The Journal of Chemical Physics

Thermodiffusion of aqueous solutions of various potassium salts

Cite as: J. Chem. Phys. **154**, 084506 (2021); https://doi.org/10.1063/5.0038039
Submitted: 18 November 2020 . Accepted: 04 February 2021 . Published Online: 26 February 2021

Shilpa Mohanakumar, Jutta Luettmer-Strathmann, and Simone Wiegand

COLLECTIONS

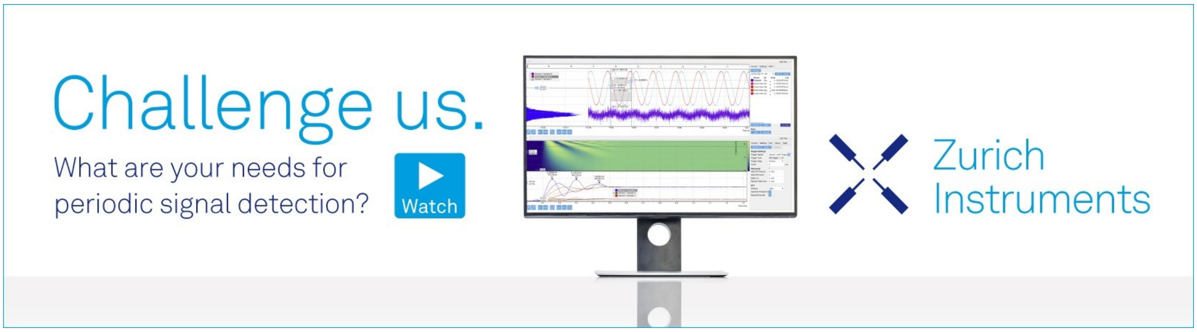
Paper published as part of the special topic on Special Collection in Honor of Women in Chemical Physics and Physical Chemistry

ARTICLES YOU MAY BE INTERESTED IN

Recent progress in simulating microscopic ion transport mechanisms at liquid–liquid interfaces
The Journal of Chemical Physics **154**, 080901 (2021); https://doi.org/10.1063/5.0039172

Can we define a unique microscopic pressure in inhomogeneous fluids?
The Journal of Chemical Physics **154**, 084502 (2021); https://doi.org/10.1063/5.0044487

Generalized equation of state for fluids: From molecular liquids to colloidal dispersions
The Journal of Chemical Physics **154**, 084902 (2021); https://doi.org/10.1063/5.0037630



AIP Publishing

J. Chem. Phys. **154**, 084506 (2021); https://doi.org/10.1063/5.0038039 **154**, 084506

The Journal of Chemical Physics ARTICLE scitation.org/journal/jcp

Thermodiffusion of aqueous solutions of various potassium salts

Cite as: J. Chem. Phys. 154, 084506 (2021); doi: 10.1063/5.0038039
Submitted: 18 November 2020 • Accepted: 4 February 2021 •

Shilpa Mohanakumar,[1] **Jutta Luettmer-Strathmann,**[2,a)] **and Simone Wiegand**[1,b)]

AFFILIATIONS

[1] IBI-4: Biomacromolecular Systems and Processes, Forschungszentrum Jülich GmbH, D-52428 Jülich, Germany
[2] Department of Physics and Department of Chemistry, The University of Akron, Akron, Ohio 44325-4001, USA

Note: This paper is part of the JCP Special Collection in Honor of Women in Chemical Physics and Physical Chemistry.
[a)] **Electronic mail:** jutta@uakron.edu
[b)] **Also at**: Chemistry Department – Physical Chemistry, University Cologne, D-50939 Cologne, Germany.
Author to whom correspondence should be addressed: s.wiegand@fz-juelich.de

ABSTRACT

Thermophoresis or thermodiffusion has become an important tool to monitor protein–ligand binding as it is very sensitive to the nature of solute–water interactions. However, the microscopic mechanisms underlying thermodiffusion in protein systems are poorly understood at this time. One reason is the difficulty to separate the effects of the protein system of interest from the effects of buffers that are added to stabilize the proteins. Due to the buffers, typical protein solutions form multicomponent mixtures with several kinds of salt. To achieve a more fundamental understanding of thermodiffusion of proteins, it is therefore necessary to investigate solutions of buffer salts. For this work, the thermodiffusion of aqueous potassium salt solutions has been studied systematically. We use thermal diffusion forced Rayleigh scattering experiments in a temperature range from 15 °C to 45 °C to investigate the thermodiffusive properties of aqueous solutions of five potassium salts: potassium chloride, potassium bromide, potassium thiocyanate, potassium acetate, and potassium carbonate in a molality range between 1 mol/kg and 5 mol/kg. We compare the thermophoretic results with those obtained for non-ionic solutes and discuss the thermophoresis of the salts in the context of ion-specific solvation according to the Hofmeister series.

I. INTRODUCTION

Thermophoresis, also known as thermodiffusion or the Ludwig–Soret effect, is sensitive to the nature of solute–solvent interactions.[1,2] Nowadays, there are two major applications of this effect in aqueous solutions of biological and biocompatible compounds. The first is the accumulation of molecules in thermophoretic traps by a combination of thermodiffusion and convection.[3,4] The second application is based on the change in the thermophoretic response of a protein when a ligand binds.[5,6] This is the operating principle of MicroScale Thermophoresis (MST) that allows the determination of binding constants.[5] The origin for the change in the thermophoretic behavior of the molecules upon binding is not understood on a microscopic level. Recent studies suggest that changes in the hydration layer of the protein upon ligand binding and electrostatic effects influence the thermophoretic response.[2,6,7]

In a macroscopic description, the diffusion flux $\vec{j}$ in a binary fluid of mass density ρ not only originates from a concentration but also from a temperature gradient,

$$\vec{j} = -\rho D \nabla w - \rho w(1-w) D_T \nabla T, \tag{1}$$

where w is the mass fraction of the solute, and D and D_T are mass and thermal diffusion coefficients, respectively. In the steady state with $\vec{j} = 0$, the Soret coefficient $S_T = D_T/D$ is proportional to the established concentration difference divided by the applied temperature difference. S_T can be positive indicating that the solute accumulates in the colder region (thermophobic response) or negative indicating that the solute moves toward the warmer region (thermophilic response).[2,8]

Thermophoresis of protein–ligand systems relevant to biomedical applications is complicated as those systems are stabilized in buffer solutions containing a variety of salts. This makes protein solutions examples of multi-component mixtures, a class of systems known to have complex thermodiffusive properties.[9] In addition, salt concentrations in protein solutions are typically low to moderate (physiological concentration is 150 mM) and beyond the Debye–Hückel and Poisson–Boltzmann approximations. To gain a better understanding of the thermophoretic response of protein–ligand systems, it is therefore essential to separate the effects of the protein system of interest from the effects of the buffer. As a first step, we investigate thermal diffusion in aqueous salt solutions in this work.

For salts in protein solutions, it is well known that not just the charges but the types of the ions affect protein solubility, stability, and function. Ion specific effects are also important in aqueous salt solutions and may be described by the Hofmeister series,[10,11] which ranks ions according to their degree of hydration.[11] In general, ion specific effects are larger for anions than for cations. Since hydration/solvation dominates the thermodiffusive behavior of non-ionic solutes in water, we expect differences in ion-specific hydration to lead to differences in thermophoretic behavior. Furthermore, salts are known to modify the dynamics and thermodynamics of aqueous solutions,[12] which will certainly have an impact on the heat transfer thus influencing thermodiffusion. To explore these effects, we focus in this work on salts with a common cation and a series of anions. In the following, we briefly summarize what is known about the thermophoresis of ionic and non-ionic water soluble solutes.

Ionic water soluble solutes: The majority of the recent thermophoretic studies of charged systems concentrate on large solutes such as (bio)macromolecules and colloids.[13–24] So far, there are no recent systematic temperature and concentration dependent studies of aqueous salt solutions. Almost a century ago, Tanner reported positive Soret coefficients for more than 20 different salts as a function of concentration at a fixed temperature around 35 °C.[25] In his studies, S_T of half of the investigated salts increased with increasing salt concentration, while S_T of the other salts showed a decrease. An unusual concentration dependence of S_T has been reported by Gaeta *et al.*[26] for sodium and potassium chloride. They found two sign inversions and a minimum of S_T in a very low concentration range of the order 10^{-1} mol/L. A more recent study[27] could not reproduce this observation because it was not possible to get reliable data below 0.5 mol/L. Another indication for a minimum of S_T as a function of concentration was observed experimentally[28] and by computer simulations[1] for lithium chloride.

Non-ionic water soluble solutes: Hydrogen-bond contributions to the Soret effect have been systematically investigated in recent years.[2] As illustrated in Fig. 1, a weakening of hydrogen bonds between the solute molecules and water leads to an increase in S_T and a decrease in $\Delta S_T(\Delta T) = S_T(T + \Delta T) - S_T(T)$, the change of S_T in a certain temperature range ΔT. It turns out that $\Delta S_T(\Delta T)$ for many systems shows a clear correlation with the logarithm of a partition coefficient P, which is a measure for the hydrophilicity of the solute.[2] Most commonly P describes the

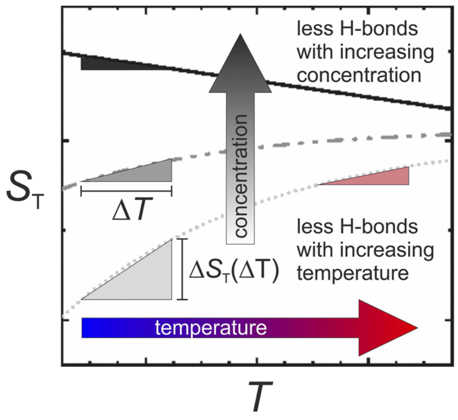


FIG. 1. Illustration of the temperature dependence of the Soret coefficient S_T for diluted and concentrated non-ionic solutes. The lines represent Soret coefficients for high (solid), intermediate (dashed-dotted), and low (dotted) concentrations. The colored triangles illustrate $\Delta S_T(\Delta T) = S_T(T + \Delta T) - S_T(T)$, the change of S_T in a certain temperature range ΔT. By increasing the solute concentration or the temperature, the number of hydrogen bonds between the solute and water is reduced. This leads to an increase in S_T and a decrease in $\Delta S_T(\Delta T)$.

concentration ratio in the two phases 1-octanol and water ($c_{\text{octanol}}/c_{\text{water}}$). The influence of temperature on S_T can be described by an equation proposed by Iacopini and Piazza,[15]

$$S_T^{\text{hyd}} = S_T^{\infty}\left[1 - \exp\left(\frac{T^* - T}{\tilde{T}}\right)\right], \tag{2}$$

where S_T^{∞}, T^*, and $\tilde{T}$ are empirical parameters that refer to the Soret coefficient at infinite temperature, the temperature at which a sign change of S_T^{hyd} occurs, and a parameter to describe the curvature, respectively. The superscript hyd indicates that S_T is mainly determined by hydration effects. This equation holds for numerous biological systems[2,29] but fails to describe the temperature dependence of certain substances such as ethanol[30] or ethylene glycol oligomers in water.[31] For solutes such as formamide, Eq. (2) holds at dilute concentrations and deviates at higher concentrations.[4] Note that a sign change of S_T with increasing temperature and concentration may occur if the solute shows thermophilic behavior at low concentrations and temperatures. The sign change with temperature was explained qualitatively using a concept of free energy minimization.[32]

Reichl *et al.*[21] expanded Eq. (2) by adding an electric double layer contribution (S_T^{DL}), a contribution from the Seebeck effect (S_T^{SE}), and an ideal gas term ($1/T$) to describe the Soret coefficient of DNA strands of different lengths in aqueous solutions of various salts as a function of temperature as follows:

$$S_T = S_T^{\text{DL}} + S_T^{\text{SE}} + S_T^{\text{hyd}} + 1/T. \tag{3}$$

While there are explicit expressions for S_T^{DL} and S_T^{SE}, there is no theory for hydration effects. Reichl *et al.*[21] accounted for those effects by applying Eq. (2) with adjustable parameters. In accordance with the Hofmeister series,[10] we expect that the hydration layer will depend on the chemical nature of the salt. Therefore, the hypothesis of the additivity of the various contributions to the Soret coefficient underlying Eq. (3) has to be carefully examined for different salts.

Wittko and Köhler[33] proposed another empirical ansatz to describe the temperature and concentration dependence of the Soret coefficient $S_T(m, T)$,

$$S_T(m,T) = \alpha(m)\beta(T) + S_T^i, \tag{4}$$

with polynomial serial expansions for $\alpha(m)$ and $\beta(T)$,

$$\begin{aligned} \alpha(m) &= a_0 + a_1 m + a_2 m^2 + a_3 m^3 + \cdots, \\ \beta(T) &= 1 + b_1(T - T_0) + b_2(T - T_0)^2 + \cdots. \end{aligned} \tag{5}$$

While Wittko and Köhler used the molar fraction as the concentration variable, we employ the molality m of the solution. The parameter T_0 is an arbitrary reference temperature, set to $T_0 = 25\,^\circ\mathrm{C}$, and S_T^i is a temperature and concentration independent constant. For non-polar systems, S_T^i can be expressed as

$$S_T^i = a_M \delta M + b_I \delta I, \tag{6}$$

where δM and δI are the mass and moment of inertia difference (between the solute and solvent), respectively, and a_M and b_I are adjustable parameters. Recent work shows that Eqs. (4)–(6) may be used to describe the Soret coefficients of amides in water. However, the relation between S_T^i and the mass and moment of inertia differences expressed in Eq. (6) fails in general for polar solutes.[34]

Some insight into microscopic processes underlying thermophoresis can be gained by discussing diffusion in the absence of temperature gradients. Due to ion pairing and complex formation, the diffusing entities in electrolyte solutions are changing with increasing concentration, which also implies that different entities respond to an applied temperature gradient. For example, in LiCl aqueous solutions, single ions diffuse at very low concentrations ($c < 0.1$ mol/L), ion pairs at intermediate concentrations (0.1 mol/L $< c <$ 1 mol/L), and ions with clouds of counter ions at high concentrations ($c > 1$ mol/L).[1] In experiments on aqueous KSCN solutions, Bian *et al.*[35] observed cluster formation, with clusters containing multiple anions and the cluster size increasing with concentration. In the case of organic salts, hydrogen bonding may also play an important role so that water molecules might be pulled with the moving entities thereby slowing down the diffusion. The theoretical description of diffusion in electrolyte solutions dates back to Nernst[36] and Onsager and Fuoss.[37] The latter employed the Debye–Hückel ion-atmosphere model to derive an expression for the diffusion coefficient that includes electrophoretic effects. This approach has been extended and improved over the years.[37–45] Most theoretical approaches predict that the diffusion coefficients of simple salts show a minimum at low concentrations (0.1 mol/L $< c^* <$ 1 mol/L) and a monotonous increase at higher concentrations. Theories based on the mean-spherical approximation are limited to concentrations less than about 2 mol/L because they assume that the solvent may be described as a dielectric continuum.[42] For the best description of experimental data, the hydration layer of the cations has to be taken into account, which is accomplished by assigning effective diameters to the cations.[42–44] For example, Gao *et al.*[43] described the cationic diameter as $\sigma^+ = \sigma_0^+ + \lambda_{\text{hyd}}(m)$, where σ_0^+ is the Pauling diameter and the parameter λ_{hyd}, being twice the thickness of the hydration layer, is assumed to depend on the salt concentration. They were able to reproduce the minimum in the mutual diffusion coefficient observed for many solutions of simple salts as well as the monotonous decay of the diffusion coefficient with concentration observed in aqueous ammonium nitrate solutions.[46] For this last system, the infinite dilution value λ_0 of λ_{hyd} was roughly a factor five larger than σ_0^+. Gao *et al.* assumed that the diffusion slows down due to the formation of ion pairs. However, as the obtained hydration layer thickness $\lambda_{\text{hyd}}^0/2$ at infinite dilution corresponds to a large number of water layers around the ion, other explanations might be considered.

To achieve a more fundamental understanding of thermodiffusion of aqueous salt solutions, we investigated the five potassium salts displayed in Fig. 2 together with their probable position according to the Hofmeister series.[10,11] For potassium chloride (KCl), potassium bromide (KBr), and potassium thiocyanate (KSCN), we expect that the thermophoretic behavior is predominantly determined by ionic effects, while for potassium acetate (CH_3COOK) and potassium carbonate (K_2CO_3), contributions due to hydrogen bonds should become more important. There are two reasons for including the divalent salt K_2CO_3: first, we can investigate how much its behavior deviates or follows the general trend of monovalent salts, and second, carbonate is very hydrophilic and allows us to cover a wide hydrophilicity range of anions. To investigate whether ionic and non-ionic contributions to the Soret coefficient can be separated, we performed systematic measurements in a temperature range from 15 °C to 45 °C and a concentration range of 1 mol/kg–5 mol/kg.

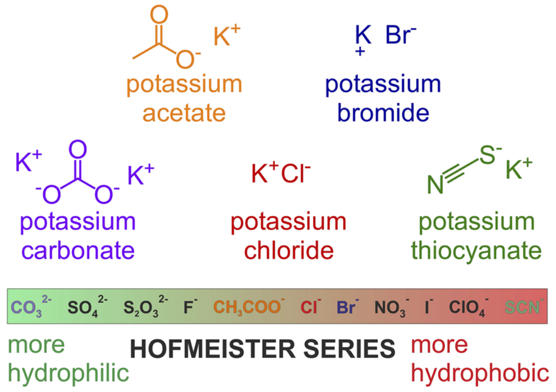


FIG. 2. Sketch of the investigated potassium salts and their probable position according to the Hofmeister series.[10,11] From left to right in the series, the salts generally become more hydrophobic.

II. METHODS AND MATERIAL

A. Sample preparation and properties

The investigated substances, potassium chloride, potassium bromide, potassium acetate, potassium carbonate, and potassium thiocyanate, were purchased from Sigma Aldrich and were used without further purification. The salts used were of purity ≥99%. The solutions were prepared with distilled and deionized water. Before filling solutions into an optical quartz cell (Hellma) with an optical path length of 0.2 mm, they were filtered through a 0.2 μm filter (Whatman Anotop 10). A stock solution of the highest concentration was prepared, and the required concentrations were made up from this stock solution. The stock solution was made by weighing the required amount of salt and adding water into it. We filled at least two cells and measured each cell at least two times at the same temperature.

A crucial point in the interpretation of S_T is the number of ionic species present in the solution. Since CH_3COOK and K_2CO_3 are salts of weak acids, the pH value and with it the valency of the anion are expected to depend on the salt concentration. We performed pH-measurements, calculated microspecies distributions, and found that, in the concentration range investigated in this work, only the anions CH_3COO^- and CO_3^{--} exist in the solution (cf. Sec. VI and Fig. 23 of the supplementary material). Thus, a distribution of anions with different valencies was ruled out.

The auxiliary parameters, concentration and temperature dependence of the refractive index, were measured independently. The refractive index as a function of concentration was measured with an Abbe refractometer (Anton Paar Abbemat MW) at a wavelength of 632.8 nm. We measured the refractive index for seven concentrations to determine $(\partial n/\partial c)_{p,T}$. The refractive index change on temperature, $(\partial n/\partial T)_{p,c}$, was measured interferometrically.[47] All data are shown in the supplementary material.

B. Thermal diffusion forced Rayleigh scattering

Infrared-Thermal diffusion forced Rayleigh scattering (IR-TDFRS), a transient grating technique, is employed to measure the thermodiffusion.[8,18] Two infrared laser beams are used to create a holographic grating inside the sample, which in turn creates a temperature grating due to the inherent absorption of water in that wavelength range. This leads to the migration of particles in the temperature gradient resulting in a concentration grating. Both temperature and concentration gradients give rise to changes in the refractive index of the sample. The heterodyne scattering intensity $\zeta_{het}(t)$ of the readout beam is measured and fitted with

$$\zeta_{\text{het}}(t) = 1 - \exp\left(-\frac{t}{\tau_{\text{th}}}\right) - A(\tau - \tau_{\text{th}})^{-1} \times \left\{\tau\left[1 - \exp\left(-\frac{t}{\tau}\right)\right] - \tau_{\text{th}}\left[1 - \exp\left(-\frac{t}{\tau_{\text{th}}}\right)\right]\right\}. \tag{7}$$

With the lifetimes $\tau_{th} = (D_{th}q^2)^{(-1)}$ and $\tau = (Dq^2)^{(-1)}$ of the temperature and concentration grating, respectively, where q, D_{th}, and D denote the grating wave vector, the thermal diffusivity, and the mutual diffusion coefficient, respectively. When the so-called contrast factors, the change of refractive index with temperature and concentration, $(\partial n/\partial T)_{c,p}$ and $(\partial n/\partial c)_{T,p}$, are known, the Soret coefficient can be calculated from the amplitude A as follows:

$$A = \left(\frac{\partial n}{\partial w}\right)_{p,T}\left(\frac{\partial n}{\partial T}\right)_{p,w}^{-1} S_T w(1 - w). \tag{8}$$

Low concentrations and small S_T values will result in a small amplitude of A, which makes the analysis difficult.

III. RESULTS

A. Concentration dependence

The concentration dependence of the Soret coefficient S_T for all considered aqueous salt solutions is shown in Fig. 3. The lines in Fig. 3 are fits to Eq. (4), which gives a satisfactory description of all studied systems. In all cases, third order and second order polynomials have been used to describe the concentration and temperature dependence of S_T, respectively. The simplest salts investigated in this study are potassium chloride (KCl) and potassium bromide (KBr). The concentration dependence of S_T of KCl solutions was studied

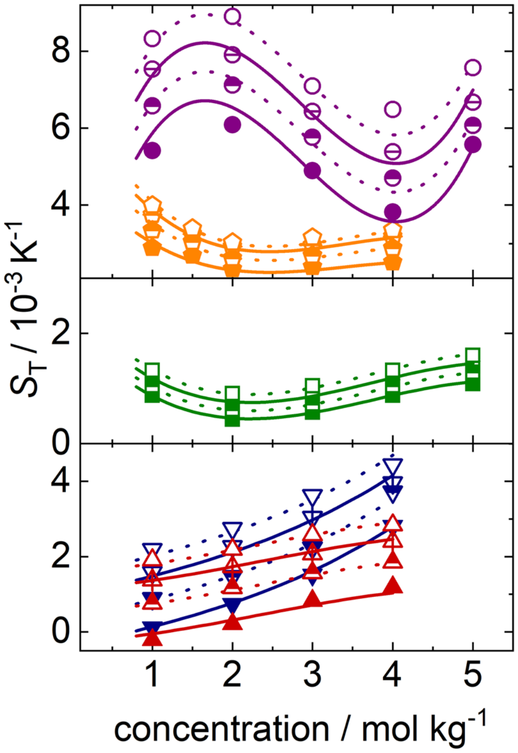


FIG. 3. Soret coefficients of all investigated systems as a function of concentration for temperatures between 15 °C and 45 °C. The markers indicate the temperature, filled symbols (15 °C), half filled symbols (25 °C), half crossed symbols (35 °C), and open symbols (45 °C), and the salts, KCl (red up-pointing triangles), KBr (blue down-pointing triangles), KSCN (green squares), CH_3COOK (orange pentagons), and K_2CO_3 (violet circles). The lines are fits to Eq. (4).

before by Gaeta *et al.*[26] at 30 °C and by Tanner[25] at 36.4 °C. Deviations between our experimental measurements at 30 °C and the reported values lie around 4%–51% with the highest difference observed for a molality of 4 mol/kg (Fig. 1 of the supplementary material). The study by Gaeta *et al.*[26] reported a minimum of S_T at 0.4 mol/L. Due to experimental constraints, we were not able to measure at concentrations below 1 mol/kg. Our S_T values show a monotonous increase with concentration for these two systems, and there is no indication for a minimum at low concentrations.

We also studied aqueous solutions of potassium thiocyanate (KSCN), potassium acetate (CH_3COOK), and potassium carbonate (K_2CO_3). In the case of KSCN, S_T initially shows a decrease with concentration up to 2 mol/kg and then increases again at higher concentrations. Such a minimum has been previously reported for some salts systems such as KCl, NaCl, and LiCl.[26,28] The range over which S_T varies with concentration for KSCN is smaller compared to that of KCl and KBr. In the forthcoming parts, we will refer to the concentration at which the minimum of S_T is observed as m^*. The other investigated salts, CH_3COOK, a monovalent salt, and K_2CO_3, a divalent salt, exhibit a more complex behavior of S_T. Both salts show a minimum in S_T with concentration as observed for KSCN. For CH_3COOK, S_T decays with concentration until m^* and saturates at higher concentrations. S_T of K_2CO_3, on the other hand, shows a weak increase between 1 mol/kg and 2 mol/kg, then it drops until a minimum is reached at $m^* \approx 4$ mol/kg, and then S_T increases once more at higher concentrations. The increase in S_T at high concentrations is a general observation, which holds for all investigated salt systems.

The diffusion coefficient D and its concentration dependence differ between the systems. On the basis of the obtained results, salts can be classified into two groups. KCl, KBr, and CH_3COOK belong to the first group, where D increases with concentration. The diffusion coefficient of the divalent salt K_2CO_3 has a slight decrease with concentration, which is more pronounced at higher temperatures. For KSCN, there is a clear decay in the magnitude of D with concentration at all temperatures. Figure 4 shows the diffusion coefficients of KCl and KSCN as two representatives of the two classes at 25 °C in comparison with literature results.[48–50] The measured diffusion coefficients for all potassium salts and temperatures are shown in the supplementary material.

The concentration dependence of the thermodiffusion coefficient D_T is similar to that of S_T. In the case of KSCN, K_2CO_3, and CH_3COOK, D_T shows a minimum, as was also observed for S_T. For CH_3COOK and K_2CO_3, the spread of D_T observed at the highest temperature of 45 °C is a factor two to three larger compared to that at 15 °C. All results for D_T are included in the supplementary material.

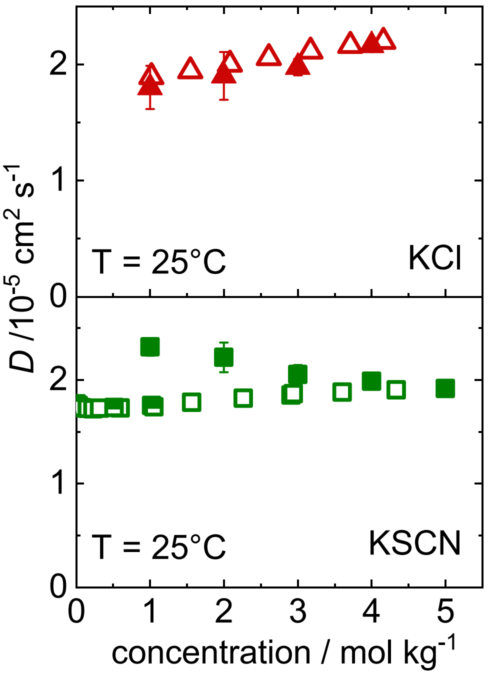


FIG. 4. Diffusion coefficients of KCl (red triangles) and KSCN (green squares) compared with literature values. Filled symbols correspond to our results, and open and half filled symbols correspond to literature results for KSCN by Mitchell *et al.*[48] (open squares) and Ribeiro *et al.*[49] (half filled squares) and for KCl by Gosting (open triangles).[50]

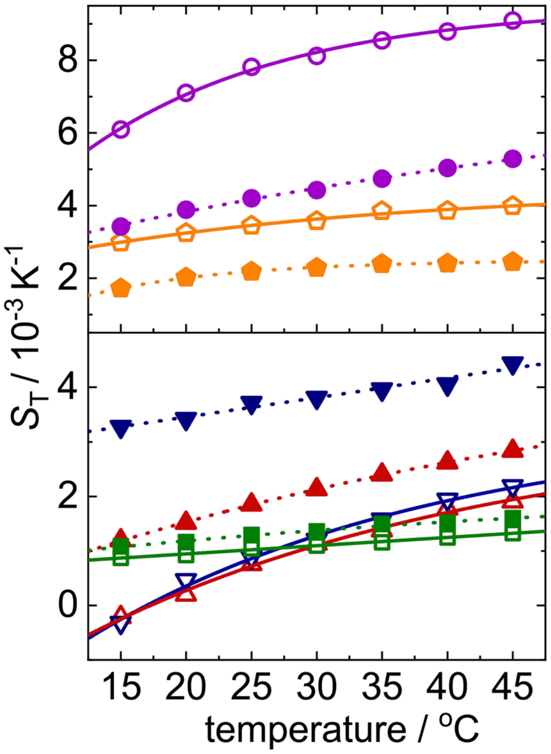


FIG. 5. Soret coefficients as a function of temperature for all investigated aqueous solutions of potassium salts at 4 mol/kg (solid symbols) and 1 mol/kg (open symbols): KCl (red up-pointing triangles), KBr (blue down-pointing triangles), KSCN (green squares), CH_3COOK (orange pentagons), and K_2CO_3 (violet circles). The lines are fits to Eq. (2).

B. Temperature dependence

The Soret coefficient against temperature for the lowest and highest concentration of 1 mol/kg (open symbols) and 4 mol/kg (solid symbols) of the studied potassium salts in water is shown in Fig. 5. Curves are fitted according to Eq. (2). For all studied systems, S_T shows an increase with temperature indicating a more thermophobic behavior with increasing temperature. A more detailed look into the temperature dependence of S_T and its change from low to high concentrations suggest that the investigated systems can be divided into two groups. For salts such as KCl, KBr, and KSCN, the magnitude of S_T increases with concentration, while the temperature dependence of S_T, characterized by $\Delta S_T(\Delta T)$ (cf. Sec. I), shows a decrease with increasing concentration. Note that $\Delta S_T(\Delta T)$ of KSCN is almost concentration independent, and its temperature dependence is weak. The scenario is different for K_2CO_3 and CH_3COOK. For these salts, the magnitude of S_T decreases with increasing concentration. While the temperature dependence of S_T is weak for CH_3COOK at both concentrations, for K_2CO_3, $\Delta S_T(\Delta T)$ decreases with concentration. The thermal diffusion coefficient D_T behaves similar to S_T and shows a monotonous increase with temperature. The temperature dependence of the diffusion coefficient D is dominated by the decrease in viscosity with increasing temperature leading to a monotonous increase of D with temperature for all systems (see the supplementary material for more details).

IV. DISCUSSION

A. Concentration dependence

1. Soret coefficient: Empirical fitting

As mentioned in Sec. I, the Soret coefficient of nonpolar systems can be described successfully with Eq. (4), and the temperature and concentration independent parameter S_T^i can be expressed as a function of differences of mass and moment of inertia of the solute and solvent [see Eq. (6)]. We applied Eq. (4) to describe the temperature and concentration dependence of the investigated aqueous potassium salt solutions and determined S_T^i from fits to our experimental data. Additionally, we have included previously investigated aqueous solutions of amides.[34] To compare with Eq. (6), we calculated absolute mass and moment of inertia differences as described in the supplementary material. The fitting of S_T^i to Eq. (6) yields $a_M = (-1.2 \pm 0.1)\ \mathrm{K^{-1}\ g\ mol^{-1}}$ and $b_I = (-2.1 \pm 0.4)\ \mathrm{K^{-1}\ g\ mol^{-1}}\text{Å}^2$. Rutherford[51] and Debuschewitz and Köhler[52] analyzed S_T^i for benzene systems. Converted to absolute mass and moment of inertia differences (see the supplementary material), Rutherford's values for substituted benzene systems are $a_M = (-1.0 \pm 0.1)\ \mathrm{K^{-1}\ g\ mol^{-1}}$ and $b_I = (-1.5 \pm 0.4)\ \mathrm{K^{-1}\ g\ mol^{-1}}\text{Å}^2$ and those by Debuschewitz and Köhler for benzene–cyclohexane mixtures are $a_M = (-1.1 \pm 0.1)\ \mathrm{K^{-1}\ g\ mol^{-1}}$ and $b_I = (-3.5 \pm 0.4)\ \mathrm{K^{-1}\ g\ mol^{-1}}\text{Å}^2$. Our values are close to the literature values.

Figure 6 shows the correlation between the calculated $S_T^i(\mathrm{calc})$ using a_M and b_I with Eq. (6) and S_T^i obtained from the fit of the experimental data according to Eq. (4). The linear regression of $S_T^i(\mathrm{calc})$ vs S_T^i results in a regression coefficient of $R = 0.7$. The amide solutes have comparatively a low mass difference and do not vary much among themselves in terms of S_T^i. The masses of the potassium salts cover a larger range: KCl shows the highest negative value, whereas K_2CO_3 (divalent salt) has the highest positive value of S_T^i.

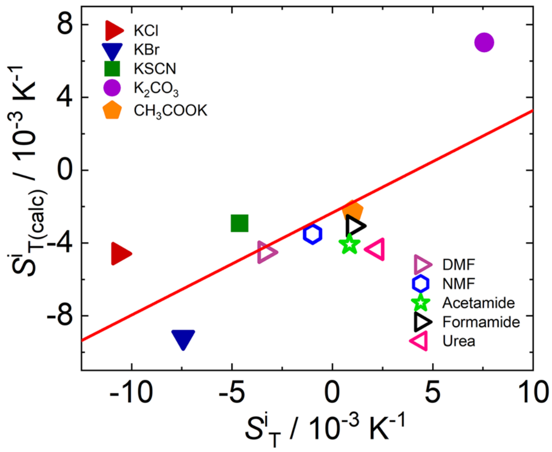


FIG. 6. Comparison of the constant contribution to the Soret coefficient, S_T^i, determined from fits of experimental data to Eq. (4) with values calculated from the correlation $S_T^i(calc) = a_M\delta M + b_I\delta I$ with $a_M = -1.2\ \mathrm{K^{-1}\ g\ mol^{-1}}$ and $b_I = -2.1\ \mathrm{K^{-1}\ g\ mol^{-1}}\text{Å}^2$ for all systems investigated in this work and for aqueous solutions of amides.[34] The solid line represents a linear regression as discussed in the text.

In a recent study of aqueous solutions of amides,[34] it was found that S_T^i decays linearly with log *P*, where log *P* is a parameter describing the hydrophilicity of the solute molecule, determining the interactions with water. Notice that the hydrophilicity scale defined by log *P* is not completely identical to Hofmeister's order. In particular, the SCN^- anion is not the least hydrophilic anion but slightly more hydrophilic than Cl^- and Br^- according to the log *P*-scale. To study whether a similar dependence holds for potassium salts, we present in Fig. 7 S_T^i values as a function of log *P* for all investigated salts. For

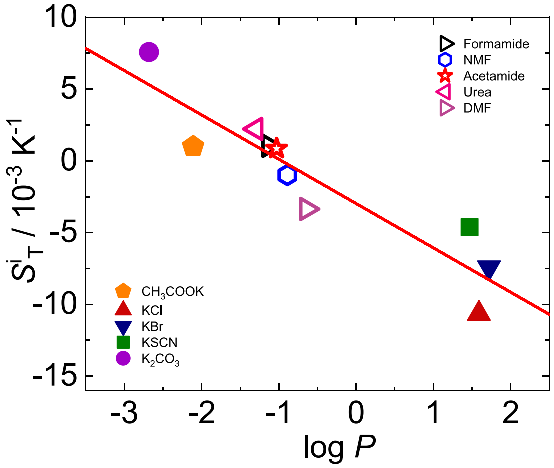


FIG. 7. S_T^i values for all investigated systems as a function of log *P* containing ionic and non-ionic contributions.

comparison, we include also previously investigated amide systems. Note that, for salts, log P has contributions from ionic and nonionic species. S_T^i shows a decrease with log P, and the linear correlation leads to a slightly better regression coefficient of $R = 0.9$ compared to the fit using a_M and b_I [cf. Fig. (6)]. This confirms that, in the case of polar substances, the thermophoretic behavior is more influenced by specific interactions than by physical parameters such as mass and moment of inertia. Due to the strong correlation between S_T^i and log P for ionic and non-ionic water soluble solutes, we suggest expressing S_T^i by

$$S_T^i = \gamma_P \log P + \sigma_{\text{intercept}}, \tag{9}$$

where the parameter γ_P represents the slope obtained in a fit of the data to a straight line and $\sigma_{\text{intercept}}$ is the intercept. We find $\gamma_P = (-3.1 \pm 0.5) \times 10^{-3}\ \text{K}^{-1}$ and $\sigma_{\text{intercept}} = (-3.0 \pm 0.7) \times 10^{-3}\ \text{K}^{-1}$. The correlation between log P and S_T^i may be related to the solute's ability to form hydrogen bonds. Consequently, this relation is probably limited to molecules, which are small enough not to coil or fold, so that the entire surface of the molecules is accessible by the solvent. Although there is certainly also a correlation between S_T^i and δM and δI, it is not possible to separate this contribution from the influence of the solute–water interactions described by log P.

Another relevant parameter obtained from a fit to Eq. (4) is b_1 describing the temperature dependence in first order. For amide systems, it was observed that b_1 increases non-linearly with log P and the b_1-values spread over a three-times larger range compared to non-polar systems.[34] If we include the b_1-values of potassium salts, we can no longer identify a correlation between b_1 and log P (cf. Fig. 24 of the supplementary material). While in the case of the amide systems the solute molecule with the most negative log P-value shows also the most negative b_1-value, we find for CH_3COOK with log $P = -2.1$ a positive b_1. Therefore, the correlation between b_1 and the capacity of the solute to form hydrogen bonds are altered by charge effects.

2. Diffusion coefficient

Since the amplitude of the concentration signal [cf. Eq. (8)] becomes very small below 0.5 mol/kg, we could not obtain reliable values for the diffusion coefficient in the concentration range where typically a minimum can be observed. The minimum of D with concentration is often related to ion-pair formation, which reduces the movement of the ions.[48] Apart from ion pairing, solvent–solute association can also contribute to the behavior of D. When solute–solvent interactions are more favored, the probability of ions being surrounded by solvent molecules increases leading to a larger size and reduced diffusion coefficient of the entity.[48,53]

In the intermediate to high concentration range investigated in this work, the diffusion coefficients of aqueous solutions of KCl and KBr show a monotonous increase with concentration for all temperatures. Except for the lowest temperature, the same holds true for the diffusion coefficient of CH_3COOK in water (cf. Fig. 14 of the supplementary material). This observed trend follows the theoretically predicted behavior for simple aqueous electrolyte solutions.[37,40,43] While for KCl and KBr the concentration dependent slope is almost the same for all temperatures, the slope decreases for CH_3COOK with decreasing temperature. At the lowest investigated temperature of $T = 15\,^\circ$C, the diffusion coefficient of CH_3COOK is almost temperature independent. This slightly different behavior might be related to the capability to form hydrogen bonds between the two oxygens of the acetate group of CH_3COO^- and water. With increasing temperature, the influence due to the hydrogen bonds diminishes so that at higher temperatures the diffusion is dominated by the charge of the salt. This idea is supported by the observation that the measured diffusion coefficients of non-ionic amides in water also show a decrease with increasing concentration (cf. Fig. 8). For most of the investigated amides, the derivative of the diffusion coefficient with concentration decreases slightly with lowering the temperature (cf. Fig. 27 of the supplementary material).

The measured diffusion coefficients of aqueous K_2CO_3 and KSCN solutions decrease with concentration (cf. Figs. 4 and 18 of the supplementary material). In the case of KSCN, the derivative of the diffusion coefficient with concentration is temperature independent within the error bars. For the divalent salt K_2CO_3, the negative slope becomes more pronounced with increasing temperature. The decreasing diffusion coefficient of KSCN with concentration can be explained by cluster formation, which was reported by Bian *et al.*[35] In the investigated concentration regime between 1 mol/kg and 5 mol/kg, the percentage of ion clusters increases approximately from 30% to 70%, whereas also the number of anions in the cluster doubles from 3 to 6. Both effects will lead to a decrease in the mutual diffusion coefficient. The thermal diffusion and the Soret coefficient of KSCN show a minimum around 2 mol/kg. On the one hand, it is known that D_T is very sensitive to the solute–solvent interface. On the other hand, it is not expected that the water interfaces of the formed clusters change with concentration. This suggests that the minimum might be a concentration effect. While at low concentrations interactions between water and salt clusters dominate, at higher concentrations interactions between the clusters become more important. With K_2CO_3, we have a divalent

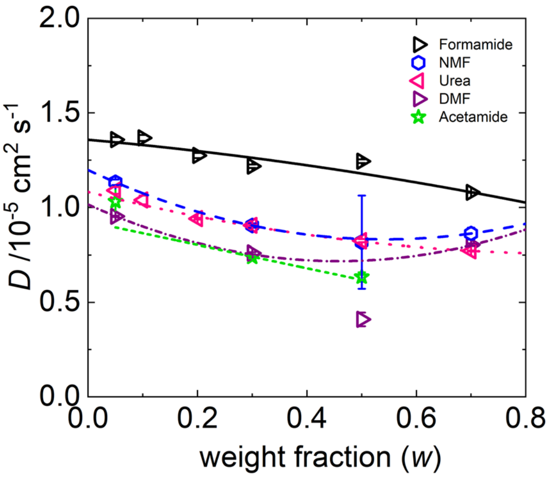


FIG. 8. Diffusion coefficients of various aqueous solutions of amides at $T = 20\,^\circ$C. The unpublished diffusion coefficients have been determined in the thermophoretic study by Niether *et al.*[34] The lines are a guide to the eye.

salt, which can also form hydrogen bonds. At this time, we can only conclude that this particular divalent salt does not follow the same trend as the monovalent salts and that more experiments are required.

B. Temperature dependence

As shown in Fig. 5, the temperature dependence of S_T of all salts, even those with a positive $\log P$, can be described by Eq. (2) at low and high concentrations. This is in contrast to the aqueous solutions of amides. Only S_T of the two most hydrophilic amides, urea and formamide, exhibited the typical temperature dependence at low concentrations in water, while S_T of the other amides shows a decrease with temperature.[34] Furthermore, for many non-ionic water soluble solutes, the change of the Soret coefficient with temperature $\Delta S_T(\Delta T)$ decays linearly with log P (cf. Fig. 7 of Ref. 34). The underlying physical reason for this correlation is the solutes' ability to form hydrogen bonds. In the case of the salts investigated here, the correlation between $\Delta S_T(\Delta T)$ and $\log P$ observed for non-ionic solutes cannot be confirmed (cf. Fig. 26 of the supplementary material). Note that only for two of the salts investigated here, potassium acetate and potassium carbonate, both being able to form hydrogen bonds and both being very hydrophilic, $\Delta S_T(\Delta T)$ shows a similar trend in respect of $\log P$ as the non-ionic amides (cf. Fig. 26 of the supplementary material).

The aqueous solutions of amides, which cannot be described by Eq. (2), tend to form micro-heterogeneities.[54–57] The physical reason is probably connected to their more hydrophobic nature leading to the formation of clusters instead of the formation of hydrogen bonds with water. Experiments and simulations on aqueous salt solutions[35,58–60] reveal the formation of ion clusters at concentrations above about 1 mol/kg.[58–60] However, for potassium salts, we do not observe a decay of the Soret coefficient with temperature as in the case of the non-ionic solutes. Ren *et al.*[60] simulated highly concentrated (16.7M) aqueous KSCN solutions over a wide range of temperatures (300 K–800 K) at constant density and investigated the cluster size distributions. They find shifts to larger clusters for the anions and to smaller clusters for the cations as the temperature increases. They also examine cluster size distributions as a function of concentration for a temperature of 300 K and find smaller clusters at lower concentrations. If the temperature trends persist at lower concentrations and for a system at constant pressure, one would expect a very small change in cluster size distribution over the temperature range investigated in this work. This suggests that the observed changes in the diffusion and Soret coefficients are due to thermodynamics and changes in the interactions at the interface between salt clusters and water.

One striking difference between non-ionic and ionic solutes is in the effect of concentration on the temperature dependence of the Soret coefficient, as illustrated in Fig. 9. For a typical non-ionic solute, the behavior of S_T changes from increasing with temperature to decreasing with temperature as the concentration increases. This is correlated with the solvation of the solutes, which decreases as the concentration increases. Only very hydrophilic non-ionic solutes have S_T values that increase with temperature for all concentrations. In contrast, the Soret coefficients of ionic solutes show the typical temperature dependence of very hydrophilic solutes over the entire concentration range. This can be explained by cluster formation and growth of the salts with increasing concentrations. Even at high salt concentrations, the clusters are hydrated by water since the fraction of ions in the interfaces decreases when more ions are part of larger clusters.

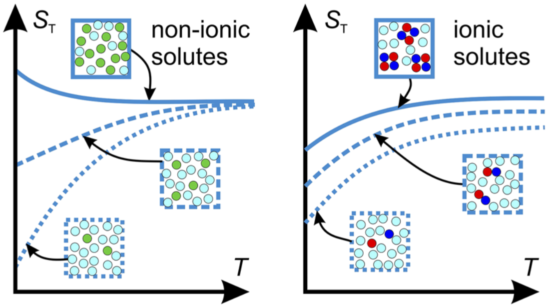


FIG. 9. Schematic comparison of the temperature dependence of S_T for non-ionic and ionic solutes at different concentrations: low (dotted line), intermediate (dashed line), and high (solid line).

V. CONCLUSION

Thermophoresis is an excellent tool to monitor protein–ligand binding as it is very sensitive to the nature of solute–solvent interactions. The process involves hydrophobic, hydrophilic, and ionic entities as chemical (side) groups of the proteins and ligands and as buffer components. In this work, we studied systematically a set of potassium salts to gain a better understanding of thermodiffusion in electrolyte solutions. We initiated the study of aqueous salt solutions to reduce the complexity compared to protein–ligand systems. However, due to the presence of charges and the complex nature of *water*, even aqueous salt solutions are complex systems. This study shows how sensitive the Soret effect is to the ion species.

For all salts studied in this work, it is possible to describe the temperature and concentration dependence of S_T with Eq. (4), an ansatz originally developed for non-polar binary mixtures. While for non-polar compounds, the temperature and concentration independent parameter S_T^i correlates well with mass and moment of inertia differences, for the salts, S_T^i is more closely correlated with $\log P$. The previously investigated amides also follow this relation, which suggests that solute–water interactions dominate mass and size effects for charged and polar systems. Other correlations[34] found for aqueous solutions of non-ionic solutes are no longer valid for salt solutions. In particular, the correlations between $\Delta S_T(\Delta T)$ and $\log P$ as well as $\Delta S_T(\Delta c)$ and $\log P$ fail in the case of salts (cf. Figs. 25 and 26 of the supplementary material).

Previous studies[21] express the Soret coefficient as a sum [cf. Eq. (3)] including two ionic contributions, one due to the electric double layer and another due to the Seebeck effect. The latter leads to an ion-specific offset, and the double layer contribution is constant for thin double layers (in the sub-nanometer range) expected at high salt concentrations. It is also assumed that the hydration contribution in Eq. (3) can be described by the empirical approach of Iacopini *et al.*[15] and is the same for all ions. For the high salt concentrations studied here, this assumption is not correct since we find an ion-specific effect on S_T that correlates with both the Hofmeister series and log P. This shows that, at higher salt concentrations, salt-specific properties become more important than the non-specific ionic contributions due to the double layer and the Seebeck effect.

To study the influence of the double layer thickness, very low salt concentrations between 2 mM and 20 mM would have to be investigated. To our best knowledge, there are no existing methods that work for small molecules in the millimolar range. Due to insufficient optical contrast, optical techniques such as beam deflection, thermal lens, and digital interferometry have similar problems to measure small molecules at low concentrations as the TDFRS method employed here. MicroScale thermophoresis (MST) requires fluorescent labeling, which would lead to inaccurate results for small molecules. Thermogravitational columns could be used to measure at concentrations up to one order of magnitude below our range, however, this is still too concentrated and requires measurement times several 100 times longer.

Another important question to address is what is diffusing. With increasing concentration, the diffusing entities change from single ions over ion pairs to ion clusters. The salt solutions investigated here are in the concentration range of ion clusters. For KSCN, it has been observed that the number and size of clusters increases with concentration.[35] This explains the decrease in the diffusion coefficient with increasing concentration, while the observed minima in D_T and S_T are more difficult to understand. A possible explanation could be that at higher concentrations, interactions between clusters become more important than cluster–water interactions, which dominate at lower concentrations. In addition, the interface between diffusing entity and solvent may change with concentration, which can have a pronounced effect on the thermophoretic properties. To achieve a deeper understanding of thermodiffusion in aqueous salt solutions, more systematic experiments need to be carried out, accompanied by computer simulations.

SUPPLEMENTARY MATERIAL

The supplementary material shows the diffusion and thermal diffusion coefficients and Soret for potassium bromide (KBr), potassium chloride (KCl), potassium carbonate (K_2CO_3), potassium acetate (CH_3COOK), and potassium thiocyanate (KCNS) in water at various temperatures, the refractive index contrast factors as a function of temperature, and the refractive index values as a function of temperature and concentration. pH dependence on concentration of CH_3COOK and K_2CO_3 is also shown. Fitting parameters of the investigated systems to Eqs. (4) and (5), dependence of b_1 on $\log P$(ionic + non-ionic), dependence of $\Delta S_T(c)$ and $\Delta S_T(T)$ on $\log P$(ionic + non-ionic), and selected diffusion coefficients of aqueous amide solutions from previous studies that have been used here for comparison have also been included.

DEDICATION

This paper honors Johanna (Anneke) Maria Henrica Levelt Sengers, who performed groundbreaking work on critical phenomena. Anneke has mentored and inspired many students, including one of the authors, to pursue careers in physical chemistry/chemical physics, during her career at NIST. She has received many awards such as the 2003 Women in Science Award and was elected to the National Academy of Sciences (NAS).

ACKNOWLEDGMENTS

We thank Fernando Bresme, Wim Briels, Sandra Greer, Doreen Niether, and Annette Schmidt for fruitful discussions. We are grateful to Jan Dhont for inspiring ideas and his generous support of our work. S.M. acknowledges support from the International Helmholtz Research School of Biophysics and Soft Matter (BioSoft). Calculator Plugins were used for calculation (of log *P* and pKa values), Marvin 16.5.2.0, 2016, ChemAxon (http://www.chemaxon.com).

DATA AVAILABILITY

The data that support the findings of this study are available within the article and its supplementary material and from the corresponding author upon reasonable request.

REFERENCES

[1] S. Di Lecce, T. Albrecht, and F. Bresme, "The role of ion-water interactions in determining the Soret coefficient of LiCl aqueous solutions," Phys. Chem. Chem. Phys. **19**, 9575–9583 (2017).

[2] D. Niether and S. Wiegand, "Thermophoresis of biological and biocompatible compounds in aqueous solution," J. Phys.: Condens. Matter **31**, 503003 (2019).

[3] P. Baaske, F. M. Weinert, S. Duhr, K. H. Lemke, M. J. Russell, and D. Braun, "Extreme accumulation of nucleotides in simulated hydrothermal pore systems," Proc. Natl. Acad. Sci. U. S. A. **104**, 9346–9351 (2007).

[4] D. Niether, D. Afanasenkau, J. K. G. Dhont, and S. Wiegand, "Accumulation of formamide in hydrothermal pores to form prebiotic nucleobases," Proc. Natl. Acad. Sci. U. S. A. **113**, 4272–4277 (2016).

[5] M. Jerabek-Willemsen, T. André, R. Wanner, H. M. Roth, S. Duhr, P. Baaske, and D. Breitsprecher, "Microscale thermophoresis: Interaction analysis and beyond," J. Mol. Struct. **1077**, 101–113 (2014).

[6] D. Niether, M. Sarter, B. W. Koenig, J. Fitter, A. M. Stadler, and S. Wiegand, "Thermophoresis: The case of streptavidin and biotin," Polymers **12**, 376 (2020).

[7] M. Sarter, D. Niether, B. W. Koenig, W. Lohstroh, M. Zamponi, N. H. Jalarvo, S. Wiegand, J. Fitter, and A. M. Stadler, "Strong adverse contribution of conformational dynamics to Streptavidin–Biotin binding," J. Phys. Chem. B **124**, 324–335 (2020).

[8] *Thermal Nonequilibrium Phenomena in Fluid Mixtures*, Lecture Note in Physics, edited by W. Köhler and S. Wiegand (Springer, Berlin, 1 edition, 2002), Vol. LNP584.

[9] W. Köhler and K. I. Morozov, "The Soret effect in liquid mixtures—A review," J. Non-Equilb. Thermodyn. **41**, 151–197 (2016).

[10] Y. Zhang and P. S. Cremer, "Interactions between macromolecules and ions: The Hofmeister series," Curr. Opin. Chem. Biol. **10**, 658–663 (2006).

[11] A. Salis and B. W. Ninham, "Models and mechanisms of Hofmeister effects in electrolyte solutions, and colloid and protein systems revisited," Chem. Soc. Rev. **43**, 7358–7377 (2014).

[12] M. Andreev, A. Chremos, J. de Pablo, and J. F. Douglas, "Coarse-grained model of the dynamics of electrolyte solutions," J. Phys. Chem. B **121**, 8195–8202 (2017).

[13] E. Bringuier and A. Bourdon, "Colloid transport in nonuniform temperature," Phys. Rev. E **67**, 011404 (2003).

[14] S. Duhr and D. Braun, "Why molecules move along a temperature gradient," Proc. Natl. Acad. Sci. U. S. A. **103**, 19678–19682 (2006).

[15] S. Iacopini, R. Rusconi, and R. Piazza, "The 'macromolecular tourist': Universal temperature dependence of thermal diffusion in aqueous colloidal suspensions," Eur. Phys. J. E **19**, 59–67 (2006).

[16] J. K. G. Dhont, S. Wiegand, S. Duhr, and D. Braun, "Thermodiffusion of charged colloids: Single-particle diffusion," Langmuir **23**, 1674–1683 (2007).

[17] J. K. G. Dhont and W. J. Briels, "Single-particle thermal diffusion of charged colloids: Double-layer theory in a temperature gradient," Eur. Phys. J. E **25**, 61–76 (2008).

[18] P. Blanco, H. Kriegs, M. P. Lettinga, P. Holmqvist, and S. Wiegand, "Thermal diffusion of a stiff rod-like mutant Y21M *fd*-virus," Biomacromolecules **12**, 1602–1609 (2011).

[19] A. Majee and A. Würger, "Collective thermoelectrophoresis of charged colloids," Phys. Rev. E **83**, 061403 (2011).

[20] K. A. Eslahian, A. Majee, M. Maskos, and A. Würger, "Specific salt effects on thermophoresis of charged colloids," Soft Matter **10**, 1931–1936 (2014).

[21] M. Reichl, M. Herzog, A. Götz, and D. Braun, "Why charged molecules move across a temperature gradient: The role of electric fields," Phys. Rev. Lett. **112**, 198101 (2014).

[22] B. T. Huang, M. Roger, M. Bonetti, T. J. Salez, C. Wiertel-Gasquet, E. Dubois, R. Cabreira Gomes, G. Demouchy, G. Mériguet, V. Peyre, M. Kouyaté, C. L. Filomeno, J. Depeyrot, F. A. Tourinho, R. Perzynski, and S. Nakamae, "Thermoelectricity and thermodiffusion in charged colloids," J. Chem. Phys. **143**, 054902 (2015).

[23] J. Burelbach, D. Frenkel, I. Pagonabarraga, and E. Eiser, "A unified description of colloidal thermophoresis," Eur. Phys. J. E **41**, 7 (2018).

[24] Z. Wang, D. Niether, J. Buitenhuis, Y. Liu, P. R. Lang, J. K. G. Dhont, and S. Wiegand, "Thermophoresis of a colloidal rod: Contributions of charge and grafted polymers," Langmuir **35**, 1000–1007 (2019).

[25] C. C. Tanner, "The Soret effect. Part 1," Trans. Faraday Soc. **23**, 75–95 (1927).

[26] F. S. Gaeta, G. Perna, G. Scala, and F. Bellucci, "Non-isothermal matter transport in sodium-chloride and potassium chloride aqueous solutions. 1. Homogeneous system (thermal-diffusion)," J. Phys. Chem. **86**, 2967–2974 (1982).

[27] F. Römer, Z. Wang, S. Wiegand, and F. Bresme, "Alkali halide solutions under thermal gradients: Soret coefficients and heat transfer mechanisms," J. Phys. Chem. B **117**, 8209–8222 (2013).

[28] J. Colombani, J. Bert, and J. Dupuy-Philon, "Thermal diffusion in (LiCl, RH$_2$O)," J. Chem. Phys. **110**, 8622–8627 (1999).

[29] Y. Kishikawa, S. Wiegand, and R. Kita, "Temperature dependence of Soret coefficient in aqueous and nonaqueous solutions of pullulan," Biomacromolecules **11**, 740–747 (2010).

[30] A. Königer, B. Meier, and W. Köhler, "Measurement of the Soret, diffusion, and thermal diffusion coefficients of three binary organic benchmark mixtures and of ethanol–water mixtures using a beam deflection technique," Philos. Mag. **89**, 907–923 (2009).

[31] K. Maeda, N. Shinyashiki, S. Yagihara, S. Wiegand, and R. Kita, "Ludwig-Soret effect of aqueous solutions of ethylene glycol oligomers, crown ethers, and glycerol: Temperature, molecular weight, and hydrogen bond effect," J. Chem. Phys. **143**, 124504 (2015).

[32] Z. Wang, H. Kriegs, and S. Wiegand, "Thermal diffusion of nucleotides," J. Phys. Chem. B **116**, 7463–7469 (2012).

[33] G. Wittko and W. Köhler, "On the temperature dependence of thermal diffusion of liquid mixtures," Europhys. Lett. **78**, 46007 (2007).

[34] D. Niether, H. Kriegs, J. K. G. Dhont, and S. Wiegand, "Peptide model systems: Correlation between thermophilicity and hydrophilicity," J. Chem. Phys. **149**, 044506 (2018).

[35] H. Bian, X. Wen, J. Li, H. Chen, S. Han, X. Sun, J. Song, W. Zhuang, and J. Zheng, "Ion clustering in aqueous solutions probed with vibrational energy transfer," Proc. Natl. Acad. Sci. U. S. A. **108**, 4737–4742 (2011).

[36] W. Nernst, "Zur Kinetik der in Lösung befindlichen Körper," Z. Phys. Chem. **2**, 613 (1888).

[37] L. Onsager and R. M. Fuoss, "Irreversible processes in electrolytes diffusion, conductance, and viscous flow in arbitrary mixtures of strong electrolytes," J. Phys. Chem. **36**, 2689–2778 (1932).

[38] H. J. V. Tyrrell and K. R. Harris, *Diffusion in Liquids* (Butterworths, London, 1984).

[39] M. J. Pikal, "Ion-pair formation and the theory of mutual diffusion in a binary electrolyte," J. Phys. Chem. **75**, 663–675 (1971).

[40] O. Bernard, T. Cartailler, P. Turq, and L. BIum, "Mutual diffusion coefficients in electrolyte solutions," J. Mol. Liq. **73-74**, 403–411 (1997).

[41] J. F. Dufrêche, O. Bernard, and P. Turq, "Mutual diffusion coefficients in concentrated electrolyte solutions," J. Mol. Liq. **96-97**, 123–133 (2002).

[42] S. Van Damme, J.-F. Dufrêche, and J. Deconinck, "Influence of ion properties on the equilibrium and transport properties of electrolyte solutions," J. Phys. Chem. B **110**, 1015–1019 (2006).

[43] G.-H. Gao, H.-B. Shi, and Y.-X. Yu, "Mutual diffusion coefficients of concentrated 1:1 electrolyte from the modified mean spherical approximation," Fluid Phase Equilib. **256**, 105–111 (2007).

[44] S. Van Damme and J. Deconinck, "Relaxation effect on Onsager coefficients of mixed strong electrolytes in the mean spherical approximation," J. Phys. Chem. B **111**, 5308–5315 (2007).

[45] A. C. F. Ribeiro, J. J. S. Natividade, A. J. M. Valente, and V. M. M. Lobo, "Diffusion of electrolytes and non-electrolytes in aqueous solutions: A useful strategy for structural interpretation of chemical systems," in *Advances in Kinetics and Mechanism of Chemical Reactions*, edited by G. E. Zaikov, A. J. M. Valente and L. L. Iordanskiĭ (Apple Academic Press, Oakville, Ont., Point Pleasant, N.J., 2013), pp. 21–33.

[46] G. J. Janz, G. R. Lakshminarayanan, M. P. Klotzkin, and G. E. Mayer, "Diffusion of silver nitrate in concentrated aqueous solutions," J. Phys. Chem. **70**, 536–539 (1966).

[47] A. Becker, W. Köhler, and B. Müller, "A scanning Michelson interferometer for the measurement of the concentration and temperature derivative of the refractive index of liquids," Ber. Bunsen-Ges. Phys. Chem. **99**, 600–608 (1995).

[48] J. P. Mitchell, J. B. Butler, and J. G. Albright, "Measurement of mutual diffusion coefficients, densities, viscosities, and osmotic coefficients for the system KSCN-H$_2$O at 25 °C," J. Solution Chem. **21**, 1115 (1992).

[49] A. C. F. Ribeiro, V. M. M. Lobo, and J. J. S. Natividade, "Diffusion coefficients in aqueous solutions of potassium sulfocyanate at 298.15 K," J. Mol. Liq. **94**, 61–66 (2001).

[50] L. J. Gosting, "A study of the diffusion of potassium chloride in water at 25° with the Gouy interference method," J. Am. Chem. Soc. **72**, 4418–4422 (1950).

[51] W. M. Rutherford, "Effect of mass distribution on the isotopic thermal diffusion of substituted benzenes," J. Chem. Phys. **81**, 6136–6139 (1984).

[52] C. Debuschewitz and W. Köhler, "Molecular origin of thermal diffusion in benzene plus cyclohexane mixtures," Phys. Rev. Lett. **87**, 055901 (2001).

[53] A. Katz and S. Ben-Yaakov, "Diffusion of seawater ions. Part II. The role of activity coefficients and ion pairing," Mar. Chem. **8**, 263–280 (1980).

[54] Y. Lei, H. Li, H. Pan, and S. Han, "Structures and hydrogen bonding analysis of *N,N*-dimethylformamide and *N,N*-dimethylformamide–water mixtures by molecular dynamics simulations," J. Phys. Chem. A **107**, 1574–1583 (2003).

[55] A. K. H. Weiss, T. S. Hofer, B. R. Randolf, A. Bhattacharjee, and B. M. Rode, "Hydrogen bond formation of formamide and *N*-methylformamide in aqueous solution studied by quantum mechanical charge field-molecular dynamics (QMCD-MD)," Phys. Chem. Chem. Phys. **13**, 12173–12185 (2011).

[56] V. Vasudevan and S. H. Mushrif, "Force field parameters for *N,N*-dimethylformamide (DMF) revisited: Improved prediction of bulk properties and complete miscibility in water," J. Mol. Liq. **206**, 338–342 (2015).

[57] J. A. Aguilar-Pineda, G. A. Méndez-Maldonado, E. Núñez-Rojas, and J. Alejandre, "Parametrisation of a force field of acetamide for simulations of the liquid phase," Mol. Phys. **113**, 2716–2724 (2015).

[58] S. A. Hassan, "Computer simulation of ion cluster speciation in concentrated aqueous solutions at ambient conditions," J. Phys. Chem. B **112**, 10573–10584 (2008).

[59] J.-H. Choi and M. Cho, "Ion aggregation in high salt solutions. II. Spectral graph analysis of water hydrogen-bonding network and ion aggregate structures," J. Chem. Phys. **141**, 154502 (2014).

[60] G. Ren, L. Chen, and Y. Wang, "Dynamic heterogeneity in aqueous ionic solutions," Phys. Chem. Chem. Phys. **20**, 21313–21324 (2018).