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PAPER

Caffeine and taurine slow down water molecules

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Abstract

In this work we study the effect of caffeine and taurine on the mobility of water molecules at 298 K using femtosecond mid-infrared and dielectric relaxation spectroscopy. We observe both molecules to have a slowing down effect on the mobility of surrounding water molecules: a single caffeine molecule slows down ∼9 water molecules, a single taurine molecule slows down ∼4 water molecules. The reorientation time constant of these slow water molecules is 4–5 times longer than the reorientation time constant of 2.5 ps of water molecules in bulk liquid water.

Introduction

Caffeine is considered to be the most widely used drug in the world [1]. It enjoys enormous popularity in beverages like coffee, tea, soft drinks, and energy drinks. Caffeine stimulates the central nervous system [2] and boosts the human performance by speeding up reaction times [3, 4] and by increasing alertness [5]. Caffeine binds to adenosine receptors in the central nervous system. Adenosine is a neuromodulator that slows down neural activity and makes one feel sleepy. By competing with adenosine, caffeine speeds up neural activity [6]. Taurine is ubiquitous in mammalian tissues [7] and is a frequently-used constituent of energy drinks. Taurine is one of the most important nutrients of the heart muscle. Increasing the taurine concentration is thus believed to stimulate the heart activity [8].

    Both caffeine and taurine are ubiquitously surrounded by water in the human body. Water is the medium in which most biochemical processes, including many receptor-activator interactions, take place, and these interactions will be dependent on the molecular dynamics of the water matrix. In this work we report on a study of the dynamics of water in aqueous solution of caffeine and taurine. The water dynamics is studied using two complementary experimental techniques. We use polarization-resolved infrared pump-probe spectroscopy to study the reorientation dynamics of the water OH groups. With dielectric relaxation spectroscopy we measure the reorientation dynamics of the molecular dipoles of both the water solvent and the solute molecules. The combination of these spectroscopic techniques allows for a direct measurement of the orientational mobility of the water molecules in the hydration shells of caffeine and taurine.

Experimental methods

In figure 1 the molecular structures of caffeine and taurine are presented. We prepare aqueous solutions of caffeine and taurine at their maximal concentrations. At room temperature the solubility of caffeine is 0.11 M, and the solubility of taurine is 0.76 M [9].

    We study the reorientation dynamics of water in aqueous solutions of caffeine and taurine at room temperature (298 K) with femtosecond pump-probe spectroscopy. In these experiments we use an isotopic dilution of 8% HDO in H_2O as the solvent. This solvent is formed by adding 4% of heavy water (D_2O) to H_2O. The OD stretch vibrations of the HDO molecules are excited with an intense 100 fs laser pulse at a mid-infrared wavelength of 4 μm (2500 cm^{-1}). This excitation leads to an anisotropic change of the absorption, because the pump pulse preferentially excites OD groups that are aligned parallel to the polarization direction of the pump

Figure 1. Molecular structure of caffeine and taurine.
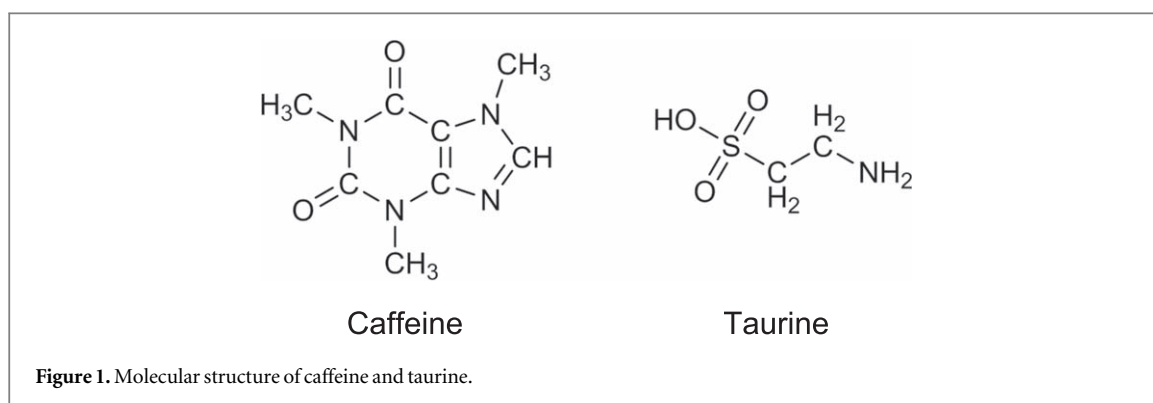
pulse. This absorption change is detected with a delayed 100 fs mid-infrared probe pulse. From the parallel $(\Delta\alpha_\parallel)$ and the perpendicular $(\Delta\alpha_\perp)$ absorption changes, the isotropic signal can be constructed:

$$\Delta\alpha_{\text{iso}}(\omega,\,t) = \frac{1}{3}[\Delta\alpha_\parallel(\omega,\,t) + 2\Delta\alpha_\perp(\omega,\,t)] \tag{1}$$

Here ω is the angular frequency and t is the time-delay between the pump and probe pulses. The isotropic signal decays with the lifetime of the OD stretch vibration and is independent of molecular reorientation. Due to the spontaneous dynamics of the liquid, the excited molecules will reorient with increasing pump—probe delay t. This leads to a decay of the anisotropy of the absorption change. The parallel $(\Delta\alpha_\parallel)$ and the perpendicular $(\Delta\alpha_\perp)$ absorption changes are used to construct the anisotropy parameter R:

$$R(\omega,\,t) = \frac{\Delta\alpha_\parallel(\omega,\,t) - \Delta\alpha_\perp(\omega,\,t)}{\Delta\alpha_\parallel(\omega,\,t) + 2\Delta\alpha_\perp(\omega,\,t)} \tag{2}$$

The isotropic absorption changes are divided out in the denominator. Therefore, the anisotropy directly reflects the reorientation dynamics of the OD groups of HDO molecules [10]. A detailed description of the experimental parameters and setup is given in Reference [11].

We also measure the reorientation of water molecules at 298 K with dielectric relaxation spectroscopy. In this case we use pure water (Milli-Q) as the solvent, and we measure the polarization response of the solution to an applied oscillatory electric field. The dielectric response to the alternating electric field can be expressed as a complex permittivity spectrum $\hat{\varepsilon}(\omega) = \varepsilon'(\omega) - i\varepsilon''(\omega)$, where ω is the angular frequency. The real part $\varepsilon'(\omega)$ is the dielectric dispersion and represents the in-phase polarization of the sample. The imaginary part $\varepsilon''(\omega)$ is the dielectric loss and expresses the energy dissipation due to the induced molecular reorientation mobility. The measured permittivity can often be described by a Debye relaxation model:

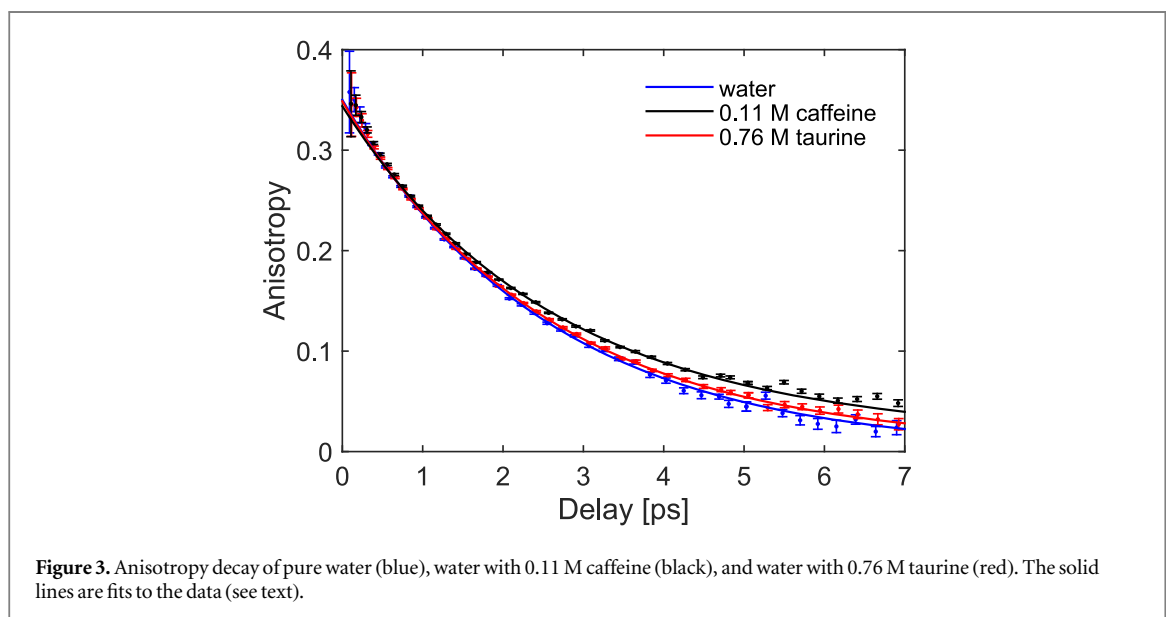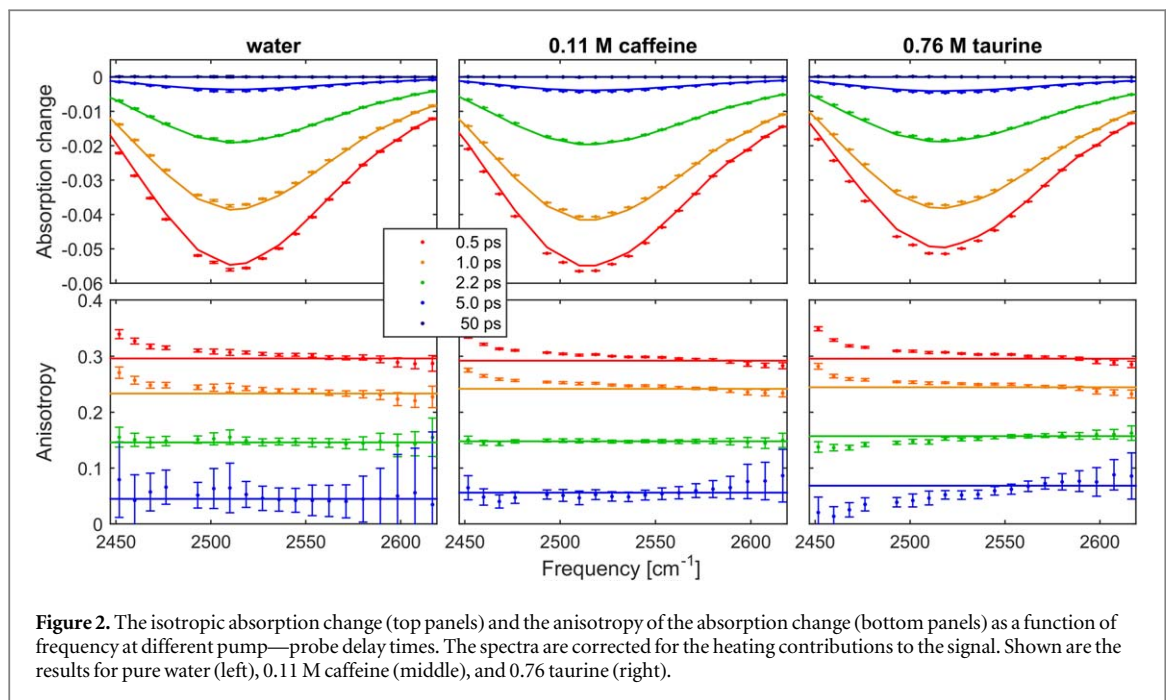$$\hat{\varepsilon}(\omega) - \varepsilon_\infty = \frac{S}{1 + i\omega\tau_{\text{D}}} \tag{3}$$

Here ε_∞ is the infinite frequency permittivity, S is the dielectric amplitude of the system, and τ_{D} is the macroscopic Debye reorientation time. For a mixture of different dipolar species with distinct reorientation time constants, each species can be described with a separate Debye mode. The amplitude of each relaxation mode is proportional to the corresponding concentration of dipoles and their squared effective dipole strength [12]. A detailed description of the experimental setup used for the dielectric relaxation experiments can be found in Reference [13].

Results

Femtosecond pump-probe spectroscopy

The top panel of figure 2 displays the isotropic absorption change of pure water, the 0.11 M caffeine solution, and the 0.76 M taurine solution. The spectra are corrected for heating effects contributing to the signal [10]. The negative absorption (bleach) for short delay times results from the depletion of the vibrational ground state due to excitation of OD stretching vibrations by the pump pulse. The bleach decays with increasing delay time as a result of vibrational relaxation. The dynamics of the isotopic absorption changes are similar for the three different samples. The corresponding frequency dependent anisotropy is shown in the bottom panel of figure 2. These spectra show that the anisotropy decay is not frequency dependent. The weighted average of the anisotropy is used to construct the anisotropy decays shown in figure 3.

The anisotropy of neat liquid water decays exponentially with a time constant of $\tau = 2.5 \pm 0.1$ ps (95% confidence interval), in agreement with previous work [10]. This time constant represents the reorientation time

Figure 2. The isotropic absorption change (top panels) and the anisotropy of the absorption change (bottom panels) as a function of frequency at different pump—probe delay times. The spectra are corrected for the heating contributions to the signal. Shown are the results for pure water (left), 0.11 M caffeine (middle), and 0.76 taurine (right).

Figure 3. Anisotropy decay of pure water (blue), water with 0.11 M caffeine (black), and water with 0.76 M taurine (red). The solid lines are fits to the data (see text).

of water molecules [10]. In the aqueous solution of 0.11 M caffeine, the decay of the anisotropy contains a small component with a much longer time constant. A similar effect is observed for the 0.76 M taurine solution. From a detailed study of the amplitude of the slow water fraction as a function of concentrations it follows that the slow water molecules are associated with the dissolved molecules, i.e. the slow water molecules are hydrating the solute molecules [14]. The anisotropy decay is thus the sum of two components. The first component represents water molecules that are far away from the dissolved caffeine or taurine molecules and that behave the same as water molecules in bulk water showing a reorientation time of $\tau_{\mathrm{bulk}} = 2.5$ ps. The second component represents water molecules in the hydration shells of the solutes having a molecular reorientation time τ_{slow} that is much longer, even longer than the time scale of the anisotropy experiment ($\sim$10 ps). As a result, the value of τ_{slow} cannot be accurately determined from the anisotropy decay.

Dielectric relaxation

We determine the relaxation time of the slow water molecules using dielectric relaxation spectroscopy. The complex permittivity of the 0.76 M taurine solution is depicted in figure 4. The spectrum is fitted with a sum of three Debye relaxation modes (equation (3)) pertaining to taurine, slow water, and bulk-like water, respectively [15]. The fit yields a macroscopic Debye reorientation time of the slow-water mode of $\tau_{\mathrm{D,slow}} = 42 \pm 3$ ps. The
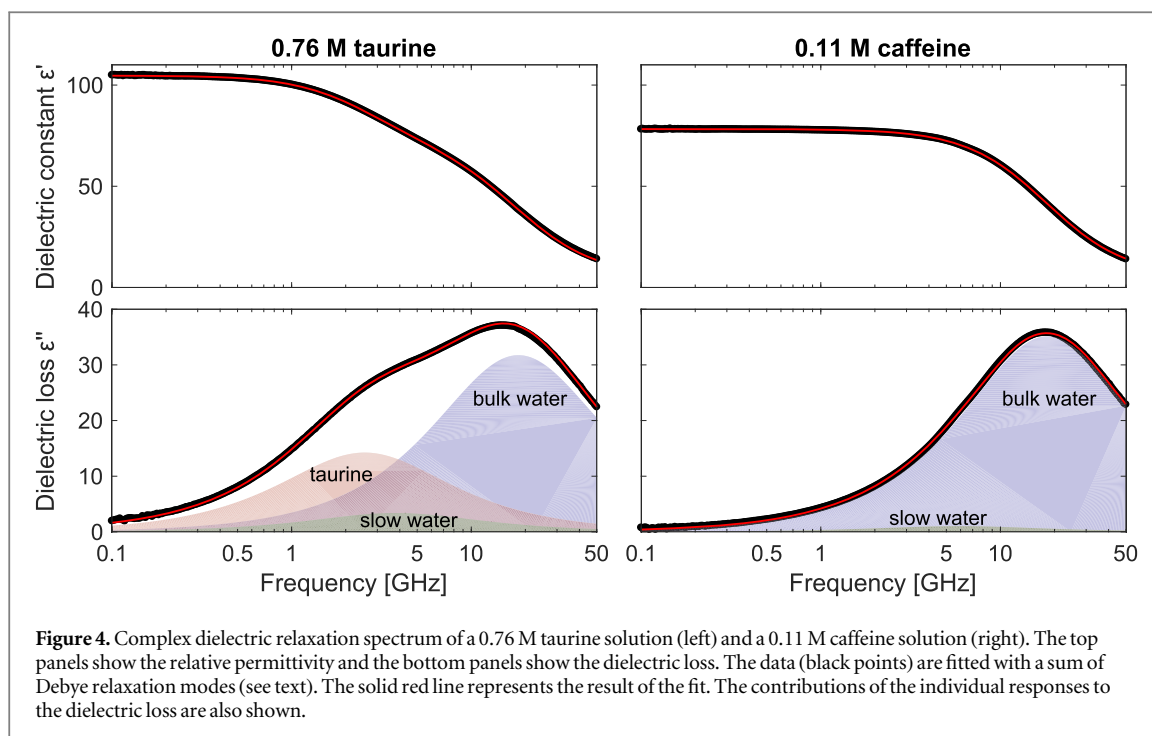
Figure 4. Complex dielectric relaxation spectrum of a 0.76 M taurine solution (left) and a 0.11 M caffeine solution (right). The top panels show the relative permittivity and the bottom panels show the dielectric loss. The data (black points) are fitted with a sum of Debye relaxation modes (see text). The solid red line represents the result of the fit. The contributions of the individual responses to the dielectric loss are also shown.

Debye reorientation time is related to the molecular reorientation time by a factor of 0.3 [16], yielding a molecular reorientation time of the slow water of $\tau_{slow} = 12 \pm 1$ ps. The reorientation time of the slow water molecules in the hydration shell of taurine is thus about 5 times longer than the reorientation time of the water molecules in bulk liquid water. This result is comparable with other solute molecules of similar size, for which a retardation by a factor of 4–5 has been observed [17–19].

In figure 4 we also show the dielectric spectrum of the 0.11 M caffeine solution. The complex permittivity is fitted by a sum of two Debye relaxation modes pertaining to slow water and bulk-like water, respectively. The dielectric relaxation response of caffeine is too small to be detectable due to the low solubility in combination with the small dipole moment of caffeine. For the slow water, we observe a Debye relaxation time constant of $\tau_{D,slow} = 30 \pm 10$ ps, corresponding to a molecular reorientation time of $\tau_{slow} = 9 \pm 3$ ps of the water molecules in the hydration shell of caffeine, i.e. similar to that of taurine. The large uncertainty in this reorientation time constant results from the low amplitude of this mode due to the low solubility of caffeine.

Determination of the slow water fraction
With the molecular reorientation times of bulk water molecules and slow water molecules, i.e. $\tau_{bulk} = 2.5$ ps and $\tau_{slow} = \sim 12$ ps, we can now accurately fit the anisotropy decays shown in figure 3. The anisotropy is fitted with the sum of two exponential decaying functions, i.e. $R(t) = A\,e^{-t/\tau_{bulk}} + B e^{-t/\tau_{slow}}$, where A and B are the amplitudes of the bulk-like and slow water components, respectively. From the parameter B the number of slow OH groups per caffeine/taurine molecule can be calculated by the formula $(C_{water}/C_{solute}) \times (B/(A + B))$, where C_{water} is the molar concentration of water (55.3 M), C_{solute} is the molar solute concentration [20]. For a 0.11 M caffeine solution, the water to caffeine ratio (C_{water}/C_{solute}) is 500. For the 0.76 M taurine solution, the water to taurine ratio (C_{water}/C_{solute}) is 73. It follows that one caffeine molecule is responsible for the retardation of 19 ± 2 OH groups of water, corresponding to ~ 9 water molecules. The number of slow OH groups per taurine molecule is 7.7 ± 0.5, corresponding to ~ 4 water molecules. The number of water molecules that are slowed down by caffeine is thus approximately half the number of water molecules that are slowed down by caffeine. Caffeine thus appears to be more efficient in reducing the mobility of surrounding water molecules. To explain this difference it is of interest to consider the size of the molecule. An interesting parameter in this respect is the number of CH bonds per molecule: caffeine contains 10 CH bonds and taurine contains 4 CH bonds per molecule. The number of slow OH groups per CH bond is thus 1.9 ± 0.2 for caffeine and 1.9 ± 0.1 for taurine. Hence, the slowing down of the hydration water appears to scale with the number of hydrophobic CH groups contained in the caffeine/taurine molecule. This result agrees with previous studies showing that hydrophobic groups have a significantly stronger retardation effect on surrounding water molecule than hydrophilic groups [14, 21, 22].

Discussion

Both caffeine and taurine are observed to slow down the reorientational dynamics of surrounding water molecules. For other organic and biological solutes a similar slowing down of the water molecules in their hydration shells has been observed [11, 17, 22, 23]. It is also quite generally found that in the case of dilute solution (no aggregation), the number of slow water molecules scales quite well with the size of the solute. In the case of aggregation [21] or folding [22] the number of slow water molecules per solute molecule is reduced because the hydrophobic groups are partly shielded from the interaction with water.

In view of the above it is interesting that molecular dynamics simulations indicate that caffeine and taurine acquire quite distinct molecular conformations in liquid water. Caffeine molecules are found to be planar and to form large self-aggregates in water in which the flat faces are stacked against one another like coins [24, 25]. In contrast, the zwitterionic taurine (at neutral pH) dominantly has a folded conformation with an intramolecular hydrogen bond [26]. Based on these results the water-exposed hydrophobic surface of taurine is expected to be larger than that of caffeine. Nevertheless, the number of slow water molecules observed for taurine and caffeine is found to scale quite well with the number of hydrophobic CH groups contained in the molecules, which suggests that the molecular dynamics simulations may overestimate the degree of self-aggregation of caffeine.

Recent theoretical and experimental work showed that the reorientation of water proceeds via a jump model in which the original hydrogen-bonded partner water molecule is exchanged for a new partner [27–29]. A crucial step in this exchange is the formation of a new hydrogen bond with an approaching water molecule, and the simultaneous weakening of the existing hydrogen bond. A strong slowing down of the reorientation of water thus points at a strong decrease of the local translational mobility of the water molecules, and an enhancement of the rigidity of the water hydrogen-bond network. Previous studies have indeed shown that the reorientation dynamics of water molecules are strongly correlated to the translational mobility [21]. When water molecules move slower and the water hydrogen-bond network is more rigid, diffusion processes will also become slower. Hence, the interaction of caffeine and taurine with their water molecules is expected to lead to a local slowing down of the transport of other ions and molecules through the surrounding water matrix.

Conclusions

Caffeine and taurine slow down the molecular reorientation of their hydrating water molecules by a factor of 5, to a reorientation time constants of 12 ± 1 ps at 298 K (cf bulk water has a reorientation time constant of 2.5 ± 0.1 ps). A caffeine molecule slows down ∼9 water molecules, a taurine molecule slows down ∼4 water molecules.

Acknowledgments

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