Measurement and Modeling of Activities of Amino Acids in Aqueous Salt Systems

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Activity-coefficient data were measured for NaCl in the system water – NaCl – DL-valine at 25°C. The activity coefficients of DL-valine were then calculated through rigorous thermodynamic relations. The activity coefficients of the amino acids in this and other aqueous systems containing electrolytes were modeled using an expression for the excess Gibbs free energy of the solution. The model combines a contribution for long-range interactions, given either by the Bromley equation or the K-V equation, and a contribution of short-range interactions represented by a ternary NRTL or Wilson expression. The model accurately correlates the activity coefficients of ten amino acids in aqueous solutions and of six amino acids in aqueous electrolyte solutions.

Introduction

The cost involved in the separation and concentration of biomaterials may be as high as 90% of the total cost of their manufacturing (Eyal and Bressler, 1993). Amino acids are the simplest biomolecules and are the building blocks of other biomolecules, such as proteins and peptides. Thus we focus the attention here on aqueous systems containing electrolytes and amino acids.

A knowledge of the activity coefficient of amino acids in aqueous electrolyte solutions is a key element for the design of equilibrium-based separation processes. Since the pioneering work of Kirkwood (1934, 1939) for the interaction between amino acids and ions, few investigations have been conducted in this area. The Kirkwood's models describe the amino acids using various shapes and consider various positions for the charges on them. They can qualitatively represent the behavior of the water–electrolyte–amino-acid systems at low electrolyte and amino-acid concentrations. Chen et al. (1989) used their own version of the electrolyte NRTL model (Chen et al., 1982), which contains a long-range interaction term represented by a Pitzer–Debye–Hückel form (Pitzer, 1980) and an interaction term given by a modified form of the NRTL equation (Renon and Prausnitz, 1968). Fernández-Mérida et al. (1994) and Rodriguez-Raposo et al. (1994) used the modified Pitzer model (Pitzer, 1991) for aqueous solutions of an electrolyte and a nonelectrolyte to model the activity coefficients of the components in water–electrolyte–amino-acid systems. The Pitzer's model employs a combination of an electrostatic term and a virial series expansion to account for all other interactions.

Among the studies of amino acids in water–amino-acid systems without the presence of an electrolyte, Nass (1988) used the Wilson equation (Wilson, 1964), with Bondi's volumes (Bondi, 1968) for pure compound liquid volumes and assumed the activity coefficients of the amino acids to be a product of two terms due to chemical-reaction equilibria and physical interactions. The introduction of a reaction equilibrium in the model was suggested by the fact that amino acids undergo equilibrium reactions to lose or gain a proton in aqueous solutions. Gupta and Heidemann (1990) described the activity coefficient of amino acids in water using a modified UNIFAC model (Larsen et al., 1987). Their work has the advantage of being predictive for the solubility of antibiotics in water, but suffers from the definition of too large groups. Pinho et al. (1994) developed a model for the activity coefficients of amino acids based on a combination of physical and chemical equilibrium using the original UNIFAC group contribution method (Fredenslund et al., 1975). They defined new groups that are smaller in size than those suggested by Gupta and Heidemann (1990). On the other hand, in contrast to the work of Gupta and Heidemann (1990), Pinho et al. (1994) introduced a Debye–Hückel term. This term seems to be unnecessary for amino-acid–water systems in the absence of an electrolyte, and in the present work it is omitted.

Two major techniques that have been used for the measurement of the activity coefficients of amino acids in aqueous electrolyte solutions are the isopiestic method (Bower and

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Robinson, 1965; Schrier and Robinson, 1971; Schrier and Robinson, 1974) and the electrochemical cells (Briggs et al., 1974; Kelley and Lilley, 1979; Rodriguez-Raposo et al., 1994). Electrochemical methods that use ion-selective electrodes, due to recent improvements in their production, are receiving more attention. Most measurements of the activity coefficients of amino acids in aqueous electrolyte solutions using ion-selective electrodes (ISE) (Briggs et al., 1974; Phang and Steel, 1974; Rodriguez-Raposo et al., 1994) have used a single ion-selective electrode, usually a cation-ion-selective electrode, vs. a reference electrode, and calibrated the potential difference so obtained with the mean ionic activity coefficient of the electrolyte. Since in this method of measurement the effect of the counterion of the electrolyte is neglected, it may lead to erroneous results. We have recently reported the measurement of activity coefficients of DL-alanine and of glycine in aqueous sodium chloride solutions using a sodium and a chloride ion selective electrode, each vs. a double-junction reference electrode (Khoshkbarchi and Vera, 1996b) and discussed the advantages of using two ion-selective electrodes over the methods that use only a single ion-selective electrode.

In this work the mean ionic activity coefficients of sodium chloride in the system water–NaCl–DL-valine at 25°C were measured using ion-selective electrodes. From these values, the activity coefficients of DL-valine were evaluated using rigorous thermodynamics. A model for the excess Gibbs free energy of the systems containing water–electrolyte–amino acid is proposed. The model has one electrostatic term to represent long-range interactions, and one term for short-range interactions. To represent the long-range interactions, the Bromley model (Bromley, 1973) and the K-V model (Khoshkbarchi and Vera, 1996) were tested. For the representation of the short-range interactions, the NRTL model (Renon and Prausnitz, 1968) and the Wilson model (Wilson, 1964) were tested. The results of the correlation of the activity coefficients of amino acids in aqueous electrolyte solutions using these contributions are compared. The parameters for electrolyte–water and for water–amino acid were obtained from experimental data reported in the literature for binary systems. Only two parameters were regressed from the experimental data of ternary water–electrolyte–amino-acid systems.

Theory of Experimental Method

According to the Nernst equation the difference between the potentials, ΔE_1, of the two cells of type (1),

Cation ISE | electrolyte (m_S) | reference electrode

Anion ISE | electrolyte (m_S) | reference electrode

is related to the mean ionic activity coefficient of the electrolyte at molality m_S, $\gamma_{\pm}^{(1)}$, by

$$\Delta E_1 = \Delta E^o + S \ln(m_S \gamma_{\pm}^{(1)}), \tag{1}$$

where ΔE^o is the difference between the standard potentials of the cells, including the asymmetry potentials of the ion-selective electrodes, and S is the slope of ΔE_1 vs. $\ln(m_S \gamma_{\pm}^{(1)})$. Equation 1 is only valid when the same reference electrode is used vs. both the anion- and cation-ion-selective electrodes. From Eq. 1 it is evident that the value of S can be calculated from a linear regression of the values of ΔE_1 vs. $\ln(m_S \gamma_{\pm}^{(1)})$ with values of $\gamma_{\pm}^{(1)}$ obtained, at each molality m_S, from the literature (Zemaitis et al., 1986). Due to the interactions between the electrolyte and other solutes, the presence of other solutes changes the mean ionic activity coefficients of the electrolyte and consequently the potential of the electrochemical cells. Therefore, the difference between the potentials, ΔE_2, of the cells of type (2),

Cation ISE | electrolyte (m_S) + solute (m_A) | reference electrode

Anion ISE | electrolyte (m_S) + *solute* (m_A) | reference electrode

is related to the mean ionic activity coefficient of the electrolyte at molality m_S in the presence of a solute at molality m_A, $\gamma_{\pm}^{(2)}$, by

$$\Delta E_2 = \Delta E^0 + S \ln(m_S \gamma_{\pm}^{(2)}). \tag{2}$$

Equation 2 indicates that the mean ionic activity coefficient of the electrolyte, in the presence of a solute, can be measured from a series of e.m.f. measurements in the previously mentioned cells. Subtracting Eq. 2 from Eq. 1 and rearranging gives

$$\ln\left(\frac{\gamma_{\pm}^{(2)}}{\gamma_{\pm}^{(1)}}\right) = \frac{\Delta E_2 - \Delta E_1}{S}. \tag{3}$$

Equation 3 provides a relation between $\gamma_{\pm}^{(2)}$ and $\gamma_{\pm}^{(1)}$ that is useful for correlational purposes. It is important to note that, in this method, by using two ion-selective electrodes, the contribution of the nonelectrolyte solute on the activity coefficients of both anion and cation of the electrolyte is measured. In contrast to this study, previous works that employed ion-selective electrodes to measure the mean ionic activity coefficients of an electrolyte in the presence of a nonelectrolyte (Briggs et al., 1974; Phang and Steel, 1974; Rodriguez-Raposo et al., 1994) identified the mean ionic activity coefficient of the electrolyte with the difference in potentials between a cation-ion-selective electrode and a reference electrode only. According to the Nernst equation the response of a cation-ion-selective electrode is only related to the ionic activity coefficient of the cation, γ_+, whereas the mean ionic activity coefficient, $\gamma_{\pm}$, is a combination of the anion and cation activity coefficients defined as

$$\gamma_{\pm} = (\gamma_+^{\nu_+} \gamma_-^{\nu_-})^{1/(\nu_+ + \nu_-)} \tag{4}$$

In Eq. 4, the plus and minus signs represent cation and anion, respectively and ν is the stoichiometric number of the corresponding ion. From Eqs. 2, 3 and 4 it can be inferred that using only a cation-ion-selective electrode to represent the mean ionic activity coefficient of the electrolyte can be correct only when either the anion activity coefficients over the whole range of electrolyte concentration is equal to the cation activity coefficient or the anion activity coefficient remains constant over the whole range of nonelectrolyte concentration. Both of these assumptions are not correct (Khoshkbarchi and Vera, 1996b), and introduce unnecessary errors in the measurements that can be avoided by using the method just discussed. The theoretical basis and applicability of the method used here have been discussed with more detail elsewhere (Khoshkbarchi and Vera, 1996b).

Materials and Methods

Sodium chloride of 99.9% purity and DL-valine 99.9% were obtained from A&C American Chemicals Ltd. (Montreal, QC). DL-Valine was used as received. Sodium chloride was oven-dried for 72 hours prior to use. During the drying period, the salt was taken out of the oven after 48 hours and 72 hours, and after cooling it in a vacuum desiccator, it was weighed. After 48 hours, no change in weight was observed. A Ross sodium-ion-selective-electrode glass-body model 84-11, a chloride-ion-selective-electrode polymer-body model 94-17, and a double-junction reference-electrode model 13-620-46 were obtained from Orion (Boston, MA). An Orion pH/ISE meter (Boston, MA) model EA 920, with a resolution of ±0.1 mV, was used to monitor the e.m.f measurements with two Bayonet Neil-Concelman connectors for ion-selective electrodes and two pin-tip connectors for the reference electrode. During the experiments, the solutions were stirred continuously with a magnetic stirrer and the temperature was kept constant at 298.15±0.02 K with a thermostatic bath. In all experiments deionized water with the conductivity of less than 0.8 μS/cm was used. Before using it to prepare samples, the distilled water was passed through ion-exchange columns type Easy pure RF, Compact Ultrapure Water System, Barnstead Thermoline.

The sodium-ion-selective electrode was immersed in its conditioning solution number 841101 24 hours prior to the measurement. The cell was a jacketed glass beaker containing 200 mL of solution. To avoid the bias potential between reference electrodes, in each experiment the response of both chloride- and sodium-ion-selective electrodes were simultaneously measured vs. the same reference electrode. All the instruments were grounded prior to and during the experiments. Each set of experiments was performed at fixed electrolyte concentration and the concentration of amino acid was increased by addition of solid amino acid. The error on the molality of the electrolyte caused by the outgoing flow of the internal solution of the reference electrode was minimized by choosing KNO_3 solution as the internal outer-body solution of the reference electrode. In order to minimize the risk of the presence of concentration gradients in the beaker, a vigorous stirring was maintained during the experiments. All the solutions were prepared based on molality and the water was also weighed. The compositions of the initial solutions were accurate within ±0.01 wt. %. The readings of the potentiometer were made only when the drift was less than 0.1 mV. For each set of experiments the electrodes were calibrated by measuring the e.m.f. of the electrochemical cell without the presence of amino acid and the slope, S, was measured. The typical value obtained for the slope of the electrodes was 50.28 mV, with a correlation coefficient of 99.99%, while the theoretical value according to the Nernst equation is 51.38 mV at 298.15 K. All the experiments were replicated three times and the data reported here are the average of the replicas. Sample variances were obtained from the replicas for each point and a pooled standard deviation was calculated using these values. The 95% confidence interval in mean ionic activity coefficient of the electrolyte, $\gamma_\pm$, was calculated to be ±0.004.

Results and Discussion

Measurements were performed at 298.15 K over the range of NaCl molalities from 0.05 to 1 m with 0.1 increments, except for the first two concentrations, and DL-valine molalities ranging from 0.05 to 0.4 m with 0.05 increments. In order to analyze the experimental data obtained, a procedure based on a combination of Debye–Hückel and virial expansion contributions, similar to that suggested by Scatchard (1968), was adopted:

$$\nu \ln \frac{\gamma_\pm^{(2)}}{\gamma_\pm^{(1)}} = C_1 m_A + C_2 m_S m_A + C_3 m_A^2 + C_4 m_A m_S^2 + C_5 m_A^3 + C_6 m_s m_A^2, \quad (5)$$

where C_i are numerical parameters. From the cross-differential relation we have

$$\nu \left(\frac{\partial \ln \gamma_\pm}{\partial m_A} \right)_{m_S,T,P} = \left(\frac{\partial \ln \gamma_A}{\partial m_S} \right)_{m_A,T,P}. \quad (6)$$

Applying Eq. 6 to Eq. 5, the activity coefficient of amino acid, $\gamma_A^{(2)}$, can be calculated as

$$\ln \frac{\gamma_A^{(2)}}{\gamma_A^{(1)}} = C_1 m_S + \frac{1}{2} C_2 m_S^2 + 2 C_3 m_A m_S + \frac{1}{3} C_4 m_S^3 + 3 C_5 m_A^2 m_S + C_6 m_S^2 m_A, \quad (7)$$

where $\gamma_A^{(2)}$ and $\gamma_A^{(1)}$ are the unsymmetric activity coefficients of amino acid in the presence of electrolyte and without electrolyte, respectively. The values of mean ionic activity coefficients of sodium chloride in water used in Eq. 5 were those reported by Robinson and Stokes (1959). The values of the parameters of Eq. 5 were calculated by a least-square analysis of the experimental data. The result of the evaluation of parameters using Eq. 5 showed a root mean square error of 1.1×10^{-3} and the values of parameters obtained were $C_1 = 5.7467 \times 10^{-2}$, $C_2 = -1.2617 \times 10^{-2}$, $C_3 = 6.6026 \times 10^{-2}$, $C_4 = 1.0374 \times 10^{-1}$, $C_5 = 7.6180 \times 10^{-2}$, $C_6 = -5.1883 \times 10^{-2}$. The coefficient of the leading term in Eq. 6, C_1, represents pairwise interactions between the sodium chloride (considered undissociated and as one species) and the amino acid. The small absolute value of C_1 indicates that the presence of DL-valine does not significantly affect the activity coefficient of the electrolyte. Table 1 presents the numerical value of the mean ionic activity coefficients of NaCl in the aqueous solutions of DL-valine. Figure 1 shows the change in the mean ionic activity coefficient of sodium chloride at different concentrations as a function of concentration of DL-valine. As shown in this figure, at fixed molality of sodium chloride, the

Table 1. Mean Ionic Activity Coefficient of NaCl in Aqueous Solutions of DL-Valine at Different NaCl and DL-Valine Molalities

m (NaCl) → m (DL-valine) ⇓	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.9	1.0
					γ ±(NaCl)				
0.00	0.7780	0.7350	0.7100	0.6930	0.6810	0.6730	0.6670	0.6590	0.6570
0.05	0.7795	0.7360	0.7110	0.6943	0.6830	0.6737	0.6683	0.6612	0.6596
0.10	0.7803	0.7372	0.7121	0.6957	0.6843	0.6758	0.6709	0.6634	0.6609
0.20	0.7834	0.7407	0.7150	0.6984	0.6878	0.6791	0.6748	0.6662	0.6668
0.30	0.7858	0.7444	0.7192	0.7021	0.6912	0.6835	0.6774	0.6733	0.6715
0.40	0.7920	0.7478	0.7241	0.7074	0.6960	0.6876	0.6834	0.6781	0.6780

mean ionic activity coefficient of sodium chloride increases as the concentration of DL-valine increases. This increase is more evident at higher sodium chloride concentrations.

Figure 2 shows the activity coefficients of DL-valine at different concentrations of DL-valine as a function of sodium chloride concentration as calculated by Eq. 7. The values of the activity coefficients of DL-valine in aqueous solution in Eq. 7 were obtained from the *Handbook of Biochemistry and Molecular Biology* (Fasman, 1976). As can be seen from this figure, the activity coefficient of DL-valine increases by increasing the sodium chloride concentration. The increase in the activity coefficient of DL-valine by increasing the sodium chloride concentration suggests a salting out effect. This behavior is different from the behavior of some other previously investigated water–electrolyte–amino-acid systems (Schrier and Robinson, 1971; Briggs et al., 1974; Khoshkbarchi and Vera, 1996b).

Figure 3 shows the comparison between the logarithm of the ratio of the activity coefficients of five amino acids with 0.5 molality sodium chloride and without the presence of sodium chloride, as a function of amino-acid concentration. The amino acids compared are glycine, β-alanine, γ-aminobutyric acid, ϵ-aminocaproic acid, and DL-valine and the references for the source of data are those listed in Table 3. These amino acids have in common a carboxilic and an amino group, and the structures of their hydrocarbon backbones differ from each other by one $-CH_2$ group. Figure 3 suggests that the interactions of the hydrocarbon part of amino acid play an important role in its behavior in solutions. It can also be observed from Figure 3 that at a fixed electrolyte concentration, the change in the ratio of the activity coefficients of an amino acid in the presence of an electrolyte to that, without the presence of an electrolyte, at the same amino-acid molality, can be approximately considered to be a linear function of amino-acid concentration.

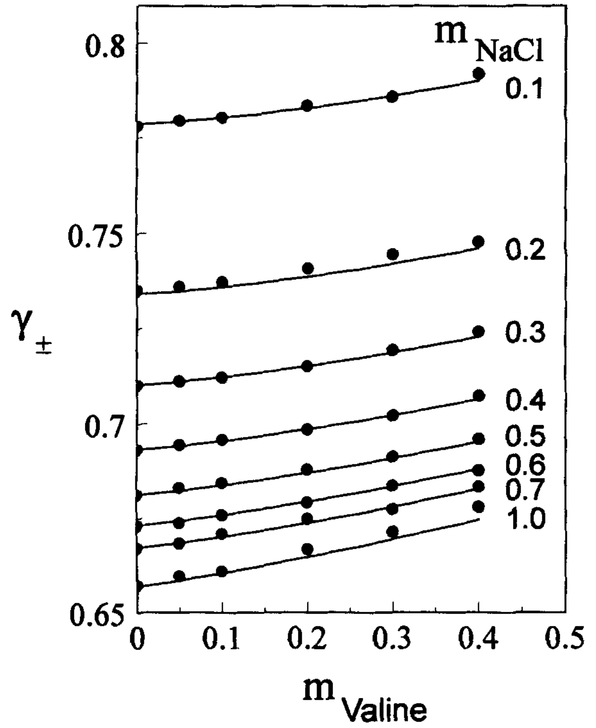

Figure 1. Mean ionic activity coefficients of NaCl in water–NaCl–DL-valine system at different NaCl and DL-valine molalities.

●: Experimental data; —: correlation of the experimental data using Eq. 15.

An Excess Gibbs Free Energy Model

In this study we propose a new excess Gibbs free energy model for aqueous solutions containing amino acids and electrolytes. The model proposed here consists of contributions

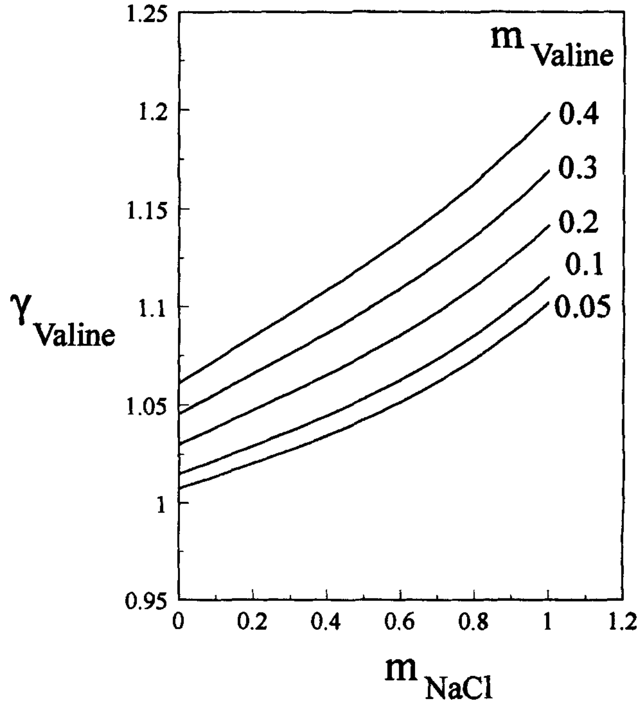

Figure 2. Activity coefficients of DL-valine in water–NaCl–DL-valine system at different NaCl and DL-valine molalities.

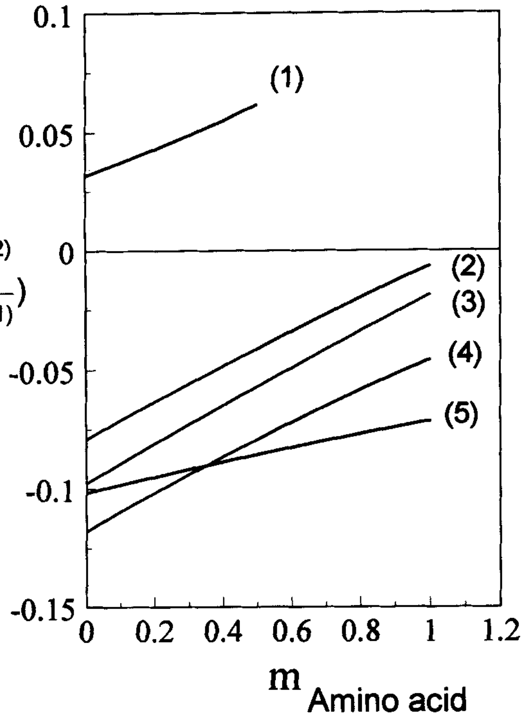

Figure 3. Comparison of the logarithm of the ratio of the activity coefficients of five amino acids with 0.5-molality NaCl and without the presence of NaCl at different amino-acid concentrations.

(1) DL-valine; (2) ϵ-aminocaproic acid; (3) γ-aminobutyric acid; (4) β-alanine; (5) glycine.

of two main terms: a long-range interaction term and a short-range interaction term:

$$G^E = G^E_{LR} + G^E_{SR}, \tag{8}$$

where subscripts LR and SR stand for the long-range and short-range interaction terms, respectively. The long-range interaction term takes into account all interactions in a binary water–electrolyte system, whereas the short-range interaction term accounts for all interactions between water–amino acid, amino acid–electrolyte, and also the change in the interaction between electrolyte–water due to the presence of the amino acid. The long-range interaction excess Gibbs free energy term, G^E_{LR}, considers all interactions in a water–electrolyte system. Thus, the short-range interaction excess Gibbs free energy term, G^E_{SR}, should be such that the total excess Gibbs free energy of the system reduces to the excess Gibbs free energy of the binary water–electrolyte system in the absence of amino acid and to the excess Gibbs free energy of the binary amino-acid–water system in the absence of electrolyte. To achieve this behavior, we propose the following form for the short-range interaction contribution to the excess Gibbs free energy of the system as

$$G^E_{SR} = G^E_{SR}(n_W, n_S, n_A) - G^E_{SR}(n_W, n_S, n_A = 0), \tag{9}$$

where n_A, n_S, and n_W are number of moles of the amino acid, electrolyte, and water present in the system, respectively. The symbols within the parentheses show the dependency of each term with respect to the number of moles of species present in the solution. The total excess free energy of the system can be obtained by combining Eqs. 8 and 9 as

$$G^E = G^E_{LR}(n_W, n_S, n_A = 0) + G^E_{SR}(n_W, n_S, n_A) - G^E_{SR}(n_W, n_S, n_A = 0). \tag{10}$$

In this study we have tested two electrostatic models, the Bromley model (Bromley, 1973) and the K-V model (Khoshkbarchi and Vera, 1995), to represent G^E_{LR}, and two local composition models, the NRTL model (Renon and Prausnitz, 1968) and the Wilson model (Wilson, 1964), to represent G^E_{SR}. Since both the Bromley and the K-V models provide expressions for the mean ionic activity coefficients of electrolytes based on a molality scale, whereas the local composition models such as NRTL and Wilson provide activity coefficients based on a mole fraction scale, to combine these models the activity coefficients should be based on the same scale. The derivation of the required conversion factor between both forms of activity coefficients, which is not available in the literature, is presented in the Appendix. This conversion factor was not required by previous models that combine electrolytes and nonelectrolytes (Cheluget et al., 1994; Zerres and Prausnitz, 1994) since no contribution to the activity coefficient of the electrolyte was generated by the short-range interaction part of the model. In those models a mean spherical approximation model or a term of Born type were used to introduce the correction to the activity coefficient of the electrolyte due to the presence of other solutes (or solvents). In this work, the short-range interactions are directly considered in the respective contribution to the excess Gibbs free energy. Thus, with the proper conversion for the composition base, the expression for the long-range interactions is written as

$$(G^E_{LR})^{(x)} = (G^E_{LR})^{(m)} + n_S RT \ln\left([\nu_+^{\nu_+}\nu_-^{\nu_-}]\, m_S^{\nu-1}\left(1 + 0.001\, M_W \sum_j m_j\right)\right). \tag{11}$$

Similarly, the expression for the short-range interactions with the proper conversion is written as

$$(G^E_{SR})^{(x)} = (G^E_{SR})^{(m)} + n_A RT \ln\left(1 + 0.001 M_W \sum_j m_j\right), \tag{12}$$

where superscripts (m) and (x) indicate the excess Gibbs free energy normalized based on molality and mole fraction scale, respectively, M_W is the molecular weight of water, and the sum runs over all solutes.

In Eq. 10 it is important to note that the excess Gibbs free energy models used must be internally consistent in terms of conventions used for standard and reference states. In Eq. 10, the models used to represent the long-range interactions excess Gibbs free energy term, the Bromley model, and the K-V model are inherently unsymmetric. To convert the local composition models employed to represent the short-range interaction excess Gibbs free energy terms, NRTL, and Wilson, to unsymmetric normalization, the following general relation can be used:

$$\frac{G^{*E}}{RT} = \frac{G^E}{RT} - \sum_i x_i \ln \gamma_i^{\infty}, \qquad (13)$$

where γ_i^{∞} is the symmetric activity coefficient of component i at infinite dilution and the sum runs over all solutes. The superscript * indicates the unsymmetric convention for the excess Gibbs free energy. This relation renders the total excess Gibbs free energy of the system to be in the unsymmetric convention, that is, with $\gamma_i \to 1$ as $x_i \to 0$ for all solutes. The reference state for water is its pure state, while that of the electrolyte and amino acid are their states at infinite dilution in water. Further, the difference between the McMillan–Mayer standard state, arising from the Debye–Hückel term in the Bromley and the K-V models, and the Lewis–Randall standard state, arising from the local composition models, is ignored. The relation between the McMillan–Mayer and Lewis–Randall standard states has been discussed in detail by Cardoso and O'Connell (1987) and Hartounian et al. (1994), who proved it was a good approach to ignore this difference. As discussed by Cheluget et al. (1992), the mean ionic activity coefficient of electrolyte can be obtained from the following relation:

$$\ln \gamma_{\pm} = \frac{1}{\nu}\left(\frac{\partial G^E/RT}{\partial n_S}\right)_{T,P,n_A,n_W} + 1 - \frac{1}{\nu}(x_W + x_A). \qquad (14)$$

Combining Eqs. 10 to 14, the mean ionic activity coefficient of the electrolyte can be calculated as

$$\ln \gamma_{\pm}^{(m)} = \ln \gamma_{\pm}^{(m),LR} + \frac{1}{\nu}\Bigg\{\ln \gamma_S^{(x),SR} - \lim_{x_A \to 0} (\ln \gamma_S^{(x),SR}) + \ln\left(\frac{1+0.001\, M_W m_S}{1+0.001\, M_W (m_S + m_A)}\right)\Bigg\}. \qquad (15)$$

From Eq. 15 it can be seen that as the amino-acid mole fraction approaches zero, the mean ionic activity coefficient of the electrolyte reduces to a binary long-range interaction activity-coefficient model. In fact, the structure of this model is such that it allows the use of any kind of binary electrolyte model without introducing new adjustable parameters. Similarly, by combining Eq. 12 and the following relation:

$$\ln \gamma_A = \left(\frac{\partial G^E/RT}{\partial n_A}\right)_{T,P,n_S,n_W} + 1 - (x_S + x_W) \qquad (16)$$

the activity coefficient of the amino acid can be derived as

$$\ln \gamma_A^{(m)} = \ln \gamma_A^{(x),SR} - \lim_{x_A \to 0,\, x_S \to 0} \ln \gamma_A^{(x),SR} - \ln[1 + 0.001\, M_W (m_A + m_S)]. \qquad (17)$$

From Eq. 17 it is evident that as the mole fraction of electrolyte approaches zero, Eq. 17 reduces to a binary short-range interaction model. As discussed below, the same binary parameters obtained from binary water–amino-acid short-range interaction models can be used for the ternary water–electrolyte–amino-acid system. From Eq. 17 the mole fraction scale, an unsymmetric activity-coefficient expression, for a binary water–amino-acid system can be obtained by setting the electrolyte mole fraction in the model to zero.

As was stated earlier, the long-range interaction term in this study is represented either by the Bromley model (Bromley, 1973) or by the K-V model (Khoshkbarchi and Vera, 1996), whose expressions for the molality-scale mean ionic activity coefficient of an electrolyte in a binary mixture of water and electrolyte are given by Eqs. 18 and 20.

The Bromley model

$$\ln \gamma_{\pm}^{Br} = -\frac{A\,|z_+ z_-|\sqrt{I}}{1+\sqrt{I}} + \frac{(0.138 + 0.6\,B)\,|z_+ z_-|\,I}{(1 + [1.5\,I/|z_+ z_-|])^2} + BI, \qquad (18)$$

where A is the Debye-Hückel parameter, which at 25°C is equal to 1.1761 $\text{kg}^{1/2}$ $\text{mole}^{1/2}$; B is an adjustable parameter; and I is the ionic strength of the solution, defined by

$$I = \frac{1}{2}[\nu_+ z_+^2 + \nu_- z_-^2]\, m_S, \qquad (19)$$

where the molality of electrolyte in undissociated form is represented by m_S.

The K-V model

$$\ln \gamma_{\pm}^{K-V} = \frac{-A_x\,|z_+ z_-|\sqrt{I_x}}{1+\rho\sqrt{I_x}} + B_x \frac{I_x^{3/2}}{1+\rho\sqrt{I_x}} + C_x \ln(1 + \rho I_x^{2/3}), \qquad (20)$$

where A_x is the usual Debye-Hückel constant, which in mole fraction basis, at 298.2 K, is equal to 8.766 $\text{kg}^{1/2} \cdot \text{mol}^{1/2}$; $\rho = 9$; B and C are two adjustable parameters; and I_x is defined as

$$I_x = \frac{1}{2} \Sigma x_i' z_i^2, \qquad (21)$$

where x_i' is the mole fraction of ion i in the mixture defined as

$$x_i' = \frac{\nu_i n_S}{\nu n_S + n_W}. \qquad (22)$$

The short-range interaction terms are represented by one of the following two local composition models, the NRTL (Renon and Prausnitz, 1968) or the Wilson (Wilson, 1964). The expressions for the NRTL and the Wilson models for the mole fraction scale activity coefficient of a component in a multicomponent mixture are given by Eqs. 23 and 25.

The NRTL model

$$\ln \gamma_i = \frac{\sum\limits_{j=1} \tau_{ji} G_{ji} x_j}{\sum\limits_{j=1} G_{ji} x_j} + \sum_{j=1} \frac{x_j G_{ij}}{\sum\limits_{k=1} x_k G_{kj}} \left(\tau_{ij} - \frac{\sum\limits_{k=1} x_k \tau_{kj} G_{kj}}{\sum\limits_{k=1} x_k G_{kj}} \right), \tag{23}$$

$$G_{ij} = \exp(-\alpha \tau_{ij}). \tag{24}$$

where α is the nonrandomness factor, which is an adjustable parameter; τ_{ij} is the binary energy parameter with $\tau_{ii} = 0$; and G_{ij} is the binary energy parameter function.

The Wilson model

$$\ln \gamma_i = 1 - \ln\left(\sum_{j=1} x_j \Lambda_{ji} \right) - \sum_{j=1} \frac{x_j \Lambda_{ji}}{\sum\limits_{k=1} x_k \Lambda_{jk}}, \tag{25}$$

where Λ_{ij} is the binary energy parameter with $\Lambda_{ii} = 0$.

It should be emphasized that in this work, in both the NRTL and the Wilson models, the electrolyte is treated as a molecular species and is regarded as undissociated. Therefore, the mole fraction of electrolyte is defined as

$$x_S = \frac{n_S}{n_W + n_S + n_A}. \tag{26}$$

At this point it is necessary to mention that amino acids form different ionic species when dissolved in aqueous media. Amino acids in water can loose a proton and form a negatively charged molecule, or gain a proton and become a positively charged molecule. They can also possess in the same molecule a positively charged amino group (NH_3^+) and a negatively charged carboxilic group (COO^-); in such a case they are called zwitterion. In the absence of a strong proton donor (an acid) or proton acceptor (a base), more than 99% of amino-acid molecules stay in the zwitterionic form (Cohn and Edsall, 1965). Because of this fact, we assume that the activity coefficients of all ionic forms of an amino acid are equal or, in other words, the amino-acid molecules are assumed to be in the solution in their zwitterionic forms.

Evaluation of the Parameters of the Model

To correlate the experimental data of activity coefficients for systems containing water–electrolyte–amino acid, the proposed model requires the evaluation of some parameters. The nature and number of the required parameters depend on the choice of expressions for the long-range and short-range interaction terms. In what follows, the method of evaluation of parameters for the different long- and short-range interaction terms are discussed.

The Bromley equation contains one adjustable parameter that depends on the nature of the electrolyte. The Bromley equation parameter for a large number of water–electrolyte systems has been compiled by Zemaitis et al. (1986). The K-V equation contains two adjustable parameters that depend on the nature of the electrolyte. The K-V equation parameters for few water–electrolyte systems have been reported by Khoshkbarchi and Vera (1996), and for other aqueous systems they can be evaluated by regressing mean ionic activity-coefficient data reported in literature. The NRTL and the Wilson models each contain six binary interaction energy parameters, that is, two binary parameters for each of the constituent binary systems. Two of these energy parameters, which correspond to water–amino acid, were evaluated in this work by correlating the available experimental data for water–amino-acid systems (Fasman, 1976). The same energy parameters obtained from the binary water–amino-acid system were used for the ternary system. As a simplifying assumption, the binary amino-acid–electrolyte and electrolyte–water parameters were assumed to be symmetric for both models, that is, it was assumed that $\tau_{W-S} = \tau_{S-W}$ and $\tau_{A-S} = \tau_{S-A}$ in the case of the NRTL model, and that $\Lambda_{W-S} = \Lambda_{S-W}$ and $\Lambda_{A-S} = \Lambda_{S-A}$ in the case of the Wilson model. The value of the short-range amino-acid–electrolyte and water–electrolyte interaction parameters were evaluated by regressing the ternary experimental data. The NRTL model also contains a nonrandomness factor, which in this work was set in all cases equal to 0.3.

Thus, the model proposed here contains two parameters that should be regressed from ternary experimental data, and is flexibile enough that two more ternary parameters can be added. The rest of the parameters can be evaluated from binary water–amino-acid and binary water–electrolyte data. In all cases, to estimate the values of the parameters, the following objective function was minimized:

$$O.F. = \Sigma[\ln \gamma_i^{\exp} - \ln \gamma_i^{cal}]^2. \tag{27}$$

Results and Discussion

The binary NRTL and Wilson models were employed to correlate the experimental data of water–amino-acid systems. For aqueous solutions of glycine, alanine, α-amino n-butyric acid, proline, serine, threonine, and valine the data reported in *Handbook of Biochemistry and Molecular Biology* (Fasman, 1976) were used, and for aqueous solutions of β-alanine, γ-aminobutyric acid, and ϵ-aminocaproic acid the experimental data reported by Scherier and Robinson (1971) were used. The data reported in the literature are all in molality scale and in the unsymmetric normalization basis. To make the experimental data compatible with our model, they were converted to mole fraction unsymmetric convention using the relation derived in the Appendix as follows:

$$\gamma_i^{(x)} = \gamma_i^{(m)}\left(1 + 0.001\, M_W \sum_i m_i\right), \tag{28}$$

where the sum runs over all solute species. The results for the correlation of the data for eight amino acids with the NRTL model are shown in Figures 4 and 5. As is evident from Figure 4, the NRTL model correlates well the activity coefficient of water–amino-acid systems over all the concentration range. Table 2 presents the binary interaction parameters and root-mean-square deviations of the correlation for several water–amino-acid systems using the NRTL and the Wilson models, respectively. The comparison of the root-

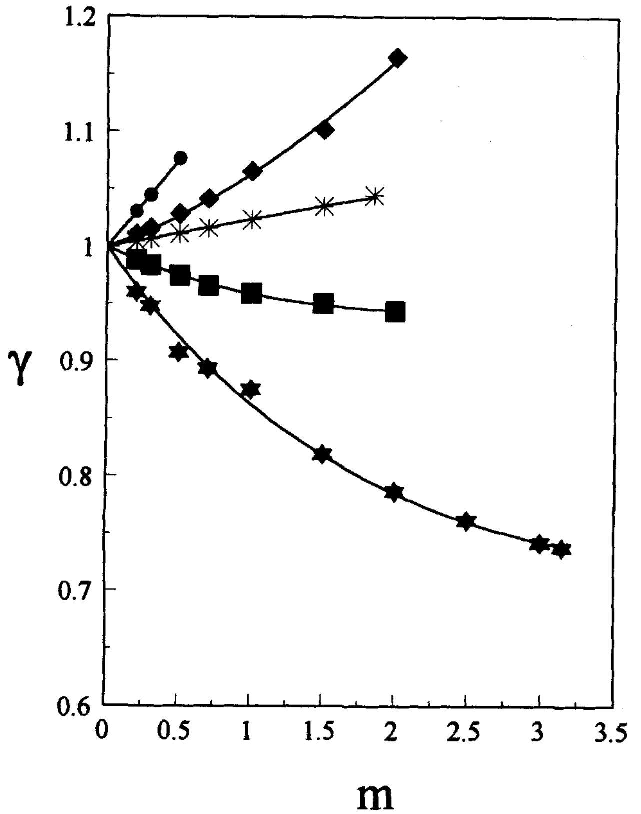

Figure 4. Activity coefficients of five amino acids in water–amino-acid systems at different amino-acid molalities.

●: Valine; ◆: α-aminobutyric acid; *: alanine; ■: α-aminovaleric acid; ✸: glycine; —: correlation of the experimental data using NRTL model.

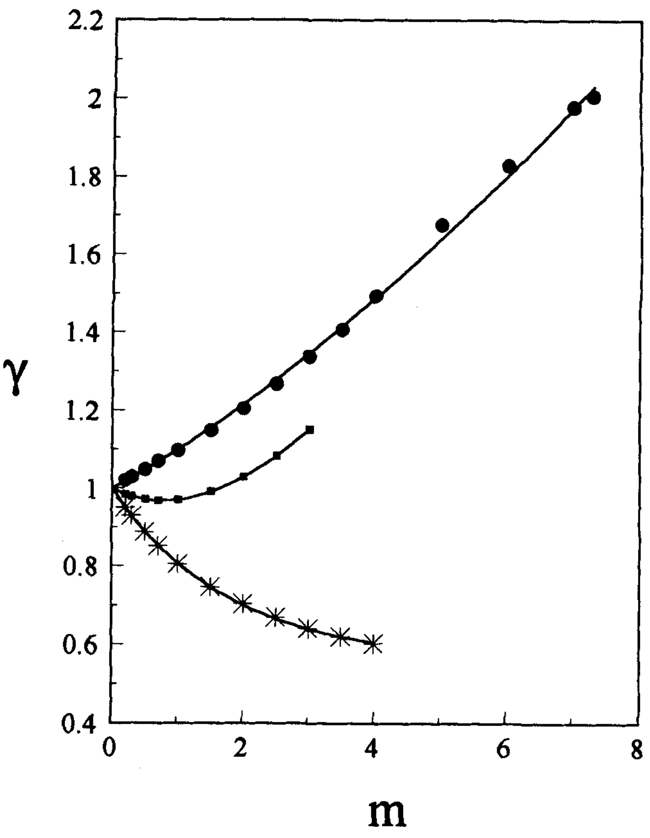

Figure 5. Activity coefficients of three amino acids in water–amino-acid systems at different amino-acid molalities.

●: Proline: ■: ε-aminocaproic acid; *: serine; —: correlation of the experimental data using NRTL model.

mean-square errors presented in Table 2 shows that both the NRTL and Wilson models can correlate the activity coefficient of amino acids in water–amino-acid systems with good accuracy.

As discussed before, in view of the fact that the dissociation of amino acids in pure water is insignificant and the zwitterionic species are predominant, no term has been introduced in the binary water–amino-acid model to take into account the presence of ionic species in solution. This is similar to the procedure followed by Chen et al. (1989), and it contrasts with the procedure followed by Pinho et al. (1994) and Peres and Macedo (1994). In fact, the consideration of the terms that take into account the effect of ionic forms of amino-acid molecules other than their zwitterionic form, only makes the modeling more complex. Since the available experimental data for the activity coefficient of amino acids do not include the ionization of amino acids in water, consideration of the ionization term seems unnecessary at this point.

The ternary excess Gibbs free energy model proposed in this study by Eqs. 15 and 17, with the NRTL or the Wilson models for the short-range interaction term, and the Bromley or the K-V models for the long-range interactions term, were applied to correlate the experimental activity coefficient data of water–electrolyte–amino-acid systems. The results of the

Table 2. Parameters of the NRTL and Wilson Models for Water–Amino-Acid Systems

Amino Acid	$\tau_{A,W}$ NRTL Model	$\tau_{W,A}$	r.m.s.d × 100	$\Lambda_{A,W}$ Wilson Model	$\Lambda_{W,A}$	r.m.s.d × 100	Reference
Glycine	−1.961	4.580	0.60	0.086	3.564	0.56	Fasman (1976)
α-Alanine	1.000	−0.289	0.26	0.172	3.581	0.02	Fasman (1976)
Valine	−0.823	−2.540	0.04	0.064	4.490	0.06	Fasman (1976)
Serine	−1.957	4.823	0.23	0.076	3.335	0.03	Fasman (1976)
Threonine	−1.962	4.124	0.10	0.104	3.978	0.07	Fasman (1976)
Proline	−2.179	3.789	1.50	0.064	3.564	1.40	Fasman (1976)
α-Amino *n*-butyric acid	−2.512	4.581	0.29	0.047	5.915	0.39	Fasman (1976)
β-Alanine	−2.633	5.204	0.15	0.057	5.272	0.03	Schrier and Robinson (1971)
γ-Amino *n*-butyric acid	−2.904	5.578	0.24	0.047	5.915	0.28	Schrier and Robinson (1971)
ε-Aminocaproic acid	−3.078	5.888	1.12	0.037	5.272	0.11	Schrier and Robinson (1971)

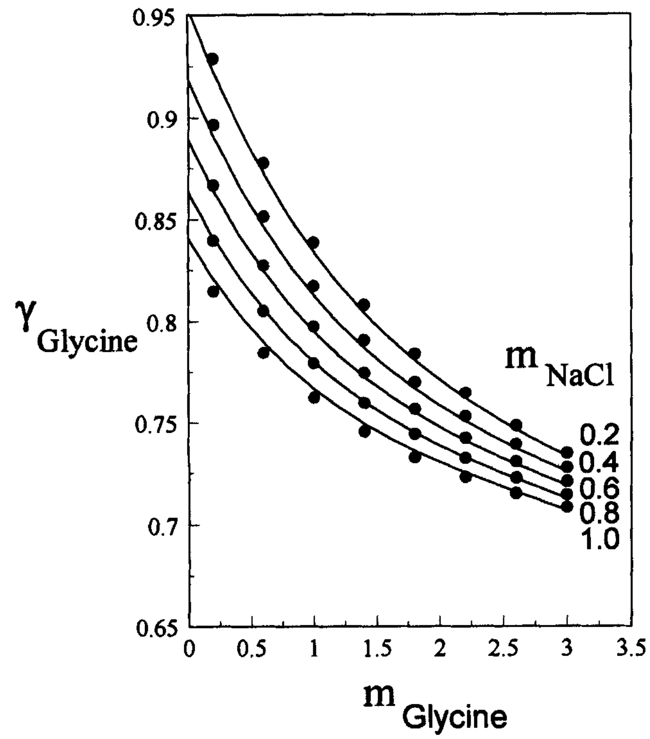

Figure 6. Activity coefficients of glycine in water–NaCl–glycine system at different NaCl and glycine molalities.

●: Experimental data; —: correlation of the experimental data using Eq. 17.

correlation of the experimental data, using Eq. 15 with the NRTL model as the short-range interaction term and the Bromley equation as the long-range interaction term, for the system water–NaCl–DL-valine measured in this study, are shown as solid lines in Figure 1. Equation 17 with the NRTL model is used to correlate the activity coefficient of glycine, which is the simplest amino acid, for the system water–NaCl–glycine, and the results are shown in Figure 6 as a function of glycine molality with NaCl concentration as a parameter. The NRTL and the Wilson models coupled with the Bromley model were also used to correlate the experimental data for some other water–electrolyte–amino-acid systems reported in the literature. The results of modeling in the form of root-mean-square deviation together with the regressed parameters are presented in Table 3. As can be seen from Figures 1 and 6, and also from the results presented in Table 3, the model proposed in this study can accurately correlate the activity coefficients of components in water–electrolyte systems over a wide range of concentrations. The comparison of the root-mean-square deviation presented in Table 3 indicates that the both the NRTL and Wilson models can correlate well the activity coefficient experimental data, and that the NRTL model, coupled with the Bromley model, provides a better correlation than the Wilson model. The combinations of the K-V model with NRTL and Wilson models were also used to correlate the experimental data for the water–electrolyte–amino-acid systems. The results, not presented in detail here, showed that both the K-V and the Bromley models can be used along with both the NRTL and the Wilson models, and no significant difference was found in the root-mean-square deviation due to the use of one or the other model. This can be explained by the fact that the short-range interaction term in Eq. 15 contains a water–electrolyte interaction parameter that can absorb part of the error arising from the long-range interactions terms. The result of the correlation of mean ionic activity coefficients of the electrolyte for some water–electrolyte–amino-acid systems using the NRTL model for the short-range interaction term and the K-V or the Bromley models for the long-range interaction term are compared in Table 4.

Conclusions

Activity coefficient data for the system water–NaCl–DL-valine were measured using an electrochemical cell and are reported in this work. The cell consisted of a cation- and an

Table 3. Parameters of the NRTL and Wilson Models Combined with the Bromley Model for Water–Electrolyte–Amino-Acid Systems

	$\tau_{A,S}$	$\tau_{W,S}$	r.m.s.d	$\Lambda_{A,S}$	$\Lambda_{W,S}$	r.m.s.d	
Amino Acid + Electrolyte	NRTL Model			Wilson Model			Reference
Glycine + NaCl	0.2077	−0.3762	0.0046	1.1394	0.8813	0.0042	Schrier and Robinson (1971)
Glycine + KCl	1.7700	1.0886	0.0035	0.4074	0.4573	0.0041	Bower and Robinson (1965)
DL-Valine + NaCl	2.7099	−0.6969	0.0044	0.5789	3.1478	0.0100	This work
β-Alanine + NaCl	−1.1621	−5.3564	0.0077	1.1817	0.8813	0.0152	Schrier and Robinson (1971)
γ-Amino *n*-butyric acid + NaCl	−1.4072	−3.0336	0.0080	10.5198	5.2522	0.0370	Schrier and Robinson (1971)
ε-Aminocaproic acid + NaCl	−1.1791	−2.9912	0.0093	11.7930	27.0283	0.0177	Schrier and Robinson (1971)

Table 4. Comparison of the Root-Mean-Square Deviations of Results Obtained from the NRTL Model Combined with Bromley Model or K-V Model for Water–Electrolyte–Amino-Acid Systems

Amino Acid + Electrolyte	r.m.s.d. Bromley	r.m.s.d. K-V	Reference
Glycine + NaCl	0.0046	0.0039	Schrier and Robinson (1971)
Glycine + KCl	0.0035	0.0032	Bower and Robinson (1965)
DL-Valine + NaCl	0.0044	0.0052	This work
β-Alanine + NaCl	0.0077	0.0074	Schrier and Robinson (1971)
γ-Amino *n*-butyric acid + NaCl	0.0080	0.0084	Schrier and Robinson (1971)
ε-Aminocaproic acid + NaCl	0.0093	0.0112	Schrier and Robinson (1971)

anion-ion-selective electrode, each measured vs. a double-junction reference electrode. Activity coefficients of amino acids in aqueous electrolyte solutions were modeled using an expression for G^E based on the contribution of a long-range interaction term represented by the Bromley or the K-V models and short-range interaction term represented by the NRTL or the Wilson models. All versions of the model require two parameters that should be regressed from ternary data. All other parameters were evaluated from binary experimental data of water–amino-acid and water–electrolyte systems. The model accurately correlated ten binary water–amino-acid systems and six water–electrolyte–amino-acid systems.

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Notation

F = Faraday number
R = universal gas constant
T = absolute temperature
x = mole fraction

Superscript

$^\circ$ = reference state

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Appendix

The mean ionic activity coefficient model developed in this study combines the contributions of a long-range interaction term, represented by a Bromley or a K-V model, and a short-range interaction term represented by a local composition model such as NRTL or Wilson. The interactions of the electrolyte with other components of the system are considered in both long-range and short-range interaction terms. Since the long-range interaction term expressions used in this study give the mean ionic activity coefficient based on a molality scale, while the short-range interaction term expression gives the activity coefficient based on a mole fraction scale, they can be added only through the use of a suitable conversion factor. In what follows, we discuss the conversion of a mole-fraction-based activity coefficient, $\gamma^{(x)}$, to a molality-based activity coefficient, $\gamma^{(m)}$, and to molality-based normalized mean ionic activity coefficient, $\gamma_{\pm}$, of an electrolyte in multicomponent solution containing an indeterminate number of electrolytes and nonelectrolytes. For our purposes here, we consider the unsymmetrical normalization of the activity coefficient for the solute. The fugacity of an electrolyte S in a solution is related to its mole-fraction-based and molality-based activity coefficient through the following relations:

$$f_S = x_S \gamma_S^{*(x)} f_g^{\theta,(x)} = m_S \gamma_S^{*(m)} f_S^{\theta,(m)}, \qquad \text{(A1)}$$

where f_S^{θ} is the fugacity of electrolyte in its corresponding (x or m) standard state. Applying the limits of $\gamma_S^{*(x)} \to 1$ and $\gamma_S^{*(m)} \to 1$ as $n_S \to 0$ to Eq. A1, and substituting the result back into Eq. A1, yields

$$\ln \gamma_S^{*(x)} = \ln \gamma_S^{*(m)} + \ln \left[1 + 0.001\, M_W \sum_j m_j \right], \qquad \text{(A2)}$$

where the sum runs over all solutes in the solution and M_W is the molecular weight of water. The mean ionic activity coefficient of an electrolyte is related to the molality-based activity coefficient of the electrolyte by (Lewis and Randall, 1961)

$$[\nu_+^{\nu_+} \nu_-^{\nu_-}] m_S^{\nu} \gamma_{\pm}^{\nu} = m_S \gamma_S^{(m)}. \qquad \text{(A3)}$$

Substituting Eq. A2 into Eq. A3 provides

$$\ln \gamma_S^{*(x)} = \nu \ln \gamma_{\pm} + \ln \left\{ [\nu_+^{\nu_+} \nu_-^{\nu_-}] m_S^{\nu-1} \left(1 + 0.001\, M_W \sum_j m_j \right) \right\}. \qquad \text{(A4)}$$

Equation A4 provides the conversion to a mole-fraction-based activity coefficient from a molality-based mean ionic activity coefficient of an electrolyte. This conversion is not available in the literature. It should be noted that $\gamma_S^{*(x)}$ is normalized in the symmetrical convention. If the symmetrically normalized activity coefficient based on mole fraction is desired, an additional conversion factor is required. This additional conversion factor is available in standard texts (Prausnitz, 1969).

It is interesting to observe that Eqs. A1 and A3 are the basis for applying the Gibbs-Duhem equation to electrolyte solutions. Considering, for example, a system formed by an electrolyte (S), water (W), and an amino acid (A), from Eq. A1 for the amino acid we have

$$d \ln (x_A \gamma_A^{*(x)}) = d \ln (m_A \gamma_A^{*(m)}). \qquad \text{(A5)}$$

Combining Eqs. A1 and A3 for the electrolyte, we can write

$$d \ln (x_S \gamma_S^{*(x)}) = \nu d \ln (m_S \gamma_{\pm}^{(m)}). \qquad \text{(A6)}$$

On the other hand, at constant temperature, when the standard states are all defined at the pressure of the system, the Gibbs-Duhem equation can be written as

$$x_A d \ln (x_A \gamma_A^{*(x)}) + x_W d \ln (x_W \gamma_W) + x_S d \ln (x_S \gamma_S^{*(x)}) = \frac{\nu^E}{RT} dP, \qquad \text{(A7)}$$

where ν^E is the excess molar volume of the system. Combining Eqs. A5 to A7 gives

$$x_A d \ln (m_A \gamma_A^{*(m)}) + x_W d \ln (x_W \gamma_W) + \nu x_S d \ln (m_s \gamma_{\pm}) = \frac{\nu^E}{RT} dP, \qquad \text{(A8)}$$

which is the form that the Gibbs-Duhem equation takes for the water-electrolyte-amino-acid system. In fact, the availability of the conversion factors for activity coefficients presented here, opens the possibility of working with models for G^E in a different way. In order to combine molality-based with mole-fraction-based excess Gibbs free energy models, one can proceed as follows. First, express the activity coefficients of the molality-based model in terms of the mole-fraction-based form, and obtain the long-range interaction excess Gibbs free energy with respect to the mole-fraction-based standard states as:

$$(G_{LR}^E)^{(x)} = (G_{LR}^E)^{(m)} + n_S RT \ln \left\{ [\nu_+^{\nu_+} \nu_-^{\nu_-}] m_S^{\nu-1} \times \left(1 + 0.001\, M_W \sum_j m_j \right) \right\}. \qquad \text{(A9)}$$

Then the excess Gibbs free energies for long-range and short-range interactions can be directly added and the activity coefficients evaluated as

$$\ln \gamma_i^{(x)} = \left(\frac{\partial G^{(x)E}/RT}{\partial n_i} \right)_{T,P,n_{j \neq i}}. \qquad \text{(A12)}$$

Finally it is necessary to back-convert the activity coefficients to molality-based scale using Eq. A4. This procedure requires a double conversion of activity coefficients, but keeps the conventional form of the relation between activity coefficients and excess Gibbs free energy, Eq. A10.

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