Structure, Organization and Heterogeneity of Water-Containing Deep Eutectic Solvents

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Abstract

The spectroscopy and structural dynamics of a deep eutectic mixture (KSCN/acetamide) with varying water content is investigated from 2D IR (with the C–N stretch vibration of the SCN− anions as the reporter) and THz spectroscopy. Molecular dynamics simulations correctly describe the non-trivial dependence of both spectroscopic signatures depending on water content. For the 2D IR spectra, the MD simulations relate the steep increase in the cross relaxation rate at high water content to parallel alignment of packed SCN− anions. Conversely, the non-linear increase of the THz absorption with increasing water content is mainly attributed to the formation of larger water clusters. The results demonstrate that a combination of structure sensitive spectroscopies and molecular dynamics simulations provides molecular-level insights into emergence of heterogeneity of such mixtures by modulating their composition.
Introduction

Deep eutectic solvents (DESs) are multicomponent mixtures prepared by combining hydrogen bond acceptors (HBAs) and hydrogen bond donors (HBDs), sometimes along with electrolytes at a particular eutectic molar ratio.\(^1\)\(^-\)\(^4\) These systems are characterized by a pronounced depression of their melting point compared to their components and remain in the liquid phase over a wider temperature interval.\(^5\) It is believed that the high entropy gain in liquid range is supported by strong H-bonding networks permeating the system, besides other specific interactions of the various components in DES. DESs gained considerable attention as potential substitutes for room temperature ionic liquids due to their non-toxicity.\(^6\) In addition low vapor pressure, low melting point, high thermal stability, and cheap production costs are some of the beneficial properties that make these solutions interesting in chemical, biological, and industrial applications.\(^7\)\(^-\)\(^12\)

For further improvement and optimization of such liquids, a more molecularly resolved, microscopic understanding of their structural and dynamical properties is required. DESs have been studied with a range of approaches, including dielectric,\(^13\)\(^-\)\(^16\) viscoelastic,\(^17\),\(^18\) nuclear magnetic\(^16\),\(^17\) and ultrasonic relaxation,\(^17\),\(^19\) optical Kerr effect spectroscopy,\(^20\) fluorescence measurements,\(^21\)\(^-\)\(^24\) wide-angle and quasi-elastic neutron scattering,\(^16\) simulated X-ray scattering structure function calculations\(^25\)\(^-\)\(^27\) empirical potential structure refinement (EPSR),\(^28\) and molecular dynamics (MD) simulations.\(^16\),\(^29\),\(^30\) For instance, femtosecond Raman-induced Kerr-effect spectroscopy measurements allowed, in some cases, direct observation of intermolecular hydrogen-bonding.\(^20\) An important characteristic of DESs - “dynamic heterogeneity” - is suggested by the fractional dependence of a solutes solvation \(\langle \tau_s \rangle\) or rotation \(\langle \tau_r \rangle\) time on viscosity \(\eta\) and temperature \(T\), which scales as \(\langle \tau_{s/r} \rangle \propto (\eta/T)^p\) with an exponent \(0.4 < p < 0.7\).\(^31\) In contrast, conventional Stokes-Einstein and Stokes-Einstein-Debye would predict \(p = 1\). Multi- or stretched-exponential relaxation of dynamic structure factors observed in MD simulations explain this viscosity dependence through the existence of spatially varying relaxation rates,
reinforcing the idea of a high degree of solution heterogeneity and the formation of domains. These domains were found to exhibit either collective small amplitude rotation or orientational jump motions followed by H-bond relaxation similar to what was found for liquid water or around hydrated ions. The formation of ion aggregates leading to charged structures in equilibrium with the liquid amide has also been suggested by dielectric relaxation measurements.

Optical spectroscopy is a versatile and powerful method to interrogate and characterize the structural dynamics of condensed phase systems. With regard to the present problem, an extensive literature exists on the vibrational energy exchange between ions in solution (especially water), establishing two-dimensional infrared (2D IR) spectroscopy as a tool to investigate structural and dynamical properties of multi-component liquids through vibrational energy transfer between some of its components. For pairwise two molecules, the vibrational energy transfer rate is expected to have a steep, i.e. inverse 6th-power, distance dependence, similar to NOESY in NMR spectroscopy, or Förster energy transfer between electronic chromophores. The presence of cross-peaks in a 2D spectrum has been directly related to the formation of aggregated structures, like ion clusters.

Terahertz (THz) spectroscopy, on the other hand, is sensitive to the more collective excitations in a sample involving particle motion leading to structural relaxations. Specifically, hydrogen bond networks exhibit intermolecular vibrations in the THz spectral range. In turn, changes in THz absorption often carry information on structural modifications of the hydrogen bond network in a sample. For instance, when bulk water molecules become bound, such as on surfaces or in proteins, the THz absorption changes. Similarly, DESs are expected to exhibit specific THz signatures for the heterogeneous mixture, because a hydrogen-bonded DES constituent in aggregated structures is closer to its bulk form as compared to being embedded in a homogeneous mixture.
One of the great challenges is to relate spectroscopic responses to underlying structural motifs, their dynamics, and their change in time. A typical example is ligand recombination in myoglobin\textsuperscript{49} for which time resolved experiments were combined with atomistic simulations to characterize complex, heterogeneous systems at molecular level.\textsuperscript{50} In the area of molecular and ionic liquids, neutron scattering\textsuperscript{51} and X-ray\textsuperscript{52} techniques were used for structural characterization combined with molecular dynamics simulations. The present work reports on the structural dynamics of the (0.75 acetamide + 0.25 KSCN) DES and its aqueous solutions by replacing acetamide with 0 to 100\% water. The physical properties around the eutectic temperature of 298 K have been studied to verify its liquidous range.\textsuperscript{53,54} It has been found that addition of inorganic salts lowers the melting point of acetamide containing mixtures and are extensively used as reaction media and in thermal salt cells to produce electricity.\textsuperscript{22,53,55,56} In general, DESs are hygroscopic, hence it is important to understand how their microscopic properties change with increasing water content.\textsuperscript{57} Also, adding water changes the physical properties of a DES, such as its viscosity or density, by up to one order of magnitude.\textsuperscript{58} Hence to use DESs as effective solvents, it is important to know how water - which is both a HBD as well as a HBA - alters the arrangements of the DES components, in particular the spectroscopically responsive part which is SCN\textsuperscript{−} in the present case. Thiocyanate (SCN\textsuperscript{−}) is an ideal spectroscopic probe as the CN-stretch vibration absorbs in an otherwise empty region of the infrared region, and has also been used in recent work on urea/choline chloride mixtures which probed the effect of water addition.\textsuperscript{59}

In the present work two complementary spectroscopic techniques - 2D IR spectroscopy and THz spectroscopy - are combined with atomistic simulations to probe the structural dynamics of a multi-component DES. The experiments are sensitive to the aggregation of the various components and characterization of a heterogeneous condensed phase systems on multiple length and time scales. Combining both spectroscopies with MD simulations, which essentially quantitatively reproduce the spectroscopic experiments, allows one to portray the short- and
long-range order in DESs to a degree that is largely inaccessible to other, more traditionally employed methods such as NMR or dielectric spectroscopy, neutron scattering, or fluorescence measurements.

Methods

2D IR Spectroscopy

The 2D IR spectrometer in pump-probe geometry used in this work is a slight modification of our previously reported setup. In brief, the output of a 5 kHz Ti:Sapphire amplifier producing \( \approx 100 \) fs pulses was used to pump a home-built mid-IR OPA, delivering \( \approx 2 \mu\text{J} \), ca. 120 fs pulses centered around 2020 cm\(^{-1}\). A small fraction of the mid-IR light was split off with a BaF\(_2\) wedge to be used as the probe and reference beams. Absorptive 2D IR spectra were obtained by fast scanning the coherence delay between the two pump pulses (up to 5 ps, revealing a \( \omega_1 \) resolution of \( \approx 2 \text{ cm}^{-1} \) after zero-padding) generated in a Mach-Zehnder interferometer for a given population delay \( t_2 \). The second output of the Mach-Zehnder interferometer was measured with a pyroelectric detector, revealing the information to phase the 2D IR spectra. The pump and probe beams were overlapped at the sample position. Afterwards, the probe and reference beams were dispersed in a spectrograph with a 150 l/mm grating, and simultaneously recorded with a 2 \times 32 pixels MCT detector, yielding a \( \omega_3 \) resolution of \( \approx 5 \text{ cm}^{-1} \). Scatter suppression was achieved by quasi-phase cycling using a librating ZnSe window introduced in the pump beam at Brewster angle. 2D IR spectra were measured in transmission with pump and probe pulses polarized in parallel.
**THz Spectroscopy**

The THz spectrometer is home-build and covers the frequency range between 3 cm$^{-1}$ (0.1 THz) and 66 cm$^{-1}$ (2 THz). Terahertz pulse generation and detection is based on a femtosecond erbium fiber laser providing pulses with a duration of 100 fs, a repetition rate of 80 MHz, and an average output power of 130 mW at around 780 nm. The laser pulses are split and sent to a photo-conductive emitter and detector. For lock-in detection, the bias voltage of the emitter is modulated with 2 kHz. The THz source is imaged by four aspheric lenses with $f_1 = 100$ mm, $f_2 = 50$ mm, $f_3 = 50$ mm and $f_4 = 100$ mm, each with a diameter of two inches, to the detection unit. The cuvette containing the different DES/water mixtures was located at the intermediate image position. The transmitted THz electric field during 6 ps was measured in delay steps of 33 fs. A reference signal (i.e., without sample) was measured before and after every DES/water mixture.

Terahertz spectra were obtained by Fourier transforming the measured time dependent electric field. The spectrally resolved THz absorption was calculated from the ratio of a sample and a reference spectrum and the mean absorption is the absorption averaged between 13 cm$^{-1}$ (0.4 THz) and 34 cm$^{-1}$ (1 THz). The relative error was determined as 2%.

**Sample Preparation**

For the 2D IR experiments the salt was first prepared in a 50%/50% mixture of the two isotopologues, KS$^{12}$C$^{14}$N and KS$^{13}$C$^{15}$N. Solutions were prepared with constant total salt concentration of 4.4 M, and the molar ratio of D$_2$O vs. acetamide varied from 0% to 100% in steps of 10%. The sample was squeezed between two CaF$_2$ windows without any spacer, revealing a sample thickness of about 1 µm.

For the THz measurements the same preparation recipe was applied, but using H$_2$O instead.
of D$_2$O and without specific measures to control the relative isotope concentration. The DES/water mixtures were filled in a 100 µm thick fused silica cuvette with a 1.3 mm thick base plate and a 1.2 mm thick cover plate. All samples were measured at a temperature of 295 K.

**MD Simulations**

Molecular dynamics (MD) simulations were performed using CHARMM$^{63}$ with the all atom force field CHARMM36.$^{64}$ The intramolecular and intermolecular potential of acetamide, water and KS$^{12}$C$^{14}$N are determined by the bond parameters of CGenFF$^{65}$ and the TIP3P model$^{66}$ for water because CGenFF was parametrized at 300 K with this water model. The CN and SC bond potential in SCN$^-$ are replaced by a Morse potential and electrostatic multipole moments of SCN$^-$ up to the quadruple moment are included in the force field. The electrostatic moments$^{67–69}$ and Morse parameters are fitted to the respective *ab initio* data for a SCN$^-$ anion at MP2/aug-cc-pVDZ level of theory using Gaussian09.$^{70}$ All force field parameters used for the present study are summarized in the supporting information, see Table S1. Bonds involving hydrogen atoms were constrained using the SHAKE algorithm.$^{71}$ For the nonbonded interactions the long-range cutoff was 14 Å and electrostatic interactions were controlled using the Particle Mesh Ewald algorithm.$^{72}$ The molar composition of the systems was changed by modifying the number of water and acetamide molecules while keeping constant the total concentration of KSCN. The number of molecules and molar fractions are reported in Table S2. In total, 10 independent random initial configurations for each of the 12 system compositions were set up using PACKMOL.$^{73}$ Following 180 ps of equilibrium, dynamics simulation in the $NpT$ ensemble at 300 K and normal pressure, production simulations were performed for 5 ns with a time step of 1 fs using the leap-frog integrator and a Hoover thermostat.$^{74}$ In total, 50 ns for each system composition were sampled. The densities of the different system compositions is reported in the supporting infor-
For computing the 2D IR spectra the frequency trajectories $\omega_i(t)$ for each oscillator are required. These were determined from an instantaneous normal mode (INM) analysis for the CN vibrational frequencies $\omega_i$ on snapshots of the trajectories each 200 fs in 250 ps time interval at $0 - 0.25$ ns, $2 - 2.25$ ns and $4 - 4.25$ ns on all SCN$^-$ ions. For this the structure of every SCN$^-$ ion was optimized while freezing the position of all remaining atoms in the system, followed by a normal mode analysis using the same force field that was employed for the MD simulations. Previously, such an approach has been validated for N$^-_3$ in solution by comparing with rigorous quantum bound state calculations.

**Simulation and Analysis of 2D IR Spectra**

To calculate 2D IR spectra from the output of the MD simulations, we started from the exciton Hamiltonian for $N$ oscillators:

$$H(t) = \sum_{i=1}^{N} \left[ \omega_i(t) b_i^\dagger b_i - \frac{\Delta}{2} b_i^\dagger b_i^\dagger b_i b_i \right] + \sum_{i \neq j}^{N} V_{ij}(t) b_i^\dagger b_j$$

$$+ \sum_{i=1}^{N} \vec{\mu}_i(t) \cdot \vec{E}(t) \left[ b_i^\dagger + b_i \right],$$

with

$$V_{ij} = \frac{1}{4\pi\varepsilon_0} \left[ \frac{\vec{\mu}_i \cdot \vec{\mu}_j}{r_{ij}^3} - 3 \frac{(\vec{r}_{ij} \cdot \vec{\mu}_i)(\vec{r}_{ij} \cdot \vec{\mu}_j)}{r_{ij}^5} \right].$$

Here, $b_i^\dagger$ and $b_i$ are the harmonic creation and annihilation operators of a vibrational quantum on SCN$^-$ anion $i$, $\omega_i(t)$, $\vec{\mu}_i(t)$ and $\Delta = 27$ cm$^{-1}$ its instantaneous frequency, transition dipole and anharmonicity, respectively, $r_{ij}$ the distance between both sites, $\varepsilon_0$ the vacuum permittivity, and $\vec{E}(t)$ the applied external field from the laser pulses. The instantaneous frequencies $\omega_i(t)$, directions of the transition dipoles $\vec{\mu}_i(t)$ and connecting vectors $\vec{r}_{ij}(t)$ are
time-dependent and can be extracted directly from the MD trajectory. To that end, the
directions of the transition dipoles $\vec{\mu}_i(t)$ were assumed to be along the CN bond of each
SCN$^-$ ion, its origin in the middle of the CN bond, and the strength 0.35 D,\textsuperscript{41} while the
frequencies $\omega_i(t)$ were derived from INM calculations (see above).

2D IR spectra were calculated from this Hamiltonian by formulating the 6 response functions
of ground state bleach (GB), stimulated emission (SE) and excited state absorption (EA)
in the two phase matching directions that contribute to purely absorptive 2D IR spectra,
see Eq. 15 of Ref. 81. As in the experiments, the polarizations of all field interactions
was set parallel to each other, and $(\langle xxxx \rangle + \langle yyyy \rangle + \langle zzzz \rangle)/3$ has been calculated to
to better average over the orientations of the SCN$^-$ anions. For the time-evolution of the
wave functions, however, a somewhat different approach was taken than in Ref. 81. In
brief, the Trotter expansion in Ref. 81 was replaced by the Chebyshev method,\textsuperscript{82} which
allows for larger time-steps and thus speeds up the calculation significantly, as discussed
in Ref. 43. Since the computational cost scales with the inverse 3rd power of the time
step in the time-propagation of the wavefunction, a relatively long time step of 200 fs was
chosen. This is longer than the decay time of the initial spike in the FFCF (see Figure S2,
Supplementary Material), and thus overestimates the homogeneous width of the simulated
spectra. However, for the present analysis only the total peak volumes are required as a
measure for the overall populations. Inhomogeneity causes the peaks to be tilted, expressed
by the correlation parameter $c$ in Eq. 3 below, and is accounted for in the calculation of the
total peak volume, see Eq. 4. Working in a rotating frame, 2D IR spectra were calculated
with coherence times of 3.2 ps and the population time was varied in steps of 1 ps up to 100 ps.

A sliding average along the 250 ps long sequences of the trajectories was performed in steps
of 5 ps in order to increase the signal-to-noise ratio of the calculated 2D IR spectra. For each
sample in this sliding average, a new 50%/50% distribution of the two isotopologues of the
SCN\(^-\) anion was randomly selected in order to generate samples as statistically independent as possible. The instantaneous frequencies \(\omega_i(t)\) of those anions, which were selected to be KS\(^{13}\)C\(^{15}\)N, were lowered by 75 cm\(^{-1}\) to account for the isotope shift. The 2D IR spectra for each mixing ratio were obtained by averaging the 30 (3 time intervals per 10 samples for each mixing ratio) 2D IR spectra for each 250 ps long fragments.

To extract the essential information from the 2D IR spectra, i.e., the frequency correlation of the diagonal peaks as well as the cross-peak intensities, they were fit globally similar to Ref. 43. To that end, each 2D IR peak was modelled as a correlated 2D-Gaussian function:

\[
G(\omega_1, \omega_3) = A \exp \left\{ -\frac{1}{2(1-c^2)} \left[ \left( \frac{\omega_1 - \omega_{1,0}}{\Delta\omega} \right)^2 + \left( \frac{\omega_3 - \omega_{3,0}}{\Delta\omega} \right)^2 - \frac{2c(\omega_1 - \omega_{1,0})(\omega_3 - \omega_{3,0})}{\Delta\omega^2} \right] \right\},
\]

where \(A\) is an amplitude, \(\omega_{i,0}\) the center frequencies along frequency axis \(i\), \(\Delta\omega\) the frequency width, and \(c\) a correlation coefficient as a measure of spectral diffusion. In total 8 such peaks were defined for a 2D IR spectrum, with many parameters set equal to minimize their total number in the fitting. That is, two pairs of diagonal peaks were defined for the two isotopologues with different central frequencies \(\omega_{i,0}\) and amplitudes \(A\), but identical width \(\Delta\omega\) and correlation \(c\), since the latter two parameters describe the identical interaction of the ions with the solvent environment. Each diagonal peak consists of ground state bleach (GB)/stimulated emission (SE) as well as excited state absorption (EA), where the latter has been down-shifted in the \(\omega_3\)-direction by the anharmonicity \(\Delta = 27\) cm\(^{-1}\). The amplitudes \(A\) and correlations \(c\) of the two contributions to each diagonal peak were assumed to be the same. In addition, two cross peak pairs were introduced, each again consisting of GB/SE and EA contributions, for which center frequencies and width were assumed to be the same as for the corresponding diagonal peaks along the two frequency axes. The amplitudes \(A\) of the two cross peak pairs were set to be the same, and we assumed \(c = 0\) for the correlation.
since cross-relaxation randomizes the frequency. To further stabilize the fitting procedure, the center frequencies $\omega_{i,0}$ and the width $\Delta \omega$ of the two diagonal peaks were first determined from the earliest 2D IR spectrum at $t_2 = 0.25$ ps, and then kept as fixed parameter when fitting a population time series of 2D IR spectra.

The population is proportional to the peak volume $\Phi$, which was calculated from the obtained fitting parameters according to

$$\Phi = 2\pi A \Delta \omega^2 \sqrt{1 - c^2}. \quad (4)$$

The intensity of a cross peak scales with $\|\vec{\mu}_{pu}\|^2 \|\vec{\mu}_{pr}\|^2$, where $pu$ and $pr$ stand for the pumped and probed oscillators, respectively. With this in mind, the energy transfer kinetics can then be retrieved by normalizing the cross peak volumes with $\sqrt{\Phi_{pu} \Phi_{pr}}$, where $\Phi_{pu}$ and $\Phi_{pr}$, respectively, are the volumes of the corresponding diagonal peaks at early population times. The fitting was performed in the same way for both experimental and simulated spectra.

**Computation of the THz Spectra**

The THz absorption spectra are determined from the MD simulations by evaluating the Fourier transform of the $\langle \dot{\vec{\mu}}(t) \dot{\vec{\mu}}(0) \rangle$ auto-correlation function

$$I_{THz}(\omega) \propto \text{Im} \int_0^\infty dt e^{i\omega t} \langle \dot{\vec{\mu}}_{tot}(t) \cdot \dot{\vec{\mu}}_{tot}(0) \rangle$$ \quad (5)

Here, $\dot{\vec{\mu}}$ is the time derivative of the dipole moment $\vec{\mu}$ of the entire simulation system with periodic boundary conditions correctly resolved for molecules that cross boundaries. Partial THz absorption spectra were computed by the Fourier transform from the auto-correlation $\langle \dot{\vec{\mu}}_\alpha(t) \dot{\vec{\mu}}_\alpha(0) \rangle$ where $\alpha$ denotes a respective species $\alpha = \{\text{SCN}^-, \text{K}^+, \text{H}_2\text{O}, \text{acetamide}\}$ of the system. The Fourier transform of the cross-correlation $\langle \dot{\vec{\mu}}_\alpha(t) \dot{\vec{\mu}}_\beta(0) \rangle$ between species $\alpha$ and
\( \beta \) determines the contribution of the two species due to their interplay to the absorption intensity. Figure S3 shows partial THz absorption spectra and the Fourier transform of cross-correlation for a selected species and species combinations, respectively. The integrated absorption or cross correlation is the integral of the experimental or computed THz absorption spectra, the computed partial absorption or the cross correlation intensities in the range from 13 to 34 cm\(^{-1}\).

**Results**

The sample for the present work is a multi-component DES system, which allows for continuous tuning of the hydration state and consequently the viscosity. That is, the eutectic system acetamide/KSCN is mixed with water, which is especially well suited for the purpose of this work, since the CN vibration in the thiocyanate anion (SCN\(^-\)) is an ideal molecular probe for 2D IR spectroscopy. Moreover the expected hydrogen bonding water network in this mixture can be readily probed via THz spectroscopy. Similar eutectic mixtures, i.e., acetamide, potassium thiocyanate together with ethanol have been characterized experimentally using thermodynamic measurements\(^{86}\) in view of their industrial applications and the acetamide-KSCN mixture with water has been reported to remain liquid down to 303 K.\(^{87}\)

For the 2D IR experiments the salt was first prepared in a 50%/50% mixture of the two isotopologues, K\(^{12}\)C\(^{14}\)N and K\(^{13}\)C\(^{15}\)N. The two isotopologues are needed in the 2D IR experiment in order to have two resolved vibrational bands, between which vibrational energy transfer can be observed. Figure 1, top, shows selected 2D IR spectra at early (left) and late (right) population times for the sample with a 50/50% molar ratio of D\(_2\)O/acetamide. At early population times (left) in essence only diagonal peaks arise. They are tilted along the diagonal due to a correlation between pump- and probe frequency, reflecting the spatial
inhomogeneity of the sample. At later population times (right), this correlation is lost (no tilt along the diagonal) but additional cross peaks arise due to cross-relaxation between the resonances of the two isotopologues $\text{KS}^{12}\text{C}^{14}\text{N}$ and $\text{KS}^{13}\text{C}^{15}\text{N}$. For such a cross peak to appear, one of the isotopologues is excited at its vibrational frequency, its vibrational energy is transferred to the other isotopologue during the population time, and is then probed at the vibrational frequency of the second isotopologue.

Figure 1: Experimental (top) and simulated (bottom) 2D IR spectra at early (left) and late (right) populations times (which are indicated in the panels), exemplified here for the sample with a 50%/50% mixture of $\text{D}_2\text{O}/\text{acetamide}$. The contour lines have been normalized to the peak of each spectrum, thereby suppressing $T_1$-relaxation.

The vibrational energy transfer rate is expected to have a steep, i.e. inverse 6th-power, distance dependence for pairwise two molecules. To that end, an analytical expression has
been derived

\[ k = \frac{2}{1 + \exp \left( -\frac{\hbar \Delta \omega}{k_B T} \right)} \left( \frac{V^2 \tau^{-1}}{\Delta \omega^2 + 4V^2 + \tau^{-2}} \right) \], \quad (6)

with \( \Delta \omega \) the frequency difference between both molecules, \( \tau \) a dephasing correlation time, and the transition dipole coupling \( V \) taken from Eq. 2. The physical picture behind this model is the following: Due to the coupling \( V \), excitation energy is initially transferred from the donor to the acceptor in a coherent sense, as described by the time-propagation of the time-dependent Schrödinger equation. The coherence between donor and acceptor state is then abruptly terminated by a random dephasing event after an average time \( \tau \),\(^{42}\) revealing a first-order kinetics with rate described by Eq. 6. The length scale over which vibrational energy transfer can be observed, i.e., the equivalent of a “Förster radius”, is 4-5 Å in the very best case, depending on the strength of the transition dipoles and the lifetime of the vibrational excitation. Histograms for vibrational coupling strengths \( V \) for the different mixtures are reported in Figure S4. Previously, it has been verified by numerical propagation of the Schrödinger equation that the analytical model Eq. 6 is valid for dimers.\(^{43}\) It has, however, also been shown that the situation is more complex when networks of interacting vibrational transitions exist, with a percolation threshold at a certain level of dilution.\(^{43}\) Therefore, the fully coupled systems are considered here.

The starting point for calculating 2D IR spectra are all-atom MD simulations with the same relative concentrations of the various components as in the experiments and a multipolar representation of the electrostatics for the SCN\(^-\) ions.\(^{67}\) The instantaneous frequencies \( \omega_i(t) \), the couplings \( V_{ij}(t) \) between oscillators \( i \) and \( j \) and accompanying parameters are all determined from the MD trajectories as input for the time-dependent Frenkel exciton Hamiltonian Eq. 1. Computed 2D IR spectra are reported in (Figure 1, bottom) and agree with the experimental ones (Figure 1, top) extremely well. Typical frequency-frequency correlation functions (FFCFs) determined from the INM frequencies are reported in Figure S2.
For this comparison it is important to stress that the force field used in the MD simulations has been derived independently and has not been adapted to reproduce the experimental 2D results. Only one additional parameter was added for the calculation of the 2D IR spectra: the modulus of the transition dipole $\mu$ of the SCN$^-$ oscillators. The value used here was 0.35 D, which has been determined experimentally before.\textsuperscript{41} Additional electronic structure calculations confirmed this value ($\sim 0.33$ D), but also showed that considerable charge fluxes on the SCN$^-$ ion are responsible for its magnitude. This effect is not accounted for in the force field used here. Overall, cross relaxation is faster in the simulation, which can be seen from the ratio of cross vs. diagonal peaks (also note the different population times in Figure 1, right: 60 ps for the experimental vs. 15 ps for the simulation spectra). Since the cross relaxation rate is expected to scale with the 4th power of the transition dipole moment,\textsuperscript{42} it is concluded that the assumed value overestimates the true transition dipole strength by only a modest factor. Furthermore, Eq. 6 suggests that the cross-relaxation rate scales as $1/\tau$ of the FFCF, and therefore the long time step in the simulation (see Methods) underestimates the cross-relaxation rate.

The cross peak volumes as determined from Eq. 3 from the experimental (blue) and simulated (red) 2D IR spectra as a function of time for the sample with a 50%/50% mixture of D$_2$O/acetamide are shown in Figure 2A. For the simulated spectra the cross-peak volume exponentially approaches an equilibrium and the cross-relaxation rate can be obtained by single-exponential fitting of this data (revealing a time constant of 25 ps for the example shown in Figure 2A). In contrast, cross relaxation in the experiments competes with $T_1$ relaxation, an effect that is not included in the exciton Hamiltonian Eq. 1. The cross peak volume therefore rises initially and decays again later due to $T_1$ relaxation, see Figure 2A, blue. These data are fit with a bi-exponential function, $-a_0(e^{-t/\tau_1} - e^{-t/\tau_2})$, revealing time constants of 1.4 ps and 56 ps for the example shown in Figure 2A. Since $\tau_1 \ll \tau_2$, the amplitude $a_0$ reflects in essence
Figure 2: (A) Cross peak volumes of the experimental (filled blue squares) and simulated (filled red squares) 2D IR spectra for the sample with a 50%/50% mixture of D$_2$O/acetamide. The cross peak volumes have been normalized to the diagonal peak volumes at the earliest population times. The open red squares show the simulated data after phenomenologically multiplying them with a $T_1$ lifetime of 56 ps. The solid lines show the respective fits. (B) Comparison of the cross-relaxation rate as a function of mixing ratio. For the simulated 2D IR spectra, the inverse time constants from single exponential fits are shown (right scale); in the case of the experimental 2D IR spectra the peak amplitude $a_0$ (left scale). Both data sets are scaled relative to each other.
the peak of the signal, and serves as a measure of the efficiency of cross relaxation. The open red squares in Figure 2A show the simulated data after phenomenologically multiplying them with a $T_1$ lifetime of 56 ps. The data is qualitatively the same as the experimental ones, but the peak amplitude is higher since the simulation overestimates the transition dipole strength (as discussed above).

Figure 2B shows the results of this analysis as a function of acetamide/water mixing ratio, i.e., the single exponential cross relaxation rate for the simulated 2D IR spectra, and the amplitude $a_0$ for the experimental 2D IR spectra. While these two quantities cannot be compared one-to-one, when properly scaling them relative to each other, one can see very good agreement. In both cases, cross relaxation varies non-monotonically as a function of the water content, with a dip after an initial rise and a steep increase towards higher water content. Since the cross-relaxation rate is a steep function of the intermolecular distances between the SCN$^-$ anions, the cross relaxation rate reflects the clustering of the SCN$^-$ anions. Overall, the theoretical curve is shifted somewhat towards a lower water content as compared to the experimental curve, indicating that the MD force field slightly overestimates SCN$^-$ clustering. A simulation with 100% water content no longer gave reasonable results due to ion aggregation, and 95% water content is the highest value considered in all subsequent simulation results. Nonetheless, the fact that the simulations are able to qualitatively capture this non-trivial dependence of the cross relaxation rate on the mixing ratio is remarkable.

Measured Terahertz spectra are reported in Figure 3A for different water/acetamide mixing ratios in the frequency range from 13 cm$^{-1}$ and 34 cm$^{-1}$. The samples were the same as for the 2D IR experiment, except for the fact that H$_2$O and only naturally abundant KS$^{12}$C$^{14}$N at 4.4 M concentration was used. The THz absorption monotonically increases with wavenumber, consistent with a broad band whose peak is outside of the measurement frequency range. Its amplitude scales nonlinearly with mixing ratio across the entire spec-
Figure 3: Experimental (A) and simulated THz spectra (B) between 13 cm$^{-1}$ to 34 cm$^{-1}$. Results are shown for different water/acetamide mixing ratios, including 0% (blue), 20% (red), 50% (green), 80% (violet), 90% (orange), 95% (magenta) and 100% (brown). Panel C shows the THz absorption spectra from all H$_2$O molecules. Panel D compares the integrated intensity of the experimental (blue squares) and simulated (red circles) THz spectra between 13 cm$^{-1}$ and 34 cm$^{-1}$ for different water/acetamide mixing ratios. The data are shifted and scaled to best overlap the lowest and highest integrated absorptions from experiments and simulations. Panel E compares the integrated absorption intensity of the simulated THz spectra with the contribution from the water-water autocorrelation function (light blue). The magenta line with marker shows the average coordination number $\langle n_{H_2O} \rangle$, which corresponds to the number of water molecules surrounding a central water molecule in mixtures with different mixing ratios. Water molecules are counted as in vicinity if the oxygen-oxygen distance is shorter than 4.5 Å. The vertical lines show the standard deviation of the coordination number distribution $P(\langle n_{H_2O} \rangle)$. 

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tral range, which is seen best when plotting the absorption integrated between 13 cm$^{-1}$ and 34 cm$^{-1}$ against the mixing ratio, as shown in Figure 3D (blue squares). The non-linear increase is indicative of a non-trivial structural rearrangement with increasing mixing ratio.

The simulated THz absorption spectra (Figure 3B) agree well with the measurements (Figure 3A) in that they reproduce the increase in absorption with wavenumber and in particular the nonlinear increase with mixing ratio. For a quantitative comparison, the simulated integrated absorption was scaled such that it matches with the measured results for its lowest and highest values, as shown in Figure 3D, and the nonlinear increase for intermediate mixing ratios is reproduced very well.

Contributions from individual components to the total THz absorption spectrum were determined from \( \dot{\mu}_{tot} = \dot{\mu}_{water} + \dot{\mu}_{SCN^-} + \dot{\mu}_{K^+} + \dot{\mu}_{acetamide} \), where \( \dot{\mu}_\alpha \) is the contribution of species \( \alpha \) to the total dipole moment time derivative of the simulation system (even for single charged atoms there is a contribution to the total system dipole moment). This gives rise to 4 auto-correlations and 6 cross-correlations when evaluated in Eq. 5. The largest contribution to the THz absorption spectrum, as well as its nonlinear dependence on the mixing ratio, can be traced back to the water-water autocorrelation function in the mixture, see Figures 3C and the red vs. light blue line in 3E. All other contributions to the total absorption spectrum are comparably small, and are essentially flat as a function of mixing ratio, see Figure S3.

To summarize this part, the MD simulations can almost quantitatively reproduce the results of both the 2D IR and THz spectroscopy, and in particular capture correctly the highly non-trivial changes of the spectroscopic responses for different mixing ratios. 2D IR spectroscopy is primarily sensitive to short range SCN$^-$/SCN$^-$ contacts and reveals more rapid intermolecular energy redistribution between the CN stretch vibrations of SCN$^-$ in systems with higher water ratios. The striking feature is the sharp increase of these contacts at
...water content and above which is also what the simulations find but already at 80% water content. On the other hand, THz spectroscopy, which is mostly sensitive to the water in the sample, shows a similar sharp increase in absorption above 80% water ratio. Both spectroscopic observations reflect and report on different structural properties of the liquid. Based on this agreement between experiments and simulations the structural properties, which can be directly assessed from the MD simulations, will be analyzed in the following.

Discussion

Figure 4A reports the partial radial distribution function $g_{\text{SCN}^-\text{SCN}^-}(r_{CC})$ computed from the MD trajectories. Here, $r_{CC}$ is the carbon-carbon distance between the SCN$^-$ anions. The first maximum occurs at $r_{CC} \sim 3.8$ Å for mixtures with larger water content, especially for 80% and larger. This peak does not exist in pure acetamide (blue) and then increases gradually for mixtures with 20% to 80% water content. At above 50% water content the peak height increases sharply, by a factor of close to two. As the vibrational energy transfer rate depends on the inverse 6th power of the separation of the oscillators, it is concluded that it is this peak in the $g_{\text{SCN}^-\text{SCN}^-}(r_{CC})$ radial distribution function that is responsible for the cross relaxation. Indeed, the cross-relaxation rate follows the height of this peak in particular with respect to the step-like rise beyond 80% water content (Figure 2). It is also noted that the position of the first maximum in $g_{\text{SCN}^-\text{SCN}^-}(r_{CC})$ changes only marginally (except for the water-free system) but the peak height increases by a factor of three between 20% and 95% water content. This indicates that predominantly, an angular reorientation of neighboring SCN$^-$ ions occurs upon increased water content.

The rise of the first peak in $g_{\text{SCN}^-\text{SCN}^-}(r_{CC})$ correlates with the decrease of the first peaks in $g_{\text{SCN}^-\text{K}^+}(r_{\text{CK}^+})$ at $r_{\text{CK}^+} = 3.65$ Å and 4.35 Å (Figure 4B). These peaks are related to K$^+$...
Figure 4: Radial distribution function $g(r)$ for the C atom of SCN$^-$ to (A) the C atom of SCN$^-$, (B) K$^+$, (C) the O atom of H$_2$O and (D) the N atoms of in acetamide (multiplied by its density $\rho$(H$_2$O) and $\rho$(acetamide), respectively) of the MD simulation of the different mixtures of H$_2$O/acetamide. See Figure S5 for $g_{\text{SCN}^-\text{SCN}^-}(r_{CC})$ at the experimental density of 1.14 g/cm$^3$ for high water content.

interacting with the N- and S-ends in axial position of SCN$^-$, respectively. The plateau at even shorter distances ($r < 3.65$ Å) originates from K$^+$ in an equatorial position relative to the SCN$^-$ anion (T-shaped configuration). With increasing water content, the decrease of the peak amplitudes in Figure 4B indicates preferential solvation of K$^+$ by water molecules.

Concomitantly, the radial distribution function $g_{\text{SCN}^-\text{H}_2\text{O}}(r_{CO})$ for SCN$^-$ and the water oxygen atom in Figure 4C indicates preferred interaction of these molecules. Water solvent and, in particular, the positively charged H$^{\delta^+}$ are more frequently attached along the axial position to the S atom of SCN$^-$ (second peak in Figure 4C) and preferably to the N atom (first peak in Figure 4C), thereby substituting K$^+$. The higher the water content, the higher the proportion of K$^+$ solvated by water molecules which prevents K$^+$ from directly interacting with an SCN$^-$ ion. Equatorial close attachment of water around SCN$^-$ occurs proportionally more often compared with axial attachment at much higher water ratios (initial plateau.
Figure 5: SCN$^-$-SCN$^-$ radial-angular alignment distribution SCN$^-$ anions with increasing water content from left to right. The orientation angle $\alpha$ is defined between the CN bond vector (green arrow) of the center SCN$^-$ and the C-C connection vector (red arrow) to the second SCN$^-$. The alignment $\theta$ denotes the angle between both CN bond vectors and $r_{CC}$ is the distance between the C atoms of neighboring SCN$^-$ anions. The distribution along the $r_{CC}$ is normalized as in the radial distribution function. Features A to E correspond to high density points in the distribution. The values for $\phi$ in all relative orientations ($r, \theta, \alpha$) are unspecified, see panel X.

in Figure 4C). Conversely, acetamide was found to attach preferentially in an equatorial position around SCN$^-$ (first broad peak in Figure 4D). Acetamide attached axially by the partially positively charged amine hydrogen atoms to the N and S atom of SCN$^-$ becomes prevented by already low water content in the mixture as observable by the diminishing second and third peak in Figure 4D with increasing water ratio. The rapid increase in the radial distribution function between SCN$^-$ anions at 3.8 Å in Figure 4A for water ratios 80% to 90% correlates with a significant change in the system composition. The ratio between the number of SCN$^-$ anions $N$(SCN$^-$) and acetamide molecules $N$(acetamide) in the simulation system changes from $N$(SCN$^-$) < $N$(acetamide) to $N$(SCN$^-$) > $N$(acetamide) for mixtures 80% and 90%, respectively.
The increase of the first maximum of $g_{\text{SCN}^-\text{SCN}^-}(r_{\text{CC}})$ in Figure 4A and shift towards shorter $r_{\text{CC}}$ with increasing water content indicates that the arrangement of SCN$^-$ anions becomes more dense and forms clusters. The denser packing correlates with increased order in the orientation between neighboring SCN$^-$ anions. This effect is shown in Figure 5, which reports projections $P(\alpha, \theta)$ (green), $P(\alpha, r_{\text{CC}})$ (red), and $P(\theta, r_{\text{CC}})$ (blue) of the 3-dimensional probability distribution function $P(\alpha, \theta, r_{\text{CC}})$ of the relative configurations of all SCN$^-$ anions with carbon-carbon distances $r_{\text{CC}} < 8$ Å. In pure acetamide (left panel Figure 5), the angular orientation between two SCN$^-$ molecules is broadly distributed over a larger angular range in $\alpha$ and $\theta$. As the water content increases (middle and right panels), SCN$^-$ is more inclined for equatorial stacking with parallel or antiparallel alignment. This becomes evident as the angular distribution in $\alpha$ (red contour plot) and $\theta$ (blue contour plot) against the SCN$^-$-SCN$^-$ distance $r_{\text{CC}}$ contracts towards a parallel ($\alpha \sim 90^\circ$, $\theta \sim 0^\circ$, Figure 5E) and anti-parallel ($\alpha \sim 90^\circ$, $\theta \sim 180^\circ$, Figure 5D) alignment. Increased order in the angular orientation for neighboring SCN$^-$ anions increases the tendency for smaller SCN$^-$-SCN$^-$ separations and leads to the peak at 3.8 Å in the partial radial distribution function $g_{\text{SCN}^-\text{SCN}^-}(r_{\text{CC}})$ for increasing water ratios (Figure 4A).

The transition dipole coupling not only depends on inter-ion distance, but also on the relative orientation, see Eq. 2. For an equatorial stacking with parallel or antiparallel alignment (structures D and E in Figure 5), the transition dipole coupling is positive since the first term in Eq. 2 dominates given that $\vec{r}_{ij} \perp \vec{\mu}_i = 0$. Such structures are called H-aggregates.\(^{88}\) On the other hand, the second term overcompensates the first one for a tail-to-tail arrangement (structure A in Figure 5, J-aggregates). In between, there are magic angle configurations similar to structure B or C, where both terms cancel each other. Figure 5 shows that the most sharply defined structures are in fact H-aggregates with a population that increases with water content. At the same time, they reveal the shortest $r_{\text{CC}}$ distance, and hence dominate the cross-relaxation rate. For positive transition dipole coupling, the higher frequency state
will be the symmetric (in-phase) linear combination of SCN local states, and thus will gain oscillator strength at the expense of the out-of-phase, lower-frequency state.\textsuperscript{88} 2D-IR spectroscopy amplifies this effect due to the 4th-power dependence of the peak intensity on the transition dipole (in contrast to a quadratic dependence of linear absorption spectroscopy). Indeed, the higher frequency band is stronger in the simulated 2D IR spectra (Fig. 1, bottom) due to this effect (but one can not rule out that the KS\textsuperscript{13}C\textsuperscript{15}N/KS\textsuperscript{12}C\textsuperscript{14}N mixture has not been exactly 50%/50% in the experiment.)

THz spectroscopy is sensitive to structural changes on larger spatial scales. As an example, \textit{ab initio} MD simulations of liquid water concluded that solutes can impact the hydrogen bond network on length scales corresponding to at least two layers of solvating water molecules, i.e. \( \sim 10 \text{ Å} \), and affect the THz spectrum.\textsuperscript{89} Here, it is found that the integrated absorption increases in a nonlinear fashion as water content in the system increases; see Figure 3D. Such a nonlinear dependence indicates that water is not only a dilution component. Rather, the simulations suggest that as the water content increases, microheterogeneous patches of water develop. Microheterogeneity has already been reported for acetonitrile/water mixtures which have been linked to anomalous thermodynamic properties of such mixtures.\textsuperscript{90–92} Similarly, mixtures of very dilute methanol and acetonitrile lead to clustering of methanol as tetramers or larger clusters\textsuperscript{93} and from small angle neutron scattering experiments on sorbitol-water mixtures which also reported microheterogeneous clustering of the water.\textsuperscript{94} Here, microheterogeneous clustering of water molecules can be gleaned from Figure 3E, which implies that the integrated THz absorption as a function of the mixing ratio follows the same nonlinear behaviour as the size distribution of water clusters in the system. The nonlinearity may arise from the fact that the number of interactions one specific water molecule in a water cluster is involved in scales as \( \propto n^2 \). It is likely that including polarizability in the simulations - in particular for water - further improves quantitative agreement with the experiments. For pure water it is known that point charge models capture the 600 cm\(^{-1}\) absorption correctly.
whereby the line shape extends well beyond the 200 cm$^{-1}$ feature due to the oxygen–oxygen low frequency motion without, however, accounting for the spectral density due to neglect of polarizability. Including polarization in the model leads to the spectral response in better agreement with experiment. However, whether and in which way these observations for pure water translate to the heterogeneous system considered in the present work is unclear.

The $g_{\text{SCN}^- - \text{SCN}^-}(r_{CC})$ radial distribution functions in Figure 4A show that with increasing hydration the probability to find two SCN$^-$ ions at their most likely separation ($r_{CC} \sim 3.8$ Å) increases whereas the position of the maximum is largely unaffected. Based on the dielectric constants for water (80) compared with acetamide (60) it would be expected that hydration of SCN$^-$ is facilitated by increasing water content that results in increased probability to populate longer $r_{CC}$ separations or a shift of the maximum value for $P(r_{CC})$ to larger values of $r_{CC}$, or both. However, for complex and electrostatically demanding mixtures such as DESs it is likely that expectations governing bulk solvation do not simply translate. In other words: “local solvation” as is operative in DESs is governed by molecular driving forces which may result in phenomenologically different observations compared with what is known from “bulk solvation”.

**Conclusion**

In conclusion, spectroscopic responses in two different regions of the optical spectrum (infrared and THz) for a heterogeneous, electrostatically dominated system are realistically described from atomistic simulations for a range of acetamide/water ratios. The integrated THz absorption increases in a nonlinear fashion due to the quadratic dependence of the number of interactions in the water clusters that form with increasing water content and to which this spectroscopy is sensitive to. Conversely, 2D IR spectroscopy probes the closer
environment of an oscillator (here the CN-stretch) and coupling between the oscillators. With increasing water content the relative orientation of two adjacent SCN$^-$ anions changes from predominantly linear or angled to a more parallel arrangement. The agreement between simulations and experiments points to an adequate description of the intra- and intermolecular interactions in the complex system that can provide insights in the physical and chemical properties not only for SCN$^-$ clustering in eutectic acetamide:water solvent but for ion clustering in DESs in general.

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**Supporting Information Available**

The experimental and computational setup, the sample preparation and supplementary figures are provided in the supporting information.

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Deep eutectic KSCN/acetamide mixtures with varying water content are investigated experimentally by 2D infrared and terahertz spectroscopy and by molecular dynamics simulations to characterize the heterogeneity of such mixtures by modulating their composition.
Supporting Information:
Structure, Organization and Heterogeneity of Water-Containing Deep Eutectic Solvents

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## Force Field Parametrization

Table S1: Bonded and non-bonded parameters.

| Residues     | Parameters          |
|--------------|---------------------|
| Acetamide    | CGenFF S1           |
| Water        | TIP3P S2            |

### K⁺

| Non-bonded   | ε (kcal/mol) | r<sub>min</sub> (Å) | q (e) |
|--------------|--------------|----------------------|-------|
| K⁺S<sup>3</sup> | 0.087        | 3.5275               | +1    |

### SCN⁻

| Bond (Morse Potential) | r<sub>eq</sub> (Å) | β (Å⁻¹) | D₀ (kcal/mol) |
|------------------------|---------------------|---------|---------------|
| C-N *                  | 1.21706             | 1.61348 | 373.811       |
| S-C *                  | 1.66867             | 1.69773 | 124.360       |

| Angle (Harmonic Potential) | k<sub>θ</sub> (kcal/mol/rad²) | θ<sub>min</sub> (°) |
|----------------------------|-------------------------------|---------------------|
| S-C-N                      | 21.20                         | 1.61348             |

| Non-bonded | ε (kcal/mol) | r<sub>min</sub> (Å) | q (e) |
|------------|--------------|----------------------|-------|
| S          | 0.45         | 4.00                 | -0.183|
| C          | 0.18         | 3.58                 | -0.362|
| N          | 0.18         | 3.74                 | -0.455|

| Atomic Multipoles ** | S   | C   | N   |
|----------------------|-----|-----|-----|
| Q₁₀                  | -1.83| -0.362| -0.455|
| Q₁₁c                 | 1.179| 0.163| 0.319|
| Q₁₁s                 | 0.0  | 0.0  | 0.0  |
| Q₂₀                  | -1.310| -0.929| -3.114|
| Q₂₁c                 | 0.0  | 0.0  | 0.0  |
| Q₂₁s                 | 0.0  | 0.0  | 0.0  |
| Q₂₂c                 | 0.0  | 0.0  | 0.0  |
| Q₂₂s                 | 0.0  | 0.0  | 0.0  |

* MP2/cc-aug-pVDZ
** within Local Reference Axis System and in atomic units - see MTPL documentation: [www.charmm.org/archive/charmm/documentation/by-version/c45b1/mtpl.html](http://www.charmm.org/archive/charmm/documentation/by-version/c45b1/mtpl.html)
System compositions

Table S2: Molar fraction and number of molecules used on the MD simulations for each component of the systems at a given water/acetamide mixing ratio.

| Mixing Ratio | Molar Fraction | Number of Molecules |
|--------------|----------------|---------------------|
|              | H$_2$O | Acetamide | KSCN | H$_2$O | Acetamide | KSCN |
| 100          | 0.901 | 0.000     | 0.099 | 685   | 0        | 75   |
| 95           | 0.844 | 0.044     | 0.111 | 570   | 30       | 75   |
| 90           | 0.791 | 0.092     | 0.118 | 506   | 59       | 75   |
| 80           | 0.686 | 0.179     | 0.135 | 381   | 100      | 75   |
| 70           | 0.586 | 0.263     | 0.152 | 290   | 130      | 75   |
| 60           | 0.490 | 0.342     | 0.168 | 219   | 153      | 75   |
| 50           | 0.399 | 0.418     | 0.183 | 164   | 171      | 75   |
| 40           | 0.312 | 0.490     | 0.198 | 119   | 186      | 75   |
| 30           | 0.229 | 0.559     | 0.212 | 81    | 198      | 75   |
| 20           | 0.149 | 0.626     | 0.225 | 50    | 209      | 75   |
| 10           | 0.073 | 0.689     | 0.238 | 23    | 217      | 75   |
| 0            | 0.000 | 0.750     | 0.250 | 0     | 225      | 75   |
Densities

Figure S1: Average density of the simulation systems for different mixing ratios in the NPT at 300 K (red full circles). Average densities from MD simulation with Lennard-Jones parameters for SCN$^-$ from Bian et al.$^5$ are shown with open red circles and from MD simulation with the SPC/E water parametrization for the 100% mixture are shown as green circle.$^6$ Experimental values at 298 K for KSCN in acetamide$^6$ and in water$^7$ are shown with blue squares. The experimental density for KSCN in water is linearly interpolated between the closest reference values to fit the molality of KSCN in the simulated system at 95% mixing ratio (3.77 mol/kg).
Figure S2: Averaged frequency-frequency correlation function (FFCF) of the INM frequencies of all C-N vibrations in the SCN\(^-\) anion in different mixing ratios of acetamide and water. The FFCF are computed from INM frequency sequences of length $t = 250$ ps with time steps of $\Delta t = 0.01$ ps (top left panel) and of length $t = 1000$ ps with time steps of $\Delta t = 0.05$ ps (top right panel). Bottom left and right panels directly compare the FFCFs for mixture 20% and 90% with different time steps, respectively.
THz Spectra

Figure S3: Components of the THz absorption spectra from the Fourier transform of the (A-D) auto-correlation of the dipole sequences of all (A) SCN$^-$ anions, (B) K$^+$ cations, (C) H$_2$O and (D) acetamide molecules. Panels E-K shows the Fourier transform of the cross-correlation functions of the 6 possible dipole sequence combinations. The integrated intensity of the single component THz absorption spectra is given in panel L and of the cross correlation functions in panel M. Panel N compares the integrated absorption of the experimental THz spectra (blue line) for different mixtures with the simulated spectra from the total dipole sequence (red line) and the sum of the single components in panel L and cross components in panel M (red dashed line).
Vibrational Coupling

Figure S4: Vibrational transition coupling strength $V$ (A) between all SCN$^-$-SCN$^-$ ion pairs and (B) for pair distances shorter than 5 Å. Each curve shows the change in amplitude for different mixing ratios of the histogram of ion pair number vs. transition coupling with bin size of 1 cm$^{-1}$. The coupling is computed for the same data selection used for the computation of the 2D IR spectra ($\sim 10^8$ ion pairs per mixture). The line shapes of the curves for medium and high coupling strengths are unaffected by the exclusion of ion pairs with distances larger than 5 Å.
Radial Distribution Function at Experimental Density

The computed system density of the NPT ensemble at 300 K and normal pressure is almost linearly increasing from 1.26 g/cm$^3$ (0%) to 1.35 g/cm$^3$ (95%). Experimentally obtained reference densities yield a decrease from 0% to 100% water content from 1.207 g/cm$^3$ to 1.14 g/cm$^3$. Experimental densities for a KSCN:acetamide DES mixed in different ratios with water are reported in reference S8, however, in their work the KSCN concentration decreases with increasing water ratio. Additional simulation for a subset of mixing ratios were performed using Lennard-Jones Parameters for SCN$^-$ from the work of Bian et al. (open red circles). Additionally, one MD simulation for the 100% mixture using the SPC/E water model was performed that yields an average density of 1.31 g/cm$^3$. One final simulation was carried out for KSCN in 100% water at the experimentally determined density of 1.14 g/cm$^3$ to determine the sensitivity of the SCN$^-$/SCN$^-$ ordering on the density of the simulated system, see Figure S2. It is found that the radial distribution function $g_{SCN^- - SCN^-}(r_{CC})$ only marginally changes if the density increases from 1.14 g/cm$^3$ to 1.35 g/cm$^3$. 

S-8
Figure S5: Radial Distribution function $g_{\text{SCN}^-\text{SCN}^-}(r_{CC})$ between the C atoms of SCN$^-$ anions from MD simulations with parametrization used throughout this work (see Table S1) of a NV$T$ ensemble of KSCN in water with a respective box size to match the experimentally observed density of 1.14 g/cm$^3$ (dashed brown line) with KSCN molality of 3.77 mol/kg. The radial distribution function in the $NPT$ ensemble of KSCN in a 95% mixture of water and acetamide with average density of 1.35 g/cm$^3$ is shown by the solid magenta line, see also Figure 4.
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