Thermodynamics, Experimental, and Modelling of Aqueous Electrolyte and Amino Acid Solutions

Breil, Martin Peter; Mollerup, Jørgen

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Martin P. Breil

2001

IVC-SEP

Department of Chemical Engineering

Technical University of Denmark

DK-2800 Kongens Lyngby, Denmark

Preface

This thesis is submitted as a partial fulfilment of the Ph.D. degree at the Technical University of Denmark.

The project, granted by the IVC-SEP, has been carried out from October 1998 to September 2001 at the Department of Chemical Engineering, Technical University of Denmark under the supervision of Jørgen Mollerup. I wish to thank my supervisor for his guidance, his ideas, and his ability to encourage me.

I would also like to thank Kaj Thomsen for our many discussions on matters of electrolytes and for letting me borrow articles from his extensive library when necessary.

My thanks also extend to the people that I met during my sabbatical at the Kluyver Laboratory for Biotechnology, Delft University of Technology in the Netherlands. Especially, Luuk van der Wielen and Marcel Ottens who made the stay possible, and Susanne Rudolph who was my supervisor.

Finally, I wish to thank the staff of the IVC-SEP and of the Kluyver Laboratory for making the past three years so successful.

Martin Peter Breil

Kongens Lyngby, September 2001

Summary

The thesis addresses the thermodynamics involved when describing the properties of solutions of amino acids and dipeptides. Furthermore, it presents the solubility measurements of two dipeptides (glycylglycine and glycyl-L-alanine) in aqueous salt solutions and electrode potential measurements of the same two dipeptides in aqueous NaCl solutions.

Chapter 1 is an introduction to the chemistry of amino acids and dipeptides. It presents the principles of the Bjerrum diagram and the isoelectric point of a polyvalent compound. The industrial and medical use of amino acids is briefly touched.

Chapter 2 is the main thermodynamic chapter where most of the required properties are presented and defined. The schism of defining the activity coefficient at infinite dilution in a non-binary mixture is pointed out as well as the alternative types of concentration scales.

In Chapter 3 the four most common types for experimental methods for determination of solvent or solute activity are described by using the thermodynamic properties of the proceeding chapter.

Chapter 4 focuses on the thermodynamics of electrochemistry and is based on the principles of Chapter 2. As an example experimental data obtained on a so-called Harned cell is presented.

Chapter 5 presents the results of the experimental work carried out during the sabbatical, namely the solubility of glycylglycine and glycyl-L-alanine in aqueous NaCl, Na_2SO_4, and $(NH_4)_2SO_4$ solutions - and electrode potential measurements with ISE's of solutions containing NaCl and the two dipeptides mentioned above.

Chapter 6 presents the basis for the so-called McMillan-Mayer framework in relation to statistical thermodynamics and in relation to the usual (Lewis-Randall) framework.

In Chapter 7, the osmotic equilibrium and limitations of the van't Hoff equation are examined.

In Chapter 8, the continuum concept is described and related to the McMillan-Mayer framework. Different types of electrolyte models are presented: Debye-Hückel, extended UNIQUAC, and HS-MSA. The usually approach to model solubility data is presented.

In Chapter 9, the modelling results of the extended UNIQUAC model on binary and ternary aqueous solutions containing amino acid are presented. The solubility prediction of the extended UNIQUAC model commented. Furthermore, an analysis of the behaviour of the HS-MSA model in electrolyte solutions is carried out and commented.

Chapter 10 is giving an overview of the extent of the database created during this project.

Chapter 11 is a conclusion, summarising the results achieved during this project.

Three appendices are included: one on Euler's theorem, one on equilibrium, and one on electrostatics.

Resumé på dansk

Afhandlingen omhandler den termodynamik, der er involveret, når man skal beskrive egenskaberne af opløsninger af aminosyrer og dipeptider. Ydermere præsenteres opløselighedsmålinger af to dipeptider (glycylglycin og glycyl-L-alanin) i vandige salt-opløsninger og målinger af elektrode-potentialer af de samme to dipeptider i vandig NaCl opløsninger.

Kapitel 1 er en introduktion til aminosyrer og dipeptiders kemi. Det præsenterer principperne ved Bjerrum-diagrammerne og det isoelektriske punkt af et fler-valent stof. Den industrielle og medicinale brug af aminosyrer er kort berørt.

Kapitel 2 er det centrale termodynamiske kapitel, hvor de fleste af de krævede egenskaber er præsenteret og defineret. Skismaet ved definitionen af aktivitetskoefficienten ved uendelig fortynding i en ikke-binær blanding er belyst, ligeledes som alternative koncentrationsskalaer.

I Kapitel 3 er de fire mest almindelige typer af eksperimentelle metoder til bestemmelse af aktiviteten af opløsningsmidlet eller det opløste stof beskrevet af hjælp af de termodynamiske egenskaber fra det foregående kapitel.

Kapitel 4 fokuserer på termodynamikken i elektrokemien og er baseret på principperne fra Kapitel 2. Som et eksempel er eksperimentelle data fra en såkaldt Harned-celle præsenteret.

Kapitel 5 præsenterer resultaterne af det eksperimentelle arbejde, som er udført under det eksterne forskningsophold, nemlig opløseligheden af glycylglycin og glycyl-L-alanin i vandig NaCl, Na_2SO_4 og $(NH_4)_2SO_4$ opløsninger - og målinger af elektrode-potentialer med ionselektive elektroder i opløsninger indeholdende NaCl og de to ovennævnte dipeptider.

Kapitel 6 præsenterer grundlaget for det såkaldte McMillan-Mayer framework i relation til statistisk termodynamik og i relation til det sædvanlige (Lewis-Randall) framework.

I Kapitel 7 forklares den osmotiske ligevægt og begrænsningerne af van't Hoff-ligningen.

I Kapitel 8 beskrives kontinuum-konceptet og relateres til McMillan-Mayer framework'et. Forskellige typer af elektrolyt-modeller er præsenterede: Debye-Hückel, udvidet UNIQUAC og HS-MSA. Den sædvanlige måde, hvorpå opløselighedsdata modelleres, er præsenteret.

I Kapitel 9 præsenteres modelleringsresultaterne fra den udvidede UNIQUAC-model på binære og ternære vandige opløsninger indeholdende aminosyre. Den udvidede UNIQUAC-

models forudsagte opløseligheder er kommenteret. Ydermere er der udført en analyse af forløbet af HS-MSA-modellen i elektrolyt-opløsninger og kommenteret.

Kapitel 10 giver et overblik over omfanget af den database, som er skabt i løbet af projektet.

Kapitel 11 er en konklusion, der opsummerer de opnåede resultater.

Tre appendices er inkluderede: ét om Euler's theorem, ét om ligevægt og ét om elektrostatik.

Table of Contents

1. Introduction to the Chemistry of Amino Acids

Amino acids are found in all living organisms on Earth. Also in meteorites traces of amino acids have been discovered, Jakubke and Jeschkeit (1982). But despite their universal presence, their structure and their behaviour are not equally widespread. This chapter gives an introduction to the chemistry of amino acids and its purpose is to present some of the fundamental properties of amino acids.

1.1 Structure of amino acids

From a chemical viewpoint an amino acid is a base as well as an acid; i.e. it consists both of an amino group and a carboxylic group. The amino acid is therefore an ampholyte since it can react both as a base and as an acid. The most common amino acids are the α-amino acids, which are amino acids where the amino group is located at the α-carbon atom of the carboxylic group as shown in Figure 1.1. The α-carbon atom (usually) has hydrogen and a side chain at the last two sites.

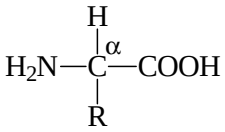


Figure 1.1: Basic structure of an α-amino acid.

If also the side chain is hydrogen, the compound is the simplest of amino acids, namely glycine, as presented in Figure 1.2.

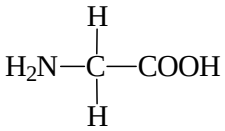


Figure 1.2: Glycine - the simplest α-amino acid.

Among the α-amino acids, it is only glycine that does not have a chiral α-carbon atom since two of the neighbouring groups are hydrogen. However, in nature more than 180 different amino acids are encountered (Jakubke and Jeschkeit, 1982). Twenty of these are denoted

natural amino acids (or primary protein amino acids), of which 19 are α-amino acids and one is a cyclic α-amino acid (proline). These are presented in Table 1.1 on page 9. The reason for naming them 'natural' is that they are the building blocks of those proteins encountered in nature. Two amino acids linked together by a peptide bond are called a dipeptide, which is shown in Figure 1.3. Continuing this process of dehydration will eventually lead to the formation of protein. By convention, peptides of molecular weight up to 10,000 are known as polypeptides and above that as proteins, Morrison and Boyd (1992).

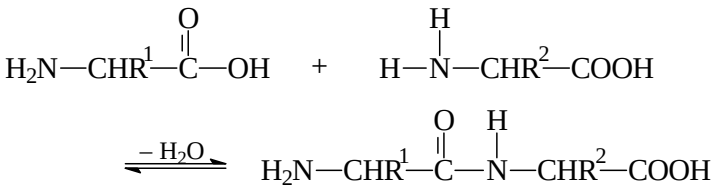


Figure 1.3: The principle of dehydration of two amino acids forming a dipeptide.

Contrary to plants and some microorganisms, animals and humans are only capable of synthesising 10 of the 20 naturally occurring amino acids. The rest must be included in the diet; these amino acids are classified as *essential*. An asterisk in Table 1.1 marks these essential amino acids.

The naturally occurring amino acids all have trivial names. The names are related to either the material from which the amino acid was isolated for the first time, the method applied to isolated them, or a structural resemblance to known compounds (Jakubke and Jeschkeit, 1982). The naming of dipeptides is based on the trivial names of the amino acids. The dipeptide is written with the amino group on the left and the carboxyl group on the right, and then the dipeptide is named according to the sequence of the amino acids, read from left to right. Two dipeptides are shown at the end of Table 1.1.

1.2 Stereochemistry

Because of the chirality of the α-carbon atom the amino acids exist in two enantiomers. These mirror images are able to rotate polarised light. They are said to be optically active. An amino acid that rotates the light clockwise (+) is denoted D, and anti-clockwise (–) L. The DL-notation is experimentally based, only. All naturally occurring amino acids have the same direction of rotation as L-(–)-glyceraldehyde, Morrison and Boyd (1992), see Figure 1.4.

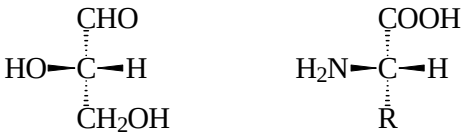


Figure 1.4: Projections of L-glyceraldehyde and an L-amino acid, respectively. The groups vertically attached to the central carbon atom are pointing away from the observer and those groups attached horizontally are pointing towards the observer.

1.3 The influence of pH

Amino acids have a higher solubility in polar solvents (e.g. water, ammonia) than in non-polar solvents (e.g. ethanol, methanol, acetone), Jakubke and Jeschkeit (1982). The reason for this is the equilibrium

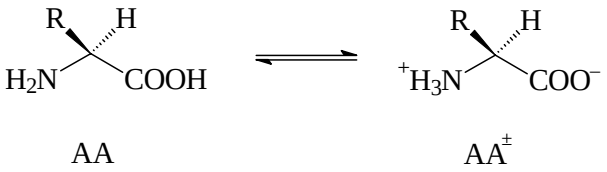


Figure 1.5: Equilibrium of the uncharged species AA and the zwitterion $AA^{\pm}$.

which is a reaction that lies far to the right in polar solvents. The gain in energy is 44.8 - 51.5 kJ / mole (Jakubke and Jeschkeit, 1982). $AA^{\pm}$ is the amino acid in the so-called *zwitterionic* form. The German word *Zwitter* means hybrid or hermaphrodite. The unchanged amino acid, AA, will have a dipolar moment due to the two functional groups. The zwitterion do not have a dipole, but on the other hand nor is it an ion since its ionic groups are not entitled to move freely. In Anglo-Saxon literature the zwitterion is sometimes referred to as the *dipolar ion*.

Furthermore, the amino acid is capable of assuming a cationic and an anionic form. Depending on the side chain there might be even more ionic configurations. For the naturally occurring amino acids the pK_a-values for the amino group are approximately 1.8 - 2.8 (CRC Handbook of Chemistry and Physics, 78th Edition). Consequently, the amino acid will be fully protonised at low pH (pH < 1). In the other end of the acidity scale (pH > 13) the amino acid will be stripped of all acidic hydrogen since the pK_a-values for the carboxylic group are 8.9 - 10.6.

Assuming ideal solution theory (see Chapter 2. Basic Thermodynamics) all dissociation reactions arisen from one amino acid can, generally, be written as eq. (1.1).

$$\begin{aligned} A^m &= A^{m-1} + H^+ & K_1^c &= \frac{[A^{m-1}][H^+]}{[A^m]} \\ &\vdots & &\vdots \\ A^{m-(n-1)} &= A^{m-n} + H^+ & K_n^c &= \frac{[A^{m-n}][H^+]}{[A^{m-(n-1)}]} \end{aligned} \qquad (1.1)$$

where n is the number dissociation reactions (there are n + 1 species of any given amino acid), m is the maximum number of positive charge on the amino acid, and K_j^c is the equilibrium constant for the dissociation of reaction j based on molarities. The unit of K_j^c is mole per litre. Greenstein and Winitz (1961) presented tables listing the apparent pK'_a values of many amino acids. The apparent K'_j values are identical to the dissociation constants K_j^c as defined in eq. (1.1) except that it is the proton activity instead of the proton concentration. Therefore the K'_j values are dimensionless. However, under the present assumptions (ideal solution) K' is equal to K^c. Greenstein and Winitz (p. 482) state that for all practical purposes, the apparent K' values may be employed with nearly equal validity in eq. (1.1).

In total there are n equations (n dissociation reactions, eq. (1.1)) to describe 2n + 1 unknowns, $[A^m]$, …, $[A^{m-n}]$, $[H^+]$, and $K_0^c, ..., K_n^c$). Specifying the dissociation constants and the pH the problem is feasible. In order to have dimensionless concentrations the relative concentration of any given species *k* of the amino acid is introduced

$$\alpha_k = \frac{[A^{m-k}]}{c_T} \qquad \text{for } k = 0, \ldots, n \qquad (1.2)$$

where c_T is the total concentration of the amino acid given by

$$c_T = \sum_{i=0}^{n} [A^{m-i}] \qquad (1.3)$$

Because of eq. (1.3) the concentration of the products of the n dissociation reactions are rewritten as

$$\begin{aligned} [A^{m-1}] &= \frac{K_1^c [A^m]}{[H^+]} \\ &\vdots \quad \vdots \\ [A^{m-n}] &= \frac{K_n^c [A^{m-(n-1)}]}{[H^+]} \end{aligned} \qquad (1.4)$$

All the concentrations are then expressed by means of the dissociation constants, the concentration of hydrogen, and the concentration of A^m.

$$\begin{aligned} [A^{m-1}] &= \frac{K_1^c [A^m]}{[H^+]} \\ &\vdots \qquad\qquad \vdots \\ [A^{m-n}] &= \frac{K_1^c K_2^c \cdots K_n^c [A^m]}{[H^+]^n} \end{aligned} \tag{1.5}$$

These expressions for concentrations, eq. (1.5), are then inserted in eq. (1.3) to determine c_T.

$$\begin{aligned} c_T &= [A^m] + \sum_{i=1}^{n} \frac{[A^m]}{[H^+]^i} \prod_{j=1}^{i} K_j^c \\ &= [A^m] \left(1 + \sum_{i=1}^{n} \frac{1}{[H^+]^i} \prod_{j=1}^{i} K_j^c \right) \\ &= \frac{[A^m]}{[H^+]^n} \left(\sum_{i=0}^{n} [H^+]^{n-i} \prod_{j=0}^{i} K_j^c \right) \qquad , K_0^c \equiv 1 \end{aligned} \tag{1.6}$$

Note that for the sake of simplicity K_0^c has been defined as unity. With eq. (1.6) the relative concentration for any given species *k* of the amino acid is expressed as a function of pH and the dissociation constants.

$$\begin{aligned} \alpha_k(\mathrm{pH}, \mathbf{K}^c) &= \frac{1}{c_T} \frac{K_1^c K_2^c \cdots K_k^c}{[H^+]^k} [A^m] = \frac{1}{c_T} \frac{[A^m]}{[H^+]^k} \prod_{j=0}^{k} K_j^c \\ &= \frac{[H^+]^n}{[H^+]^k} \frac{\prod_{j=0}^{k} K_j^c}{\sum_{i=0}^{n} [H^+]^{n-i} \prod_{j=0}^{i} K_j^c} = \frac{[H^+]^{-k} \prod_{j=0}^{k} K_j^c}{\sum_{i=0}^{n} [H^+]^{-i} \prod_{j=0}^{i} K_j^c} \end{aligned} \tag{1.7}$$

One way of illustrating the relative concentrations of any polyfunctional compound is the so-called Bjerrum diagram as shown in Figure 1.6.

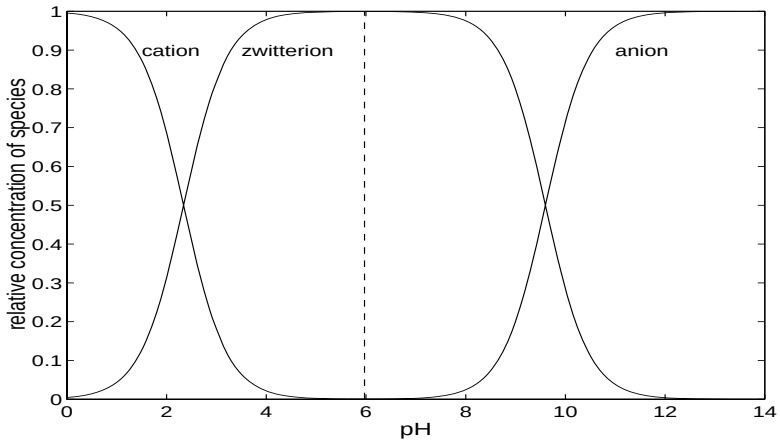


Figure 1.6: The Bjerrum diagram of glycine. The relative concentrations of cation, zwitterion, and anion as a function of pH. The dotted line is at the isoelectric point, pI = 5.97. The pK'_a values are 2.34 and 9.60 of Greenstein and Winitz, 1961.

The pK'_a values are graphically represented in Figure 1.6 as the intercepts between cation and zwitterion, pH = 2.34, and between zwitterion and anion, pH = 9.60.

1.4 The isoelectric point

The isoelectric point is defined as the pH where the number of the positively charged ions (cations) of the amino acid is equal to the number of the negatively charged ions (anions). So the net charge of all the species of the ampholyte are zero. "*Historically, this (the isoelectric point) is defined as the point at which an amphoteric electrolyte when subjected in a solution to a source of direct current will move towards neither positive nor negative pole*", Greenstein and Winitz, p. 482; their reference is W.B. Hardy, Proceedings of the Royal Society (London), B, 66, 110 (1900). Writing up a charge balance at the isoelectric point gives

$$\begin{aligned} &m \cdot \alpha_0 + (m-1) \cdot \alpha_1 + ... + (m-m) \cdot \alpha_m + ... \\ &\qquad +(m-(n-1)) \cdot \alpha_{n-1} + (m-n) \cdot \alpha_{m-n} = 0 \qquad \text{, or} \qquad (1.8) \\ &\sum_{k=0}^{n} (m-k) \cdot \alpha_k = 0 \end{aligned}$$

Inserting eq. (1.7) and assuming that the proton concentration is not zero gives

$$\sum_{k=0}^{n} (m-k) \cdot [H^+]_{iso}^{-k} \prod_{j=0}^{k} K_j^c = 0 \qquad (1.9)$$

Note that eq. (1.9) is independent of the total amino acid concentration. Consequently, the isoelectric point is a property that is specific for each compound. Solving eq. (1.9) for glycine gives an isoelectric point of 5.97. In the case of glycine, the isoelectric point is more like an isoelectric band between pH 5 and pH 7 as shown in Figure 1.6.

Having the relative concentrations of the species of the amino acid the net charge z_{net} of the molecule is easily deducted.

$$z_{net}(\mathrm{pH}, \mathbf{K}^c) = \sum_{k=0}^{n} (m - k) \cdot \alpha_k(\mathrm{pH}, \mathbf{K}^c) \tag{1.10}$$

From eq. (1.10) it is seen that the net charge is a function of pH and dissociation constants wherefore Figure 1.7 shows the average charge of a glycine solution as a function of pH. It is clearly observed that glycine is a divalent amino acid since it has two equivalence points.

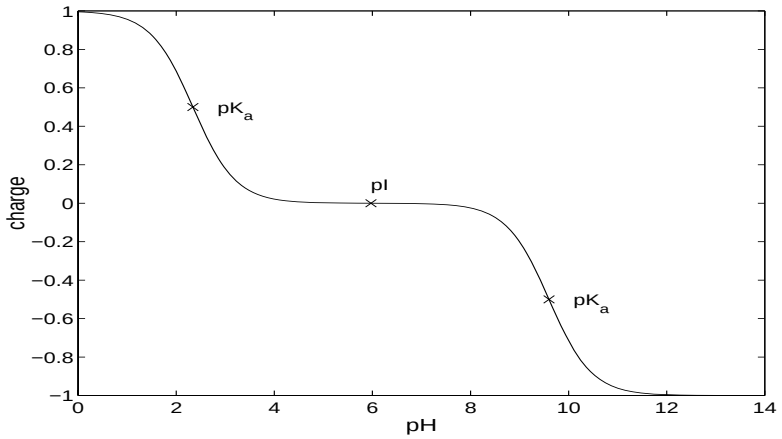


Figure 1.7: The average charge of glycine as function of pH. This is almost an equivalent to a titration curve. Both the pK'_a values and the isoelectric point, pI, are shown.

When a given amount of an amino acid is dissolved in pure water, the pH will begin to approach the pH of the isoelectric point, pI, as shown in Figure 1.8. If the amount of amino acid was not sufficient to reach the pI, the pH of the solution will be somewhere between pH = 7 (that of pure water) and pH = pI.

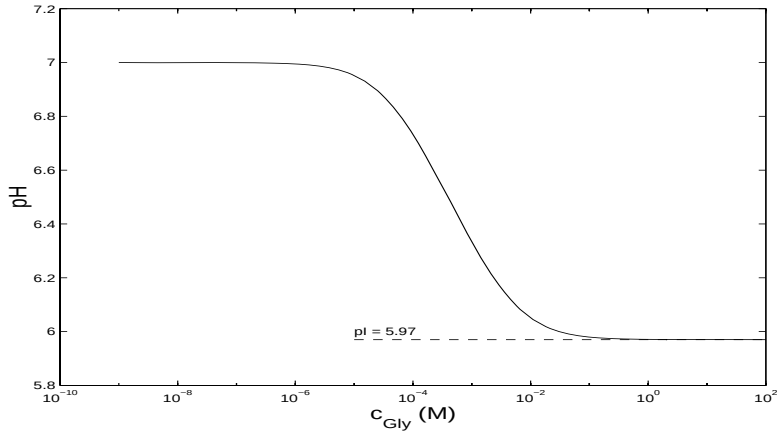


Figure 1.8: The pH as a function of molarity of glycine.

By comparing the Bjerrum diagram, Figure 1.6, and Figure 1.8 we can see that the only configuration of glycine present in any glycine - water solution will be the neutral zwitterion - whatever the amino acid concentration.

For some of the amino acids with functional groups in the side chain, e.g. aspartic acid, the zwitterionic form will not be the only form present at pI as shown in Figure 1.9. At the isoelectric point only 80% of the aspartic acid is in the zwitterionic configuration. In these cases it will be inappropriate to treat the amino acid solution as if the solution contained the zwitterionic form, only.

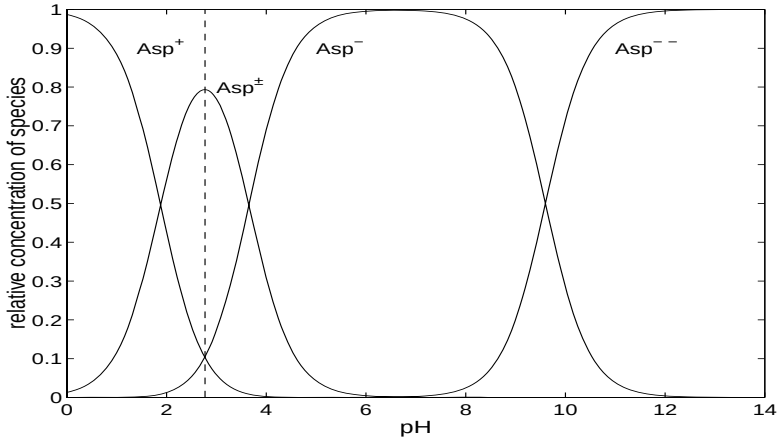


Figure 1.9: The Bjerrum diagram of aspartic acid. The relative concentrations of cation (Asp^+), zwitterion ($Asp^\pm$), and anions (Asp^- and Asp^{--}) as a function of pH. The dotted line is at the isoelectric point, pI = 2.77. The pK'_a values are 1.88, 3.65, and 9.60 (Greenstein and Winitz, 1961).

1.5 The use of amino acids

Amino acids have a broad spectrum of applications. One of the main uses of amino acids is as an additive in the food industry, e.g. glycine is used for sweet jams and salted vegetables, sauce, vinegar and fruit juice. The reason is that the taste of the naturally occurring amino acids is categorised as either bitter or sweet, Barrett (1985), p.8. As previously mentioned the naturally occurring amino acids are L-enantiomer but changing the configuration to the D-enantiomer gives a sweeter taste. Furthermore, interactions between amino acids and sugar can give rise to pleasant odours. An example is proline and glucose that together produce an odour of newly baked bread, Barrett (1985), p.8.

The other major use of amino acids is as buffers or acid correctors. Glycine is used as such in wine and soft beverage. Likewise glycine also finds use as an anti-oxidant in e.g. cream and cheese. Because glycine also retains the reproduction of bacteria, e.g. E. coli., is used as an antiseptic agent for fish flakes.

Glycine is medically used in amino acid injection solution as nutritional infusion and as a raw material for making L-Dopa, a pharmaceutical for treating Parkinson's disease.

In the fertiliser industry glycine is used as a solvent for removing CO_2. Glycine is also an intermediate in the production of pesticides.

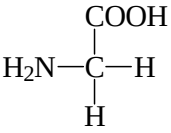
The application of a number chemical compounds and pharmaceuticals are given on the internet at the address http://www.gtamart.com/mart/products/chemical/zhitgaa.htm.

Table 1.1: Most chemicals have a three-dimensional structure and to visualise that in the two-dimensional space calls for a projection. In organic chemistry the Fisher projection is designed to accomplish just that. The two groups to the left and right of the α carbon atom are pointing out of the plane towards the observer whereas the other two groups are pointing into the plane away from the observer.

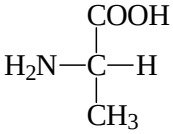
Fisher projection

The amino acids are sometimes divided into four subsections: non-polar, polar, acidic, and basic amino acids.

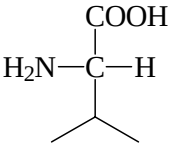
Non-polar amino acids (hydrophobic)



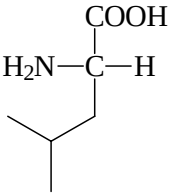
glycine



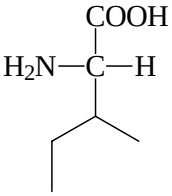
L-alanine



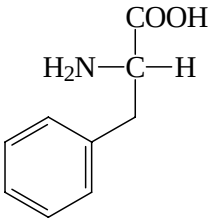
L-valine*



L-leucine*



L-isoleucine*



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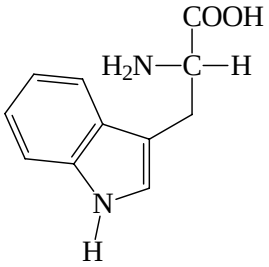

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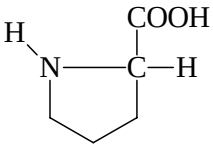
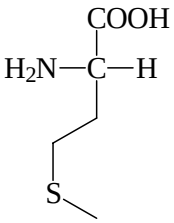
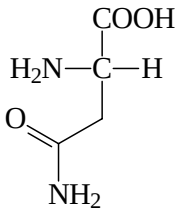


L-proline

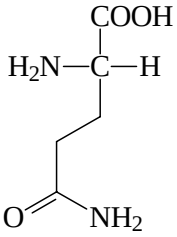


L-methionine*

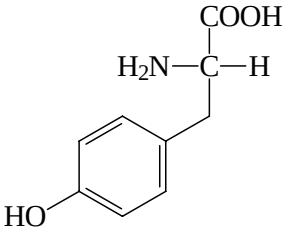
Polar amino acids (hydrophilic)



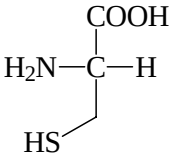
L-asparagine



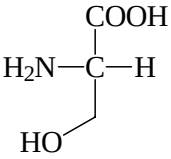
L-glutamine



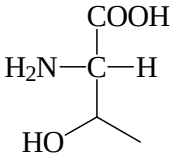
L-tyrosine



L-cysteine

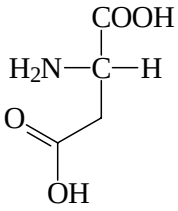


L-serine

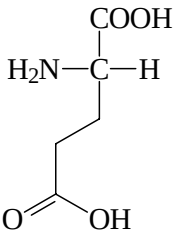


L-threonine*

Acidic amino acids

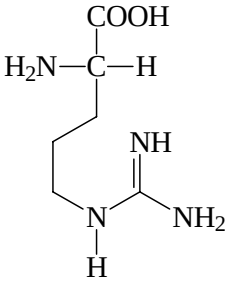


L-aspartic acid

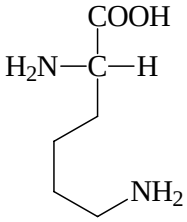


L-glutamic acid

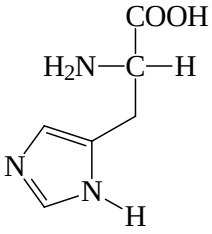
Basic amino acids



L-arginine*

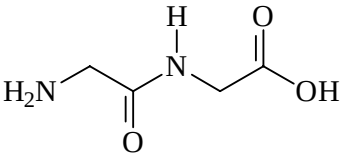


L-lysine*

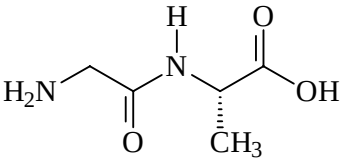


L-histidine*

Two dipeptides



glycylglycine



glycyl-L-alanine

* essential amino acids

Now having the basic knowledge of the structure and behaviour of amino acids the attention is turned to the thermodynamics. This is necessary in order to describe - in detail - the chemical behaviour of amino acid solutions.

2. Basic Thermodynamics

The purpose of this chapter is to derive the thermodynamic properties that will be used in this thesis. The philosophy of this derivation is to begin by defining the residual property and then define one ideal and one real solution. The rest of the properties are derived from these definitions.

2.1 States

The state of a system is usually described by one of the following two sets of variables (T,P,**n**) or (T,V,**n**). It is possible to describe the state of a system by specifying another set of variables, but these two are the most common ones. Among the variables there is a distinction between intensive and extensive variables. The latter variables are additive, e.g. volume, mole numbers, contrary to the former variables, e.g. temperature and pressure. Each intensive variable has a conjugated extensive variable; entropy and temperature, volume and pressure, mole and chemical potential, Michelsen and Mollerup (2000), p. 6.

The distinction between intensive and extensive variables is essential when dealing - for instance - with the Gibbs-Duhem equation, see Appendix A, which states

$$\sum_i \left(\frac{\partial M}{\partial a_i}\right)_{a_j,\mathbf{b}} da_i - \sum_i b_i \, d\left(\frac{\partial M}{\partial b_i}\right)_{\mathbf{a},b_j} = 0 \tag{2.1}$$

where M is a state function, **a** is the vector of intensive variables, and **b** is the vector of extensive variables. A property M can be can by the state (T,P,**n**) and by the state (T,V,**n**). The Gibbs-Duhem equation will look different for these two states due to the fact the second variable is intensive and extensive, respectively, in the two state descriptions,

$$\left(\frac{\partial M}{\partial T}\right)_{P,\mathbf{n}} dT + \left(\frac{\partial M}{\partial P}\right)_{T,\mathbf{n}} dP - \sum_i n_i \, d\left(\frac{\partial M}{\partial n_i}\right)_{T,P,n_j} = 0 \tag{2.2}$$

and

$$\left(\frac{\partial M}{\partial T}\right)_{V,\mathbf{n}} dT - V \, d\left(\frac{\partial M}{\partial V}\right)_{T,\mathbf{n}} - \sum_i n_i \, d\left(\frac{\partial M}{\partial n_i}\right)_{T,V,n_j} = 0 \tag{2.3}$$

2.2 The residual property of the Gibbs energy

A property M at the state (T,P,**n**) can be expressed by two terms

$$M(T,P,\mathbf{n}) = M^{*}(T,P,\mathbf{n}) + M^{r}(T,P,\mathbf{n}) \tag{2.4}$$

where $M^{*}(T,P,\mathbf{n})$ is the property M as a hypothetical ideal gas at the state (T,P,**n**). The difference between the property M at the state (T,P,**n**) and $M^{*}(T,P,\mathbf{n})$ is called the residual property of M, $M^{r}(T,P,\mathbf{n})$.

2.3 Pure phase

A pure phase is a phase that consists of one species, only. Therefore, the state of a pure phase is specified by (T,P,n) or (T,V,n). (Note that n is a scalar and not a vector).

The residual Gibbs energy of a pure phase at the state (T,P,n) is written as $G^{r}(T,P,n)$. The unit of $G^{r}(T,P,n)$ is joules, J. The molar residual Gibbs energy of the pure phase, $g^{r}(T,P)$, has the unit joules per mole, J/mole. Note that this property does not depend on the mole number - but only on temperature and pressure. As a consequence we have

$$G^{r}(T,P,n) = n \cdot g^{r}(T,P) \tag{2.5}$$

The partial molar residual Gibbs energy of a pure phase at the state (T,P,n) is called the residual chemical potential of a pure phase, $\mu^{r}(T,P)$. This property has the unit of joules per moles, J/mole. By definition it is independent of the mole number.

$$\mu^{r}(T,P) = \overline{G}^{r}(T,P) \equiv \left(\frac{\partial G^{r}(T,P,n)}{\partial n}\right)_{T,P} = \left(\frac{\partial n \cdot g^{r}(T,P)}{\partial n}\right)_{T,P} = g^{r}(T,P) \tag{2.6}$$

2.4 The one species in the pure phase

Logically, the properties of the pure phase are identical to those of the one species *i* forming that phase. Therefore the residual Gibbs energy of species *i* in a pure phase, the molar residual Gibbs energy of species *i* in a pure phase, and the residual chemical potential of species *i* in a pure phase are denoted by a subscript *i*, $G_i^{r}(T,P,n_i)$, $g_i^{r}(T,P)$, and $\mu_i^{r}(T,P)$, respectively. Eq. (2.5) is valid as eq. (2.7)

$$G_i^r(T,P,n_i) = n_i \cdot g_i^r(T,P) \tag{2.7}$$

and as a consequence one has

$$\mu_i^r(T,P) = \overline{G}_i^r(T,P) \equiv \left(\frac{\partial G_i^r(T,P,n_i)}{\partial n_i}\right)_{T,P} = \left(\frac{\partial n_i \cdot g_i^r(T,P)}{\partial n_i}\right)_{T,P} = g_i^r(T,P) \tag{2.8}$$

Utilising eq. (2.4) the chemical potential of the species *i* in a pure phase at the state (T,P,n_i) is

$$\mu_i(T,P) = \mu_i^*(T,P) + \mu_i^r(T,P) \tag{2.9}$$

where $\mu_i^*(T,P)$ is the (hypothetical) chemical potential of the pure species *i* as an ideal gas at T and P. This potential is achieved as

$$\begin{aligned} G_i^*(T,P,n_i) - G_i^*(T,P^o,n_i) &= \int_{P^o}^{P}\left(\frac{\partial G_i^*}{\partial P}\right)_T dP \\ &= \int_{P^o}^{P} V^* dP \end{aligned} \tag{2.10}$$

where P^o is an arbitrarily chosen set point pressure. The phase is treated as an ideal gas wherefore we make use of the ideal gas law

$$PV = nRT \qquad \text{or} \qquad PV = n_i RT \quad \text{for pure solutions} \tag{2.11}$$

so eq. (2.10) is rewritten as

$$\begin{aligned} G_i^*(T,P,n_i) - G_i^*(T,P^o,n_i) &= \int_{P^o}^{P}\frac{n_i RT}{P} dP \\ &= n_i RT \ln\frac{P}{P^o} \end{aligned} \tag{2.12}$$

Since the set point pressure is constant, the second term on the left-hand side is only a function of temperature

$$G_i^*(T,P^o,n_i) = n_i \mu_i^o(T) \tag{2.13}$$

Inserting eq. (2.13) into eq. (2.12) and formulate the corresponding (hypothetical) Helmholtz energy of the pure species *i* as an ideal gas one has

$$
\begin{aligned}
A_i^*(T,V,n_i) &= G_i^*(T,P,n_i) - (PV)^* \\
&= n_i\mu_i^o(T) + n_i RT \ln\frac{P}{P^o} - n_i RT \\
&= n_i\mu_i^o(T) + n_i RT\left(\ln\frac{n_i RT}{P^o V} - 1\right)
\end{aligned}
\tag{2.14}
$$

The (hypothetical) chemical potential of pure species *i* as an ideal gas is then

$$
\begin{aligned}
\mu_i^*(T,V) &= \left(\frac{\partial A^*(T,V,n_i)}{\partial n_i}\right)_{T,V} \\
&= \mu_i^o(T) + RT\ln\frac{n_i RT}{P^o V} \qquad \Rightarrow \\
\mu_i^*(T,P) &= \mu_i^o(T) + RT\ln\frac{P}{P^o}
\end{aligned}
\tag{2.15}
$$

This is the chemical potential of a pure phase treated as an ideal gas at T and P. One, then, postulates that the chemical of a pure phase treated as a real gas is

$$
\mu_i(T,P) = \mu_i^o(T) + RT\ln\frac{f_i(T,P)}{P^o} \tag{2.16}
$$

Thus defining fugacity f_i at T and P. The residual chemical potential of the pure phase of species *i* is expressed in terms of its fugacity

$$
\mu_i^r(T,P) = RT\ln\frac{f_i(T,P)}{P} = RT\ln\varphi_i(T,P) \tag{2.17}
$$

where $\varphi_i(T,P)$ by definition is the fugacity coefficient at T and P of species *i* in the pure phase.

2.5 Mixture

A mixture is a phase that consists of more than one species. Therefore, the state of a mixture is specified by (T,P,**n**) or (T,V,**n**).

The residual Gibbs energy, of a mixture, at the state (T,P,**n**) is written as $G^r(T,P,\mathbf{n})$. The unit of $G^r(T,P,\mathbf{n})$ is joules, J. The molar residual Gibbs energy of the mixture, $g^r(T,P,\mathbf{n})$, has the unit joules per mole, J/mole. Even though $g^r(T,P,\mathbf{n})$ depends on the vector of the mole numbers, it is independent of the total number of moles; it is only dependent of the composition of the mixture. So it would have been appropriate to give g^r in terms of (T,P,**x**)

instead, but this gives some disadvantages in regards to molar derivatives. **x** is the vector of the mole fractions.

2.6 Species in the mixture

The unit of the molar residual chemical potential of species *i* in the mixture is still joules per mole. It should be stressed that $\mu_i^r(T,P,\mathbf{n})$ is not dependent on the total number of moles but dependent on the composition of the mixture, **x**.

Utilising eq. (2.4) the chemical potential of the species *i* in a mixture at the state (T,P,**n**) is

$$\mu_i(T,P,\mathbf{n}) = \mu_i^*(T,P,\mathbf{n}) + \mu_i^r(T,P,\mathbf{n}) \tag{2.19}$$

where $\mu_i^*(T,P,\mathbf{n})$ is the (hypothetical) chemical potential of species *i* in the mixture treated as an ideal gas at the state (T,P,**n**). This potential is achieved by postulating that the (hypothetical) Helmholtz energy treated as an ideal gas is

$$A^*(T,V,\mathbf{n}) = \sum_k n_k \mu_k^o(T) + RT\sum_k n_k\left(\ln\frac{n_k RT}{P^o V} - 1\right) \tag{2.20}$$

in analogy to eq. (2.14). The potential is

$$\left(\frac{\partial A^*(T,V,\mathbf{n})}{\partial n_i}\right)_{T,V,n_{j\neq i}} = \mu_i^o(T) + RT\ln\frac{n_i RT}{P^o V} \tag{2.21}$$

when applying the ideal gas law, PV = nRT

$$\mu_i^*(T,P,\mathbf{n}) = \mu_i^o(T) + RT\ln\frac{x_i P}{P^o} \tag{2.22}$$

Since a chemical potential is a molar derivative, see Appendix A eq. (A.5), we have

$$G^*(T,P,\mathbf{n}) = \sum_i n_i \mu_i^*(T,P,\mathbf{n}) \tag{2.23}$$

For consistency eq. (2.22) is inserted into eq. (2.23) and the relation A = G – PV is used, and eq. (2.20) reappears. Finally, one postulates that the chemical potential of a species *i* in a real mixture is

$$\mu_i(T,P,\mathbf{n}) = \mu_i^o(T) + RT\ln\frac{\hat{f}_i(T,P,\mathbf{n})}{P^o} \tag{2.24}$$

where $\hat{f}_i(T, P, \mathbf{n})$ is the fugacity of species *i* in the mixture at the state (T,P,**n**). As a consequence, the fugacity coefficient of species *i* in the mixture, $\hat{\varphi}_i(T, P, \mathbf{n})$ is defined by

$$\mu_i^r(T, P, \mathbf{n}) = RT \ln \frac{\hat{f}_i(T, P, \mathbf{n})}{P x_i} = RT \ln \hat{\varphi}_i(T, P, \mathbf{n}) \tag{2.25}$$

Note that by subtracting eq. (2.15) from eq. (2.22), i.e. the two (hypothetical) chemical potentials of species *i* (ideal gas), one will arrive at the most often used description of an ideal solution, eq. (2.29).

2.7 Reference state

Since the chemical potential is a state function (independent of the way of integration, exact differential), one can choose the set point arbitrarily.

A reference state is arbitrary by definition. Choosing a reference state of species *i* in a system as the state where T and P are identical to those of the system and where species *i* is the only one, $\mu_i(T,P)$, the difference between the chemical potential of species *i* in the system and its reference is

$$\begin{aligned}
&\mu_i(T, P, \mathbf{n}) - \mu_i(T, P) \\
&\quad = \mu_i^*(T, P, \mathbf{n}) + \mu_i^r(T, P, \mathbf{n}) - \mu_i^*(T, P) - \mu_i^r(T, P) \\
&\quad = \mu_i^*(T, P, \mathbf{n}) - \mu_i^*(T, P) + \mu_i^r(T, P, \mathbf{n}) - \mu_i^r(T, P) \\
&\quad = RT \ln(P x_i) - RT \ln P + RT \ln \hat{\varphi}_i(T, P, \mathbf{n}) - RT \ln \varphi_i(T, P) \\
&\quad = RT \ln x_i + RT \ln \frac{\hat{\varphi}_i(T, P, \mathbf{n})}{\varphi_i(T, P)}
\end{aligned} \tag{2.26}$$

Defining the activity of species *i* as

$$a_i(T, P, \mathbf{n}) \equiv \frac{\hat{\varphi}_i(T, P, \mathbf{n}) \cdot x_i}{\varphi_i(T, P)} = \frac{\hat{f}_i(T, P, \mathbf{n})}{f_i(T, P)} \tag{2.27}$$

one has from eq. (2.26)

$$\mu_i(T, P, \mathbf{n}) = \mu_i(T, P) + RT \ln a_i(T, P, \mathbf{n}) \tag{2.28}$$

This is the chemical potential of species *i* at the state (T,P,**n**) in a real solution or a non-ideal solution.

2.8 Ideal solution

Besides defining the real solution, the ideal solution must also be defined. There is no unique definition of an ideal solution. However, normally the ideal solution is regarded as a solution without interactions among the species. Consequently, the ideal solution is based on pure component properties and the composition of the solution.

$$\mu_i^{id}(T,P,\mathbf{n}) = \mu_i(T,P) + RT \ln x_i \,. \tag{2.29}$$

The chemical potential of the ideal solution is denoted by superscript id. By defining the ideal solution by setting the activities equal to the mole fractions, one obtains a convenient state; the ideal gas will be an ideal solution - but not vice versa. Other concentration scales (e.g. molalities and molarities) are equally valid but the subsequent excess properties will differ from those derived in this work.

2.9 Definition of the activity coefficient

A real solution approaches the ideal solution when the system is approaching the limit where species *i* is the only one.

$$\lim_{x_i \to 1} \hat{f}_i(T,P,\mathbf{n}) = f_i(T,P) \qquad \text{and} \qquad \lim_{x_i \to 1} \hat{\varphi}_i(T,P,\mathbf{n}) = \varphi_i(T,P) \tag{2.30}$$

It follows from eqs. (2.27) and (2.30) that the activity is unity in this limit. Furthermore, the activity coefficient is defined from eq. (2.27) as

$$\gamma_i(T,P,\mathbf{n}) \equiv \frac{a_i(T,P,\mathbf{n})}{x_i} = \frac{\hat{\varphi}_i(T,P,\mathbf{n})}{\varphi_i(T,P)} = \frac{\hat{f}_i(T,P,\mathbf{n})}{x_i \cdot f_i(T,P)} \tag{2.31}$$

In the same limit (eq. (2.30)) the activity coefficient of species *i* is unity

$$\lim_{x_i \to 1} \gamma_i(T,P,\mathbf{n}) = 1 \tag{2.32}$$

2.10 The excess property of the Gibbs energy

As a residual property is defined as the difference between the real property and the (hypothetical) property as an ideal gas, eq. (2.4), so is the excess property defined as the difference between the real property and the property as an ideal solution

$$M^E(T,P,\mathbf{n}) = M(T,P,\mathbf{n}) - M^{id}(T,P,\mathbf{n}) \tag{2.33}$$

In case of the Gibbs energy one has

$$\begin{aligned} G^E(T,P,\mathbf{n}) &= G(T,P,\mathbf{n}) - G^{id}(T,P,\mathbf{n}) \\ &= \sum_i n_i\mu_i(T,P,\mathbf{n}) - \sum_i n_i\mu_i^{id}(T,P,\mathbf{n}) \end{aligned} \tag{2.34}$$

Inserting eqs. (2.28) and (2.29) in eq. (2.34)

$$\begin{aligned} G^E(T,P,\mathbf{n}) &= \sum_i n_i\mu_i(T,P) + n_i RT\ln a_i(T,P,\mathbf{n}) - \sum_i n_i\mu_i(T,P) + n_i RT\ln x_i \\ &= RT\sum_i n_i \ln\gamma_i(T,P,\mathbf{n}) \end{aligned} \tag{2.35}$$

The unit of G^E is joules, J. The molar excess Gibbs energy g^E has the unit of joules per mole, and is independent of the total number of moles, but dependent on the composition. Since $\ln\gamma_i$ is a molar property, it follows that

$$RT\ln\gamma_i(T,P,\mathbf{n}) = \left(\frac{\partial G^E(T,P,\mathbf{n})}{\partial n_i}\right)_{P,T,n_{j\neq i}} = \left(\frac{\partial n\cdot g^E(T,P,\mathbf{n})}{\partial n_i}\right)_{P,T,n_{j\neq i}} \tag{2.36}$$

Eq. (2.36) is the way of achieving the activity coefficient once a g^E model has been presented. One way of testing the correctness of a proposed model follows from the corollary of Euler's theorem, given in Appendix A.

$$\sum_i n_i\left(\frac{\partial^2 G^E(T,P,\mathbf{n})}{\partial n_i \partial n_k}\right)_{T,P,n_{j\neq i,k}} = 0 \tag{2.37}$$

Since the order of differentiation is immaterial, eq. (2.37) is split into

$$\sum_i n_i\left(\frac{\partial \ln\gamma_i}{\partial n_k}\right)_{T,P,n_{j\neq k}} = 0 \qquad \text{or} \qquad \sum_i n_i\left(\frac{\partial \ln\gamma_k}{\partial n_i}\right)_{T,P,n_{j\neq i}} = 0 \tag{2.38}$$

Eq. (2.38) is an appropriate test for the consistency of the second molar derivative of a g^E model.

2.11 The reference state for the asymmetric activity coefficient

In some cases it is more convenient to replace the pure component reference state in eq. (2.28) by a reference state that includes the partial molar excess Gibbs energy at infinite dilution. Adding and subtracting this term gives

$$\mu_i(T,P,\mathbf{n}) = \mu_i(T,P) + RT\ln\gamma_i^{\infty} + RT\ln\frac{\gamma_i x_i}{\gamma_i^{\infty}} \tag{2.39}$$

where γ_i^{∞} is the activity coefficient of species *i* at infinite dilution. Consequently, the reference state in eq. (2.39) is

$$\mu_i^{ref} = \mu_i(T,P) + RT\ln\gamma_i^{\infty} \tag{2.40}$$

For a binary mixture the concept of the infinite dilution is unequivocal; as x_1 approaches zero x_2 approaches unity. But for systems consisting of more than two components several possibilities arise as to define the activity coefficient at infinite dilution. Here, three manners to define the infinite dilution are discussed.

1. *Constant composition reference*. Let n_i approach zero while all other mole numbers are kept constant. This definition leads to an asymmetric activity coefficient of species *i* that approaches unity as n_i approaches zero

$$\gamma_i^{\infty}(T,P,\mathbf{n},n_i=0) = \lim_{n_i\to 0}\gamma_i(T,P,\mathbf{n}) \quad n_{j\neq i} \text{ constant} \tag{2.41}$$

   The advantage of this definition is that it is straightforward. The drawback, however, is that the reference state depends on the composition of all other components present, eq. (2.40).

2. *Mixed solvent reference.* For this definition it is essential to distinguish between solutes and solvents. Solvents are components that are miscible in all proportions at the system's temperature and pressure. The activity coefficient at infinite dilution of solute *i* is then defined as the activity coefficient when the concentrations of all solutes approach zero while the mole numbers of all solvent components are kept constant.

$$\gamma_i^{\infty}(T,P,\mathbf{n},\mathbf{n}_{solutes}=0) = \lim_{\mathbf{n}_{solutes}\to 0}\gamma_i(T,P,\mathbf{n}) \quad \mathbf{n}_{solvents} \text{ constant} \tag{2.42}$$

   This definition has the advantage that addition of solutes does not change γ_i^{∞}. However, the reference state is still dependent on the solvent composition. Therefore, the phase behaviour of the solvent system as a function of the temperature, the pressure, and the composition has to be known in order to avoid artefacts due to phase splits.

3. *One reference solvent*. In this definition one of the solvents is chosen as the reference solvent. The activity coefficient of component *i* at infinite dilution in the pure reference solvent γ_i^{∞} is then defined as

$$\gamma_i^{\infty}(T, P, x_{rs} = 1) = \lim_{x_{rs} \to 1} \gamma_i(T, P, \mathbf{n}) \tag{2.43}$$

where subscript rs denotes the reference solvent. In this manner γ_i^{∞} is independent of all changes in the system's composition. Moreover γ_i^{∞} is equal to the activity coefficient at infinite dilution in the binary mixture, $\gamma_{i,rs}^{\infty,bin}(T, P)$ which is only a function of temperature, pressure, and the specified reference solvent.

Assuming water as the reference solvent allows the use of thermodynamic tables of the Gibbs energy of formation, the enthalpy of formation, etc, for solutes. The reference state of these tables is commonly the infinite dilution in water. A drawback of this definition is, however, the fact that the solvent interactions are not taken into account (*vanishing solvent effect*). This can be illustrated by considering a binary mixture of a solid or a salt dissolved in water. The definition of the activity coefficient at infinite dilution for the salt, γ_s^{∞}, is unequivocal since water is logically chosen as the reference solvent. If a small amount of water is replaced by ethanol, γ_s^{∞} stays the same. Even if more water is replaced by ethanol until a solvent system is obtained, which only consists of ethanol and no water, γ_s^{∞} is not changing. This definition does not recognise that the solvent properties have changed completely. The solvent in the physical sense is ethanol but in the thermodynamic sense it is still water, which is no longer present. In other words a truly hypothetical reference.

The definitions of the infinite dilution in sections 1. and 2. require a g^E-model to describe a change in the reference state. If such a model were available, there would be no need for the asymmetric normalisation. Either way, there are advantages and disadvantages in using asymmetric activity coefficients.

In this work, the activity coefficient at infinite dilution is defined by eq. (2.43). The asymmetric activity coefficient is then by definition

$$\tilde{\gamma}_{i,rs}(T, P, \mathbf{n}) \equiv \frac{\gamma_i(T, P, \mathbf{n})}{\gamma_{i,rs}^{\infty,bin}(T, P)}. \tag{2.44}$$

Eq. (2.44) shows that the asymmetric activity coefficient $\tilde{\gamma}_{i,rs}(T,P,\mathbf{n})$ is normalised such that it is unity in the pure reference solvent, only. If a third component is present, the limit of the activity coefficient at infinite dilution is no longer 1. Consequently, the reference state of the chemical potential is

$$\tilde{\mu}_{i,rs}(T,P) = \mu_i(T,P) + RT\ln\gamma_{i,rs}^{\infty,bin}(T,P) \tag{2.45}$$

This reference state is a function not only of temperature and pressure but also of the nature of the pure reference solvent, since the activity coefficient at infinite dilution is not the same in different solvents. When an asymmetric activity coefficient is used, the equivalent of eq. (2.28) is

$$\mu_i(T,P,\mathbf{n}) = \tilde{\mu}_{i,rs}(T,P) + RT\ln\tilde{\gamma}_{i,rs}(T,P,\mathbf{n}) + RT\ln x_i \tag{2.46}$$

2.12 The reference state for the molality activity coefficient

Concentrations given as molalities m_i are commonly used in electrolyte solutions. The molality is defined as the number of moles of solute per kg of solvent. To convert from mole fractions to molalities the following identity is used

$$x_i = \frac{n_i}{n} = \frac{n_i}{\frac{n_{solvent}M_{solvent}}{1000\,{}^{g}\!/_{kg}}}\frac{n_{solvent}}{n}\frac{M_{solvent}}{1000\,{}^{g}\!/_{kg}} = m_i x_{solvent}\frac{M_{solvent}}{1000\,{}^{g}\!/_{kg}} = \frac{m_i}{m_0}x_{solvent} \tag{2.47}$$

where n_i is the moles of solute, n the total number of moles in the solution, $n_{solvent}$ is the moles of solvent, $M_{solvent}$ is the molecular mass of the solvent (g/mole), m_i is the molality of the solute, $x_{solvent}$ is the mole fractions of the solvent, and m_0 is the molality of the pure solvent. Inserting eq. (2.47) into eq. (2.46) together with eq. (2.44) gives the following expression

$$\mu_i(T,P,\mathbf{n}) = \mu_i(T,P) + RT\ln\gamma_{i,rs}^{\infty,bin}(T,P) + RT\ln\tilde{\gamma}_{i,rs}(T,P,\mathbf{n}) + RT\ln x_{solvent}\frac{m_i}{m_0} \tag{2.48}$$

In electrochemistry, the chemical potential of a solute - and not for the solvent - is often written as

$$\mu_i = \mu_i^{ref,m} + RT\ln\gamma_i^m m_i \tag{2.49}$$

However, it is worth noting that it is only possible to take the logarithm of the product $\gamma_i^m m_i$ when the product is dimensionless. The superscript m indicates that the solute concentrations are in moles per kg of solvent. To be conform with eq. (2.48) the reference state in eq. (2.49) has to be

$$\mu_i^{ref,m} = \mu_i(T,P) + RT\ln\gamma_{i,rs}^{\infty,bin}(T,P) - RT\ln m_0 \tag{2.50}$$

while the molality activity coefficient γ_i^m has to be

$$\gamma_i^m = \tilde{\gamma}_{i,rs}(T,P,\mathbf{n})\cdot x_{solvent} \tag{2.51}$$

which is a rather peculiar expression for an activity coefficient. If molalities are used, it is more appropriate to use following definition

$$\mu_i(T,P,\mathbf{n}) = \tilde{\mu}_{i,rs}(T,P) + RT\ln\gamma_i^m\frac{m_i}{m_0} \tag{2.52}$$

and thus preserving $\tilde{\mu}_{i,rs}(T,P)$ of eq. (2.45) as the reference state chemical potential which has a well-defined physical significance.

2.13 The reference state for the molarity activity coefficient

Another concentration unit that is often encountered in aqueous solution chemistry is molarity, moles per litre, c. Expressing the activity of a species by the product of its molarity and an 'molarity activity coefficient'

$$\mu_i = \mu_i^{ref,c} + RT\ln\gamma_i^c\cdot c_i \tag{2.53}$$

This has some peculiar consequences in regards to the reference state. The relation between the mole fraction and the molarity of a species *i* is

$$x_i = \frac{n_i}{n_{total}} = \frac{n_i}{V_{solution}}\cdot\frac{V_{solution}}{n_{total}} = \frac{c_i}{c_0} \tag{2.54}$$

Inserting eq. (2.54) into eq. (2.46) together with eq. (2.44) gives the following expression

$$\mu_i(T,P,\mathbf{n}) = \mu_i(T,P) + RT\ln\gamma_{i,rs}^{\infty,bin}(T,P) + RT\ln\tilde{\gamma}_{i,rs}(T,P,\mathbf{n}) + RT\ln\frac{c_i}{c_0} \tag{2.55}$$

Conforming eq. (2.55) to eq. (2.53) gives a reference state chemical potential

$$\mu_i^{ref,c} = \mu_i(T,P) + RT\ln\gamma_{i,rs}^{\infty,bin}(T,P) - RT\ln c_0 \tag{2.56}$$

However, the product of $c_i\gamma_i$ has to be dimensionless in order to be able to take the logarithm. This results in a rather strange activity coefficient. Instead the chemical potential should be expressed as

$$\mu_i(T,P,\mathbf{n}) = \tilde{\mu}_{i,rs}(T,P) + RT\ln\tilde{\gamma}_{i,rs}(T,P,\mathbf{n})\cdot\frac{c_i}{c_0} \tag{2.57}$$

in which case the reference chemical potential remains physical sensible, eq. (2.45).

This concludes the chapter on the basic thermodynamics. Now one has the tools to describe the experimental methods for determining the activity of the solvent in a thermodynamic consistent way. This is the topic for the next chapter.

3. Thermodynamics of Experimental Methods

The experimental data of amino acid that are found in the literature are mostly isopiestic measurements and electrode potential measurements. The former experimental method is presented in this chapter. The isopiestic method is a method that is based on a reference, which has been experimentally determined by the use of other experimental methods (vapour pressure measurements and freezing point depression). It is these (reference) methods and the isopiestic method itself that is the topic of this chapter. The electrode potential method is presented in the next chapter of electrochemistry.

3.1 The thermodynamics of vapour pressure measurements

Vapour pressure measurements are essentially measurements of pressure differences, ΔP, between two systems at constant temperature T. Figure 3.1 is a schematic drawing of this method.

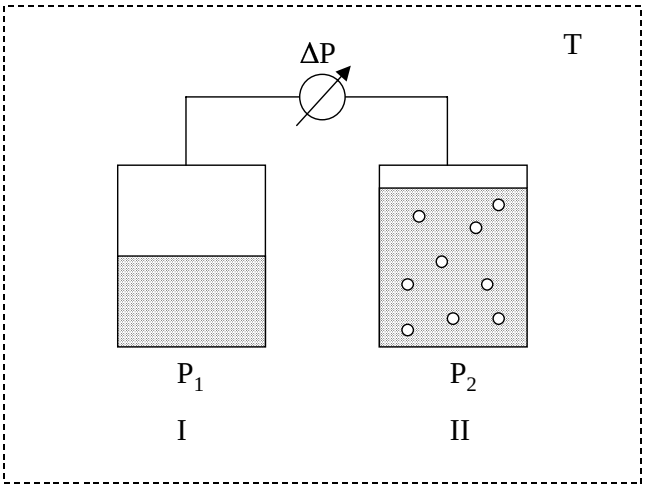


Figure 3.1: A schematic drawing of an experimental set-up for vapour pressure measurements. The compartment on the left (I) is containing a pure solvent liquid phase that is at equilibrium with a pure solvent vapour phase at a vapour pressure P_1. The compartment on the right (II) is containing one solvent - solute liquid phase that is at equilibrium with a vapour phase of pure solvent at a vapour pressure P_2. There is only an infinitesimal amount of vapour in the compartment II in order to avoid too great an evaporation of solvent and consequently an unknown solute concentration in the liquid phase.

The vapour pressure of the pure solvent, P_1, is (nearly) always known at the given temperature so with the measurement of ΔP, the vapour pressure of the solvent-solute solution, P_2, is easily determined. It is assumed that the solute is involatile.

Since both phases in compartment I are pure and at equilibrium at a vapour pressure P_1, the solvent fugacity, f_w, will be same in the two phases. This is known as the isofugacity criterion,

$$f_w^V(T, P_1) = f_w^L(T, P_1) \tag{3.1}$$

where V denotes the vapour phase and L the liquid phase.

In compartment II, a *pure vapour* phase (V) and a *solvent-solute liquid* phase (L) are at equilibrium at a vapour pressure of P_2. The difference in chemical potentials of the two phases is

$$\begin{aligned} &\mu_w^V(T, P_2) - \mu_w^L(T, P_2) = RT\ln\left(f_w^V(T, P_2)\right) - RT\ln\left(\hat{f}_w^L(T, P_2, \mathbf{n})\right) && \Rightarrow \\ &0 = RT\ln\left(f_w^V(T, P_2)\right) - RT\ln\left(\hat{f}_w^L(T, P_2, \mathbf{n})\right) && \Leftrightarrow \\ &f_w^V(T, P_2) = \hat{f}_w^L(T, P_2, \mathbf{n}) \end{aligned} \tag{3.2}$$

From eq. (2.17) one can express the pressure ratio as

$$\frac{P_2}{P_1} = \frac{f_w^V(T, P_2)}{f_w^V(T, P_1)} \cdot \frac{\varphi_w^V(T, P_1)}{\varphi_w^V(T, P_2)} \tag{3.3}$$

From the isofugacity criterion in eqs. (3.1) and (3.2)

$$\frac{P_2}{P_1} = \frac{\hat{f}_w^L(T, P_2, \mathbf{n})}{f_w^L(T, P_1)} \cdot \frac{\varphi_w^V(T, P_1)}{\varphi_w^V(T, P_2)} \tag{3.4}$$

Pressure adjustment of f_w^L from P_1 to P_2, in order to obtain the activity at P_2.

$$\begin{aligned} \ln f_w^L(T, P_2) &= \ln f_w^L(T, P_1) + \int_{P_1}^{P_2} \left(\frac{\partial \ln f_w^L}{\partial P} \right)_{T,\mathbf{n}} dP \\ &= \ln f_w^L(T, P_1) + \int_{P_1}^{P_2} \frac{v_w^L}{RT} dP \end{aligned} \tag{3.5}$$

where v_w^L is the molar volume of pure liquid water. Eq. (3.5) is inserted in eq. (3.4)

$$\frac{P_2}{P_1} = \frac{\hat{f}_w^L(T,P_2,\mathbf{n})}{f_w^L(T,P_2)} \cdot \frac{\varphi_w^V(T,P_1)}{\varphi_w^V(T,P_2)} \cdot \exp\left(-\int_{P_1}^{P_2} \frac{v_w^L}{RT} dP \right) \quad \Rightarrow$$
$$a_w^L(T,P_2,\mathbf{n}) = \frac{P_2}{P_1} \cdot \frac{\varphi_w^V(T,P_2)}{\varphi_w^V(T,P_1)} \cdot \exp\left(+\int_{P_1}^{P_2} \frac{v_w^L}{RT} dP \right) \tag{3.6}$$

The way that the activity is determined in eq. (3.6) indirectly sets the reference state as the state (T,P_2).

3.2 Simplifications on the vapour pressure measurements

The usual assumptions are that the two fugacity coefficients $\varphi_w^V(T,P_2)$ and $\varphi_w^V(T,P_1)$ are identical and that the partial molar volume is pressure independent. The modified expression for the activity is then

$$a_w^L(T,P_2,\mathbf{n}) = \frac{P_2}{P_1} \cdot \exp\left(\frac{v_w^L}{RT}(P_2 - P_1) \right) \tag{3.7}$$

at the state $(T,P_2,\mathbf{n})$. So a series of measurements will almost certainly have a new reference for each data point since P_2 is changing. An almost similar experimental method is the osmotic pressure measurements. The thermodynamic description of this method is given in Chapter 7. Osmotic Equilibrium.

3.3 The thermodynamics of freezing point depression measurements

Freezing point depression measurements are essentially measurements of temperature differences, ΔT, between two systems. Figure 3.2 is a schematic drawing of this method.

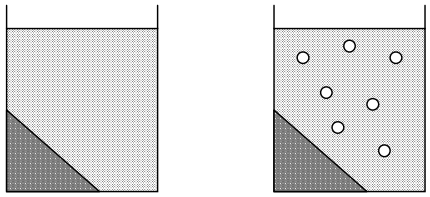


Figure 3.2: A schematic drawing of the experimental set-up for freezing point depression measurements. The cup on the left (I) is only containing solvent - in a solid phase and a liquid phase at equilibrium at a temperature T_0 and a pressure P_0. The other cup (II) only differs from cup I by having a solute in the liquid phase as well. The solid phase and the liquid phase of cup II are at equilibrium at a temperature T_2 and a pressure P_2.

The influence of the pressure on the freezing point is not great and is only given in order to complete the picture.

Since cup I is only containing the pure solvent, one has isofugacity of the solvent.

$$f_w^S(T_0, P_0) = f_w^L(T_0, P_0) \tag{3.8}$$

where S denotes the solid phase and L the liquid phase.

In the other cup, cup II, a *pure solid* phase (S) and a *solvent-solute liquid* phase (L) are at equilibrium at a temperature T_2 and a pressure P_2. The chemical potentials of the solvent in two phases are subtracted from each other

$$\begin{aligned} &\mu_w^S(T_2, P_2) - \mu_w^L(T_2, P_2) = RT_2 \ln\left(f_w^S(T_2, P_2)\right) - RT_2 \ln\left(\hat{f}_w^L(T_2, P_2, \mathbf{n})\right) && \Rightarrow \\ &0 = RT_2 \ln\left(f_w^S(T_2, P_2)\right) - RT_2 \ln\left(\hat{f}_w^L(T_2, P_2, \mathbf{n})\right) && \Leftrightarrow \\ &f_w^S(T_2, P_2) = \hat{f}_w^L(T_2, P_2, \mathbf{n}) \end{aligned} \tag{3.9}$$

In order to obtain the activity of the solvent the fugacity on the left-hand side of eq. (3.9) has to refer to the liquid phase. Therefore the left-hand side is temperature and pressure adjusted to the reference state (T_0,P_0).

$$\begin{aligned} \ln f_w^S(T_2, P_2) &= \ln f_w^S(T_0, P_0) + \int_{T_0}^{T_2} \left(\frac{\partial \ln f_w^S}{\partial T} \right)_P dT + \int_{P_0}^{P_2} \left(\frac{\partial \ln f_w^S}{\partial P} \right)_T dP \\ &= \ln f_w^S(T_0, P_0) - \int_{T_0}^{T_2} \frac{h_w^{r,S}}{RT^2} dT + \int_{P_0}^{P_2} v_w^S dP \end{aligned} \tag{3.10}$$

where $h_w^{r,S}$ is the residual molar enthalpy of the pure solid solvent and v_w^S is the molar volume of the pure solid solvent. At the reference state (T_0,P_0) eq. (3.8) is valid. Doing the same adjustments on the liquid phase from the reference state to the state (T_2,P_2) gives

$$\begin{aligned} \ln f_w^L(T_2,P_2) &= \ln f_w^L(T_0,P_0) - \int_{T_0}^{T_2} \frac{h_w^{r,L}}{RT^2}\,dT + \int_{P_0}^{P_2} v_w^L\,dP \qquad \Leftrightarrow \\ \ln f_w^L(T_0,P_0) &= \ln f_w^L(T_2,P_2) + \int_{T_0}^{T_2} \frac{h_w^{r,L}}{RT^2}\,dT - \int_{P_0}^{P_2} v_w^L\,dP \end{aligned} \tag{3.11}$$

where $h_w^{r,L}$ is the residual molar enthalpy of the pure liquid solvent and v_w^L is the molar volume of the pure liquid solvent. Inserting eqs. (3.8) and (3.11) into eq. (3.10) gives

$$\begin{aligned} \ln f_w^S(T_2,P_2) &= \ln f_w^L(T_2,P_2) + \int_{T_0}^{T_2} \frac{h_w^{r,L}}{RT^2}\,dT - \int_{P_0}^{P_2} v_w^L\,dP - \int_{T_0}^{T_2} \frac{h_w^{r,S}}{RT^2}\,dT + \int_{P_0}^{P_2} v_w^S\,dP \\ &= \ln f_w^L(T_2,P_2) + \int_{T_0}^{T_2} \frac{h_w^{r,L} - h_w^{r,S}}{RT^2}\,dT - \int_{P_0}^{P_2} \left(v_w^L - v_w^S\right) dP \\ &= \ln f_w^L(T_2,P_2) + \int_{T_0}^{T_2} \frac{\Delta_S^L h_w}{RT^2}\,dT - \int_{P_0}^{P_2} \Delta_S^L v_w\,dP \end{aligned} \tag{3.12}$$

where $\Delta_S^L M = M^L - M^S$ is a property of fusion. Inserting eq. (3.12) into eq. (3.9) gives

$$\begin{aligned} \ln \hat{f}_i^L(T_2,P_2,\mathbf{n}) &= \ln f_w^L(T_2,P_2) + \int_{T_0}^{T_2} \frac{\Delta_S^L h_w}{RT^2}\,dT - \int_{P_0}^{P_2} \Delta_S^L v_w\,dP \qquad \Rightarrow \\ \ln a_i^L(T_2,P_2,\mathbf{n}) &= \int_{T_0}^{T_2} \frac{\Delta_S^L h_w}{RT^2}\,dT - \int_{P_0}^{P_2} \Delta_S^L v_w\,dP \end{aligned} \tag{3.13}$$

The way that the activity is determined in (3.13) indirectly sets the reference state as the state (T_2,P_2). Again we note that the reference will most probably change in a series of measurements due to changing T and P.

3.4 Simplifications on freezing point depression methods

The usual assumptions are that $\Delta_S^L h_w$ is temperature independent and the pressure is constant. The modified expression for the activity is then

$$\ln a_i^L(T_2, P, \mathbf{n}) = \frac{\Delta_S^L h_w}{R}\int_{T_0}^{T_2}\frac{1}{T^2}dT = \frac{\Delta_S^L h_w}{R}\left(-\frac{1}{T_2}+\frac{1}{T_0}\right) = \frac{\Delta_S^L h_w}{R}\left(\frac{1}{T_0}-\frac{1}{T_2}\right)$$
$$= \frac{\Delta_S^L h_w}{RT_0}\frac{\Delta}{\Delta - T_0} \qquad (3.14)$$

where $\Delta = T_0 - T_2$. Since $T_0 >> \Delta > 0$ and $\Delta_S^L h_w > 0$ (for water it is 6.008 kJ/mole, Aktins, p. 936), the logarithmic activity will be negative according to eq. (3.14). This is also what is expected.

3.5 Boiling point elevation

There is a third experimental method by which the solvent activity is determined, namely the boiling point elevation. The thermodynamics of the boiling point elevation measurements are in principle the same as the freezing point depression measurements - except that $\Delta_S^L h_w$ is replaced by $-\Delta_L^V h_w$ in eq. (3.14) where T_0 then is the boiling temperature of the pure solvent and Δ is the temperature elevation, $T_{\text{with solute}} - T_0$.

3.6 The thermodynamics of isopiestic measurements

It is based on obtaining equilibrium between a number of subsystems (or cups each containing a solvent - solute phase) in a common atmosphere. There is only one common solvent in all the subsystems and this solvent is also the only volatile compound. In one of the subsystems the solvent activity is known as a function of concentration, i.e. the reference system. This makes the isopiestic method a relative method; it is based on results from other experiments.

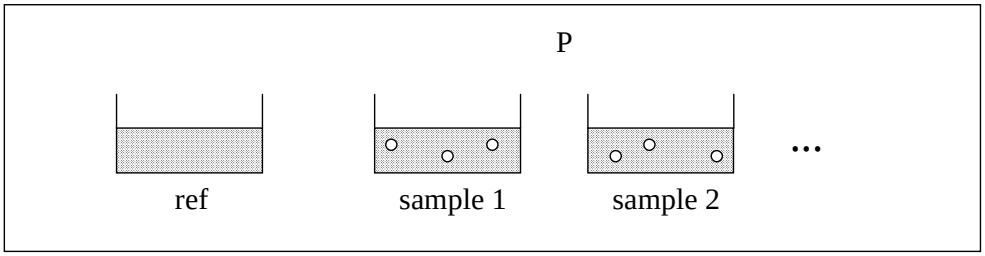


Figure 3.3: A schematic drawing of the general experimental set-up for isopiestic measurements. The cup on the left (ref) is the reference system where the solvent activity is known as a function of concentration. The other cups (sample 1, sample 2, …) contain solvent - solute solutions. When equilibrium is reached, the concentrations of the all cups have to be determined.

In the literature the solvent activity of both the reference system as well as the sample are often given in terms of osmotic coefficients, ϕ. The practical osmotic coefficient is defined as

$$\phi = \frac{-\ln a_w}{M_w \sum_i \nu_i m_i} \qquad , i\text{ - solutes} \tag{3.15}$$

where a_w is the solvent activity, M_w is molar mass of the solvent, ν_i is the stoichiometric coefficients of the solutes when dissociated, and m_i is the molalities of the undissociated solutes.

When the osmotic coefficients are given both for the reference system and the sample, these are related as

$$\begin{aligned}
& a_w^{ref} = a_w^{sample} && \Leftrightarrow \\
& -\frac{\ln a_w^{ref}}{M_w} \frac{1}{\sum_i \nu_i m_i^{ref}} \frac{1}{\sum_i \nu_i m_i^{sample}} = -\frac{\ln a_w^{sample}}{M_w} \frac{1}{\sum_i \nu_i m_i^{sample}} \frac{1}{\sum_i \nu_i m_i^{ref}} && \Leftrightarrow \\
& \phi^{ref} \frac{1}{\sum_i \nu_i m_i^{sample}} = \phi^{sample} \frac{1}{\sum_i \nu_i m_i^{ref}} && \Leftrightarrow \\
& \phi^{sample} = \phi^{ref} \frac{\sum_i \nu_i m_i^{ref}}{\sum_i \nu_i m_i^{sample}}
\end{aligned} \tag{3.16}$$

The reason for using the osmotic coefficient is that the solvent activity is usually very close to unity at low solute concentrations. By this definition one gets a more detailed information on the solvent activity.

Traditionally, sodium chloride, potassium chloride, and sucrose have been used as reference systems because the water activities in these aqueous solutions are well established. However, these solvent activities are derived from the two methods presented in this chapter, vapour pressure and freezing point depression. A third experimental method is also used as a basis for the references and that is the osmotic pressure measurements, which is presented in Chapter 7. Osmotic Equilibrium.

Another experimental method is the potentiometric method by which the activities of electrolytes are determined. The next chapter presents the theory of electrochemistry and the principles of the Harned cell. At the end of the next chapter the relativity of experimental

methods, i.e. how they are dependent on the results obtained by other experiments, is discussed.

4. Electrochemistry

Electrode potential measurements are an essential part of the experimental data available on amino acids and peptides as mentioned in the introduction to the previous chapter. In order to connect the electrochemistry to the basic thermodynamics – at times the two subjects seem to be disconnected in the literature – this chapter on electrochemistry is given. The Nernst equation is derived from a purely thermodynamic starting point, the internal energy, in consistency with the basic thermodynamics presented in Chapter 2.

Once the fundamentals of the electrochemistry are clear, it enables one to describe the experimental methods by which the activities of electrolytes are obtained. Two such methods are measurements on a Harned cell and measurements using ion-selective electrodes, see Chapter 5.

4.1 Electrochemical equilibrium

In electrochemistry, the internal energy U is given by the state (S, V, **n**, **q**) where **q** is the charge and therefore has the unit of coulomb, C. All variables given are extensive properties so the internal energy is

$$\begin{aligned} U &= \sum_i (\text{intensive property})_i \cdot (\text{conjugated extensive property})_i \\ &= TS - PV + \sum_i \mu_i n_i + \sum_i \Phi q_i \end{aligned} \tag{4.1}$$

The last term on the right-hand side of eq. (4.1) is due to the work done when a particle of charge q_i is moved into an electric potential, Φ. In general, all work terms should be added in eq. (4.1), such as $\Sigma_i \sigma_i A_i$ for surface tension, $\Sigma_i g \cdot m_i$ for gravity. From the definitions of Gibbs energy and enthalpy

$$G \equiv H - TS \quad , \qquad H \equiv U + PV \tag{4.2}$$

one has

$$\begin{aligned} G &= U + PV - TS \\ &= \sum_i \mu_i n_i + \sum_i \Phi q_i \end{aligned} \tag{4.3}$$

It is observed that the Gibbs energy now includes a second term. Normally, this term is not included since the systems considered are restricted to a system without any electrical influences. The so-called electrochemical potential, μ_i^{elec} is defined as

$$\sum_i n_i \mu_i^{elec} = \sum_i n_i \mu_i + q_i \Phi \tag{4.4}$$

For a single species *i* the electrochemical potential is

$$\begin{aligned} n_i \mu_i^{elec} &= n_i \mu_i + q_i \Phi \qquad \Rightarrow \\ \mu_i^{elec} &= \mu_i + \frac{q_i}{n_i} \Phi \end{aligned} \tag{4.5}$$

The ratio between the charge and the matter (q_i/n_i) is usually referred to by the Faraday constant which is defined as the elementary charge times Avogadro's number, $F = e \cdot N_A$ = 96,485 C/mole. The hydrogen ion or proton has the charge of + *e* and the molar charge of + $e \cdot N_A$. The molar charge is, therefore, equally well expressed as + F. In general, the molar charge of a species *i* is given as $z_i \cdot F$ where z_i is the ratio between a given molar charge and the molar charge of a proton, H^+. Eq. (4.5) is rewritten to the more familiar form of

$$\mu_i^{elec} = \mu_i + z_i F \Phi \tag{4.6}$$

Observe, that if $\Phi > 0$ and species *i* is a cation ($z_i > 0$), the electrochemical potential will be greater than the chemical potential and thus energetically a less favourable state. On the other hand, a negative electric potential results in an energetically more favourable state.

The total differential of eq. (4.1)

$$\begin{aligned} dU = &\sum_i d(\text{intensive property})_i \cdot (\text{conjugated extensive property})_i \\ &+ \sum_i (\text{intensive property})_i \cdot d(\text{conjugated extensive property})_i \end{aligned} \tag{4.7}$$

where the Gibbs-Duhem equation (Appendix A) is

$$0 = \sum_i d(\text{intensive property})_i \cdot (\text{conjugated extensive property})_i \tag{4.8}$$

wherefore one has

$$\begin{aligned} dU &= \sum_i (\text{intensive property})_i \cdot d\,(\text{conjugated extensive property})_i \\ &= TdS - PdV + \sum_i \mu_i dn_i + \sum_i \Phi\, dq_i \end{aligned} \tag{4.9}$$

The total differential of the Gibbs energy, eq. (4.3), is

$$\begin{aligned} dG &= dU + VdP + PdV - SdT - TdS \\ &= TdS - PdV + \sum_i \mu_i dn_i + \sum_i \Phi\, dq_i + VdP + PdV - SdT - TdS \\ &= \sum_i \mu_i dn_i + \sum_i \Phi\, dq_i + VdP - SdT \end{aligned} \tag{4.10}$$

As previously described the charge q_i is equal to $z_i n_i F$, so at constant T and P, eq. (4.10) reduces to

$$\begin{aligned} dG &= \sum_i \mu_i dn_i + \sum_i \Phi\, d(z_i n_i F) \\ &= \sum_i \mu_i dn_i + z_i F \Phi\, dn_i \\ &= \sum_i (\mu_i + z_i F \Phi)\, dn_i \end{aligned} \tag{4.11}$$

The amount of species *i* that reacts will be $\nu_i\, d\xi$ where ν_i is the stoichiometric coefficients.

$$dG = \sum_i \nu_i (\mu_i + z_i F \Phi) d\xi \tag{4.12}$$

At equilibrium, one has (see Appendix B)

$$0 = \sum_i \nu_i (\mu_i + z_i F \Phi) \tag{4.13}$$

4.2 Equilibrium of an electrochemical cell

An electrochemical cell is characterised by having an anode and a cathode. The reactions at both electrodes are written as reduction reactions, i.e. the electron is a reactant, $\nu_e < 0$.

$$\text{ox} + |\nu_e|\, e^- \rightarrow \text{red} \tag{4.14}$$

These reactions are also called the two half-cell reactions. The cell reaction (i.e. the reaction of the cell) is obtained by subtracting the half-cell reaction at the anode from that at the cathode. At the cathode at equilibrium the following is valid

$$\begin{aligned} 0 &= \sum_{i} \left(\nu_i \mu_i + \nu_i z_i F \Phi \right) \\ &= \sum_{i \neq e} \left(\nu_i \mu_i + \nu_i z_i F \Phi \right) + \nu_e \mu_e + \nu_e z_e F \Phi \end{aligned} \tag{4.15}$$

and equally at the anode

$$0 = \sum_{j \neq e} \left(\nu_j \mu_j + \nu_j z_j F \Phi \right) + \nu_e \mu_e + \nu_e z_e F \Phi \tag{4.16}$$

In order to maintain electroneutrality ν_e must be the same at both electrodes. Subtracting the molar Gibbs energy of the anode from that of the cathode consequently gives

$$\begin{aligned} 0 &= \left[\sum_{i \neq e} \left(\nu_i \mu_i + \nu_i z_i F \Phi \right) + \nu_e \mu_e + \nu_e z_e F \Phi \right]_{\text{cathode}} \\ &\qquad - \left[\sum_{j \neq e} \left(\nu_j \mu_j + \nu_j z_j F \Phi \right) + \nu_e \mu_e + \nu_e z_e F \Phi \right]_{\text{anode}} \\ &= \left[\sum_{i \neq e} \nu_i \mu_i + \nu_i z_i F \Phi \right]_{\text{cathode}} - \left[\sum_{j \neq e} \nu_j \mu_j + \nu_j z_j F \Phi \right]_{\text{anode}} \\ &\qquad + \nu_e z_e F \left(\Phi_{\text{cathode}} - \Phi_{\text{anode}} \right) \end{aligned} \tag{4.17}$$

All the ions (z_i and $z_j \neq 0$) experience the same electric potential; that of the solution, Φ_S, so eq. (4.17) is

$$\begin{aligned} 0 &= \left[\sum_{i \neq e} \nu_i \mu_i \right]_{\text{cathode}} - \left[\sum_{j \neq e} \nu_j \mu_j \right]_{\text{anode}} \\ &\qquad + F \Phi_S \left(\left[\sum_{i \neq e} \nu_i z_i \right]_{\text{cathode}} - \left[\sum_{j \neq e} \nu_j z_j \right]_{\text{anode}} \right) - \nu_e F \Delta\Phi_{\text{cell}} \end{aligned} \tag{4.18}$$

where $\Delta\Phi_{\text{cell}}$ is the electric potential difference of the cell. Due to electroneutrality the total charge at the cation is equal to that of the anion. Consequently, the third term on the right-hand side of eq. (4.18) is zero. Furthermore, the first two terms are the sum of the chemical potentials of the cell reaction.

$$0 = \sum_{i} \nu_i^{\text{cell}} \mu_i^{\text{cell}} - \nu_e F \Delta\Phi_{\text{cell}} \tag{4.19}$$

The figure ν_e is always negative since the electrons are reactants in a reduction. To eliminate any confusion regarding the sign convention of the stoichiometric coefficient for the electron eq. (4.19) is reformulated

$$0 = \sum_i \nu_i^{cell} \mu_i^{cell} + |\nu_e| F \Delta\Phi_{cell} \tag{4.20}$$

where $|\nu_e|$ is the numerical value of the stoichiometric coefficient for the electron. It is noticed that the electric potential difference is also an intensive property as the electric potential is, i.e. independent of the extent of reaction.

4.3 The electric potential in an electrochemical cell

The electric potential difference is also called the zero-current electrode potential of the cell (E_{cell}) or in short the electrode potential. An older notation for the electrode potential is electromotive force, emf. This is misleading since a force has the unit of newton and the electrode potential that of volt.

Substituting the electric potential difference by the electrode potential in eq. (4.19) a familiar relation emerges

$$\sum_i \nu_i^{cell} \mu_i^{cell} = -|\nu_e| F E_{cell} \tag{4.21}$$

or if the stoichiometric coefficient of the electron is regarded signless

$$\sum_i \nu_i \mu_i = -\nu_e F E \tag{4.22}$$

It is worth noting that due to the convention of achieving the cell reaction, (and thus defining the electrode potential of the cell) gives a positive electrode potential for any spontaneous reaction since the sum of the chemical potentials is negative for such a spontaneous reaction. It is from this fundamental relation between the summation of chemical potentials and the electrode potential of a cell that experimental measurements of electrode potentials of a given cell are applicable to determine the activity coefficients. However, it is necessary that the reaction is reversible in order to obtain equilibrium, zero-current electrode potential. That is the electrodes have to be reversible - and if not the measurements obtained are not at equilibrium.

4.4 The Nernst equation

When the expression for the chemical potential eq. (2.28) is inserted into eq. (4.22), the well-known Nernst equation emerges

$$\begin{aligned} E(T,P,\mathbf{n}) &= -\frac{1}{\nu_e F}\sum_i \nu_i\left(\mu_i(T,P)+RT\ln a_i(T,P,\mathbf{n})\right) \\ &= -\frac{1}{\nu_e F}\sum_i \nu_i\mu_i(T,P)-\frac{RT}{\nu_e F}\sum_i \nu_i \ln a_i(T,P,\mathbf{n}) \\ &= E(T,P)-\frac{RT}{\nu_e F}\sum_i \ln\left(a_i(T,P,\mathbf{n})\right)^{\nu_i} \\ &= E(T,P)-\frac{RT}{\nu_e F}\ln\prod_i \left(a_i(T,P,\mathbf{n})\right)^{\nu_i} \end{aligned} \tag{4.23}$$

Since the activity coefficient is defined as eq. (2.31), eq. (4.23) is

$$E(T,P,\mathbf{n}) = E(T,P)-\frac{RT}{\nu_e F}\ln\prod_i x_i^{\nu_i}\gamma_i^{\nu_i}(T,P,\mathbf{n}) \tag{4.24}$$

where E(T,P) is the reference electrode potential which is only a function of temperature and pressure.

4.5 The reference electrode potential for the asymmetric activity coefficient

The Nernst equation, eq. (4.24), is based in activity coefficients of the symmetric convention. When the activity coefficients are changed to the asymmetric convention the reference state is changed, too.

$$\begin{aligned} E(T,P,\mathbf{n}) &= E(T,P)-\frac{RT}{\nu_e F}\ln\prod_i x_i^{\nu_i}\gamma_i^{\nu_i}(T,P,\mathbf{n}) \\ &\quad +\frac{RT}{\nu_e F}\ln\prod_i\left(\gamma_{i,rs}^{\infty,bin}(T,P)\right)^{\nu_i}-\frac{RT}{\nu_e F}\ln\prod_i\left(\gamma_{i,rs}^{\infty,bin}(T,P)\right)^{\nu_i} \\ &= \tilde{E}_{rs}(T,P)-\frac{RT}{\nu_e F}\ln\prod_i x_i^{\nu_i}\tilde{\gamma}_{i,rs}^{\nu_i}(T,P,\mathbf{n}) \end{aligned} \tag{4.25}$$

where by definition $\tilde{E}_{rs}(T,P)$ is a reference electrode potential when the asymmetrical activity coefficient is applied,

$$\begin{aligned}\tilde{E}_{rs}(T,P) &= E(T,P) - \frac{RT}{\nu_e F}\ln\prod_i\left(\gamma_{i,rs}^{\infty,bin}(T,P)\right)^{\nu_i}\\ &= -\frac{1}{\nu_e F}\sum_i \nu_i\mu_i(T,P) - \frac{RT}{\nu_e F}\ln\prod_i\left(\gamma_{i,rs}^{\infty,bin}(T,P)\right)^{\nu_i}\\ &= -\frac{1}{\nu_e F}\sum_i \nu_i\left(\mu_i(T,P) - RT\ln\gamma_{i,rs}^{\infty,bin}(T,P)\right)\\ &= -\frac{1}{\nu_e F}\sum_i \nu_i\tilde{\mu}_{i,rs}(T,P)\end{aligned} \tag{4.26}$$

As discussed earlier in Chapter 2. Basic Thermodynamics the infinite dilution limit of an activity coefficient is unequivocal in a binary mixture, only. Inserting eqs. (2.47) and (2.51) into eq. (4.25) gives eq. (4.27) describing the electrode potential of the cell

$$\begin{aligned}E &= \tilde{E}_{rs}(T,P) - \frac{RT}{\nu_e F}\ln\prod_i m_0^{-\nu_i} - \frac{RT}{\nu_e F}\ln\prod_i\left(m_i\,\gamma_{i,rs}^{m}(T,P,\mathbf{n})\right)^{\nu_i}\\ &= E^{m} - \frac{RT}{\nu_e F}\ln\prod_i\left(m_i\,\gamma_{i,rs}^{m}(T,P,\mathbf{n})\right)^{\nu_i}\end{aligned} \tag{4.27}$$

where by definition E^m is a reference electrode potential when the concentrations are on a molality basis,

$$E^{m} \equiv \tilde{E}_{rs}(T,P) - \frac{RT}{\nu_e F}\ln\prod_i m_0^{-\nu_i} \tag{4.28}$$

E(T,P) and $\tilde{E}_{rs}(T,P)$ have the unit of electrode potential, namely volt; E^m does not.

4.6 Harned cell

A specific type of electrochemical elements has been named after H.S. Harned who pioneered in the field of electrochemistry and electrochemical cells (Harned and Åkerlöf, 1926; Harned and Owen, 1930a-b; and Harned and Hamer, 1933). A Harned cell is a cell without liquid junction (salt bridge). The schematic design of this cell is

(Anode) (Cathode)

$$\mathrm{Pt} \mid \mathrm{H_{2\,(g)}} \mid \mathrm{H^{+}_{(aq)}}, \mathrm{Cl^{-}_{(aq)}} \mid \mathrm{AgCl_{(s)}}, \mathrm{Ag_{(s)}} \tag{4.29}$$

where the concentration of hydrochloric acid is known. Sometimes the cathode is a calomel electrode, instead. The cell reaction, by definition, is

$$\tfrac{1}{2}\mathrm{H_{2\,(g)}} + \mathrm{AgCl_{(s)}} \rightarrow \mathrm{H^{+}_{(aq)}} + \mathrm{Cl^{-}_{(aq)}} + \mathrm{Ag_{(s)}} \tag{4.30}$$

The stoichiometric coefficient of the electron is one. Assuming the solid silver/silver chloride electrode is pure, the Nernst equation for the Harned cell becomes

$$E_{cell}(T,P,\mathbf{n}) = E_{cell}(T,P) - \frac{RT}{F}\ln\frac{a_{H^+}(T,P,\mathbf{n})\,a_{Cl^-}(T,P,\mathbf{n})}{a_{H_2}^{½}(T,P,\mathbf{n})} \tag{4.31}$$

If the gas phase only consists of hydrogen, then the activity of $H_{2\,(g)}$ will be unity

$$a_{H_2}(T,P,\mathbf{n}) = \frac{\hat{f}_{H_2}(T,P,\mathbf{n})}{f_{H_2}(T,P)} = \frac{f_{H_2}(T,P)}{f_{H_2}(T,P)} = 1 \tag{4.32}$$

and the electrode potential of the cell will be

$$E_{cell}(T,P,\mathbf{n}) = E_{cell}(T,P) - \frac{RT}{F}\ln a_{H^+}(T,P,\mathbf{n})\,a_{Cl^-}(T,P,\mathbf{n}) \tag{4.33}$$

Eq. (4.33) implies that the reference electrode potential $E_{cell}(T,P)$ is indeed a hypothetical property. It is impossible that both activities are unity. That would imply that each of the components should have a mole fraction of one - and that would violate the principle of electroneutrality. The only way that one can measure $E_{cell}(T,P)$ would be if the product of the activities incidental should be unity.

From the definition of the activity coefficient, eq. (2.31), eq. (4.33) is equally well represented by

$$E_{cell}(T,P,\mathbf{n}) = E_{cell}(T,P) - \frac{RT}{F}\ln x_{H^+}x_{Cl^-}\gamma_{H^+}(T,P,\mathbf{n})\,\gamma_{Cl^-}(T,P,\mathbf{n}) \tag{4.34}$$

To facilitate the nomenclature the ionic mean activity coefficient $\gamma_\pm$ and the corresponding mole fraction is $x_\pm$ are defined as

$$\nu \ln\gamma_\pm = \sum_i \nu_i \ln\gamma_i(T,P,\mathbf{n}) \qquad \text{and} \qquad \nu\, x_\pm = \sum_i \nu_i x_i \tag{4.35}$$

where ν is the sum of the stoichiometric coefficients in question, ν_i. In the case of the Harned cell the electrode potential of the cell is then

$$E_{cell}(T,P,\mathbf{n}) = E_{cell}(T,P) - \frac{2RT}{F}\ln x_\pm\gamma_\pm \tag{4.36}$$

As a simple check it is seen that in the limit $x_\pm \to 0$ that the electrochemical potential of the cell is approaching infinity, which is in accordance with the observed, as shown in Figure 4.1.

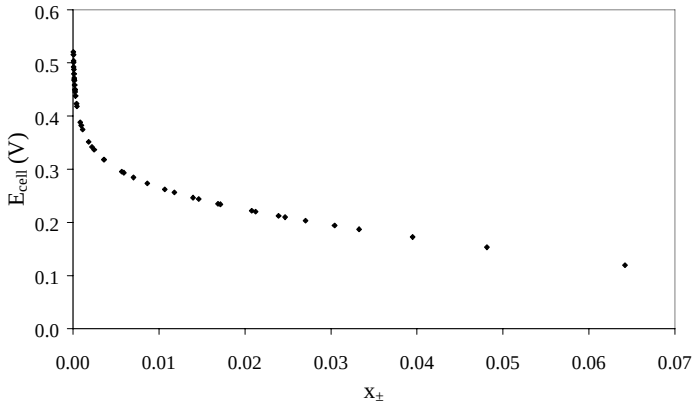


Figure 4.1: The measured electrode potential of a Harned cell as a function of the mole fraction of $x_{\pm}$. The experimental data are from Harned and Ehlers, 1932 and 1933. The temperature is 298.15 K and the pressure is 1 atm.

The provisional standard potential, E' as it is suggested by Pitzer (1991, pp. 158) is eq. (4.33) rearranged so that the known variables are on left-hand side of the equality sign and the unknown on the right-hand side.

$$E' = E_{cell}(T, P, \mathbf{n}) + \frac{2RT}{F} \ln x_{\pm} = E_{cell}(T, P) - \frac{2RT}{F} \ln \gamma_{\pm} \tag{4.37}$$

The limit of provisional standard potential, E' is

$$\begin{aligned} \tilde{E}_{rs}(T, P) &= \lim_{x_{\pm} \to 0} E' = \lim_{x_{\pm} \to 0} \left(E_{cell}(T, P, \mathbf{n}) + \frac{2RT}{F} \ln x_{\pm} \right) \\ &= \lim_{x_{\pm} \to 0} \left(E_{cell}(T, P) - \frac{2RT}{F} \ln \gamma_{\pm} \right) \\ &= E_{cell}(T, P) - \frac{2RT}{F} \ln \gamma_{\pm,rs}^{\infty,bin} \end{aligned} \tag{4.38}$$

It is noted that eq. (4.38) is in accordance with eq. (4.26) and that $\tilde{E}_{rs}(T, P)$ will have a finite value. At low concentrations the Debye-Hückel equation or more correctly a function in that mathematical form, is a good approximation to the activities. As a consequence the provisional standard potential has the mathematical form

$$E' = \tilde{E}_{rs}(T, P) + \frac{A_2 \sqrt{I}}{1 + A_3 \sqrt{I}} + A_4 I \tag{4.39}$$

where I is the ionic strength (given as $\frac{1}{2}\Sigma x_i z_i^2$). That this is the case (at low concentrations) is shown in Figure 4.2.

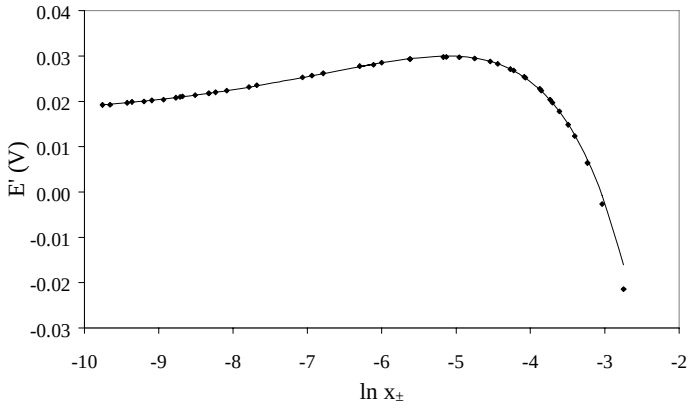


Figure 4.2: The provisional standard potential as a function of logarithm of $x_{\pm}$. The data points are those of Figure 4.1. The fitted curve is eq. (4.39).

In the presented case the estimated value of $\tilde{E}_{cell,rs}(T,P)$ is 0.0163V. This is *not* in agreement with what one can find in a table listing standard electrode potentials. The reason why this is so, is that these tabulated standard electrode potentials are derived from a different basis; the molality basis. The conversion from the asymmetric convention to the molality reference potential is an artefact of another way of defining an activity coefficient, the so-called molality based activity coefficient or activity coefficient on molal scale. From the thermodynamic theory and eq. (4.28) we have the 'molality reference potential' given as

$$E^m = \tilde{E}_{cell,rs}(T,P) - \frac{2RT}{F}\ln\frac{M_{solvent}}{1000\,{}^{g}\!/_{kg}} \qquad (4.40)$$

Since the solvent in the presented case is water, $M_{solvent}$ = 18.01528 g/mole, this 'molality reference potential' is 0.223 "V". This is exactly what one finds in the tables. However, the unit is physically unwise since it involves the logarithm of (kg/mole).

4.7 Discussion on the relativity of experimental methods

In principle, all measurements are relative since they are related to a set point, e.g. temperature is often related to the temperature at which water melts or to the temperature

where all motion stops; the magnitude of the potential energy of mechanics depends on an arbitrarily chosen reference height. However, some set points are more logically chosen than others are. For instance, the absolute temperature is defined by referring to the temperature at which all motion stops as the set point and is then called absolute temperature and denoted kelvin.

Vapour pressure measurements, osmotic pressure measurements, freezing point depression, and boiling point elevation are experimental methods, by which the solvent activity is determined. However, the solvent activity is only determined by these four methods if the solvent molar volume, the solvent molar enthalpy of fusion, and the solvent molar enthalpy of evaporation are known. These solvent properties are usually determined quite precisely and therefore the four above mentioned experimental methods could be regarded as so-called 'absolute' experimental methods.

Contrary to these 'absolute' experimental methods, the isopiestic method is a 'relative' method. The solvent activity of the reference solution has been calculated from vapour pressure measurements, osmotic pressure measurements, or freezing point measurements as a function of the reference solute concentration (Smith and Smith, 1937).

The ionic mean activity coefficient of the Harned cell is only determined if the reference electrode potential of the cell is known. The reference electrode potentials that are tabulated in the literature are determined by the procedure sketched in Section 4.6. This only gives the ionic mean asymmetric activity coefficient, which is relative to the activity coefficient at infinite dilution. One way to circumvent the problem of the unknown reference electrode potential of a given cell is presented in Section 5.2.6. The idea is to observe the changes in the ionic mean activity coefficient - instead of its absolute value.

5. Experimental Results

During the project a number of experiments were carried out at the Kluyver Laboratory at the Delft University of Technology. The procedures and the results of the experimental work are presented in this chapter. The chapter is divided into two parts: the first part addresses the solubility of the two dipeptides (glycylglycine and glycyl-L-alanine) in aqueous salt solutions and the densities of these solutions. The second part is concerned with the electrode potential measurements of aqueous NaCl - dipeptide solutions.

5.1 Densities, mixing volumes, and solubilities of dipeptides

Since the 1930's the experimental determination of the phase behaviour of systems containing proteins, dipeptides, and amino acids, has received a considerable amount of attention, (McMeekin et al., 1935; Cohn and Edsall, 1943; Nozaki and Tanford, 1963, 1965; Needham et al., 1971; Orella and Kirwan, 1989; Jin and Chao, 1992; Gude et al., 1996a, 1996b; Khoshkbarchi and Vera, 1997; Coen et al., 1997; Pradhan and Vera, 1998; and Rudolph et al., 2001). The 13 references quoted are a minor selection among the vast number of data available.

Experimental data is essential in the development, design, and modelling of separation process. Traditionally, thermodynamic models have not been widely used in the biotechnological industry as is the case in the chemical industry, but it is becoming more prevalent because of the increasing demand for computer aided design and optimisation of processes.

Density and solubility measurements of dipeptides in solution are properties that may contribute to a better understanding of their thermodynamic behaviour in solution and eventually the behaviours of polypeptides and proteins. Traditionally, the dry mass method (McMeekin et al., 1935; Nozaki and Tanford, 1963, 1965) has been used to determine the solubility of amino acids and peptides. However, in this work a spectroscopic method was used.

Glycylglycine is the simplest of all possible peptides since it consists only of the amino acid, glycine. Glycyl-L-alanine differs from glycylglycine by having a methyl group on the α-

carbon instead of hydrogen. The salts are NaCl, Na_2SO_4, and $(NH_4)_2SO_4$; salts most often used in industrial separation processes.

5.1.1 Materials

Glycylglycine (> 99 % purity) and glycyl-L-alanine (> 98 % purity, $[\alpha]_D^{24} = -59.7°$ (in 0.5 N HCl)) were purchased from Bachem A.G. (Bubendorf, Switzerland). Sodium chloride (NaCl, ≥ 99.5 % purity) was obtained from J.T. Baker (Deventer, The Netherlands). Sodium sulphate (Na_2SO_4, > 99 %, extra pure) and ammonium sulphate ($(NH_4)_2SO_4$, ≥ 99.5 % purity) were obtained from Merck (Darmstadt, Germany). The water was cleaned in a milli-Q system from Millipore to a conductivity of 0.06 $\mu S \cdot cm^{-1}$.

5.1.2 Experimental procedure

The solubility of the dipeptide in aqueous electrolyte solutions at various salt concentrations as well as in pure water was determined experimentally. The salt solutions were prepared gravimetrically by use of a Mettler Toledo AG204 DeltaRange (Greifensee, Switzerland) balance with a resolution of ± 0.1 mg. The salt concentrations range from 0.1 molal to saturation for solutions containing NaCl, from 0.1 to 1.0 molal for the Na_2SO_4 and $(NH_4)_2SO_4$ solutions. The dipeptide was added in abundant to the salt solutions to ensure saturation. The solutions were stirred for 18 to 24 hours at 298.15 K (± 0.1 K) in a thermostated water bath (Thermomix 1419, B. Braun, Germany). After equilibration samples were taken with a syringe with an attached 0.20 μm filter (Schleicher & Schuell GmbH, Dassel, Germany). The densities of the solutions at 298.15K were determined on a density meter (Density meter DMA 48, AP Paar - Austria, accuracy ± 10^{-4} g/cm³ for 0.5 - 1.5 g/cm³). The density meter was calibrated by water and ethanol at 298.15 K. Prior to spectroscopic analysis, the samples were diluted gravimetrically.

5.1.3 Analysis of the dipeptide

The dipeptide concentration was analysed by UV spectrophotometry (Varian DMS 90 UV visual spectrophotometer) at a wave length of 210 nm. Calibration curves for the dipeptide

were determined in pure water. Preliminary experiments showed that, at this wave length, the influence of the salt on the absorption was insignificant. The samples were diluted in different proportions. The glycylglycine samples were diluted gravimetrically by a factor of 2000 or 2400. The glycyl-L-alanine samples were diluted gravimetrically by a factor of 10,000 or 12,000. In order to exclude the possibility of unrecognised degradation of the dipeptide some samples randomly chosen were analysed by HPLC. No degradation was observed.

5.1.4 Analysis of the NaCl concentration

For NaCl molalities less than 5 it was assumed that no salt precipitates when the solution was saturated with dipeptide. Consequently, the salt concentrations in the solutions were not analysed. For higher concentrations, 5 molal to saturation, it was likely that the solubility of NaCl might have been influenced by the presence of the dipeptide. Therefore, the sodium concentration in the liquid sample was determined by flame atomic absorption spectroscopy (flame-AAS, Perkin-Elmer 1100B) to detect the sodium content in the solution. A dilution factor of 8000 was required. The relative error of this method is in general 3-5%.

Besides the successful sodium determination by flame-AAS, determinations of the chloride content were carried out as well. The analysis was done by an absorption technique, the so-called Dr. Lange CADAS 50S Spektralphotometer. The principle of this analysis is the following. The Dr. Lange company (Dr. Bruno Lange GmbH & Co. KG) that produces the photometer also supplies different test tubes containing specific reagents. A volumetric specified amount of the solution of the unknown chloride content is applied to a test tube. In the case of the chloride analysis the following reaction is occurring

$$2\ Cl^- + Hg(SCN)_2 \ <=>> \ HgCl_2 + 2\ SCN^-$$

$$FeX_3 + 3\ SCN^- \ —> \ Fe(SCN)_3 + 3\ X^-$$

where FeX_3 represents iron(III) salts - not specified by the manufacturer. The iron(III) thiocyanate complexes are colouring the solution in the test tubes brownish. The photometer is then measuring the absorbance of the solution and calculates the chloride content. The result is given on the display of the photometer. This analysis is relatively appealing. However, it has some shortcomings. The concentration range in which the test tubes are applicable is very low < 70 mg Cl^- / L, which is comparable with the flame-AAS.

Furthermore, the effect of the amount of chloride added seems to be ignored; the guidelines only say that 1 mL should be added. Whether that is 0.9 or 1.1 mL is not addressed. Last but not least, the effect of the temperature. The test tubes containing the reagents must be kept at < 5 °C, but when the chloride solution is applied and the test tube is placed in the photometer, the temperature should be ambient (15-25 °C). However, the temperature dependence on the iron(III) thiocyanate complex seems to be quite significant since the chloride readings are fluctuating by approximately 2%. This is a high precision, but the accuracy is not always acceptable, i.e. a determination of the NaCl solubility in water gives more than 7 molal, while the literature value is 6.14 molal. Out of curiosity the 'chloride' content of the 'pure' test tubes was measured before the chloride solution was added. The readings were never zero, but around 2 mg Cl^- / L. A calibration tube supplied by the Dr. Lange company was used to calibrate the photometer. I would not recommend this technique to determine the chloride content but I would rely on the flame-AAS determination of sodium.

5.1.5 Results and discussion

The density of the saturated dipeptide solution, the calculated volume expansion by dissolving the dipeptide in water, and the solubility of the dipeptide in pure water are given in Tables 5.1 and 5.2. The calculated volume expansion is given as cm³ per kg of pure water. The average and sample standard deviation, *s*, is also given (Skoog et al., 1992). The volume expansion when dissolving a solute in water $\Delta_{mix}V$ is calculated as the difference between the volume of the solution V and the volume of water V_w.

$$\Delta_{mix} V = V - V_w \tag{5.1}$$

When the volume expansion is calculated per kg of water, then the volume of water is

$$V_w = \frac{1000\,g}{\rho_w} \tag{5.2}$$

where ρ_w is the density of water. The volume of a solution containing 1 kg of water is

$$V = \frac{1000\,g + \sum_{solutes} m_s M_s}{\rho_{solution}} \tag{5.3}$$

where m_s is the molality of the solute, M_s is the molar mass of the solute, and $\rho_{solution}$ is the density of the solution.

To ease the readability the Tables 5.1 - 5.11 are placed at the end of this chapter. The values in Tables 5.1 and 5.2 show that by saturating water with glycylglycine the volume increases by 138 cm³ per kg of water whereas for glycyl-L-alanine the volume increase is 465 cm³ per kg of water. This huge volume expansion reduces the density of the saturated solution to a specific gravity of 1.157 only.

Tables 5.3 - 5.5 show the measured densities of the salt solutions, data available in the literature (CRC Handbook of Chemistry and Physics, 78th Ed., 1997-1998 and 62nd Ed., 1981-1982) at 293 K, the correlation of Söhnel and Novontý (1985) at 298 K, and the calculated volume expansion when the salt is dissolved in 1 kg of water. The volume expansions when dissolving NaCl and Na_2SO_4 are similar whereas $(NH_4)_2SO_4$ gives rise to a much larger volume expansion.

Tables 5.6 - 5.11 show the measured densities of the salt - dipeptide - water solutions, the solubilities, and the calculated volume expansions when dissolving salt + dipeptide in 1 kg of water. Experimental results of the solubility of glycyl-L-alanine in NaCl in the range of 2-5 molal have been disregarded due to an experimental error.

When dissolving salt + glycylglycine in 1 kg of water the volume expansions range between 140 and 240 cm³ whereas it ranges from 470 to 540 cm³ for dissolving salt + glycyl-L-alanine.

The approximate volume expansion by dissolving salt and dipeptide in 1 kg water is

$$\Delta V_{salt+dipeptide} = \Delta V_{salt} + \Delta V_{dipeptide,S=S_0} \frac{S}{S_0} \tag{5.4}$$

where S is the solubility of the dipeptide in the salt solution and S_0 is the solubility in pure water. This relationship is within 5-10 % of the experimentally determined volume expansion.

The results in Tables 5.6 - 5.11 show that the solubility of the glycylglycine increases moderately with increasing salt concentration. The solubility of glycyl-L-alanine show a minor or no salting-in effect at low salt concentrations and a moderate salting-out effect at higher salt concentrations in NaCl and Na_2SO_4, and in $(NH_4)_2SO_4$ the solubility is almost constant. Similar results were observed for some amino acids investigated by Carta, 1998.

As presented in the next chapter the activity coefficient of the dipeptides in NaCl solutions (ranging from 0.1 to 1.0 molal NaCl) relative to the activity coefficient of the dipeptide in pure water has been determined. The results show that the activity coefficient ratio of glycylglycine at saturation decreases with increasing salt concentration whereas the activity coefficient ratio of glycyl-L-alanine increases slightly with increasing salt concentration. Given this and the assumption that the standard state of the precipitate is invariant one would expect a salting-in of glycylglycine and a minor salting-out of glycyl-L-alanine.

The solubility of NaCl in pure water is 6.14 molal (Clarke and Glew, 1985) and saturation with glycylglycine does not reduce the salt solubility whereas the solubility limit is reduced by 17% when saturated with glycyl-L-alanine.

Authors	Solubility of glycylglycine (mol / kg water)
This work	1.74
McMeekin et al., 1935	1.72
Smith and Smith, 1940c	1.87
Nozaki and Tanford, 1963, 1965	1.76; 1.72
Conio et al., 1973	1.91
Bruskov and Klimov, 1973	1.74
Gekko, 1981	1.72

Table 5.12: The solubility of glycylglycine in pure water at 298.15 K.

The solubility data of glycylglycine in pure water determined spectroscopically are compared with data available in the literature in Table 5.12. The data from the literature were all determined by the dry weight method. There is a good agreement between the literature data and the results of this work. Neither the solubility of glycylglycine nor of glycyl-L-alanine in aqueous electrolyte solutions have been reported in the literature. The solubility of glycyl-L-alanine is more than twice that of glycylglycine which is in agreement with an investigation (Sijpkes et al., 1994) of the solubility of cyclic dipeptides, cyclo(glycylglycine) and cyclo(glycyl-L-alanine). The solubilities of these dipeptides are 0.15 and 0.56 molal, respectively.

The reason why the solubilities of the cyclic dipeptides are significantly lower than non-cyclic ones could be because they are unchanged in a highly polar solvent. It could be interesting to

investigate whether or not the trend of the solubility of cyclic dipeptides is similar in a non-polar solvent such as ethanol.

The pH values of the solutions were not measured but a saturated dipeptide - water solution will have a pH value corresponding to the isoelectric point, i.e. 5.65 for glycylglycine and 5.70 for glycyl-L-alanine where the dipeptide is a zwitterion. The influence of the carbon dioxide from the air was considered since the dipeptide solutions had a buffer effect, see Figures 5.2a and 5.2b. Furthermore, the samples were capped during the equilibration time.

	$\rho_{glycylglycine}$ (g/cm³)	Solubility (mol / kg H_2O)	$\Delta_{mix}V$ (cm³ / kg H_2O)
	1.0759	1.72	138
	1.0778	1.81	147
	1.0785	1.75	138
	1.0782	1.73	136
	1.0773	1.71	135
	1.0778	1.72	136
Average	1.0776	1.74	138
s	0.0009	0.04	5.3

Table 5.1: The density of a saturated glycylglycine - water solution, the solubility of glycylglycine in water, and the volume expansion by dissolving glycylglycine in water at 298.15K.

	$\rho_{glycyl\text{-}L\text{-}alanine}$ (g/cm³)	Solubility (mol / kg H_2O)	$\Delta_{mix}V$ (cm³ / kg H_2O)
	1.1568	4.79	467
	1.1568	4.74	458
	1.1564	4.77	465
	1.1562	4.78	466
	1.1584	4.74	458
	1.1573	4.88	477
Average	1.1570	4.78	465
s	0.0008	0.05	6.9

Table 5.2: The density of a saturated glycyl-L-alanine - water solution, the solubility of glycyl-L-alanine in water, and the volume expansion by dissolving glycyl-L-alanine in water at 298.15K.

NaCl (mol/kg H_2O)	Reference 293.15K ρ_{NaCl} (g / cm³)	Reference 298.15K ρ_{NaCl} (g / cm³)	Measured 298.15K ρ_{NaCl} (g / cm³)	$\Delta_{mix}V$ (cm³ / kg H_2O)
0.1003	1.0024	1.0012	1.0012	1.8
0.2012	1.0065	1.0054	1.0045	4.4
0.4041	1.0146	1.0136	1.0124	8.3
0.5071	1.0187	1.0176	1.0173	9.3
0.6082	1.0227	1.0216	1.0210	11.4
0.8151	1.0307	1.0296	1.0291	15.2
0.9182	1.0346	1.0335	1.0330	17.2
1.0217	1.0386	1.0374	1.0370	19.1

Table 5.3: Measured and tabulated values of the density of NaCl - water solutions and the volume expansion by dissolving NaCl in water at 298.15K. The reference at 293.15K is CRC Handbook of Chemistry and Physics, 78th Ed., 1997-1998, and the reference at 298.15K is Söhnel and Novotný, 1985.

Na_2SO_4 (mol/kg H_2O)	Reference 293.15K ρ_{Na2SO4} (g / cm³)	Reference 298.15K ρ_{Na2SO4} (g / cm³)	Measured 298.15K ρ_{Na2SO4} (g / cm³)	$\Delta_{mix}V$ (cm³ / kg H_2O)
0.1003	1.0107	1.0098	1.0119	– 0.5
0.1735	1.0197	1.0189	1.0202	1.6
0.2012	1.0231	1.0223	1.0240	1.7
0.3524	1.0414	1.0405	1.0429	4.0
0.5054	1.0591	1.0583	1.0606	7.7
0.6078	1.0708	1.0700	1.0724	10.2
0.8146	1.0941	1.0930	1.0956	15.5
1.0241	1.1171	1.1156	1.1186	21.2

Table 5.4: Measured and tabulated values of the density of Na_2SO_4 - water solutions and the volume expansion by dissolving Na_2SO_4 in water at 298.15K. The reference at 293.15K is CRC Handbook of Chemistry and Physics, 78th Ed., 1997-1998, and the reference at 298.15K is Söhnel and Novotný, 1985.

$(NH_4)_2SO_4$ (mol/kg H_2O)	Reference 293.15K $\rho_{(NH4)2SO4}$ (g / cm³)	Reference 298.15K $\rho_{(NH4)2SO4}$ (g / cm³)	Measured 298.15K $\rho_{(NH4)2SO4}$ (g / cm³)	$\Delta_{mix}V$ (cm³ / kg H_2O)
0.1012	1.0061	1.0052	1.0072	3.3
0.2028	1.0137	1.0129	1.0145	9.3
0.4095	1.0287	1.0278	1.0294	21.2
0.5150	1.0360	1.0351	1.0365	27.6
0.6217	1.0432	1.0422	1.0436	34.1
0.8411	1.0574	1.0562	1.0574	48.0
0.9524	1.0642	1.0630	1.0644	54.9
1.0652	1.0710	1.0697	1.0712	62.1

Table 5.5: Measured and tabulated values of the density of $(NH_4)_2SO_4$ - water solutions and the volume expansion by dissolving $(NH_4)_2SO_4$ in water at 298.15K. The reference at 293.15K is CRC Handbook of Chemistry and Physics, 62nd Ed., 1981-1982, and the reference at 298.15K is Söhnel and Novotný, 1985.

NaCl (mol/kg H_2O)	$\rho_{sat'd\ sol.}$ (g / cm³)	Solubility (mol/kg H_2O)	Average $\Delta_{mix}V$ (cm³ / kg H_2O)
0.1003	1.0807	1.73	140
	1.0825	1.76	
0.2012	1.0841	1.74	144
	1.0869	1.80	
0.4041	1.0856	1.80	157
	1.0943	1.83	
0.5071	1.0984	1.85	156
	1.0985	1.84	
0.6082	1.1024	1.87	160
	1.1021	1.85	
0.8151	1.1098	1.87	165
	1.1095	1.89	
0.9182	1.1130	1.88	168
	1.1129	1.88	
1.0217	1.1163	2.10	183
	1.1162	1.89	
2.0436		1.98	
3.0061		1.97	
3.9870		2.01	
4.9859		2.07	
5.5928		2.10	
5.6093		2.12	
5.6202		2.08	
5.6300		2.10	

Table 5.6: The density of NaCl - glycylglycine - water solutions, the solubility of glycylglycine in NaCl - water solutions, and the volume expansion by dissolving NaCl plus glycylglycine in water at 298.15K.

Na_2SO_4 (mol/kg H_2O)	$\rho_{sat'd\ sol.}$ (g / cm³)	Solubility (mol/kg H_2O)	Average $\Delta_{mix}V$ (cm³ / kg H_2O)
0.1003	1.0920	1.84	147
	1.0914	1.82	
0.1735	1.1042	1.89	153
	1.1042	1.85	
0.2012	1.1213	1.91	155
	1.1201	1.88	
0.3524	1.1005	2.01	167
	1.0996	1.94	
0.5054	1.1376	2.11	176
	1.1376	1.97	
0.6078	1.1478	2.09	180
	1.1469	2.00	
0.8146	1.1669	2.03	182
	1.1665	2.00	
1.0241	1.1860	2.07	192
	1.1850	2.03	

Table 5.7: The density of Na_2SO_4 - glycylglycine - water solutions, the solubility of glycylglycine in Na_2SO_4 - water solutions, and the volume expansion by dissolving Na_2SO_4 plus glycylglycine in water at 298.15K.

$(NH_4)_2SO_4$ (mol/kg H_2O)	$\rho_{sat'd\ sol.}$ (g / cm³)	Solubility (mol/kg H_2O)	Average $\Delta_{mix}V$ (cm³ / kg H_2O)
0.1012	1.0878	1.82	150
	1.0868	1.81	
0.2028	1.0958	1.89	161
	1.0951	1.87	
0.4095	1.1102	2.00	184
	1.1093	1.98	
0.5150	1.1169	2.05	194
	1.1155	2.01	
0.6217	1.1237	2.07	203
	1.1223	2.05	
0.8411	1.1344	2.12	221
	1.1331	2.07	
0.9524	1.1401	2.12	229
	1.1389	2.08	
1.0652	1.1452	2.14	238
	1.1439	2.10	

Table 5.8: The density of $(NH_4)_2SO_4$ - glycylglycine - water solutions, the solubility of glycylglycine in $(NH_4)_2SO_4$ - water solutions, and the volume expansion by dissolving $(NH_4)_2SO_4$ plus glycylglycine in water at 298.15K.

NaCl (mol/kg H_2O)	$\rho_{sat'd\ sol.}$ (g / cm³)	Solubility (mol/kg H_2O)	Average $\Delta_{mix}V$ (cm³ / kg H_2O)
0.1003	1.1577	4.82	469
	1.1577	4.73	
0.2012	1.1592	4.88	476
	1.1600	4.74	
0.4041	1.1637	4.80	476
	1.1638	4.74	
0.6082	1.1675	4.71	471
	1.1676	4.67	
0.8151	1.1710	4.68	475
	1.1713	4.68	
1.0217	1.1757	4.73	481
	1.1749	4.62	
5.3123 (saturation)		3.86	
5.3365 (saturation)		3.91	

Table 5.9: The density of NaCl - glycyl-L-alanine - water solutions, the solubility of glycyl-L-alanine in NaCl - water solutions, and the volume expansion by dissolving NaCl plus glycyl-L-alanine in water at 298.15K.

Na_2SO_4 (mol/kg H_2O)	$\rho_{sat'd\ sol.}$ (g / cm³)	Solubility (mol/kg H_2O)	Average $\Delta_{mix}V$ (cm³ / kg H_2O)
0.1003	1.1631	4.98	494
	1.1646	4.98	
0.1735	1.1693	4.77	470
	1.1707	4.77	
0.2012	1.1687	4.80	475
	1.1692	4.80	
0.6078	1.1936	4.56	464
	1.1952	4.56	
0.8146	1.2055	4.47	463
	1.2067	4.47	
1.0241	1.2173	4.34	458
	1.2188	4.34	

Table 5.10: The density of Na_2SO_4 - glycyl-L-alanine - water solutions, the solubility of glycyl-L-alanine in Na_2SO_4 - water solutions, and the volume expansion by dissolving Na_2SO_4 plus glycyl-L- alanine in water at 298.15K.

$(NH_4)_2SO_4$ (mol/kg H_2O)	$\rho_{sat'd\ sol.}$ (g / cm³)	Solubility (mol/kg H_2O)	Average $\Delta_{mix}V$ (cm³ / kg H_2O)
0.1012	1.1601	4.81	482
	1.1620	4.91	
0.2028	1.1631	4.79	487
	1.1667	4.91	
0.4095	1.1698	4.81	503
	1.1715	4.90	
0.6217	1.1758	4.81	518
	1.1783	4.87	
0.8411	1.1820	4.78	529
	1.1838	4.81	
1.0652	1.1878	4.75	542
	1.1899	4.78	

Table 5.11: The density of $(NH_4)_2SO_4$ - glycyl-L-alanine - water solutions, the solubility of glycyl-L-alanine in $(NH_4)_2SO_4$ - water solutions, and the volume expansion by dissolving $(NH_4)_2SO_4$ plus glycyl-L-alanine in water at 298.15K.

5.2 Electrode potential measurements of NaCl - dipeptide - water

Experimental determination of activity coefficients of amino acids, peptides, and proteins in solution is a prerequisite to develop thermodynamic models describing the phase behaviour in bioprocesses. Three methods commonly used to determine the solvent activity in biological systems are freezing point depression (Pitzer, 1991, pp. 17-19), vapour pressure (Pitzer, 1991, pp. 214-220) and isopiestic methods (Pitzer, 1991, p. 241). The solute activity can only be obtained indirectly by means of the Gibbs-Duhem equation. For systems containing more than two components, a solute and a solvent, only the solvent activity is accessible by these methods. The freezing point depreciation has frequently been used for systems containing amino acids (Roth, 1903; Hoskins et al., 1930; Frankel, 1930; Lewis, 1931; Cann, 1932; Scatchard and Prentiss 1934a, 1934b, Lilley and Scott, 1976b), whereas the vapour pressure method has seldom been used (Kuramochi et al., 1997), as it requires a very high precision in measuring the pressure. The principle of the isopiestic method is to equilibrate two solutions in a common atmosphere where the solvent is the only volatile component and one of the solutions serves as the reference solution where the activity of the solvent is known. At equilibrium the solvent activity in the two solutions is identical. This method has been used extensively to determine activity coefficients in aqueous amino acid solutions (Smith and Smith, 1937, 1940a-c; Richards, 1938; Robinson and Sinclair, 1934; Anslow, 1933; Robinson, 1952; Hutchens et al., 1963; Bower and Robinson, 1965; Schrier and Robinson, 1971, 1974; Lilley and Scott, 1976a; Bonner, 1981, 1982; Kuramochi et al., 1996). A thermodynamic description of the isopiestic method is given in Chapter 3. The Thermodynamics of Experimental Methods.

Another way to determine the activity coefficient of an electrolyte in a binary solution is to measure the electrode potential. The electrode potential is directly affected by all species present in the solution. Khoshkbarchi and Vera (1996) review applications of different electrochemical cells used prior to 1995. Only recently, reliable ion-selective electrodes have become available and applied in salt - amino acid - water systems (Khoshkbarchi and Vera, 1996a-c; Khoshkbarchi et al., 1997, Soto-Campos et al., 1997, 1998). The solute activity coefficient was obtained by means of the cross-differential equation. In this investigation two ion-selective electrodes have been used to determine the activity coefficients of glycylglycine and glycyl-L-alanine in aqueous sodium chloride solutions.

5.2.1 Materials

The materials are identical to those of Section 5.1.1.

5.2.2 Experimental procedure

The experimental set-up comprises of a sodium ion-selective and a chloride ion-selective electrode (ISE) which measure the electrode potential of NaCl in a NaCl - dipeptide - water solution. The experimental set-up resembles that of Haghtalab and Vera (1991). When the chloride ISE is used as reference electrode for the sodium ISE, the liquid-junction potential can be eliminated (Haghtalab and Vera, 1991). The ion-selective electrodes (315-75 C Sodium Electrode) and (301-75 Chloride Mono) were from Sentek (Braintree, Essex, UK). The ISE's were immersed in a solution contained in a U-shaped glass tube and connected to a digital voltmeter (Metrohm - 654 pH Meter, error = $\pm 5 \cdot 10^{-5}$ V + 1 digit, resolution = 0.1 mV) from Metrohm, (Herisau, Switzerland). The dimensions of the U-tube were a height of 102 mm and an inner diameter of 14 mm. The radius of the bend was equal to the diameter of the tube. The position of and the distance between the electrodes relative to the U-tube were kept constant. The U-tube was placed in a thermostatically controlled water bath (Lauda RM6, Königshofen, Germany) at 298.15 ± 0.1 K. Magnetic stirrers agitated both the water bath and the solution in the U-tube.

Salt solutions ranging from 0.1 to 1.0 molal were prepared gravimetrically by the use of a Mettler Toledo AG204 DeltaRange (Greifensee, Switzerland) balance with a resolution of ± 0.1 mg. The water was cleaned in a milli-Q water system from Millipore to a conductivity of 0.06 $\mu S \cdot cm^{-1}$.

A volume of approximately 3 mL of the salt solution (mass known) was nearly saturated with dipeptide (mass known). After dissolving the peptide the solution was put in the U-tube and the ISE's were immersed and the electrode potential was observed. When the electrode potential became constant the value was taken down. The sample was then diluted (mass known) with the salt solution whereby the salt molality was kept constant whereas the dipeptide molality decreased. Measurements were performed at NaCl molalities up to 1 molal.

5.2.3 Theory

Each ISE only allows specified ions to penetrate its membrane. For the two half cells the reduction reactions can be written as

$$\begin{aligned} Na^+ + e^- &= Na - ISE\,(s) && n_e = 1 \\ Cl - ISE\,(s) + e^- &= Cl^- && n_e = 1 \end{aligned} \tag{5.5}$$

where n_e is the number of moles of electrons transferred per mole of reaction. The electrode potentials of the two half cells are according to the Nernst equation

$$\begin{aligned} E_{Na^+/Na-ISE} &= E^*_{Na^+/Na-ISE} - \frac{RT}{F}\ln\frac{a_{Na-ISE}}{a_{Na^+}} \\ E_{Cl-ISE/Cl^-} &= E^*_{Cl-ISE/Cl^-} - \frac{RT}{F}\ln\frac{a_{Cl^-}}{a_{Cl-ISE}} \end{aligned} \tag{5.6}$$

where E_i^* is the reduction potential when the activity ratio is unity. Defining the activities as shown in Chapter 2, eq. (2.27), E_i^* is the hypothetical reduction potential when all components are pure, and thus only a function of temperature and pressure.

5.2.4 The reference electrode potential for the symmetric activity coefficient

The electrode potential of a galvanic cell ($E_{cell} > 0$) is

$$\begin{aligned} E &= E_{cation} - E_{anion} \\ &= E^*_{Na^+/Na-ISE} - \frac{RT}{F}\ln\frac{a_{Na-ISE}}{a_{Na^+}} - E^*_{Cl-ISE/Cl^-} + \frac{RT}{F}\ln\frac{a_{Cl^-}}{a_{Cl-ISE}} \\ &= E^*_{Na^+/Na-ISE} - E^*_{Cl-ISE/Cl^-} + \frac{RT}{F}\ln\frac{a_{Na^+}a_{Cl^-}}{a_{Na-ISE}\,a_{Cl-ISE}} \\ &= E^{ref} + \frac{RT}{F}\ln(a_{Na^+}a_{Cl^-}) \end{aligned} \tag{5.7}$$

where E^{ref} is the reference electrode potential

$$E^{ref} = E^*_{Na^+/Na-ISE} - E^*_{Cl-ISE/Cl^-} - \frac{RT}{F}\ln(a_{Na-ISE}\,a_{Cl-ISE}) \tag{5.8}$$

It is assumed that the product of the ISE activities is constant. However, it might be possible that the presence of another solute might effect the ISE activities as discussed in paragraph

5.2.7. E and E^{ref} refer to the electrode potential and the reference electrode potential of the cell, respectively. With $a_i = x_i \gamma_i$, eq. (5.7) becomes

$$E = E^{ref} + \frac{RT}{F} \ln (x_{Na^+} x_{Cl^-} \gamma_{Na^+} \gamma_{Cl^-}) \tag{5.9}$$

Defining the mole fractions and the activity coefficient of the salt (NaCl) as

$$x_{\pm} \equiv x_{Na^+} = x_{Cl^-} \tag{5.10}$$

and

$$2 \ln \gamma_{\pm} \equiv \ln \gamma_{Na^+} + \ln \gamma_{Cl^-} \tag{5.11}$$

the electrode potential is

$$E = E^{ref} + \frac{2RT}{F} \ln (x_{\pm} \gamma_{\pm}) \tag{5.12}$$

where E^{ref} is the reference electrode potential.

The advantage of expressing the electrode potential as shown in eq. (5.12) instead of the commonly used molality based expression, as discussed in Chapter 4. Electrochemistry, is that the reference electrode potential E^{ref}, is independent of the concentrations of the non-ionic species present. Consequently, E^{ref} remains constant even though dipeptide is added to the salt - water solution.

The works of Harned and Åkerlöf (1926), Harned and Owen (1930a-b), Harned and Hammer (1933), Smith and Smith (1942), and Owens and King (1943) all use cells without liquid junction, the so-called Harned cells (see Chapter 4. Electrochemistry). The goal of these works was the determination of the dissociation constants of weak acids and bases, e.g. amino acids. The electrodes of these works were predominately hydrogen and silver chloride electrodes or sometimes mercury chloride electrodes; i.e. not ion-selective electrodes. Consequently, the activity product in the Nernst equation consists of all ionic species in the solution. This was solved by assuming the values of activity coefficients and by knowing the concentrations (molalities) and then solve for the dissociation constant by extrapolation to infinite dilution. This method obviously demands that the values of activity coefficients are known, so one can solve for the dissociation constants. That these constants then sometimes

are used - in other works - to determine the very same activity coefficients will of course lead to an excellent agreement between experimental results and those found in the literature.

5.2.5 The pH of the solutions

In a ternary system of NaCl - dipeptide - water more than three species are present. The electrolyte dissociates fully and the dipeptide is capable of forming three species: a cation, a zwitterion, and an anion. Finally, water autoprotolyses itself to H^+ (or H_3O^+) and OH^-. However, some of the species will be present in very small amounts. The apparent pK_a values of glycylglycine are 3.12 and 8.17 and of glycyl-L-alanine 3.15 and 8.25 (Greenstein and Winitz, 1961). The isoelectrical point of glycylglycine pI is 5.65 and for glycyl-L-alanine pI is 5.7. pH of an aqueous dipeptide solution depends on the concentration of the dipeptide. The NaCl - water system has a pH of approximately pH 7, and upon addition of dipeptide pH declines rapidly to a pH close to the isoelectrical point of the dipeptide as depicted in Figures 5.1a and 5.1b. If one calculates the Bjerrum diagram (Skoog et al., 1992, p. 258) of the dipeptide, assuming the solution is ideal, one will observe that more than 99% of the dipeptide will be present in its zwitterionic form because pH equals pI when the dipeptide concentration exceeds 10 mM. Because of this the amount of dipeptide cations and anions are negligible as shown in Figures 5.2a and 5.2b. Furthermore, it is not expectable that a change of the H_3O^+ concentration from ~10^{-7} M to ~$10^{-5.7}$ M has a significant effect on $\gamma_{\pm}$.

5.2.6 Data reduction

The difference in the electrode potentials between the ternary system of salt - dipeptide - water and the binary system of salt - water gives the ratio of the salt activity coefficients

$$\begin{aligned}\Delta E &= E^{ter} - E^{bin} \\ &= E^{ref} + \frac{2RT}{F}\ln a_{\pm}^{ter} - E^{ref} - \frac{2RT}{F}\ln a_{\pm}^{bin} \\ &= \frac{2RT}{F}\ln\frac{x_{\pm}^{ter}}{x_{\pm}^{bin}} + \frac{2RT}{F}\ln\frac{\gamma_{\pm}^{ter}}{\gamma_{\pm}^{bin}}\end{aligned} \tag{5.13}$$

and finally

$$\ln \frac{\gamma_{\pm}^{ter}}{\gamma_{\pm}^{bin}} = \frac{F}{2RT}\Delta E - \ln \frac{x_{\pm}^{ter}}{x_{\pm}^{bin}} \tag{5.14}$$

The right-hand side of eq. (5.14) can easily be evaluated from the experimentally determined electrode potentials. Some authors have used an experimentally estimated slope instead of the Nernstian slope. This is addressed later in paragraph 5.2.7. In eq. (5.14) all additive constant potentials, e.g. the boundary potential or the asymmetry potential cancel because they are similar in the binary and the ternary system. In order to determine the activity coefficients of the dipeptides in NaCl - water solutions we must fit the activity coefficient ratio in eq. (5.14) and use the cross-differential equation to estimate the corresponding activity coefficient ratio of the dipeptide. The following empirical expression fits the activity coefficient ratio in eq. (5.14) quite well. A denotes dipeptide and ± salt.

$$f(z) = \frac{a_1 z_A}{(1+b_1 z_A)(1+b_2 z_{\pm})} + (c_1 + c_2 z_{\pm}) z_A + d_1 z_A^2 \tag{5.15}$$

where z_i is either the mole fraction $x_i = n_i/n_{total}$ or the molar solute-solvent ratio $y_i = n_i/n_w$ in the ternary mixture wherefore $f(z_A = 0) = 0$. Since the solutions are diluted, the total mole number is almost equal to the mole number of water and, consequently, x_i and y_i are almost identical. Using the independent variables **x** or **y** give approximately identical sample standard deviations, wherefore, due to the facilitation of the mathematics involved when evaluation the cross-differential, we use **y**. The parameters and the sample standard deviations of the estimates are given in Table 5.13.

	Glycylglycine	Glycyl-L-alanine
a_1	– 41.3160	– 31.0537
b_1	106.8204	80.4917
b_2	770.8665	165.9538
c_1	– 5.3985	1.4654
c_2	106.9840	15.7241
d_1	51.7459	1.5088
s	0.0031	0.0078

Table 5.13: Parameters in eq. (5.15) and sample standard deviation s of the estimate.

With the parameters estimated, eq. (5.15) does not have any inflection points at constant salt molality since the second derivative with respect to y_A is always positive whatever the salt concentration. Consequently, at each salt molality, eq. (5.15) is only capable of producing one extremum, a minimum. Figures 5.3 and 5.4 show the logarithm of the ratio of the activity

coefficients of the electrolyte in the ternary system to the binary electrolyte - water system as function of the dipeptide molality at various constant salt molalities. The effect of adding dipeptide to the NaCl - H_2O system is stronger at low salt concentration than at higher salt concentration. Eq. (5.15) correlates the activity coefficient ratio of the electrolyte in the ternary and the binary system reasonably.

The asymmetric activity coefficient of salt in pure water (Clarke and Glew, 1985) can empirically be correlated as

$$\ln \frac{\gamma_{\pm}^{\mathrm{bin}}}{\gamma_{\pm,\mathrm{w}}^{\infty,\mathrm{bin}}} = \ln \tilde{\gamma}_{\pm,\mathrm{w}}^{\mathrm{bin}} = \frac{A\sqrt{y_{\pm}}}{1 + B\sqrt{y_{\pm}}} + C\, y_{\pm} + D\, y_{\pm}^{\,2} \tag{5.16}$$

The salt activity coefficient at infinite dilution in pure water $\gamma_{\pm,\mathrm{w}}^{\infty,\mathrm{bin}}$ is a function of temperature and pressure, only. Note that the chosen reference solvent is water so the subscript rs (from the Chapter 2. Basic Thermodynamics) is replaced by w. The parameters and the sample standard deviation of the estimate are given in Table 5.14.

	NaCl
A	– 8.5462
B	9.4329
C	6.5537
D	13.9653
s	$9.14 \cdot 10^{-5}$

Table 5.14: Parameters for eq. (5.16) and sample standard deviation s of the estimate.

If we add eq. (5.16), the logarithm of the asymmetric salt activity coefficient in pure water, to eq. (5.14), the logarithm of the ratio of the activity coefficients of the electrolyte in the ternary system to the binary electrolyte - water system, the result is the logarithm of the ratio of the salt activity coefficient in the ternary system to the salt activity coefficient at infinite dilution in pure water

$$\ln \frac{\gamma_{\pm}^{\mathrm{ter}}}{\gamma_{\pm,\mathrm{w}}^{\infty,\mathrm{bin}}} = \ln \frac{\gamma_{\pm}^{\mathrm{ter}}}{\gamma_{\pm}^{\mathrm{bin}}} + \ln \frac{\gamma_{\pm}^{\mathrm{bin}}}{\gamma_{\pm,\mathrm{w}}^{\infty,\mathrm{bin}}} \tag{5.17}$$

Figures 5.5 and 5.6 show the activity coefficients of salt in the electrolyte - dipeptide - water solutions at constant salt molalities in proportion to the activity coefficient of salt at infinite dilution in pure water as a function of dipeptide concentration. The change of the electrolyte activity coefficient caused by adding dipeptide is most pronounced at low salt concentration.

Another way of illustrating the same effect is to depict the same activity coefficient ratio at constant dipeptide molality as a function of salt concentration, as shown in Figures 5.7 and 5.8. It is noted that the top line is the asymmetric activity coefficient of NaCl in pure water which is only one that is zero at infinite dilution.

Since one does not know $\ln\gamma_{\pm}^{ter}$ but only $\ln\gamma_{\pm}^{ter} - \ln\gamma_{\pm,w}^{\infty,bin}$, one can calculate the reference electrode potential E^{ref} of the cell except for a constant of $2RT/F \ln\gamma_{\pm,w}^{\infty,bin}$, only.

$$\begin{aligned} E &= E^{ref} + \frac{2RT}{F}\ln(x_{\pm}^{ter}\,\gamma_{\pm}^{ter}) \\ &= E^{ref} + \frac{2RT}{F}\ln x_{\pm}^{ter} + \frac{2RT}{F}\ln\frac{\gamma_{\pm}^{ter}}{\gamma_{\pm,w}^{\infty,bin}} - \frac{2RT}{F}\ln\frac{1}{\gamma_{\pm,w}^{\infty,bin}} \\ &= \tilde{E}_w + \frac{2RT}{F}\ln\frac{x_{\pm}^{ter}\,\gamma_{\pm}^{ter}}{\gamma_{\pm,w}^{\infty,bin}} \end{aligned} \qquad (5.18)$$

where the electrode potential $\tilde{E}_w$ is defined as

$$\tilde{E}_w \equiv E^{ref} + \frac{2RT}{F}\ln\gamma_{\pm,w}^{\infty,bin} \qquad (5.19)$$

The estimated reference potential $\tilde{E}_w$ is 337 mV for the glycylglycine system and 338 mV for the glycyl-L-alanine system. Ideally, $\tilde{E}_w$ should have been identical since it is independent of the mixture composition and a function of E^{ref} and $\gamma_{\pm,w}^{\infty,bin}$ of the salt, only. The results are shown in Figures 5.9 and 5.10. To get maximum sensitivity when fitting the ternary activity coefficients one has to use eq. (5.14) and not eq. (5.18).

The activity coefficient of the dipeptide are calculated from the activity coefficient of the electrolyte using the cross-differential equation (equivalent to Maxwell's equations) - readily obtained from any homogeneous differentiable function (Bjerrum, 1923)

$$\frac{\partial^2 G^E}{\partial n_{\pm}\partial n_A} = \frac{\partial^2 G^E}{\partial n_A \partial n_{\pm}} \qquad \Rightarrow \qquad \nu\frac{\partial\ln\gamma_{\pm}}{\partial n_A} = \frac{\partial\ln\gamma_A}{\partial n_{\pm}} \qquad (5.20)$$

Since $\ln\gamma_{\pm}^{bin}$ is independent of n_A,

$$\frac{\partial\ln\gamma_{\pm}^{ter}}{\partial n_A} - \frac{\partial\ln\gamma_{\pm}^{bin}}{\partial n_A} = \frac{\partial\ln\gamma_{\pm}^{ter}}{\partial n_A} \qquad (5.21)$$

Combining eqs. (5.20) and (5.21) the activity coefficient ratio of the dipeptide can be obtained by integration

$$\int_{n_\pm=0}^{n_\pm} \nu \frac{\partial \ln \gamma_\pm^{ter}}{\partial n_A} dn_\pm = \int_{n_\pm=0}^{n_\pm} \frac{\partial \ln \gamma_A^{ter}}{\partial n_\pm} dn_\pm \quad \Rightarrow$$
$$\nu \int_{n_\pm=0}^{n_\pm} \frac{\partial \ln \gamma_\pm^{ter}}{\partial n_A} dn_\pm = \ln \gamma_A^{ter} - \ln \gamma_A^{bin} \tag{5.22}$$

Differentiating the fitting function eq. (5.15) with respect to the n_A and subsequently integrating it with respect to $n_\pm$ gives the function g which is merely a mathematical representation of eq. (5.22).

$$g(\mathbf{y}) = \nu \left(\frac{a_1 / b_2}{(1 + b_1 y_A)^2} \ln(1 + b_2 y_\pm) + c_1 y_\pm + 1/2\, c_2 y_\pm^2 + 2 d_1 y_A y_\pm \right) \tag{5.23}$$

Figures 5.11 and 5.12 show the resulting activity coefficient ratios of the dipeptides as a function of the salt concentration at constant dipeptide molality. The change of the activity coefficient ratio of the dipeptide is most pronounced at low concentrations of both solutes. Close to saturation glycyl-L-alanine shows salting-in.

Ellerton et al. (1964) and Smith (1940c) have published experimental activity coefficients (asymmetric convention) of the dipeptides in water at concentrations less than 1 mole per kg of water. Adding the logarithm of this asymmetric activity coefficient to eq. (5.22), the outcome is the logarithm of the activity coefficient of the dipeptide in proportion to $\gamma_{A,w}^{\infty,bin}$ in water. Figures 5.13 and 5.14 show the activity coefficients of the two dipeptides in dipeptide - salt - water solutions at constant dipeptide molalities in proportion to the activity coefficient of the dipeptide at infinite dilution in pure water in dependence of the salt concentration. Figures 5.15 and 5.16 show plots of the activity coefficient ratio in dependence of the molal concentration of the dipeptide. The intersections with the ordinate axis display the activity coefficients of the dipeptide at infinite dilution in the salt - water solution.

To form a general view over the result three-dimensional plots of the activity coefficient of the dipeptide in proportion to the that of the dipeptide at infinite dilution (in pure water) are presented in Figures 5.17 and 5.18.

5.2.7 The experimental slope and the Nernstian slope in the Nernst equation

Vera and co-workers (Khoshkbarchi and Vera, 1996a-c; Khoshkbarchi et al., 1997, Soto-Campos et al., 1997, 1998) have used experimentally estimated slopes instead of the Nernstian slope, 2RT/F, in the Nernst equation. The reference electrode potentials and slopes are determined from the electrode potentials measured for the binary electrolyte - water system. The intercepts, $\tilde{E}_w^S$, and the slopes, S, in eq. (5.24) are fitted to the experimental electrode potentials using activities available in literature Clarke and Glew (1985) and Zemaitis et al., 1986. The literature standards are based on the methods such as freezing point depression, vapour pressure, and the isopiestic method.

$$E = \tilde{E}_w^S + S \cdot \ln(x_\pm \tilde{\gamma}_{\pm,w}) \tag{5.24}$$

In this work, the intercept and slope determined in such a manner are 330.6 mV and 50.08 mV, respectively, with a correlation coefficient of 0.997. Using the slope S instead of the Nernstian slope corresponds to making the reference electrode potential a function of the salt concentration in the Nernst equation.

$$E = \tilde{E}_w^S + \tilde{E}_w^{add}(x_{NaCl}) + \frac{2RT}{F}\ln(x_\pm \tilde{\gamma}_{\pm,w}) \tag{5.25}$$

Where the additional electrode potential $\tilde{E}_w^{add}$ is

$$\tilde{E}_w^{add}(x_{NaCl}) = \left(S - \frac{2RT}{F}\right)\ln(x_\pm \tilde{\gamma}_{\pm,w}) \tag{5.26}$$

Consequently, the concentration dependent reference electrode potential can be compared to the residuals, res

$$res = E - \frac{2RT}{F}\ln(x_\pm \tilde{\gamma}_{\pm,w}) \tag{5.27}$$

which have been estimated from the experimental measurements and $\tilde{\gamma}_{\pm,w}$ from Clarke and Glew (1985). Figure 5.19 shows a comparison of res and the corresponding $\tilde{E}_w^S + \tilde{E}_w^{add}$ as a function of the salt concentration.

Although there is some scattering of the experimental data, it can be concluded that ($\tilde{E}_w^S + \tilde{E}_w^{add}$) as a function of the salt concentration describes the experimental data better than

using a constant E^{∞} of approximately 337 mV. Defining α as the ratio of the slope S and the Nernstian slope

$$\alpha = \frac{S}{2RT/F}, \tag{5.28}$$

gives an α value of 0.97. However, in this work the Nernstian slope has been used because it makes the data reduction independent of the choice of $\tilde{\gamma}_{\pm,w}$. If the data are recalculated using S determined from the data of Clarke and Glew (1985) as the reference for $\tilde{\gamma}_{\pm,w}$, the estimated results change by only 3% which we consider to be less than the experimental uncertainty. The deviation from the Nernstian slope cannot be explained by uncertainties in the temperature but could be due to concentration dependent variations in the ISE activities or some neglected potentials across the ISE membranes.

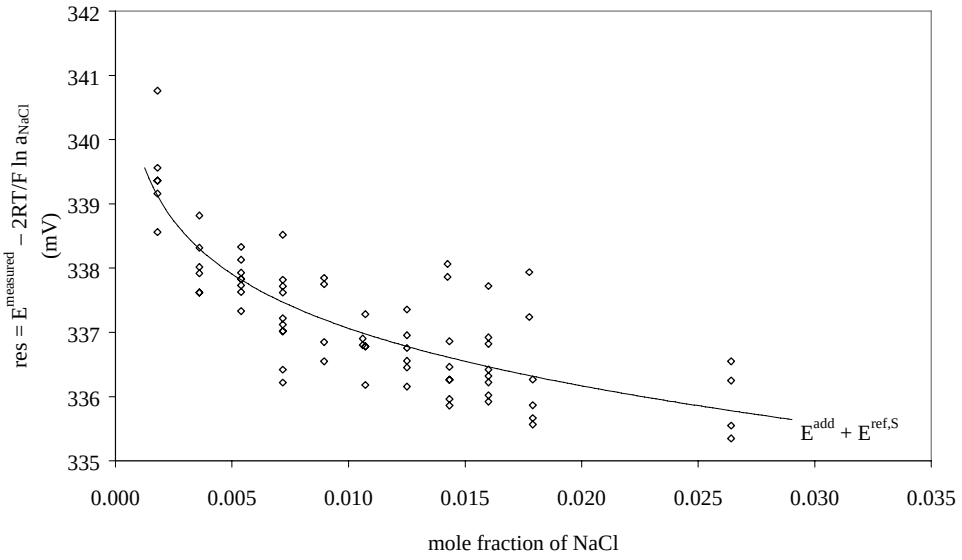


Figure 5.19: A comparison of the residuals, res, defined in eq. (5.27), ◊, and $\tilde{E}_w^S + \tilde{E}_w^{add}$, —, as functions of the NaCl concentration.

5.2.8 Discussion

The two ternary mixtures investigated in this work have not been investigated previously. However, Khoshkbarchi and Vera (1996a) have published results of the systems NaCl - glycine - H_2O and NaCl - DL-alanine - water. These two amino acids are the building blocks

of the two dipeptides investigated in this work. The activity coefficient ratios of NaCl (ternary to binary) as a function of the amino acid concentration resemble those of the corresponding salt - dipeptide - water systems, i.e. increasing the salt concentration increases the activity coefficient ratio of the electrolyte. In order to compare this work with the work of Khoshkbarchi and Vera (1996a) some conversions of their data have to be performed due to the fact that their reference state depends on the solute concentration. Khoshkbarchi and Vera (1996a) have defined the activity coefficient on a molality basis as shown in eq. (A.19). Consequently, the logarithmic ratio of the mole fraction of water in the ternary and the binary solutions must be subtracted from the activity coefficients published in Khoshkbarchi and Vera (1996a).

The NaCl activity coefficient ratios at two different compositions of NaCl and amino acid or dipeptide are listed in Table 5.15. The figures in Table 5.15 show that the amino acids have less effect on the activity coefficient ratio of NaCl than the dipeptides. It is noted that the presence of DL-alanine has the least effect on the electrolyte activity coefficient ratio.

$\ln\left(\frac{\gamma_{\pm}^{ter}}{\gamma_{\pm}^{bin}}\right)$	glycine*	DL-alanine*	glycylglycine	glycyl-L-alanine
0.1 molal NaCl 1.0 molal A	–0.09	–0.05	–0.18	–0.15
1.0 molal NaCl 0.1 molal A	–0.15	–0.06	–0.36	–0.34

Table 5.15: The activity coefficient ratio of NaCl in solutions containing amino acid or dipeptide (A). *Results from the Khoshkbarchi and Vera (1996a)

5.2.9 Conclusion

The thermodynamic theory of ion-selective electrodes (ISE's) has been presented. The experimental method is similar to the one suggested and applied by Haghtalab and Vera (1991). The experimental procedure to determine activity coefficients of the salt in the ternary systems, NaCl - glycylglycine - H_2O, and NaCl - glycyl-L-alanine - H_2O, was tested, and has proven to be suitable to determine the effect that the salt has on the activity coefficient of a non-electrolyte in a salt - water solution. Furthermore, if the activity coefficient of the non-electrolyte in the binary aqueous system is available, the activity coefficient of the non-

electrolyte in the ternary system in proportion to the activity coefficient of the non-electrolyte at infinite dilution in pure water can be determined. This ratio displays the effect the electrolyte has on the non-electrolyte.

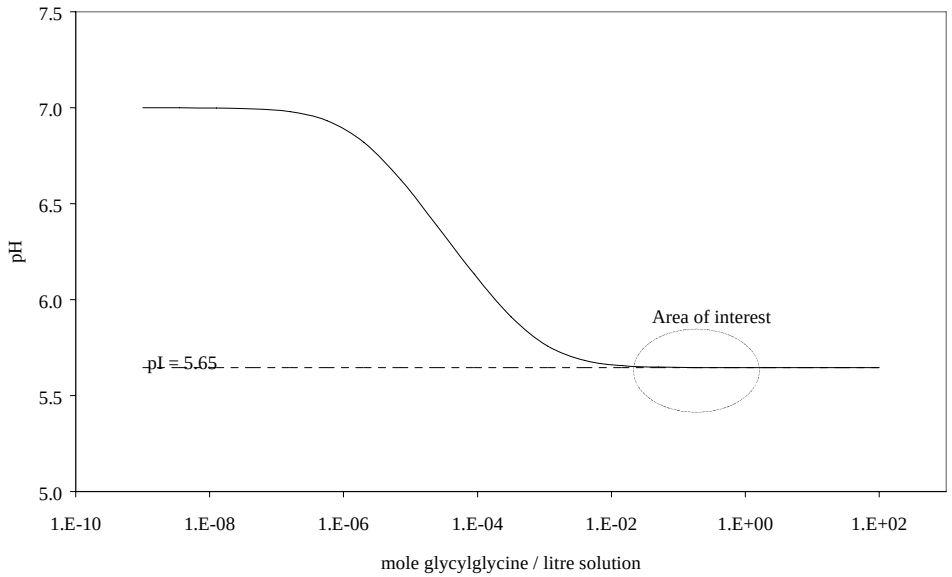


Figure 5.1a: pH as a function of glycylglycine molarity at 298.15 K.

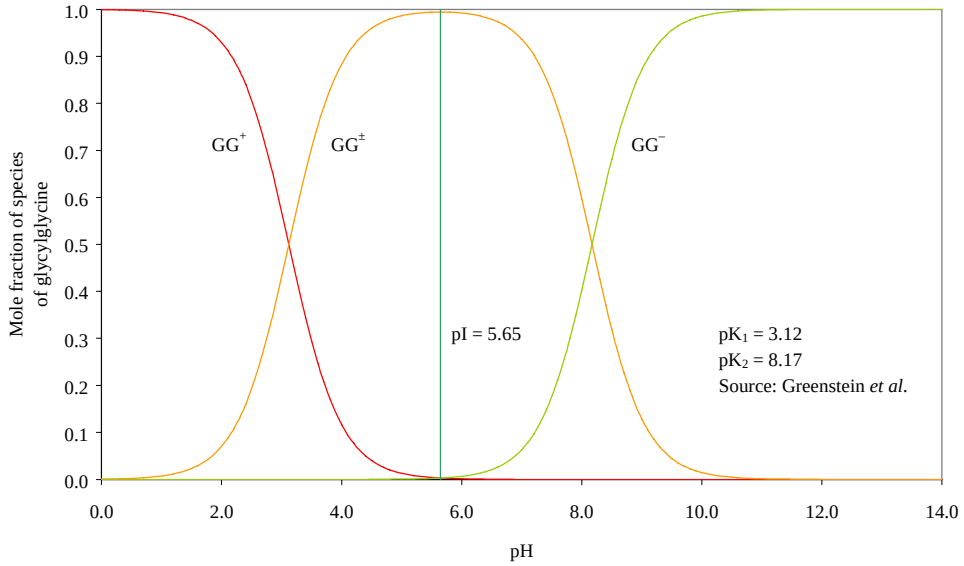


Figure 5.2a: Bjerrum diagram of glycylglycine at 298.15 K. GG^+, $GG^\pm$, and GG^- denote the cation, zwitterion, and anion of glycylglycine, respectively.

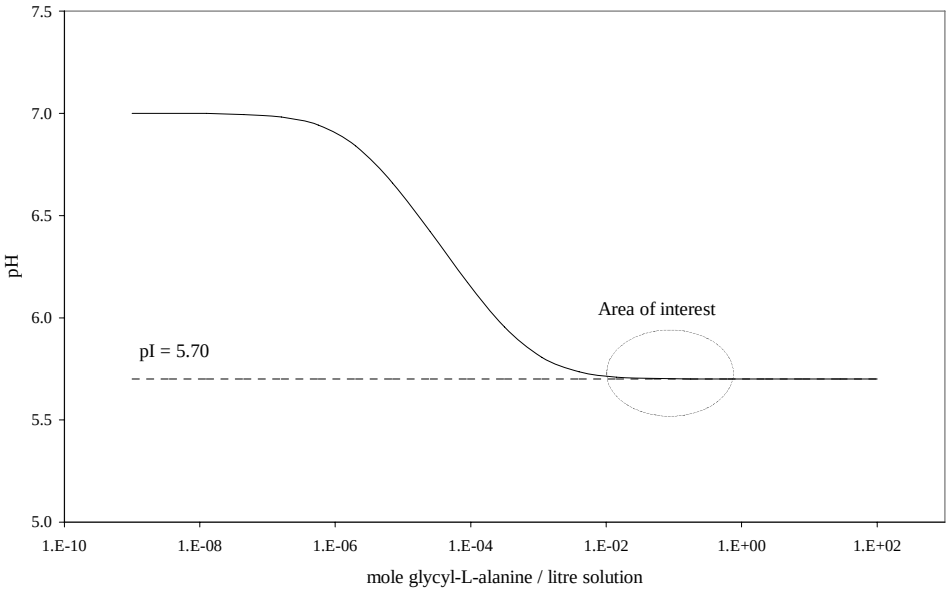


Figure 5.1b: pH as a function of glycyl-L-alanine molarity at 298.15 K.

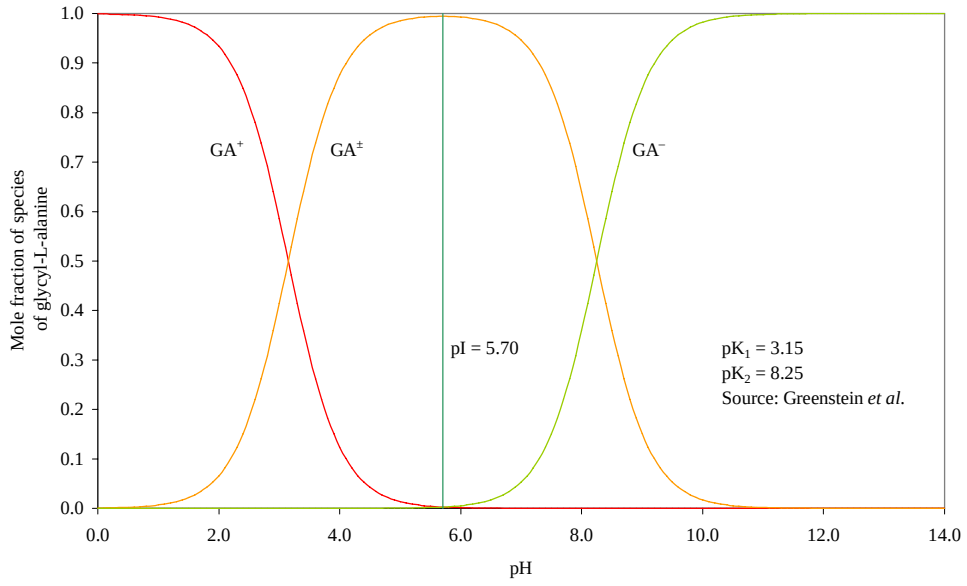


Figure 5.2b: Bjerrum diagram of glycyl-L-alanine at 298.15 K. GG^{+}, $GG^{\pm}$, and GG^{-} denote the cation, zwitterion, and anion of glycyl-L-alanine, respectively.

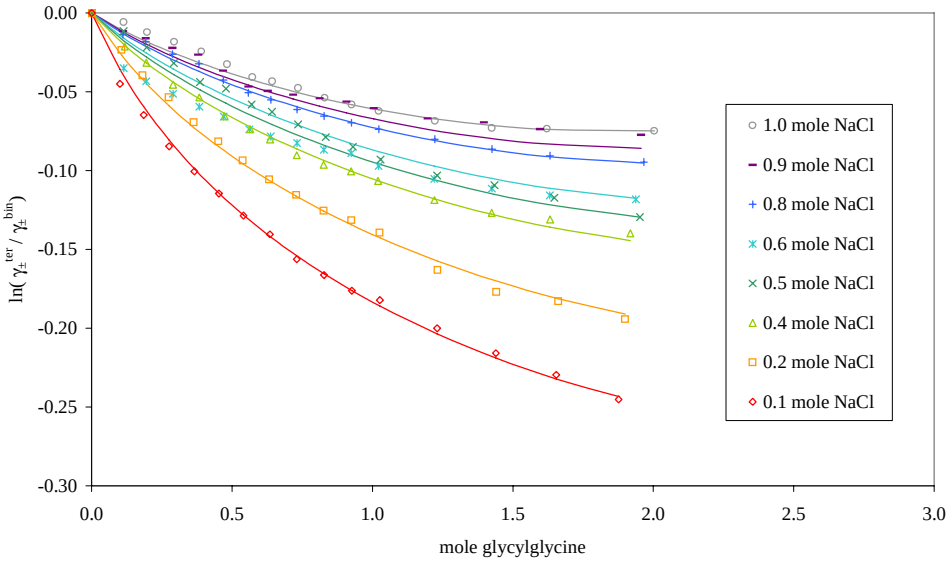


Figure 5.3: The activity coefficient of salt in glycylglycine - water at constant salt molalities in proportion to the activity coefficient of salt in water at 298.15 K. All mole numbers are per kg of water.

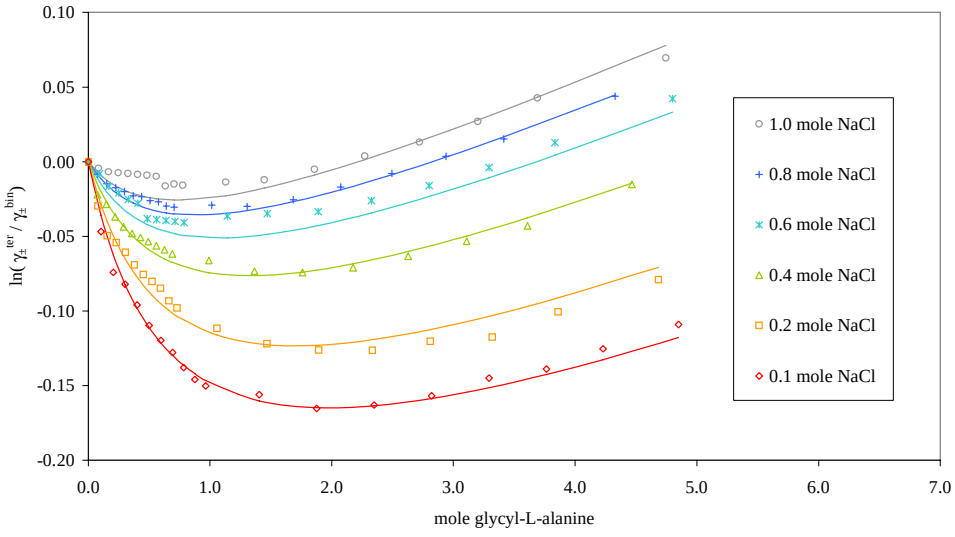


Figure 5.4: The activity coefficient of salt in glycyl-L-alanine - water at constant salt molalities in proportion to the activity coefficient of salt in water at 298.15 K. All mole numbers are per kg of water.

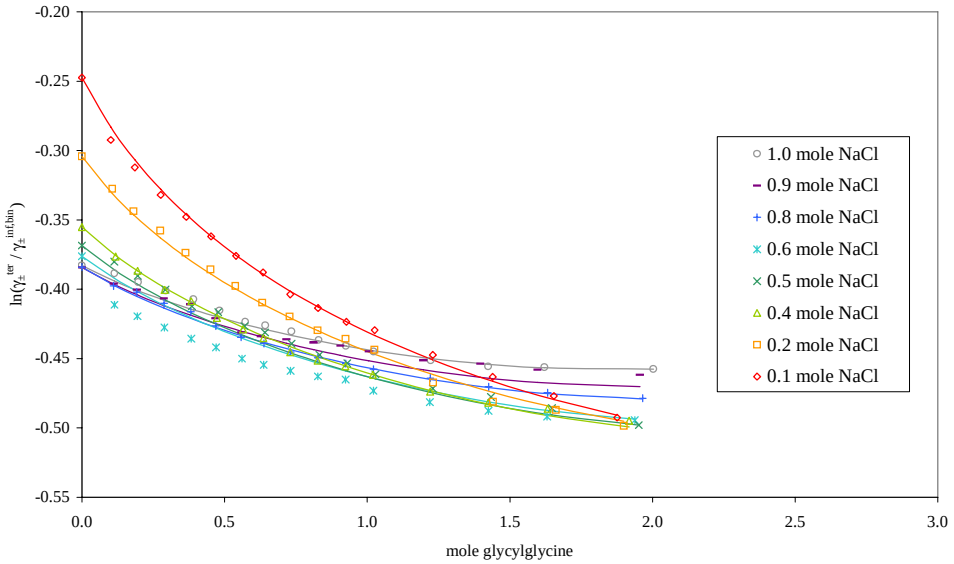


Figure 5.5: The activity coefficient of salt in glycylglycine - water at constant salt molalities in proportion to the activity coefficient of salt at infinite dilution in pure water at 298.15 K. All mole numbers are per kg of water.

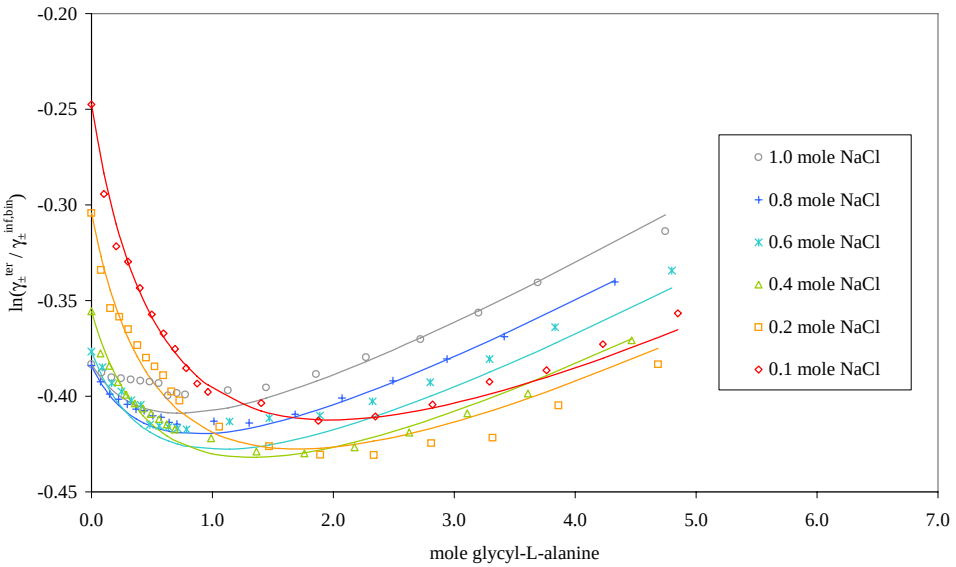


Figure 5.6: The activity coefficient of salt in glycyl-L-alanine - water at constant salt molalities in proportion to the activity coefficient of salt at infinite dilution in pure water at 298.15 K. All mole numbers are per kg of water.

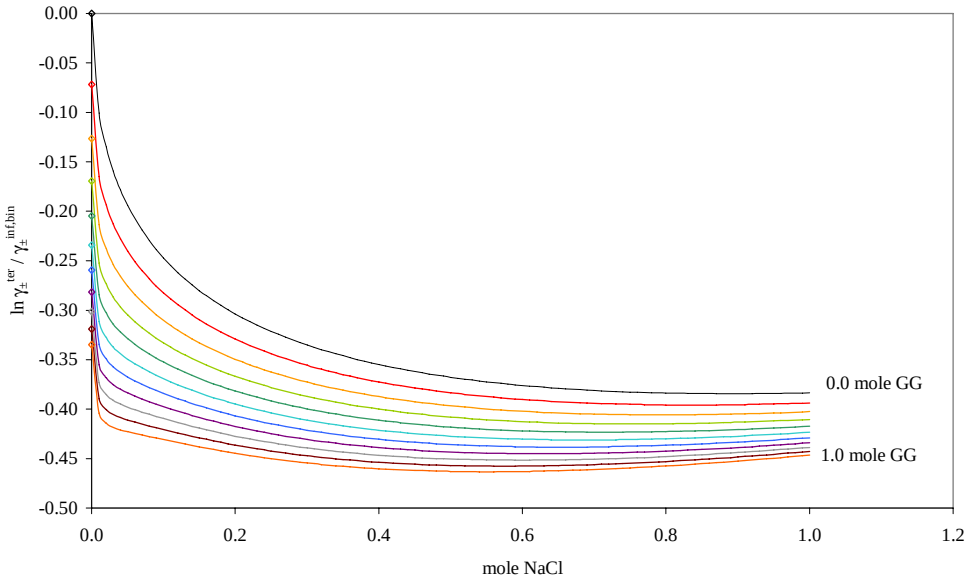


Figure 5.7: The activity coefficient of salt in glycylglycine (GG) - water at constant glycylglycine molalities in proportion to the activity coefficient of salt at infinite dilution in pure water at 298.15 K. All mole numbers are per kg of water.

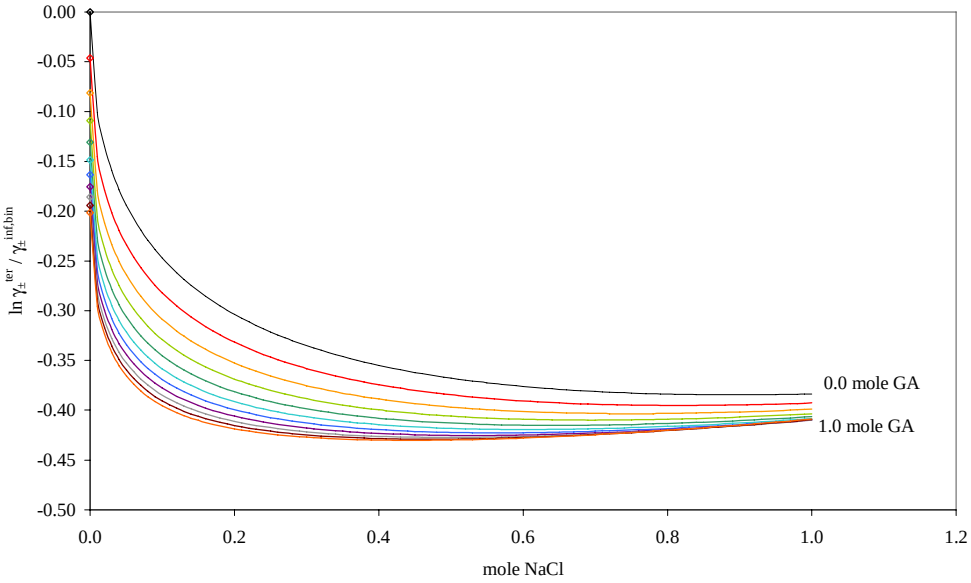


Figure 5.8: The activity coefficient of salt in glycyl-L-alanine (GA) - water at constant glycyl-L-alanine molalities in proportion to the activity coefficient of salt at infinite dilution in pure water at 298.15 K. All mole numbers are per kg of water.

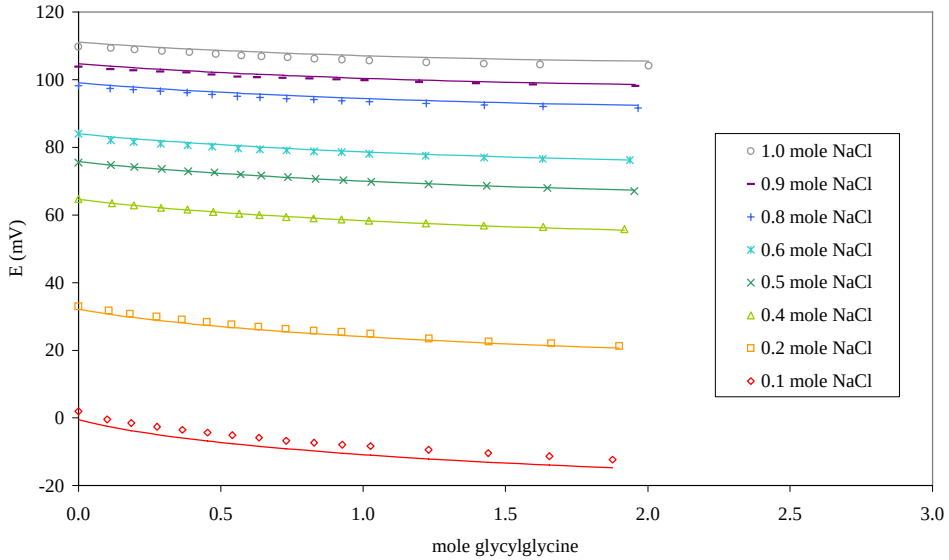


Figure 5.9: Experimental and correlated electrode potentials for glycylglycine. All mole numbers are per kg of water.

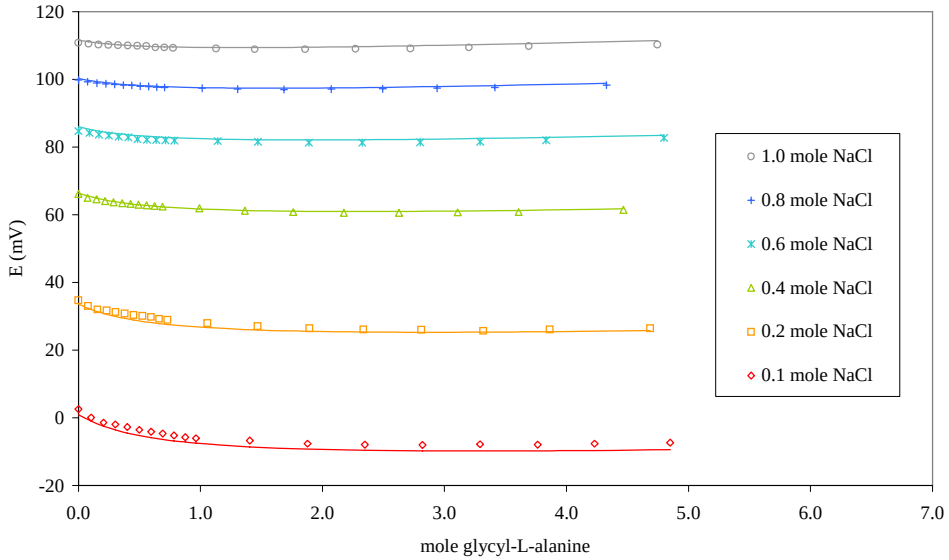


Figure 5.10: Experimental and correlated electrode potentials for glycyl-L-alanine. All mole numbers are per kg of water.

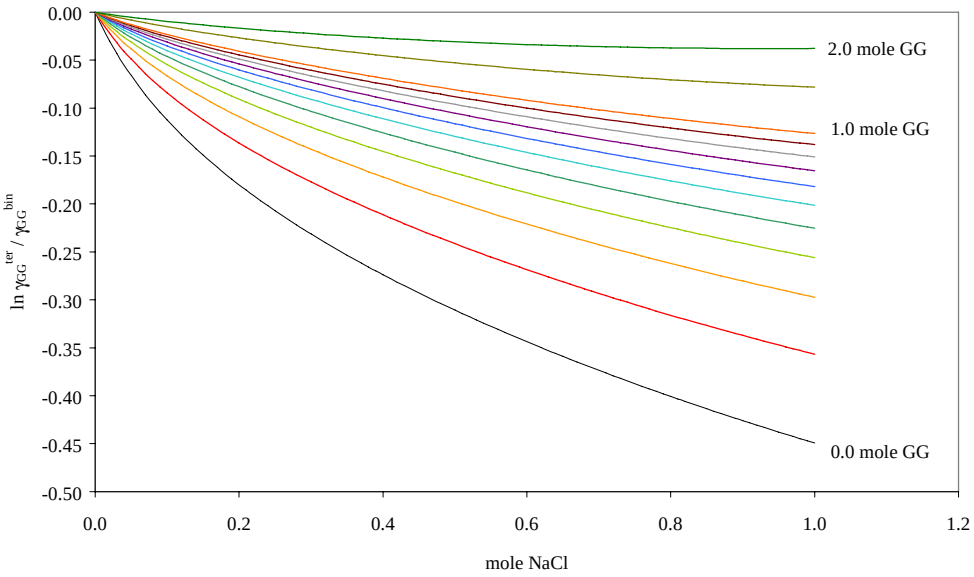


Figure 5.11: The activity coefficient of glycylglycine (GG) in salt - water at constant GG molalities in proportion to the activity coefficient of GG in water at 298.15 K. 0.0 mole GG corresponds to GG infinite diluted. All mole numbers are per kg of water.

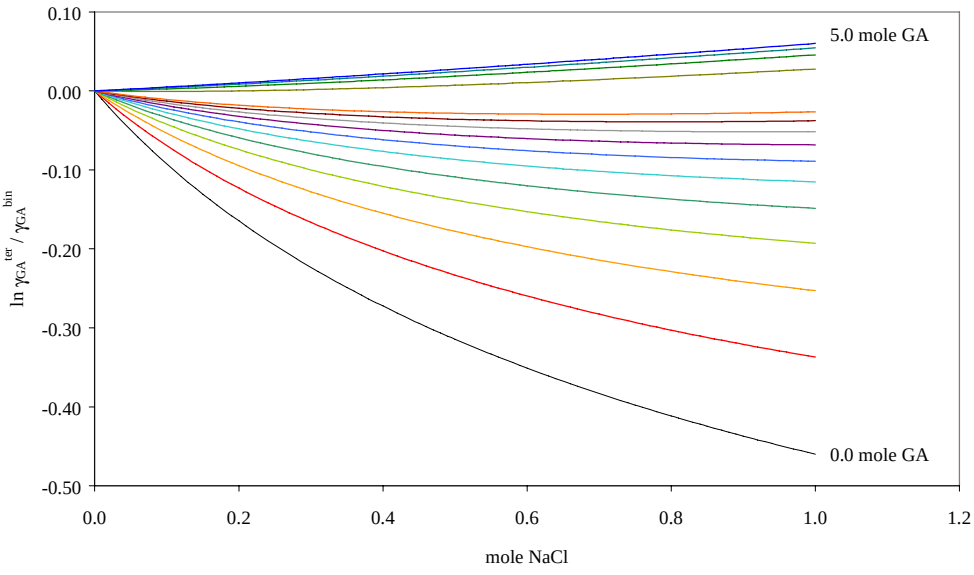


Figure 5.12: The activity coefficient of glycyl-L-alanine (GA) in salt - water at constant GA molalities in proportion to the activity coefficient of GA in water at 298.15 K. 0.0 mole GA corresponds to GA infinite diluted. All mole numbers are per kg of water.

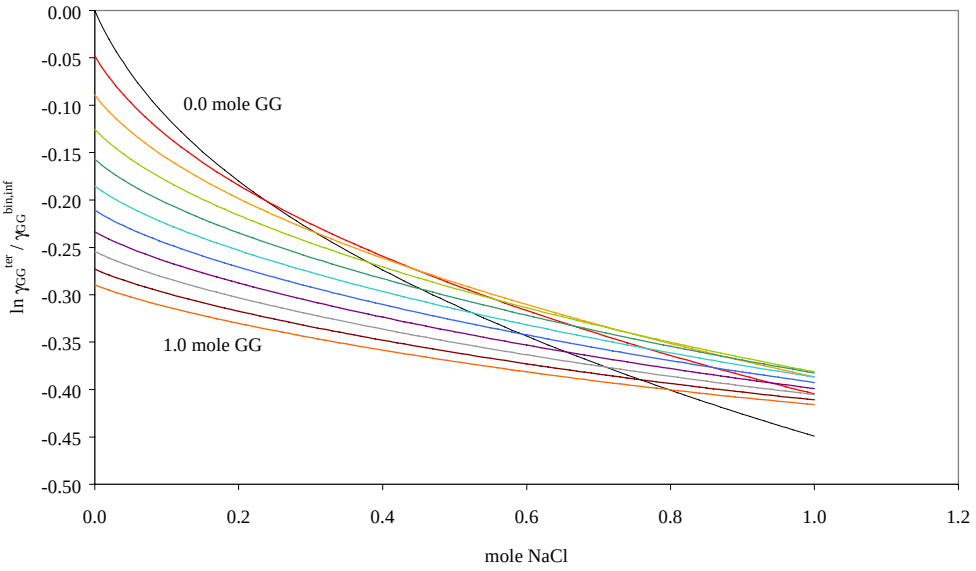


Figure 5.13: The activity coefficient of glycylglycine (GG) in salt - water at constant GG molalities in proportion to the activity coefficient of GG at infinite dilution in pure water at 298.15 K. 0.0 mole GG corresponds to GG infinite diluted. All mole numbers are per kg of water.

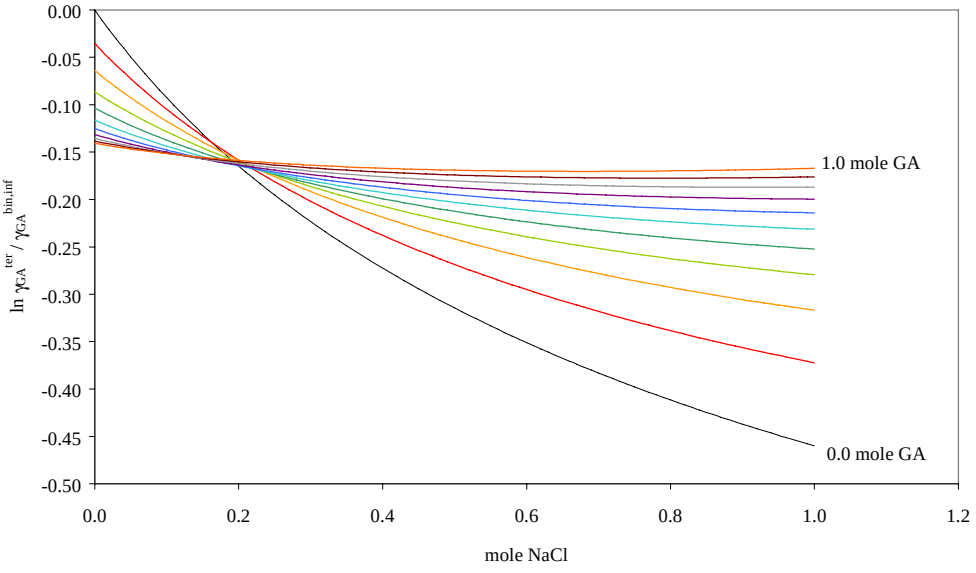


Figure 5.14: The activity coefficient of glycyl-L-alanine (GA) in salt - water at constant GA molalities in proportion to the activity coefficient of GA at infinite dilution in pure water at 298.15 K. 0.0 mole GA corresponds to GA infinite diluted. All mole numbers are per kg of water.

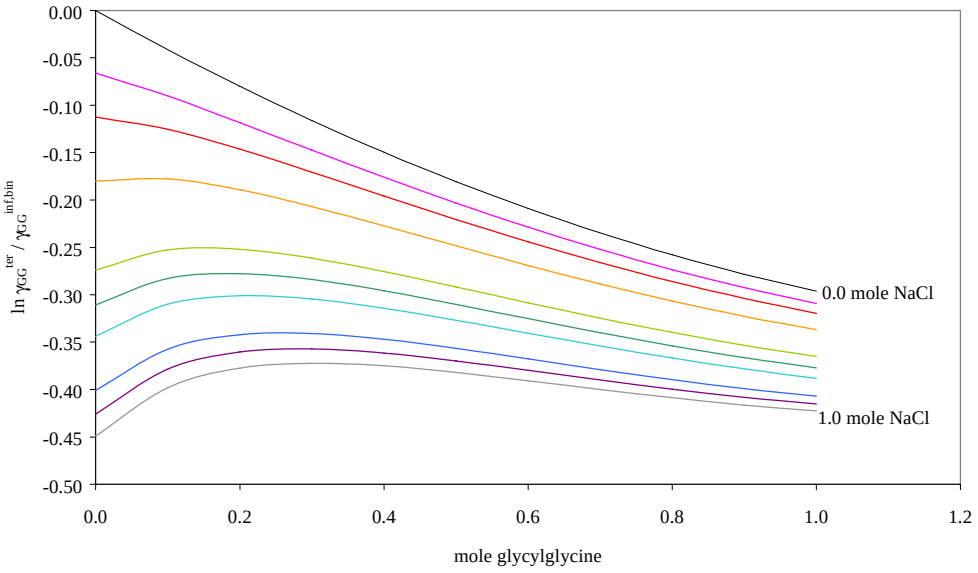


Figure 5.15: The activity coefficient of glycylglycine (GG) in salt - water at constant salt molalities in proportion to the activity coefficient of GG at infinite dilution in pure water at 298.15 K. All mole numbers are per kg of water.

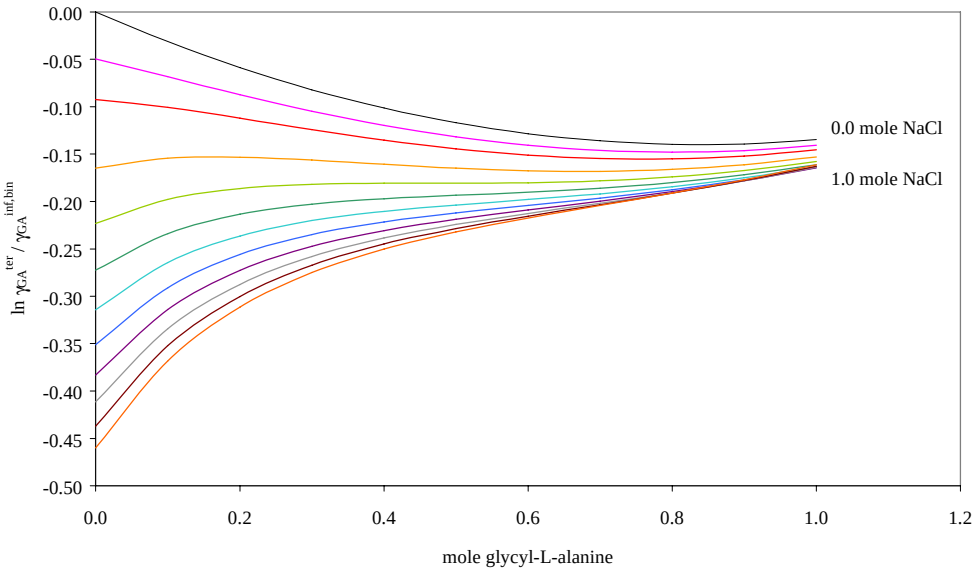


Figure 5.16: The activity coefficient of glycyl-L-alanine (GA) in salt - water at constant salt molalities in proportion to the activity coefficient of GA at infinite dilution in pure water at 298.15 K. All mole numbers are per kg of water.

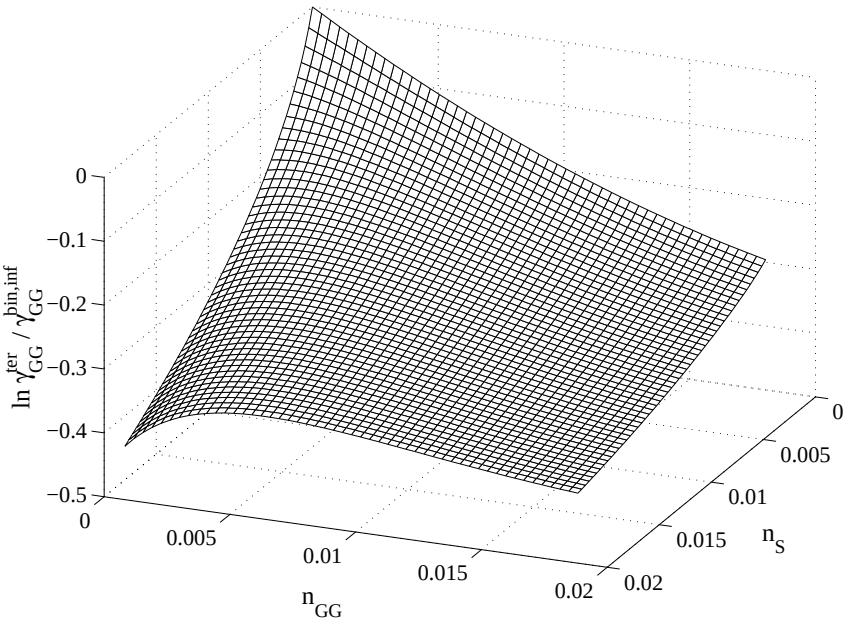


Figure 5.17: The activity coefficient of glycylglycine (GG) in salt - water at constant salt molalities in proportion to the activity coefficient of GG at infinite dilution in pure water at 298.15 K. All mole numbers are per kg of water.

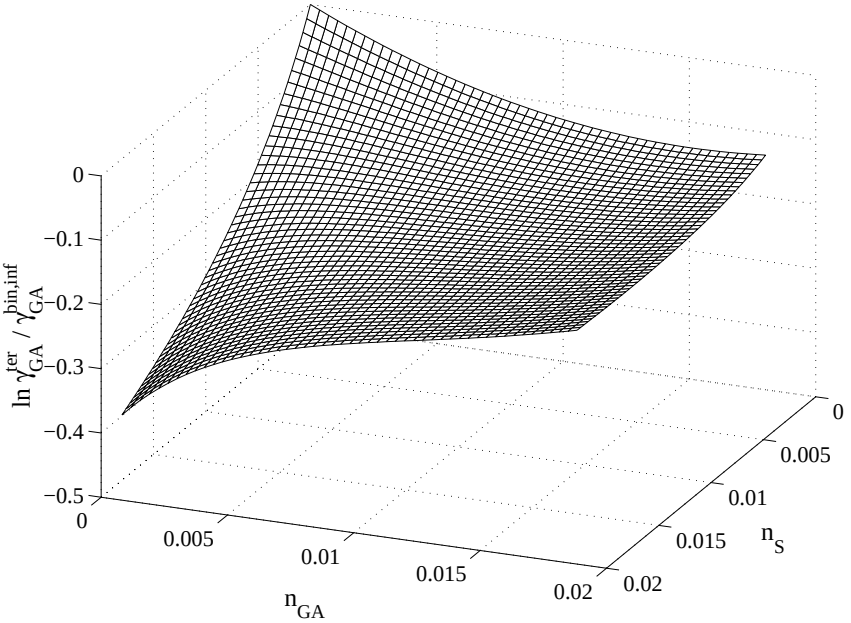


Figure 5.18: The activity coefficient of glycyl-L-alanine (GA) in salt - water at constant salt molalities in proportion to the activity coefficient of GA at infinite dilution in pure water at 298.15 K. All mole numbers are per kg of water.

6. Statistical Mechanics

This chapter and the succeeding one are written in order to explain how the so-called McMillan-Mayer framework is related to the usual (Lewis-Randall) framework. The level of description in the McMillan-Mayer framework is different from the usual one since it - instead of the usual state description (T,P,**n**) or (T,V,**n**) - is using (T,V,**n**\$n_0$,$\mu_0$) where n_0 is the solvent mole number and μ_0 is the solvent chemical potential. The notation **n**\$n_0$ means the vector [n_1, n_2, n_3, …], that is all mole numbers except n_0. But there is some apparent confusion on how the McMillan-Mayer level of description is related to the classical one - wherefore Chapters 6 and 7 address this question.

Chapter 6 gives a statistical mechanical description of the modified excess Helmholtz energy, and its relation to the usual thermodynamic properties, e.g. activity coefficient. Chapter 7 focuses on the relation between the McMillan-Mayer framework and the osmotic pressure.

For a far more thorough insight into the field of statistical mechanics and statistical thermodynamics one should consult e.g. Hill, 1962 and McQuarrie, 1976. What is presented in this chapter and the next chapter is far from covering the entire area of statistical mechanics.

The energy of a system is usually given by means of its Gibbs energy, its Helmholtz energy, or its internal energy. All of these energies can be expressed by statistical mechanics. For instance, the Helmholtz energy is the characteristic thermodynamic function of the canonical ensemble. An ensemble is a (vast) collection of systems, each of which is described by the same independent variables.

6.1 The canonical ensemble

Consider a container separated into a finite (large) number of cells or systems each having the same number of molecules (of each species) and the same volume. At equilibrium each and every cell has the same temperature since the walls separating the cells are heat conducting but impermeable. The ensemble of systems is described by three independent variables: temperature T, volume V, and molecular numbers **N**. The energies of the species in each system are not identical wherefore the ensemble energy has to be evaluated by statistical

mechanics, McQuarrie pp. 35. From a canonical ensemble is the Helmholtz energy is achieved by

$$A = -kT \ln Q(T, V, \mathbf{N}) \tag{6.1}$$

where Q(T,V,**N**) is the canonical partition function. The differential of the Helmholtz energy is

$$dA = -S\,dT - p\,dV + \sum_i \mu_i^m dN_i \tag{6.2}$$

where μ_i^m is the molecular chemical potential which is equal to $\mu_i \cdot N_A$. As a consequence of eq. (6.2) the canonical ensemble is uniquely described by the state (T,V,**N**).

6.2 The grand canonical ensemble

Like the canonical ensemble a grand canonical ensemble can be imagined by considering a container divided into a finite (large) number of cells or systems. The cell walls are still heat conducting but this time permeable to the molecules. The ensemble is described by three independent variables: temperature T, volume V, and molecular chemical potential $\boldsymbol{\mu}^m$ of each species. The partition function for this ensemble is

$$\Xi(T, V, \boldsymbol{\mu}^m) = \sum_{N_0} \cdots \sum_{N_S} \exp\left(\frac{\sum_{i=0}^{S} N_i \mu_i^m}{kT} \right) Q(T, V, \mathbf{N}) \tag{6.3}$$

where S is the total number of species. The energy corresponding to the grand canonical ensemble is pV

$$pV = kT \ln \Xi(T, V, \boldsymbol{\mu}^m) \tag{6.4}$$

The differential of pV is

$$d(pV) = S\,dT + p\,dV + \sum_i N_i d\mu_i^m \tag{6.5}$$

Note, that adding eqs. (6.2) and (6.5) will give the differential of the Gibbs function.

6.3 Semi-grand canonical ensemble

A semi-grand canonical ensemble is derived from the canonical ensemble. The mole number of the solvent (in the canonical ensemble) is replaced by its chemical potential. The semi-grand canonical partition function is denoted $\Psi(T, V, \mathbf{N}\backslash N_0, \mu_0^m)$. This semi-grand canonical partition function is given by both McQuarrie (1976), p. 66 and Haynes and Newman (1998). The relations between the semi-grand canonical partition function and those of the canonical and grand canonical ensembles are

$$\Xi(T, V, \mathbf{N} \setminus N_0, \mu_0^m) = \sum_{N_1} \cdots \sum_{N_S} \exp\left(\frac{\sum_{i=1}^{S} N_i \mu_i^m}{kT} \right) \Psi(T, V, \mathbf{N} \setminus N_0, \mu_0^m) \tag{6.6}$$

and

$$\Psi(T, V, \mathbf{N} \setminus N_0, \mu_0^m) = \sum_{N_0} \exp\left(\frac{N_0 \mu_0^m}{kT} \right) Q(T, V, \mathbf{N}) \tag{6.7}$$

By inserting eq. (6.7) into eq. (6.6), the partition function for the grand canonical ensemble is achieved, eq. (6.3). The theory of fluctuation (McQuarrie, p. 63) states that if N (the total number of molecules) is large enough then there will be an average number of solvent molecules, $\overline{N}_0$. This average will be the only one that effectively counts in the summation wherefore eq. (6.7) is equally well represented by

$$\Psi(T, V, \mathbf{N} \setminus N_0, \mu_0^m) = \exp\left(\frac{\overline{N}_0 \mu_0^m}{kT} \right) Q(\overline{N}_0, N_1, ..., N_S, T, V) \tag{6.8}$$

The characteristic thermodynamic function of the partition function Ψ is then

$$-kT \ln \Psi(T, V, \mathbf{N} \setminus N_0, \mu_0^m) = -\overline{N}_0 \mu_0^m - kT \ln Q(\overline{N}_0, N_1, ..., N_S, T, V) \tag{6.9}$$

Inserting eq. (6.1) into eq. (6.9) gives

$$-kT \ln \Psi(T, V, \mathbf{N} \setminus N_0, \mu_0^m) = -n_0 \mu_0 + A(T, V, \mathbf{N}) \tag{6.10}$$

where μ_0 is the molar chemical potential of the solvent (J/mole) and n_0 is the number of moles of solvent. The corresponding energy of this semi-grand canonical ensemble is denoted as a modified Helmholtz energy, B.

$$B(\mu_0, n_1, ..., n_S, T, V) = -kT \ln \Psi(\mu_0, N_1, ..., N_S, T, V) \tag{6.11}$$

Strictly speaking B is not a Helmholtz energy at all - modified or not. It is worth noting that B is only indirectly dependent on the number of solvent molecules. The direct solvent - solute interaction is deactivated. From eq. (6.10) the relation between the modified Helmholtz energy and the Helmholtz energy is

$$B(\mu_0, \mathbf{n} \setminus n_0, T, V) = -n_0\mu_0 + A(\mathbf{n}, T, V) \tag{6.12}$$

Normally, the chemical potential of the solvent is unknown and the interchange of frameworks is impossible.

As demonstrated it is important to remember which properties that are dependent and which that are independent in the McMillan-Mayer framework. Table 6.1 shows the independent and the dependent variables in the ideal and the real systems in the McMillan-Mayer framework.

	Independent variables	Dependent variables
Ideal system	T, V, $\mathbf{n} \setminus n_0$, μ_0	P^{id}, n_0^{id}
Real system	T, V, $\mathbf{n} \setminus n_0$, μ_0	P, n_0

Table 6.1: Relation between the dependency of the variable in the McMillan-Mayer framework and the type of system.

The modified Helmholtz energy is related to the Helmholtz energy - and vice versa - through differential equations, eqs. (6.14) and (6.15). The starting point is the differential of the modified Helmholtz energy as given in eq. (6.12) is

$$\begin{aligned} dB &= dA - d(n_0\mu_0) \\ &= -S\,dT - P\,dV + \sum_i \mu_i dn_i - \mu_0 dn_0 - n_0 d\mu_0 \\ &= -S\,dT - P\,dV + \sum_{i\neq 0} \mu_i dn_i - n_0 d\mu_0 \end{aligned} \tag{6.13}$$

Differentiating eq. (6.13) with respect to μ_0 at constant T, V, and $\mathbf{n}\setminus n_0$ gives $-n_0$. Substituting this into eq. (6.12)

$$A(T, V, \mathbf{n}) = B(T, V, \mathbf{n} \setminus n_0, \mu_0) - \mu_0 \left(\frac{\partial B}{\partial \mu_0} \right)_{T,V,\mathbf{n}\setminus n_0} \tag{6.14}$$

gives an expression for the Helmholtz energy once the modified Helmholtz energy is known. Conversely, B is obtained from A via eq. (6.2) since the chemical potential of the solvent is molar derivative of A with respect to n_0 when T, V, and the rest of the mole number kept constant.

$$B(T, V, \mathbf{n} \setminus n_0, \mu_0) = A(T, V, \mathbf{n}) - n_0 \left(\frac{\partial A}{\partial n_0} \right)_{T,V,\mathbf{n}\setminus n_0} \tag{6.15}$$

Eq. (6.15) states that having an expression for the Helmholtz energy makes it fairly simple to calculate the modified Helmholtz energy.

6.4 McMillan-Mayer

The statistical mechanical background for the McMillan-Mayer framework is not always presented with the greatest clarity. One of the reasons for this is that the 1945 article of McMillan and Mayer is difficult to follow. But they do quite clear state that the framework is equal to that of an imperfect gas where the vacuum has been replaced by a solvent (McMillan and Mayer, 1945). This is identical to the continuum concept presented in Chapter 8. Modelling Electrolyte Systems.

Furthermore, McMillan and Mayer (1945) say that "The equations for the osmotic pressure are developed and found to be entirely analogous to those for pressure of an imperfect gas". This is in agreement with Simonin's statement (1996): "An important feature of the McMillan-Mayer description level is that the thermodynamic functions are calculated at constant solvent chemical potential". That is, if the solvent chemical potential is that of the pure solvent, then the pressure of the solution will be $P° + \Pi$, where $P°$ is the vapour pressure of the pure solvent and Π is the osmotic pressure, see Chapter 7. Osmotic Equilibrium. In other words the state of a McMillan-Mayer description is equivalent to the description of an osmotic equilibrium, i.e. the solvent chemical potential is constant. Whether it is the solvent chemical potential of the pure solvent or not is not essential. The solvent chemical potential is still an independent variable in the McMillan-Mayer framework.

6.5 Derivation of the excess modified Helmholtz energy, B^E

If a thermodynamic model can not be related to the fundamental functions such as the Gibbs energy or the Helmholtz energy and obey the Gibbs-Duhem equation, the application of that model is purely mathematical and is of no scientific use. One has merely produced a very advanced fitting function that most properly could be replaced by a simple polynomial fitting function. The modified Helmholtz energy obtained from statistical mechanics (6.12) is

$$\begin{aligned} B(T, V, \mathbf{n} \setminus n_0, \mu_0) &= A(T, V, \mathbf{n}) - n_0\mu_0 \\ &= G(T, P, \mathbf{n}) - PV - n_0\mu_0 \end{aligned} \tag{6.16}$$

Logically, the modified Helmholtz energy of an ideal solution is defined as

$$B^{id}(T, V, \mathbf{n} \setminus n_0, \mu_0) \equiv \left[G(T, P, \mathbf{n}) - PV - n_0\mu_0\right]^{id} \tag{6.17}$$

Since independent variables cannot be regarded as either ideal or real, the volume and the solvent chemical potential are identical to those of the real solution; hence one has

$$V = V^{id} \qquad \text{and} \qquad \mu_0 = \mu_0^{id} \tag{6.18}$$

and consequently

$$B^{id}(T, V, \mathbf{n} \setminus n_0, \mu_0) = \left[G(T, P, \mathbf{n})\right]^{id} - P^{id}V - n_0^{id}\mu_0 \tag{6.19}$$

However, the solvent mole number is a dependent variable and hence different in the two cases.

$$n_0 = \frac{V - \sum_{i\neq 0} n_i \overline{V}_i}{\overline{V}_0} \qquad \text{and} \qquad n_0^{id} = \frac{V - \sum_{i\neq 0} n_i v_i}{v_0} \tag{6.20}$$

where $\overline{V}_i$ is the partial molar volume and v_i is the molar volume.

The Gibbs energy of the ideal solution at P^{id} and n_0^{id} in relation to that at P and n_0 is

$$
\begin{aligned}
\left[G(T,P,\mathbf{n})\right]^{id} &\equiv G^{id}(T,P^{id},\mathbf{n}\setminus n_0^{id},n_0^{id}) \\
&= G^{id}(T,P,\mathbf{n}\setminus n_0,n_0)+\int_{P}^{P^{id}}\left(\frac{\partial G^{id}}{\partial P}\right)_{T,\mathbf{n}} dP+\int_{n_0}^{n_0^{id}}\left(\frac{\partial G^{id}}{\partial n_0}\right)_{T,P,\mathbf{n}\setminus n_0} dn_0 \\
&= G^{id}(T,P,\mathbf{n})+\int_{P}^{P^{id}} V^{id}dP+\int_{n_0}^{n_0^{id}}\mu_0^{id}dn_0 \\
&\cong G^{id}(T,P,\mathbf{n})+V^{id}(P^{id}-P)+\mu_0^{id}(n_0^{id}-n_0) \\
&= G^{id}(T,P,\mathbf{n})+V(P^{id}-P)+\mu_0(n_0^{id}-n_0)
\end{aligned}
\tag{6.21}
$$

where V^{id} is considered pressure independent and $\mu_0{}^{id}$ is independent of solvent mole number as a consequence of the framework definition, that states that $\mu_0{}^{id}$ is constant. Inserting eq. (6.21) into eq. (6.19) gives the final definition of the ideal solution

$$
\begin{aligned}
B^{id}(T,V,\mathbf{n}\setminus n_0,\mu_0) &= G^{id}(T,P,\mathbf{n})+V(P^{id}-P)+\mu_0(n_0^{id}-n_0)-P^{id}V-n_0^{id}\mu_0 \\
&= G^{id}(T,P,\mathbf{n})-PV-n_0\mu_0
\end{aligned}
\tag{6.22}
$$

The resulting excess energy $B^E(T, V, \mathbf{n} \setminus n_0, \mu_0)$ is given by subtracting eq. (6.22) from eq. (6.16)

$$
B^{E}(T,V,\mathbf{n}\setminus n_0,\mu_0) = G^{E}(T,P,\mathbf{n}) \tag{6.23}
$$

There is no difference between $B^E(T, V, \mathbf{n} \setminus n_0, \mu_0)$ and $G^E(T, P, \mathbf{n})$. Differentiate $G^E(T, P, \mathbf{n})$ with respect to n_i at constant temperature, pressure, and mole numbers of the remaining species, gives

$$
\begin{aligned}
\left(\frac{\partial G^{E}(T,P,\mathbf{n})}{\partial n_i}\right)_{T,P,\mathbf{n}\setminus n_i} &= \left(\frac{\partial B^{E}(T,V,\mathbf{n}\setminus n_0,\mu_0)}{\partial n_i}\right)_{T,P,\mathbf{n}\setminus n_i} \\
&= \left(\frac{\partial B^{E}(T,V,\mathbf{n}\setminus n_0,\mu_0)}{\partial n_i}\right)_{T,V,\mathbf{n}\setminus\{n_i,n_0\},\mu_0} \\
&\quad+\left(\frac{\partial B^{E}(T,V,\mathbf{n}\setminus n_0,\mu_0)}{\partial V}\right)_{T,\mathbf{n}\setminus n_0,\mu_0}\left(\frac{\partial V}{\partial n_i}\right)_{T,P,\mathbf{n}\setminus n_i} \\
&\quad+\left(\frac{\partial B^{E}(T,V,\mathbf{n}\setminus n_0,\mu_0)}{\partial \mu_0}\right)_{T,V,\mathbf{n}\setminus n_0}\left(\frac{\partial \mu_0}{\partial n_i}\right)_{T,P,\mathbf{n}\setminus n_i}
\end{aligned}
\tag{6.24}
$$

The total differential of B^E is achieved by

$$\begin{aligned} dB^E &= dB - dB^{id} \\ &= -S^E dT - P^E dV + \sum_{i\neq 0} \mu_i^E dn_i - n_0^E d\mu_0 \end{aligned} \tag{6.25}$$

which is analogous to eq. (6.13). Applying eq. (6.25) for the differentiation in eq. (6.24) gives

$$RT \ln \gamma_i = RT \ln \gamma_i^{MM} - P^E \overline{V}_i - n_0^E \left(\frac{\partial \mu_0}{\partial n_i} \right)_{T,P,\mathbf{n}\backslash n_i} \tag{6.26}$$

As mentioned earlier in this chapter "an important feature of the McMillan-Mayer description level is that the thermodynamic functions are calculated at constant solvent chemical potential.", Simonin (1996). Consequently, eq. (6.26) is reduced to

$$RT \ln \gamma_i = RT \ln \gamma_i^{MM} - P^E \overline{V}_i \tag{6.27}$$

This is the same expression as Haynes and Newman concluded (1998). The following chapter will focus on what the physical significance of P^E is.

7. Osmotic Equilibrium

7.1 Osmotic pressure

Osmotic equilibrium is an equilibrium between two compartments: the first one (denoted I) is filled by pure solvent and the second one (denoted II) by a solution of a composition of **n**. The two compartments are only separated by a semi-permeable membrane that only allows the solvent to pass.

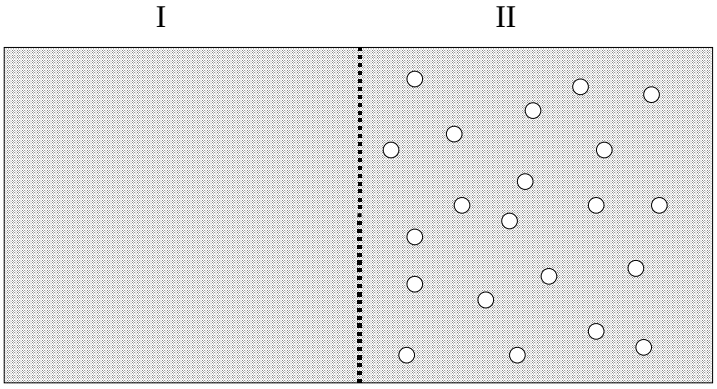


Figure 7.1: A schematic representation of an osmotic equilibrium. A compartment I without solutes and a compartment II with solutes divided by a membrane that only allows the solvent to penetrate.

There will be a pressure difference between the two compartments of a magnitude Π, the osmotic pressure. At equilibrium the chemical potential of the solvent will be the same in both compartments.

$$\mu_w^I(T, P^o) = \mu_w^{II}(T, P^o + \Pi, \mathbf{n}) \tag{7.1}$$

In order to determine the osmotic pressure a pressure adjustment in compartment I from P° to P° + Π is done.

$$\begin{aligned} \mu_w^I(T, P^o) &= \mu_w^I(T, P^o + \Pi) - \int_{P^\circ}^{P^\circ+\Pi} \left(\frac{\partial \mu_w(T, P)}{\partial P} \right)_T dP \\ &= \mu_w^I(T, P^o + \Pi) - \int_{P^\circ}^{P^\circ+\Pi} v_w dP \\ &= \mu_w^I(T, P^o + \Pi) - < v_w > \Pi \end{aligned} \tag{7.2}$$

$\langle v_w \rangle$ is an average molar volume of the solvent between the pressures P° and P° + Π. The solvent chemical potential in compartment II is

$$\mu_w^{II}(T, P^\circ + \Pi, \mathbf{n}) = \mu_w^{II}(T, P^\circ + \Pi) + RT \ln a_w^{II}(T, P^\circ + \Pi, \mathbf{n}) \tag{7.3}$$

Inserting eqs. (7.2) and (7.3) into eq. (7.1) gives

$$0 = \frac{\langle v_w \rangle \Pi}{RT} + \ln a_w^{II}(T, P^\circ + \Pi, \mathbf{n}) \tag{7.4}$$

The molar volume of the pure solvent is

$$v_w = \frac{V_w}{n_w} \tag{7.5}$$

Another way of determining the osmotic pressure is to pressure adjust the right-hand side of eq. (7.1) instead.

$$\begin{aligned} \mu_w^{II}(T, P^\circ + \Pi, \mathbf{n}) &= \mu_w^{II}(T, P^\circ, \mathbf{n}) + \int_{P^\circ}^{P^\circ + \Pi} \left(\frac{\partial \mu_w(T, P, \mathbf{n})}{\partial P} \right)_{T, \mathbf{n}} dP \\ &= \mu_w^{II}(T, P^\circ, \mathbf{n}) + \int_{P^\circ}^{P^\circ + \Pi} \overline{V}_w dP \\ &= \mu_w^{II}(T, P^\circ, \mathbf{n}) + \langle \overline{V}_w \rangle \Pi \end{aligned} \tag{7.6}$$

where $\langle \overline{V}_w \rangle$ is the average partial molar volume of the solvent from P° to P° + Π. Furthermore, the chemical potential $\mu_w^{II}(T, P^\circ, \mathbf{n})$ can be expanded

$$\begin{aligned} \mu_w^{II}(T, P^\circ + \Pi, \mathbf{n}) &= \mu_w^{II}(T, P^\circ, \mathbf{n}) + \langle \overline{V}_w \rangle \Pi \\ &= \mu_w^{II}(T, P^\circ) + RT \ln a_w^{II}(T, P^\circ, \mathbf{n}) + \langle \overline{V}_w \rangle \Pi \end{aligned} \tag{7.7}$$

Equalising eqs. (7.1) and (7.7) gives

$$0 = \frac{\langle \overline{V}_w \rangle \Pi}{RT} + \ln a_w^{II}(T, P^\circ, \mathbf{n}) \tag{7.8}$$

Eqs. (7.4) and (7.8) are both valid at any solute concentration. If the solvent activity is defined as $x_w \cdot \gamma_w(T,P,\mathbf{n})$ and the model for the activity coefficient is indifferent to pressure, it follows that the average molar volume of the solvent is equal to the average partial molar volume of the solvent, and as a consequence the osmotic pressure is defined by eq. (7.4) only. Contrary to $\langle \overline{V}_w \rangle$ the molar volume of the solvent is usually a known property.

7.2 Ideal solution

In an ideal solution the solvent activity is often set equal to the solvent mole fraction, $a_w = x_w$, as discussed in Chapter 2. Basic Thermodynamics, page 19. Furthermore, the solvent molar volume is considered to be independent of pressure. This implies that eq. (7.4) is rewritten as

$$0 = \frac{v_w \Pi^{id}}{RT} + \ln(1 - x_S) \tag{7.9}$$

where x_S is the total mole fraction of salt and Π^{id} is the ideal osmotic pressure. One could equally easy arrived at eq. (7.9) from eq. (7.8) since the partial molar volume in an ideal solution is the molar volume and the solvent activity is $1 - x_S$. A virial expansion of the ideal osmotic pressure in the concentration scale of molarities is

$$\Pi = RTc_S + RT\sum_{j\geq 2} B_j c_S^j \tag{7.10}$$

where **B** are the virial coefficients (Hill, p. 345).

7.3 Dilute ideal solution

Taking eq. (7.9) one step further is to consider a dilute ideal solution $x_S << 1$.

$$0 = \frac{v_w \Pi_o^{id}}{RT} - x_s \tag{7.11}$$

Furthermore, the molar volume of the solvent, eq. (7.5), will be

$$v_w = \frac{V_{total}}{n_{total}} \tag{7.12}$$

Inserting eq. (7.12) into eq. (7.11) produces the equation of van't Hoff and the definition of the ideal osmotic pressure at dilute solution, Π_o^{id}.

$$\Pi_o^{id} \equiv c_s RT \tag{7.13}$$

where c_S is total molarity of the solutes. The van't Hoff equation is therefore only valid for dilute ideal solutions. At low solute concentrations the higher order terms of eq. (7.10) will be vanishing and the van't Hoff equation will appear.

7.4 Osmotic coefficients

In the usual (Lewis-Randall) framework the osmotic coefficient, ϕ^{LR}, is defined as

$$\phi^{LR} = -\frac{x_w}{x_s} \ln a_w \tag{7.14}$$

where x_w is the solvent mole fraction and a_w is the solvent activity (Atkins (1992), p. 186 and Pitzer (1991), p. 12). For a dilute solution the osmotic coefficient can be expressed as the ratio of the osmotic pressure of the real solution and the ideal osmotic pressure. Considering eq. (7.4) for a dilute solution and inserting eq. (7.14) would give

$$\begin{aligned} \Pi_o &= -\frac{RT\, n_w}{V} \ln a_w \\ &= +\frac{RT}{V} n_S \ln a_w = c_S RT \phi \end{aligned} \tag{7.15}$$

which relative to the osmotic pressure of a dilute ideal solution, eq. (7.13), gives the osmotic coefficient for a dilute solution.

In the McMillan-Mayer framework, the osmotic coefficient, ϕ^{MM}, is defined as the ratio of the real osmotic pressure and the ideal osmotic pressure, Simonin (1999).

$$\phi^{MM} = \frac{\Pi}{\Pi^{id}} \tag{7.16}$$

The difference between the real and the ideal osmotic pressure is logically denoted the excess osmotic pressure, i.e. the osmotic pressure difference between what is defined as the ideal solution and the actual, real solution.

$$\Pi = \Pi^{id} + \Pi^{E} \tag{7.17}$$

Inserting eq. (7.17) into eq. (7.16) gives

$$\phi^{MM} = 1 + \frac{\Pi^{E}}{\Pi^{id}} \tag{7.18}$$

In case that the solution considered is an ideal solution, the osmotic coefficient ϕ^{MM} is unity since an excess property must be zero in an ideal solution.

7.5 Dilute solution

A dilute solution is characterised by having all the solutes at a low concentration and the solvent approaching unity (in terms of mole fractions). Often when dilute solutions are considered, there is a tendency to replace the ideal osmotic pressure in eq. (7.18) by the van't Hoff equation, Friedman (1972). However, this is only valid when one is considering a dilute *ideal* solution and then the osmotic coefficient, ϕ^{MM}, is unity. A dilute solution is *not* an ideal solution and hence the solute activity coefficient is *not* unity. In fact, the activity coefficient usually has its greatest gradient at low concentrations. This is obvious when comparing the electrode potential measurements at high and low concentration in Chapter 5. Experimental Results.

However, the solvent activity coefficient in a dilute solution is for any practical purpose unity.

7.6 Dilute solution having solvent activity coefficient of unity

Assuming that the solvent activity coefficient is unity at dilute solution, the van't Hoff equation can be applied in eq. (7.18)

$$\phi_o^{MM} = 1 + \frac{\Pi_o^E}{c_s RT} \tag{7.19}$$

This is in accordance with McQuarrie (pp. 337) if one considers the excess osmotic pressure as "der elektrische Zusatzdruck" that Debye and Hückel (1923) present.

Using the same assumptions (dilute solute, unit solvent activity coefficient), an often-encountered relation between the Lewis-Randall and McMillan-Mayer framework is derived. By inserting eq. (7.11) into the expression for the osmotic coefficient, eq. (7.14), one has an expression for the osmotic coefficient of a dilute solution, ϕ_o^{LR}.

$$\phi_o^{LR} = -\frac{x_w}{x_s}\left(-\frac{v_w \Pi_o}{RT}\right) \tag{7.20}$$

where Π_o is the osmotic pressure in the dilute solution. Substituting RT by the van't Hoff equation and utilise the definition of ϕ^{MM}, eq. (7.16)

$$\begin{aligned}\phi_o^{LR} &= \frac{x_w}{x_s} c_s v_w \left(\frac{\Pi_o}{\Pi_o^{id}} \right) \\ &= \frac{x_w}{x_s} c_s v_w \phi_o^{MM} \\ &= x_w \phi_o^{MM}\end{aligned} \tag{7.21}$$

This is the same limit that Simonin (1999) and Lee (2000) have for the conversion between the two frameworks. It is worth noting that in the limit where the solvent is almost pure (x_w = 1) - and where the solution is definitively ideal - both osmotic coefficients are unity. That the Lewis-Randall osmotic coefficient ϕ^{LR} is unity can be proofed from the definition, eq. (7.14).

$$\begin{aligned}\phi_o^{LR} &= \\ \lim_{n_S \to 0} \phi^{LR} &= \lim_{n_S \to 0} \left(-\frac{n_w}{n_S} \ln a_w \right) && = -\lim_{n_S \to 0} \left(\frac{n_w}{n_S} \ln(\gamma_w x_w) \right) \\ &= -\lim_{n_S \to 0} \left(\frac{n_w}{n_S} \ln \gamma_w + \frac{n_w}{n_S} \ln x_w \right) && = -\lim_{n_S \to 0} \frac{n_w}{n_S} \ln x_w \\ &= -\lim_{n_S \to 0} \frac{n_w}{n_S} \ln \frac{n_w}{n_w + n_S} && = \lim_{n_S \to 0} \frac{n_w}{n_S} \ln \frac{n_w + n_S}{n_w} \\ &= \lim_{n_S \to 0} \frac{n_w}{n_S} \ln \left(1 + \frac{n_S}{n_w} \right) && \approx \frac{n_w}{n_S} \frac{n_S}{n_w} = 1\end{aligned} \tag{7.22}$$

7.7 Excess pressure

Having defined the osmotic pressure and the osmotic coefficients (both in the Lewis-Randall and the McMillan-Mayer framework) one can return to eq. (6.27) where an excess pressure, P^E, appears. An excess property is per definition the difference between the property of the real solution and that of the ideal solution.

$$P^E = P - P^{id} \tag{7.23}$$

Since the solvent chemical potential is kept constant in the McMillan-Mayer framework, the difference between the real and the ideal solution is conceptually comparable to an osmotic equilibrium. The osmotic pressure Π is defined as the difference between the real pressure, P, and the pressure of the pure solvent, P°.

$$\Pi = P - P^\circ \tag{7.24}$$

However, in the McMillan-Mayer description level, the ideal phase is *not* a pure solvent phase, but the real solution treated ideally, i.e. $\gamma_i = 1$. So the pressure difference (between the real and the ideal solution) is *not* the osmotic pressure, but rather the excess pressure of eq. (7.23). The pressure P is eliminated from eq. (7.24) by eq. (7.23)

$$\Pi = P^E + P^{id} - P^\circ \tag{7.25}$$

The last two terms of eq. (7.25) could be interpreted as an ideal osmotic pressure, Π^{id}, in analogy to eq. (7.24).

$$\Pi = P^E + \Pi^{id} \tag{7.26}$$

Eq. (7.26) is indirectly defining an excess osmotic pressure that is identical to P^E and could be regarded as the non-ideality correction of the osmotic pressure.

7.8 Dilute solutions with unit solvent activity

For dilute solutions where the solvent activity is approximately unity, the last term of eq. (7.26) could be replaced by the van't Hoff equation

$$P_o^E = \Pi_o - c_S RT \tag{7.27}$$

and eq. (7.16) rearranged to

$$\Pi_o = c_S RT \phi_o^{MM} \tag{7.28}$$

This is in accordance with Friedman (1972), Simonin (1996), and McQuarrie (1976) for the osmotic coefficient in the McMillan-Mayer description level dilute solutions. Eliminating Π_o in eq. (7.27) by eq. (7.28) gives an expression for the excess pressure in a dilute solution as

$$P_o^E = c_S RT(\phi_o^{MM} - 1) \tag{7.29}$$

Inserting eq. (7.29) into eq. (6.27)

$$\begin{aligned} RT \ln \gamma_i &= RT \ln \gamma_i^{MM} - c_S RT(\phi_o^{MM} - 1)\,\overline{V}_i \quad \Leftrightarrow \\ \ln \gamma_i &= \ln \gamma_i^{MM} - c_S(\phi_o^{MM} - 1)\,\overline{V}_i \\ &= \ln \gamma_i^{MM} - c_S \overline{V}_i \phi_o^{MM} + c_S \overline{V}_i \end{aligned} \tag{7.30}$$

Simonin (1999) does not have the last term of eq. (7.30). But if P^E and Π were identical, the last term of eq. (7.30) would vanish. Simonin (1999) has based his work on that of Friedman (1972), in which there are some unfortunate descriptions of the frameworks.

7.9 Friedman

One of the often-cited articles in the field of the McMillan-Mayer framework is an article by Friedman (1972). This article describes the LR framework by using a state (T, P, **m**) where **m** is the vector of the molalities of the solutes. But by specifying a molality vector, the energy of the state is only described as a molar property, since it is only the composition of the state that is given. It is impossible to calculate the total energy of that state without the knowing the total number of moles. Normally, the composition is given in terms of mole numbers and hence the state is unequivocally described.

In the description of the MM framework Friedman is using a state (T, P_o, **c**) where P_o is the pressure of the pure solvent in equilibrium with solution and **c** is the vector of solute molarities. This state description differs from the one given in the previous Chapter 6. Statistical Mechanics at two points. The first point is that Friedman specifies a pressure. The semi-canonical ensemble responsible for the modified Helmholtz energy B is not specified by a pressure at all, eq. (6.12). The second point is that the molarity is used instead of mole numbers of the solutes, the total volume, and the chemical potential of the solvent. As is the case for Friedman's LR description the energy of the specified state is 'only' a molar energy - and not the total energy.

Furthermore, Friedman defines an 'excess Helmholtz energy per unit volume', A^{excess}, as an integration of the difference in osmotic pressures $\Pi - c_S RT$ from zero solutes to the real solution. This implies that the assumption for this energy function is a dilute ideal solution because then the van't Hoff equation is valid.

$$A^{excess} = -c_S \int_{c_S'=0}^{c_S'=c_S} [\Pi_o - c_S' RT] d\left(\frac{1}{c_S'}\right) \tag{7.31}$$

It should be emphasised that A^{excess} is *not* a traditional excess Helmholtz energy but a defined energy function and the working equations of Friedman are only valid where the van't Hoff equation is valid. By application of eq. (7.27), eq. (7.31) is rewritten into

$$A^{excess} = -c_S \int_{c_S'=0}^{c_S'=c_S} P_o^E \, d\left(\frac{1}{c_S'}\right) \qquad \Rightarrow \qquad \left(\frac{\partial (A^{excess}/c_S)}{\partial (1/c_S)}\right) = -P_o^E \tag{7.32}$$

Inserting eq. (7.29) into eq. (7.31)

$$\left(\frac{\partial (A^{excess}/c_S)}{\partial (1/c_S)}\right) = c_S RT(1-\phi_o^{MM}) \tag{7.33}$$

one obtains precisely the expression for that 'excess Helmholtz energy per unit volume' which is given by Friedman (1972). The 'excess Helmholtz energy per unit volume' of Friedman is not based on a statistical mechanical background as the modified Helmholtz energy B is. This lack of sound background and the fact that Friedman's equations only are valid for dilute solutions makes his results limited and not generally applicable.

8. Modelling Electrolyte Systems

In this chapter the Debye-Hückel theory will be derived as Debye and Hückel did, and then compared with the approach implied by McQuarrie. A few of the 'electrolyte' g^E terms inspired by the Debye-Hückel theory are presented as well. Furthermore one electrolyte g^E model (the extended UNIQUAC model) and one continuum concept based model (the HS-MSA model) are presented and the most-often used approach towards modelling of solubility data is sketched.

8.1 An simple explanation of the continuum concept

Consider a very dilute solution of water and fully dissociated sodium chloride. Since the amount of water molecules is much greater than the total amount of sodium and chloride ions, it is reasonable to regard water (the solvent) as a dielectric continuum - contrary to individual molecules. The ions are still regarded as individual spheres. The NaCl solution has to be electrical neutral overall; the number of protons equals that of electrons. If one chooses the reference of the system to that where all the 'ions' are uncharged, then all the 'ions' can be regarded as atoms which then again can be regarded as spheres. The Debye-Hückel theory deals with the charging-up of this reference system to the real solution.

8.2 The Debye-Hückel theory and derivatives

The 1923 work of Debye and Hückel is one of the first theoretical papers on electrolytes that deals with the continuum concept. The basis of the concept is to regard a continuum in which spheres are located. This is a simplified representation of a very dilute solution where the solvent is regarded as the continuum and the ions as the spheres.

The Debye-Hückel theory only concerns the energetic of charging-up a system. In other words, there has to be an uncharged system of molecules that needs to be charged. When Debye and Hückel (1923) mentioned the classical term in the internal energy function, it is the difference between the real (or actual) internal energy and that of charging-up the system. "Die Rechnungen, welche in Folgenden auszuführen sind, unterscheiden sich von den klassischen durch Berücksichtigung der elektrischen Ionenwirkungen. Dementsprechend

zerlegen wir U in zwei Bestandteile, einen klassischen Anteil U_k und eine elektrische Zusatzenergie U_e: U = U_k + U_e". Translated: The calculations, which are carried out subsequently, differ from the classical ones by consideration of the influence of the ions. Because of that we give U in two terms, a classical term U_k and an electrical additional energy U_e: U = U_k + U_e. (Debye and Hückel (1923), pp. 187)

If a Debye-Hückel model is used without any additional configurational models, the modelling is limited to (very) dilute solutions and the configurational contribution of the molecules has to be negligible.

The continuum is characterised by its dielectric constant or permittivity. For a polar solvent such as water the relative permittivity ε_r is 78.54 at 25°C whereas an organic solvent such as ethanol has a relative permittivity of 24.30 at 25°C (CRC 78th, p. 8-115). The dielectric constant of a continuum is thus $\varepsilon = \varepsilon_r\varepsilon_0$ where ε_0 is the dielectric constant of vacuum.

The relative permittivity is in the following considered to be independent of the system's temperature, volume, and composition. However, this is a simplification since there exist a number of quantitative relations for the relative permittivity and the electric properties of the solvent. One of these is the Debye equation (Atkins, 1992)

$$\frac{\varepsilon_r - 1}{\varepsilon_r + 2} = \frac{n_0 N_A}{V}\frac{1}{3\varepsilon_0}\left(\alpha + \frac{\mu^2}{3kT}\right) \tag{8.1}$$

where n_0 is the mole number of the solvent, a is the polarizability (unit C^2m^2/J), and μ is the electric dipole moment (unit C·m).

The starting point for the Debye-Hückel theory is the Poisson equation

$$\nabla^2\Phi = -\frac{\rho}{\varepsilon} \tag{8.2}$$

where Φ is the electric potential (unit volt, V), ρ is the volumetric charge density (unit coulomb per volume, C/m^3), and ε is the dielectricity of continuum (unit $C^2/(J\cdot m)$).

The work required to move a cation of charge z_+e (where *e* is the elementary charge) towards the electric potential Φ is $z_+e\cdot\Phi$; for an anion of charge z_-e the work is $z_-e\cdot\Phi$. Furthermore, Debye and Hückel assume that the ionic distribution follows the Boltzmann principle, wherefore the volumetric charge density can be expressed as

$$\begin{aligned}\rho &= e\,N_A \sum_i z_i c_i \exp\left(-z_i \frac{e\Phi}{kT}\right) \\ &= F\sum_i z_i c_i \exp\left(-z_i \frac{F\Phi}{RT}\right)\end{aligned} \tag{8.3}$$

where F is Faraday constant and c_i is the molarity of ionic species *i*. Inserting eq. (8.3) into the Poisson equation yields a differential equation, the Poisson-Boltzmann equation. Normally, eq. (8.3) is linearised

$$\rho \cong -\frac{F^2}{RT}\sum_i z_i^2 c_i \Phi \tag{8.4}$$

and the linearised Poisson-Boltzmann equation is obtained

$$\begin{aligned}\nabla^2\Phi &= \frac{F^2}{\varepsilon RT}\sum_i z_i^2 c_i \Phi \\ &= \kappa^2 \Phi \qquad\qquad , \kappa^2 = \frac{F^2}{\varepsilon RT}\sum_i z_i^2 c_i\end{aligned} \tag{8.5}$$

where κ is the Debye (shielding) length, which has the unit of reciprocal metre. The solution of eq. (8.5) is

$$\Phi(r) = \frac{A}{r}e^{-\kappa r} + \frac{A'}{r}e^{\kappa r} \tag{8.6}$$

Obviously, A' must be zero since Φ has to be zero at an infinite great distance

$$\Phi(r) = \frac{A}{r}e^{-\kappa r} \tag{8.7}$$

In the Debye-Hückel theory the ion *i* is regarded as a sphere of radius a_i. The radius a_i is not the ionic radius but the closest distance that any other ion can approach the ion in question, the so-called Annäherungsabstand, the distance of closest approach, Debye and Hückel (1923, p. 192). The electric potential at distances greater than a_i is given by eq. (8.7). The inside of this ionic sphere is regarded as a continuum of a given permittivity and the charge is regarded as a point charge placed at the origin. The electric potential inside the ionic sphere is given by

$$\Phi(r) = \frac{z_i e}{4\pi\varepsilon}\frac{1}{r} + B \tag{8.8}$$

The expression of an electric potential is presented in the Appendix C on Electrostatics, eq. (C.8). The additional term B is a constant background electric potential. The boundary conditions of the model described by eqs. (8.7) and (8.8) are that both Φ and its gradient are continuous at $r = a_i$. The solution is given by the two constants

$$A = \frac{z_i e}{4\pi\varepsilon}\frac{e^{\kappa a_i}}{1+\kappa a_i} \qquad \text{and} \qquad B = -\frac{z_i e}{4\pi\varepsilon}\frac{\kappa}{1+\kappa a_i} \tag{8.9}$$

The potential energy per molecule is given by the product of the charge and the background electric potential, B, accordingly to Debye and Hückel, p. 193.

$$u_i = z_i e\, B = -\frac{z_i^2 e^2}{4\pi\varepsilon}\frac{\kappa}{1+\kappa a_i} \tag{8.10}$$

Consequently, the total electrostatic (internal) energy is given by

$$\begin{aligned} U^{elec} &= \sum_i \frac{N_i}{2} u_i \qquad \Leftrightarrow \\ \frac{U^{elec}}{RT} &= -\sum_i \frac{n_i z_i^2}{2}\frac{F^2\kappa}{4\pi\varepsilon RT}\frac{1}{N_A}\frac{1}{1+\kappa a_i} \\ &= -\frac{F^2\kappa}{8\pi\varepsilon RT}\frac{1}{N_A}\sum_i \frac{n_i z_i^2}{1+\kappa a_i} \end{aligned} \tag{8.11}$$

The unit of U^{elec} is joule. The Helmholtz energy is related to the internal energy by

$$d\left(\frac{A}{T}\right) = U\, d\left(\frac{1}{T}\right) - \frac{P}{T}dV + \frac{1}{T}\sum_i \mu_i dn_i \qquad \Rightarrow \qquad \frac{A}{T} = \int U\, d\frac{1}{T} \tag{8.12}$$

at constant volume and composition. The total electrostatic Helmholtz energy (unit joule) becomes

$$\begin{aligned} &\frac{A^{elec}(T,V,\mathbf{n})}{RT} \\ &\quad = -\frac{1}{4\pi\sum_j c_j z_j^2}\frac{1}{N_A}\sum_i \frac{n_i z_i^2}{a_i^3}\left[\frac{3}{2} + \ln(1+\kappa a_i) - 2(1+\kappa a_i) + \frac{1}{2}(1+\kappa a_i)^2\right] \\ &\quad = -\frac{F^2}{4\pi\varepsilon RT}\frac{1}{N_A}\frac{1}{\kappa^2}\sum_i \frac{n_i z_i^2}{a_i^3}\left[\frac{3}{2} + \ln(1+\kappa a_i) - 2(1+\kappa a_i) + \frac{1}{2}(1+\kappa a_i)^2\right] \\ &\quad = -\frac{F^2}{4\pi\varepsilon RT}\frac{1}{N_A}\sum_i \frac{n_i z_i^2}{3}\kappa\chi_i \end{aligned} \tag{8.13}$$

where

$$\chi_i = \frac{3}{(\kappa a_i)^3}\left[\frac{3}{2} + \ln(1+\kappa a_i) - 2(1+\kappa a_i) + \frac{1}{2}(1+\kappa a_i)^2\right] \tag{8.14}$$

The volume change due to the charging-up is so insignificant that A^{elec} approximates the electrostatic Gibbs energy (Debye-Hückel, p. 188). "Mit Rücksicht darauf aber, daß die Kompressibilität des Wassers so gering ist, daß 20 Atm. nur eine relative Volumänderung von 0,001 hervorrufen, kann für die meisten Anwendenungen der elektrischen Zusatz zu V (als Funktion von p und T) vernachlässig werden". Translated: Because of the small compressibility of water (a pressure of 20 atmospheres only gives a relative volume change of 0.001), the volume change (as a function of pressure and temperature) due to charging-up is for the most cases negligible. So by assuming the PV work to be insignificant one has the Debye-Hückel electrostatic Gibbs energy.

$$\frac{G^{elec,DH}(T,P,\mathbf{n})}{RT} = -\frac{F^2}{4\pi\varepsilon RT}\frac{1}{N_A}\sum_i \frac{n_i z_i^2}{3}\kappa\chi_i \tag{8.15}$$

The activity coefficient of any ionic species j is determined as the molar derivative of eq. (8.15) at constant temperature and pressure.

$$\begin{aligned} RT\ln\gamma_j^{elec,DH} &= \left(\frac{\partial G^{elec,DH}}{\partial n_j}\right)_{T,P,\mathbf{n}\backslash n_j,\kappa\boldsymbol{\chi}} \\ &\quad + \sum_k \left(\frac{\partial G^{elec,DH}}{\partial(\kappa\chi_k)}\right)_{T,P,\mathbf{n},\kappa\boldsymbol{\chi}\backslash\kappa\chi_k}\left(\frac{\partial(\kappa\chi_k)}{\partial\kappa}\right)_{T,P,\mathbf{n}}\left(\frac{\partial\kappa}{\partial n_j}\right)_{T,P,\mathbf{n}\backslash n_j} \\ &= -\frac{F^2}{4\pi\varepsilon}\frac{\kappa}{6N_A}\left(2z_j^2\chi_j + (z_j^2 - \overline{V}_j\sum_i c_i z_i^2)\frac{\sum_k n_k z_k^2\sigma_k}{\sum_i n_i z_i^2}\right) \end{aligned} \tag{8.16}$$

where $\overline{V}_j$ is the partial molar volume of species j,

$$\sigma_k = \left(\frac{d(\kappa\chi_k)}{d\kappa}\right)_{T,P,\mathbf{n}} = \frac{3}{(\kappa a_k)^3}\left[1+\kappa a_k - \frac{1}{1+\kappa a_k} - 2\ln(1+\kappa a_k)\right] \tag{8.17}$$

and

$$\left(\frac{\partial\kappa}{\partial n_j}\right)_{T,P,\mathbf{n}\backslash n_j} = \frac{1}{2}\frac{\kappa}{\sum_i z_i^2 n_i}(z_j^2 - \overline{V}_j\sum_i c_i z_i^2) \tag{8.18}$$

Eq. (8.16) reduces when the partial molar volume of an ion is assumed to be much less than that the total volume

$$\ln \gamma_j^{elec}(T,P,\mathbf{n}) = -\frac{F^2}{4\pi\varepsilon RT}\frac{\kappa z_j^2}{6N_A}\left(2\chi_j + \frac{\sum_i n_i z_i^2 \sigma_i}{\sum_i n_i z_i^2}\right) \tag{8.19}$$

It is noted that $RT\sum_j n_j \ln \gamma_j^{elec}(T,P,\mathbf{n})$ is not $G^{elec,DH}(T,P,\mathbf{n})$ due to the assumption of the insignificant partial molar volume relative to the total volume.

At very dilute solutions the function χ_j is almost constantly unity and if all radii are assumed identical, the activity coefficient of the ionic species is

$$\begin{aligned}\ln \gamma_j^{elec}(T,P,\mathbf{n}) &= -\frac{F^2}{4\pi\varepsilon RT}\frac{\kappa z_j^2}{2N_A} \\ &= -\frac{F^3}{4\pi N_A}\sqrt{\frac{1}{2(\varepsilon RT)^3}}z_j^2\sqrt{I} \\ &= -A_{DH} z_j^2 \sqrt{I}\end{aligned} \tag{8.20}$$

where I is the ionic strength

$$I = \frac{1}{2}\sum_i c_i z_i^2 \tag{8.21}$$

and the A_{DH} parameter or the Debye-Hückel parameter is

$$A_{DH} = \frac{F^3}{4\pi N_A}\sqrt{\frac{1}{2(\varepsilon RT)^3}} \tag{8.22}$$

and has the units of $m^{3/2}\cdot mol^{-1/2}$. For a continuum of water at 298.15K $A_{DH} = 3.7084\cdot 10^{-2}$ $m^{3/2}\cdot mol^{-1/2}$. Eq. (8.20) is the end result of Debye and Hückel (1923) for the activity coefficient of an ionic species in an infinitely diluted solution. The expression is valid up to approximately 0.01 M, (Thomsen, 1997). As presented Debye and Hückel have not assumed that the distances of closest approach are identical in order to derive an expression for the activity coefficient, eq. (8.19).

However, instead of assuming that the PV work of the charging process and the partial molar volumes relative to the total volume are negligible as Debye and Hückel did, the correct

electrostatic Gibbs is obtainable from the expression of A^{elec}, eq. (8.13), in two different ways (McQuarrie, pp. 336).

The first way of deriving the electrostatic Gibbs energy is given by

$$G^{elec}(T,V,\mathbf{n}) = A^{elec}(T,V,\mathbf{n}) + P^{elec}(T,V,\mathbf{n})\,V \tag{8.23}$$

where P^{elec} is the electrostatic pressure due to the charging process which is derived as

$$\begin{aligned} -P^{elec} &= \left(\frac{\partial A^{elec}}{\partial V}\right)_{T,\mathbf{n}} \\ &= \left(\frac{\partial A^{elec}}{\partial V}\right)_{T,\mathbf{n},\kappa\boldsymbol{\chi}} + \sum_k \left(\frac{\partial A^{elec}}{\partial \kappa\chi_k}\right)_{T,\mathbf{n},V} \left(\frac{\partial \kappa\chi_k}{\partial \kappa}\right)_{T,\mathbf{n},V} \left(\frac{\partial \kappa}{\partial V}\right)_{T,\mathbf{n}} \\ &= \frac{F^2}{24\pi\varepsilon}\frac{\kappa}{N_A}\sum_k c_k z_k^2 \sigma_k \end{aligned} \tag{8.24}$$

Eqs. (8.13) and (8.24) are inserted into eq. (8.23) and the $G^{elec}(T,V,\mathbf{n})$ is determined

$$\begin{aligned} G^{elec}(T,V,\mathbf{n}) &= -\frac{F^2}{4\pi\varepsilon}\frac{1}{N_A}\sum_i \frac{n_i z_i^2}{3}\left(\kappa\chi_i + \frac{\kappa\sigma_i}{2}\right) \\ &= -\frac{F^2}{4\pi\varepsilon}\frac{1}{N_A}\sum_i \frac{n_i z_i^2}{2}\frac{\kappa}{1+\kappa a_i} \end{aligned} \tag{8.25}$$

By comparing eqs. (8.15) and (8.25) it is obvious that Debye and Hückel's assumptions only are valid if $\sigma_i << \chi_i$. But σ_i and χ_i are of the same order of magnitude.

The other way of deriving the electrostatic Gibbs energy involves the electrostatic chemical potentials which are the molar derivative of $A^{elec}(T,V,\mathbf{n})$ at constant T and V.

$$\begin{aligned} \mu_j^{elec}(T,V,\mathbf{n}) &= \left(\frac{\partial A^{elec}}{\partial n_j}\right)_{T,V,\mathbf{n}\backslash n_j} \\ &= \left(\frac{\partial A^{elec}}{\partial n_j}\right)_{T,V,\mathbf{n}\backslash n_j,\kappa\boldsymbol{\chi}} \\ &\qquad + \sum_k \left(\frac{\partial A^{elec}}{\partial(\kappa\chi_k)}\right)_{T,V,\mathbf{n},\kappa\boldsymbol{\chi}\backslash\kappa\chi_k} \left(\frac{\partial(\kappa\chi_k)}{\partial\kappa}\right)_{T,V,\mathbf{n}} \left(\frac{\partial\kappa}{\partial n_j}\right)_{T,V,\mathbf{n}\backslash n_j} \\ &= -\frac{F^2}{4\pi\varepsilon}\frac{\kappa z_j^2}{6N_A}\left[2\chi_j + \frac{\sum_k n_k z_k^2 \sigma_k}{\sum_k n_k z_k^2}\right] \end{aligned} \tag{8.26}$$

where

$$\left(\frac{\partial \kappa}{\partial n_j}\right)_{T,V,\mathbf{n}\setminus n_j} = \frac{F^2}{\varepsilon RT}\frac{z_j^2}{V}\frac{1}{2\kappa} = \frac{\kappa}{2}\frac{z_j^2}{\sum_k n_k z_k^2} \tag{8.27}$$

which is a simpler expression than eq. (8.18) since eq. (8.27) is the derivative of κ at constant V. The electrostatic Gibbs energy is then calculated as

$$\begin{aligned} G^{elec}(T,V,\mathbf{n}) &= \sum_j n_j \mu_j^{elec}(T,V,\mathbf{n}) \\ &= -\frac{F^2}{4\pi\varepsilon}\sum_j n_j \frac{\kappa z_j^2}{6N_A}\left[2\chi_j + \frac{\sum_k n_k z_k^2 \sigma_k}{\sum_k n_k z_k^2}\right] \\ &= -\frac{F^2}{4\pi\varepsilon}\frac{1}{N_A}\sum_j \frac{n_j z_j^2}{3}\left(\kappa\chi_j + \frac{\kappa\sigma_j}{2}\right) \end{aligned} \tag{8.28}$$

which is identical to eq. (8.25). The total Gibbs energy of the solution is given by

$$G = G_o + G^{elec} \tag{8.29}$$

where G_o is the Gibbs energy of the uncharged system and the excess Gibbs energy of the solution is

$$\begin{aligned} G^E &= (G_o - G_o^{id}) + G^{elec} \\ &= G_o^E + G^{elec} \end{aligned} \tag{8.30}$$

where G_o^{id} is the Gibbs energy of the ideal uncharged system. There is no ideal electrostatic Gibbs energy since the charging process is immaterial. From eq. (8.30) it follows that

$$RT\ln\gamma_i = RT\ln\gamma_{o,i} + RT\ln\gamma_i^{elec} \tag{8.31}$$

and consequently,

$$G^{elec}(T,V,\mathbf{n}) = RT\sum_i n_i \ln\gamma_i^{elec}(T,V,\mathbf{n}) \tag{8.32}$$

which implicitly gives the activity coefficient of an ionic species

$$\ln\gamma_j^{elec}(T,V,\mathbf{n}) = -\frac{F^2}{4\pi\varepsilon RT}\frac{\kappa z_j^2}{6N_A}\left(2\chi_j + \frac{\sum_k c_k z_k^2 \sigma_k}{\sum_k c_k z_k^2}\right) \tag{8.33}$$

which is identical to eq. (8.19). The two assumptions of Debye and Hückel are that 1: the PV work of the charging process is negligible and 2: the partial molar volumes of the ions are insignificant relative to the total volume. However, both of these assumptions are equivalent

of ignoring the partial molar volume of the ions - and the following paragraph will show that these assumptions are unnecessary.

In principle, the deviation of the logarithmic activity coefficient of Debye and Hückel, eq. (8.16), is given by eq. (8.34).

$$\begin{aligned}\mu_i(T,P,\mathbf{n}) &= \left(\frac{\partial G(T,P,\mathbf{n})}{\partial n_i}\right)_{T,P,\mathbf{n}\backslash n_i} = \left(\frac{\partial A(T,V,\mathbf{n})}{\partial n_i}\right)_{T,P,\mathbf{n}\backslash n_i} + P\left(\frac{\partial V}{\partial n_i}\right)_{T,P,\mathbf{n}\backslash n_i} \\ &= \left(\frac{\partial A(T,V,\mathbf{n})}{\partial n_i}\right)_{T,P,\mathbf{n}\backslash n_i} + P\overline{V}_i\end{aligned} \tag{8.34}$$

But since Debye and Hückel implicitly say that $\overline{V}_i$ is zero, and consequently eq. (8.16) reduces to eq. (8.19). However, it is not necessary to assume anything about $\overline{V}_i$, since eq. (8.34) is

$$\begin{aligned}\mu_i(T,P,\mathbf{n}) &= \left(\frac{\partial A(T,V,\mathbf{n})}{\partial n_i}\right)_{T,V,\mathbf{n}\backslash n_i} + \left(\frac{\partial A(T,V,\mathbf{n})}{\partial V}\right)_{T,\mathbf{n}}\left(\frac{\partial V}{\partial n_i}\right)_{T,P,\mathbf{n}\backslash n_i} + P\overline{V}_i \\ &= \mu_i(T,V,\mathbf{n}) + (-P)\,\overline{V}_i + P\overline{V}_i \\ &= \mu_i(T,V,\mathbf{n})\end{aligned} \tag{8.35}$$

Therefore the expression for the activity coefficient derived as Debye and Hückel did it (two assumptions and end up as eq. (8.19)) is equivalent to the procedure implied by McQuarrie which does not include any assumptions, eq. (8.33).

In order for the consistency of the model to be fulfilled the electrostatic chemical potentials obtained from $G^{elec}(T,V,\mathbf{n})$ have to be identical to the those obtained from $A^{elec}(T,V,\mathbf{n})$. Therefore the electrostatic Gibbs energy is differentiated by n_j at constant T, P, and **n** to check that the result is identical to the electrostatic chemical potential.

$$\begin{aligned}\left(\frac{\partial G^{elec}(T,V,\mathbf{n})}{\partial n_j}\right)_{T,P,\mathbf{n}\backslash n_j} &= \left(\frac{\partial G^{elec}(T,V,\mathbf{n})}{\partial n_j}\right)_{T,V,\mathbf{n}\backslash n_j} \\ &\quad + \left(\frac{\partial G^{elec}(T,V,\mathbf{n})}{\partial V}\right)_{T,\mathbf{n}}\left(\frac{\partial V}{\partial n_j}\right)_{T,P,\mathbf{n}\backslash n_j}\end{aligned} \tag{8.36}$$

Eq. (8.23) is inserted in eq. (8.36), which then is evaluated

$$\begin{aligned}\left(\frac{\partial G^{elec}(T,V,\mathbf{n})}{\partial n_j}\right)_{T,P,\mathbf{n}\backslash n_j} &= \left(\frac{\partial A^{elec}(T,V,\mathbf{n})}{\partial n_j}\right)_{T,V,\mathbf{n}\backslash n_j} + \left(\frac{\partial (P^{elec}V)}{\partial n_j}\right)_{T,V,\mathbf{n}\backslash n_j} \\ &+ \left(\left(\frac{\partial A^{elec}(T,V,\mathbf{n})}{\partial V}\right)_{T,\mathbf{n}} + \left(\frac{\partial (P^{elec}V)}{\partial V}\right)_{T,\mathbf{n}}\right)\left(\frac{\partial V}{\partial n_j}\right)_{T,P,\mathbf{n}\backslash n_j} \\ &= \mu_j^{elec}(T,V,\mathbf{n}) + V\left(\frac{\partial P^{elec}}{\partial n_j}\right)_{T,V,\mathbf{n}\backslash n_j} \\ &+ \left((-P^{elec}) + V\left(\frac{\partial P^{elec}}{\partial V}\right)_{T,\mathbf{n}} + P^{elec}\right)\overline{V}_j \\ &= \mu_j^{elec}(T,V,\mathbf{n}) + V\left(\frac{\partial P^{elec}}{\partial n_j}\right)_{T,V,\mathbf{n}\backslash n_j} + V\left(\frac{\partial P^{elec}}{\partial V}\right)_{T,\mathbf{n}}\overline{V}_j\end{aligned} \tag{8.37}$$

Since the state is given by (T,V,**n**), the pressure is to be regarded as a function of T, V, and **n**. Therefore the total differential of the pressure is

$$dP = \left(\frac{\partial P}{\partial T}\right)_{V,\mathbf{n}} dT + \left(\frac{\partial P}{\partial V}\right)_{T,\mathbf{n}} dV + \sum_k \left(\frac{\partial P}{\partial n_k}\right)_{T,V,\mathbf{n}\backslash n_k} dn_k \tag{8.38}$$

The differentiation considered, eq. (8.36), is at constant pressure (dP = 0) and temperature (dT = 0), so one has that the molar derivative of eq. (8.38) is

$$\begin{aligned}0 &= \left(\frac{\partial P}{\partial V}\right)_{T,\mathbf{n}}\left(\frac{\partial V}{\partial n_j}\right)_{T,P,\mathbf{n}\backslash n_j} + \sum_k \left(\frac{\partial P}{\partial n_k}\right)_{T,V,\mathbf{n}\backslash n_k}\left(\frac{\partial n_k}{\partial n_j}\right)_{T,P,\mathbf{n}\backslash n_j} \quad \Rightarrow \\ \left(\frac{\partial P}{\partial V}\right)_{T,\mathbf{n}}\overline{V}_j &= -\left(\frac{\partial P}{\partial n_j}\right)_{T,V,\mathbf{n}\backslash n_j}\end{aligned} \tag{8.39}$$

Eq. (8.39) is applied in eq. (8.37) whereby the molar derivative of the electrostatic Gibbs energy at constant temperature, pressure, and composition is equal to the chemical potential.

$$\left(\frac{\partial G^{elec}(T,V,\mathbf{n})}{\partial n_j}\right)_{T,P,\mathbf{n}\backslash n_j} = \mu_j^{elec}(T,V,\mathbf{n}) \tag{8.40}$$

The result of the differentiation, eq. (8.40), shows that there is internal consistency of the model.

In order to simplify the expression of the activity coefficient eq. (8.33), the distances of closest approach, a_i, are assumed identical for all ions. This reduces the expression to the so-called extended Debye-Hückel equation

$$\begin{aligned}\ln\gamma_j^{elec} &= -\frac{F^2}{12\pi\varepsilon RT}\frac{\kappa z_j^2}{N_A}\left(\chi+\frac{\sigma}{2}\right)\\ &= -\frac{F^2}{8\pi\varepsilon RT}\frac{\kappa z_j^2}{N_A}\frac{1}{1+\kappa a}\\ &= -\frac{F^2}{4\pi N_A}\sqrt{\frac{F^2}{2(\varepsilon RT)^3}}\frac{z_j^2\sqrt{I}}{1+\kappa a}\\ &= -A_{DH}\frac{z_j^2\sqrt{I}}{1+b\sqrt{I}}\end{aligned} \tag{8.41}$$

where A_{DH} is the same as given by eq. (8.22) and the b parameter

$$b = a\sqrt{\frac{2F^2}{\varepsilon RT}} \tag{8.42}$$

which has the units of $m^{3/2}\cdot mol^{-1/2}$. All the state descriptions given so far in this chapter have either been (T,V,**n**) or (T,P,**n**). But the mole number of the solvent is not explicitly given in any of the equations, i.e. the vector **n** is strictly speaking only a vector of **n**\n_0. In order for the state description to be complete, it is required that the solvent mole number is included (a Lewis-Randall level of description) or the solvent chemical potential (a McMillan-Mayer level of description). Since the Debye-Hückel theory regards the solvent as a continuum, it would be natural to assume that the Debye-Hückel theory is conceived at a McMillan-Mayer level of description. But the theory does not mention the chemical potential of the solvent, and hence it is not a complete description. As a consequence the derivation of the chemical potential of the solvent (the continuum) is not possible without an additional assumption regarding the solvent mole number or the solvent chemical potential.

8.3 Electrostatic g^E model terms

To achieve a complete description Fowler and Guggenheim (1949) constructed an excess Gibbs energy model, which they based on an expression similar to eq. (8.41) except that the

ionic strength was replaced by a 'molal' ionic strength, I_m, and the distance of closest approach was assumed the same for all ions.

$$\ln \gamma_j = -A_{DH} \frac{z_j^2 \sqrt{d_w} \sqrt{I_m}}{1 + b_m \sqrt{I_m}} \tag{8.43}$$

where the 'molal' ionic strength is

$$I_m = \frac{1}{2} \sum_i m_i z_i^2 \tag{8.44}$$

Consequently, the b parameter has to redefined as b_m

$$b_m = b\sqrt{d_w} = a\sqrt{\frac{2 d_w F^2}{\varepsilon RT}} \tag{8.45}$$

where d_w is the pure solvent density. The b_m parameter has the units of $kg^{1/2} \cdot mol^{-1/2}$. In this work the value of b_m is 1.5 $kg^{1/2} \cdot mol^{-1/2}$. This is in accordance with the work of Thomsen (1997) which is the basis for the modelling with the Fowler-Guggenheim model in this work. The integration of $\ln \gamma_j$ with respect to n_j gives the excess Gibbs energy and thus

$$\frac{G^E}{RT} = -n_w M_w \sqrt{d_w} \frac{4A_{DH}}{b_m^3} \left[\ln\left(1 + b_m \sqrt{I_m}\right) - b_m \sqrt{I_m} + \frac{1}{2} b_m^2 I_m \right] \tag{8.46}$$

where n_w is the mole number of solvent and M_w is the molar mass of the solvent (kg/mole). This model is valid up to approximately 0.1 molal, (Thomsen, 1997). Notice that where Debye and Hückel present a Gibbs energy for the charging process, Fowler and Guggenheim present an excess Gibbs energy model. That is, Fowler and Guggenheim's model includes the solvent; it is possible to differentiate the excess Gibbs energy and obtain the activity coefficient of the solvent.

$$\ln \gamma_w = +M_w \sqrt{d_w} \frac{2A_{DH}}{b_m^3} \left[1 + b_m \sqrt{I_m} - \frac{1}{1 + b_m \sqrt{I_m}} - 2\ln\left(1 + b_m \sqrt{I_m}\right) \right] \tag{8.47}$$

Furthermore, Fowler and Guggenheim use a molality based ionic strength; the model has to include the density of the solvent. The addition of an uncharged compound, a non-solvent, to an electrolyte solution would not have an effect according to eq. (8.46).

However, the addition of a non-electrolyte will at least dilute the electrolyte solution and hence the charge density. The Poisson-Boltzmann equation states that a change in the charge density will change the electric potential and eventually the excess Gibbs energy. Concluding that the model of Fowler and Guggenheim is insensitive to uncharged species since the molalities of the electrolytes are not affected by the uncharged species.

In 1980, Pitzer derived a generalised model also originating from the work of Debye and Hückel. Unlike Fowler and Guggenheim, Pitzer defines the ionic strength as

$$I_x = \frac{1}{2}\sum_i x_i z_i^2 \tag{8.48}$$

where x_i includes water. Since the ionic strength, eq. (8.48), is affected by the amount of uncharged species present, this definition of the ionic strength seems more reasonable than the definition of eq. (8.44), where the ionic strength is indifferent to the amount of uncharged species.

$$\frac{G^{E,elec}}{RT} = -\left(\sum_k n_k\right)\sqrt{\frac{d_w}{M_w}}\,\frac{4A_{DH}I_x}{3\rho}\ln\left(1+\rho\sqrt{I_x}\right) \tag{8.49}$$

where d_w is the density of the solvent, M_w is the molar mass of the solvent, ρ is a 'closest approach' parameter (and has a value of 8.94), and the sum includes all species, neutral as well as ions (Pitzer, 1980). The Bromley model (Bromley, 1973) is an electrolyte model that calculates the mean ionic activity coefficient of aqueous salt solution based on single parameter B. The model is based on the Debye-Hückel equation plus two additional terms that both are functions of the ionic strength alone.

$$\log\gamma_{\pm} = \frac{-A_{DH}\sqrt{d_w}\,|z_+z_-|\,I_m^{½}}{\ln 10\,(1+I_m^{½})} + \frac{(0.06+0.6B)\,|z_+z_-|\,I_m}{\left(1+\dfrac{1.5}{|z_+z_-|}I_m\right)^2} + B\,I_m \tag{8.50}$$

where d_w is the density of the pure solvent, I_m is the molal ionic strength, and B is an estimated parameter significant for each salt. These parameters are tabulated by Bromley, 1973. This model is in comparison with the Debye-Hückel equation valid up to 6 molal. The reason for Bromley to include a first order polynomial function of the ionic strength in eq. (8.50) is because of experimental evidence that such a relation exists: "Inspection of the curves of Figure 22-8 in Pitzer and Brewer's revision (1961) of Lewis and Randall's

Thermodynamics led this author to believe that the curves are linear in *I* and approach constant values at large *I*.", Bromley, 1973.

Recently, modifications to the original Bromley electrolyte model have been published (Borge et al., 1996a-b, and Raposo et al., 1999). The modifications are to regard the ionic strength as a volumetric property (mole per litre) and use a mixing rule for the B parameter given the cations and anions. Based on these modifications the model is now applicable up to 9 molal. However, both Bromley models lack any temperature dependence; the B parameters are only estimated at 298 K.

The Poisson-Boltzmann equation can of course be solved numerically. If only radial dimension is considered, the numerical solution and the approximate one of the linearised Poisson-Boltzmann equation are identical (McQuarrie, p. 332). This is illustrated by Figure 8.1. The Poisson-Boltzmann equation is solved by an ordinary differential equation solver provided by MATLAB, ode45.m.

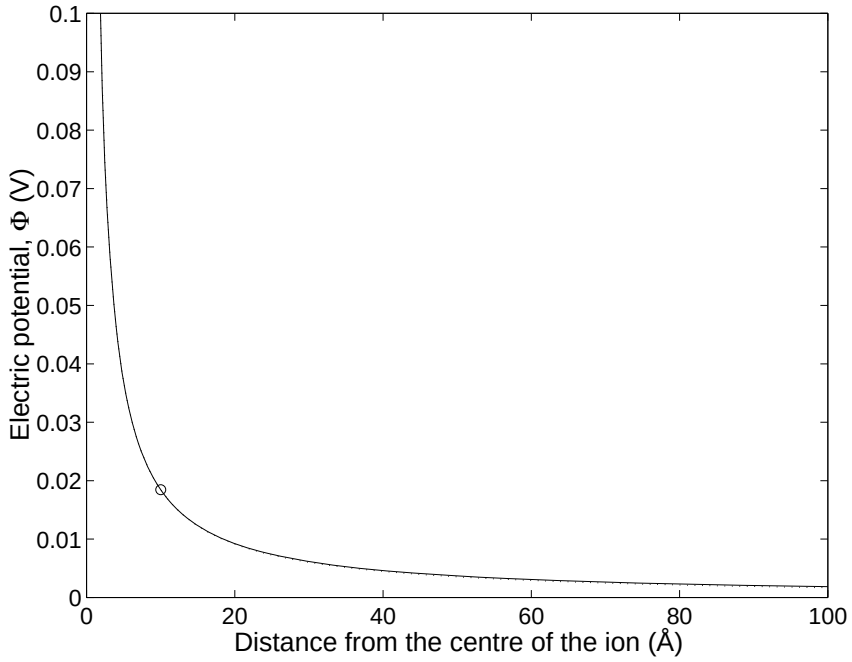


Figure 8.1: The electric potential as a function of the radial distance from the centre of an ion. The distance of closest approach a, der Annäherungsabstand, is arbitrarily chosen as a = 10 Å, the concentration is c_{NaCl} = 0.01 M, and the temperature is 298.15 K. The distance of closest approach is indicated by o, the Poisson-Boltzmann equation by —, and the linearised Poisson-Boltzmann equation by - -.

8.4 Electrolyte g^E models

As mentioned previously a Debye-Hückel model needs configurational terms from another model in order to describe other solutions than very dilute ones. Examples of those additional terms are g^E models. The three classical g^E models NRTL, UNIFAC, and UNIQUAC all have electrolyte versions where a Debye-Hückel-like term is added to the classical g^E model in order to account for the ionic behaviour. These modified models are called the electrolyte NRTL, UNIFAC + DH, and the extended UNIQUAC, respectively.

The electrolyte NRTL model was presented by Chen and Evans (1986). This g^E model consists of two terms, a long-range interaction contribution (Pitzer-Debye-Hückel formula, described by Pitzer, 1980) and a short-range interaction contribution where the original NRTL formula as described by Renon and Prausnitz (1968) is slightly modified by Chen and Evans (1986). The modification is that the ionic species are contributing differently to the excess Gibbs energy than the non-ionic species. The electrolyte NRTL model has been extended by a third term (Chen et al., 1989). The additional term is the Born term which accounts for the effects of mixed solvents. (There are no further comments to this model.)

The modified UNIFAC model (Larsen et al., 1987) plus a Debye-Hückel-like term have been used to model the activity coefficients of amino acids and antibiotics (Pinho et al. (1996), Fiol et al. (1995), Gupta and Heidemann (1990), and Kuramochi et al. (1996a-b, 1997)). The strength of the UNIFAC model is that it in principle is a predictive model once the contributing groups have been determined. In the case of amino acids, Pinho et al. (1996) have determined the groups significant of zwitterionic amino acids, e.g. the carboxylate group ($-COO^-$) and the α-amino group ($-CH_2NH_3^+$). However, all these charged 'new' groups are identical to the already conventional uncharged groups, (-COOH and $-CH_2NH_2$, respectively).

The extended UNIQUAC model of Sander et al. (1986) is made up of two parts; a usual UNIQUAC contribution as presented by Abrams and Prausnitz (1975) and the Debye-Hückel-like contribution of Fowler and Guggenheim, eq. (8.46).

In turn, the UNIQUAC model itself consists of two terms, a combinatorial (enthalpic) and a residual (entropic) term, eqs. (8.51) and (8.52), respectively.

$$\frac{g^{E,comb}}{RT} = \sum_i x_i \ln \frac{\phi_i}{x_i} + \frac{Z}{2} \sum_i x_i q_i \ln \frac{\theta_i}{\phi_i} \tag{8.51}$$

$$\frac{g^{E,res}}{RT} = -\sum_i x_i q_i \ln \sum_j \theta_j \exp\left(-\frac{\Delta U_{ji}}{RT}\right) \tag{8.52}$$

where Z is the lattice co-ordination number which normally is set to a value of 10, the variable

$$\phi_i = \frac{x_i r_i}{\sum_j x_j r_j} \tag{8.53}$$

is the volume fraction, r_i is the volume parameter of component *i*, the variable

$$\theta_i = \frac{x_i q_i}{\sum_j x_j q_j} \tag{8.54}$$

is the surface area fraction, q_i is the surface area parameter of component *i*, and interaction energy differences

$$\Delta U_{ji} = U_{ji} - U_{ii} \quad , \quad \Delta U_{ij} = U_{ij} - U_{jj} \quad \text{, and} \quad \Delta U_{ii} = \Delta U_{jj} = 0 \tag{8.55}$$

It is noted that ΔU_{ji} is not identical to ΔU_{ij}. The results of the application of the extended UNIQUAC model are given in Chapter 9. Modelling results.

8.5 The HS-MSA model

As mentioned in the introduction of this chapter there are two types of frameworks. This section describes a model that is fully based in the McMillan-Mayer framework.

The model considered consists of two parts: a configurational term and an electrostatic term. The configurational term is the hard-sphere term (HS) of Mansoori et al. (1971) and the electrostatic term is the mean spherical approximation term (MSA) of Blum and Høye (1977). This model is identical to that presented by Simonin et al. (1996). For consistency, the combined model is named the HS-MSA model in this work.

When the solvent is treated as a dielectric continuum and not molecularly, the model is called a *primitive* model. Consequently, a *non-primitive* model does treat all components molecularly. These hard spheres have neither a charge nor a dipole moment. Furthermore, the hard spheres are assumed to have different sizes.

The 'excess' MSA Helmholtz energy, ΔA^{MSA}, as it is presented by Simonin et al., 1996, is given by

$$\frac{\Delta A^{MSA}}{kT} = \frac{\Delta U^{MSA}}{kT} + \frac{\Gamma^3}{3\pi} \tag{8.56}$$

where the 'excess' MSA internal energy is

$$\Delta U^{MSA} = -\frac{e^2}{4\pi\varepsilon}\sum_i \rho_i z_i \frac{\Gamma z_i + \eta\sigma_i}{1+\Gamma\sigma_i} \tag{8.57}$$

where σ_i is the diameter of species i. The reason for writing ΔA and 'excess' is that it is relative to the dielectric continuum. This description level is called the McMillan-Mayer framework (Simonin et al., 1996) and is further described in Chapter 6. Statistical mechanics. The three properties η, Ω, and Δ are defined by eqs. (8.58) - (8.60). It is worth noting that η is zero when all the ionic diameters are identical due the overall charge balance.

$$\eta = \frac{1}{\Omega}\frac{\pi}{2\Delta}\sum_k \frac{\rho_k \sigma_k z_k}{1+\Gamma\sigma_k} \tag{8.58}$$

$$\Omega = 1 + \frac{\pi}{2\Delta}\sum_k \frac{\rho_k \sigma_k^3}{1+\Gamma\sigma_k} \tag{8.59}$$

$$\Delta = 1 - \frac{\pi}{6}\sum_k \rho_k \sigma_k^3 \tag{8.60}$$

The screening parameter Γ must satisfy the closure equation

$$\Gamma^2 = \frac{e^2}{4\varepsilon kT}\sum_i \rho_i \left[\frac{z_i - \eta\sigma_i^2}{1+\Gamma\sigma_i}\right]^2 \tag{8.61}$$

For comparison the Debye length of eq. (8.4) is rewritten as

$$\kappa^2 = \frac{e^2}{\varepsilon kT}\sum_i \rho_i z_i^2 \tag{8.62}$$

It is worth noting that for identical radii ($\eta = 0$) the parameters Γ and κ are interrelated as

$$4\Gamma^2(1+\Gamma\sigma)^2 = \kappa^2 \tag{8.63}$$

The hard-sphere term, as it is given by Simonin et al., 1996, is identical to the expression of Mansoori et al., 1971.

$$\frac{\pi}{6kT}\Delta A^{HS} = \left(\frac{X_2^3}{X_3^2} - X_0\right)\ln(1-X_3) + \frac{3X_1X_2}{1-X_3} + \frac{X_2^3}{X_3(1-X_3)^2} \tag{8.64}$$

where

$$X_n = \frac{\pi}{6}\sum_k \rho_k \sigma_k^n \tag{8.65}$$

where ρ_k is the number density. Originally, the hard-sphere model (Mansoori et al., 1971) is not a primitive model, but it is treated as such by the HS-MSA model. The HS-MSA model is designed to describe the behaviour of electrolyte solutions. Furthermore, the cation diameters and the dielectric constant are made functions of the solute concentration by Simonin et al., 1996, as shown in eqs. (9.9) and (9.10). The argument of Simonin et al. (1996) for applying a concentration dependent cation diameter is the hydration of the cation. However, they are regarding the solvent as a dielectric continuum, which is equivalent to regard the solvent as inert. Nonetheless, they permit the solvent to react molecularly with the cation (hydration). This is a contradiction in terms. The reason for a concentration dependent dielectric constant has an experimental foundation. Helgeson et al. (1981) have correlated experimental determined dielectric constants as a function of the 'molal' ionic strength.

Additionally, Simonin (1999) has suggested to model non-electrolytes by an additional van der Waals contribution to account for the short-range interactions (dipole-dipole interactions). Khoshkbarchi and Vera (1996d) presented a model where the hard-sphere term of Mansoori et al., 1971, was the reference and perturbation terms were added (dispersion, dipole-dipole, dipole-induced dipole, and angle-average charge - dipole). Amino acids have relatively high dipoles. Furthermore, the electrostatic term of Blum and Høye (1977) was added for electrolytes. However, the contributions of the additional terms are very scarce (except that of dispersion), so for any practical purposes these terms should be omitted. This model is known as the perturbed hard-sphere model with mean spherical approximation. This model has been simplified so it only consists of two perturbation terms besides the hard-sphere term (Khoshkbarchi and Vera, 1996e). These two terms account for the dispersion (Lennard-Jones) and the dipole-dipole interaction (angle-average Keesom). This simplified model is made for non-electrolyte solutions and is consequently without a long-ranging electrostatic term.

However, the concept of describing a system with the solvent as a reference seems to have some shortcomings. By definition the interactions between solvent and solutes are eliminated because of the choice of having the solvent as a dielectric continuum.

When Hill (1962), p. 327, gives an expression for the hard-sphere activity coefficient for a continuum model in terms of virial coefficients, he approximates the dilute solution by a gas mixture since that is the idea of the McMillan-Mayer level of description. The hard-sphere term presented by Hill, like that of Khoshkbarchi and Vera (1996d), is deprived of any direct interactions between the solvent and the solute. In fact, all primitive model terms must be. (In a gas mixture there is nothing called a solvent. That is a major difference between a gas mixture and a dilute solution). Consequently, a hard-sphere term in a primitive model is not a classical model as mentioned by Debye and Hückel. From a physical viewpoint, it seems unfortunate to formulate a model that does not include solvent - solute interactions.

The results of the HS-MSA model are given in Chapter 9. Modelling results.

8.6 Modelling of solubility

Many attempts have been made to model the solubility of amino acids (Chen et al. (1989), Peres and Macedo (1994), Pinho et al. (1994), Fiol et al. (1995), Gupta and Heidemann (1990), Nass (1988), and Kuramochi et al. (1996a-b)). The approach has almost been the same as well. Firstly, the activity coefficient model is tuned by estimating the activity coefficients of the amino acids at different concentrations but at constant temperature (298 K). The activity coefficients most often used are those tabulated by Fasman (1976). Secondly, the tuned activity coefficient model is then used to model the solubility of the amino acids as a function of temperature. Fasman (1976) also gives most of the solubilities. They are calculated by the correlations derived by Dalton and Schmidt (1933 and 1935) who have correlated the logarithmic solubilities of a number of amino acids as a second order polynomial function of the temperature.

$$\ln x_{AA^{\pm}} = A + BT + CT^2 \tag{8.66}$$

where A, B, and C are adjustable parameters. The temperature range is 273 - 373 K. An evident shortcoming of this procedure is that the model tuning is done at 298 K but the modelling of the solubility is done over a much wider temperature range.

In order to model the solubility, the equilibrium constant K of dissolving the amino acid has to be known.

$$AA\,(s) \;=\; AA^{\pm}\,(aq) \qquad\qquad K = a_{AA^{\pm}(aq)} \tag{8.67}$$

The equilibrium constant is usually correlated by eq. (8.68)

$$\ln K = A + \frac{B}{T} + C \ln T \tag{8.68}$$

where A, B, and C are adjustable parameters. The form of the correlation originates from

$$\left(\frac{\partial (\Delta G / T)}{\partial (1/T)} \right)_P = \Delta H \tag{8.69}$$

where ΔG and ΔH are the change in Gibbs energy and the change in enthalpy due to the reaction. The fact that the Gibbs energy is interrelated with the equilibrium constant

$$\Delta G = -RT \ln K \tag{8.70}$$

gives by inserting eq. (8.70) into eq. (8.69) the so-called Gibbs-Helmholtz equation

$$\left(\frac{\partial \ln K}{\partial T} \right)_P = \frac{\Delta H}{RT^2} \tag{8.71}$$

or in the integral form

$$\ln K_T = \ln K_{T_o} + \int_{T_o}^{T} \frac{\Delta H}{RT^2} dT \tag{8.72}$$

where T_o is the reference temperature. The temperature derivative of the enthalpy at constant pressure is by definition the heat capacity, ΔC_p.

$$\left(\frac{\partial \Delta H}{\partial T} \right)_P = \Delta C_p \tag{8.73}$$

Assuming a constant heat capacity will result in the following expression for the equilibrium constant

$$\begin{aligned} R \ln K_T &= R \ln K_{T_o} - \Delta H_{T_o}\left(\frac{1}{T} - \frac{1}{T_o}\right) + \Delta C_p\left(\ln\frac{T}{T_o} + \frac{T_o}{T} - 1\right) \\ &= \left(R \ln K_{T_o} + \frac{\Delta H_{T_o}}{T_o} - \Delta C_p \ln T_o - \Delta C_p\right) + \frac{\Delta C_p T_o - \Delta H_{T_o}}{T} + \Delta C_p \ln T \end{aligned} \tag{8.74}$$

where eq. (8.74) has the same form as eq. (8.68).

If the amino acid solution is assumed ideal (γ_i = 1), the correlation for the equilibrium constant is able to describe the solubility curve, eq. (8.66), (a second order polynomial function of the temperature), since

$$\begin{aligned} \ln K &= A + \frac{B}{T} + C \ln T \\ &= A + \frac{B}{T} + C \ln\left(\frac{T_r + T - T_r}{T_r}\right) + C \ln T_r \\ &= A + C \ln T_r + \frac{B}{T} + C \ln\left(1 + \frac{T - T_r}{T_r}\right) \end{aligned} \tag{8.75}$$

where T_r is a reference temperature, chosen such that

$$\frac{T - T_r}{T_r} \le 1 \qquad \Rightarrow \qquad \xi \le 1 \tag{8.76}$$

Using the series expansion of the natural logarithm

$$\begin{aligned} \ln K &= A + C \ln T_r + \frac{B}{T} + C \ln(1 + \xi) \\ &= A + C \ln T_r + \frac{B}{T} + C \sum_{i=1}^{\infty} (-1)^{i+1} \xi^i \\ &\approx A + C \ln T_r + \frac{B}{T} + C\left(\left[\frac{T - T_r}{T_r}\right] - \frac{1}{2}\left[\frac{T - T_r}{T_r}\right]^2\right) \\ &= \left(A + C \ln T_r - \frac{3C}{2}\right) + \frac{B}{T} + \frac{2C}{T_r} T - \frac{C}{2T_r^2} T^2 \end{aligned} \tag{8.77}$$

In this way the logarithmic equilibrium constant K can be modelled by a second order polynomial function - like to the logarithm of the solubility. That is why the correlation for the equilibrium constant is capable of correlating the solubility of an ideal solution. However, the activity coefficient model makes up for the small discrepancies between the two expressions. Or in other words: the equilibrium constant correlation has three adjustable

parameters that are fitted so that the activity coefficient model can describe the solubility curve.

9. Modelling Results

The purpose of this chapter is to impart the experience gained in this project of how the extended UNIQUAC model is describing binary and ternary systems containing amino acids or peptides and how the behaviour of a continuum concept based model, the HS-MSA model, is performing in an electrolyte system. Both models are applied as they were described in the previous chapter, 8. Modelling Electrolyte Systems.

This chapter is made up of two parts. The first part is focussing on the modelling with the extended UNIQUAC model. Firstly, the flexibility of the model is investigated by fitting only binary data with and without the residual term of the model. Secondly, an investigation of the modelling results of binary as well as ternary systems, i.e. osmotic coefficients from isopiestic measurements and electrode potential measurements, is performed.

In the second part of this chapter the modelling results concerning the HS-MSA model are given. The model has been applied as it is presented in Chapter 8. Furthermore, the effects of changing the HS-MSA model from its original primitive basis to a non-primitive basis have been done in order to see how well the HS-MSA model performs. A primitive model treats the solvent as a dielectric continuum and not as uncharged molecules. A non-primitive model treats the solvent molecularly.

9.1 Flexibility of the UNIQUAC model

As mentioned in the introduction of this chapter the model flexibility is investigated by modelling binary systems of water and amino acid. In binary systems of water and amino acid the extended UNIQUAC model is losing its electrolyte extension since the amino acid at the present pH will assumes its zwitterionic configuration; a net charge of zero. The experimental data are osmotic coefficients, which are obtained by isopiestic measurements.

The maximum number of UNIQUAC parameters that one possibly can estimate for a binary system is 2 surface area parameters, 2 volume parameters, and 2 interaction parameters, ΔU_{12} and ΔU_{21}. The surface area parameter and the volume parameter of water are assigned to those of Abrams and Prausnitz (1975). This leaves 4 estimable parameters per binary system. The (extended) UNIQUAC model has no difficulties in fitting the experimentally determined

osmotic coefficients of the 3 representative systems that are shown in Figures 9.1, 9.3, and 9.5 by the full lines.

However, it is possible to model these systems without the residual term of the UNIQUAC model quite well, i.e. the surface area parameter and the volume parameter of the amino acids are re-estimated while the interaction parameters are set to zero. The results of these re-estimations are also shown in Figures 9.1, 9.3, and 9.5 by the dotted lines. The reason for this success is that the UNIQUAC model is flexible enough to accomplish satisfactory fits. In the case of glycine the osmotic coefficient calculated by the two versions of the UNIQUAC model coincide.

As presented in the previous chapter, the UNIQUAC model consists of two terms: the combinatorial term, eq. (8.51), and the residual term, eq. (8.52). However, the combinatorial term can be split into two contributions

$$\frac{g^{E,comb,I}}{RT} = \sum_i x_i \ln \frac{\phi_i}{x_i} \tag{9.1}$$

and

$$\frac{g^{E,comb,II}}{RT} = \frac{Z}{2} \sum_i x_i q_i \ln \frac{\theta_i}{\phi_i} \tag{9.2}$$

To illustrate the flexibility of the model the individual terms of the logarithmic activity coefficients of the amino acid are shown as function of the amino acid molality. The Figures 9.2, 9.4, and 9.6 are for the 'full' model, i.e. the model including the residual term.

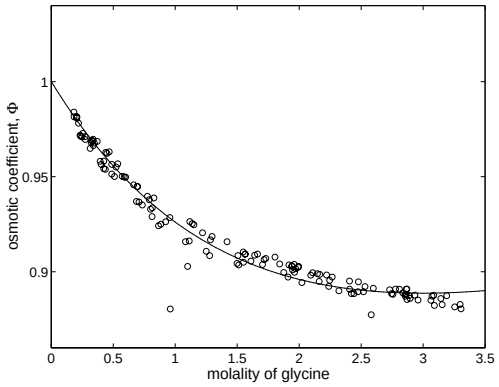


Figure 9.1: The osmotic coefficient of the glycine - water system as a function of the glycine molality. The UNIQUAC model with (–) and without (···) its residual term. The experimental points (o): Smith and Smith (1937), Richards (1938), and Ellerton et al. (1964).

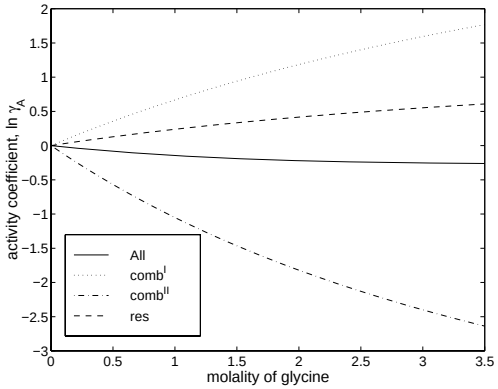


Figure 9.2: The logarithmic activity coefficient of glycine as a function of the glycine molality. 'All' is the full UNIQUAC model, 'comb^{I}' is eq. (9.1), 'comb^{II}' is eq. (9.2), and 'res' is eq. (8.52).

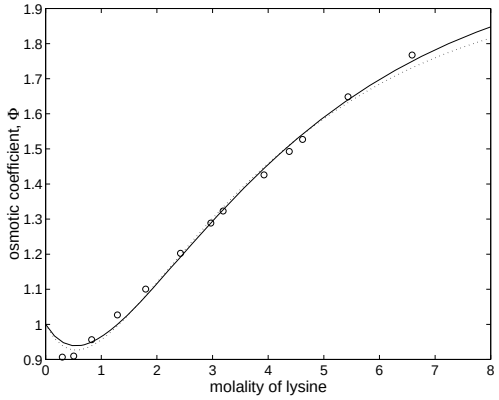


Figure 9.3: The osmotic coefficient of the lysine - water system as a function of the lysine molality. The UNIQUAC model with (–) and without (···) its residual term. The experimental points (o): Bonner (1982).

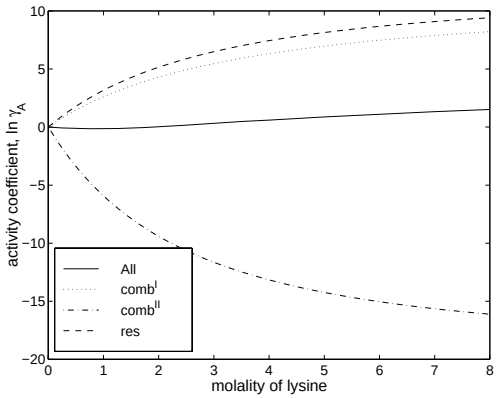


Figure 9.4: The logarithmic activity coefficient of lysine as a function of the lysine molality. 'All' is the full UNIQUAC model, 'comb^{I}' is eq. (9.1), 'comb^{II}' is eq. (9.2), and 'res' is eq. (8.52).

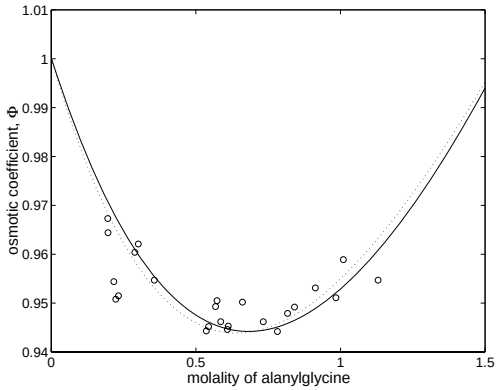


Figure 9.5: The osmotic coefficient of the glycylalanine - water system as a function of the glycylalanine molality. The UNIQUAC model with (–) and without (···) its residual term. The experimental points (o): Smith and Smith (1940c).

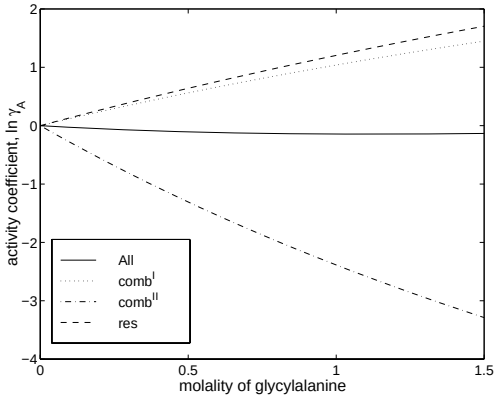


Figure 9.6: The logarithmic activity coefficient of glycylalanine as a function of the glycylalanine molality. 'All' is the full UNIQUAC model, 'comb^{I}' is eq. (9.1), 'comb^{II}' is eq. (9.2), and 'res' is eq. (8.52).

Figures 9.2, 9.4, and 9.6 show that the combinatorial term consists of two opposing terms. This gives a huge flexibility in the model. This is the reason that the reduced version of the UNIQUAC model is still performing acceptable.

The phenomenon, which is illustrated by Figures 9.2, 9.4, and 9.6, is popularly called 'weighing the ship's captain'; the mass of the captain is determined by weighing the ship with and without the captain. A small value is determined by subtracting two large values. If the residual term is left out, the two parts of the combinatorial term, eqs. (9.1) and (9.2), will just find a new internal ratio so that the reduced model fits the data again.

In conclusion, the UNIQUAC model is a very flexible model to model binary water-amino acid systems. The extended UNIQUAC model has no difficulties in describing the binary systems of amino acid (or peptides) and water.

9.2 Binary and ternary systems modelled by the extended UNIQUAC

Knowing that the flexibility of the UNIQUAC model is significant, the focus is shifted towards the fitting of experimental data in binary as well as ternary systems by the use of the extended UNIQUAC model. The binary (osmotic coefficients) and the ternary (electrode

potentials) systems were modelled simultaneously. The application of the extended UNIQUAC model for solute-electrolyte solutions was greatly facilitated by the work of Thomsen (1997) since all the needed parameters for aqueous electrolyte systems were available. Consequently, only the parameters involving the additional amino acids or peptides had to be estimated. The estimated parameters are given in Tables 9.1 and 9.2. Contrary to the non-electrolytes the ions of the dissolved salts still have an electrostatic contribution.

The graphic presentations of the model fits to the binary data also include the so-called ideal osmotic coefficient, ϕ^{id}.

$$\phi^{id} = -\frac{x_w}{x_s} \ln x_w \tag{9.3}$$

which is identical to the osmotic coefficient (in the Lewis-Randall framework, eq. (O.15)) except that the solvent activity is replaced by the solvent mole fraction, hence the notation ideal, ($\gamma_i = 1$). Figure 9.7 shows the ideal osmotic coefficient, ϕ^{id}, as a function of the solute mole fraction. The osmotic coefficient is another way of formulating the solvent activity. However, often the solvent activity is close to unity because the solution is diluted. The advantage of the osmotic coefficient is that it magnifies the behaviour of the solvent activity. A reasonable fit to the osmotic coefficient is therefore a good fit to the solvent activity.

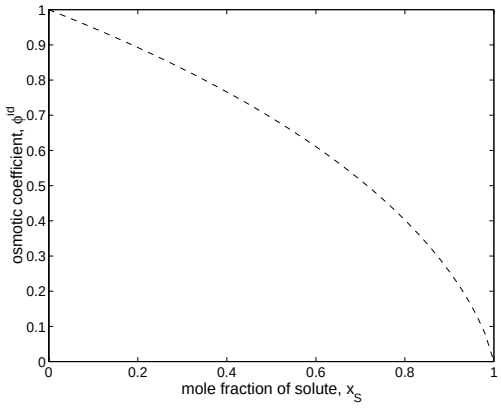


Figure 9.7: The osmotic coefficient of an ideal binary solution as a function of the solute mole fraction. The two end points, (0,1) and (1,0) are valid even for the osmotic coefficient of a real solution.

When the osmotic coefficient of a solution is exhibiting a behaviour resembling that of Figure 9.7, there is reason to believe that the solution in question can be treated as an ideal solution.

For comparison the ideal osmotic coefficient, eq. (9.3), is shown as the dashed line in Figures 9.12, 9.16, 9.20, 9.23, 9.26, 9.28, and 9.30.

This section will present the relation between the osmotic coefficient and the activity coefficient of the solute in a binary solution. Based on the behaviour of the osmotic coefficient with respect to the solute concentration, it is possible to describe the behaviour of the activity coefficient of the solute and of the solvent in a binary solution. If the deviation from the ideal osmotic coefficient is negative,

$$\begin{aligned} &\phi - \phi^{id} < 0 && \Leftrightarrow \\ &-\frac{x_w}{x_S}\ln a_w + \frac{x_w}{x_S}\ln x_w < 0 && \Rightarrow \\ &\ln \gamma_w > 0 && \Rightarrow \quad \gamma_w > 1 \end{aligned} \tag{9.4}$$

the activity coefficient of the solvent is greater than unity. From the definition of the activity coefficient one has the limit

$$\lim_{x_i \to 1} \gamma_i(T, P, \mathbf{n}) = 1 \tag{2.32}$$

and finally the gradient of the activity coefficients are determined from the Gibbs-Duhem equation at constant temperature and pressure - implying that the reference chemical potentials are constants.

$$\begin{aligned} &\sum_i n_i d\mu_i = 0 && \Rightarrow \\ &d\ln a_S = -\frac{n_w}{n_S} d\ln a_w \end{aligned} \tag{9.5}$$

From the definition of real solution ($a_i = x_i\gamma_i$) one obtains for a binary system at constant temperature and pressure

$$\frac{\partial \ln \gamma_S}{\partial n_S} = -\frac{x_w}{x_S}\frac{\partial \ln \gamma_w}{\partial n_S} \tag{9.6}$$

Since the ratio x_w / x_S always is positive, the gradient of ln γ_S with respect to n_S has the opposite sign of the gradient of ln γ_w with respect to n_S. The knowledge of the deviation from the ideal osmotic coefficient gives information of the activity coefficients of the two species in the solution. When the deviation is negative, the usual behaviour of the activity coefficients

is encountered as illustrated by Figures 9.8 and 9.9. Both the solute and the solvent activity coefficients are greater than unity.

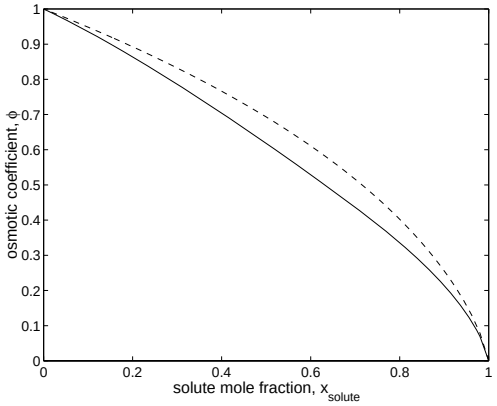


Figure 9.8: A negative deviation from the ideal osmotic coefficient. The osmotic coefficient (–) and the ideal osmotic coefficient (- -).

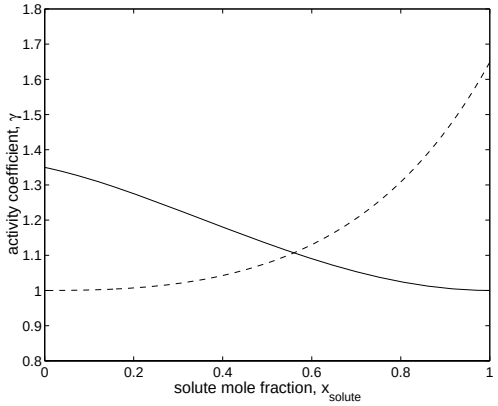


Figure 9.9: The corresponding activity coefficients of the solute (–) and the solvent (- -) at a negative deviation from the ideal osmotic coefficient.

However, when the deviation is positive, the behaviour of the activity coefficients is laterally reversed along the ordinate axis at a value of one, so that the activity coefficients are less than unity as shown in Figures 9.10 and 9.11. The proof of this is analogous to eq. (9.4).

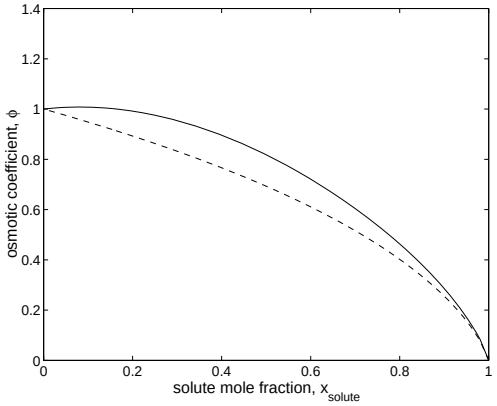


Figure 9.10: A positive deviation from the ideal osmotic coefficient. The osmotic coefficient (–) and the ideal osmotic coefficient (- -).

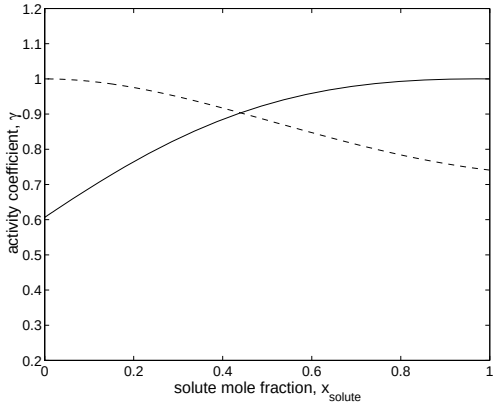


Figure 9.11: The corresponding activity coefficients of the solute (–) and the solvent (- -) at a positive deviation from the ideal osmotic coefficient.

The six binary systems of glycine, serine, threonine, and glycylglycine (Figures 9.16, 9.20, 9.23, and 9.28) all have decreasing osmotic coefficients, ϕ, as a function of the solute molality in common but none of them are identical to the ideal osmotic coefficient, ϕ^{id}. This implies that none of these solutions are ideal solutions despite a decreasing osmotic coefficient at increasing amino acid (or peptide) concentration. They all exhibit a negative deviation from the ideal osmotic coefficient, $\phi - \phi^{id} < 0$, which indicates that the solvent activity coefficient is greater than unity. This is usually the case for binary mixtures.

The two binary systems of alanine and valine (Figures 9.12 and 9.26) are obviously non-ideal systems since the osmotic coefficients of these solutions are increasing at increasing amino acid concentration. This is emphasised by the fact that there is a positive deviation from the ideal osmotic coefficient, $\phi - \phi^{id} > 0$.

Figure 9.30 shows that the osmotic coefficient of glycyl-L-alanine has a minimum in the osmotic coefficient. The significance of a minimum is that the activity coefficient of the solute also has a minimum.

For alanine, threonine, and valine (Figures 9.12, 9.23, and 9.26) the ordinate axis has a small scale so the scattering of the data is insignificant.

Measurements of the electrode potentials of ternary aqueous solute-electrolyte systems have been practised since the 1920s (e.g. Harned and Åkerlöf (1926), Harned and Owen (1930a-b), and Roberts and Kirkwood (1941)). In case the solution is at the isoelectric point of the amino acid (or the peptide), it is only the inorganic salt that is able to conduct current. By the introduction of ion-selective electrodes it was possible to conduct experiments at a pH different from the isoelectric point and still only measure the electrode potential due to the inorganic salt. Since 1996, Vera and co-workers (Khoshkbarchi and Vera, 1996a-c; Khoshkbarchi et al., 1997, Soto-Campos et al., 1997a-b, 1998) have performed measurements of this sort for 6 amino acids in combination with a few salts: NaCl, KCl, and $NaNO_3$. There is a practical limitation to the number of salts available for electrode potential measurements using ion-selective electrodes - and that is the types of ISE's available on the market. However, all the systems investigated by Vera and co-workers are at a pH identical to the isoelectric point of the amino acids.

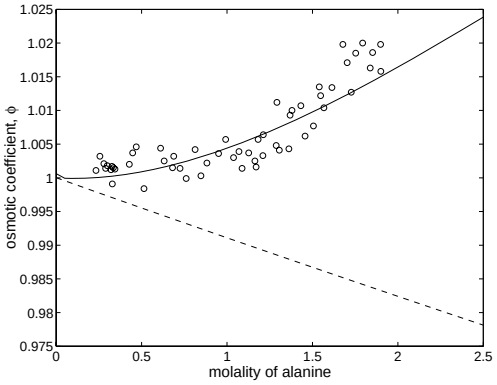


Figure 9.12: The osmotic coefficient of the alanine - water system as a function of the alanine molality. The UNIQUAC model with its residual term (–) and the ideal osmotic coefficient (- -). The experimental points (o): Smith and Smith (1937b) and Robinson (1952).

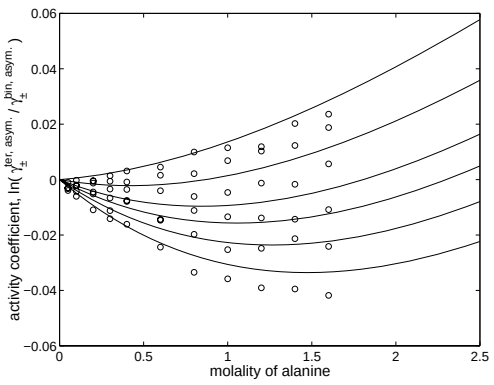


Figure 9.13: The activity coefficient ratio of NaCl in alanine - water. The salt concentrations are from top to bottom: 0.9, 0.6, 0.4, 0.3, 0.2, and 0.1 molal. Experimental points (o): Khoshkbarchi and Vera (1996a).

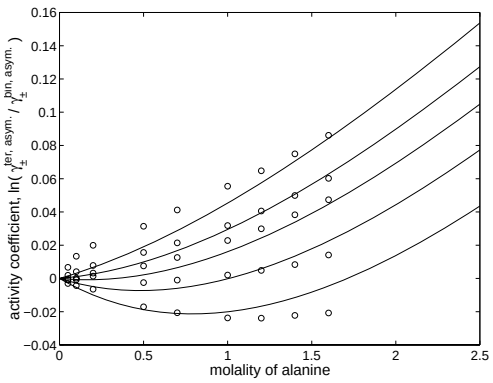


Figure 9.14: The activity coefficient ratio of KCl in alanine - water. The salt concentrations are from top to bottom: 1.0, 0.7, 0.5, 0.3, and 0.1 molal. Experimental points (o): Soto-Campos et al. (1997).

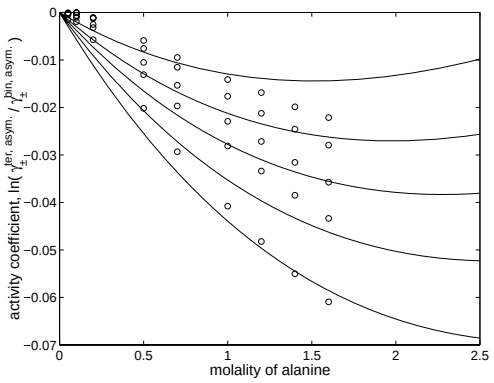


Figure 9.15: The activity coefficient ratio of $NaNO_3$ in alanine - water. The salt concentrations are from top to bottom: 1.0, 0.7, 0.5, 0.3, and 0.1 molal. Experimental points (o): Soto-Campos et al. (1997).

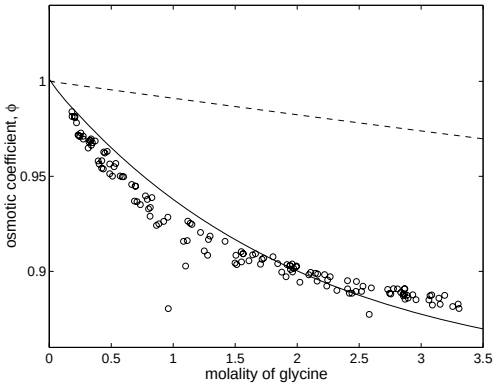


Figure 9.16: The osmotic coefficient of the glycine - water system as a function of the glycine molality. The UNIQUAC model with its residual term (–) and the ideal osmotic coefficient (- -). The experimental points (o): Smith and Smith (1937), Richards (1938), and Ellerton et al. (1964).

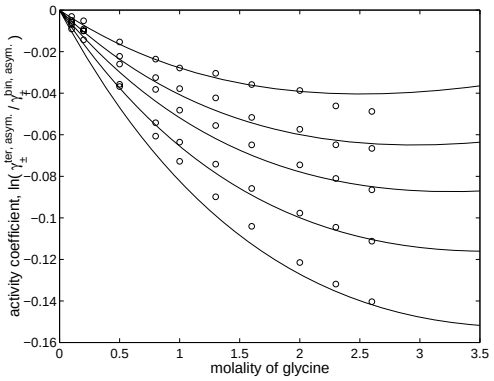


Figure 9.17: The activity coefficient ratio of NaCl in glycine - water. The salt concentrations are from top to bottom: 1.0, 0.7, 0.5, 0.3, and 0.1 molal. Experimental points (o): Khoshkbarchi and Vera (1996a).

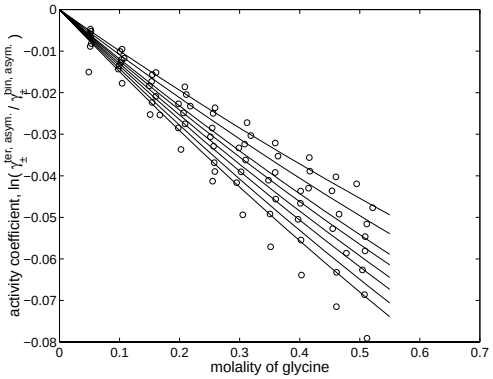


Figure 9.18: The activity coefficient ratio of KCl in glycine - water. The salt concentrations are from top to bottom: 0.50, 0.40, 0.30, 0.25, 0.20, 0.15, 0.10, and 0.05 molal. Experimental points (o): Roberts and Kirkwood (1941).

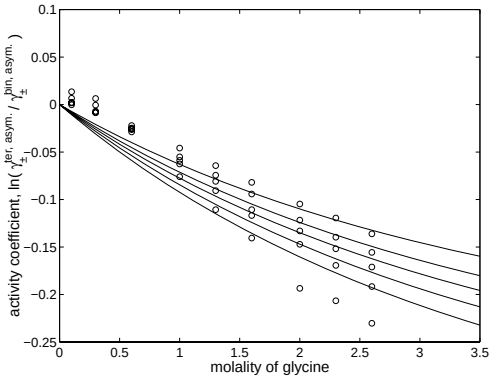


Figure 9.19: The activity coefficient ratio of $NaNO_3$ in glycine - water. The salt concentrations are from top to bottom: 1.0, 0.7, 0.5, 0.3, and 0.1 molal. Experimental points (o): Soto-Campos et al. (1997b).

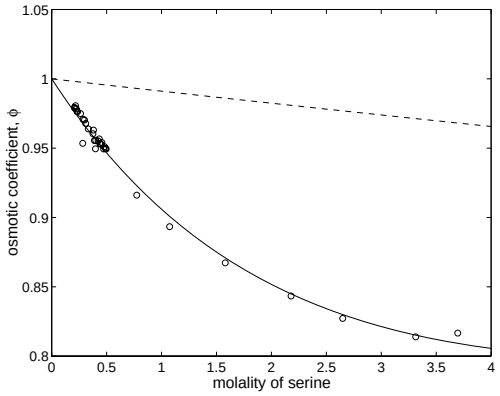


Figure 9.20: The osmotic coefficient of the serine - water system as a function of the serine molality. The UNIQUAC model with its residual term (–) and the ideal osmotic coefficient (- -). The experimental points (o): Smith and Smith (1940b) and Hutchens et al. (1963).

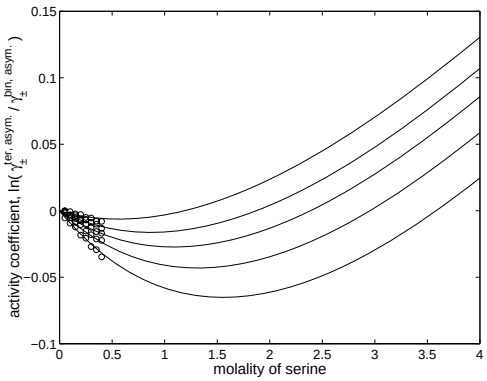


Figure 9.21: The activity coefficient ratio of NaCl in serine - water. The salt concentrations are from top to bottom: 1.0, 0.7, 0.5, 0.3, and 0.1 molal. Experimental points (o): Khoshkbarchi et al. (1997).

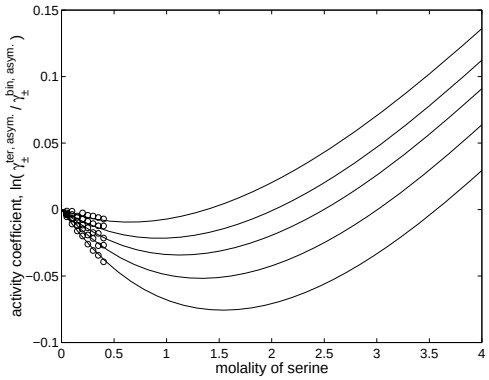


Figure 9.22: The activity coefficient ratio of KCl in serine - water. The salt concentrations are from top to bottom: 1.0, 0.7, 0.5, 0.3, and 0.1 molal. Experimental points (o): Khoshkbarchi et al. (1997).

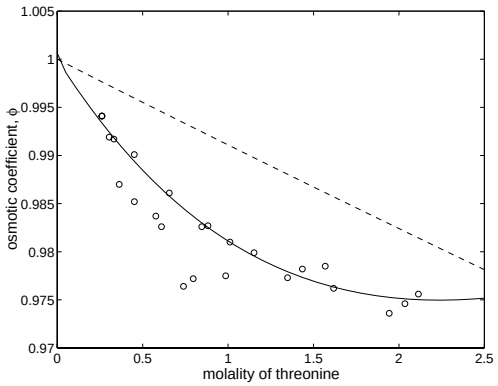


Figure 9.23: The osmotic coefficient of the threonine - water system as a function of the threonine molality. The UNIQUAC model with its residual term (–) and the ideal osmotic coefficient (- -). The experimental points (o): Smith and Smith (1940b).

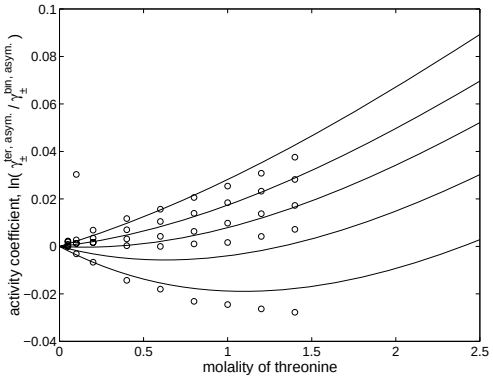


Figure 9.24: The activity coefficient ratio of NaCl in threonine - water. The salt concentrations are from top to bottom: 1.0, 0.7, 0.5, 0.3, and 0.1 molal. Experimental points (o): Soto-Campos et al. (1997a).

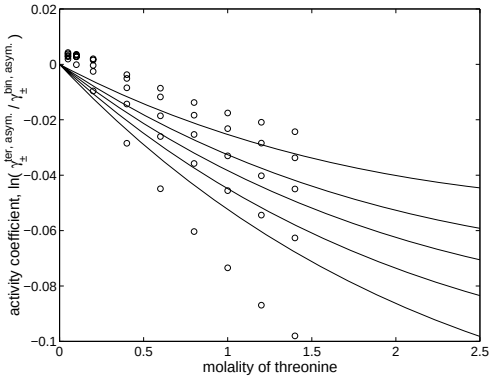


Figure 9.25: The activity coefficient ratio of $NaNO_3$ in threonine - water. The salt concentrations are from top to bottom: 1.0, 0.7, 0.5, 0.3, and 0.1 molal. Experimental points (o): Soto-Campos et al. (1997a).

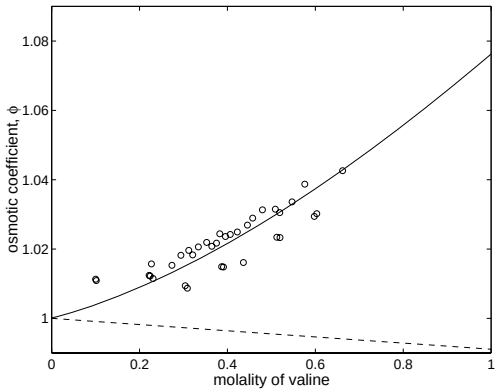


Figure 9.26: The osmotic coefficient of the valine - water system as a function of the valine molality. The UNIQUAC model with its residual term (–) and the ideal osmotic coefficient (- -). The experimental points (o): Bonner (1982), Ellerton et al. (1964) and Smith and Smith (1937b).

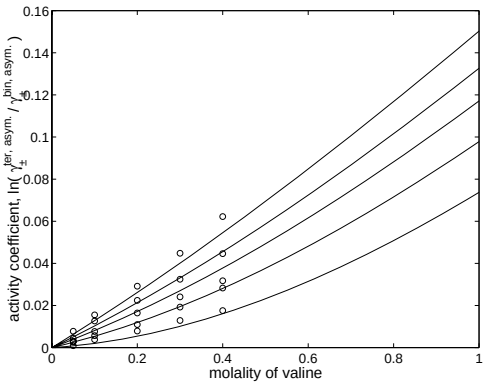


Figure 9.27: The activity coefficient ratio of KCl in valine - water. The salt concentrations are from top to bottom: 1.0, 0.7, 0.5, 0.3, and 0.1 molal. Experimental points (o): Khoshkbarchi and Vera (1996c).

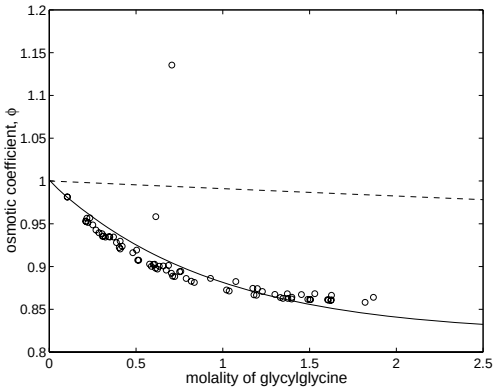


Figure 9.28: The osmotic coefficient of the glycylglycine - water system as a function of the glycylglycine molality. The UNIQUAC model with its residual term (–) and the ideal osmotic coefficient (- -). The experimental points (o): Ellerton et al. (1964) and Smith and Smith (1940c).

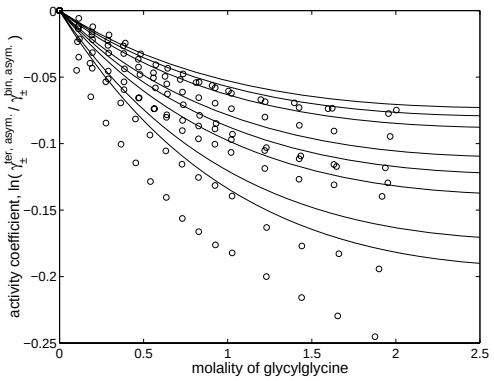


Figure 9.29: The activity coefficient ratio of NaCl in glycylglycine - water. The salt concentrations are from top to bottom: 1.0, 0.9, 0.8, 0.6, 0.5, 0.4, 0.2, and 0.1 molal. Experimental points (o): This work.

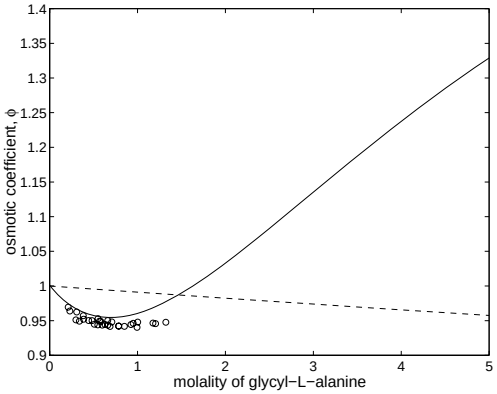


Figure 9.30: The osmotic coefficient of the glycyl-L-alanine - water system as a function of the glycyl-L-alanine molality. The UNIQUAC model with its residual term (–) and the ideal osmotic coefficient (- -). The experimental points (o): Smith and Smith (1940c).

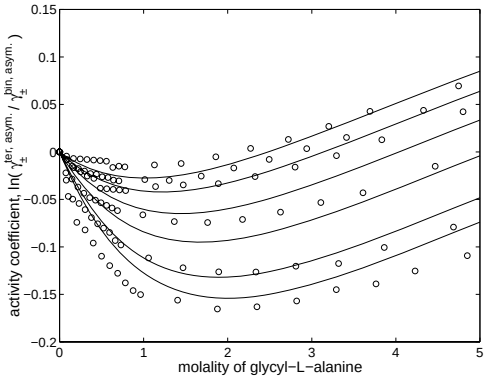


Figure 9.31: The activity coefficient ratio of NaCl in glycyl-L-alanine - water. The salt concentrations are from top to bottom: 1.0, 0.8, 0.6, 0.4, 0.2, and 0.1 molal. Experimental points (o): This work.

In general, the extended UNIQUAC model can fit NaCl - amino acid - water systems quite satisfactorily. The uncertainty lies at low concentrations of both the salt and the amino acid, i.e. in the region where the electrode potential is most sensitive to changes in the salt concentration - and consequently in the amino acid concentration. However, it is in this region (almost a binary solution) that the osmotic coefficients are represented quite well by the model. Since the physics involved are presumed to be continuous, the divergence in the electrode potential representation cannot be due to the model, but is more likely due to the experimental uncertainties at low salt concentrations. This is illustrated by comparing all the binary systems (Figures 9.12, 9.16, 9.20, 9.23, 9.26, 9.28, and 9.30) to the ternary systems.

It is noted that the description of the osmotic coefficient in Figures 9.16 and 9.28 is less satisfactory compared with Figures 9.1 and 9.5. However, this is a consequence of fitting the surface area parameters, volume parameters and the interaction energy parameters, ΔU_{ji}, on ternary as well as binary experimental data. In Figures 9.1 and 9.5, only binary data have been used.

Besides sodium chloride, potassium chloride in aqueous amino acid solutions can be described by the model. In all cases only two additional interaction parameters between K^+ and the amino acid had to be estimated in order to obtain Figures 9.14, 9.18, 9.22 and 9.27. It is worth noting that the experimental data of Figure 9.18 is not measured by application of ion-selective electrodes. Roberts and Kirkwood applied Ag/AgCl electrodes and a cell with a liquid junction of KCl. However, the disagreement between data points and model could equally well be due to the general uncertainty of measurements at low concentration.

As mentioned earlier in this chapter, electrode potential measurements have been carried out on a third salt as well, sodium nitrate, by Vera and his co-workers. The experimental results of this salt are not described very well by the model. The reason for this obvious discrepancy is not clear. The experiments of $NaNO_3$ - alanine, $NaNO_3$ - glycine, and $NaNO_3$ - threonine (Figures 9.15, 9.19, 9.25) all show a different behaviour than the other salts. The data points of the $NaNO_3$ systems lie very close at low amino acid concentrations. For the $NaNO_3$ - glycine system the activity coefficient ratio even has a minimum. It is this narrow span of activity coefficient ratio at low glycine concentration that the model has difficulties in describing. Another possibility could be that the nitrate ion-selective electrode is not working

properly. A reason for this could be that the solution contains also amino acids that perhaps is fouling the membrane in the ion-selective electrode.

9.3 Solubility predicted by the extended UNIQUAC model

As mentioned in the previous chapter, the modelling of solubility as a function of temperature often leads to the estimation of three parameters for the correlation of the equilibrium constant. However, adding an electrolyte to an aqueous amino acid solution will change the solubility conditions of the amino acid. Assuming that the amino acid precipitate is invariant (the same compound is precipitating), the equilibrium constant K_S must also be invariant.

$$AA_{(s)} = AA^{\pm}_{(aq)} \qquad K_S = a_{AA^{\pm}_{(aq)}} = x_{AA^{\pm}_{(aq)}} \cdot \gamma_{AA^{\pm}_{(aq)}} \tag{9.7}$$

The activity coefficients of species *i* obtained from the extended UNIQUAC model is asymmetric - except for the solvent, water, where the activity coefficient is symmetric. Multiplying the solubility (in terms of mole fraction) and the (asymmetric) activity coefficient gives the equilibrium constant expect for a factor of $\gamma^{\infty}_{w,AA^{\pm}}$, the activity coefficient of amino acid at infinite dilute in water. This factor is only a function of temperature and pressure. The asymmetric equilibrium constant

$$\tilde{K}_S = x_{AA} \cdot \tilde{\gamma}_{AA^{\pm}}(T, P, \mathbf{n}) \tag{9.8}$$

is determined in the binary solution of water and amino acid. For the ternary systems of electrolyte - amino acid - water the solubility of the amino acid is calculated by eq. (9.8) since it is one equation with one unknown, x_{AA}. The solubilities of glycine and alanine in aqueous NaCl and KCl solutions as well as the solubilities of glycylglycine and glycyl-L-alanine in aqueous NaCl solutions are estimated by the extended UNIQUAC model and are shown in Figures 9.32 - 9.35.

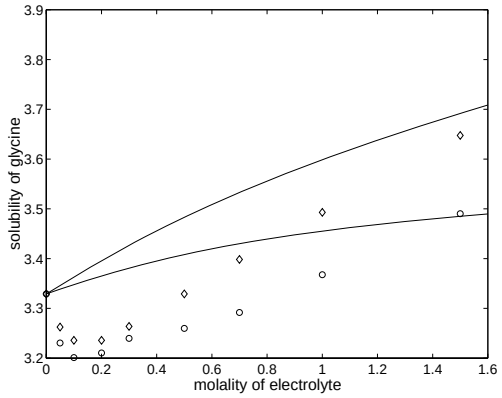


Figure 9.32: The solubility (in molality) of glycine in NaCl - water and in KCl - water as a function of the electrolyte molality. Extended UNIQUAC model (–). Experimental points: NaCl (o) and KCl (◊) from Khoshkbarchi and Vera (1997).

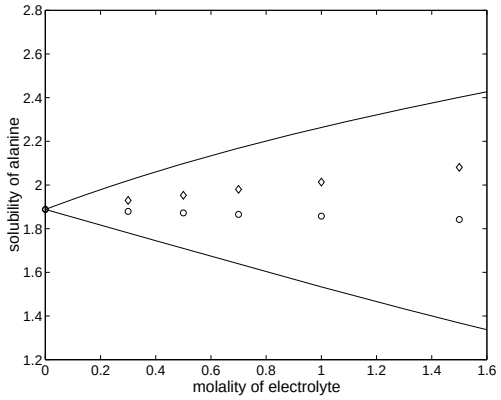


Figure 9.33: The solubility (in molality) of alanine in NaCl - water and in KCl - water as a function of the electrolyte molality. Extended UNIQUAC model (–). Experimental points: NaCl (o) and KCl (◊) from Khoshkbarchi and Vera (1997).

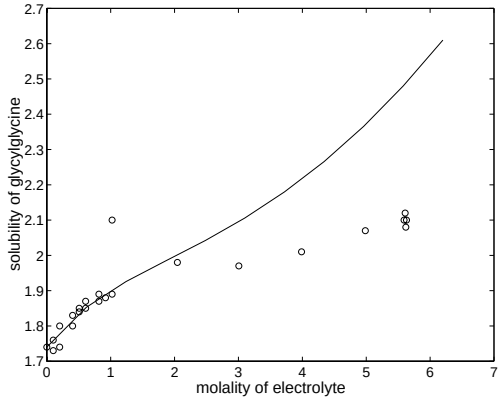


Figure 9.34: The solubility (in molality) of glycylglycine in NaCl - water as a function of the electrolyte molality. Extended UNIQUAC model (–). Experimental points: NaCl (o) from this work.

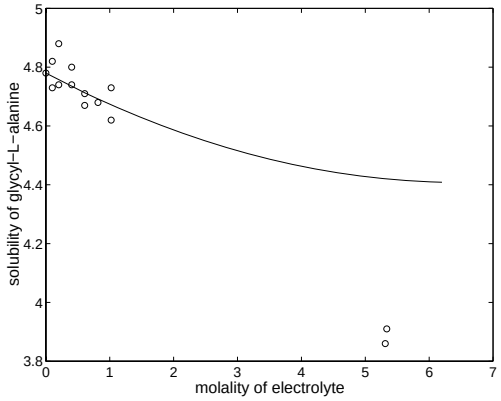


Figure 9.35: The solubility (in molality) of glycyl-L-alanine in NaCl - water as a function of the electrolyte molality. Extended UNIQUAC model (–). Experimental points: NaCl (o) from this work.

The model does a poor prediction of the amino acid and dipeptide solubility in the aqueous salt solutions, Figures 9.32-9.35. In particular the glycine solubilities at low electrolyte concentrations are displeasing; the experimental points contradict the trend of the model. The model is not able to make the steep decrease at the low electrolyte concentrations. The reason

is that the extended UNIQUAC model is reduced to the original UNIQUAC model for the non-electrolyte species, such as the zwitterion of an amino acid. Because of that the extended UNIQUAC model is not capable of predicting the solubility of glycine.

The behaviour of the alanine solubility is monotonic, Figure 9.33, but the model underpredicts the solubility in NaCl and overpredicts it in KCl. The reason for the lack of a minimum in the solubility of alanine in Figure 9.33 could be due to the fact that the experiment is not conducted at electrolyte concentrations that are not low enough. The minimum in Figure 9.32 is below 0.2 molal salt.

The model predicts the solubility of glycylglycine, Figure 9.34, well in aqueous NaCl solutions up to 2 molal NaCl but overpredicts the solubility at higher salt concentrations by approximately 20%. The prediction of glycyl-L-alanine, Figure 9.35, is acceptable at the low electrolyte concentrations but the model overpredicts the solubility at higher concentrations by approximately 15%.

In conclusion, it is evident that the extended UNIQUAC model has difficulties in describing the solubility of an amino acid in a ternary solution based on parameter estimation on experimental data of ternary electrode potential measurements and binary isopiestic measurements. However, the solubility trend, salting-in and salting-out effects, is correctly predicted. With the results at hand, it would seem to be an idea to replace the Fowler-Guggenheim g^E term of the extended UNIQUAC model by the g^E term of Pitzer in order to obtain an electrostatic contribution to the uncharged, non-solvent species as well as the solvent and the ions.

The UNIQUAC parameters for some amino acids and small peptides have been estimated on the basis of osmotic coefficient data and electrode potential data. These parameters are presented in Tables 9.1 and 9.2.

	q	r		q	r
water	1.4000 *	0.9200 *	glycine	5.4490	5.5814
Na^+	1.1990 *	1.4034 *	serine	6.5805	6.3607
K^+	2.4306 *	2.2304 *	threonine	4.9885	5.0114
Cl^-	10.197 *	10.386 *	valine	6.5653	7.4288
NO_3^-	6.2074 *	5.4041 *	glycylglycine	10.549	10.688
alanine	5.1778	5.0807	glycyl-L-alanine	9.7327	10.601

Table 9.1: The surface area parameters, q, and the volume parameters, r, of the UNIQUAC model as it is presented in eqs. (8.51) and (8.52). The asterisk denotes the parameters from the work of Thomsen (1997).

	H_2O	Na^+	K^+	Cl^-	NO_3^-	Ala	Gly	Ser	Thr	Val	GG	GA
H_2O	0	5964.5 *	4351.9 *	–5624.0 *	–14273.5 *	–1073.2	–1330.4	275.81	–1633.1	– 2962.1	–1159.5	–2489.7
Na^+	5964.5 *	0		–6276.0 *	–15912.0 *	– 4043.0	3772.2	107.48	–1.2318		–263.23	–763.05
K^+	4.3519 *		0	–6097.5 *		–3309.1	1339.1	5431.8		908.61		
Cl^-	12391.3 *	11739.2 *	11917.8 *	0		5582.7	–417.23	1006.2	161.04	2851.0	841.02	–1528.2
NO_3^-	8125.2 *	6486.7 *			0	2309.4	–2011.6		–1404.9			
Ala	887.68	3411.7	909.54	– 2091.2	4500.9	0						
Gly	2332.4	5949.8	3110.2	–1893.0	–28.078		0					
Ser	263.65	4707.5	2110.6	–792.23				0				
Thr	1988.6	4300.0		–461.21	209.55				0			
Val	388.17		2559.5	1026.9						0		
GG	3825.1	3930.8		–3446.5							0	
GA	4565.8	5395.0		–164.49								0

Table 9.2: The interaction energy parameters, ΔU_{ij}, as defined by eq. (8.55). The unit of ΔU_{ij} is that of RT = J/mole. The asterisk denotes the parameters calculated from the parameters estimated by Thomsen (1997) whose parameters are U_{ij} (=U_{ji}) and U_{ii} but of the same unit. The transformation from U_{ij} and U_{ii} to ΔU_{ij} is given by eq. (8.55). All parameters are estimated on data obtained at 298.15 K.

9.4 Modelling with the HS-MSA model

The application of the HS-MSA model in this work is based on the work of Simonin et al. (1996). They assume that both the diameter σ_+ of the cation and the dielectric constant are functions of the salt molarity, c_S.

$$\sigma_+ = \sigma_+^{(0)} + \sigma_+^{(1)} \cdot c_S \tag{9.9}$$

Eq. (9.9) accounts for the hydration of the cation. The hydration of the anion is much less and in this context presumed negligible (Simonin et al., 1996 and Helgeson et al., 1981). Hence the diameter of the anion is kept concentration independent and equal to twice its ionic radius, Table 9.3.

$\sigma^{(0)}_{Cl-} = 2 \cdot 1.81 = 3.62$ Å	$\sigma^{(0)}_{Br-} = 2 \cdot 1.96 = 3.92$ Å	$\sigma^{(0)}_{I-} = 2 \cdot 2.20 = 4.40$ Å
$\sigma^{(0)}_{Li+} = 2 \cdot 0.76 = 1.52$ Å	$\sigma^{(0)}_{Na+} = 2 \cdot 1.02 = 2.04$ Å	$\sigma^{(0)}_{K+} = 2 \cdot 1.38 = 2.76$ Å

Table 9.3: Crystal ionic radii are taken from p. 12-14 in CRC 78th Edition.

The functionality of the dielectric constant with respect to molarity, eq. (9.10), is in accordance with experimental observations, e.g. Åkerlöf (1932) and Helgeson et al. (1981). The latter of the two is an impressive work on the dielectric constants in salt solutions in which the reciprocal dielectric constant is assumed a first order function of the ionic strength. The same behaviour is assumed by Simonin et al. (1996) by their expression.

$$\varepsilon = \frac{4\pi\varepsilon_0\varepsilon_r}{1+\alpha c_S} \tag{9.10}$$

The results of this work are not obtained by the expression for the mean activity coefficient of the hard-sphere term given by Simonin et al. (1996) but from the partial molar derivative of the Helmholtz energy function of the hard-sphere term, eq. (8.64). The reason is that there is an error in the expression for the mean hard-sphere activity coefficient, eq. (9.11), given by Simonin et al., 1996.

$$\Delta \ln \gamma_m^{HS} = \left(\frac{X_2^3}{X_0 X_3^2} - 1 \right) \ln x + \frac{X_3}{x} + \frac{X_2^3(1+2X_3-X_3^2)}{X_0 X_3 x^2} + \frac{3X_1X_2(2-X_3)}{X_0 x^2} + \frac{1}{\rho_t} \sum_j \rho_j Q_j D(\sigma_j) \tag{9.11}$$

The correct equation is

$$\Delta \ln \gamma_m^{HS} = \left(\frac{X_2^3}{X_0 X_3^2} - 1 \right) \ln x + \frac{X_3}{x} + \frac{X_2^3 (1 + 2X_3 - X_3^2)}{X_0 X_3 x^3} + \frac{3 X_1 X_2 (2 - X_3)}{X_0 x^2} + \frac{1}{\rho_t} \sum_j \rho_j Q_j D(\sigma_j) \tag{9.12}$$

The difference is the third term of eq. (9.11); Simonin et al. (1996) have $X_0 X_3 x^2$ in the denominator instead of the correct $X_0 X_3 x^3$. Unfortunately, this is not a misprint. Using the erroneous equation of Simonin et al. one obtains their results.

The experimental data used in the rest of this chapter are identical to those used by Simonin et al.; i.e. the activity coefficients collected by Robinson and Stokes, 1959. The conversion of the activity coefficients from the Lewis-Randall framework to the McMillan-Mayer framework is done in accordance to Simonin et al., eq. (9.13). The molal mean activity coefficient (in the Lewis-Randall framework) is converted to a molar mean activity coefficient is (in the McMillan-Mayer framework).

The three parameters $\sigma_+^{(0)}$, $\sigma_+^{(1)}$, and α binary systems of water and salt are estimated. Table 9.4 shows a comparison of the results of this work and those of Simonin et al. (1996) when all three parameters are unconstrained.

'Salt'	$\sigma_+^{(0)}$ (Å)		$10^2\ \sigma_+^{(1)}$ (Å mol L^{-1})		$10^2\ \alpha$ (mol^{-1} L)		AARD (%)	
	Simonin et al.	This work	Simonin et al.	This work	Simonin et al.	This work	Simonin et al.	This work
HCl	5.00	4.76 ± 0.30	– 8.83	– 8.14 ± 0.21	6.76	3.44 ± 6.23	0.07	0.66
LiCl	4.76	5.20 ± 0.09	– 6.60	– 8.73 ± 0.20	6.96	12.7 ± 2.34	0.26	1.54
NaCl	3.90	3.95 ± 0.21	– 3.03	– 3.12 ± 1.64	8.18	8.64 ± 3.73	0.22	0.22
NaBr	3.99	4.00 ± 0.22	– 3.92	– 4.03 ± 3.41	8.60	8.97 ± 5.05	0.05	0.07
KCl	3.34	3.35 ± 0.28	– 0.93	– 1.10 ± 5.81	7.75	7.74 ± 5.20	0.12	0.12
KBr	3.13	3.22 ± 0.23	– 3.09	– 3.16 ± 4.24	6.51	7.38 ± 4.16	0.07	0.12
KI	3.22	3.27 ± 0.35	– 7.08	– 6.67 ± 8.83	7.51	9.05 ± 7.48	0.13	0.17

Table 9.4: The parameters $\sigma_+^{(0)}$ and $\sigma_+^{(1)}$ of the cations and α are estimated. The values of the work of Simonin et al. (1996) are compared with the results obtained in this work when all three parameters were estimated freely. The standard deviations are given for the parameters estimated as well. The stopping criteria used in the Marquardt estimation of the parameters are: $\|\mathbf{F}'\|_\infty \le 10^{-4}$, and $\|\mathbf{h}\|_2 \le 10^{-4} \cdot (10^{-4} + \|\mathbf{x}\|_2)$. **F'** is the gradient and **h** is the next step in the parameter vector **x**. The fourth column gives the average relative deviation.

$$\gamma_i^{MM} = \gamma_i^{m}(1 + m_S M_S)\frac{d_0}{d} \tag{9.13}$$

where m_S is the molality of the salt, M_S is the molar mass, d_0 is the density of the pure solvent, and d is the density of the solution. Eq. (9.13) does not include all of the corrections when converting between the two frameworks, according to Simonin et al. In order to follow the procedure of Simonin et al. the conversion of eq. (9.13) has been applied. The correct conversion between the two frameworks is given by eq. (6.27).

In the cases where the 95% confidence interval of an estimated parameter includes zero in Table 9.4, the parameter in question is set to zero and the other parameters are re-estimated, but only so that one parameter at a time is set to zero. The 95% confidence interval is $[\bar{x} - 1.96\, s_x;\ \bar{x} + 1.96\, s_x]$. $\bar{x}$ is the estimated mean value and s_x is the standard deviation. These re-estimations are shown in Table 9.5 and in Figure 9.36.

'Salt'	$\sigma_+^{(0)}$ (Å)		$10^2\,\sigma_+^{(1)}$ (Å mol L^{-1})		$10^2\,\alpha$ (mol^{-1} L)		AARD (%)	
	Simonin et al.	This work	Simonin et al.	This work	Simonin et al.	This work	Simonin et al.	This work
HCl	5.00	4.50 ± 0.02	– 8.83	– 7.74 ± 0.19	6.76	0 *	0.07	0.94
LiCl	4.76	5.20 ± 0.09	– 6.60	– 8.73 ± 0.20	6.96	12.7 ± 2.34	0.26	1.54
NaCl	3.90	2.71 ± 0.07	– 3.03	0 *	8.18	0 *	0.22	3.40
NaBr	3.99	2.91 ± 0.09	– 3.92	0 *	8.60	0 *	0.05	2.76
KCl	3.34	3.39 ± 0.21	– 0.93	0 *	7.75	8.58 ± 2.45	0.12	0.34
KBr	3.13	2.51 ± 0.15	– 3.09	– 12.1 ± 4.44	6.51	0 *	0.07	0.98
KI	3.22	2.54 ± 0.16	– 7.08	– 19.4 ± 5.93	7.51	0 *	0.13	0.82

Table 9.5: The estimated parameters ($\sigma_+^{(0)}$, $\sigma_+^{(1)}$, and α) and the standard deviation thereof. The values of the work of Simonin et al. (1996) are compared with the results obtained in this work when the parameters estimated were within the 95% confidence interval. The asterisk denoted a fixed value.

Comparing the estimated cation diameters of Tables 9.4 and 9.5 with the ionic ones of Table 9.3 indicates that the estimated ones are greater than the ionic cation diameters - except for KBr and KI in Table 9.5. However, the standard deviations on $\sigma_+^{(1)}$ of these two salts are

relatively large, c. 30% of the parameter value. Furthermore, it is noticed that two salts (NaCl and NaBr) can be described by only one parameter, $\sigma_+^{(0)}$.

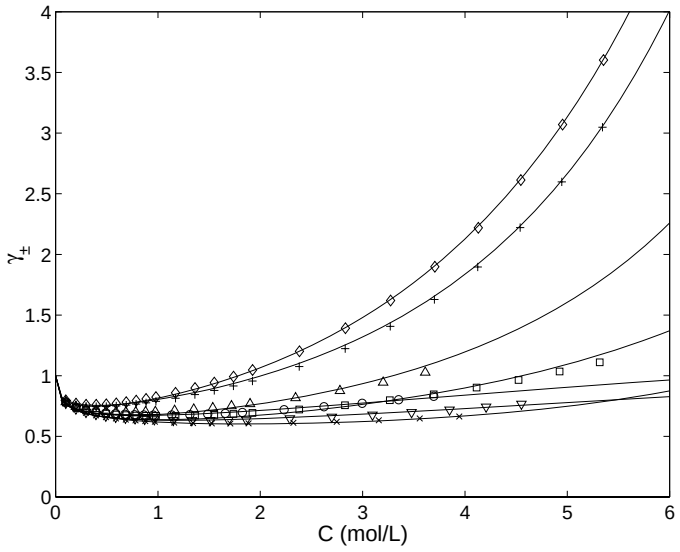


Figure 9.36: The mean activity coefficients of the seven 'salts', HCl (◊), LiCl (+), NaCl (□), NaBr (Δ), KCl (×), KBr (∇), and KI (o) as functions of the molarity at a temperature of 298.15 K. The model parameters are those of Table 9.5.

9.5 The functionality of dielectric constant

The behaviour of the dielectric constant as a function of the salt concentration has been reported thoroughly by Helgeson et al., 1981. That work compares - very likely - all published data and finds that there are inconsistencies and sometimes contradictions (pp. 1307) among the various authors - even among papers of the same author. Nevertheless, a correlation between the dielectric constant and the molal ionic strength is presented. An explanation of why the molal ionic strength is used in this correlation instead of e.g. molarity is not given. However, it seems more obvious that the dielectric constant would have a volumetric dependency as it describes the permittivity of a volume rather than that of a mass. Comparing the expressions of Simonin et al. (1996) and Helgeson et al. (1981)

$$\varepsilon_r = \frac{\varepsilon_{r,water}}{1+\alpha c_S} \qquad \text{and} \qquad \varepsilon_r^{-1} = \varepsilon_{r,water}^{-1} + \hat{b}\, m_S \qquad \text{(9.14a) and (9.14b)}$$

where $\varepsilon_{r,water}$ is the relative dielectric constant of water, gives an interrelation of the two parameters

$$\alpha = \frac{\varepsilon_{r,water}}{d_0 - c_S M_S} \cdot \hat{b} \tag{9.15}$$

where d_0 is the density of the pure solvent. In other words, the ratio of α and $\hat{b}$ is not a constant, but a function of the concentration. Recalling the reported inconsistencies on dielectric constant data of ionic solutions a description of the permittivity by molal ionic strength or molarity seems equally acceptable.

Taking the $\hat{b}$ values of Helgeson et al. as a starting point and calculating the dielectric constant as a function of the molal ionic strength, will produce a number of fictive data points to which the α values are fitted using eq. (9.14a). The obtained estimates of α are presented in Table 9.6. For comparison α values estimated on real experimental data (Harris and O'Konski, 1957) are also presented. From Table 9.6 it is clear that the α values obtained from Helgeson et al. are concurrent with the α values estimated from the experimental data of Harris and O'Konski. A further comparison to the freely estimated α values of Table 9.4 reveals a better correspondence between the α values of this work and those of Harris and O'Konski.

	Helgeson et al., 1981	Harris and O'Konski, 1957
HCl	16.5	—
LiCl	21.7	12.6
NaCl	19.7	17.3
NaBr	19.4	16.5
KCl	18.4	6.61
KBr	18.1	8.07
KI	15.9	7.99

Table 9.6: Comparison of the α values, eq. (9.13), indirectly obtained from Helgeson and directly from Harris and O'Konski.

Extrapolating the HS-MSA model beyond the saturation limit of the salt gives some remarkable behaviour. The most noticeable one is that of lithium chloride. Figure 9.37 shows an extrapolation of the lithium chloride activity coefficient up to 25 moles per litre.

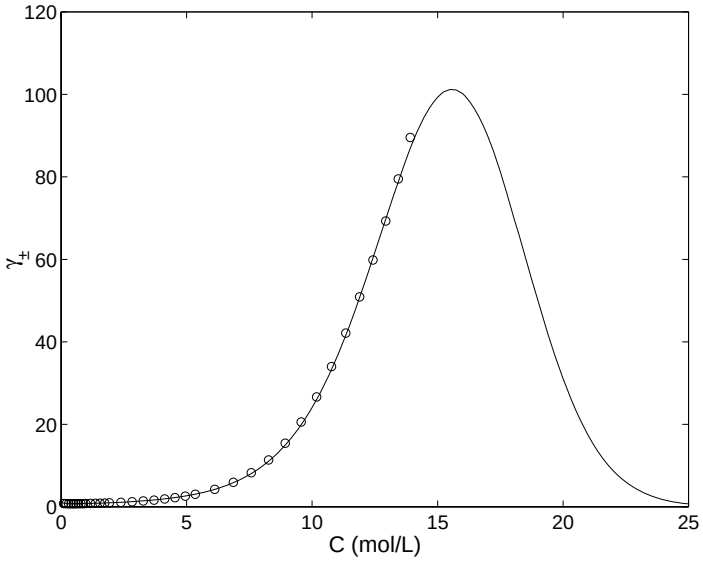


Figure 9.37: The activity coefficient of LiCl as a function of molarity. The model parameters are those of Table 9.5.

Since the electrostatic term (of the activity coefficient) of LiCl in the entire concentration range is nearly zero, the hard-sphere term (of the activity coefficient) must have a horizontal tangent at some concentration in order for the activity coefficient to have a maximum. This implies that the reason for the peaking activity coefficient curve is not the concentration dependent dielectric constant but rather the concentration dependency of the cation; the hard-sphere term is not a function of permittivity. Only HCl shows a similar behaviour. The rest of the salts have an increasing exponential behaviour. The two terms of the HS-MSA are plotted individually in Figure 9.38 for LiCl. Here it is obvious that the electrostatic contribution is vanishing and the hard-sphere contribution consequently is the dominating one.

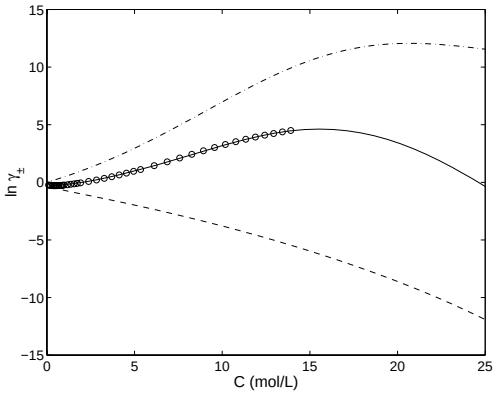
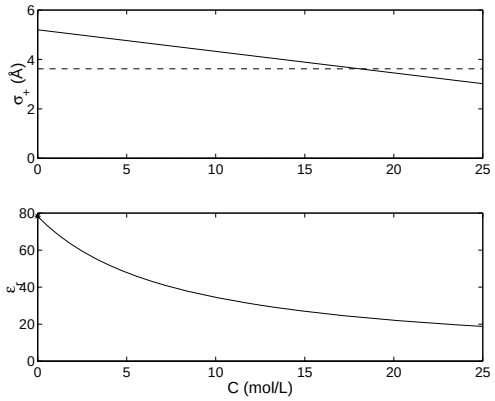


Figure 9.38: The logarithmic activity coefficient of LiCl (—), the hard-sphere term ln $\gamma_{\pm}^{HS}$ (· –), and the electrostatic term ln $\gamma_{\pm}^{elec}$(- -) as a function of molarity. The parameters of Table 9.5.



Figures 9.39a-b: The parameters of LiCl as functions of molarity. The top figure shows the diameter of lithium (—) and the diameter of chloride (- -), in ångstöms. The bottom figure the relative dielectric constant, ε_r, dimensionless. The parameters of Table 9.5.

It is noted that the relative dielectric constant in Figure 9.39b is comparable to that of ethanol (page 100) at the saturation limit. This is in accordance with what is reported by Helgeson et al., 1981.

9.6 Constant solution density

However, there is a huge disadvantage using a Helmholtz energy in the independent variables T, V, and **n** - and that is that nearly all experimental data are reported in the variables T, P and **n** which requires the knowledge of the density in order to convert to T, V, and **n**. This limitation is overcome in binary salt-water solutions by the impressive work of Söhnel and Novotný (1985) whose correlations of the solution density as a function of molarity makes this interrelation possible.

But for more seldom encountered solutions the density is unknown - and a correlation is called for. However, that there is no mixing rules for densities. So because of this limitation the application of the HS-MSA model is limited to systems whose densities are known. It is known from the experiments of determination of the solubilities of glycylglycine and glycyl-L-alanine that the volume expansion when adding the dipeptide is considerable, Chapter 5.

This means that even though the dipeptide has a relatively large molar mass the volume expansion has a reducing effect on the value of the density.

However, assuming a constant density - that of the pure solvent - one can get an impression of how flexible the model is. Again the same seven 'salts' have been used and as for Table 9.5, only parameters with reasonable standard deviations are estimated, i.e. their 95% confidence interval does not include zero. The rest of the parameters are set to zero.

'Salt'	$\sigma_+^{(0)}$ (Å)	$10^2\ \sigma_+^{(1)}$ (Å mol L solvent^{-1})	$10^2\ \alpha$ (mol^{-1} L solvent)	AARD (%)
HCl	4.19 ± 0.03	– 8.51 ± 0.20	0 *	5.87
LiCl	4.43 ± 0.03	– 7.62 ± 0.17	2.77 ± 0.94	1.05
NaCl	3.11 ± 0.13	– 8.27 ± 2.83	0 *	1.39
NaBr	3.33 ± 0.14	– 12.5 ± 4.80	0 *	0.82
KCl	2.65 ± 0.16	– 12.8 ± 4.92	0 *	0.90
KBr	2.53 ± 0.14	– 13.9 ± 3.34	0 *	1.02
KI	2.56 ± 0.15	– 21.8 ± 4.44	0 *	0.90

Table 9.7: The estimated parameters ($\sigma_+^{(0)}$, $\sigma_+^{(1)}$, and α) and the standard deviation thereof. The asterisk denoted a fixed value.

That $\alpha = 0$ for almost all of the salts, indicates that the use of mole per litre solvent as the concentration unit, gives a dielectric constant that is concentration independent. From the AARD column of Table 9.7 it is obvious that HCl is the only 'salt' that is difficult to describe by this approach. Based on Table 9.7 it seems that the density of the pure solvent is applicable if the density of the solution is unknown - at least for these binary systems.

9.7 A non-primitive model

In the original work of Mansoori et al. (1971) the hard-sphere Helmholtz energy function is not limited to the 'primitive' models. A 'primitive' model is a model where the solvent is disregard on the molecular level and treated as a dielectric continuum. Applying the hard-sphere term as well as the electrostatic term as non-primitive, i.e. include the solvent on the same molecular level as the solutes, implies a basic change: the dielectric constant ε (= $\varepsilon_0\varepsilon_r$) is equal to that of vacuum, ε_0. This might inflict on the theory of the MSA theory but not of the Debye-Hückel theory. The electrostatic term as presented by Debye and Hückel (1923) is a charging-up process of an existing neutral charged system. Treating water molecularly merely

suggests that water is charged-up to zero charge - in order to keep the analogy with the ions. The results obtained by this approach is presented in Table 9.8. The parameterisation is also a bit different: α is constantly kept equal to zero since the dielectric constant is constantly that of vacuum.

The diameter of water is taken as 1.58 Å based on the bond length and angle of gaseous water as described in Figure 9.40.

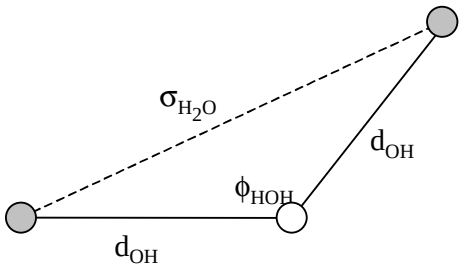


Figure 9.40: A schematic representation of a water molecule. The shaded circles are hydrogen atoms and the white one is oxygen. d_{OH} is the distance between oxygen and hydrogen 0.9575 Å, ϕ_{HOH} is angle of the O–H bonds 104.51°, and σ_{H2O} is estimated diameter of water, (p. 9-19, CRC).

'Salt'	$\sigma_+^{(0)}$ (Å)	$10^2\ \sigma_+^{(1)}$ (Å mol L solvent^{-1})	$10^2\ \alpha$ (mol^{-1} L solvent)	AARD (%)
HCl	3.64 ± 0.03	– 5.28 ± 0.27	0 *	1.69
LiCl	3.57 ± 0.05	– 5.15 ± 0.40	0 *	6.96
NaCl	2.69 ± 0.25	– 6.90 ± 3.09	0 *	1.66
NaBr	2.94 ± 0.33	– 10.7 ± 4.73	0 *	0.94
KCl	2.70 ± 0.35	– 11.7 ± 4.13	0 *	0.83
KBr	2.49 ± 0.34	– 13.9 ± 3.76	0 *	0.94
KI	2.86 ± 0.38	– 24.1 ± 3.46	0 *	0.59

Table 9.8: The estimated parameters ($\sigma_+^{(0)}$ and $\sigma_+^{(1)}$) and the standard deviation thereof. The hard-core diameter of water is set to 1.58 Å. The asterisk denoted a fixed value.

In order to obtain the asymmetric activity coefficient, the activity coefficient calculated by the non-primitive model is subtracted by the activity coefficient at infinite dilution; the same approach as for the UNIQUAC model. As Table 9.8 shows this approach is able to describe the seven binary salt - water systems equally well by the use of two parameters as was the case for original approach of Simonin et al. Only the LiCl system has a less acceptable an AARD.

10. The Database

The project was started by a literature survey on the work in the field of the solubility of amino acids and small peptides. The database now consists of some 300 articles. The experimental data contained in these articles are the basis for the database. It distinguishes between the L-, D-, and DL-forms of the amino acids. When no specification on the optic rotation is made in an article, it is assumed that the applied amino acid is racemic, DL.

The database contains three types of experimental data, solid-liquid equilibrium (SLE) data (solubility data and freezing point depression data), isopiestic data, and electrode potential data. The reported experimental data are ordered in separate files as to the order of the system: binary SLE, ternary SLE, and quaternary SLE plus one file for isopiestic data and one file for electrode potential measurements. The temperatures for the SLE data are mostly 298.15 K. The temperature range for the electrode potential measurements are 298 - 333 K, but mostly 298.15 K.

The SLE data cover systems such as

amino acid or peptide – water	840 datapoints (binsle.dat)
amino acid or peptide – salt – water	167 datapoints (tersle.dat)
amino acid – acid / base – water	186 datapoints (tersle.dat)
amino acid – amino acid – water	523 datapoints (tersle.dat)
amino acid – acid / base – salt – water	343 datapoints (quasle.dat)

The isopiestic data cover systems such as

amino acid or peptide – water	1128 datapoints (isop.dat)

The emf data cover systems such as

amino acid – salt – water	767 datapoints (elec.dat)
amino acid – acid / base – water	832 datapoints (elec.dat)
amino acid – acid / base – salt – water	1815 datapoints (elec.dat)

10.1 Compound index

In order to identify each amino acid in a simple way in the databases, a six-digit code - or compound index - was assigned to each of them. The first 3 digits are assigned in a systematic manner. First digit in the compound index is 1 for amino acids, 2 for dipeptides, and 3 for tripeptides. The next two digits are assigned accordingly to which subgroup the amino acid belongs. The first subgroup is the natural occurring amino acid (including cystine and hydroxylproline); the second subgroup (5x) long α-amino acids; the third subgroup (6x) β-amino acids, etc. The explanation of the last three digits is given on the next page.

amino acids	
alanine	101
arginine	102
asparagine	103
aspartic acid	104
cysteine	105
glutamine	106
glutamic acid	107
glycine	108
histidine	109
isoleucine	110
leucine (α-amino-iso-caproic acid)	111
lysine	112
methionine	113
phenylalanine	114
proline	115
serine	116
threonine	117
tryptophan	118
tyrosine	119
valine	120
cystine	121
hydroxyproline	122

α-amino-*n*-butyric acid	150
α-amino-*iso*-butyric acid	151
α-amino-*n*-valeric acid	152 (norvaline)
α-amino-*n*-caproic acid	153 (norleucine)
β-alanine	160
β-amino-*n*-butyric acid	161
β-amino-*n*-valeric acid	162
γ-amino-*n*-butyric acid	170
γ-amino-*n*-valeric acid	171
ε-aminocaproic acid	180

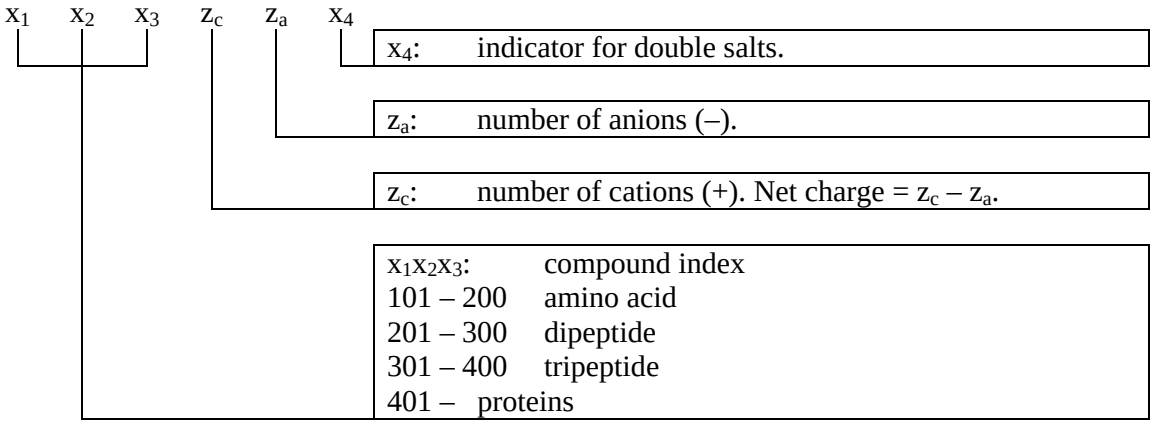
dipeptides	
alanylalanine	201
alanylglycine	202
glycylalanine	203
glycylglycine	204

tripeptides	
tri-glycine	301

Besides the biomolecules the database also contains some inorganic salts (and sugar).

sucrose	7	$CaCl_2$	346
NaCl	310	NaOH	383
Na_2SO_4	322	KOH	391
KCl	323	$(NH_4)_2SO_4$	441
$NaNO_3$	324	HNO_3	652
KNO_3	325	HCl	647

10.2 The index system



Examples:

The zwitterion of glycine (one cation and one anion): 108110
- glycine has index 108.

The salt of glycine, Gly $_{(s)}$ 108000

The salt of DL-alanine, DL-Ala $_{(s)}$ 101000
The salt of L-alanine, L-Ala $_{(s)}$ 101001
The salt of D-alanine, D-Ala $_{(s)}$ 101002

Sodium glycinate, $Gly^{-},{}^{+}Na$ $_{(s)}$ 108003
(The summation of z_c and z_a is still the net charge.)

Arginine hydrochloride, Arg·HCl $_{(s)}$ 102004
Aspartic acid hydrid, Asp·H_2O $_{(s)}$ 104005

The cation of glycylglycine, $GlyGly^{+}$ (one cation): 204100
- glycylglycine has index 204.

The anion of triglycine, $GlyGlyGly^{-}$ (one anion): 301010
- triglycine has index 301.

Tyr^{+}: 119100
$Tyr^{\pm}$: 119110
Tyr^{-}: 119010
Tyr^{--}: 119020
- tyrosine has index 119.

As the example for tyrosine shows, the number of cations, z_c, is not identical to the number of amino groups, as well as the number of anions, z_a, is not identical to the number of hydroxylic and carboxylic groups.

11. Conclusion

This thesis has addressed the chemistry and thermodynamics of amino acids and dipeptides and the modelling of systems containing these biomolecules. The main conclusions are summarised in this final chapter.

The solubility of two dipeptides, glycylglycine and glycyl-L-alanine, have been determined in three salts, NaCl, Na_2SO_4, and $(NH_4)_2SO_4$, at various salt concentrations. It is found that the solubility behaviour of glycylglycine exhibits a moderate salting-in effect; i.e. a moderate increase in the dipeptide solubility as the salt concentration is increasing. Also the solubility behaviour of glycyl-L-alanine exhibits a salting-in effect, but only at low salt concentrations and the effect is less pronounced and in the case of ammonium sulphate the dipeptide solubility is almost constant. At higher salt concentrations of sodium chloride and sodium sulphate the solubility behaviour of glycyl-L-alanine shows a moderate salting-out effect, whereas the dipeptide solubility remains unaffected by the presence of ammonium sulphate.

The usual procedure of modelling the solubility of amino acids has been addressed. It is concluded that a correct model procedure of such data would demand the knowledge of the Gibbs energy of formation of the amino acids prior to the fitting of the solubility data and the activity coefficients.

Furthermore, density measurements have been carried out on aqueous NaCl, Na_2SO_4, and $(NH_4)_2SO_4$ solutions saturated with glycylglycine and glycyl-L-alanine in order to determine to the volume expansions of water due to dissolving salt and dipeptide. A correlation for the approximate volume expansion by dissolving salt and dipeptide in 1 kg water is presented.

The use of ion-selective electrodes to determine activity coefficients of the salt in the ternary systems, NaCl - glycylglycine - H_2O, and NaCl - glycyl-L-alanine - H_2O, is investigated experimentally. The application of such electrodes has proven to be suitable to determine the effect that the salt has on the activity coefficient of a dipeptide. Furthermore, if the activity coefficient of the non-electrolyte in the binary aqueous system is available, the activity coefficient of the dipeptide in the ternary system in proportion to the activity coefficient of the dipeptide at infinite dilution in pure water can be determined. This ratio displays the effect that the electrolyte has on the dipeptide (non-electrolyte). The results show that the activity

coefficient ratio of glycylglycine at saturation is decreasing with increasing salt concentration whereas the activity coefficient ratio of glycyl-L-alanine is increasing slightly with increasing salt concentration. Given this and the assumption that the standard state of the precipitate is invariant one would expect a salting-in of glycylglycine and a minor salting-out of glycyl-L-alanine. This was confirmed by the experiments on the solubilities of the dipeptides.

The problems using models in the McMillan-Mayer framework because of the decoupling of the direct solvent-solute interaction have been presented. The fact that most experimental data in the literature are reported in terms of T, P, and **n** makes it nearly impossible to convert them to the state of a Helmholtz energy model (T, V, **n**) - unless a correlation for the density as a function of the concentration is available.

The derivation of the Debye-Hückel theory as they themselves did it, and as McQuarrie implies it, have thoroughly been discussed and it is concluded that the state description of the Debye-Hückel equation is lacking either one independent variable or one assumption. The lacking independent variable is either the mole number of the solvent (a classical description) or the chemical potential of solvent (a McMillan-Mayer description).

The modelling of salt - amino acid - water systems by means of the extended UNIQUAC model has lead to 68 new parameters which are valid at 298.15 K and are presented in Tables 9.1 and 9.2. However, the extended UNIQUAC model is either unable to model $NaNO_3$ - amino acid - water systems or the applied nitrate ion-selective electrodes are giving erroneous readings in the presence of biomolecules. The prediction of the solubilities of amino acids and dipeptides using the parameters estimated are not acceptable. The model contradicts the experimentally determined solubility of glycine when the model parameters are determined using isopiestic and electrode potential measurements.

It seems that the model lacks a term to account for the physics of the zwitterion wherefore it might be an idea to replace the electrostatic term of Fowler and Guggenheim (in the extended UNIQUAC model) by that of the Pitzer model. The Pitzer g^E model is also taking the influence of uncharged, non-solvent species into account.

An analysis of the HS-MSA model on six salts and HCl were conducted and the model parameters were estimated for a number of different assumptions concerning these parameters: the model parameters have considered being functions of the salt concentration,

the solution having constant density, and the model concept being non-primitive. The model is performing well in these binary mixtures.

A database on amino acid related literature has been established and the experimental data found in this literature have been organised in 5 databases: one for binary SLE data, one for ternary SLE data, one for quaternary SLE data, one for isopiestic data, and one for electrode potential data.

The fundamentals of thermodynamics and electrochemistry have been addressed extensively and hopefully also consistently.

Appendix A on Euler's Theorem for a Homogeneous Function

A.1 Euler's theorem

Given a function M in the variables **a** and **b**. This function is a homogeneous function of degree *m* in variable **b** if when multiplying the variable **b** by a factor of λ the value of the function will increase by a factor of λ^m.

$$M(\mathbf{a}, \lambda\,\mathbf{b}) = \lambda^m\, M(\mathbf{a}, \mathbf{b}) \tag{A.1}$$

Theorem: Given the function M(**a**, **b**) which is homogeneous of degree *m* in variable **b** then

$$m\, M(\mathbf{a}, \mathbf{b}) = \sum_i b_i \left(\frac{\partial\, M(\mathbf{a}, \mathbf{b})}{\partial\, b_i} \right)_{\mathbf{a}, b_j} \tag{A.2}$$

The proof is the following. The differential of eq. (A.1) with respect to the factor λ is

$$\begin{aligned}
&\left(\frac{\partial}{\partial\,\lambda} M(\mathbf{a}, \lambda\,\mathbf{b}) \right)_{\mathbf{a},\mathbf{b}} = \left(\frac{\partial}{\partial\,\lambda} \left[\lambda^m M(\mathbf{a}, \mathbf{b}) \right] \right)_{\mathbf{a},\mathbf{b}} && \Leftrightarrow \\
&\sum_i \left(\frac{\partial\, M(\mathbf{a}, \lambda\,\mathbf{b})}{\partial\,(\lambda\, b_i)} \right)_{\mathbf{a}, b_{j\neq i}} \left(\frac{\partial\,(\lambda\, b_i)}{\partial\,\lambda} \right)_{\mathbf{a},\mathbf{b}} = m\,\lambda^{m-1}\, M(\mathbf{a}, \mathbf{b}) && \Leftrightarrow \\
&\sum_i b_i \left(\frac{\partial\, M(\mathbf{a}, \lambda\,\mathbf{b})}{\partial\,(\lambda\, b_i)} \right)_{\mathbf{a}, b_{j\neq i}} = m\,\lambda^{m-1}\, M(\mathbf{a}, \mathbf{b})
\end{aligned} \tag{A.3}$$

and the differential of eq. (A.1) with respect to the variable b_i is

$$\begin{aligned}
&\left(\frac{\partial}{\partial\, b_i} M(\mathbf{a}, \lambda\,\mathbf{b}) \right)_{\mathbf{a}, b_{j\neq i}, \lambda} = \left(\frac{\partial}{\partial\, b_i} \left[\lambda^m M(\mathbf{a}, \mathbf{b}) \right] \right)_{\mathbf{a}, b_{j\neq i}, \lambda} && \Leftrightarrow \\
&\left(\frac{\partial\, M(\mathbf{a}, \lambda\,\mathbf{b})}{\partial\,(\lambda\, b_i)} \right)_{\mathbf{a}, b_{j\neq i}} \left(\frac{\partial\,(\lambda\, b_i)}{\partial\, b_i} \right)_{\mathbf{a}, b_{j\neq i}, \lambda} = \lambda^m \left(\frac{\partial\, M(\mathbf{a}, \mathbf{b})}{\partial\, b_i} \right)_{\mathbf{a}, b_{j\neq i}, \lambda} && \Leftrightarrow \\
&\lambda \left(\frac{\partial\, M(\mathbf{a}, \lambda\,\mathbf{b})}{\partial\,(\lambda\, b_i)} \right)_{\mathbf{a}, b_{j\neq i}} = \lambda^m \left(\frac{\partial\, M(\mathbf{a}, \mathbf{b})}{\partial\, b_i} \right)_{\mathbf{a}, b_{j\neq i}, \lambda} && \Rightarrow \\
&\left(\frac{\partial\, M(\mathbf{a}, \lambda\,\mathbf{b})}{\partial\,(\lambda\, b_i)} \right)_{\mathbf{a}, b_{j\neq i}} = \lambda^{m-1} \left(\frac{\partial\, M(\mathbf{a}, \mathbf{b})}{\partial\, b_i} \right)_{\mathbf{a}, b_{j\neq i}, \lambda}
\end{aligned} \tag{A.4}$$

By inserting eq. (A.4) into eq. (A.3) one has

$$\sum_i b_i \left[\lambda^{m-1} \left(\frac{\partial M(\mathbf{a},\mathbf{b})}{\partial b_i} \right)_{\mathbf{a},b_{j\neq i},\lambda} \right] = m\,\lambda^{m-1} M(\mathbf{a},\mathbf{b}) \quad \Rightarrow$$
$$\sum_i b_i \left(\frac{\partial M(\mathbf{a},\mathbf{b})}{\partial b_i} \right)_{\mathbf{a},b_{j\neq i},\lambda} = m\,M(\mathbf{a},\mathbf{b}) \tag{A.5}$$

Eq. (A.5) is Euler's theorem for a homogeneous function of degree *m* in **b**.

There is a corollary to the Euler's theorem stating that "if M(**a**,**b**) is a homogeneous function of degree one in **b**, then the first derivatives with respect to variable **b** are themselves homogeneous functions of degree zero" [Internet: http://cepa.newschool.edu/het/essays/math/euler.htm]. The proof of this is

$$\left(\frac{\partial}{\partial b_k} M(\mathbf{a},\mathbf{b}) \right)_{\mathbf{a},b_{l\neq k}} = \left(\frac{\partial}{\partial b_k} \left[\sum_i b_i \left(\frac{\partial M(\mathbf{a},\mathbf{b})}{\partial b_i} \right)_{\mathbf{a},b_{j\neq i}} \right] \right)_{b_{l\neq k}}$$
$$= \sum_i \delta_{ik} \left(\frac{\partial M(\mathbf{a},\mathbf{b})}{\partial b_i} \right)_{\mathbf{a},b_{j\neq i}} + \sum_i b_i \left(\frac{\partial^2 M(\mathbf{a},\mathbf{b})}{\partial b_i \partial b_k} \right)_{\mathbf{a},b_{j\neq i,k}}$$
$$= \left(\frac{\partial M(\mathbf{a},\mathbf{b})}{\partial b_k} \right)_{\mathbf{a},b_{j\neq k}} + \sum_i b_i \left(\frac{\partial^2 M(\mathbf{a},\mathbf{b})}{\partial b_i \partial b_k} \right)_{\mathbf{a},b_{j\neq i,k}} \quad \Rightarrow$$

$$\sum_i b_i \left(\frac{\partial^2 M(\mathbf{a},\mathbf{b})}{\partial b_i \partial b_k} \right)_{\mathbf{a},b_{j\neq i,k}} = 0 \tag{A.6}$$

A.2 Gibbs-Duhem equation

The differential of M(**a**, **b**) is

$$dM(\mathbf{a},\mathbf{b}) = \sum_i \left(\frac{\partial M}{\partial a_i} \right)_{a_j,\mathbf{b}} da_i + \sum_i \left(\frac{\partial M}{\partial b_i} \right)_{\mathbf{a},b_j} db_i \tag{A.7}$$

The differential of Euler's theorem for a homogeneous of degree one gives

$$dM(\mathbf{a},\mathbf{b}) = \sum_i \left(\frac{\partial M}{\partial b_i} \right)_{\mathbf{a},b_j} db_i + \sum_i b_i\, d\left(\frac{\partial M}{\partial b_i} \right)_{\mathbf{a},b_j} \tag{A.8}$$

Subsequently,

$$\sum_i \left(\frac{\partial M}{\partial a_i}\right)_{a_j,\mathbf{b}} da_i - \sum_i b_i \, d\left(\frac{\partial M}{\partial b_i}\right)_{\mathbf{a},b_j} = 0 \qquad \text{(A.9)}$$

which is known as the Gibbs-Duhem equation.

Appendix B on Equilibrium

This appendix is deriving the condition of equilibrium for a system that is influenced by an electrical potential, Φ. The system considered is described by four independent extensive variables: the entropy, the volume, the mole numbers, and the charges. From Euler's theorem for a homogeneous of degree one gives (Appendix A, eq. (A.9))

$$dU(S, V, \mathbf{n}, \mathbf{q}) = TdS + (-P)\,dV + \sum_{i}^{m} \mu_i dn_i + \sum_{i}^{m} \Phi\, dq_i \tag{B.1}$$

where m is number species in the system. Rearranging eq. (B.1) by expressing the change in the entropy gives

$$dS = \frac{dU}{T} + \frac{P\,dV}{T} - \sum_{i}^{m} \frac{\mu_i dn_i}{T} - \sum_{i}^{m} \frac{\Phi\, dq_i}{T} \tag{B.2}$$

For a multiphase system, this is valid for each phase of the system. Since entropy is an extensive property, the change in entropy of each phase is an additive property. Furthermore, one has from the second law of thermodynamics that the entropy is ever-increasing ($dS > 0$) or at equilibrium at its maximum ($dS = 0$).

$$dS = \sum_{j}^{\pi} \frac{dU^{(j)}}{T^{(j)}} + \sum_{j}^{\pi} \frac{P^{(j)} dV^{(j)}}{T^{(j)}} - \sum_{j}^{\pi} \sum_{i}^{m} \frac{\mu_i^{(j)} dn_i^{(j)}}{T^{(j)}} - \sum_{j}^{\pi} \sum_{i}^{m} \frac{\Phi^{(j)} dq_i^{(j)}}{T^{(j)}} \geq 0 \tag{B.3}$$

where π is the number of phases in the system. The system is considered to be isolated so that no matter or work is exchanged with the surroundings and no reactions within the system are occurring.

By state description the total internal energy (U), the total volume (V), the overall system composition (**n**), and the overall charge (**q**) is given. This implies that the extensive independent variables are subject to the some constraints

$$U = \sum_{j}^{\pi} U^{(j)} \qquad \Rightarrow \qquad \sum_{j}^{\pi} dU^{(j)} = 0 \tag{B.4}$$

$$V = \sum_{j}^{\pi} V^{(j)} \qquad \Rightarrow \qquad \sum_{j}^{\pi} dV^{(j)} = 0 \tag{B.5}$$

$$\mathbf{n} = \sum_{j}^{\pi} n_i^{(j)} \qquad \Rightarrow \qquad \sum_{j}^{\pi} dn_i^{(j)} = \mathbf{0} \tag{B.6}$$

$$\mathbf{q} = \sum_{j}^{\pi} q_i^{(j)} \qquad \Rightarrow \qquad \sum_{j}^{\pi} dq_i^{(j)} = \mathbf{0} \tag{B.7}$$

The condition of equilibrium is that eq. (B.3) is zero.

$$\begin{aligned} dS &= \sum_{j}^{\pi} \frac{dU^{(j)}}{T^{(j)}} + \sum_{j}^{\pi} \frac{P^{(j)} dV^{(j)}}{T^{(j)}} - \sum_{j}^{\pi} \sum_{i}^{m} \left\{ \frac{\mu_i^{(j)} dn_i^{(j)}}{T^{(j)}} + \frac{\Phi^{(j)} dq_i^{(j)}}{T^{(j)}} \right\} \\ &= \sum_{j \neq \alpha}^{\pi} \frac{dU^{(j)}}{T^{(j)}} + \frac{dU^{(\alpha)}}{T^{(\alpha)}} + \sum_{j \neq \alpha}^{\pi} \frac{P^{(j)} dV^{(j)}}{T^{(j)}} + \frac{P^{(\alpha)} dV^{(\alpha)}}{T^{(\alpha)}} \\ &\quad - \sum_{j \neq \alpha}^{\pi} \sum_{i}^{m} \left\{ \frac{\mu_i^{(j)} dn_i^{(j)}}{T^{(j)}} + \frac{\Phi^{(j)} dq_i^{(j)}}{T^{(j)}} \right\} - \sum_{i}^{m} \left\{ \frac{\mu_i^{(\alpha)} dn_i^{(\alpha)}}{T^{(\alpha)}} + \frac{\Phi^{(\alpha)} dq_i^{(\alpha)}}{T^{(\alpha)}} \right\} = 0 \end{aligned} \tag{B.8}$$

where α is one of the π phases in the system. From the constraints one has

$$dU^{(\alpha)} = -\sum_{j \neq \alpha}^{\pi} dU^{(j)} \tag{B.9}$$

$$dV^{(\alpha)} = -\sum_{j \neq \alpha}^{\pi} dV^{(j)} \tag{B.10}$$

$$dn_i^{(\alpha)} = -\sum_{j \neq \alpha}^{\pi} dn_i^{(j)} \tag{B.11}$$

$$dq_i^{(\alpha)} = -\sum_{j \neq \alpha}^{\pi} dq_i^{(j)} \tag{B.12}$$

which are used to simplify eq. (B.8) by eliminating the independent variables of phase α.

$$
\begin{aligned}
dS = &\sum_{j\neq\alpha}^{\pi}\frac{dU^{(j)}}{T^{(j)}} + \frac{1}{T^{(\alpha)}}\left[-\sum_{j\neq\alpha}^{\pi} dU^{(j)}\right] + \sum_{j\neq\alpha}^{\pi}\frac{P^{(j)}dV^{(j)}}{T^{(j)}} + \frac{P^{(\alpha)}}{T^{(\alpha)}}\left[-\sum_{j\neq\alpha}^{\pi} dV^{(j)}\right] \\
&-\sum_{j\neq\alpha}^{\pi}\sum_{i}^{m}\left\{\frac{\mu_i^{(j)}dn_i^{(j)}}{T^{(j)}} + \frac{\Phi^{(j)}dq_i^{(j)}}{T^{(j)}}\right\} \\
&-\sum_{i}^{m}\left\{\frac{\mu_i^{(\alpha)}}{T^{(\alpha)}}\left[-\sum_{j\neq\alpha}^{\pi} dn_i^{(j)}\right] + \frac{\Phi^{(\alpha)}}{T^{(\alpha)}}\left[-\sum_{j\neq\alpha}^{\pi} dq_i^{(j)}\right]\right\} \\
= &\sum_{j\neq\alpha}^{\pi}\left(\frac{1}{T^{(j)}} - \frac{1}{T^{(\alpha)}}\right)dU^{(j)} + \sum_{j\neq\alpha}^{\pi}\left(\frac{P^{(j)}}{T^{(j)}} - \frac{P^{(\alpha)}}{T^{(\alpha)}}\right)dV^{(j)} \\
&-\sum_{j\neq\alpha}^{\pi}\sum_{i}^{m}\left\{\frac{\mu_i^{(j)}dn_i^{(j)} + \Phi^{(j)}dq_i^{(j)}}{T^{(j)}} - \frac{\mu_i^{(\alpha)}dn_i^{(j)} + \Phi^{(\alpha)}dq_i^{(j)}}{T^{(\alpha)}}\right\} = 0
\end{aligned}
\tag{B.13}
$$

The reason, why the charges (**q**) and mole numbers (**n**) are independent variables, is that the relative charges, **z**, are independent of the mole numbers

$$q_i^{(j)} = z_i F n_i^{(j)} \qquad \Rightarrow \qquad dq_i^{(j)} = z_i F dn_i^{(j)} \tag{B.14}$$

The electrochemical potential is defined as

$$\mu_i^{elec(j)} = \mu_i^{(j)} + \Phi^{(j)} z_i F \tag{B.15}$$

and thus eq. (B.13) is rewritten as

$$
\begin{aligned}
dS = &\sum_{j\neq\alpha}^{\pi}\left(\frac{1}{T^{(j)}} - \frac{1}{T^{(\alpha)}}\right)dU^{(j)} + \sum_{j\neq\alpha}^{\pi}\left(\frac{P^{(j)}}{T^{(j)}} - \frac{P^{(\alpha)}}{T^{(\alpha)}}\right)dV^{(j)} \\
&-\sum_{j\neq\alpha}^{\pi}\sum_{i}^{m}\left(\frac{\mu_i^{elec(j)}}{T^{(j)}} - \frac{\mu_i^{elec(\alpha)}}{T^{(\alpha)}}\right)dn_i^{(j)} = 0
\end{aligned}
\tag{B.16}
$$

This equation must be satisfied for any changes in the independent variables since these variables are constrained by eqs. (B.9) - (B.11) plus the constraint of electroneutrality

$$\sum_{i}^{m} n_i^{(j)} z_i^{(j)} = \sum_{i}^{m} q_i^{(j)} = \mathbf{0} \tag{B.17}$$

Consequently,

$$T^{(j)} = T^{(\alpha)} \qquad \text{for all j phases} \tag{B.18}$$

$$P^{(j)} = P^{(\alpha)} \qquad \text{for all j phases} \tag{B.19}$$

$$\mu_i^{elec(j)} = \mu_i^{elec(\alpha)} \qquad \text{for all j phases and for each species i} \tag{B.20}$$

In other words, the temperature and the pressure are uniform throughout the system. At equilibrium the electrochemical potential of species i is the same in all phases.

For a single phase reacting system the condition of equilibrium eq. (B.16) is reduced to

$$dS = \sum_{i}^{m} \mu_i^{elec} dn_i = \sum_{i}^{m} \nu_i \mu_i^{elec} d\xi \geq 0 \tag{B.21}$$

where $d\xi$ is the change in reaction extent. At equilibrium ($dS = d\xi = 0$)

$$\sum_{i}^{m} \nu_i \mu_i^{elec} = 0 \tag{B.22}$$

which is identical to $dG = 0$ at constant temperature and pressure, see eq. (4.4).

Appendix C on Electrostatics

During my study of electrolyte theory I have realised that it is closely related to the fundamentals of electricity and to some extent magnetism. The fundamental equations of electrostatics are depending on the choice of the system of units; the cgs system of units, which is used in 'old' literature, or the SI system of units of today - it was adopted in 1960 (CRC Handbook of Chemistry and Physics, 78th Ed, p. **1**-19). In this appendix (and the thesis as a whole) only SI units have been applied. The motivation for this appendix on electricity and magnetism which is based on excerpts from *Electricity and Magnetism* of W.N. Cottingham and D.A. Greenwood, 1991, is to present the fundamental equations in terms of the SI system of units.

C.1 Coulomb's law

All the equations in this appendix are for free space system; i.e. the permittivity is that of vacuum. The starting point is Gauss's theorem which states that the electric flux appearing when an electric field **E** (due to a point charge Q) is passing through a closed surface **S** is either Q/ε_0 (if the point charge is within the closed surface) or else zero.

$$\int_S \mathbf{E}\cdot d\mathbf{S} = \begin{cases} Q/\varepsilon_0 & \mathbf{R}\ \text{inside S} \\ 0 & \mathbf{R}\ \text{outside S} \end{cases} \tag{C.1}$$

where S is a closed surface, **E** is the electric field (unit: V/m), Q is a point charge (unit: C), and ε_0 is permittivity of vacuum (unit: C/V/m). Using the superposition principle Gauss's theorem results in

$$\int_S \mathbf{E}\cdot d\mathbf{S} = \frac{1}{\varepsilon_0}\int_V \rho\, dV \tag{C.2}$$

where ρ is the volumetric charge density. The divergence theorem used on the left-hand side of eq. (C.2) gives

$$\int_V \nabla\cdot\mathbf{E}\, dV = \frac{1}{\varepsilon_0}\int_V \rho\, dV \qquad \Rightarrow \qquad \nabla\cdot\mathbf{E}(\mathbf{r}) = \frac{\rho(\mathbf{r})}{\varepsilon_0} \tag{C.3}$$

This is a field equation. The electric potential Φ (unit: volt) is defined as

$$\mathbf{E}(\mathbf{r}) = -\nabla\Phi(\mathbf{r}) \tag{C.4}$$

Inserting eq. (C.3) into the field equation results in the relation known as the Poisson equation

$$\nabla^2\Phi(\mathbf{r}) = -\frac{\rho(\mathbf{r})}{\varepsilon_0} \tag{C.5}$$

For a space where are no particles ($\rho = 0$) the Poisson equation reduces to the Laplace equation.

Since the electric potential is a function of the variable **r** only, eq. (C.5) is rewritten as

$$\frac{1}{r^2}\frac{\partial}{\partial r}\left(r^2\frac{\partial\Phi}{\partial r}\right) = -\frac{\rho(\mathbf{r})}{\varepsilon_0} \tag{C.6}$$

The solution to the differential equation of the potential is

$$\begin{aligned}
r^2\frac{\partial\Phi}{\partial r} &= -\frac{1}{\varepsilon_0}\int\rho(\mathbf{r}')\,r'^2\,dr' \quad , \qquad dV' = 4\pi r'^2\,dr' \\
r^2\frac{\partial\Phi}{\partial r} &= -\frac{1}{4\pi\varepsilon_0}\int\rho(\mathbf{r}')\,dV' \qquad \Rightarrow \\
\Phi(\mathbf{r}) &= +\frac{1}{4\pi\varepsilon_0}\int\rho(\mathbf{r}')\,dV'\frac{1}{r} \qquad r = |\mathbf{r}-\mathbf{r}'| \\
\Phi(\mathbf{r}) &= \frac{1}{4\pi\varepsilon_0}\int\frac{\rho(\mathbf{r}')}{|\mathbf{r}-\mathbf{r}'|}dV'
\end{aligned} \tag{C.7}$$

The solution is obtained through the spherical co-ordinate system, which is the reason for the 4π factor. For a *point* charge Q_1 at position $\mathbf{r}_1$ the potential reduces to

$$\Phi_1(\mathbf{r}) = \frac{1}{4\pi\varepsilon_0}\frac{Q_1}{|\mathbf{r}-\mathbf{r}_1|} \tag{C.8}$$

The electric field of the electric potential given by eq. (C.8) is derived from eq. (C.4)

$$\begin{aligned}
\mathbf{E}(\mathbf{r}) &= -\nabla\Phi(\mathbf{r}) \\
&= -\frac{Q_1}{4\pi\varepsilon_0}\frac{-1}{|\mathbf{r}-\mathbf{r}_1|^2}\mathbf{e}_r = \frac{1}{4\pi\varepsilon_0}\frac{Q_1}{|\mathbf{r}-\mathbf{r}_1|^2}\mathbf{e}_r
\end{aligned} \tag{C.9}$$

The force on a second particle (of charge Q_2) due to the first particle is

$$\begin{aligned}
\mathbf{F}_{21}(\mathbf{r}) &= Q_2\,\mathbf{E}(\mathbf{r}) \\
&= \frac{1}{4\pi\varepsilon_0}\frac{Q_1Q_2}{|\mathbf{r}-\mathbf{r}_1|^2}\mathbf{e}_r
\end{aligned} \tag{C.10}$$

where $\mathbf{e}_r$ is the radial unit vector. Eq. (C.10) is Coulomb's law. In the SI system of units the unit of charge is the *coulomb* (C), and in these units the force between two 'point' charges is given by eq. (C.10).

When the system considered is not a free space system, the permittivity of vacuum, ε_0, is replace by $\varepsilon_0\varepsilon_r$, where ε_r is the relative dielectric constant.

In the cgs system of units the unit of charge was esu, the electrostatic unit. Its definition was based on Coulomb's law. Two point charges, each of 1 esu and 1 cm apart, will act with a force of 1 dyn (= 10^{-5} newton) on each other. Inserting this length and force in eq. (C.10) will give a charge of $3.33564\cdot10^{-10}$ C (= 1 esu). Consequently, the equations presented in this appendix would appear differently in the 'old' literature. Coulomb's law in the cgs system of units was

$$\mathbf{F}_{21}(\mathbf{r}) = \frac{1}{D}\frac{Q_1Q_2}{|\mathbf{r}-\mathbf{r}_1|^2}\mathbf{e}_r \qquad \text{cgs system of units}$$

where D is the relative dielectric constant and D is unity in vacuum.

C.2 Maxwell's equations in a vacuum

Consider a region of space which is empty of everything except electric fields **E** and magnetic fields **B.** Maxwell's equations are then

$$\begin{aligned} &\nabla\cdot\mathbf{E}=0 \quad \text{(a)}, \qquad &&\nabla\times\mathbf{B}-\mu_0\varepsilon_0\frac{\partial\mathbf{E}}{\partial t}=0 \quad \text{(b)}\\ &\nabla\cdot\mathbf{B}=0 \quad \text{(c)}, \qquad &&\nabla\times\mathbf{E}+\frac{\partial\mathbf{B}}{\partial t}=0 \quad \text{(d)} \end{aligned} \tag{C.11}$$

where μ_0 is the permeability of vacuum and t is time. Taking the curl of eq. (C.11d), the vector identity

$$\nabla\times(\nabla\times\mathbf{E}) = \nabla(\nabla\cdot\mathbf{E}) - \nabla^2\mathbf{E} \tag{C.12}$$

gives, with eq. (C.11a)

$$-\nabla^2\mathbf{E} + \nabla\times\frac{\partial\mathbf{B}}{\partial t} = 0 \tag{C.13}$$

The ∇ and $\partial/\partial t$ operations can be interchanged, so that using eq. (C.11b) one obtains

$$\nabla^2 \mathbf{E} = \mu_0 \varepsilon_0 \frac{\partial^2 \mathbf{E}}{\partial t^2} \tag{C.14}$$

Similarly, taking the curl of eq. (C.11b) and using eqs. (C.11c) and (C.11d), gives

$$\nabla^2 \mathbf{B} = \mu_0 \varepsilon_0 \frac{\partial^2 \mathbf{B}}{\partial t^2} \tag{C.15}$$

Thus both the **E** and **B** fields satisfy the *wave equation*, with the wave velocity $(\mu_0\varepsilon_0)^{-½}$. Noting that the numerical value of $(\mu_0\varepsilon_0)^{-½}$ (which indeed has the dimensions of velocity) was consistent with the values found for the velocity of light, Maxwell concluded that light was an electromagnetic phenomenon, and $c = (\mu_0\varepsilon_0)^{-½}$.

From 1983, the velocity of light, *c*, together with the unit of time has been taken to define the unit of length: the metre is such that *c* in a vacuum is *exactly* $2.99792458 \cdot 10^8$ m/s. Since

$$\mu_0 = 4\pi \cdot 10^{-7} \frac{\mathrm{N}}{\mathrm{A}^2} = 4\pi \cdot 10^{-7} \frac{\mathrm{kg \cdot m}}{\mathrm{C}^2} \tag{C.16}$$

and

$$c^2 = \frac{1}{\mu_0 \varepsilon_0} \tag{C.17}$$

it follows that the value of $(4\pi\varepsilon_0)^{-1}$ is also exactly defined

$$\frac{1}{4\pi\varepsilon_0} = \frac{\mu_0 c^2}{4\pi} = 10^{-7} c^2 \frac{\mathrm{N}}{\mathrm{A}^2} \tag{C.18}$$

Hence Coulomb's law (C.10) determines the unit of charge exactly; which is identical to the unit of charge as defined from the force between current carrying wires (eq. (C.19)). This is a consequence of the consistency of the overall theory.

Consider the simple geometry of two thin parallel wires, distance ρ apart, carrying currents I_1 and I_2. If the currents are in the same direction, the magnetic force per unit length on each wire is attractive and of magnitude

$$\mathrm{d}F = \frac{\mu_0}{2\pi} \frac{I_1 I_2}{\rho} \mathrm{d}l \tag{C.19}$$

Hence μ_0 has the dimensions $kg \cdot m/C^2$. The SI unit of current, the ampere, and the SI unit of charge, the coulomb (1 A = 1 C/s), are thereby determined. Thus two currents, each of 1 A, flowing in wires 1 m apart give a force per unit length of $2 \cdot 10^{-7}$ N/m. This example indicates how in principle absolute standards of current (and hence charge) may be established in terms of the forces between circuits.

References

Abrams, D.S. and J.M. Prausnitz, 1975, *Statistical thermodynamics of liquid mixtures: A new expression for the excess Gibbs energy of partly or completely miscible systems,* AIChE Journal, volume 21, pp. 116-128.

Åkerlöf, G., 1932, *Dielectric constants of some organic solvent-water mixtures at various temperatures*, Journal of the American Chemical Society, volume 54, pp. 4125-4139.

Atkins, P.W., 1992, *Physical Chemistry*, 4th Edition, Oxford University Press, Oxford, England.

Anslow, G.A., M.L. Foster, and C. Klingler, 1933, *The absorption spectra of glycine solutions and their interpretation,* Journal of Biological Chemistry, volume 103, pp. 81-92.

Barrett, G.C., 1985, *Chemistry and Biochemistry of the Amino Acids*, Chapman and Hall, London.

Bett, K.E., J.S. Rowlingson, and G. Saville, 1975, *Thermodynamics for Chemical Engineers*, The Athlone Press, London.

Bjerrum, N., 1923, *Zur Thermodynamik des Aktivitätskoeffizienten und des osmotischen Koeffizienten*, Zeitschrift für physikalische Chemie, volume 104, pp. 406-432.

Blum, L. and J.S. Høye, 1977, *Mean spherical model for asymmetric electrolytes. 2. Thermodynamic properties and the pair correlation function*, Journal of Physical Chemistry, volume 81, pp. 1311-1316.

Bonner, O.D., 1981, *Osmotic and activity coefficients of sodium and potassium glutamate at 298.15K*, Journal of Chemical and Engineering Data, volume 26, pp. 147-148.

Bonner, O.D., 1982, *Osmotic and activity coefficients of some amino acids and their hydrochloride salts at 298.15 K*, Journal of Chemical and Engineering Data, volume 27, pp. 422-423.

Borge, G., R. Castaño, M.P. Carril, M.S. Corbillón, and J.M. Madariaga, 1996a, *Development of a modified Bromley's methodology (MBM) for the estimation of ionic media effects*

on solution equilibria. Part 1. Calculation of the interaction parameters in the molar and molal scales at 25 degrees celsius, Fluid Phase Equilibria, volume 121, pp. 85-98.

Borge, G., N. Etxebarria, L.A. Fernández, M.A. Olazabal, and J.M. Madariaga, 1996b, *Development of a modified Bromley's methodology (MBM) for the estimation of ionic media effects on solution equilibria. Part 2. Correlation of the molar and molal interaction parameters with the charge and crystal radii of the ions*, Fluid Phase Equilibria, volume 121, pp. 99-109.

Bower, V.E. and R.A. Robinson, 1965, *Thermodynamics of the ternary system: Water-glycine-potassium chloride at 25 degrees C. From vapor pressure measurements*, Journal of Research of NBS - A. Physics and Chemistry, volume 69A, pp. 131-135.

Bromley, L.A., 1973, *Thermodynamic properties of strong electrolytes in aqueous solutions*, AIChE Journal, volume 19, pp. 313-320.

Bruskov, V.I. and A.I. Klimov, 1973, *Solubility of L-amino acids and oligomers of glycine in light and heavy water. Connexion with the heat stability of proteins*, Biofizika (Biophysics), volume 18, pp. 1022-1027.

Cann, J.Y., 1932, *Glycine in water solution*, Journal of Physical Chemistry, volume 36. pp. 2813-2816.

Carta, R., 1998, *Solubilities of L-cystine, L-tyrosine, L-leucine, and glycine in sodium chloride solutions at various pH values*, Journal of Chemical Thermodynamics, volume 30, pp. 379-387.

Chen, C.C. and L.B. Evans, 1986, *A local composition model for the excess Gibbs energy of aqueous electrolyte systems*, AIChE Journal, volume 32, pp. 444-454.

Chen, C.C., Y. Zhu, and L.B. Evans, 1989, *Phase partitioning of biomolecules: solubilities of amino acids*, Biotechnology Progress, volume 5, pp. 111-118.

Clarke, E.C.W. and D.N. Glew, 1985, *Evaluation of the thermodynamic functions for aqueous sodium chloride from equilibrium and calorimetric measurements below 154°C*, Journal of Physical Chemistry Reference Data, volume 14, No. 2, pp. 489-610.

Coen, C. J., J.M. Prausnitz, and H.W. Blanch, 1997, *Protein salting-out: Phase equilibria in two-protein systems*, Biotechnology and Bioengineering, volume 53, pp. 567-574.

Cohn, E.J. and J.T. Edsall, 1943, *Protein, Amino Acids and Peptides as Ions and Dipolar Ions*, American Chemical Society, Monograph Series, Reinhold Publishing Corporation: New York, Chapter 8.

Conio, G., L. Curletto, and E. Patrone, 1973, *On the temperature coefficient of the solubility of some glycyl peptides in water-ethanol mixtures*, Journal of Biological Chemistry, volume 218, pp. 5448-5450.

Cottingham, W.N. and D.A. Greenwood, 1991, *Electricity and Magnetism*, Cambridge University Press, United Kingdom.

CRC Handbook of Chemistry and Physics, 78th Ed., 1997-1998.

CRC Handbook of Chemistry and Physics, 62nd Ed., 1981-1982.

Dalton, J.B. and C.L.A. Schmidt, 1933, *The solubility of certain amino acids in water. The densities of their solutions at twenty-five degrees, and the calculated heats of solution and partial molal volumes*, Journal of Biological Chemistry, volume 103, pp. 549-578.

Dalton, J.B. and C.L.A. Schmidt, 1935, *The solubility of certain amino acids in water. The densities of their solutions at twenty-five degrees, and the calculated heats of solution and partial molal volumes. II*, Journal of Biological Chemistry, volume 109, pp. 241-248.

Debye, P. and E. Hückel, 1923, *Zur Theorie der Electrolyte*, Physikalische Zeitschrift, volume 24, pp. 179-207.

Ellerton, H.D., G. Reinfels, D.E. Mulcahy, and P.J. Dunlop, 1964, *Activity, density, and relative viscosity data for several amino acids, lactamide, and raffinose in aqueous solution at 25°*, Journal of Physical Chemistry, volume 68, pp. 398-402.

Fasman, G.D., 1976, *Handbook of Biochemistry and Molecular Biology, Physical and Chemical Data*, CRC, pp. 109-120.

Fiol, S., I. Brandariz, and M. Sastre de Vicente, 1995, *The ionization constants of α-alanine in NaCl at 25°. Effect of the ionic strength based on three models*, Talanta - Oxford, volume 42, pp. 797-802.

Frankel, M., 1930, *Zur Kenntnis der Assoziationstendenz von Aminosäuren in wässeriger Lösung*, Biochemische Zeitschrift, volume 217, pp. 378-388.

Friedman, H.L., 1972, *Lewis-Randall to McMillan-Mayer conversion for the thermodynamic excess functions of solutions. Part I. Partial free energy coefficients*, Journal of Solution Chemistry, volume 1, pp. 387-412.

Gekko, K., 1981, *Mechanism of polyol-induced protein stabilization: Solubility of amino acids and diglycine in aqueous polyol solutions*, Journal Biochemistry, volume 90, pp. 1633-1641.

Greenstein, J.P. and M. Winitz, 1961, *Chemistry of the Amino Acids, vol. 1*, Wiley and Sons, Inc., New York, p. 488.

Gude, M.T., H.H.J. Meeuwissen, L.A.M. van der Wielen, and K.Ch.A.M. Luyben, 1996, *Partition coefficients and solubilities of α-amino acids in aqueous 1-butanol solutions*, Industrial and Engineering Chemistry Research, volume 35, pp. 4700-4712.

Gude, M.T., L.A.M. van der Wielen, and K.Ch.A.M. Luyben, 1996, *Phase behavior of α-amino acids in multicomponent aqueous alkanol solutions*, Fluid Phase Equilibria, volume 116, pp. 110-117.

Gupta, R.B. and R.A. Heidemann, 1990, *Solubility models for amino acids and antibiotics*, AIChE Journal, volume 36, pp. 333-341.

Haghtalab, A. and J.H. Vera, 1991, *Mean activity coefficients in the ternary system NaCl - $NaNO_3$ - H_2O and NaBr-$NaNO_3$-H_2O systems at 298.15 K*, Journal of Chemical and Engineering Data, volume 36, pp. 332-340.

Harned, H.S. and G. Åkerlöf, 1926, *Experimentelle Untersuchungen an wässerigen Lösungen einfacher gewöhnlicher Elektrolyte*, Physikalische Zeitschrift, volume 27, pp. 411-448.

Harned, H.S. and W.J. Hamer, 1933, *The ionization constant of water and the dissociation of water in potassium chloride solutions from electromotive forces of cells without liquid junction*, Journal of the American Chemical Society, volume 55, pp. 2194-2206.

Harned, H.S. and B.B. Owen, 1930a, *The thermodynamic properties of weak acids and bases in salt solutions, and an exact method of determining their dissociation constants*, Journal of the American Chemical Society, volume 52, pp. 5079-5091.

Harned, H.S. and B.B. Owen, 1930b, *The acid and base constants of glycine from cells without liquid junction*, Journal of the American Chemical Society, volume 52, pp. 5091-5102.

Harris, F.E. and C.T. O'Konski, 1957, *Dielectric properties of aqueous ionic solutions at microwave frequencies*, Journal of Physical Chemistry, volume 61, pp. 310-319.

Haynes, C.A. and J. Newman, 1998, *On converting from the McMillan-Mayer framework. I. Single-solvent system*, Fluid Phase Equilibria, volume 145, pp. 255-268.

Helgeson, H.C., D.H. Kirkham, and G.C. Flowers, 1981, *Theoretical prediction of the thermodynamic behavior of aqueous electrolytes at high pressures and temperatures: IV. Calculations of activity coefficients, osmotic coefficients, and apparent molal and standard and relative partial molal properties to 600°C and 5 kb*, American Journal of Science, volume 281, pp. 1249-1516.

Hill, T.L., 1962, *An Introduction to Statistical Thermodynamics*, Addison-Wesley Publishing Company, Inc., London, England.

Hoskins, W.M., M. Randall, and C.L.A. Schmidt, 1930, *The conductance and activity coefficients of glutamic and aspartic acids and their monosodium salts*, Journal of Biological Chemistry, volume 88, pp. 215-239.

Hutchens, J.O., K.M. Figlio, and S.M. Granito, 1963, *An isopiestic comparison method for activities - the activities of L-serine and L-arginine-hydrochloride*, Journal of Biological Chemistry, volume 238, pp. 1419-1422.

Jakube, H.-D. and H. Jeschkeit, 1982, *Aminosäuren Peptide Proteine - Eine Einführung*, Akademie-Verlag, Berlin.

Jin, X.Z. and K.-C. Chao, 1992, *Solubility of four amino acids in water and four pairs of amino acids in the their water solutions*, Journal of Chemical and Engineering Data, volume 37, pp. 199-203.

Khoshkbarchi, M.K. and J.H. Vera, 1996a, *Measurement of activity coefficients of amino acids in aqueous electrolyte solutions: Experimental data for the systems H_2O + NaCl + glycine and H_2O + NaCl + DL-alanine at 25 °C*, Industrial and Engineering Chemistry Research, volume 35, pp. 2735-2742.

Khoshkbarchi, M.K. and J.H. Vera, 1996b, *Measurement and modelling of activities of amino acids in aqueous salt systems*, AIChE Journal, volume 42, pp. 2354-2364.

Khoshkbarchi, M.K. and J.H. Vera, 1996c, *Activity coefficients of DL-valine in aqueous solutions of KCl at 25 degree C. Measurement with ion selective electrodes and modelling*, Journal of Solution Chemistry, volume 25, pp. 865-875.

Khoshkbarchi, M.K. and J.H. Vera, 1996d, *A perturbed hard-sphere model with mean spherical approximation for the activity coefficients of amino acids in aqueous electrolyte solutions*, Industrial and Engineering Chemistry Research, volume 35, pp. 4755-4766.

Khoshkbarchi, M.K. and J.H. Vera, 1996e, *A simplified perturbed hard-sphere model for the activity coefficients of amino acids and peptides in aqueous solutions*, Industrial and Engineering Chemistry Research, volume 35, pp. 4319-4327.

Khoshkbarchi, M.K. and J.H. Vera, 1997, *Effect of NaCl and KCl on the solubility of amino acids in aqueous solutions at 298.2 K: Measurements and modeling*, Industrial and Engineering Chemistry Research, volume 36, pp. 2445-2451.

Khoshkbarchi, M.K., A.M. Soto-Campos, and J.H. Vera, 1997, *Interaction of DL-serine with NaCl and KCl in aqueous solutions*, Journal of Solution Chemistry, volume 26, pp. 941-955.

Kuramochi, H., H. Noritomi, D. Hoshino, and K. Nagahama, 1996a, *Measurements of solubilities of two amino acids in water and prediction by the UNIFAC model*, Biotechnology Progress, volume 12, pp. 371-379.

Kuramochi, H., H. Noritomi, D. Hoshino, and K. Nagahama, 1996b, *Measurements of solubilities of two amino acids in water and prediction by the UNIFAC model*, Biotechnology Progress, volume 12, p. 728, Errata to the above mentioned.

Kuramochi, H., H. Noritomi, D. Hoshino, and K. Nagahama, 1997, *Measurements of vapor pressures of aqueous amino acid solutions and determination of activity coefficients of amino acids*, Journal of Chemical and Engineering Data, volume 42, pp. 470-474.

Larsen, B.L., P. Rasmussen, Aa. Fredenslund, 1987, *A modified UNIFAC group-contribution model for prediction of phase equilibria and heat of mixing*, Industrial and Engineering Chemistry Research, volume 26, pp. 2274-.

Lee, L.L., 2000, *Thermodynamic consistency and reference scale conversion in multisolvent electrolyte solutions*, Journal of Molecular Liquids, volume 87, pp. 129-147.

Lewis, W.C.M., 1931, *Behavior of glycine. Appendix: Note on the physicochemical behavior of glycine in solution*, Chemical Reviews, volume 8, pp. 151-165.

Lilley, T.H. and P.R. Scott, 1976a, *Aqueous solutions containing amino-acids and peptides. Part 2. Gibbs function and enthalpy behaviour of the systems urea+glycine, urea+α-alanine, urea+α-aminobutyric acid and urea+glycylglycine at 298.15 K*, Journal of the Chemical Society - Faraday Transactions, volume 72, pp. 184-196.

Lilley, T.H. and R.P. Scott, 1976b, *Aqueous solutions containing amino-acids and peptides. Part 3. The osmotic coefficient at the freezing temperature of the solutions of aqueous systems containing glycine and some alkali metal chlorides and some tetra-alkylammonium bromides*, Journal of the Chemical Society - Faraday Transactions, volume 72, pp. 197-207.

Mansoori, G.A., N.F. Carnahan, K.E. Starling, and T.W. Leland, Jr., 1971, *Equilibrium thermodynamic properties of the mixture of hard spheres*, Journal of Chemical Physics, volume 54, pp. 1523-1525.

McMeekin, T.L., E.J. Cohn, and J.H. Weare, 1935, *Studies in the physics chemistry of amino acids, peptides and related substances. III. The Solubility of derivatives of the amino Acids in alcohol-water mixtures*, Journal of the American Chemical Society, volume 57, pp. 626-633.

McMillan, W.G., Jr. and J.E. Mayer, 1945, *The statistical thermodynamics of multicomponent systems*, Journal of Chemical Physics, volume 13, pp. 276-305.

McQuarrie, D.A., 1976, *Statistical Mechanics*, Harper & Row, Publishers, Inc., New York.

Michelsen, M.L. and J.M. Mollerup, 2000, *Thermodynamic models, Fundamentals, and Computational Aspects*, Department of Chemical Engineering, DTU, Denmark, Chapter 1.

Morrison, R.T. and R.N. Boyd, 1992, *Organic Chemistry*, 6th Edition, Prentice-Hall International Edition, New Jersey.

Nass, K.K., 1988, *Representation of the solubility behavior of amino acids in water*, AIChE Journal, volume 34, pp. 1257-1266.

Needham, T.E. Jr., A.N. Paruta, and R.J. Gerraughty, 1971, *Solubility of amino acids in pure solvent systems*, Journal of Pharmaceutical Sciences, volume 60, pp. 565-567.

Nozaki, Y. and C. Tanford, 1963 *The solubility of amino acids and related compounds in aqueous urea solutions*, Journal of Biological Chemistry, volume 238, pp. 4074-4081.

Nozaki, Y. and C. Tanford, 1965, *The solubility of amino acids and related compounds in aqueous ethylene glycol solutions*, Journal of Biological Chemistry, volume 240, pp. 3568-3571.

Orella, C.J. and D.J. Kirwan, 1989, *The solubility of amino acids in mixtures and aliphatic alcolhols*, Biotechnology Progress, volume 5, pp. 89-91.

Owens, B.B. and E.J. King, 1943, *The effect of sodium chloride upon the ionization of boric acid at various temperatures*, Journal of the American Chemical Society, volume 65, pp. 1612-1620.

Peres, A.M. and E.A. Macedo, 1994, *Representation of solubilities of amino acids using the* UNIQUAC model for electrolytes, Chemical Engineering Science, volume 49, pp. 3803-3812.

Pinho, S.P., C.M. Silva, and E.A. Macedo, 1994, *Solubility of amino acids: A group-contribution model involving phase and chemical equilibria*, Industrial and Engineering Chemistry Research, volume 33, pp. 1341-1347.

Pitzer, K.S., 1980, *Electrolytes. From dilute solutions to fused salts*, Journal of the American Chemical Society, volume 102, pp. 2902-2906.

Pitzer, K.S., 1991, *Activity Coefficients in Electrolyte Solutions*, 2nd Edition, CRC Press, Boca Raton.

Pradhan, A.A. and J.H. Vera, 1998, *Effect of acids and bases on the solubility of amino acids*, Fluid Phase Equilibria, volume 152, pp. 121-132.

Raposo, J.C., J. Sanz, G. Borge, M.A. Olazabal, and J.M. Madariaga, 1999, *Development of a modified Bromley's methodology (MBM) for the estimation of ionic media effects on*

solution equilibria. Part 3. Application to the construction of thermodynamic models, Fluid Phase Equilibria, volume 155, pp. 1-19.

Renon, H. and J.M. Prausnitz, 1968, *Local composition in thermodynamic excess functions for liquid mixtures*, AIChE Journal, volume 14, pp. 135-144.

Richards, M.M., 1938, *The effect of glycine upon the activity coefficient of glycine, egg albumin, and carboxyhemoglobin*, Journal of Biological Chemistry, volume 122, pp. 727-743.

Roberts, R.M. and J.G. Kirkwood, 1941, *The activity of glycine in aqueous solutions of potassium chloride, from electromotive force measurements*, Journal of the American Chemical Society, volume 63, pp. 1373-1377.

Robinson, R.A., 1952, *The vapor pressure of aqueous solutions of alanine*, Journal of Biological Chemistry, volume 199, pp. 71-73.

Robinson, R.A. and D.A. Sinclair, 1934, *The activity coefficients of the alkali chlorides and of lithium iodide in aqueous solution from vapor pressure measurements*, Journal of the American Chemical Society, volume 56, pp. 1830-1835.

Robinson, R.A. and R.H. Stokes, 1959, *The Measurement and Interpretation of Conductance, Chemical Potential and Diffusion in Solutions of Simple Electrolytes*, 2nd Edition, Butterworths, London.

Roth, W.A., 1903, *Gefrierpunktserniedrigungen durch Nichtelektrolyte in konzentriertern wässrigen Lösungen*, Zeitschrift für physikalische Chemie, volume 43, pp. 539-564.

Rudolph, E.S.J., M. Zomerdijk, M. Ottens, and L.A.M. van der Wielen, 2001, *Solubilities and partition coefficients of semi-synthetic antibiotics in water + 1-butanol systems*, Industrial and Engineering Chemistry Research, volume 40, pp. 398-.

Sander, B., A. Fredenslund, and P. Rasmussen, 1986, *Calculation of solid-liquid equilibria in aqueous solutions of nitrate salts systems using an extended UNIQUAC equation*, Chemical Engineering Science, volume 41, pp. 1197-1202.

Scatchard, G. and S.S. Prentiss, 1934a, *Freezing points of aqueous solutions. VII. Ethyl alcohol, glycine and their mixtures*, Journal of the American Chemical Society, volume 56, pp. 1486-1492.

Scatchard, G. and S.S. Prentiss, 1934b, *Freezing points of aqueous solutions. VIII. Mixtures of sodium chloride with and glycine and ethyl alcohol*, Journal of the American Chemical Society, volume 56, pp. 2314-2319.

Schrier, E.E. and R.A. Robinson, 1971, *A study of free energy relationships in some amino acid-sodium chloride-water systems*, Journal of Biological Chemistry, volume 246, pp. 2870-2874.

Schrier, E.E. and R.A. Robinson, 1974, *Free energy relationships in aqueous amino acid and peptide solutions containing sodium chloride*, Journal of Solution Chemistry, volume 3, pp. 493-501.

Sijpkes, A.H., G.J. van de Kleut, and S.C. Gill, 1994, *The solubilities of five cyclic dipeptides in water and in aqueous urea at 298.15 K: A quantitative model for the denaturation of proteins in aqueous urea solutions*, Biophysical Chemistry, volume 52, pp. 74-82.

Simonin, J.-P., L. Blum, and P. Turq, 1996, *Real ionic solutions in the mean spherical approximation. 1. Simple salts in the primitive model*, Journal of Physical Chemistry, volume 100, pp. 7704-7709.

Simonin, J.-P., 1996, *Theory of experimental-to-McMillan–Mayer conversion of thermodynamic excess functions*, Journal of the Chemical Society - Faraday Transactions, volume 92, pp. 3519-3523.

Simonin, J.-P., 1999, *Thermodynamic properties of aqueous solutions of organic nonelectrolytes: use of a simple molecular model at the MacMillan-Mayer level*, Fluid Phase Equilibria, volume 165, pp. 41-58.

Skoog, D.A., D.M. West, and F.J. Holler, 1992, *Fundamentals of Analytical Chemistry*, 6th Edition, Saunders HBJ: New York.

Smith, E.R.B. and P.K. Smith, 1937, *The activity of glycine in aqueous solution at twenty-five degrees*, Journal of Biological Chemistry, volume 117, pp. 209-216.

Smith, E.R.B. and P.K. Smith, 1937b, *Thermodynamic properties of solutions of amino acids and related substances. II: The activity of aliphatic amino acids in aqueous solution at twenty-five degrees*, Journal of Biological Chemistry, volume 121, pp. 607-613.

Smith, E.R.B. and P.K. Smith, 1940a, *Thermodynamic properties of solutions of amino acids and related substances. IV: The effect of increasing dipolar distance on the activity of aliphatic amino acids in aqueous solution at twenty-five degrees*, Journal of Biological Chemistry, volume 132, pp. 47-56.

Smith, E.R.B. and P.K. Smith, 1940b, *Thermodynamic properties of solutions of amino acids and related substances. V: The effect of some hydroxy- and n-methylamino acids and proline on aqueous solutions at twenty-five degrees*, Journal of Biological Chemistry, volume 132, pp. 57-64.

Smith, E.R.B. and P.K. Smith, 1940c, *Thermodynamic properties of solutions of amino acids and related substances. VI: The activity of some peptides in aqueous solutions at twenty-five degrees*, Journal of Biological Chemistry, volume 135, pp. 273-279.

Smith, E.R.B. and P.K. Smith, 1942, *Thermodynamic properties of solutions of amino acids and related substances. VIII The ionization of glycylglycine, ε-aminocaproic acid, and aspartic acid in aqueous solution from one to fifty degrees*, Journal of Biological Chemistry, volume 146, pp. 187-195.

Söhnel, O. and P. Novotný, 1985, *Densities of Aqueous Solutions of Inorganic Substances*, Physical Sciences Data 22, Elsevier, Amsterdam.

Soto-Campos, A.M., M.K. Khoshkbarchi, and J.H. Vera, 1997a, *Interaction of DL-threonine with NaCl and $NaNO_3$ in aqueous solutions: e.m.f. measurements with ion-selective electrodes*, Journal of Chemical Thermodynamics, volume 29, pp. 609-622.

Soto-Campos, A.M., M.K. Khoshkbarchi, and J.H. Vera, 1997b, *Activity coefficients of the electrolyte and amino acid in water + $NaNO_3$ + glycine and water + NaCl + DL-methionine systems at 298.15 K*, Biophysical Chemistry, volume 67, pp. 97-105.

Soto-Campos, A.M., M.K. Khoshkbarchi, and J.H. Vera, 1998, *Effect of the anion and the cation of an electrolyte on the activity coefficient of DL-alanine in aqueous solutions*, Fluid Phase Equilibria, volume 142, pp. 193-204.

Thomsen, K., 1997, *Aqueous electrolytes: Model parameters and process simulation*, Ph.D. Thesis, Technical University of Denmark.

Zemaitis, J.F. Jr., D.M. Clarke, M. Rafal, and N.C. Scrivner, 1986, *Handbook of Aqueous Electrolyte Thermodynamics*, DIPPR, AIChE, New York.

Notation

a_i	activity of component *i*, defined by eq. (2.27)
a	distance of closest approach, (m)
A	Helmholtz energy, (J)
A_{DH}	Debye-Hückel parameter, eq. (8.22), ($m^{3/2}\cdot mol^{-1/2}$)
b	parameter in the extended Debye-Hückel model, eq. (8.42), ($m^{3/2}\cdot mol^{-1/2}$)
b_m	parameter in Fowler-Guggenheim's model, eq. (8.45), ($m^{3/2}\cdot mol^{-1/2}$)
B	modified Helmholtz energy, defined by eq. (6.12), (J)
c_i	molarity of component *i*, (mole / litre solution)
e	elementary charge, $1.602177\cdot 10^{-19}$ C
E	electrode potential, defined by eq. (4.22), (volt)
$\tilde{E}_{rs}$	reference electrode potential, defined in eq. (4.26), (volt)
E^m	reference electrode potential, defined in eq. (4.28)
f	fugacity, defined by eq. (2.16)
F	Faraday constant, 96485 C/mole
g	molar Gibbs energy, (J / mole)
G	Gibbs energy, (J)
GA	glycyl-L-alanine
GG	glycylglycine
h	molar enthalpy, (joule / mole)
I	ionic strength, defined by eq. (8.21), ((mole / litre solution)$^{1/2}$)
I_m	molal ionic strength, defined by eq. (8.44), ((mole / kg solvent)$^{1/2}$)
I_x	mole fraction ionic strength, defined by eq. (8.48), (dimensionless)
ISE	ion-selective electrode
K^c	equilibrium constant, defined in eq. (1.1)
m_i	molality of component *i*, (mole / kg solvent)
$M_{solvent}$	molar mass of solvent, (g / mole)
n_i	mole number of component *i*, (mole)
n	vector of n_i
N	number of data points

N	molecular number
N_A	Avogadro's number, $6.02214 \cdot 10^{23}$ molecules / mole
P	pressure, (Pa)
q	charge, (C)
q	surface area parameter in the UNIQUAC model
Q	canonical ensemble partition function
r	volume parameter in the UNIQUAC model
R	gas constant, 8.314 J/(mole·K)
s	sample standard deviation, $s = \sqrt{\frac{1}{N-1}\sum_i^N (x_i - x_i^{average})^2}$
S	entropy, (J / K)
T	absolute temperature, (K)
U	internal energy, defined by eq. (4.1), (J)
ΔU_{ij}	energy interaction parameter of UNIQUAC, (J / mole)
v	molar volume (m^3 / mole)
V	volume (m^3)
x_i	mole fraction of component *i*
x	vector of x_i
y_i	molar ratio of component *i* to water
y	vector of y_i
z	either **x** or **y**
z	relative charge (to the charge of H^+), (dimensionless)

Greek letters

α_k	relative concentration of the ionic species *k* of an amino acid, eq. (1.2)
γ_i	symmetric activity coefficient of component *i*, defined by eq. (2.31)
$\gamma_{i,rs}^{\infty,bin}$	symmetric activity coefficient of component *i* at infinite dilution in a binary mixture, defined by eq. (2.43)
$\tilde{\gamma}_{i,rs}$	asymmetric activity coefficient of component *i*, defined by eq. (2.44)

γ_i^m	symmetric activity coefficient of component *i* on a molal basis, defined by eq. (2.51)
Γ	screening parameter, defined by eq. (8.61), (1/m)
ε	dielectric constant or permittivity, (C^2 / (J · m))
ε_0	permittivity of vacuum, $8.85419 \cdot 10^{-12}$ C^2 / (J · m)
ε_r	relative dielectric constant or relative permittivity, (dimensionless)
θ	surface area fraction of UNIQUAC, defined by eq. (8.54)
κ	Debye length, defined by eq. (8.5), (1/m)
μ	chemical potential, defined by eq. (2.6)
ν_i	stoichiometric coefficient of component *i*
ν	sum of all stoichiometric coefficients of the electrolytes
Ξ	grand canonical ensemble partition function
Π	osmotic pressure, (Pa)
ρ	charge density (C / m^3)
ρ	number density (molecules / m^3)
σ	molecular diameter, (m)
ϕ	volume fraction of UNIQUAC, defined by eq. (8.53)
ϕ	osmotic coefficient, defined by eq. (3.17)
φ	fugacity coefficient, defined by eq. (2.17)
Φ	electric potential, (J / C = V)
Ψ	semi-grand canonical ensemble partition function

superscript

bin	binary system
E	excess property
id	ideal solution
L	liquid
MM	McMillan-Mayer framework
r	residual property
S	solid
ter	ternary system

V	vapour
∞	infinite dilution
–	partial molar property (overbar)
*	pure component property (asterisk)
°	a set point property
^	a property of a species in a mixture (accent circonflexe)

subscript

A	solute, non-electrolyte, dipeptide
m	molality based property
rs	reference solvent
S	solute, electrolyte, salt
w	water, solvent
x	mole fraction based property
±	salt, defined in eq. (5.10)
0	solvent

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