\bar{v}_c/(z_c\bar{v}_w)}\\&\quad\cdot\frac{1}{f_c}\cdot\sum_a(a_a^L)^{-1/z_a}\left(\frac{a_w^R}{a_w^L}\right)^{-\bar{v}_a/(z_a\bar{v}_w)}\cdot f_a.\end{aligned} \tag{B12}$$

The fact that the selectivity is constant is exploited to simplify the equation. For that purpose the selectivities between the cations and H$^+$ and the selectivities between the anions and OH$^-$ are introduced. First the term concerning the cations in the right member of B12 is considered. Division of the term after the summation sign by a similar term for H$^+$ and subsequent multiplication by the same term leads to

$$\begin{aligned}&\sum_c(a_c^L)^{1/z_c}\left(\frac{a_w^R}{a_w^L}\right)^{\bar{v}_c/(z_c\bar{v}_w)}\cdot\frac{1}{f_c}\\&=\sum_c\left[(a_c^L)^{1/z_c}\left(\frac{a_w^R}{a_w^L}\right)^{\bar{v}_c/(z_c\bar{v}_w)-(\bar{v}_{\mathrm{H}^+}/z_{\mathrm{H}^+}\bar{v}_w)}\cdot\frac{f_{\mathrm{H}^+}}{f_c}\right]\\&\quad\cdot\left(\frac{a_w^R}{a_w^L}\right)^{\bar{v}_{\mathrm{H}^-}/(z_{\mathrm{H}^+}\bar{v}_w)}\cdot\frac{1}{f_{\mathrm{H}^+}}.\end{aligned} \tag{B13}$$

Combination of the selectivity for a cation over H$^+$, S_{c,H^+} as defined by Eq. B9, with Eq. B6 and subsequent substitution into the preceding equation leads to

$$\begin{aligned}&\sum_c(a_c^L)^{1/z_c}\left(\frac{a_w^R}{a_w^L}\right)^{\bar{v}_c/(z_c\bar{v}_w)}\cdot\frac{1}{f_c}\\&=\sum_c\left[(a_c^L)^{1/z_c}S_{c,\mathrm{H}^+}^{1/(z_cz_{\mathrm{H}^+})}\right]\left(\frac{a_w^R}{a_w^L}\right)^{\bar{v}_{\mathrm{H}^-}/(z_{\mathrm{H}^+}\bar{v}_w)}\cdot\frac{1}{f_{\mathrm{H}^+}}.\end{aligned} \tag{B14}$$

In an analogous manner the term in the right member of Eq. B12 concerning the anions can be modified by the introduction of the selectivity of the anions over OH$^-$. This results in the following equation:

$$\begin{aligned}\sum_a(a_a^L)^{-1/z_a}\left(\frac{a_w^R}{a_w^L}\right)^{-\bar{v}_a/z_a\bar{v}_w}\cdot f_a&=\sum_a\left[(a_a^L)^{-1/z_a}S_{a,\mathrm{OH}^-}^{1/(z_az_{\mathrm{OH}^-})}\right]\\&\quad\left(\frac{a_w^R}{a_w^L}\right)^{-\bar{v}_{\mathrm{OH}^-}/(z_{\mathrm{OH}}\ \bar{v}_w)}\cdot f_{\mathrm{OH}^-}.\end{aligned} \tag{B15}$$

Multiplication of the terms outside the summation brackets in the right members of Eqs. B14 and B15 gives

$$\left(\frac{a_w^R}{a_w^L}\right)^{\bar{v}_{\mathrm{H}^+}/(z_{\mathrm{H}^+}\bar{v}_w)} \cdot \frac{1}{f_{\mathrm{H}^+}} \cdot \left(\frac{a_w^R}{a_w^L}\right)^{-\bar{v}_{\mathrm{OH}^-}/(z_{\mathrm{OH}^-}\bar{v}_w)} \cdot f_{\mathrm{OH}^-}$$

$$= \left(\frac{a_{\mathrm{H}^+}^R}{a_{\mathrm{H}^+}^L}\right)^{1/z_{\mathrm{H}^+}} \left(\frac{a_{\mathrm{OH}^-}^L}{a_{\mathrm{OH}^-}^R}\right)^{-1/z_{\mathrm{OH}^-}}. \tag{B16}$$

Since $z_{\mathrm{H}^+} = 1$ and $z_{\mathrm{OH}^-} = -1$, it is clear that the right member of the preceding equation represents the ratio between the water dissociation constant in the resin phase and that in the liquid phase:

$$\left(\frac{a_{\mathrm{H}^+}^R}{a_{\mathrm{H}^+}^L}\right)\left(\frac{a_{\mathrm{OH}^-}^R}{a_{\mathrm{OH}^-}^L}\right) = \frac{K_w^R}{K_w^L} = 1. \tag{B17}$$

Finally, substitution of Eqs. B14 to B17 into Eq. B12 leads to a simple relation between resin-phase and liquid-phase activities that contains only selectivity constants:

$$\sum_c (a_c^R)^{1/z_c} \sum_a (a_a^R)^{-1/z_a}$$

$$= \sum_c \left[(a_c^L)^{1/z_c} S_{c,\mathrm{H}^+}^{1/(z_c z_{\mathrm{H}^+})}\right] \sum_a \left[(a_a^L)^{-1/z_a} S_{a,\mathrm{OH}^-}^{1/(z_a z_{\mathrm{OH}^-})}\right]. \tag{B18}$$

This equation forms the basis for calculation of the resin-phase composition from known liquid-phase concentrations.

Manuscript received June 12, 1995, and revision received Sept. 26, 1995.