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ARTICLE TYPE

Cooperative hydration of carboxylate groups with alkali cations

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5 **We study the orientational dynamics of water molecules in solutions of formate salts using femtosecond mid-infrared spectroscopy. We observe that combining the formate ion with small cations like Na+ or Li+ leads to a cooperative effect on the water dynamics. This observation points at the**
10 **formation of solvent-separated ion pairs.**

The mutual binding of an ion and a molecule in an aqueous medium depends on the balance of their direct interactions and the interactions with the surrounding water molecules. In the field of biology the best known example of an experiment illustrating
15 the importance of the competition of these interactions is the study performed by Franz Hofmeister in 1888, in which he ranked a series of organic salts by their ability to "salt out" hen egg white protein from aqueous solution.[1] The interaction of proteins with water is governed by the hydration of the charged
20 molecular groups located at the protein surface, in particular of the negatively charged carboxylate groups.[2] The interaction of the carboxylate groups with water and/or positive counter-ions strongly influences protein stability, association and aggregation.[3, 4] The carboxylate groups also play an important
25 role in the conduction of protons by membrane proteins[5] and in the working mechanism of Na$^+$/K$^+$ ion pumps (Na$^+$/K$^+$-ATPase).[6] Here we report on a study of the combined effects of carboxylate groups and cations on the dynamics of water. To this purpose we study the orientational dynamics of water molecules in solutions
30 of formate salts (HCOO$^-$) with different monovalent cations X$^+$= Li$^+$, Na$^+$, NH$_4^+$, K$^+$, Cs$^+$ in isotopically diluted water (10% HDO in H$_2$O) with polarization-resolved femtosecond mid-IR pump-probe spectroscopy.[7] In this method we label HDO molecules by exciting the OD stretch vibration with an ultrashort linearly
35 polarized IR pulse centered at 2500 cm^{-1}. After a variable delay time τ, we probe the absorption changes $\Delta\alpha(\tau)$ due to the excited molecules with a second weaker IR pulse whose polarization is either parallel or perpendicular to the pump polarization (for further experimental details see the Electronic Supplementary
40 Information (ESI)). A measure for the reorientation dynamics is given by the anisotropy parameter R(τ), the normalized difference of the two absorption changes:

$$R(\tau) = \frac{\Delta\alpha_{\parallel}(\tau) - \Delta\alpha_{\perp}(\tau)}{\Delta\alpha_{\parallel}(\tau) + 2\Delta\alpha_{\perp}(\tau)} \quad (1)$$

In Fig. 1a we show normalized linear IR spectra in the frequency
45 region of the OD stretch vibration for solutions of 4 m formate salts dissolved in 10% HDO in H2O. Compared to neat 10%
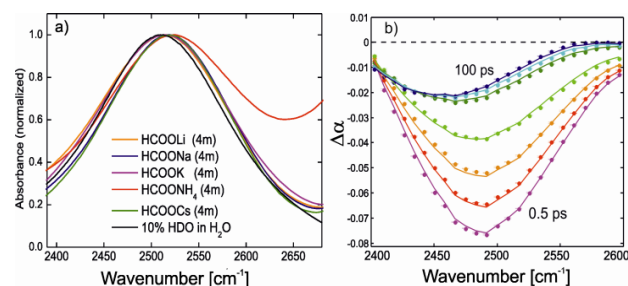

Fig. 1. a) Linear IR absorption spectra of different formate salts dissolved in 10% HDO/H$_2$O (H$_2$O background subtracted). For comparison also the
50 linear IR absorption spectrum of neat 10% HDO/H$_2$O is shown; b) Transient spectra measured for a solution of 4 m HCOONa in 10% HDO/H$_2$O for pump-probe delay times of 0.5, 0.8, 1.2, 2, 4.5, 6 and 100 ps

HDO in H$_2$O, the center frequency of the OD stretch vibration is
55 shifted to higher values by approximately 4 cm^{-1} for HCOOLi and HCOOK, and by approximately 10 cm^{-1} for HCOONa, HCOOCs and HCOONH$_4$. For the solution of HCOONH$_4$ we observe a broad shoulder in the high-frequency wing that we assign to the stretching vibrations of NH$_x$D$_y^+$.[8]
60 Fig. 1b presents transient spectra at different delay times in the frequency region of the OD stretch vibration for a 4 m solution of HCOONa. At early delay times, the transient spectra show a bleaching signal with a spectral shape that is similar to the linear absorption spectrum of the solution studied. With increasing
65 delay, the bleaching signal decays and evolves to a red-shifted bleaching signal that reflects a temperature increase of the sample. We determine the time constant of the vibrational relaxation with a kinetic model in which the excited OD vibration relaxes to an intermediate state that subsequently relaxes back to
70 the ground state at a somewhat elevated temperature (for a detailed description of the modeling see the ESI). For all studied solutions the vibrational relaxation time T$_1$ of the OD stretch vibration ranges from 1.6±0.1 to 1.8±0.1 ps, similar to the value for neat HDO/H$_2$O (1.7±0.1 ps)[9]. To determine the anisotropy
75 dynamics that exclusively represents the reorientation of the OD groups, we correct the measured $\Delta\alpha_{\parallel}(\tau)$ and $\Delta\alpha_{\perp}(\tau)$ for the spectral response of the ingrowing heated ground state. The evolution of this response is determined using the kinetic model. We subtract this response from $\Delta\alpha_{\parallel}(\tau)$ and $\Delta\alpha_{\perp}(\tau)$. The anisotropy then follows
80 from equation (1).

In Fig. 2 we present the anisotropy as a function of delay time for 4 m solutions of three different formate salts (HCOOK, HCOOLi and HCOONa). We observe that the addition of formate salts

leads to a slowing down effect on the anisotropy decay that becomes stronger in the series $Cs^+ < K^+, NH_4^+ < Li^+ < Na^+$. For all formate solutions and concentrations we fit the anisotropy decay to a bi-exponential function:

$$R(\tau) = A_{fast} \cdot e^{\frac{-\tau}{\tau_{fast}}} + A_{slow} \cdot e^{\frac{-\tau}{\tau_{slow}}} \qquad (2)$$

where A_{fast}, τ_{fast} and A_{slow}, τ_{slow} are the amplitudes and rotational relaxation times of a fast water and a slow water fraction, respectively. For all salt solutions τ_{fast} has a value of 2.5 ps. This value is similar to the reorientation time constant of a neat solution of HDO in H_2O.[9] It thus appears that there is a significant fraction of water for which the reorientation dynamics are negligibly affected, even at high salt concentrations of 4 m. The reorientation of OD groups bound to the carboxylate group likely comprises a relatively fast wobbling motion over a limited cone angle, and a slower reorientation that leads to a full decay of the anisotropy, similar to what was found for anion-bound OD groups in alkali-halide solutions.[13] In this latter work the reorientation dynamics of the anion-bound OD groups were spectrally resolved and the wobbling motion was observed to possess a time constant of ~2 ps. Since in the present work we cannot spectrally distinguish between OD groups that are carboxylate-bound or water-bound, this wobbling motion is contained in the fast 2.5 ps component.
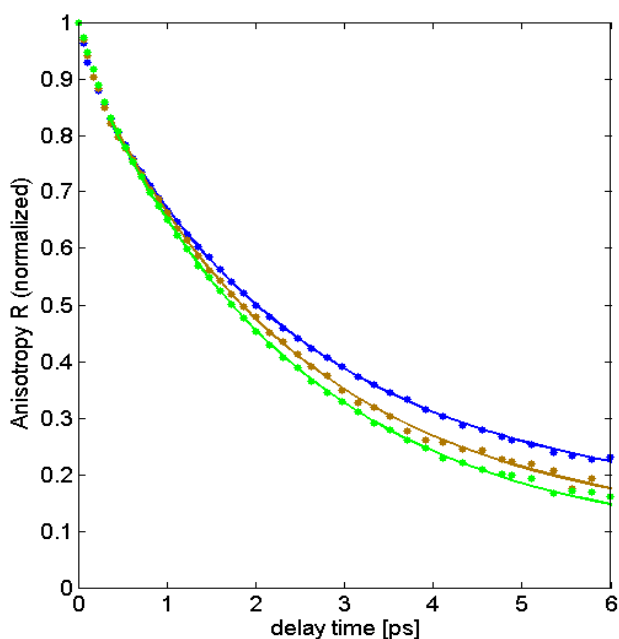

Fig. 2. Normalized anisotropy as a function of delay time for 4 m solutions of HCOOK (light green), HCOOLi (brown) and HCOONa (navy) in 10% HDO:H_2O. The points represent the experimental data and the lines the biexponential fits. Values of anisotropies were normalized to 1 at the delay time $\tau = 0$.

The time range over which we can measure the anisotropy dynamics is limited to delay times $\tau < 10$ ps, due to the fast vibrational relaxation of the OD stretch vibration. As a result, we cannot determine the precise value of τ_{slow}. To compare the effects of the different ions on the water dynamics, we set the value of τ_{slow} equal to 20 ps for all studied solutions and concentrations.

Equation (2) is fitted to the data for delay times $\tau > 400$ fs such that we avoid any contributions to the anisotropy decay due to librational motions.[10, 11] The fitted amplitudes A_{fast} and A_{slow} are used to determine the fraction f_{slow} of slow water of each solution with the following expression:

$$f_{slow} = \frac{A_{slow}}{A_{slow} + A_{fast}} \qquad (3)$$

The value of f_{slow} strongly depends on the nature of the cation and increases linearly with the concentration of dissolved salt (Fig. 3a). For HCOONa and HCOOLi the slope of the slow water fractions is much steeper than for the other formate salts. The slope of a straight line fitted to the values of f_{slow} defines the salt-specific hydration number N_h, which is the number of slow water molecules per formate + cation combination. The values of N_h depend on the nature of the cation and are shown in Fig. 3b. We find that $N_h = 3$ [12] (6 slowed hydroxyl groups) for HCOONa, $N_h = 2.5$ for HCOOLi, $N_h = 1$ for HCOONH$_4$ and HCOOK, and $N_h = 0.5$ for HCOOCs. We note that for HCOONH$_4$ the hydration number may in fact be lower than 1, because the stretch vibrations of $NH_xD_y^+$ are located in the spectral region of the OD vibration, as shown in Fig. 1a[8]. Therefore, the slow fraction observed in the anisotropy decay for HCOONH$_4$ is likely partly due to the response of the stretch vibrations of the ammonium cation.
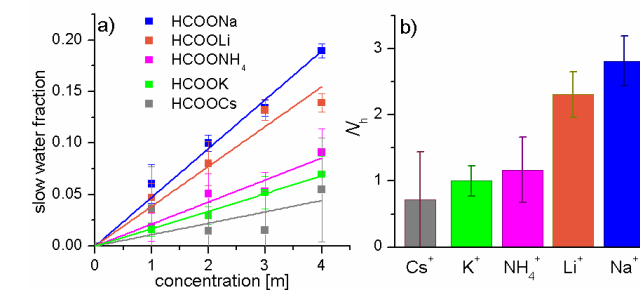

Fig.3. a) – Fraction of slow water as a function of concentration for different formate salts. The points originate from biexponential fits to the measured anisotropy curves and the lines are obtained from linear fits to these points; b) –hydration number N_h for different formate salts.

To get more insight in the influence of the individual ions on the orientational dynamics of water, we compare in Fig. 4 the anisotropy decays of HCOOK and HCOONa with the anisotropy decays of water-bound OD groups in solutions of KI and NaI. For solutions of HCOOK (Fig. 4a), the anisotropy decay curves measured at different concentrations are very similar to the anisotropy decay curve observed for neat liquid HDO:H_2O. This result shows that the combined effect of K^+ and the formate ion on the orientational dynamics of water is negligibly small, either because the effects of the two ions compensate each other (one ion accelerating the dynamics, the other decelerating the dynamics), or because both ions have a negligible effect on the dynamics of their hydrating water molecules. In Fig. 4b we show the anisotropy dynamics of OD groups bound to other water molecules measured for solutions of KI in HDO:H_2O. The contribution of OD groups bound to the I$^-$ anion was removed (according to the method described in [13]), and the curves shown thus only include the dynamics of the OD groups of bulk water
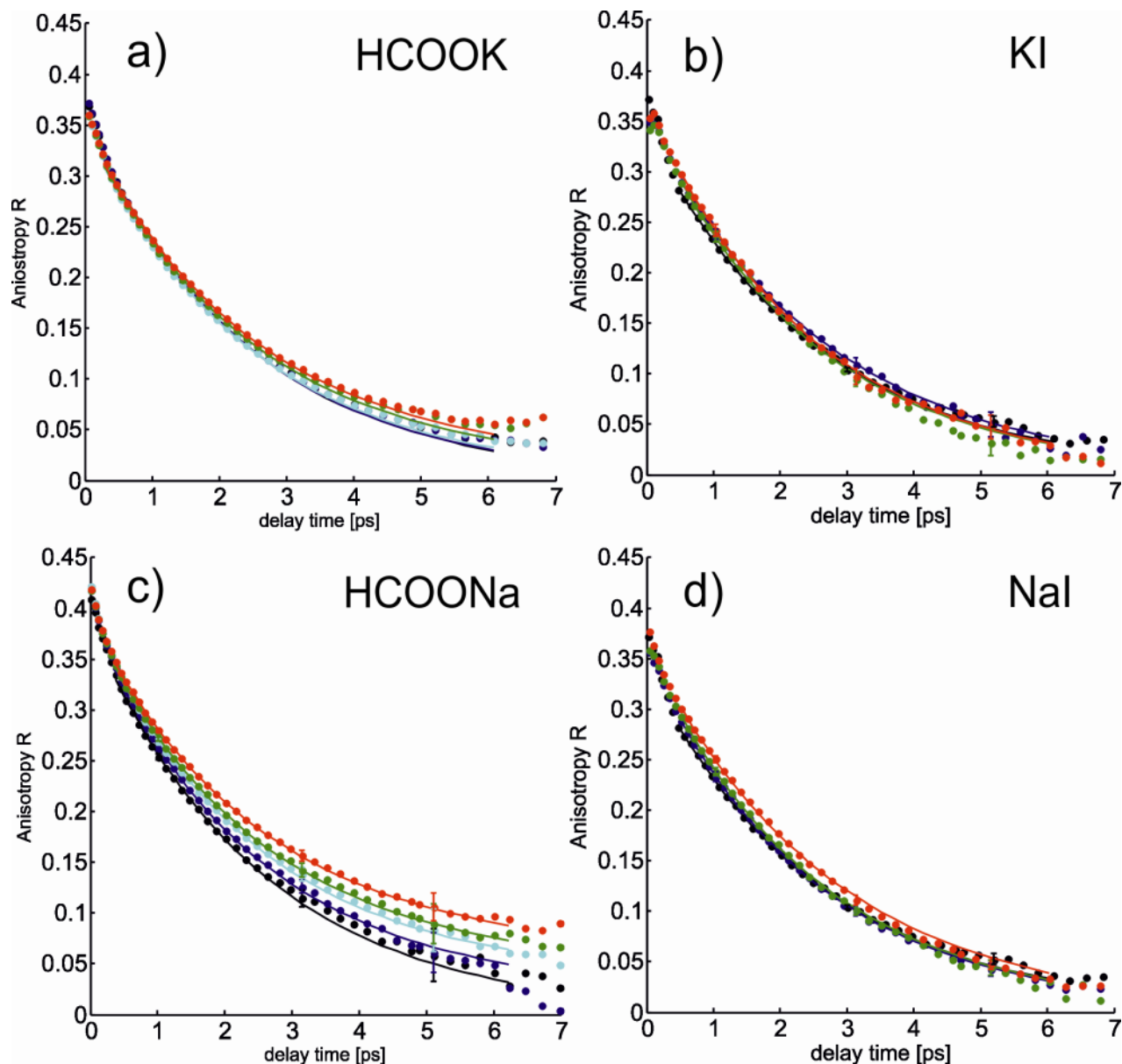
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Fig. 4. Anisotropy of the OD stretch vibration as a function of delay for different salt solutions of different concentration: 0 m (black), 1 m (navy), 2 m (cyan), 3 m (olive), 4 m (red). For clarity, the error bars are included only for delay times of 1, 3 and 5 ps.

and water molecules hydrating the cation.[13] The lack of any
5 slowing down with increasing concentration of K^+ indicates that this cation has very little effect on the orientational dynamics of the hydroxyl groups in its solvation shell, in agreement with studies on other cations.[14, 15] In these studies ([15]) it was found that the electric field exerted by a cation primarily fixes the permanent
10 dipole moments of the surrounding water molecules while leaving the reorientation of the hydroxyl groups unaffected. The

absence of any effect of the K^+ ion implies that the formate ion also has very little effect on the orientational dynamics of water, at least in case K^+ forms the counterion.
15 For solutions of HCOONa the anisotropy decay slows down significantly with increasing concentration (Fig. 4c). A comparison with the results of Fig. 4a and 4b suggests that the observed slowing down could be associated with water molecules that hydrate the Na^+ ion. However, in Fig. 4d hardly any effect is

observed on the anisotropy dynamics of the water-bound OD groups for solutions of NaI, meaning that for these solutions the effect of the Na^+ ion on the orientational dynamics of water is negligible.[13] Hence, the significant slowing down of the anisotropy decay observed in Fig. 4c points at a cooperative effect of the formate ion and the Na^+ ion on the dynamics of water. A similar difference in response is obtained for HCOOLi and LiI[15] solutions.

The effect of the negatively charged carboxylate group of the formate ion on the dynamics of water thus appears to be strongly dependent on the nature of the counter-ion, and increases in the sequence: $Cs^+ < K^+$, $NH_4^+ < Li^+ < Na^+$. A similar dependence of the nature of the cation has been observed before for solutions containing the SO_4^{2-} anion[15]. The cooperative effect of the carboxylate group and particular alkali cations may find its origin in the formation of solvent separated ion pairs. Two oppositely charged ions in a solution can interact with each other by forming a contact ion pair (CIP, no solvent in between), or a solvent-separated ion pair (SIP) in which case they share one or two solvation shells.[16] SIPs contain a limited number of water molecules in between the oxygen atoms of the carboxylate anion and the cation, and the orientational dynamics of these intervening water molecules are expected to differ from the orientational dynamics of bulk liquid water. Recent molecular dynamics simulations showed that carboxylate groups indeed form solvent-separated ion pairs (SIPs) with alkali cations, and the probability of SIP formation was observed to increase in the series: $K^+ < Na^+ < Li^+$.[17] Hence, the observed cooperative effect of the formate anion and Na^+/Li^+ cations on the reorientation dynamics of water likely finds its origin in the formation of relatively rigid solvent-separated ion pairs between the formate anion and Na^+/Li^+.

The number of slow water molecules is observed to be somewhat higher for Na^+ than for Li^+ which is surprising in view of the fact that the Li^+ ion possesses a higher charge density. The same sequence of cations ($Na^+ > Li^+$) was found in a recent X-ray absorption spectroscopy study on the formation of CIPs between alkali cations and acetate.[18] The higher number of slow water molecules observed for Na^+ may result from a better fit of the Na^+ ion in the structure of water molecules around the carboxylate group. For the Li^+ ion this structure could be somewhat more strained. As a result, it could be more favorable for the Li^+ ion to form a separate hydration structure with water instead of a hydrated CIP or SIP with the carboxylate group.

The formation of SIPs between carboxylate groups and particular alkali cations will play an important role in the hydration of proteins, and thus in the overall interaction of the protein surface with water. Particularly, the large difference between Na^+ and K^+ in forming SIPs with carboxylate groups is relevant for understanding the selectivity of Na^+/K^+ membrane ion pumps that rely on the interaction of carboxylate groups with these cations.
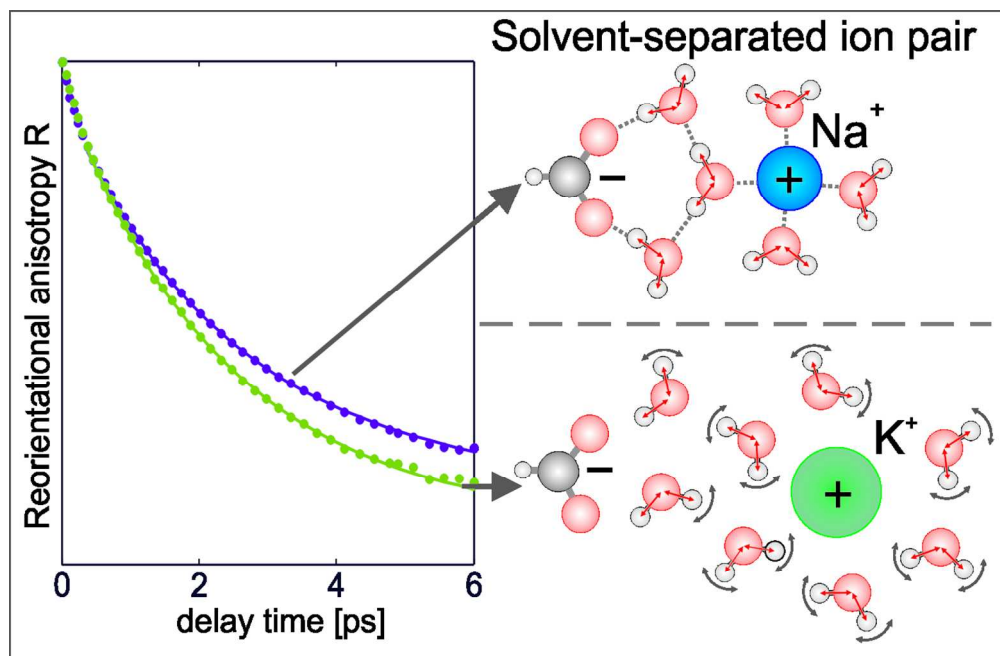
Conclusions

In summary, we studied the reorientation dynamics of water molecules in solutions of formate ions combined with different alkali cations. We found that the effect of the carboxylate group of the formate ion on the dynamics of water strongly depends on the nature of the cation. When formate is combined with a weakly

hydrating cation like Cs^+, K^+, or NH_4^+, no more than 1 water molecule is slowed down in its rotational motion. However, when combined with strongly hydrating cations like Na^+ and Li^+, the formate ion slows down the reorientation of ~3 water molecules. This cooperative effect indicates that the carboxylate group of the formate ion forms solvent-separated ion pairs (SIPs) with Na^+ and Li^+ ions.

Notes and references

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† Electronic Supplementary Information (ESI) available: description of samples prepararation, experimental setup and modelling of the time-resolved data. See DOI: 10.1039/b000000x/

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