Liquid Structure and Dynamics in Acetaline, a Choline Acetate:Urea 1:2 Deep Eutectic Solvent.

Alessandro Triolo[1,*], Maria Enrica Di Pietro[2], Andrea Mele[2], Fabrizio Lo Celso[1,3], Martin Brehm[4], Valerio Di Lisio[5], Andrea Martinelli[5], Philip Chater[6], and Olga Russina[1,5,*].

[1] Laboratorio Liquidi Ionici, Istituto Struttura della Materia, Consiglio Nazionale delle Ricerche, (ISM-CNR) Rome, Italy

[2] Department of Chemistry, Materials and Chemical Engineering "G. Natta", Politecnico di Milano, Milano, Italy.

[3] Department of Physics and Chemistry, Università di Palermo, Palermo, Italy.

[4] Institut für Chemie, Martin-Luther-Universität Halle–Wittenberg, Halle (Saale), Germany.

[5] Department of Chemistry, University of Rome Sapienza, Rome, Italy.

[6] Diamond House, Harwell Science & Innovation Campus, Diamond Light Source, Ltd., Didcot, Oxfordshire OX11 0DE, UK

Corresponding Authors: A. T. (triolo@ism.cnr.it); O.R. (olga.russina@uniroma1.it)

Abstract.

We report on the thermodynamic, structural and dynamic properties of a recently proposed Deep Eutectic Solvent (DES), formed by choline acetate and urea at the stoichiometric ratio 1:2, hereinafter indicated as acetaline. Acetaline, although melting at ca. 40 °C, can be easily supercooled in its liquid state at sub-ambient conditions. The existence of a crystalline phase has been detected, together with the glass-liquid transition at -50 °C. Synchrotron high energy X-ray scattering experiments provide the experimental data for supporting a Reverse Monte Carlo analysis to extract structural information at atomistic level. This exploration of acetaline's liquid structure reveals the major role played by hydrogen bonding in determining interspecies correlations: both acetate and urea are strong hydrogen bond acceptor sites, while both the choline hydroxyl and urea act as HB donors. All acetaline moieties are involved in mutual interactions, with acetate and urea strongly interacting through hydrogen bonding, while choline being involved mostly in van der Waals mediated interactions. Such a structural situation is mirrored by the dynamic evidences obtained by means of ^{1}H NMR techniques, that show how urea and acetate species experience higher translational activation energy than choline, fingerprinting their stronger commitments into the extended hydrogen bonding network established in acetaline.

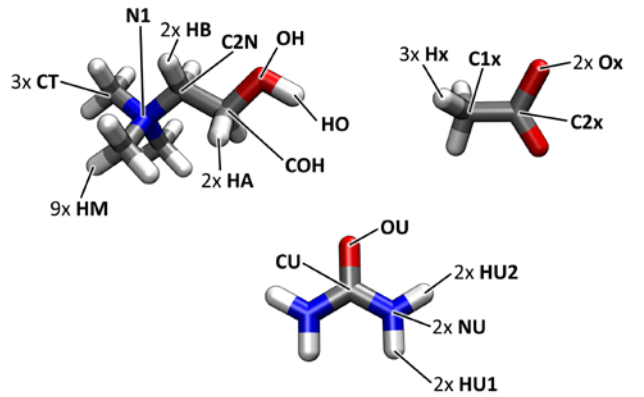
Introduction.

In the last decade large interest has been growing around deep eutectic solvents (DES)[1,2] and their applications in several fields[3–8]. After the classification proposed by Smith et al. of DES in terms of four different types[3], those belonging to type III are among the most commonly encountered ones. These latter DES are composed by a mixture of a salt (e.g. choline (i.e. the (2-hydroxyethyl)-trimethylammonium cation) chloride) with a hydrogen bonding donor (such as urea, glycerol, etc.) with, depending on the concentration ratio between the two components, a melting point depression resulting from their mixing. The large interest on these compounds stems from several appealing properties, not least their cheap production cost and easy preparation and purification. Most of them are also characterised by nonflammability, bio-compatibility and low toxicity, thus turning out to be ideal media for the development of a variety of processes. On the other hand, most of these appealing features stem from the combination of chemical-physical properties of the different components. Accordingly, by (even minor) changes to their chemical nature, one can efficiently modulate the resulting macroscopic performance, thus leading to the classification of DES as task-specific solvents.[4] Among the most well-known DES, we recall the stoichiometric 1:2 mixture of choline chloride (CC) and urea (U), sometimes referred to as reline.[9–16] Dry reline melts at ca. 31 °C[17] and has attracted huge interest over the last few years. Other CC-based DES have been proposed, including CC-glycerol (Gly) 1:2 (glyceline)[18–22], CC-ethylen glycole (EG) 1:2 (ethaline)[22–24] and, more recently, CC-water 1:3.3-4.2 (aquoline)[25–27]. The recent interest in DES stems from the opportunity that they provide to modulate their solvating properties by changes in their chemical composition. Aiming at expanding the spectrum of properties, other anions paired with choline have been explored as well. For example, choline acetate (CAc) has been recently considered as an interesting ionic liquid to be paired with an HB donor to lead to a DES. CAc is an ionic liquid with melting point at 51 °C, proposed by Fukaya et al., as an interesting example of an IL composed solely of biomaterials.[28] The opportunity to use it as a salt for preparation of a DES was presented by Zhao et al., who showed the eutectic nature of mixtures of CAc with urea (1:2), Gly and EG; these DES showed low viscosity, high biodegradability and excellent compatibility with lipase.[29] More recently CAc mixtures with different HBDs were probed for their efficiency towards enzymatic reaction with β-galactosidase.[30] In 2020, some of us used CAc-based DES in order to efficiently solubilise hemicellulose at mild conditions. [31]

This intense applicative activity calls for deeper understanding of the chemical-physical properties of CAc-based DES that have so far received negligible attention compared e.g. to their CC-based equivalents. Here we present a detailed experimental and computational study of structural and dynamic properties of liquid acetaline, a DES composed by CAc and urea at 1:2 molar ratio. The structural properties of acetaline have been obtained by merging high-energy X-ray diffraction and a Reverse Monte Carlo computational approach, aiming at extracting atomistic level structural details of the liquid organization in bulk acetaline. The same sample has also been probed with NMR techniques, aiming at extracting dynamic information related to rotational and translational processes, occurring around room temperature. Overall, this study provides a careful characterization of structural and dynamic properties of a new, eco-sustainable DES, paving the way for its application as a complementary medium to other related DES.

Experimental and Computational details.

Choline acetate (CAc) used for DSC and X-ray scattering was a TCI product; urea was a Sigma Aldrich product. CAc and urea were dried under vacuum at ambient temperature for several days. Eutectic mixtures at 1:2 CAc:U ratio were prepared in a glovebox with an inert atmosphere to reduce ambient moisture contamination, leading to acetaline formation (see **Scheme 1**). After mixing, the sealed vials were kept at 40 °C under constant agitation for at least one hour, to lead to a transparent homogeneous liquid. The sample could be maintained amorphous, when kept at ambient temperature (20 °C) in thin sealed capillaries; it would crystallise when kept inside large sealed vials.



Scheme 1. Schematic representation of choline (top, left), acetate (top, right) and urea (bottom) moieties of acetaline (choline acetate:urea=1:2). The nomenclature of the different atomic species is shown.

DSC thermograms were acquired by a Mettler Toledo DSC 822e equipped with a FRS5 sensor and a liquid nitrogen cooler. The furnace was purged during the measurement with dry nitrogen at a flow rate of 30 ml min^{-1}. A sample of about 5 mg was weighted in a 40 µl aluminium pan and rapidly sealed. DSC scans comprised of a cooling from 50 to -125 °C followed by a heating from -125 °C up to 50 °C, with a heating/cooling rate of 2/10 °C min^{-1}.

Acetaline was loaded into a borosilicate capillary of 1.5 mm outer diameter, which was glue-sealed. The total high-resolution X-ray scattering data were collected on the I15-1 beamline at Diamond Light Source, UK, using X-rays of wavelength 0.309574 Å and a Perkin Elmer XRD 4343 CT detector. The total scattering data were integrated to 1D using DAWN[32] and then normalised and corrected to extract S(Q) using GudrunX[33,34].

CAc and U for NMR experiments were purchased from Iolitec and Sigma Aldrich, respectively, and used without further purification. The DES at 1:2 molar ratio was prepared by the heating method, by mixing the two constituents at 80 °C under stirring for 1h, until a homogeneous and transparent liquid was formed. As the freshly prepared acetaline nor its starting components were dried, a residual amount of water is present in the sample (5.7 wt% by Karl Fischer titration). Controlled amounts of

water are beneficial to reduce the viscosity and allow for satisfactorily resolved NMR spectra. The sample was transferred to a 5 mm NMR tube, equipped with a capillary containing DMSO-d_6. NMR measurements were performed at 11.74 T NMR with a Bruker NEO 500 console equipped with a direct observe BBFO (broadband including fluorine) iProbe (^{1}H resonance frequency of 500.13 MHz). Measurements were performed over a temperature range of 278 K to 358 K, in 5 K increments, and a minimum of 15 min allowed for thermal equilibration. The residual amount of water together with the liquid tendency to remain in a supercooled state when slowly cooled (see Results & discussion) allowed for NMR measurements at such temperatures.

T_1 relaxation measurements were carried out without sample spinning with the inversion recovery (IR) pulse sequence, using relaxation delays at least five times the longest T_1, and the instrument was carefully tuned, shimmed, and the 90° pulses calibrated before each measurement. The spin−lattice relaxation rates were measured using data matrices of 16384 (t_2) × 16 (t_1), over a spectral width of 9 ppm for various delay times τ, ranging from 0.05−5 to 0.05−12 s, according to the temperature. A total of two transients per increment were collected for each T_1 experiment. The baselines of all arrayed T_1 spectra were corrected prior to processing the data and integrals were used to calculate relaxation times. A single exponential decay was observed for all samples over the entire temperature range investigated. Relaxation times were computed from experimental raw data by means of the Bruker T_1/T_2 relaxation module using the manual integration option and applying the standard one-component fitting function. Data were processed three times and errors were calculated from the maximum standard deviation found at the lowest temperature. Maximum errors are estimated to be 1%. Fits to extract the correlation times and rotational activation energies from the relaxation rates were performed with OriginPro 2018 using a user-defined function with the Levenberg–Marquardt algorithm. For the fit procedure, average errors were estimated to be 5%

Self-diffusion coefficients were measured by pulsed field gradient (PFG) experiments by applying sine-shaped pulsed magnetic field gradients along the z-direction up to a maximum strength of G = 53.5 G cm^{-1}. All the diffusion experiments were performed using the bipolar pulse longitudinal eddy current delay (BPP-LED) pulse sequence. All experiments were carried out over a spectral width of 9 ppm, with a total of eight transients per increment. The relaxation delay was set to at least five times T_1, and four dummy scans were programmed prior to acquisition. The pulse gradients were incremented from 2 to 95% of the maximum gradient strength in a linear ramp with 32 steps. For each DOSY experiment,

the duration of the magnetic field pulse gradients (δ) and the diffusion times (Δ) were optimized to obtain, where possible, 95% signal attenuation for the slowest diffusion species at the last step experiment. δ values were in the 2.4−6 ms range, while Δ values were 0.4−0.8 s long. The baselines of all arrayed spectra were corrected prior to processing the data. Data were processed using an exponential filter in F2 dimension (LB = 0.3 Hz), and integrals were used in calculating relaxation times. The determination of self-diffusion coefficients used the Bruker T_1/T_2 module of TopSpin for each peak. The precision of the measured diffusion coefficients is estimated to be within 3%.

2D ^{1}H-^{1}H nuclear Overhauser enhancement (NOESY) experiments were recorded at 298 K by using the phase-sensitive ge-2D NOESY pulse sequence using echo-antiecho (noesyetgp in the Bruker library). Spectra were recorded using eight transients over 4096 (t_2) × 256 (t_1) complex data points. 32 dummy scans and mixing times in the range 20 – 500 ms were used. The relaxation delay was set to 4 s. The NOESY data sets were processed by applying a sine squared window function in both dimensions (SSB = 2) prior to the Fourier transform.

The EPSR approach has been used to model the X-ray diffraction data.[35] This is a robust approach that is based on the optimization of the empirically proposed potential that leads to the best agreement with experimental diffraction data.

We used a simulation box containing 100 CAc ion pairs and 200 urea moieties (CAc:Urea=1:2) with a density of 1.17 g/cc[30] (cubic box size=35.3 Å) at 25 °C. The starting interatomic potential used for choline and urea is the one that was successfully used by Hammond et al. in their study of reline.[10,36] The acetate interaction potential parameters are the same used by Bowron et al. in their study of acetate based ionic liquids.[37] After an equilibration of ca. 6,000 steps, the EPSR was activated and further 10,000 steps delivered a good agreement of the calculated diffraction pattern with the experimental one. At this stage, further 7,000 steps were collected to achieve statistical accuracy on the structural observables (pair distribution functions, angular distributions etc.). In order to evaluate structural properties from the resulting Monte Carlo trajectories, the TRAVIS software was used.[38–40]

Results & discussion.

Acetaline's DSC trace is shown in **Figure 1**, where two thermal traces are shown with heating/cooling rates equal to 2 and 10 °C/min, respectively. At ambient conditions (i.e. at ca. 2 0 °C), crystalline acetaline is thermodynamically stable, with a melting temperature of about 40 °C. It appears that upon cooling, liquid acetaline can be easily supercooled into an amorphous solid, without crystallization intervening. The liquid-glass transition can be detected at approximately -50 °C. On the other hand, upon heating the glass material, crystallization occurs at temperatures depending on the heating rate; such a crystal eventually melts approaching 36-38 °C.

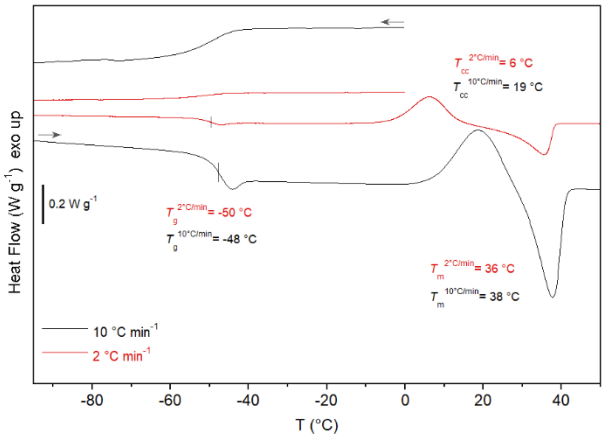


Figure 1. Thermal trace of acetaline (choline acetate: urea=1:2) at two different heating/cooling rates (2 and 10 °C/m, respectively). Indications of the liquid-glass transition at ca. -50 °C and solid melting at ca. 38 °C are highlighted.

It is notewortly that, upon cooling from the melt, acetaline remains in the liquid supercooled state at 20 °C for long time (several days). Accordingly, we determined the liquid structure of acetaline at ambient temperature, without incurring into sample crystallization during the experiment time duration. Synchrotron X-ray diffraction data collected in such a way are reported in **Figure 2**. It appears that acetaline is characterised by an X-ray diffraction pattern similar to the ones from other choline-based DES, such as reline, aquoline etc.

The quality of the agreement of experimental X-ray scattering pattern and the corresponding EPSR computed quantity is shown in **Figure 2**. The EPSR-derived X-ray weighted scattering pattern nicely accounts for the experimentally observed features, thus providing a validation support to the structural information that can be extracted from the computed trajectories. It can be appreciated that similarly to other choline-based DES, the experimental X-ray scattering pattern does not show appreciable features

at low Q values, apart from the low Q peak at ca. 1.5 $Å^{-1}$, thus suggesting that no large scale structural heterogeneities occur in this system, which could be related either to polar/apolar segregation [41–44] or to

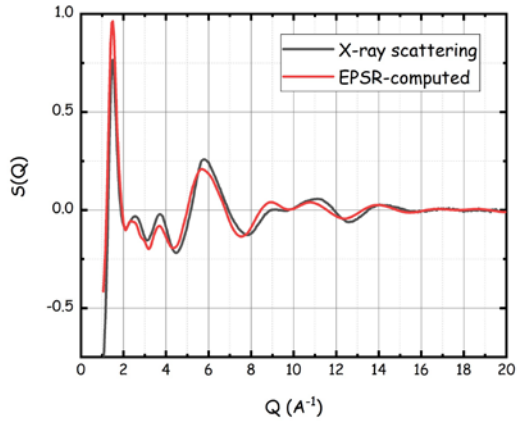


Figure 2. Comparison between experimental (black) and EPSR-computed (red) X-ray scattering patterns from acetaline at ambient temperature.

mesoscopic phase separation[45–47]. The EPSR-generated trajectories were further interrogated to extract structural information on bulk acetaline.

Figures 3 shows the center of mass pair distributions functions (pdf) for the three moieties in acetaline, namely, choline cation (C), acetate anion (A) and urea (U). It emerges that strong correlations exist between differently charged ionic species and between urea and all the components. Correlations between ionic species with the same charge are instead weaker and less well defined. CC correlations

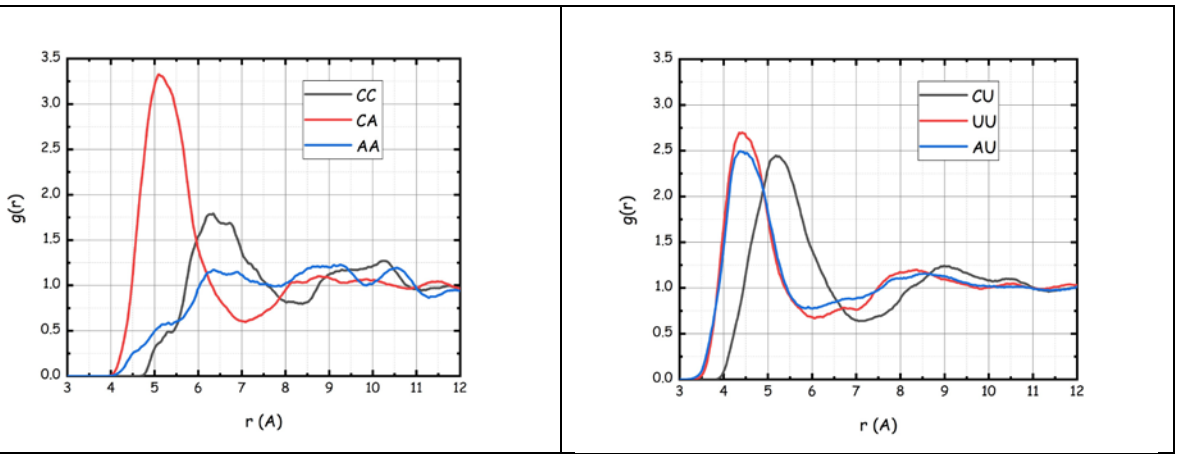


Figure 3. Pair distribution function between centers of mass of ionic species (cation (C), anion (A)) (left) and urea (U) with A and C (right) in acetaline, as obtained from the EPSR modelling.

are characterised by a weak broad peak centred at ca. 6.5 Å, building up a solvation shell containing ca. 3 moieties. This coordination number is substantially different from what is found in the case of reline, where choline is surrounded by approx. 6 other choline cations. Such a situation likely stems from the larger size, as well as the different shape and symmetry of acetate as compared to chloride anions. Each choline cation is on average surrounded by 3.4 acetate anions with a correlation peak at 5.3 Å. For comparison in reline, 4.5 chloride anions where found in the first shell[10], while 1 chloride anion was found in the same shell in malicine[48]. Urea is characterised by strong correlations both with other urea moieties and with both cations and anions. First solvation shells are detected around each ionic species, with peaks centred at 5.1 Å and 4.5 Å and 6 and 4 nearest neighbour urea moieties for choline and acetate, respectively.

Figure 4 reports a series of pdfs related to selected correlations between atomic species belonging to the different moieties building up bulk acetaline.

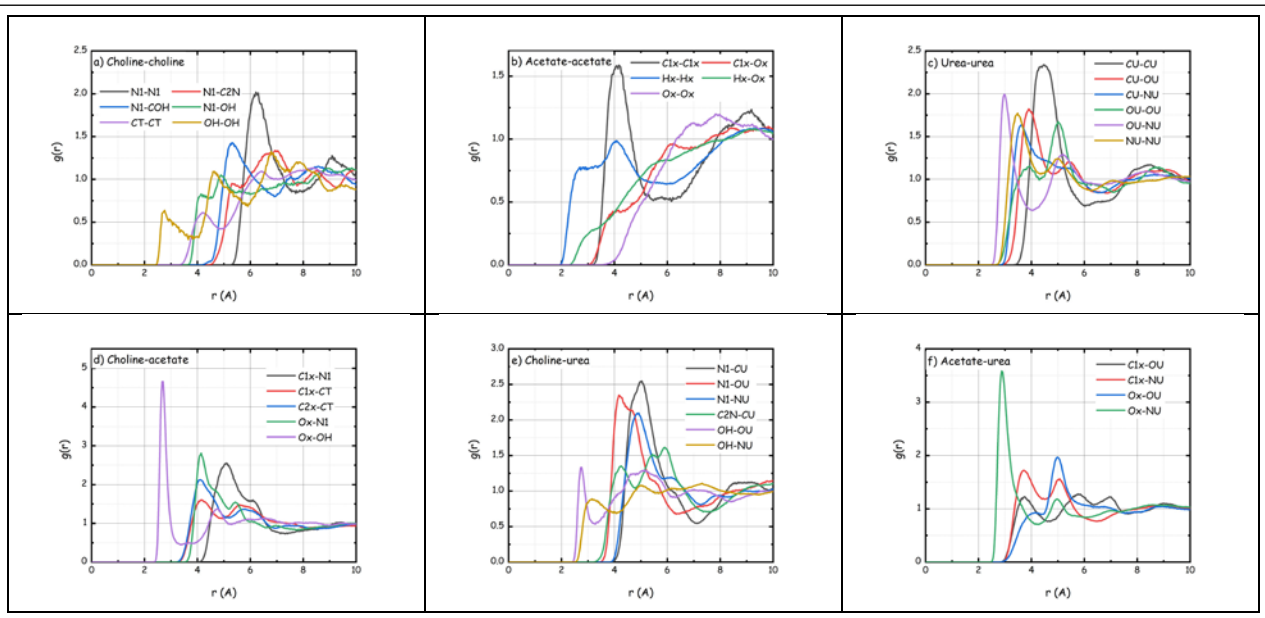


Figure 4. Selected pair distribution functions between different atomic species belonging to the three moieties in acetaline (choline, acetate and urea, respectively), after the EPSR modelling.

The selected pdfs indicate the existence of strong correlations between the different moieties. In particular, those pdfs involving acetate and either choline or urea, are characterised by strong peaks, fingerprinting hydrogen-bonding mediated interactions. Such interactions will be further explored later in the manuscript. Choline-choline correlations are rather weak and broadly distributed. The strongest correlation is between neighbour nitrogen atoms, with a peak centred at 6.5 Å, and a neighbour number

of ca. 2.5 up to 7 Å. We also detect a relatively strong N1-COH correlation centred at ca. 5.3 Å with approximately 2.5 nearest neighbours (n.n.); however there is only weak interaction of the nitrogen with the hydroxyl group (weak peaks for N1-OH between 4 and 5 Å). Neighbour acetate anions are only correlated through their methyl groups for which we detect a C1x-C1x peak at 4 Å, with one methyl group directly correlated to the reference one. Urea-urea correlations look more structured: we will see later that this is also because of the existence of hydrogen bonding interactions and accordingly we find strong peak in the OU-NU pdf at ca. 3 Å, with a n.n. population of 2 NUs around the reference OU. The other peaks reported in **Figure 4 c)** indicate the existence of strong correlations also between other urea's moieties such as NU-NU (3 n.n.), CU-OU (2 n.n.) and, in particular, CU-CU (4 n.n.). Similar observations led Edler et al. to propose the existence of urea clustering in reline.[10] Inter-species correlations are dominated, as we will see later in more detail, by HB correlations. Overall these correlations look much stronger than correlations between similar species. The selected pdfs in **Figures 4 d)-f)** reflect in an indirect way the existence of such interactions. Choline-acetate correlations are characterised by a strong Ox-OH peak at 2.7 Å, fingerprinting the HB between the two species. The broad peak related to the Cation-Anion pdf in **Figure 3** is likely related to the existence of different solvation scenarios of acetate around the reference choline: in particular, acetate will coordinate choline both at the hydroxyl side and at the ammonium side. This latter scenario is fingerprinted in the Ox-N1 and C1x-N1 pdfs by the strong peaks centred at 4.2 and 5 Å, respectively. Choline and urea appear to interact mostly through choline's ammonium: pdf peaks for N1 with CU, NU and OU are eminent at distances between 4 and 5.5 Å. Correlations mediated through choline's hydroxyl group look weaker. The competition between acetate and urea in coordinating choline's N1 leads to ca. 5 urea and 3 acetate moieties surrounding N1 by a distance of ca. 7 Å. For comparison, the OH moiety of choline is solvated by 0.6 acetate and 0.9 urea in the first shell (up to 4.5 Å) and ca. 2 choline in the first shell (up to 7 Å). Acetate and urea interact through HB involving urea's hydrogen and the carboxyl group; such an interaction, fingerprinted by the Ox-NU peak at ca 3 Å, is consistent with two different solvation environments indicated by the two peaks in the C1x-NU pdf (3.7 and 5 Å).

As mentioned, HB interactions are fundamental in driving structural correlations in acetaline. In **Figure 5**, the pair distribution functions associated to such correlations involving either the choline HOH or the urea HU1/2 donor groups. In particular, we specifically monitor the two hydrogens, HU1 and HU2, attached to the same nitrogen in urea (HU1 being the hydrogens in trans with the urea's oxygen and HU2 being the cis hydrogens), aiming at assessing differences in the HB features, due to steric

hindrance. In all cases, HB involving the acetate HB acceptor (Ox) are characterised by the shortest and

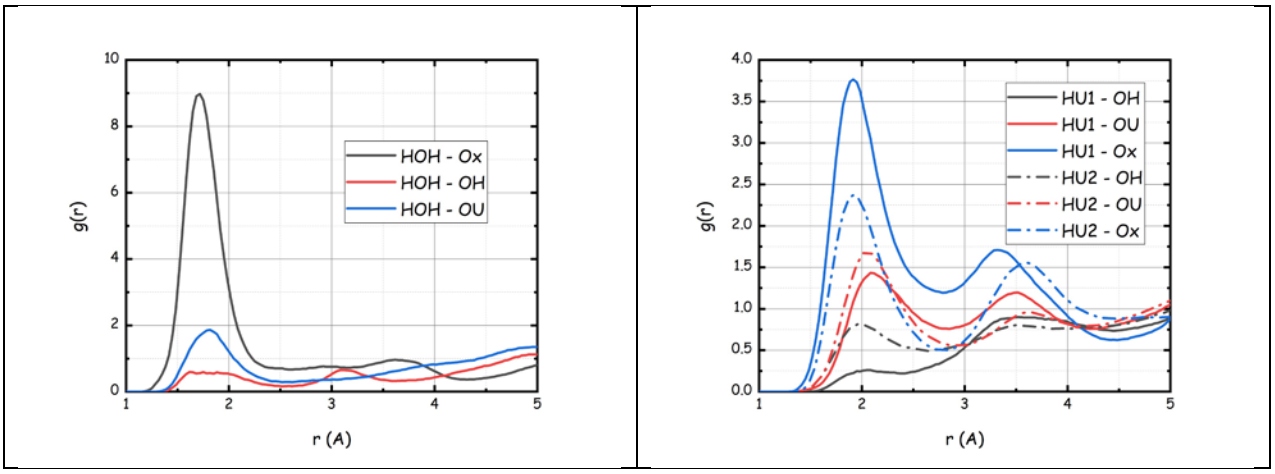


Figure 5. Pair distribution functions related to hydrogen bonding interactions in acetaline, as obtained from the EPSR modelling: (left) pdf related to the HOH donor agent in choline and (right) pdf related to the trans (HU1) and cis (HU2) hydrogens in urea.

strongest interaction. In terms of pdf peak amplitude, the next most intense peaks correspond to those involving urea's oxygen (OU) and finally choline's oxygen (OH). In order to better illustrate the balance between HB donor and acceptor capabilities of the different moieties in acetaline, we exploit the linear Sankey diagram approach of **Figure 6**, introduced recently for this kind of analysis.[39] A wealth of information can be straightforwardly extracted from such a plot, on the nature of HB networking in acetaline. The hydrogen bond donated by choline OH (HOH) (upper left) is mainly involved with the acetate Ox (lower right). There is only a tiny amount of hydrogen bonding interaction between HOH and choline OH and negligible interaction with urea. The trans and cis protons of urea (HU1 and HU2, respectively) behave differently. While the trans protons (HU1, middle left) do not form hydrogen bonds to choline OH, but form strong hydrogen bonds to both urea OU and acetate Ox, the cis protons (HU2, lower left) also form hydrogen

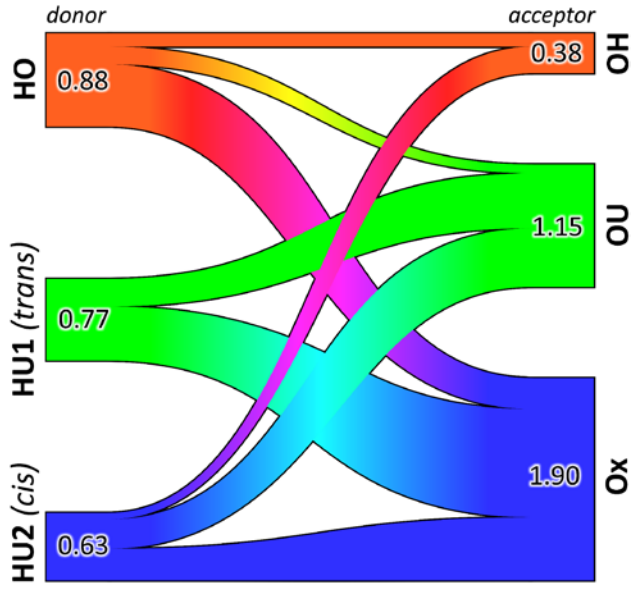


Figure 6. Linear Sankey diagram describing the hydrogen bonding topology in acetaline. Numbers correspond to the average hydrogen bond count per donor/acceptor.

bonds with choline OH. Now considering the acceptors (right side), incoming hydrogen bonds at choline OH almost exclusively come from the urea cis protons, HU2. The urea oxygen receives strong hydrogen bonds from both cis and trans urea's protons, while it almost receives no hydrogen bonds from choline HOH. A similar picture arises for acetate Ox, where the hydrogen bond received from the urea trans protons is most significant. Overall, the major role played by the acetate anion in establishing HB interactions is confirmed by this graph; analogously the minor role played by choline's OH acceptor site is also highlighted.

Additional understanding of the mutual spatial distribution of the different species with respect to each other can be obtained by inspecting the spatial distribution functions reported in **Figures 7.** The first of such plots refers to the distribution of the three different moieties surrounding a reference urea molecule. Urea is strongly correlated with acetate anions (red lobes) at spatial locations corresponding

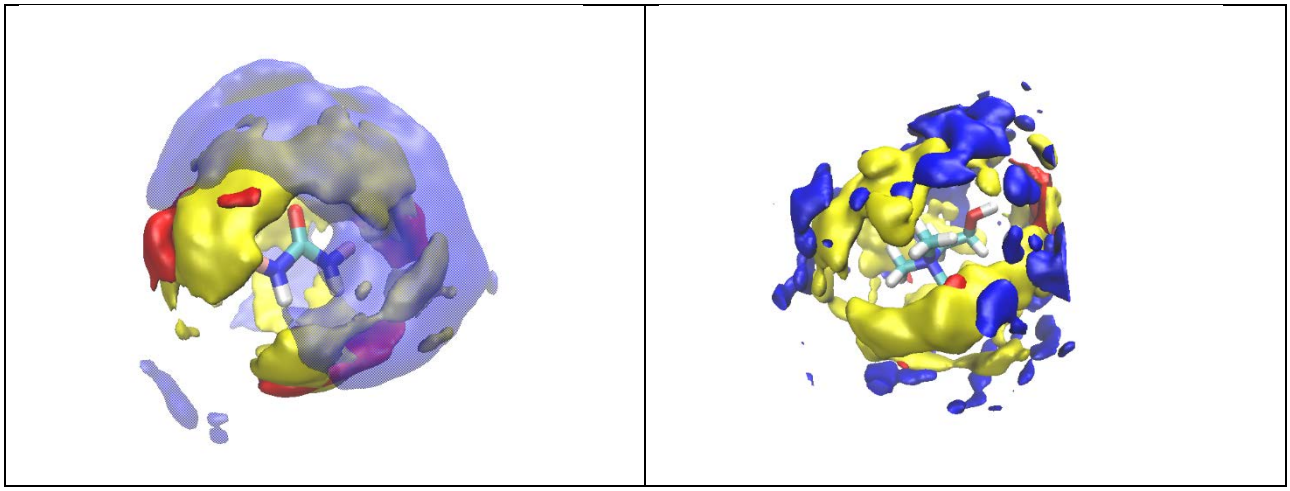


Figure 7. Spatial distribution functions around reference urea (left) and choline (right). The coloured lobes correspond to 20% most likely distribution of choline (blue), acetate (red) and urea (yellow) in acetaline

to its cis and trans hydrogens. Choline cations (blue lobes) distribute in a much more homogeneous way around urea and correlations are not driven by HB, but rather by dispersive interactions. Finally, urea (yellow lobes) competes with acetate to access the reference urea hydrogens; it moreover interacts with reference urea oxygen. It also appears that choline tends to distribute around urea, aiming at interacting also with the other species surrounding the reference one. In **Figure 7 b)** the distributions around a reference choline cation are shown. The acetate anion is strongly interacting with the hydroxyl group, with a weak competition on this site with urea; otherwise, both the choline cation and urea are

distributed rather homogeneously around the whole reference choline, with urea approaching closer than choline the reference molecule.

These pictures are consistent with the overwhelming role played by acetate in HB interacting with both urea's and choline' HB donor hydrogens. On the other hand, the amphiphilic nature of urea and the possibility of choline to interact not only with coulombic forces, but also with dispersive ones, make these two moieties able to efficiently solvate any component in acetaline. Analogously to the case of reline, an intertwining of the different species occurs in delivering an intimate mixing of these components at atomic level.

To corroborate the structural picture emerging from the combined X-ray / Reverse Monte Carlo approach, variable-temperature NMR measurements were performed. As inter-species correlations appear to be dominated by HB interactions, the upfield or downfield movement of the temperature-dependent ^{1}H chemical shift was monitored to give a preliminary insight into the strength of the HB of the detected proton. **Figure 8** shows the relative shifts of the ^{1}H NMR signals of acetaline, which are defined as $\Delta\delta = \delta - \delta_0$, with δ_0 the chemical shift of a given proton in the pure DES and δ the chemical shift of the same proton for increased temperature. [49,50] The remarkable upfield shift of urea protons is compatible with a weakening of the H-bond strength at the urea site with temperature,[51] and points towards their strong involvement in the HB network of the mixture. No relevant changes are observed for the choline signals, including the N-methyl groups, which is in line with a minor role played by the cation in the intermolecular network. Only a tiny upfield shift emerges for the methyl group of acetate, as they do not directly participate in the HB interactions but most likely feel a pale indirect effect of the major role played by the acidic group of the anion.

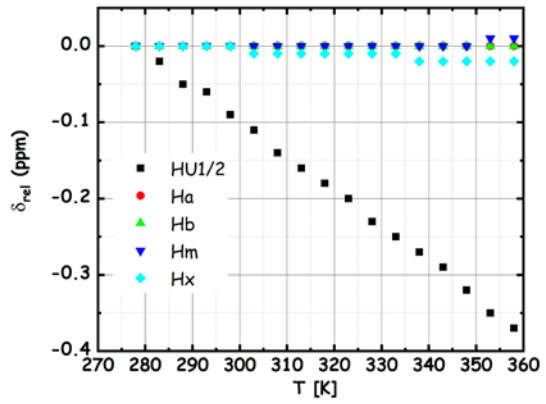


Figure 8. ^{1}H relative shift observed for acetaline as a function of the temperature.

The NMR experiments of choice to probe spatial intermolecular networks are typically based on the nuclear Overhauser enhancement (nOe). In extensively connected systems like DES it is however quite common to observe intra- and inter-correlations between all sites/species in the mixtures.[52,53] This is the case for acetaline too, as

displayed in **Figure S1** in the Supporting Information. Due to spin diffusion and/or exchange (facilitated by the residual water), all signals are positive. Choline shows intramolecular NOE signals, and intermolecular NOE are observed between all the three species, choline, acetate and urea. As expected, intense correlations are observed between the hydroxyl group proton of choline and urea, and the N-methyl groups of choline and urea. The methyl group of acetate shows the strongest correlations with the N-methyl protons of choline and with urea. This confirms the major role of these protons in the interactions holding the DES components together.

The NOESY data provide then support to the scenario of an extended HB network in the DES, which is the root of its peculiar macroscopic properties. We also exploited relaxation and diffusion NMR experiments to shed more light on the system. Intermolecular interactions and dynamics are indeed intertwined, as strong correlations reduce motion – as one can intuitively envisage. T_1 relaxation times and self-diffusion coefficients were measured over an 80 °C temperature interval and analyzed to get quantitative descriptors of the motion(s).

As displayed in **Figure S2** in the Supporting Information, all temperature-dependent T_1 curves, but that corresponding to methyl protons of acetate, pass through a minimum. This indicates that the protons of choline and urea undergo a transition from the extreme narrowing ($\omega_0\tau_C < 1$) to the diffusion limit ($\omega_0\tau_C > 1$) relaxation regime between ~25 °C and ~50 °C. Contrarily, the methyl protons of the anion fail to undergo this transition in the studied temperature range due to their higher mobility. In the case of ^{1}H T_1, where the predominant relaxation mechanism is the homonuclear dipole−dipole interaction, the relaxation rate R_1 is defined by the Bloembergen, Purcell, and Pound (BPP) approach as:[54–56]

$$R_1 = \frac{1}{T_1} = C\left(\frac{\tau_C}{1+\omega_0^2\tau_C^2} + \frac{4\tau_C}{1+4\omega_0^2\tau_C^2}\right) \quad (1)$$

with ω_0 the observe frequency (rad s^{-1}) and C a term evaluated separately for each nucleus. The correlation time of the dipolar interaction τ_C can be thought of as the time required for the vector connecting the interacting nuclei to rotate through the angle of one radian, and for small rigid molecules it commonly reflects the molecular reorientational time constant.[56] As for flexible ionic liquids[57,58], the τ_C observed for acetaline have to be rather considered as a combination of molecular reorientation and internal motions of each given segment. From the term in brackets in Eq. (1), it follows that T_1 is minimum when $\omega_0\tau_C = 2\pi\nu_0\tau_C = 0.616$ [58–60], which means here $\tau_C = 0.616/(2\pi \cdot 500.13 \cdot 10^6\ \text{Hz}) = 196$ ps. Such minimum T_1 value can be used to calculate C from Eq. (1), then

enabling the calculations of τ_C values from the T_1 values observed at any temperature. The temperature-dependent correlation times can be then used in an Arrhenius-type equation to calculate the "apparent" activation energy E_a^{rot} (averaged over several types of movements).[58,61] Alternatively, by substituting the function of the correlation time approximated as an Arrhenius expression into the BPP equation (Eq. (1)), and assuming C temperature insensitive, the combined equation can be directly solved yielding the same outputs within the experimental error. [58,62] Although the two methods are essentially the same from the theoretical standpoint, the latter nonlinear least squares method is useful in cases where an exact minimum is not reached in the examined temperature range, and is recommended even for protons where a T_1 minimum can be distinctly observed as it needs less steps with a reduced margin of error.[58] The nonlinear least squares method was used here to fit all T_1 data

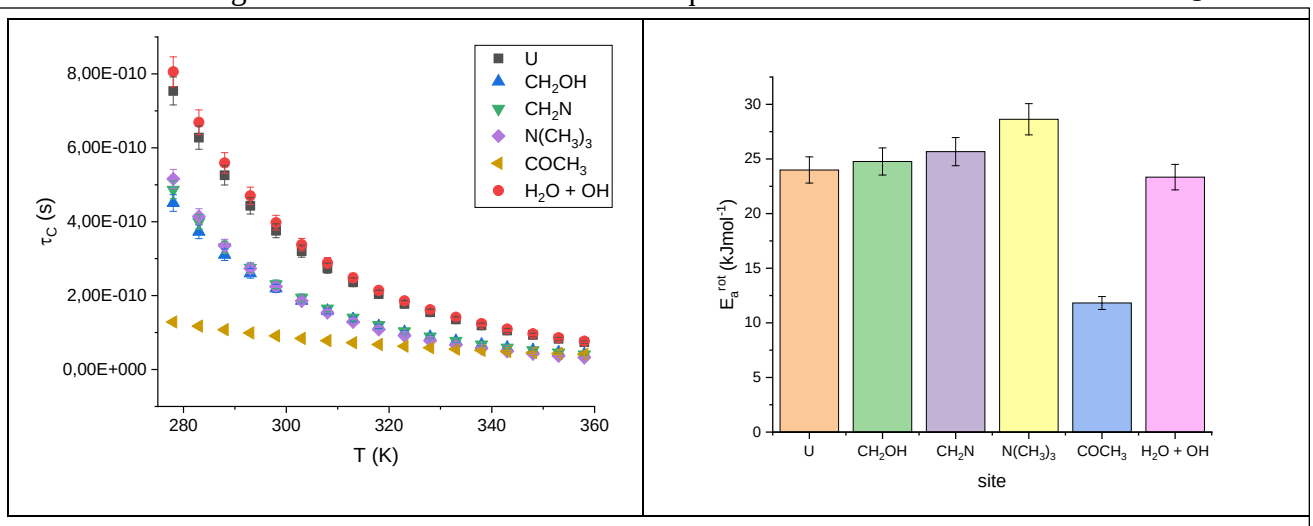


Figure 9. (a) ^{1}H correlation times τ_C vs temperature and (b) rotational activation energy E_a^{rot} (kJ mol^{-1}) obtained for the different proton sites of acetaline.

obtaining the correlation times and activation energies reported in **Figure 9**. All temperature-dependent curves followed perfectly the BPP model, which means that a single basic motion occurs in the studied temperature range.[59] The best-fit parameters are given in **Table S1** in the Supporting Information, together with those obtained by applying the most widely used method based on the T_1 minimum followed by Arrhenius plot of the activation energies, to confirm that comparable results are obtained. Urea protons show the longest τ_C values (slowest rotational motion), and the methyl protons of acetate the shortest ones (fastest rotational motion), while the three methylene and methyl sites of choline exhibited all close, intermediate τ_C values. A direct comparison between the correlation times of the different sites and species is complicated due to the contribution of different relaxation mechanisms.

More informative are the rotational activation energies, which mark a significant difference between acetate from the one side, with E_a^{rot} of ca. 12 kJ mol^{-1}, and choline and urea from the other, all with E_a^{rot} above 20 kJ mol^{-1}. Hence, the rotational motion of the acetate protons is not only the fastest, also due to the intramolecular rotation around the symmetry axis of the methyl group, but it also requires less energy to occur. For the sake of completeness, we also report the correlation times and rotational activation energy obtained from the BPP analysis of the temperature-dependent T_1 data of the peak corresponding to the residual water and the hydroxyl proton of choline (**Figures S2 and 9**). All T_1, τ_C and E_a^{rot} values essentially overlap those corresponding to urea protons, pointing towards a strong correlation between the rotational motion of the two species. Despite its relevance, the role of water in the intermolecular network of ChOAc:U is beyond the scope of the present paper and will be deepened in a separate work on hydrated acetaline. Here the focus is on the role of the DES constituents - choline, acetate and urea - and we can safely assume that the residual water molecules will participate in the intermolecular network without drastic alterations of the mutual relationships among them.

In order to monitor the translational mobility and gather a more complete overview of the system, the self-diffusion coefficients of the different acetaline moieties were measured by PFG NMR. The diffusivities, D, probed in the range 278 – 358 K are given in **Figure S3** and **Table S2** in the Supporting Information. As expected, the diffusion coefficients measured for the methylene protons of choline yielded the same value as CH_3, hence only the latter is presented. The temperature dependence of the diffusion coefficients over the whole probed temperature range was modelled in terms of an Arrhenius-activated process. Translational activation energies are reported in **Figure 10** and fit parameters in **Table S3** in the Supporting Information. While the activation energies associated with relaxation data are in the range 10−30 kJ mol^{-1}, the activation energies associated with diffusion data are larger (40−50 kJ mol^{-1}). This is due to the different molecular motion affecting these apparent activation energies, rotational *versus* translational, and is in agreement with behaviours found for instance in ionic

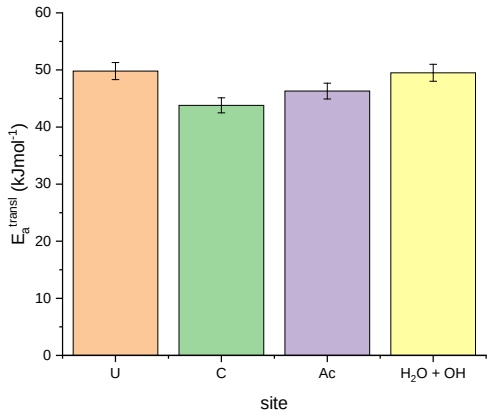


Figure 10. Translational activation energy E_a^{transl} (kJmol^{-1}) obtained for all species in acetaline.

liquids. [63,64] Noteworthy is the order of E_a^{transl}: urea ≈ H_2O + OH > acetate > choline. This is unrelated to the molecular size of the species and can be explained only by admitting that the translational motion of urea and acetate is slowed down by their strong involvement in the HB network. The major role of urea and acetate in the intermolecular network, inferred here from a dynamic parameter, fits the molecular picture outlined by means of more common techniques for structure elucidation, such as X-ray and NOESY. Note, also, that this prominent role is maintained here even in the presence of residual amounts of water (5.7 wt%). Contrarily, the activation energy of choline is the lowest one regardless of its higher size due to its less fundamental role in the intermolecular connections. As urea has proven to strongly connect with other constituents in several DES using both the oxygen and proton nuclei (see also the linear Sankey diagram in **Figure 6**), its reduced rotational and translational mobility (high E_a^{rot} and E_a^{transl}) is quite expected. The peculiar role of acetate is instead not a foregone conclusion. The key role of this small anion in the HB network keeps it on a tight leash, strongly affecting its translational mobility and increasing its E_a^{transl}, which is a dynamic indicator of the whole molecule. Contrarily, the rotational mobility of the methyl protons of acetate does not suffer from a strong effect, as they are not directly participating in the HB network. Hence the corresponding E_a^{rot} - a local dynamic parameter - is still smaller than the rotational activation energy of all other proton sites of both choline and urea.

Conclusion.

Choline acetate mixtures with urea at a stoichiometric composition of 1:2, here termed as acetaline, are deep eutectic media. Acetaline's melting point is ca. 40 °C, but it can be easily supercooled into the liquid state at sub-ambient conditions. Liquid acetaline structure at atomistic level has been investigated by means of synchrotron high energy X-ray diffraction, supported by the EPSR Reverse Monte Carlo analysis approach that allows extracting detailed information on the mutual interactions between acetaline's moieties. Hydrogen bonding plays a major role in determining structure in liquid acetaline. Radial distribution functions shows how acetate-mediated HB are among the strongest in the system; urea plays also a major role as HB donor and these correlations are straightforwardly described by the use of a Sankey diagram illustrating HB flow among the different donor and acceptor moieties. A complex intertwining of different moieties is observed with coulombic interactions (via HB correlations) mostly involving acetate and urea, while choline is involved mostly in dispersive interactions. This peculiar situation is mirrored in the dynamics monitored in acetaline. While acetate's methyl group shows the lowest correlation times and activation energy considering ^{1}H rotational motion, the anion diffuses slower than expected from its size, thus confirming its strong role in the HB network. Choline turns out to be the moiety with the lowest activation energy concerning diffusive dynamics, reflecting its secondary involvement into the HB interactions network.

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DATA AVAILABILITY.

The data that support the findings of this study are available from the corresponding authors upon reasonable request.

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