



This is a repository copy of *A study of the relationship between water and anions of the Hofmeister series using pressure perturbation calorimetry.*

White Rose Research Online URL for this paper:  
<http://eprints.whiterose.ac.uk/86005/>

Version: Accepted Version

---

**Article:**

Falconer, R.J. and Bye, J.W. (2015) A study of the relationship between water and anions of the Hofmeister series using pressure perturbation calorimetry. *Physical Chemistry Chemical Physics*. ISSN 1463-9084

<https://doi.org/10.1039/C5CP00571J>

---

**Reuse**

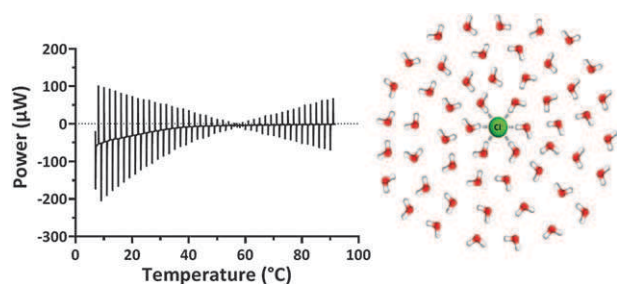
Unless indicated otherwise, fulltext items are protected by copyright with all rights reserved. The copyright exception in section 29 of the Copyright, Designs and Patents Act 1988 allows the making of a single copy solely for the purpose of non-commercial research or private study within the limits of fair dealing. The publisher or other rights-holder may allow further reproduction and re-use of this version - refer to the White Rose Research Online record for this item. Where records identify the publisher as the copyright holder, users can verify any specific terms of use on the publisher's website.

**Takedown**

If you consider content in White Rose Research Online to be in breach of UK law, please notify us by emailing [eprints@whiterose.ac.uk](mailto:eprints@whiterose.ac.uk) including the URL of the record and the reason for the withdrawal request.



[eprints@whiterose.ac.uk](mailto:eprints@whiterose.ac.uk)  
<https://eprints.whiterose.ac.uk/>



**A study of the relationship between water and anions of the Hofmeister series using pressure perturbation calorimetry**

Jordan W. Bye and Robert J. Falconer\*

Pressure perturbation calorimetry (PPC) was used to study the relationship between water and sodium salts with a range of different anions.

Q1

Q2

Q3

Please check this proof carefully. **Our staff will not read it in detail after you have returned it.**

Translation errors between word-processor files and typesetting systems can occur so the whole proof needs to be read. Please pay particular attention to: tabulated material; equations; numerical data; figures and graphics; and references. If you have not already indicated the corresponding author(s) please mark their name(s) with an asterisk. Please e-mail a list of corrections or the PDF with electronic notes attached – do not change the text within the PDF file or send a revised manuscript. Corrections at this stage should be minor and not involve extensive changes. All corrections must be sent at the same time.

**Please bear in mind that minor layout improvements, e.g. in line breaking, table widths and graphic placement, are routinely applied to the final version.**

Please note that, in the typefaces we use, an italic vee looks like this:  $\nu$ , and a Greek nu looks like this:  $\nu$ .

We will publish articles on the web as soon as possible after receiving your corrections; **no late corrections will be made.**

Please return your **final** corrections, where possible within **48 hours** of receipt, by e-mail to: [pccp@rsc.org](mailto:pccp@rsc.org)

## Queries for the attention of the authors

Journal: PCCP

Paper: c5cp00571j

Title: **A study of the relationship between water and anions of the Hofmeister series using pressure perturbation calorimetry**

Editor's queries are marked on your proof like this **Q1**, **Q2**, etc. and for your convenience line numbers are indicated like this 5, 10, 15, ...

Please ensure that all queries are answered when returning your proof corrections so that publication of your article is not delayed.

Query reference	Query	Remarks
Q1	For your information: You can cite this article before you receive notification of the page numbers by using the following format: (authors), Phys. Chem. Chem. Phys., (year), DOI: 10.1039/c5cp00571j.	
Q2	Please carefully check the spelling of all author names. This is important for the correct indexing and future citation of your article. No late corrections can be made.	
Q3	Please check that the inserted GA text is suitable.	
Q4	Ref. 37: Please provide the year of publication.	

# A study of the relationship between water and anions of the Hofmeister series using pressure perturbation calorimetry†

Jordan W. Bye and Robert J. Falconer\*

Cite this: DOI: 10.1039/c5cp00571j

Received 29th January 2015,  
Accepted 29th April 2015

DOI: 10.1039/c5cp00571j

www.rsc.org/pccp

Pressure perturbation calorimetry (PPC) was used to study the relationship between water and sodium salts with a range of different anions. At temperatures around 25 °C the heat on pressurisation ( $\Delta Q$ ) from 1 to 5 bar was negative for all solutions relative to pure water. The raw data showed that as the temperature rose, the gradient was positive relative to pure water and the transition temperature where  $\Delta Q$  was zero was related to anion surface charge density and was more pronounced for the low-charge density anions. A three component model was developed comprising bulk water, the hydration layer and the solute to calculate the molar expansivity of the hydration layer around the ions in solution. The calculated molar expansivities of water in the hydration layer around the ions were consistently less than pure water.  $\Delta Q$  at different disodium hydrogen phosphate concentrations showed that the change in molar enthalpy relative to pure water was not linear even as it approached infinite dilution suggesting that while hydration layers can be allocated to the water around ions this does not rule out interactions between water and ions extending beyond the immediate hydration layer.

## Introduction

Water is a unique solvent that plays a critical role in supporting life on earth. Despite this there is still ongoing discussion between scientists on the nature of water and its association with inorganic and organic molecules. A unique property of water is its propensity to rapidly swap protons between water molecules at a picosecond timescale, referred to as hydrogen bonding. When a salt is added to water it dissociates into anions and cations as described by Arrhenius in 1887.<sup>1</sup> These ions have electrical fields which interact with the dipolar water molecules that arrange themselves around the ions. These arranged water molecules are often referred to as the hydration layer. There is discussion around whether the ion's effect extends just to the water molecules at the interface with the ion, into a second hydration layer or beyond into more distant water.

In 1888 Franz Hofmeister published two papers on the effect salts had on protein solubility in water.<sup>2,3</sup> An English translation of these papers is available in Kunz *et al.* 2004.<sup>4</sup> The observation was made that ions could be ordered according

their ability to precipitate or solubilise protein ensembles. Hofmeister explained his observations in terms of the hydration strength of the ions (their ability to absorb water). Ions with strong hydration compete with the protein for the water and it is this that causes the protein's precipitation. A similar ordering of the ions was observed in surface tension measurements by Adolf Heydweiller in 1910.<sup>5</sup> An alternative explanation for the Hofmeister effect was published in 1930 by Cox and Wolfenden which explained the observed effect of ions on viscosity in terms of the degree of polymerisation of the solvent in the presence of the ions.<sup>6</sup> Over a period of years evolved the explanation for the Hofmeister effect as the ability of an ion to alter the hydrogen bond population of the solvent<sup>7</sup> often referred to as the structure making and structure breaking theory. This theory relied on the ions having the ability to interact with water molecules beyond its first hydration layer. In 2003, the structure making and structure breaking theory was directly challenged using data from femtosecond pump-probe spectroscopy that suggested there was no measurable interaction with water beyond the first hydration layer.<sup>8</sup> Since then evidence using neutron diffraction,<sup>9</sup> molecular dynamic simulation<sup>10</sup> and calorimetry techniques<sup>11</sup> have suggested long-range interactions beyond the first hydration layer are likely.

In this paper we add pressure perturbation calorimetry (PPC) at low pressure changes to the existing palette of techniques for studying electrolyte solutions and discuss the results with reference to the Hofmeister effect. The current PPC technology was preceded

Department of Chemical & Biological Engineering, ChELSI Institute, University of Sheffield, Sheffield, S1 3JD, UK. E-mail: r.j.falconer@sheffield.ac.uk; Fax: +44 (0)114 2227501; Tel: +44 (0)114 2228253

† Electronic supplementary information (ESI) available. See DOI: 10.1039/c5cp00571j

by instrumentation that subject the samples to high pressure changes (up to 4000 bar) which were suitable for studying phase transitions in organic solvents and polymers, and had been around since the 1970s.<sup>12–15</sup> More recently a modification to differential scanning microcalorimetry (DSC) instrumentation enabled this type of analysis to be carried out at lower pressure changes (4 bar) with a high degree of sensitivity which enabled the analysis of the heat change on pressurization for diverse solutes in water.<sup>16,17</sup> These devices measure the heat change in the solution as the pressure above the solution is altered. From this the thermal expansion coefficient ( $\alpha$ ) of the solute has been calculated and the hydrogen-bond population of the water at the solute–water interface studied.<sup>18,19</sup> This approach has been applied to a diverse range of solutes including polymers,<sup>16</sup> amino acids,<sup>17</sup> small inorganic and organic molecules,<sup>18</sup> proteins,<sup>16–28</sup> lipid micelles and bilayers,<sup>29–31</sup> and nucleic acid.<sup>32,33</sup>

The calculation of the thermal expansion coefficient from PPC data assumed a two-state model for water with a relatively low density and a denser liquid species. PPC relies on the Le Chatelier's principle, that on pressurization the water will try to equilibrate by moving towards the higher density form. The derivation of the equation that has been used to calculate the thermal expansion coefficient uses a two-component system for small molecules in solution where  $V_{\text{tot}}$  is the total volume,  $V_0$  is the molar volume of solvent and  $\bar{V}$  is the partial specific volume of the solute in the solution which includes any volume changes induced in the solvent;  $x_0$  is molar fraction of the solvent and  $x_s$  is molar fraction of the solute.<sup>17,18</sup>

$$V_{\text{tot}} = x_0 V_0 + x_s \bar{V} \quad (1)$$

An alternative approach to the two-component model is to directly take into account the population of water around the solute (referred to as the hydration layer or solvation shell in the literature) that has a molar volume which may be different to bulk water (unperturbed or pure water). Whichever model is selected for defining the boundary of the hydration layer around a solute this population of water has to be defined in terms of its own average molar volume, molar fraction and average thermal expansion coefficient. In this paper the authors propose an alternative approach to studying solutes in water taking the hydration layer into account and present the results for sodium salts with different anions to illustrate how this approach can be implemented.

## Data analysis

The authors initially calculated values for the coefficient of thermal expansion using the equation derived in Lin *et al.* 2002<sup>17</sup> using published apparent partial volume ( $\bar{V}$ ) values<sup>34</sup> and the experimental PPC results for 100 mM salt solutions (see Fig. S1 in the ESI†). While the coefficient of thermal expansion for sodium chloride, sodium bromide, sodium iodide, sodium thiocyanide and sodium perchlorate are plausible those for sodium fluoride and disodium sulphate were unusual. Sodium fluoride and disodium sulphate both have high charge density and their conventional apparent partial volume ( $\bar{V}$ ) values<sup>34</sup> are markedly lower than their intrinsic volumes ( $V_{\text{int}}$ )<sup>35</sup> (see Fig. S2 in the ESI†).

It was concluded that the two-component model was problematic for high charge density ions. It was this observation that led the authors to suggest a three-component model for salt solutions where  $V_b$  is the molar volume of bulk solvent,  $V_h$  is the average molar volume of the solvent within the hydration layer and  $V_s$  is the molar volume of solute;  $x_b$  is the molar fraction of the bulk solvent,  $x_h$  is the molar fraction of the solvent within the hydration layer and  $x_s$  is the molar fraction of the solute.

$$V_{\text{tot}} = x_b V_b + x_h V_h + x_s V_s \quad (2)$$

The heat ( $Q$ ) is derived from first principles for a single component system where  $T$  is temperature,  $\Delta P$  is change in pressure,  $\alpha$  is the thermal expansion coefficient and  $V$  is the volume.<sup>17</sup>

$$Q = -T\Delta P\alpha V \quad (3)$$

For a three component system this becomes

$$Q = -T\Delta P[x_b V_b \alpha_b + x_h V_h \alpha_h + x_s V_s \alpha_s] \quad (4)$$

where  $\alpha_b$ ,  $\alpha_h$  and  $\alpha_s$  is the thermal expansion coefficient of the bulk water, hydration layer and solute, respectively.

The difference in heat between the sample and reference cells is

$$\Delta Q = T\Delta P[x_0 V_0 \alpha_0 - x_b V_b \alpha_b - x_h V_h \alpha_h - x_s V_s \alpha_s] \quad (5)$$

where  $x_0$ ,  $V_0$  and  $\alpha_0$  is the molar fraction, molar volume and thermal expansion coefficient of the pure water in the reference cell.

As  $V_0 = V_b$ ,  $\alpha_0 = \alpha_b$  and  $x_0$  is 1 the equation can be simplified to

$$\Delta Q = T\Delta P[(1 - x_b)(V_b \alpha_b) - x_h V_h \alpha_h - x_s V_s \alpha_s] \quad (6)$$

As  $x_b = 1 - x_h - x_s$

$$\Delta Q = T\Delta P[(x_s + x_h)(V_b \alpha_b) - x_h V_h \alpha_h - x_s V_s \alpha_s] \quad (7)$$

As the  $x_h$  is defined by the multiple number ( $n$ ) of water molecules around the ions  $x_h = n x_s$ , the equation can be further simplified to

$$\Delta Q = T\Delta P[(n + 1)(x_s V_b \alpha_b) - n x_s V_h \alpha_h - x_s V_s \alpha_s] \quad (8)$$

$$\Delta Q = T\Delta P x_s [(n + 1)(V_b \alpha_b) - n V_h \alpha_h - V_s \alpha_s] \quad (9)$$

The experimental results show that as  $\Delta P$  and  $x_s$  tend to zero  $\Delta Q$  tend to zero but as  $T$  tends to zero  $\Delta Q$  is negative therefore a constant ( $A$ ) is added to the equation. Note  $A$  is undefined and may be due to the presence of the sodium cation and its interaction with the anion. Where  $T$  is the variable

$$\Delta Q = T\Delta P x_s [(n + 1)(V_b \alpha_b) - n V_h \alpha_h - V_s \alpha_s] + A \quad (10)$$

Accurate values for density, specific volume ( $V_b$ ), thermal expansivity ( $\alpha_b$ ), and compressibility of ordinary water are available in the literature.<sup>36</sup> The number of water molecules for the first and second hydration layers around anions and cations has been estimated by diffraction methods<sup>37</sup> and molecular dynamic simulation<sup>38</sup> so a value can be attributed to  $n$ . The  $V_s \alpha_s$  is known for crystalline sodium halides.<sup>39</sup> Molar

1 expansivity of the hydration layer ( $E_h$ ) can be derived using  
eqn (10) as  $E_h = V_h \alpha_h$ .

Determining the thermal expansion coefficient ( $\alpha_h$ ) is more  
difficult as an estimate as a value for  $V_h$  is needed. The difference  
5 between experimental determined apparent partial molal  
volumes<sup>34</sup> and the intrinsic molal volume<sup>35</sup> could be used to  
estimate the change in molar volume of the water within the  
hydration layer. An alternative approach would be to calculate  
10 the effect of electrostriction on the molar volume of the water  
within the hydration layer from molecular dynamic simulation  
data.<sup>38</sup> Both these method would be estimates at best so the  
calculations used by the authors were confined to calculating the  
molar expansivity of the hydration layer around the ions.

## 15 Methods and materials

### Sample preparation

Ultra-pure water and all salts were sourced from Sigma Aldrich,  
Gillingham, UK with purities >99.9%. Sodium was used as the  
20 counter-ion for all anions. 2000 mM stock solutions at pH 7  
were made for all salts (sodium fluoride stock solutions were  
made to 100 mM at pH 8.4 due to solubility limits); stock  
solution dilutions were performed by adding the required  
amount of pure water.

### Pressure perturbation calorimetry (PPC) measurements

PPC measurements were obtained using a capillary Nano-DSC  
(TA Instruments, New Castle, DE, USA). Samples were degassed

for 1 hour at 30 °C to remove dissolved gas from samples and  
eliminate bubble formation during the scan. Heat effects ( $\Delta Q$ )  
were measured during alternating pressure pulses of  $\pm 4$  bar  
from 1 bar to 5 bar at 1 °C intervals from 7–92 °C, giving a  
usable data range of 10–90 °C. A heating rate of 0.1 °C min<sup>-1</sup>  
5 was used to satisfy isothermal conditions required during  
pressure pulses; this scanning rate is slower than the instru-  
ment feedback.<sup>33</sup> The instrument was held at a constant  
temperature for 30 minutes before each scan to ensure that  
any asymmetry between the reference and sample cells was  
10 minimal. Heat changes during pressurization steps were used  
for data analysis and were calculated using the NanoAnalyze  
software (TA Instruments, New Castle, DE, USA) provided by the  
manufacturer. Water baseline scans were performed with pure  
water in reference and sample cell, scans with salt present were  
15 performed with pure water in the reference cell and salt  
solution in the sample cell. The area under each thermal power  
spike was calculated by integration using NanoAnalyze software  
(TA Instruments, New Castle, DE, USA) and was used as the  
heat change during pressurization for that temperature, shown  
20 in Fig. 1a–d.

### Calculation of molar expansivity

Application of eqn (10) is simple in practice for solutes where  
the specific volume ( $V_s$ ), thermal expansivity ( $\alpha_s$ ) are known and  
25  $n$  can be estimated. The specific volume ( $V_b$ ), thermal expan-  
sivity ( $\alpha_b$ ) of pure water are known.<sup>36</sup>  $A$  was determined by  
adjusting it till the calculated  $\Delta Q$  fitted experimental  $\Delta Q$  data.

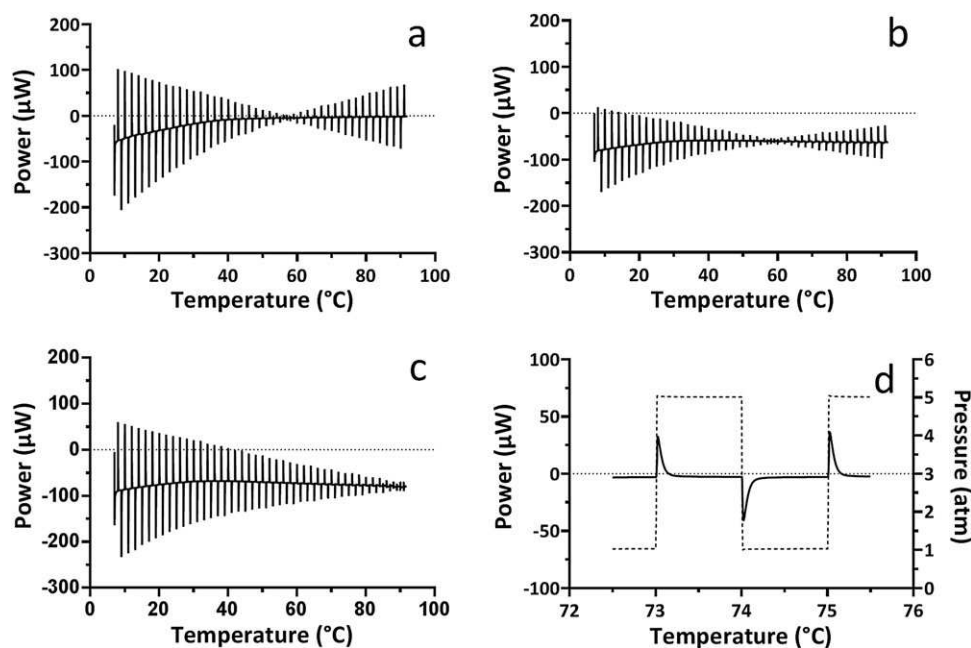


Fig. 1 (a–c) Show the raw data from a pressure perturbation scan of 1000 mM disodium hydrogen phosphate, sodium chloride and sodium thiocyanate in pure water at pH 7 respectively. Alternating pressure pulses from 1–5 bar and then 5–1 bar were applied to the sample at 1 °C intervals from 7–92 °C, with a heating rate of 0.1 °C min<sup>-1</sup>. (d) Shows a close up of (a) from 70 °C to 75 °C, with data for pressure increases and decreases shown (---). Here the area under the power spike for the pressure pulses was integrated by the software provided to calculate the energy absorbed and released by the sample relative to the reference cell containing pure water. For the pressurization steps shown in (d) the change in heat is positive (endothermic) with reference to the pure water baseline. During the depressurization steps the heat change is negative (exothermic) with reference to the pure water baseline.

Eqn (10) was rearranged as follows so molar expansivity ( $V_h\alpha_h$ ) can be calculated.

$$V_h\alpha_h = \frac{[(n+1)(V_b\alpha_b)] - V_s\alpha_s - \frac{\Delta Q - A}{T\Delta P X_s}}{n} \quad (11)$$

## Results

2 M stock solutions were made for disodium hydrogen phosphate (at pH 7.0 this is a mixture of sodium dihydrogen phosphate and disodium hydrogen phosphate), disodium sulphate, sodium fluoride, sodium chloride, sodium bromide, sodium iodide, sodium thiocyanate and sodium perchlorate at pH 7.0 (sodium fluoride at pH 8.4 was only made to 100 mM due to solubility limits). These salts were chosen so that a range of anions from the Hofmeister series could be studied, including the simple monoatomic halogen anions and more complex oxoanions.

Thermal data was collected as microwatts ( $\mu\text{W}$ ) of power required to keep the reference and sample cell temperatures identical upon pressurization and depressurization steps, the raw data for 1000 mM disodium hydrogen phosphate, sodium chloride and sodium thiocyanate, is shown in Fig. 1a–c, respectively. Fig. 1d shows a small temperature range in which the area under the thermal spikes (which was integrated) can be more clearly seen, along with the pressure change which caused the thermal spike. The power function was converted into heat absorbed or released ( $\Delta Q$ ) in micro joules ( $\mu\text{J}$ ) by the sample during pressure changes between 1–5 atm.

The  $\Delta Q$  associated with pressurization of the salt solutions at 100 mM and 1000 mM, respectively, is shown in Fig. 2a and b. The plotted heat energies show the difference in energy added to the sample cell compared to the reference cell which contained pure water. Sodium fluoride was not tested at 1000 mM due to its low solubility. For all salts tested a negative  $\Delta Q$  is observed at lower temperatures upon sample pressurization, this indicates that an exothermic process is taking place. The temperature where  $\Delta Q$  upon sample pressurization is zero ( $T_i$ ) was found to be salt dependent and independent of salt concentration. The  $T_i$  were found to be 60.5 °C for disodium hydrogen phosphate, 59.5 °C for disodium sulphate, 54 °C for

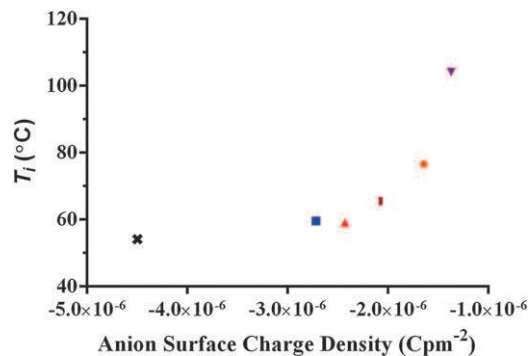


Fig. 3 Ion surface charge density against the temperature ( $T_i$ ) where the  $\Delta Q$  equals zero for 100 mM disodium sulphate (■), sodium fluoride (✕), sodium chloride (▲), sodium bromide (+), sodium iodide (●), and sodium perchlorate (▼). Note thiocyanate was omitted as it is not spherical.

sodium fluoride, 59 °C for sodium chloride, 65.5 °C for sodium bromide, 76.5 °C for sodium iodide, 90.5 °C for sodium thiocyanate and 104 °C for sodium perchlorate at all salt concentrations. The temperature where  $\Delta Q$  upon pressurization became endothermic was not reached for sodium perchlorate concentrations. The temperature where its  $\Delta Q$  became endothermic was calculated by extrapolation reached for sodium perchlorate. The surface charge density of the ions tested plotted against the temperature where the heat changes upon pressurization of the salt solution becomes endothermic at the same temperature is shown in Fig. 3. Charge, ionic and apparent ionic radii for sulphate, fluoride, chloride, bromide, iodide, thiocyanate and perchlorate were used to calculate the surface charge density of each ion.<sup>29,30</sup> It should be noted that phosphate was omitted from this graph due to phosphate being composed of a mixture of  $\text{H}_2\text{PO}_4^-$  and  $\text{HPO}_4^{2-}$  at pH 7.0. There is a trend of increasing  $T_i$  values with a decrease in surface charge density. Thiocyanate does not fit the trend as well as the other ions which may be due to it being treated as a sphere to obtain its ionic radius, when it is not spherical. It should be noted that the ordering of these ions by the  $T_i$  value closely agrees with the order seen in the Hofmeister series.<sup>2–4</sup>

The average gradient on the  $\Delta Q$  versus temperature plot for the eight salts tested at 100 mM from 9.5–91.5 °C. The average

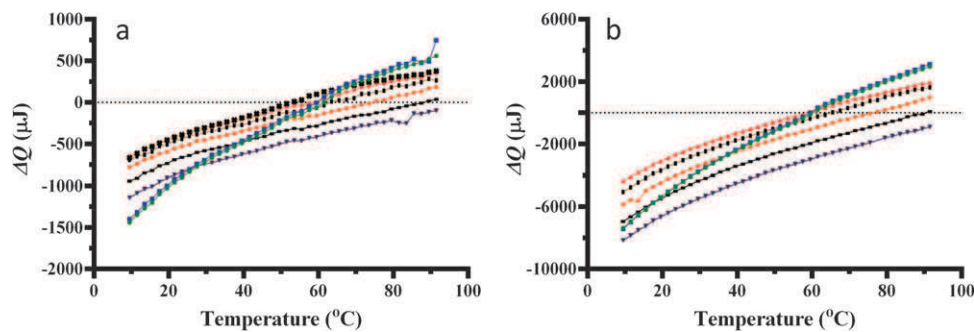


Fig. 2 (a) Heat changes for pressure increase (1 to 5 bar) from 7–92 °C for (a) 100 mM and (b) 1000 mM disodium hydrogen phosphate (●), disodium sulphate (■), sodium fluoride (✕), sodium chloride (▲), sodium bromide (+), sodium iodide (●), sodium thiocyanate (–) and sodium perchlorate (▼). The sample size was 300  $\mu\text{L}$ . Lines between data points do not represent experimental data and are only shown for guidance.

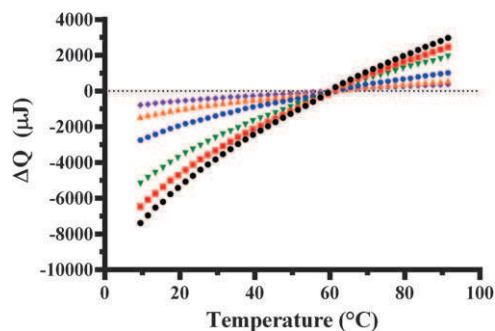


Fig. 4 Heat changes for pressure increase (1–5 bar) from 7–92 °C at different concentrations of disodium hydrogen phosphate; 50 (◆), 100 (▲), 250 (●), 500 (▼), 750 (■) and 1000 mM (●). The sample size was 300  $\mu\text{L}$ .

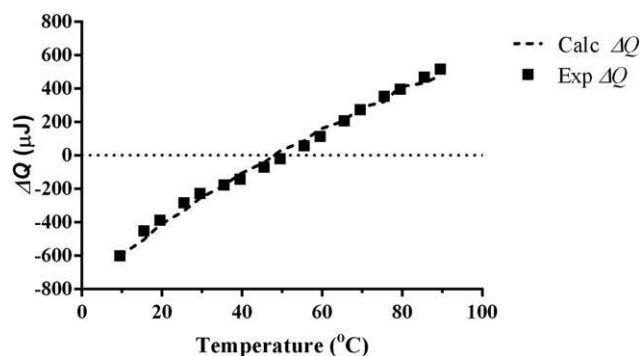


Fig. 6 Experimental values for the  $\Delta Q$  for 100 mM NaCl fitted against values for  $\Delta Q$  calculated using eqn (10) using the assumptions that  $n$  is 13.3 and the molar expansivity of the hydration layer is 0.55 that of pure water.

gradient for each salt (100 mM) was calculated by dividing the difference in  $\Delta Q$  upon pressurization at 9.5 °C and 91.5 °C. From Fig. 2 it can clearly be seen that ions with a  $-2$  charge release more energy at lower temperatures and require more energy at higher temperatures upon pressurization than ions with a  $-1$  charge. It is worth remembering that the divalent anion, sulphate has two sodium cations so the gradient cannot be ascribed to the anion alone. The gradient of ions with a  $-1$  charge was similar to each other, so is not dependent on ion charge density, size or shape.

The effect of different phosphate concentrations on  $\Delta Q$  versus temperature is shown in Fig. 4. The change in molar enthalpy relative to pure water of the  $\Delta Q$  versus temperature was dependent on phosphate concentration. The  $\Delta Q$  versus phosphate concentration at different temperatures is shown in Fig. 5a and b. It is worth noting that change in molar enthalpy relative to pure water is not linear even at concentrations around 100 mM where there are over 500 water molecules per anion and cation.

The values for the molal volume ( $V_b$ ) and thermal expansion coefficient of pure water ( $\alpha_b$ ) are known from the literature,<sup>36</sup> and  $T$ ,  $\Delta P$  and  $x_s$  values are controlled during each experiment. The variables are  $n$  and molar expansivity ( $V_h\alpha_h$ ).  $V_h$  and  $\alpha_h$  cannot be separated by this approach.  $V_s\alpha_s$  is known for crystalline salts at a set temperature.<sup>38</sup> In this paper we assume the  $V_s\alpha_s$  value for salt and the  $n$  does not vary with temperature calculations. The  $\Delta Q$  values calculated using eqn (10) for

100 mM NaCl (Fig. 6) is consistent with an  $n$  value of 13.3 and a  $V_h\alpha_h$  value 0.55 times that of the known  $V_b\alpha_b$  for bulk water at temperatures between 5 and 95 °C. The calculated values for all the sodium halide salts using both the single hydration layer and double hydration layer models are shown

Table 1 The number of water molecules in the 1st and 2nd water layers around sodium ( $n$ ) and halide ions, molar expansivity of a salt ( $V_s\alpha_s$ ), the relationship between the average molar expansivity of water in the hydration layer and the bulk phase ( $V_h\alpha_h/V_b\alpha_b$ ) and the constant  $A$  for NaF, NaCl, NaBr and NaI. The later two values derived from 100 mM experimental data using eqn (10)

	$n^a$	$V_s\alpha_s^b$ ( $\text{m}^3 \text{mol}^{-1} \text{K}^{-1}$ )	$V_h\alpha_h/V_b\alpha_b^c$	$A$ (J)
1 Layer model				
NaF	12.3	$1.48 \times 10^{-9}$	0.54	$7.35 \times 10^{-7}$
NaCl	13.3	$3.16 \times 10^{-9}$	0.55	$6.60 \times 10^{-7}$
NaBr	13.1	$4.46 \times 10^{-9}$	0.62	$7.05 \times 10^{-7}$
NaI	14.0	$5.51 \times 10^{-9}$	0.65	$7.80 \times 10^{-7}$
2 Layer model				
NaF	34.3	$1.48 \times 10^{-9}$	0.83	$7.50 \times 10^{-7}$
NaCl	40.8	$3.16 \times 10^{-9}$	0.85	$6.75 \times 10^{-7}$
NaBr	40.5	$4.46 \times 10^{-9}$	0.87	$7.50 \times 10^{-7}$
NaI	46.1	$5.51 \times 10^{-9}$	0.89	$8.10 \times 10^{-7}$

<sup>a</sup> The number of water molecules per sodium and halide ions was determined by MD simulation.<sup>40</sup> <sup>b</sup> The  $V_s\alpha_s$  is for crystalline sodium halides.<sup>41</sup> <sup>c</sup> The  $V_b\alpha_b$  is derived from pure water density measurements published in Kell, 1967.<sup>38</sup> The  $V_h\alpha_h/V_b\alpha_b$  and  $A$  values were calculated using eqn (10).

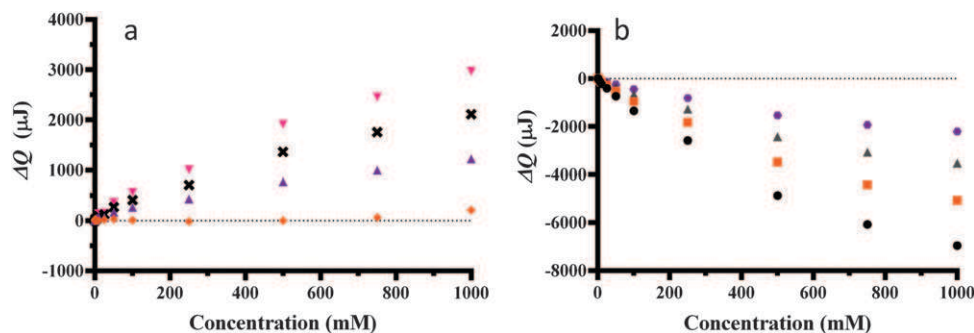


Fig. 5 Heat changes for pressure increase (1–5 bar) at different concentrations of disodium hydrogen phosphate and different temperatures; (a) 11.5 (●), 21.5 (■), 31.5 (▲), (b) 41.5 (●), 61.5 (◆), 71.5 (▲), 81.5 (x) and 91.5 °C (▼). The sample size was 300  $\mu\text{L}$ .



1 in Table 1. The  $V_h\alpha_h$  values approach that of pure water as the  
charge density reduces but are all lower than pure water.

## 5 Discussion

10 Interpretation of the PPC results for the different salt solutions  
has to take into account that the measured  $\Delta Q$  is a result of  
both the sodium and the anion and cannot be separated. The  
monovalent anions all have the same concentration of sodium  
so differences between the  $\Delta Q$  values will be due to the anion  
alone. The second factor that has to be considered is that the  
measured  $\Delta Q$  is relative to the pure water in the reference cell.  
By applying eqn (10) the  $V_h\alpha_h$  values for the hydration layer were  
15 calculated.

Heat release has been interpreted as bond formation  
between water molecules<sup>40</sup> so the initial exothermic  $\Delta Q$  can  
be interpreted as the hydration layer strengthening or forming  
additional hydrogen bonds relative to pure water. At tempera-  
20 tures over the  $T_i$  value this relationship reverses and  $\Delta Q$  became  
endothermic can be interpreted as the hydration layer weaken-  
ing or breaking more hydrogen bonds relative to pure water.  
The temperature where this transition between bond formation  
and bond breaking is observed is dependent on charge density  
25 of the anion. This is clearly seen for the halides which are  
simple spheres but the general trend is also evident with the  
more complex structure of the oxoanions and thiocyanate  
(which is more linear than spherical). It is possible that PPC  
is providing evidence about the hydrogen bond population of  
30 water around the anions. Electrostatic interaction impact on  
the hydration layer is also evident as valency of the anion has  
an obvious effect on the average gradient on the  $\Delta Q$  versus  
temperature plot though this work does not differentiate  
between this being driven by the valency of the anion or the  
35 number of sodium ions present.

The experimental data where the concentration of phos-  
phate was varied (Fig. 4, 5a and b) demonstrated that change in  
molar enthalpy relative to pure water at a temperature below  
the  $T_i$  value was reduced as the  $x_s$  increased. The non-linearity  
40 occurs below 100 mM phosphate suggests that there are longer-  
range interactions between water and ions that extends beyond  
the first two layers of water and are probably electrostatic  
interactions.<sup>10</sup> This does call into question where the  $n$  value  
should be set so the use of eqn (10) should have the assump-  
45 tions used to select the  $n$  value clearly explained.

The equation for the analysis of PPC data presented in this  
paper (eqn (10)) is based on a three component model compris-  
ing bulk water (unperturbed water); hydration water (water that  
is measurably perturbed by the ions) and the ions. Eqn (10)  
50 accepts that the hydration water has its own molar volume and  
thermal expansion coefficient that may differ from the bulk  
water and this should not be ignored. The  $n$  value is dependent  
on where boundary between the hydration layer and bulk water  
is set. Molecular dynamic simulation has been used to estimate  
55 the  $n$  value around the halides, see Table 1.<sup>38</sup> For example, if  
the boundary is set at a single layer of water molecules per ion,

a sodium and chloride would have an  $n$  value of 13.3; but if a  
double layer is chosen the  $n$  value will be 34.3. The researcher  
has a choice of a single thickness or double thickness model  
when using eqn (10) and should remember that the calculated  
 $V_h\alpha_h$  will be an average for the water molecules within the  
5 hydration layer.

The apparent partial molar volumes of water around salts at  
infinite dilution<sup>32</sup> and the ionic volume<sup>43</sup> has been observed to  
be quite different for over 50 years,<sup>6</sup> see Fig. S1 in the ESI.† This  
has been explained as electrostriction, a reduction in the  
10 volume of the water interacting with the ion's electrical field  
and is particularly noticeable for high charge density ions like  
sodium, and fluoride.<sup>34</sup> The  $V_h\alpha_h$  values calculated are consis-  
tently lower than bulk water suggesting that any decrease in the  
 $V_h$  value is due to electrostriction, the  $\alpha_h$  value or a combination  
15 of the two.

Partial molal adiabatic compressibility sodium salts in water  
at 25 °C determined from the velocity of sound through the  
sample<sup>41</sup> like the molar expansivity of the hydration layer ( $V_h\alpha_h$ )  
calculated here also follows a series that mirrors the Hofmeister  
20 series. It is attractive to think the three phenomenon are related  
and have to do with the interaction of the salt with water.

Franz Hofmeister's original observation was that certain  
salts were consistent in their ability to precipitate and dissolve  
proteins.<sup>2–4</sup> Hofmeister put this observation down to the salt  
absorbing the water. In the 1930s the idea that ions have a long-  
range effect on the hydrogen bond structure of water to explain  
25 the viscosity of electrolyte solutions.<sup>5</sup> This led to the theory of  
some ions being "structure makers" and others being "struc-  
ture breakers". Since the 1930s there has been extensive  
research undertaken to better study the interaction between  
water and ions using an incredibly diverse collection of analy-  
tical techniques including nuclear magnetic resonance, optical  
Kerr effect spectroscopy, dielectric relaxation spectroscopy,  
30 transient vibrational adsorption spectroscopy, terahertz  
spectroscopy, X-ray scattering and molecular dynamic simula-  
tion. The femtosecond pump–probe spectroscopy results first  
used to challenge the long-range effect of ions on water and  
came to the conclusion that ions had little effect on water  
beyond its immediate single molecule thick hydration layer.<sup>8</sup> A  
40 hydration layer composed of a single water layer has been used  
to explain experimental data for a range of techniques includ-  
ing nuclear magnetic resonance,<sup>42</sup> optical Kerr effect spectro-  
scopy,<sup>43</sup> transient vibrational adsorption spectroscopy,<sup>42</sup>  
terahertz spectroscopy.<sup>44</sup> The problem with the model of water  
45 being limited to a single layer of water around the ion is that it  
failed to explain the Hofmeister effect while destroying the  
established structure maker structure breaker theory. The new  
orthodoxy of a single water molecule thick hydration layer has  
been criticized using data from neutron scattering<sup>9</sup> and femto-  
50 second infrared spectroscopy<sup>45</sup> which detected a second layer  
of water around ions. When the potential long-range effects of  
the ion's electrical field is taken into consideration along with  
the dynamic nature of water the selection of a hydration layer's  
boundary is probably a measure of each analytical method's  
55 sensitivity. PPC can be used to justify either a single or double

1 water layer around ions. It can also be used to challenge the  
 idea of the interaction between water and ions being solely short  
 range. The slope on the  $\Delta Q$  versus phosphate ion concentration  
 plot shown in Fig. 5 and 6 did not show linearity as it  
 5 approached zero concentration. This phenomenon was also  
 observed when determining apparent partial molar volumes of  
 water around salts where an infinite dilution method was  
 needed to estimate the partial molar volume.<sup>34</sup> Both observa-  
 tions could be used to argue for long-range interactions  
 10 between ions and water beyond a one or two molecule thick  
 hydration layer. While the authors would not argue that struc-  
 ture making structure breaking theory is an adequate explana-  
 tion for the Hofmeister effect the femtosecond pump-probe  
 spectroscopy evidence that was used to criticise the theory<sup>8</sup> was  
 15 not as conclusive as it looked at the time.

The majority of the papers that used PPC to study amino  
 acids,<sup>17</sup> small inorganic and organic molecules,<sup>18</sup> proteins<sup>17–28</sup>  
 and DNA<sup>32,33</sup> used the equation derived in Lin *et al.* 2002<sup>17</sup> to  
 calculate the thermal coefficient of expansion of the solvent  
 20 volume. The authors of this paper suggest that eqn (10) is worth  
 applying to PPC studies of diverse solutes in aqueous solutions.  
 Small organic and inorganic molecules as well as macromole-  
 cules have hydration layers. There is an increasing body of work  
 using techniques such as terahertz spectroscopy that have been  
 25 used to detect hydration layers around diverse organic mole-  
 cules including sugars,<sup>46</sup> peptides<sup>47</sup> and proteins<sup>48–50</sup> suggest-  
 ing hydration in many cases is not limited to a single layer at  
 the solutes surface but can be extensive. Whether the boundary  
 of the hydration layer around a solute is a single layer, a double  
 30 layer or more complex this population of water has to be  
 defined in terms of its own average molar volume and thermal  
 expansion coefficient like the water around salts in this paper.  
 In studies using macromolecules such as globular proteins as  
 the solute, it is also worth noting that the molar expansivity  
 35 ( $V_{s,\alpha_s}$ ) will have to be estimated from the known partial volumes  
 of the protein's constituent groups<sup>51</sup> and that estimating a  
 value for  $n$  in eqn (10) will be problematic with the data  
 available at the time of writing.

## 40 Acknowledgements

The authors would like to thank the Department of Chemical  
 and Biological Engineering at the University of Sheffield for  
 financing Jordan Bye's studentship, and the Engineering and  
 45 Physical Sciences Research Council (EPSRC) Knowledge Transfer  
 Account for part funding the purchase of the DSC. The authors  
 would also like to thank Dr James McGregor of the University of  
 Sheffield for his advice into the interpretation of the PPC results.

## 50 References

- 1 S. Arrhenius, *Z. Phys. Chem.*, 1887, **1**, 631–648.
- 2 F. Hofmeister, *Arch. Exp. Pathol. Pharmacol.*, 1888, **24**,  
247–260.
- 3 F. Hofmeister, *Arch. Exp. Pathol. Pharmacol.*, 1888, **25**, 1–30.

- 4 W. Kunz, J. Henle and B. W. Ninham, *Curr. Opin. Colloid  
Interface Sci.*, 2004, **9**, 19–37.
- 5 A. Heydweiller, *Ann. Phys.*, 1910, **33**, 145–185.
- 6 W. M. Cox and J. H. Wolfenden, *Proc. R. Soc. London, Ser. A*,  
1934, **92**, 475–488.
- 7 R. W. Gurney, *Ionic Processes in Solution*, McGraw-Hill, New  
York, 1953.
- 8 A. W. Omta, M. F. Kropman, S. Woutersen and H. J. Bakker,  
*Science*, 2003, **301**, 347–349.
- 9 R. Mancinelli, A. Botti, F. Bruni, M. A. Ricci and A. K. Soper,  
*Phys. Chem. Chem. Phys.*, 2007, **9**, 2959–2967.
- 10 S. J. Irudayam and R. H. Henchman, *J. Chem. Phys.*, 2013,  
**137**, 034508.
- 11 J. W. Bye and R. J. Falconer, *J. Phys. Chem. B*, 2014, **118**,  
4282–4286.
- 12 L. Ter-Minassian, J. C. Petit, N. Vankiet and C. Brunaud,  
*J. Chim. Phys.*, 1970, **67**, 265–269.
- 13 L. Ter-Minassian and F. Milliou, *J. Phys. E: Sci. Instrum.*,  
1983, **16**, 450–455.
- 14 S. L. Ranzio, *J. Phys. E: Sci. Instrum.*, 1984, **11**, 1058–1061.
- 15 S. L. Ranzio, *Thermochim. Acta*, 1997, **300**, 29–41.
- 16 P. Kujawa and F. M. Winnik, *Macromolecules*, 2001, **34**,  
4130–4135.
- 17 L. N. Lin, J. F. Brandts, J. M. Brandts and V. Plotnikov, *Anal.  
Biochem.*, 2002, **302**, 144–160.
- 18 J. D. Batchelor, A. Olteanu, A. Tripathy and G. J. Pielak,  
*J. Am. Chem. Soc.*, 2004, **126**, 1958–1961.
- 19 R. Ravindra and R. Winter, *Z. Phys. Chem.*, 2003, **217**, 1221–1243.
- 20 W. Dzwolak, R. Ravindra, J. Lendermann and R. Winter,  
*Biochemistry*, 2003, **42**, 11347–11355.
- 21 C. Nicolini, R. Ravindra, B. Ludolph and R. Winter, *Biophys.  
J.*, 2004, **86**, 1385–1392.
- 22 R. Ravindra and R. Winter, *ChemPhysChem*, 2004, **5**,  
566–571.
- 23 R. Ravindra, C. Royer and R. Winter, *Phys. Chem. Chem.  
Phys.*, 2004, **8**, 1938–1943.
- 24 L. Mitra, N. Smolin, R. Ravindra and R. Winter, *Phys. Chem.  
Chem. Phys.*, 2006, **8**, 1249–1265.
- 25 R. Winter, D. Lopes, S. Grundzielanek and K. Voggt, *J. Non-  
Equilib. Thermodyn.*, 2007, **32**, 41–97.
- 26 A. Cooper, D. L. Cameron, J. Jakus and G. W. Pettigrew,  
*Biochem. Soc. Trans.*, 2007, **35**, 1547–1550.
- 27 D. L. Cameron, J. Jakus, S. R. Pauleta, G. W. Pettigrew and  
A. Cooper, *J. Phys. Chem. B*, 2010, **114**, 16228–16235.
- 28 A. D. Tsamaloukas, N. K. Pyzocha and G. I. Makhatazde,  
*J. Phys. Chem. B*, 2010, **114**, 16166–16170.
- 29 M. Nazari, H. Y. Fan and H. Heerklotz, *Langmuir*, 2012, **28**,  
14129–14136.
- 30 N. Tamai, Y. Nambu, S. Tanaka, M. Goto, H. Matsuki and  
S. Kaneshina, *Colloids Surf., B*, 2012, **92**, 232–239.
- 31 H. Y. Fan, M. Nazari, S. Chowdury and H. Heerklotz,  
*Langmuir*, 2011, **27**, 1693–1699.
- 32 G. Rayan, A. D. Tsamaloukas, R. B. Macgregor and  
H. Heerklotz, *J. Phys. Chem. B*, 2009, **113**, 1738–1742.
- 33 A. I. Dragan, D. J. Russel and P. L. Privalov, *Biopolymers*,  
2009, **91**, 95–101.

- 1 34 F. J. Millero, *Chem. Rev.*, 1971, **71**, 147–176.
- 35 Y. Marcus, *Ions Properties*, CRC Press, Boca Raton, 1997.
- 36 G. S. Kell, *J. Chem. Eng. Data*, 1967, **12**, 66–69.
- Q4 37 H. Ohtaki and T. Radai, *Chem. Rev.*, **93**, 1157–1204.
- 5 38 S. H. Lee and J. C. Rasaiah, *J. Phys. Chem.*, 1996, **100**, 1420–1425.
- 39 D. R. Lide, *CRC Handbook of Chemistry and Physics*, CRC Press, Boca Raton, 88th edn, 2008.
- 40 B. Hribar, N. T. Southall, V. Vlachy and K. A. Dill, *J. Am. Chem. Soc.*, 2002, **124**, 12302–12311.
- 10 41 F. J. Millero and J. D. Sharp, *J. Chem. Eng. Data*, 2013, **58**, 3458–3463.
- 42 H. J. Bakker, *Chem. Rev.*, 2008, **108**, 1456–1473.
- 43 I. A. Heisler, K. Mazur and S. R. Meech, *J. Phys. Chem. B*, 2011, **115**, 1863–1973.
- 15 44 M. Heyden, E. Bründermann, U. Heugen, G. Niehues, D. M. Leitner and M. Havenith, *J. Am. Chem. Soc.*, 2008, **130**, 5773–5779.
- 20
- 25
- 30
- 35
- 40
- 45
- 50
- 55
- 45 K. J. Tielrooij, N. Garcia-Araez, M. Bonn and H. J. Bakker, *Science*, 2010, **328**, 1006–1009.
- 46 M. Heyden, E. Bründermann, U. Heugen, G. Niehues, D. M. Leitner and M. Havenith, *J. Am. Chem. Soc.*, 2008, **130**, 5773–5779. 5
- 47 T. Ding, R. Li, J. A. Zeitler, T. L. Huber, L. F. Gladden, A. P. J. Middelberg and R. J. Falconer, *Opt. Express*, 2010, **18**, 27431–27444.
- 48 S. Ebbinghaus, S. J. Kim, M. Heyden, X. Yu, U. Heugen, M. Gruebele, D. M. Leitner and M. Havenith, *Proc. Natl. Acad. Sci. U. S. A.*, 2007, **104**, 20749–20752. 10
- 49 B. Born, H. Weingärtner, E. Bründermann and M. Havenith, *J. Am. Chem. Soc.*, 2009, **131**, 3752–3755.
- 50 J. W. Bye, S. C. Meliga, D. Ferachou, J. A. Zeitler and R. J. Falconer, *J. Phys. Chem. A*, 2014, **118**, 83–88. 15
- 51 G. I. Makhatadze, V. N. Medvedkin and P. L. Privalov, *Biopolymers*, 1990, **30**, 1001–1010.