The interplay between solute solvation and solute-solute interactions in solutions containing amino acids, peptides and related species

Terence H. Lilley

Biothermodynamics Laboratory, Chemistry Department, The University of Sheffield, Sheffield S3 7HF, U.K.

Abstract
A summary is presented of some of the work we and others have done on compounds containing amino acid and peptide species, or other compounds which are structurally related to these. The information is addressed from the viewpoints of solvation and solute-solute interactions and some general comments on the behaviour of solutes in solutions are made. Correlations are presented between solvational properties and interactive properties and a general chemical principal is suggested from the correlations, viz. the more strongly solutes are solvated the less they will be their tendency to interact with other solutes.

INTRODUCTION
There is currently a considerable amount of interest, much of it being driven by problems in molecular biology and environmental science, in the 'non-bonding' interactions which occur in condensed media. Many of these problems, or similar ones, have been addressed by solution physical chemists in the past although the language used today is rather different to that used previously. As an example, a phrase which is currently popular is 'molecular recognition' but in other language this can be interpreted as the balance which is reached between the tendencies molecular species or chemical groups, have to interact with each other and their propensities to be solvated by the environment in which they are present. In other words, molecular recognition is a manifestation of the compromise between the intermolecular forces of solvation and those of solute species interaction. It is worthwhile stressing that all chemical events in condensed media are also a consequence of such a balance and to solve the problems of solution chemistry necessitates having precise knowledge about both solvation and how solvated species

![Figure 1. Schematic representation of the association between two solvated species in a solvent. The solvation regions are denoted by hatching and in the associated species some of the solvent which was present in solvation regions is released.](image)
interact with each other. It is easy to represent the molecular process schematically and this is done in Fig. 1 for the extreme example in which the solvated species can form a well-defined associate. The extent to which the association occurs depends on how well the two solute species are solvated and how strongly they interact. Qualitatively, 'good' solvation inhibits the association and favorable solute species interaction promotes the association.

Some years ago, when thinking about the problems of protein folding and protein-substrate interactions, particularly in aqueous media, it soon became apparent that there was only a comparatively small amount of experimental information available on the energetics of appropriate 'model' solutes, i.e. polyfunctional species containing groups such as those which occur in proteins. Accordingly, it was decided to embark on a programme in which molecules of the types shown (Fig. 2) were synthesized and their properties in solution investigated (refs. 1-5).

The intention was to look at their solvational properties and the solute-solute intermolecular behaviour to see if it was possible to correlate these in any way and also to use the information obtained to address the problems of intermolecular interactions of more complex molecules. Some progress has been made in both of these areas but there are still many problems outstanding. In what follows, a summary of the information which is currently available on the solvation and solute-solute interactions on species of the types shown in Fig. 2 and some related species, will be presented and then some comments will be made on the interplay which occurs between these distinct events.

SOLVATION STUDIES

All of the molecules we have studied in this area contain amidic groups of one sort or another, as do all proteins, and information on the properties of hydrated peptide and other groups have been obtained in different ways. The most direct energetic measure of the solvation of solutes is obtained from experimental information obtained from the transfer of the solutes from the gas phase to to the solvent considered and a pictorial representation of the process is shown on Fig. 3.

The enthalpy of hydration of peptide groups (ref. 6)
The net interactions which occur between the primary peptide group (secondary amide group) and water is given by the energy changes for the process:

$$\text{Peptide group (gas)} \rightarrow \text{Peptide group (water)}$$  \hspace{1cm} (1)
It is not possible, of course, to study this process directly, but if we consider, say, the enthalpy of hydration of an amide

$$\text{R-CONH-R'} \text{(gas)} \rightarrow \text{R-CONH-R'} \text{(water)}$$

and assume that the experimental enthalpy of hydration is chemical group additive then

$$\Delta_{\text{hydH}_m}^{\text{m}}(\text{R-CONH-R'}) = \Delta_{\text{hydH}_m}^{\text{m}}(-\text{R}) + \Delta_{\text{hydH}_m}^{\text{m}}(-\text{R'}) + \Delta_{\text{hydH}_m}^{\text{m}}(-\text{CONH})$$

If the enthalpies of hydration of the groups -R and -R', can be obtained then the enthalpy change for the hydration of peptide groups can be deduced. Experimental data are available (refs.6,7) for the enthalpies of solution of several gaseous hydrocarbons and for hydrogen gas and so assuming, for example,

$$\Delta_{\text{hydH}_m}^{\text{m}}(\text{C}_2\text{H}_6) = \Delta_{\text{hydH}_m}^{\text{m}}(\text{C}_2\text{H}_6) - \frac{1}{2} \Delta_{\text{hydH}_m}^{\text{m}}(\text{H}_2)$$

then the hydration enthalpies of the non-peptidic functionalities on the amides can be obtained. Inclusion of these into eqn. (3) then leads to a simple relationship with the enthalpies of hydration of the amides. This is seen in Fig. 4 (upper line) and from it we obtain

$$\Delta_{\text{hydH}_m}^{\text{m}}(-\text{CONH}) = -52 \text{ kJ mol}^{-1}$$. Included in this figure are the results obtained in an analogous way from tertiary amides and these give the enthalpy of hydration of the secondary peptide group, $$\Delta_{\text{hydH}_m}^{\text{m}}(-\text{CON<}) = -35 \text{ kJ mol}^{-1}$$. The obvious conclusion to be drawn from this information is that the -CONH- group interacts with three water molecules whereas the -CON< group interacts with only two water molecules (see Fig. 5).

Figure 4. Application of the group approach to the enthalpies of hydration, at 25°C, of secondary and tertiary amides. The intercepts on the ordinate give the enthalpies of hydration of primary (upper) and secondary (lower) peptide groups.

(a)

(b)

Figure 5. Representation of the bonding of water molecules to (a) primary peptide groups, and to (b) secondary peptide groups.

Given the success of this approach, it can be extended and used to allow the calculation of the energetics of hydration of more complex molecules. As an example, a considerable amount of computer modelling work has been done (see e.g. ref. 8) on what is sometimes called the ‘alanine peptide’ ($N$-acetyl-$N'$-methylalaninamide),

$$\text{CH}_3 \text{CONHCHCONHCH}_3$$

and we estimate that for this compound, the enthalpy of hydration is -141 kJ mol$^{-1}$, when it is in its fully extended form in both the gas phase and in water.
Partial molar volumes and heat capacities (refs. 5, 9)

Properties which contain contributions from solvation effects are the partial molar properties of solutes at infinite dilution and these solvation contributions are particularly apparent in the partial molar heat capacities although they are also evident in other properties such as the partial molar volume. Table 1 gives the information on standard state partial molar volumes and heat capacities for those amino acid and peptide amides for which data are available (refs. 5, 9).

It is possible to represent these data rather well using a solvation group additivity approach in which, for example, the partial molar heat capacity is represented by the following expression:

$$C_p^m = n_{CH_3}C_{p,CH_3} + n_{CH_2}C_{p,CH_2} + n_{CH}C_{p,CH} + n_HC_{p,H} + n_{CONH}C_{p,CONH}$$

(5)

In this, $n_i$ is the number of groups of type $i$ on a solute and $C_{p,i}$ is the group molar heat capacity.

The experimental data for the substituted amino acids and peptides given in Table 1 and supplemented by information on some aliphatic simple amides, were fitted to the group approach and the group coefficients obtained (all with units of J K⁻¹ mol⁻¹) were:

$$C_{p,CH_3} = 133; C_{p,CH_2} = 90; C_{p,CH} = 65; C_{p,H} = 45; C_{p,CONH} = -13.$$

The most striking feature of these results is the low value for the heat capacity of the hydrated peptide group and this is certainly a reflection of the similarity of the hydrogen-bonding vibrational manifolds arising from water-water and water-peptide group interactions. It is also worth mentioning that this group value differs markedly from an earlier (ref. 10) value, but it seems quite clear from a comparison which has been made (ref. 5) that the above value is to be preferred. The large and positive values obtained for the heat capacity contributions of apolar residues is a manifestation of the hydrophobic hydration about these groups and the low energy vibrations resulting therefrom.

The volumetric information (ref. 5, 9), although it can be treated in a similar way, is less instructive since, a considerable part of the experimental volume arises from the intrinsic volumes of the molecules and does not reflect solvation effects. However, it is possible to get reasonable estimates of the groups present on peptides and it is possible to make estimates of the partial molar volumes of proteins, at least of their completely denatured forms.

### Table 1. Partial molar volumes and heat capacities of N-acetyl amino acid and peptide amides in water at 25°C.

<table>
<thead>
<tr>
<th>Solute</th>
<th>$V^\infty_\text{cm}^3$ mol⁻¹</th>
<th>$C_p^\infty$ J K⁻¹ mol⁻¹</th>
<th>Solute</th>
<th>$V^\infty_\text{cm}^3$ mol⁻¹</th>
<th>$C_p^\infty$ J K⁻¹ mol⁻¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>GLY</td>
<td>90.56b</td>
<td>238.4c</td>
<td>GG</td>
<td>127.37b</td>
<td>322.1c</td>
</tr>
<tr>
<td>ALA</td>
<td>108.06b</td>
<td>346.4c</td>
<td>AA</td>
<td>161.79b</td>
<td>537.5c</td>
</tr>
<tr>
<td>VAL</td>
<td>139.00b</td>
<td></td>
<td>GA</td>
<td>144.41c</td>
<td>422.0c</td>
</tr>
<tr>
<td>PRO</td>
<td>126.51b</td>
<td></td>
<td>AG</td>
<td>145.43c</td>
<td>430.9c</td>
</tr>
<tr>
<td>SAR</td>
<td>107.14b</td>
<td></td>
<td>PP</td>
<td>200.93b</td>
<td></td>
</tr>
<tr>
<td>GLYMe</td>
<td>108.93b</td>
<td></td>
<td>GP</td>
<td>161.77b</td>
<td></td>
</tr>
<tr>
<td>ALAMe</td>
<td>122.87b</td>
<td></td>
<td>PG</td>
<td>164.23b</td>
<td></td>
</tr>
<tr>
<td>LEUMe</td>
<td>174.75b</td>
<td></td>
<td>PA</td>
<td>180.67b</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>PDA</td>
<td>180.63b</td>
<td></td>
</tr>
</tbody>
</table>

a The abbreviations used are as follows. The first five entries on the left are the N-acetyl amides of glycine (G), α-alanine (A), valine, proline (P) and sarcosine. The next three entries are the N-acetyl, N'-methyl amides of glycine, α-alanine and leucine. The entries on the right are N-acetyl peptide amides. The last entry (PDA) is the D-isomer whereas the rest are all L-isomers.

b Ref. 9.  c Ref. 5.
It is worthwhile pointing out that there is a marked difference in the volumetric and heat capacity behaviour of terminally substituted amino acids and peptides and their parent compounds and this arises, largely if not entirely, from the presence of the charges on the zwitterionic structures. There are various ways of illustrating this but one way is to consider the standard state volume and heat capacity changes for the processes:

\[
nH_3N^+\text{CH(R)CO}^- = H_3N^+-[\text{CH(R)CONH}]_n\text{CH(R)CO}^- + (n - 1)H_2O
\]

\[
n\text{CH}_3\text{CONHCH(R)CONH}_2 = \text{CH}_3\text{CO}-[\text{NHCH(R)CO}]_n\text{NH}_2 + (n - 1)\text{CH}_3\text{CONH}_2
\]

In the first of these, when the peptide is formed, charge is neutralised, whereas in the second, no such effect occurs. If it is assumed that the contributions from the charged groups can be represented using a Born approach then for the formation of a peptide containing \(n\) residues, the free energy contribution, from electrostatic sources, to the standard state free energy change is of the form

\[
\Delta G^0_{\text{(elec)}} = (n - 1)Q/\varepsilon_r
\]

(6)

where, \(Q\) is a term containing, among other things, a measure of the effective radii of the charges on the species, and \(\varepsilon_r\) is the relative permittivity of the solvent. Appropriate differentiation of this gives the following expression for the ratio of the standard state heat capacity and volume changes:

\[
\frac{\Delta C_p^0_{\text{(elec)}}}{\Delta V^0_{\text{(elec)}}} = 13.0 \text{ J K}^{-1} \text{ cm}^{-3}
\]

(7)

after substitution of the appropriate (ref. 11) permittivity information. Fig. 6 shows the experimental (ref. 12) heat capacity and volume changes calculated for the formation of zwitterionic peptides at 25°C and included in this figure is the line with a slope of 13.0 J K\(^{-1}\) cm\(^{-3}\).

It is apparent from this that major contributions to the 'solvation' properties of the zwitterionic amino acids and peptides arise from electrostatic sources and have nothing to do with 'structural' properties per se. This is further illustrated in Table 2 where we compare the heat capacity changes for the formation of some zwitterionic peptides with those for the corresponding terminally substituted compounds. It is evident from this that the changes observed for the charged species are much greater than those seen for the uncharged species and that much of the difference arises purely from the presence of the charges. This is not to say that there are no contributions from 'structural' sources, these are obviously present, as evidenced by the differences shown between the values for the two structural isomers, but disentangling the two

<table>
<thead>
<tr>
<th>Side chains</th>
<th>Peptide</th>
<th>(\Delta C_p^0) (J K(^{-1}) mol(^{-1}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>gly, gly</td>
<td>100.8</td>
<td>7.7</td>
</tr>
<tr>
<td>gly, ala</td>
<td>110.7</td>
<td>-0.4</td>
</tr>
<tr>
<td>ala, gly</td>
<td>97.9</td>
<td>8.5</td>
</tr>
<tr>
<td>ala, ala</td>
<td>123.1</td>
<td>7.1</td>
</tr>
</tbody>
</table>

TABLE 2. Standard state partial molar heat capacity changes for the formation of some peptides and for their N-acetyl amides in water at 25°C.
types of contribution to peptide properties, clearly would be difficult at the present time. Some progress has been made in attempts to do this but they have met with mixed success. It is interesting that we are currently in the position of being able to measure many properties to a very high level of accuracy but the level of our interpretation is frequently fairly elementary because there is not available, at the moment, any theoretical approaches which are sufficiently refined to aid a real molecular interpretation.

SOLUTE–SOLUTE INTERACTIONS

Turning now to the interactions which occur between solvated solutes in solution, most of the information which has been obtained on such interactions, has been treated using the excess thermodynamic function approach (refs.13,14). In this one is concerned with the difference between the behaviour of a real solution and that of a defined ideal solution. For a thermodynamic property $X$, we have

$$X^{ex} = X^{real} + X^{ideal}$$

(8)

Usually, the molal scale is used to represent solute 'concentrations' and the approach is formulated in terms of unit mass (1 kg) of the solvent. Given this, then for non-electrolytes, the excess Gibbs' energy

$$G^{ex} = G^{real} + G^{ideal}$$

(9)

is represented as a power series in solute(s) molality viz.

$$G^{ex} = \sum_{ij} g_{ij}m_i m_j + \sum_{ijk} g_{ijk} m_i m_j m_k + ...$$

(10)

where the $g$ terms represent, at least in a notional sense (see below), interactions between the subscripted solvated species. Analogous expressions can be written for other thermodynamic properties.

There are various experimental ways of determining excess functions but these will not be discussed here. We also do not intend considering terms other than in the first terms in the various expansions, i.e. we will only address those terms which represent pairwise interactions between solutes. However, one aspect which is worth pointing out is that the frequently observed oscillation of signs in consecutive terms in molality expansions of excess properties and functions related to these, e.g. osmotic and activity coefficients and apparent molar enthalpies, can be rationalised using the more fundamental activity expansions (ref. 15). If, for purposes of illustration, we consider a solution of a solute A and assume that, at the molecular level, only pairwise interactions occur between solvated A species, then the excess Gibbs' energy is strictly given by

$$G^{ex} = g_{AA}a_A^2$$

(11)

where $a_A$ is the activity of A. Expanding the activity term leads to the expression

$$G^{ex} = g_{AA}m_A^2 + 4g_{AA}(g_{AA}/RT)m_A^3 + 24g_{AA}(g_{AA}/RT)^2m_A^4 + ...$$

(12)

Consequently, if there are attractions between the solvated solute molecules, i.e. $g_{AA}$ is negative, when a molality expansion is used, oscillation in signs will result but the higher order terms are artefactual and, in this instance, will not indicate that there are triplet, etc. interactions occurring between the solute species. In real situations, higher order terms may well be present in the activity expansion reflecting real interactions at the molecular level, but if one is to address and interpret these, this should only be done after due allowance has been made for the pairwise
Contributions. To illustrate the importance of this, if we consider a situation where the homotactic pairwise interaction coefficient of a solute is \(-280 \text{ J kg}^{-1} \text{ mol}^{-2}\), then the calculated contributions to the triplet and quartet terms from the pairwise term are \(+99 \text{ J kg}^{-3} \text{ mol}^{-4}\) and \(-59 \text{ J kg}^{-3} \text{ mol}^{-4}\) respectively. These 'higher order' terms are similar in magnitude to those observed experimentally (see e.g. ref. 16) and so due allowance must be made for such contributions if molecular interpretation of the higher terms in virial expansions are to be made. Similar treatments can be applied to other properties and similar conclusions can be drawn.

Interactions between amides and salts

Some years ago, Schrier and Schrier (ref. 17) proposed that when an ion interacts with a polyfunctional molecule, and implicitly if the interaction between any group on the molecule and the ion is small compared to thermal energies, the experimental measure of the net interaction contains contributions from each of the groups present. If one considers the interactions between an aliphatic amide containing methyl, methylene, methyne and secondary amide groups, and ions, then the free energetic pairwise interaction coefficient is given by

\[
\varepsilon_{\text{amide, salt}} = \varepsilon_{\text{amide, M}^+} + \varepsilon_{\text{amide, X}}
\]

\[
= n_{\text{CH}_3} G_{\text{CH}_3,M^+} + n_{\text{CH}_2} G_{\text{CH}_2,X} + n_{\text{CH}_2} G_{\text{CH}_2,M^+} + n_{\text{CH}_2} G_{\text{CH}_2,X} + n_{\text{CONH}} G_{\text{CONH},M^+} + n_{\text{CONH}} G_{\text{CONH},X} \tag{13}
\]

This contains a large number of group interaction terms and to simplify it, given the approximate nature of the procedure, it was suggested that the aliphatic groups present could be represented by equivalent methylene groups such that, \(n_{\text{CH}} = 1.5n_{\text{CH}_2}\) and \(n_{\text{CH}} = 0.5n_{\text{CH}_2}\), and using this approximation, eqn. (13) simplifies to

\[
\varepsilon_{\text{amide, salt}} = \varepsilon_{\text{amide, M}^+} + \varepsilon_{\text{amide, X}}
\]

\[
= n_{\text{CH}_2} G_{\text{CH}_2,M^+} + n_{\text{CH}_2} G_{\text{CH}_2,X} + n_{\text{CONH}} G_{\text{CONH},M^+} + n_{\text{CONH}} G_{\text{CONH},X} \tag{14}
\]

which is much more tractable. It should be noted that it is not possible to separate the individual ionic contributions without making an extrathermodynamic assumption and consequently in application this becomes

\[
\varepsilon_{\text{amide, salt}} = n_{\text{CH}_2} G_{\text{CH}_2,\text{salt}} + n_{\text{CONH}} G_{\text{CONH},\text{salt}} \tag{15}
\]

An example of the use of this expression to amide systems containing either secondary or tertiary amide groups is given in Fig. 7.

The most striking feature of this is that, the tertiary amide group interacts more strongly with all of the salts than does the secondary amide group.

In some recent papers (ref. 18) some results were considered on the heterotactic interactions between amides and urea and amides and other salts (refs. 19-21), and in all cases, the interactions between solutes are such as

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**Figure 7.** Plot of the enthalpic heterotactic interaction coefficient against the number of equivalent methylene groups, for the interaction of amides with ammonium formate in water at 25°C.
to indicate that the primary peptide group interacts less well with urea and with ions than does the secondary peptide group.

Interactions between amides and between N-acetyl amino acid and peptide amides
Tables of the free energetic and enthalpic pairwise interaction coefficients obtained for terminally substituted amino acids and peptides in water have been given elsewhere (ref. 1). There are several observations which can be made from perusal of the information which is available, but a striking feature is the wide variation in the values obtained, even for rather similar molecules. For example, if one considers the pairwise enthalpic coefficients for the derivatives of glycine, alanine, valine and leucine, these vary from about -200 to +1700 J kg\(^{-1}\) mol\(^{-1}\) and this observation alone immediately indicates that the interactions between these species in water, are not dominated by peptide group peptide group hydrogen-bonding interactions. The wide variation clearly shows that other contributions must be present.

As a first approximation, most of the experimental results can be rationalised using an approach first suggested by Savage and Wood (ref. 22) who significantly extended the Schriers' idea to give a means of representing interactions between two polyfunctional species. The resulting expression for a pairwise interaction coefficient \(x_{AB}\) is of the form

\[
x_{AB} = \sum_{ij} X_{ij} n_i^A n_j^B
\]

where \(n_i^A\) and \(n_j^B\) are the numbers of groups of types i and j on the molecules A and B, and \(X_{ij}\) is the term representing the interaction of solvated group i with solvated group j.

This type of expression has been applied to the results obtained for a large number of systems, for different excess properties, and Fig. 8 illustrates the quality of fitting obtained for the enthalpic pairwise coefficients for some amidic and peptidic solutes. The values obtained for the group free energetic and enthalpic interaction coefficients, for this coherent set of solutes and related compounds containing the secondary peptide functionality, are given in Table 3. There are several comments which could be made about these group coefficients but the most striking feature is the observation that the interaction coefficients for the amide groups indicate that the interaction between primary peptide groups is weaker than that between secondary peptide groups, i.e. removal of hydrogen-bond donors increases the interaction.

<table>
<thead>
<tr>
<th>Groups</th>
<th>(G_{ij}) (J kg mol(^{-1}))</th>
<th>(H_{ij}) (J kg mol(^{-2}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>CH(_2) CH(_2)</td>
<td>-20</td>
<td>25</td>
</tr>
<tr>
<td>CH(_2) CONH</td>
<td>22</td>
<td>80</td>
</tr>
<tr>
<td>CH(_2) CON</td>
<td>37</td>
<td>49</td>
</tr>
<tr>
<td>CONH CONH</td>
<td>-50</td>
<td>-292</td>
</tr>
<tr>
<td>CON CON</td>
<td>-62</td>
<td>-319</td>
</tr>
</tbody>
</table>

Figure 8. Comparison of fitted and experimental results obtained for the enthalpic interaction coefficients of terminally substituted amino acid and peptide amides and simple amides, containing aliphatic, primary amide and secondary amide groups. The fitted results were obtained using the group coefficients given in the text.
Correlations between solute–solute interactions and solvation

There seems to be a qualitative correlation between the tendencies solutes have to interact in solution and their solvation characteristics. This is not too unexpected and indeed it has been shown (ref. 18) from a combination of the McMillan-Mayer (ref. 23) and Kirkwood-Buff (ref. 24) theories of solution that this idea has a firm basis. However, it does seem that, for a large number of different systems that the correlation between hydration and interaction is more quantitative than one might have predicted, given the complexity of the systems studied. This will be illustrated for a few types of system.

In Fig. 9 we show the correlation between the heterotactic interaction coefficients of some amides with urea and the enthalpies of hydration of the amides. Fig. 10 gives the corresponding correlation between amides and the salt sodium chloride and Fig. 11 illustrates the variation in the heterotactic interaction coefficients for amides with the amino acids glycine and α-alanine. In each of these examples, as the enthalpy of hydration becomes more negative (i.e. thermochemically more attractive) the enthalpic interaction coefficient becomes more positive (i.e. thermochemically more repulsive).

Figure 9. Correlation between the enthalpies of hydration of amides and their heterotactic interaction coefficients with urea in water at 25°C.

![Figure 9](image1)

Figure 10. Correlation between the enthalpies of hydration of amides and their heterotactic interaction coefficients with sodium chloride in water at 25°C.

![Figure 10](image2)

Figure 11. Correlation between the enthalpies of hydration of amides and their heterotactic interaction coefficients with glycine and α-alanine in water at 25°C.

![Figure 11](image3)

Figure 12. Correlation between the enthalpies of hydration of alkali metal halide salts and the relative molar excess enthalpies (syn. relative apparent molar enthalpy) of 0.1 molal solutions in water at 25°C.

![Figure 12](image4)
There are various other illustrations which could be given which show this type of correlation, not only for the enthalpy but also for the free energy, between interaction and solvation but to illustrate the apparent broad generality an example from electrolyte solutions will be given. In Fig. 12 we plot the molar excess enthalpy, $H_m^{\text{ex}}$ (often termed the relative apparent molar enthalpy and given the symbol $\phi_m$), of 0.1 molal solutions of the alkali metal halides, against the molar enthalpy of hydration of the constituent ions and it is apparent that there is a broad correlation found between these quantities and again it is found that the more exothermic is the enthalpy of hydration, the more endothermic is the molar excess enthalpy.

It would seem therefore that correlations of the type presented could well have some general utility and the intention is that this aspect of solutions will be explored more fully in the future.

REFERENCES

1. A summary of some of the work is given in M.N. Jones (editor), Biochemical Thermodynamics (2nd. edition), chapter 1, Elsevier, Amsterdam (1988).