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MEASURING AND MODELING ACTIVITY COEFFICIENTS AND OSMOTIC COEFFICIENTS IN AQUEOUS AMINO-ACID SOLUTIONS

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ABSTRACT

The perturbed-chain statistical association theory (PC-SAFT) is applied to simultaneously describe various thermodynamic properties (density, vapor-pressure depression, activity coefficient, solubility) of aqueous solutions containing an amino acid or an oligopeptide. The 28 organic compounds considered within this work are glycine, alanine, serine, proline, hydroxyproline, valine, leucine, arginine, lysine, threonine, asparagine, tyrosine, histidine, cysteine, methionine, aspartic acid, glutamic acid, R-ABA, R-isoABA, _-ABA, γ-ABA, R-AVA, γ-AVA, diglycine, triglycine, dialanine, Gly-Ala, and Ala-Gly. If not yet available in literature, amino-acid solubility data and activity coefficients were determined experimentally. To prove the predictivity of PC-SAFT, osmotic coefficients in aqueous solutions containing two amino acids (glycine/valine and alanine/ valine) were measured and predicted without applying any additional model parameters.

KEYWORDS: Electrolytes, Amino Acids, Activity Coefficients, Osmotic Coefficients.

INTRODUCTION

Since the early years of the last century densities, vapor pressures, solubilities, and activity coefficients of amino acids and peptides in various solvents have been correlated, measured, and calculated. The modeling of such systems requires the availability of precise experimental data. As literature data does not cover the solubility and activity coefficients of all amino acids and peptides in water, some new data will be presented here. In the case of solubilities, the gravimetric method has already been applied and proven as a suitable tool for precise and fast determination of single-solute1 and multisolute[1,2] solubility data. The measurement of water activity coefficients is also well established. The oldest procedure is the isopiestic method applied for example, by Robinson and Stokes[3] to aqueous electrolyte systems. However, this method is extremely timeconsuming for small solute concentrations. This makes it inappropriate for the systems considered in this work as many amino acids are very little soluble in water. Furthermore, there exist some vapor-pressure measurements which also provide activity coefficients. They are performed as measurement of absolute vapor pressures or by vapor-pressure depressions with high certainty[4] and almost no limitations with respect to concentration, solute, or solvent. However, such measurements are as difficult as they are very sensitive (e.g., to the tempering the system or to the accuracy of weighing) and additionally expensive. Recently, vapor-pressure osmometry is more and more used as an alternative possibility for the determination of activity coefficients. Because of its simplicity and reliability it has already been applied to aqueous biomolecule solutions.[5]
For the thermodynamic modeling of amino-acid and peptide solutions, two main types of models have been applied so far: Gibbs-energy (*g*E) models and equations of state (EOS). Khoshkbarchi and Vera[6] give an excellent overview of the thermodynamic modelss*g*E models as well as EOSsapplied in the recent years to calculate activity coefficients and solubilities of amino acids in aqueous solutions. For example, Kuramochi et al.[7] used the UNIFAC model combined with a Pitzer-Debye-Hu¨ckel theory to calculate activity coefficients in aqueous solutions containing amino acids, sugars, and inorganic salts. Nass[8] applied the electrolyte NRTL model to describe amino-acid solubilities of L-alanine, L-serine, and L-threonine. Xu et al.[9] and Pazuki et al.[10,11] suggested the modified Wilson model for the calculation of activity coefficients and solubilities of several amino acids in aqueous solutions that may also contain electrolytes. Both groups compared their modeling results with other *g*E models like UNIQUAC or UNIFAC and perturbation models of varying complexity. The reported mean root square deviations indicate that perturbation models (equation of states) yield comparably good or even better results than *g*E models. Khoshkbarchi and Vera[12,13]

presented a so-called primitive model based on a first-order perturbation theory for the correlation of activity coefficients and solubilities of some amino acids and oligopeptides (up to trimers) in water. In a primitive model, the solvent (in this case water) is only considered implicitly by its dielectric constant. The amino acids and peptides were modeled as Lennard-Jones spheres which also exhibit dipole-dipole interactions (Stockmayer fluid). The model of Khoshkbarchi and Vera needs three pure-component parameters, namely the molecule diameter, the dispersion energy, and the dipole moment. While the first two are fitted to experimental data, the third is calculated by means of quantum mechanics. “Simple” models like the one by Khoshkbarchi and Vera are based on a spherical shape of the molecules. However, this assumption is not even justified for molecules like small amino acids. Aiming at the description of even more complex biological systems, where the molecules exhibit a rodlike structure, segment-based models appear to be more appropriate. The model by Liu et al.[14] is also based on a perturbation theory but it treats the solvent as a discrete molecule. Moreover, the molecules are described as chains of Lennard-Jones spheres having a dipole moment. The reference system consists of a hard-sphere mixture; chain formation, dispersion, and dipoledipole interactions are taken into account as perturbation contributions. Four pure-component parameters (segment number, segment diameter, dispersion energy, and dipole moment) were fitted to correlate activity coefficients and solubilities of some amino acids and dipeptides in aqueous solutions. PC-SAFT has already been used to describe multisolvent and multisolute amino-acid mixtures. Fuchs et al.[15] modeled the solubility of glycine, DL-alanine, and DL-methionine in water/alcohol solutions at varying pH. Also other authors used PC-SAFT to model.

EXPERIMENTAL WORK

Materials and Reagents.

The amino acids L-valine (Sigma, 97%), DL-valine (Sigma, 97%), L/DL-alanine (Sigma 99%), glycine (Sigma, 99%) DL-norleucine (Sigma, 98%), DL-norvaline (Sigma, 98%), L-cysteine (Sigma, 99.5%), Lmethionine (Sigma, 99.5%), and diglycine (Sigma, 99%) were used without further purification. For the calibration of the vapor-pressure osmometer, a sodium chloride solution (NaCl: Merck, □99.5%) was applied. All solutions were prepared gravimetrically by weighing with an accuracy of 0.01 mg. Water from the Millipore purification system was used for the preparation of all aqueous solutions.

MEASUREMENT OF ACTIVITY COEFFICIENTS.

The measurements of osmotic coefficients were performed with a Gonotec Osmomat which allows for the measurement of one-solvent solutions in the concentration range of 0.005-3.0 mol solute per kg solvent [mol/kg] up to the solvent’s boiling point. The measuring cell of the Osmomat contains two thermistors placed in a tempered closed, water-saturated atmosphere. With the help of a syringe, the thermistors are wetted, one with water and the other one with the solute solution of interest. Being at the same solvent pressure, the temperature difference between the two droplets is detected. This value can be converted into the osmotic coefficient or the solvent activity coefficient.5 Before carrying out the measurements, the Osmomat was calibrated with sodium chloride solutions between 0.05 and 1.2 mol/kg using reference values from literature.3 After that, the experiments for the amino acids were performed at 30^{0}C. For each solution the measurements were repeated until a constant temperature difference could be observed. Afterward, at stable results, the measuring signal of five measurements at equal concentration were recorded and averaged. After measurement, the calibration was controlled again to exclude any baseline drifts of the apparatus. This procedure was repeated for all measured concentrations allowing for a maximum uncertainty of (2% in experimental osmotic coefficients.

Table -1

Activity coefficients of NaCl in the NaCl-$MgCl_2$-Glycine-H_2O System at 25°C.

Conc. NaCl mol. kg^{-1}	Conc. $MgCl_2$ mol. kg^{-1}	Conc. Glycine mol. kg^{-1}	EmF Volts.	y_B	$\log\gamma_{NaCl}$	γ_{NaCl}
			I = 0.5			
0.5000	0.0000	0.0000	0.1176	0.0000	-0.1172	0.7634
0.4475	0.0525	0.0525	0.1150	0.1051	-0.1162	0.7651
0.4050	0.0950	0.0950	0.1125	0.1899	-0.1151	0.7671
0.3698	0.1302	0.1302	0.1103	0.2603	-0.1147	0.7679
0.3403	0.1597	0.1597	0.1083	0.3194	-0.1145	0.7681
0.3152	0.1848	0.1848	0.1064	0.3697	-0.1146	0.7680
0.2935	0.2065	0.2065	0.1047	0.4131	-0.1139	0.7692
0.2746	0.2254	0.2254	0.1030	0.4509	-0.1141	0.7690
0.2579	0.2421	0.2421	0.1015	0.4841	-0.1141	0.7690
0.2432	0.2568	0.2568	0.1000	0.5136	-0.1142	0.7688
0.2301	0.2699	0.2699	0.0987	0.5399	-0.1142	0.7688
0.0517	0.4483	0.4483	0.0610	0.8967	-0.1165	0.7646
0.0936	0.4064	0.4064	0.0761	0.8127	-0.1163	0.7650
0.1284	0.3716	0.3716	0.0841	0.7451	-0.1154	0.7667
0.1577	0.3423	0.3423	0.0893	0.6845	-0.1151	0.7671
0.1828	0.3172	0.3172	0.0929	0.6331	-0.1147	0.7678
0.2044	0.2956	0.2956	0.0957	0.5912	-0.1144	0.7684
0.2232	0.2768	0.2768	0.0979	0.5535	-0.1142	0.7687
0.2398	0.2602	0.2602	0.0997	0.5203	-0.1142	0.7687
0.2545	0.2455	0.2455	0.1012	0.4909	-0.1141	0.7689
I = 1.0						
1.0000	0.0000	0.0000	0.1513	0.0000	-0.1354	0.7321
0.8995	0.1005	0.1005	0.1489	0.1005	-0.1321	0.7378
0.8173	0.1827	0.1827	0.1467	0.1827	-0.1304	0.7406
0.7489	0.2511	0.2511	0.1446	0.2511	-0.1283	0.7442
0.6910	0.3090	0.3090	0.1427	0.3090	-0.1277	0.7452
0.6415	0.3585	0.3585	0.1410	0.3585	-0.1264	0.7475
0.5986	0.4010	0.4010	0.1393	0.4014	-0.1263	0.7476
0.5610	0.4390	0.4390	0.1378	0.4390	-0.1255	0.7490
0.5279	0.4721	0.4721	0.1363	0.4721	-0.1251	0.7497
0.4985	0.5015	0.5015	0.1349	0.5015	-0.1249	0.7500
0.4722	0.278	0.278	0.1336	0.5278	-0.1245	0.7507
0.1059	0.8941	0.8941	0.0964	0.8941	-0.1245	0.7507
0.1915	0.8085	0.8085	0.1113	0.8085	-0.1245	0.7507
0.2621	0.7379	0.7379	0.1192	0.7379	-0.1245	0.7507
0.3214	0.6786	0.6786	0.1242	0.6786	-0.1245	0.7507
0.3719	0.6281	0.6281	0.1278	0.6281	-0.1245	0.7507
0.4153	0.5847	0.5847	0.1305	0.5847	-0.1243	0.7511
0.4532	0.5468	0.5468	0.1326	0.5468	-0.1243	0.7511
0.4864	0.5136	0.5136	0.1343	0.5136	-0.1245	0.7507
0.5159	0.4841	0.4841	0.1358	0.4841	-0.1249	0.7500

Contd…..

Activity coefficients of NaCl in the NaCl-$MgCl_2$-Glycine-H_2O System. at 25°C.

Conc. NaCl mol. kg^{-1}	Conc. $MgCl_2$ mol. kg^{-1}	Conc. Glycine mol. kg^{-1}	EmF Volts.	y_B	$\log\gamma_{NaCl}$	γ_{NaCl}
			***I* = 2.0**			
2.0000	0.0000	0.0000	0.1877	0.0000	-0.1532	0.7027
1.7908	0.2092	0.2092	0.1853	0.1046	-0.1482	0.7109
1.6212	0.3788	0.3788	0.1832	0.1894	-0.1451	0.7160
1.4809	0.5191	0.5191	0.1812	0.2595	-0.1432	0.7191
1.3630	0.6370	0.6370	0.1973	0.3185	-0.1411	0.7226
1.2625	0.7375	0.7375	0.1776	0.3687	-0.1398	0.7248
1.1758	0.8242	0.8242	0.1760	0.4121	-0.1386	0.7267
1.1002	0.8998	0.8998	0.1744	0.4499	-0.1378	0.7281
1.0338	0.9662	0.9662	0.1730	0.4831	-0.1374	0.7288
0.9749	1.0251	1.0251	0.1716	0.5125	-0.1368	0.7298
0.9224	1.0776	1.0776	0.1703	0.5388	-0.1362	0.7308
0.2201	1.7799	1.7799	0.1353	0.8898	-0.1321	0.7377
0.3966	1.6034	1.6034	0.1500	0.8017	-0.1331	0.7360
0.5412	1.4588	1.4588	0.1576	0.7294	-0.1337	0.7350
0.6619	1.3381	1.3381	0.1625	0.6690	-0.1347	0.7333
0.7642	1.2358	1.2358	0.1659	0.6179	-0.1351	0.7326
0.8519	1.1481	1.1481	0.1685	0.5740	-0.1361	0.7310
0.9280	1.0720	1.0720	0.1705	0.5360	-0.1359	0.7313
0.9946	1.0054	1.0054	0.1721	0.5027	-0.1367	0.7299
1.0535	0.9465	0.9465	0.1734	0.4733	-0.1373	0.7289
I = 3.0						
3.0000	0.0000	0.0000	0.2118	0.0000	-0.1723	0.6725
2.6851	0.3149	0.3149	0.2095	0.1050	-0.1639	0.6856
2.4301	0.5699	0.5699	0.2074	0.1900	-0.1599	0.6920
2.2193	0.7807	0.7807	0.2055	0.2602	-0.1562	0.6979
2.0421	0.9579	0.9579	0.2037	0.3193	-0.1542	0.7011
1.8911	1.1089	1.1089	0.2020	0.3693	-0.1523	0.7042
1.7610	1.2390	1.2390	0.2004	0.4130	-0.1514	0.7057
1.6476	1.3524	1.3524	0.1989	0.4508	-0.1499	0.7081
1.5479	1.4521	1.4521	0.1975	0.4840	-0.1488	0.7099
1.4596	1.5404	1.5404	0.1961	0.5135	-0.1481	0.7110
1.3808	1.6192	1.6192	0.1949	0.5397	-0.1473	0.7124
0.3679	2.6321	2.6321	0.1630	0.8774	-0.1402	0.7241
0.6554	2.3446	2.3446	0.1772	0.7815	-0.1418	0.7214
0.8863	2.1137	2.1137	0.1845	0.7046	-0.1431	0.7193
1.0758	1.9242	1.9242	0.1891	0.6414	-0.1443	0.7172
1.2341	1.7659	1.7659	0.1923	0.5886	-0.1454	0.7155
1.3684	1.6316	1.6316	0.1947	0.5439	-0.1463	0.7140
1.4836	1.5164	1.5164	0.1965	0.5055	-0.1472	0.7125
1.5837	1.4163	1.4163	0.1980	0.4721	-0.1477	0.7117
1.6714	1.3286	1.3286	0.1992	0.4429	-0.1485	0.7104

RESULT AND DISCUSSION

The Model. One aim of this work is the calculation of various thermodynamic properties of aqueous amino-acid and oligopeptide solutions with a physically sound model and a minimal parameter set. Properties of interest are solution density, vapor-pressure depression, solute activity coefficient, and solubility. For this purpose, the PC-SAFT equation of state appears to be most appropriate. It has proved its flexibility and excellent performance in the modeling of complex systems.

Activity and Osmotic Coefficients in Amino-Acid Solutions.

In this work the osmotic coefficients of the binary amino-acid solutions water/glycine, water/valine, water/leucine, water/methionine, and water/cysteine were measured at 25 □C. Whereas in the glycine, valine, and leucine systems such data is already available in literature, the osmotic coefficients for water/methionine and water/cysteine are presented for the first time. The respective values of the aqueous leucine, cysteine, and methionine systems measured at 25^0 C.

Parameter Estimation for PC-SAFT

For the parameter regression of DL-methionine, Fuchs et al.[15] have used experimental sublimation pressures. However, only little of such experimental data is available for pure amino acids and peptides as they decompose before sublimation. Moreover, the relative mean deviations are fairly large since the absolute sublimation pressures are very low.

Ternary Systems Containing Two Amino Acids

Up to this point, binary aqueous mixtures have been investigated. Model parameters have been fitted for amino acids as well as for small peptides. In a previous paper1 we have already shown that amino-acid solubilities can be predicted in multisolute aqueous solutions based on these pure-component parameters only. In the following, the applicability of PC-SAFT for modeling osmotic coefficients of aqueous solutions containing two amino acids will be discussed briefly.

As earlier for modeling amino-acid solubilities, the interaction between the two solutes does not have to be parametrized. Thus, PC-SAFT combined with the presented amino-acid parameters is expected to predict thermodynamic properties of aqueous solutions.

CONCLUSION

Thermodynamic properties of aqueous amino-acid were investigated. water activity coefficients were determined for the first time. Such data is of crucial interest as many proteins (e.g., keratin) mainly consist of these amino acids. Osmotic coefficients in aqueous peptide solutions decrease with increasing molecular weight of the peptide. However, this is reversed in aqueous amino-acid systems: the successive addition of one methylene group to the glycyl basis in the series from glycine to R-AVA causes increasing osmotic coefficients. This apparent contradiction is caused by the enthalpy-driven behavior in amino-acid solutions: whereas glycine and its peptides induce an increasing of the partial molar excess enthalpy of water, the addition of hydrophobic amino acids to water causes decreased enthalpies. The series of water excess enthalpies is in accordance with the series of water activity coefficients, that is, unpolar solutes cause lower water activity coefficients and therewith strengthen the water-water interaction in the liquid phase and vice versa for polar solutes. Moreover, increasing osmotic coefficients (and decreasing water activity coefficients) are observed for amino-acid isomers with (1) branched instead of aliphatic methylene groups and (2) with decreasing dipole moment (from γ- to R-amino acids).

The PC-SAFT model has been applied for modeling solution densities, activity coefficients, and solubilities of the amino acids in water. Using a single parameter set per solute, PC-SAFT is able to accurately describe all the considered thermodynamic properties. Moreover, PC-SAFT allows for quantitative predictions of osmotic coefficients in systems containing two amino acids without fitting additional parameters.

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