Mechanisms of phase separation in temperature-responsive acidic aqueous biphasic systems†

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The temperature responsive solubility of ionic liquids with ‘bulky’ polar regions, such as tributyltetradecyl phosphonium chloride ([P44414]Cl), in acidic aqueous solutions is elucidated through a combined experimental and computational approach. The temperature effect in the acidic aqueous biphasic system HCl/[P44414]Cl/H2O was characterised in the range 273 K to 373 K and was found to significantly deviate from the corresponding aqueous biphasic system with NaCl. A new transferable coarse grained MARTINI model for [P44414]Cl was developed, validated and applied to provide a molecular understanding of the experimental results. It is shown that the presence of large aliphatic moieties around the central phosphorus atoms of [P44414]Cl results in a decrease in the electrostatic repulsion between the cationic moieties, leading the [P44414]+ cation to present a behaviour conventionally associated with non-ionic surfactants. This difference in behaviour between HCl and NaCl was shown to result from the greater interaction of the hydronium cation with the micelle surface, thereby enhancing the [P44414]Cl aggregation.

1. Introduction

Stimuli-responsive systems capable of changing their state or properties in response to external stimuli such as temperature, magnetism, light or pH are of crucial relevance to the design of innovative materials and more efficient catalytic and separation processes. In this context, the use of temperature-responsive ionic liquid-based systems has provided a fresh boost to liquid–liquid extraction processes in which extraction can occur under homogeneous conditions prior to the preferential partition of products and impurities into separate phases after temperature adjustment.1–7 Ionic liquids (ILs) are low-temperature melting salts that have emerged as a viable alternative to volatile organic solvents due to their negligible vapor pressure and extended solvation ability, which can be further tailored by varying the cation and anion structure.8 The temperature-responsive solubility of IL systems manifests itself by the presence of an upper or lower critical solution temperature (UCST/LCST). Such transitions are attributed to dominant entropic (LCST) or enthalpic (UCST) effects stemming from the interactions between ILs and water, the most prominent of these being hydrogen bonding and strong polar interactions.9,10

Due to the potential of thermo-responsive systems for the design of flexible and integrated extraction–separation platforms, many ILs were investigated to achieve thermo-responsive behaviour. Whilst multiple cation types in conjunction with fluorinated anions have a UCST phase separation with water, the majority of reported IL–water LCST-type phase transitions are based on variations of tetraalkyl ammonium and phosphonium cations such as tetrabutylphosphonium ([P4444]+).11–16 We recently demonstrated that ILs containing such bulky cations could form reversible biphasic mixtures in the presence of inorganic acids.7,17 Furthermore, the acidic aqueous biphasic system (AcABS) composed of tributyltetradecyl phosphonium chloride ([P44414]Cl), water and hydrochloric acid (HCl) displayed a pronounced LCST-type thermo-responsive behaviour.17,18 However, the mechanism for the liquid–liquid demixing in AcABS was shown to markedly deviate from that of the corresponding traditional aqueous biphasic systems (ABS) based on conventional inorganic salts.17 The mechanism behind the stimuli-responsive behaviour of AcABS at the molecular scale is still poorly understood.

In this work, the effects of [P44414]Cl self-aggregation, HCl concentration and temperature in driving phase separation in AcABS are investigated through a mixed experimental and computational approach. By providing a probable mechanism for the observed phase separation, a guideline for the design of new AcABS combinations can be proposed. The discussion is structured as follows. Firstly, a new coarse grained model based on the MARTINI forcefield for the [P44414]Cl IL is developed and
validated. Secondly, the AcABS based on HCl/[P_{44414}]Cl/H_2O is experimentally characterised across a range of temperatures, acid and IL concentrations along with the [P_{44414}]Cl aggregate evolution with temperature. Finally, molecular dynamic simulations of the AcABS and its ABS counterpart using NaCl were performed to provide a molecular understanding of the experimental results and of the observed differences between AcABS and ABS formation.

2. Experimental methodology

The AcABS studied in this work were established by aqueous solutions of HCl (37 wt% from Sigma-Aldrich) with the IL [P_{44414}]Cl. [P_{44414}]Cl was purchased from Iolitec in 95 wt% purity. Quantitative 1H-NMR analysis using benzene as an internal standard yielded a purity of 97.1%. The determination of the [P_{44414}]Cl purity is important as the concentration of residual phosphine oxide precursor has a non-negligible effect on the LCST transition. This can ultimately result in a temperature shift of the binodal curves between IL batches due to varying impurity content. Ultrapure, double distilled water passed through a reverse osmosis system and further treated with a Milli-Q plus 185 water purification apparatus (18.2 MΩ cm at 298 K) was used for all experiments.

The cloud points of the HCl/[P_{44414}]Cl systems at various IL to HCl ratios were measured using the cloud point method. The [P_{44414}]Cl and HCl concentration ranges probed in this study are 2–70 wt% IL and 0–35 wt% HCl respectively. The cloud point of each mixture was visually determined by identifying the temperature at which the solution became turbid. Two replicates were taken for each composition with an error of less than 1 K. The ternary system compositions were determined by the weight quantification of all components added within an uncertainty of ±10⁻² g. The systems were heated between 273 K and 373 K in a temperature-controlled water bath with a precision of ±0.01 K (ME-18 V Visco-Thermostat, Julabo). Viscosity measurements of [P_{44414}]Cl/H_2O mixtures were performed at atmospheric pressure and in the temperature range 293 K to 323 K using a SVM 3000 Antor Paar rotational Stabinger viscometer–densimeter. The uncertainty of the temperature is ±0.02 K and the relative uncertainty of the dynamic viscosity is ±0.35%.

Dynamic Light Scattering (DLS) measurements (Malvern Zetasizer Nano-ZS) were carried out to evaluate the change in aggregate size with temperature. Samples were irradiated with red light (a HeNe laser, a wavelength of 565 nm) and the intensity fluctuations of the scattered light were detected at a backscattering angle of 173° to generate an autocorrelation function. The cumulant analysis of this function provided by software DTS v 7.03 yielded the particle size and the distribution width. Each AcABS composition was analysed five separate times over a 2 h period to ensure the formation of stable aggregates, with the average aggregate size reported. All measurements were performed using ultrapure water and left to equilibrate for 30 min at the tested temperature prior to measurements.

3. Computational methodology

3.1. Simulation protocol

All simulations were carried out with the Gromacs 5.1 package within the NPT ensemble by adopting the leapfrog algorithm to integrate the equations of motion at a fixed temperature and pressure (1 bar). The energy contributions in the potential energy function for bonded interactions were bond stretching, angle bending and dihedral torsion, whilst non-bonded interactions were modelled by Lennard-Jones (LJ) and Coulombic terms. All bonds were constrained by the LINCS algorithm during the simulations. LJ and Coulombic interactions were computed up to a cut-off radius of 1.2 nm. The force-switch van der Waals potential modifier was employed for LJ, where the energy decays smoothly to zero between 0.9 and 1.2 nm, while long-range Coulombic interactions were evaluated by particle mesh Ewald (PME).

For all simulations carried out in this work, the same equilibration protocol was followed: an energy minimization step using the steepest descent algorithm to prevent short-range contacts between atoms prior to two short equilibration runs in the NVT and NPT ensembles, respectively. Simulation outputs were visualised using the VMD software package and the spatial distribution functions (SDF) were analysed with TRAVIS. The pre-packed micelles were generated using Packmol. Equilibrated micellar aggregates were characterised using in-house code based on the Hoshen–Kopelman clustering algorithm. Two individual surfactants are considered to belong to the same cluster if any of their last surfactant tail beads are separated by less than 1.2 nm. This distance corresponds to the first peak of the tail–tail radial distribution function between the last tail beads of the surfactant. The last surfactant tail beads are taken as a reference for the micelle center of mass, with distances for other molecules in the density profile estimated from this reference.

3.2. All-atom molecular dynamics (AA-MD) framework

All AA-MD systems simulated in this work consist of a cubic box with periodic boundary conditions enclosing 100 [P_{44414}]Cl ion pairs, 20 000 water molecules represented by the SPC/E model and varying concentrations of NaCl and HCl molecules. The force field parameters of [P_{44414}] were taken from the OPLS-AA all-atom force field developed for ILs by Canongia Lopes et al., whilst force field parameters from Aqvist were used for Na⁺ and Cl⁻ ions. In these simulations, HCl was considered fully dissociated to [H_3O⁺] and Cl⁻ ions, with the force field parameters developed by Baaden et al. being used for the hydronium cation. For all simulations, the run time was at least 40 ns with a time step of 2 fs. The temperature and pressure were fixed at 298 K and 1 bar through the Nose–Hoover thermostat and the Parrinello–Rahman barostat, respectively. Only mixture points in the monophasic region of the phase diagram were simulated to avoid potential simulation artefacts that could arise in highly concentrated systems such as overestimation of ion–ion pairing and clustering of ions. The composition of each simulated system
is provided in Table 1. For all systems, two simulations were performed, one starting from a random configuration and the other from a single pre-packed 100 [P44414]Cl component micelle. Thermodynamic equilibrium was considered attained if both final systems resulted in a similar micelle distribution and density profile.

3.3. Coarse grained molecular dynamics (CG-MD) framework

A new coarse-grained (CG) model for [P44414]Cl was developed to study the evolution of [P44414]Cl-based AcABS and ABS phase separation over longer timescales and larger systems. The MARTINI 2.2 forcefield\textsuperscript{35,36} was applied due to its transferability and ability to capture the self-assembly of various surfactants, including cationic surfactants.\textsuperscript{26,37} The MARTINI model provides a CG framework in which the molecules are mapped based on an energy matrix of interactions with 18 different bead types.\textsuperscript{35,36} The main advantage of the MARTINI framework is the reduction in the number of interaction centres present in the system by mapping several heavy atoms as one bead (either using a 4 : 1 bead of 0.47 nm or a 3 : 1 smaller bead of 0.43 nm). Periodic boundary conditions with isotropic pressure scaling and an integration time step of 10 fs were used in the simulations. Temperature time and pressure constants were 12 (ps) and 24 (1/bar), respectively. Equilibration during the production run was monitored by the temperature, density and a visual inspection of the simulation box. The system was considered as equilibrated when the density profile was stable for 1 µs of simulation time. All simulations ran for a minimum of 2 µs, enough time to ensure equilibration was reached for all systems.

The representative chloride and sodium beads were taken from the MARTINI forcefield, each containing six implicit water molecules.\textsuperscript{36} The [P44414]\textsuperscript{+} cation was divided into eight beads that are mapping four heavy atoms: four C1 (strongly apolar) beads for the C14 alkyl chain, a Q0 (charged) bead for the phosphonium centre including the first carbon of the butyl alkyl chains and three C3 (mildly apolar) beads for the butyl head groups. A schematic representation of the CG mapping employed is illustrated in Fig. 1. The CG mapping was chosen to match AA simulation results (further details of the CG model validation are discussed in the next section). The polarizable CG water model was employed to better capture the highly ionic nature of concentrated IL solutions and ABS.\textsuperscript{18} The polarizable water bead (PW), representing three real water molecules, reproduces the orientational polarizability of water, providing more realistic electrostatic screening with a relative dielectric constant of 2.5 rather than the empirical value of 15 used in the regular MARTINI water model. It must be taken into account that the lack of parameters in the MARTINI model to distinguish between small salts of identical valency, such as between [H$_3$O]$^+$ and Na$^+$, limits the study of the salt effect. As such, only ABS simulations containing NaCl were computed as the latter is already defined in the MARTINI forcefield. The composition of each molecular system studied within the CG-MD formalism is also provided in Table 1.

3.4. CG model validation

The CG model validation was based on experimental and AA-MD results. More specifically, on its ability to replicate the micellar behaviour of [P44414]Cl under dilute conditions and to capture the fully water miscible nature of [P44414]Cl for all concentrations. The gradual hydration at 293 K of vacuum dried [P44414]Cl was monitored experimentally by polarized light microscopy. The resulting images presented in Fig. S1 of the ESI\textsuperscript{†} do not indicate the formation of any observable crystalline phases. Instead, the IL swells upon hydration to form hydrated crystals before dissolving with no observable phase transition occurring in between. A similar behaviour was reported for aqueous mixtures of dodecylttrimethylammonium bromide.\textsuperscript{19} The AA simulations indicate that the behaviour of

<table>
<thead>
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<th>System</th>
<th>[IL] (wt%)</th>
<th>[HCl or NaCl] (wt%)</th>
<th>Temp. (K)</th>
<th>Simulation time (ns)</th>
</tr>
</thead>
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<td>2.0</td>
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</tbody>
</table>

Table 1 System composition and conditions for all AA and CG simulations
11 wt% [P44414]Cl (system 1) in aqueous solution in the absence of additives is typical of a surfactant with the formation of spherical micelles containing 20 to 35 [P44414]+ ions (Fig. S2, ESI†). The radial distribution functions (RDFs) between the phosphorus centre (P) of [P44414]+ and the surrounding water molecules and chloride anions (Fig. S3, ESI†) indicate the dissociation of the [P44414]Cl ion-pair in aqueous media and the preferential solvation of the chloride anion. The P–H2O RDF shows a first peak at 0.50 nm inside the [P44414]+ head, the distance between the phosphorus centre and the terminal butyl carbon being 0.545 nm, whilst that of P–Cl is within the first hydration shell of the cation’s polar head at 0.52 nm.

With the aim to validate the CG framework, identical dilute aqueous [P44414]Cl systems containing 25 [P44414]Cl components were prepared at both the AA and CG levels. The AA system was taken as a reference against which several CG MARTINI mapping options were attempted until the final micelle geometry, density profile and chloride anion distribution around the [P44414]+ cation (SDF) in CG matched that of the AA counterpart. All simulations were started from a random distribution of all molecules in the simulation box along 60 ns of simulation time to ensure that equilibrium was attained. The final result is summarised in Fig. 2 and presents a reasonable agreement in the micelle density profile as well as the chloride distribution (SDF, shown in the black colour) around the [P44414]+ head in both AA and CG. In a second stage, larger and more concentrated systems containing 10 wt%, 40 wt% [P44414]Cl (2000 components) with water were simulated for 2 μs at 298 K to ensure that no phase separation occurred under these conditions, in line with experimental results. A dodecahedron box was used at this stage to minimize any extra-ordering effects that could arise using a cubic box. The resulting phase for [P44414]Cl concentrations of 40 and 70 wt% is that of a mesoporous bi-continuous network observed in Fig. 4, in line with reported experimental evidence for similar systems.39 Studies of cationic quaternary ammonium surfactants with increasing polar head volumes and silicate salts indicate that bulky polar domains decrease the structure factor of the obtained phase such that the existence of highly structured phases such as cubic or lamellar becomes unlikely.40 The results in Fig. 2 and 4 indicate that the developed model can successfully replicate the behaviour of [P44414]Cl in aqueous solutions over a range of concentrations and can serve as the basis for the study of thermo-responsive systems based on [P44414]Cl.

4. Results and discussion

4.1. Remarkable thermal responsiveness of AcABS – the HCl effect

The thermal responsiveness of the HCl/[P44414]Cl/H2O system as a function of IL and acid concentration was studied over a large range of HCl and IL concentrations, with the results presented in Fig. 3 and Fig. S4 in the ESI†. Previously reported HCl/[P44414]Cl/H2O binodals18 were incorporated with new experimental results (Fig. S4 in the ESI†) when fitting the surface in Fig. 3 to improve its resolution. Fig. 3 constitutes the first full characterisation of the thermo-responsiveness of an IL system with inorganic acids. The experimental data points are represented as grey beads in Fig. 3C, whilst the black lines correspond to the interpolated points on the surface at a fixed IL concentration, HCl concentration or temperature. A 2-D projection of the HCl/[P44414]Cl/H2O AcABS surface highlighting the cloud point evolution as a function of IL concentration for a fixed HCl concentration is provided in Fig. 3A. The corresponding 2-D projection of the system binodals for a given temperature is presented in Fig. 3B. The HCl/[P44414]Cl/H2O could be either monophasic or biphasic depending on the temperature, it being possible to induce reversible phase transitions by changes in temperature. The biphasic region of the HCl/[P44414]Cl/H2O system is favoured by an increase of temperature, i.e. less HCl is required to induce an AcABS at higher temperatures, presenting a LCST type behaviour.

The addition of HCl has a pronounced effect on the LCST phase transition as well as the shape of the binodal. Whilst the cloud points of the binary [P44414]Cl/H2O system are well above 373 K, the addition of only 2.7 wt% HCl sharply decreases the cloud point to 346 K for a 10 wt% [P44414]Cl concentration (Fig. 3A). Further addition of HCl results in a non-linear decrease of the system’s cloud point to 289 K for 22.4 wt% HCl and 10 wt% [P44414]Cl (Fig. S5 in the ESI†). This non-linearity is most pronounced in the region of 10 to 40 wt% [P44414]Cl and 6 to 16 wt% HCl in which there is little variation in the cloud point temperature with increasing HCl and/or IL content. A closer analysis of the binodals in Fig. 3A indicates the presence of two different domains as a function of HCl concentration. Below 12 wt% HCl, the HCl/[P44414]Cl/H2O binodals display a well-defined critical point. The LCST-type phase diagram presents a typical concave shape in which, for a given HCl concentration, the cloud point presents little variation from 10 wt% to 40 wt% [P44414]Cl and increases thereafter.

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Fig. 2 (A) Comparison between all-atom (solid lines) and coarse-grained (dashed lines) density profiles for the [P44414]Cl/H2O system measured from the centre of mass of the obtained micelle. (B) Snapshot of the final equilibrated AA (top) and CG (bottom) systems, with water molecules removed for clarity. (C) Spatial distribution functions (SDFs) of the chloride anion around [P44414]+ in the AA (top) and CG (bottom) simulations. The colour code is: surfactant tail atoms are shown in green, carbon head atoms in purple, phosphonium head atoms in orange, water in blue, and chloride ions in black.
Above 12.5 wt% HCl, the phase diagram no longer has the same shape; it opens sharply with the critical point falling below 273 K for 60 wt% [P44414]Cl and 15 wt% HCl. At HCl concentrations of 20 wt% or higher, the monophasic region contracts rapidly, becoming fully biphasic at room temperature for all tested compositions. It is hypothesized that at high acid concentrations, the amount of free water available is no longer sufficient to adequately solvate all components in solution, resulting in the phase separation of the more hydrophobic IL. This phenomenon is more pronounced in concentrated acidic solutions in which the growth of hydronium–water aggregates with longer-range order increases.41

4.2. The influence of the [P44414]Cl concentration

The reported LCST behaviour of bulky phosphonium-based ILs is remarkable as this behaviour is traditionally associated with non-ionic surfactants or polymers and seldom reported for ionic surfactants.42 Self-assembly, which can ultimately result in phase separation, is dictated by a balance of opposing forces, namely hydrophobic van der Waals attraction of the apolar moieties, electrostatic repulsion between charged headgroups and entropic effects from counter-ions.43 Prior to discussing the IL concentration influence on the thermoresponsiveness of the system, it is important to stress the low-polarity character of tetraalkylphosphonium-based aggregates composed of C4 alkyl chains or longer. It was previously shown that the bulky C4 alkyl chains of the [P4444]+ polar head shield the localised positive charge on the phosphonium centre, resulting in an apolar accessible surface with weak hydrogen bonding interactions17 that favors cation–cation interactions through van der Waals forces. Furthermore, [P4444]+-based ILs were shown to efficiently solubilise apolar substances such as dyes, L-phenylalanine or ibuprofen.12,44,45 In this context, it is reasonable to consider electrostatic repulsion between charged headgroups as playing a secondary role compared to dispersive forces and entropic effects. The charge screening ability of the butyl moieties ultimately results in greater attractive forces between aggregates. This in turn yields greater self-organisation of the cations in aqueous solutions, thereby facilitating liquid–liquid demixing, a phenomenon exacerbated near the cloud point.46

![Cloud point curves for HCl/[P44414]Cl/H2O as a function of IL concentration for a given acid concentration.](image-url)
Focusing on the influence of the [P44414]Cl concentration, further sub-domains can be macroscopically observed by following the viscosity of [P44414]Cl/H2O solutions presented in Fig. 4A. Fig. 4A shows the presence of three domains corresponding to [P44414]Cl < 40 wt%, 70 wt% ≥ [P44414]Cl ≥ 40 wt% and [P44414]Cl > 70 wt%. To understand how these macroscopic variations in system properties are linked to the potential self-organisation of [P44414]Cl in aqueous solution, three aqueous binary systems containing 10 wt%, 40 wt% and 70 wt% [P44414]Cl (2000 components) were simulated. Final simulation snapshots are presented in Fig. 4B-D. Higher [P44414]Cl concentrations are not computationally reproducible due to the implicit water molecules associated with the CG chloride beads (Fig. 1). The results in Fig. 4 clearly depict two different phases for [P44414]Cl in aqueous solution, namely micellar for [P44414]Cl < 40 wt% (Fig. 4B) and bi-continuous for [P44414]Cl ≥ 40 wt%. A representative snapshot of the bi-continuous phase is presented in Fig. 4C and D in which isolated micellar aggregates are arranged as linked-micelle branched structures yielding a mesoporous network containing large water channels. Increasing the IL concentration from 40 wt% to 70 wt% results in a more compact bi-continuous phase intersected by water channels of smaller diameter. ILS with lipophilic domains are known to form both nanoscale and mesoscale heterogeneous domains with water. At higher IL concentrations, the formation of water nanochannels penetrate the IL system is obtained, with further dilution yielding a micellar regime.47

For concentrated [P44414]Cl solutions, the system transitions from an aqueous IL solution to a hydrated IL. These ‘solvent in salt’ systems have markedly different dynamics than their aqueous counterparts as shown in Fig. 4.40 This suggests that, as the IL content increases, the impact of temperature on the phase separation could vary based on the ‘rigidity’ of the [P44414]Cl self-organization. Importantly for the scope of this work, the surface binodals in Fig. 3C for HCl/[P44414]Cl/H2O as a function of temperature present: (i) a highly temperature dependent domain for [P44414]Cl concentrations below 50 wt% and (ii) a less temperature dependent one for [P44414]Cl concentrations above 50 wt%. In the first, the temperature dependency is evidenced by the clear separation between binodal curves with a temperature change (Fig. 3B). The situation is different above 50 wt% IL: all binodal curves merge to one region as can be easily identified by following the ‘onion’ shaped temperature curves in Fig. 3B. It is therefore important to consider the impact of the IL concentration, the ‘rigidity’ of the IL phase at a given concentration and the availability of free water, i.e. water molecules not engaged in solute solvation, when assessing the thermal-responsiveness of bulky quaternary ammonium and phosphonium ILS.

4.3. Temperature effect in AcBS formation – the micellar effect

To further probe the underlying LCST transition in the AcABS ‘micellar domain’, the temperature effect on the average [P44414]+ aggregate size for a given system composition (20 wt% [P44414]Cl/10 wt% HCl/70 wt% H2O) was determined and is presented in Fig. 5. The critical concentration of approximately 20 to 30 wt% [P44414]Cl is significantly higher than the critical micelle concentration of the system (3.3 mM or < 1 wt%) as well as higher than for non-ionic micellar systems, which are typically of around 1 wt% surfactant.17,39,49 From the phase diagram reported in Fig. 3, this ternary mixture undergoes phase separation just above 323 K.

Fig. 5 shows the exponential growth of the average aggregate diameter as the temperature is increased towards the cloud point, suggesting that IL aggregation dominates the LCST transition. Furthermore, there is little variation in the micelle size below 298 K, mirroring the temperature independent behaviour of the binodals in this temperature range (Fig. 3B). A phase transition from micelles to coacervates occurs as the temperature is increased close to the critical solution temperature, which in turns results in phase separation as the coacervate

![Fig. 5](average_micelle_diameter.png)
droplets aggregate.\textsuperscript{50,51} The coacervate aggregates first result in mesoscopic phase separation, which is the intermediate state for macroscopic phase separation. For the studied system in Fig. 5 such a transition occurs at approximately 319 K. This behaviour is remarkably similar to that observed for non-ionic surfactants as discussed by Lindman et al.\textsuperscript{52} The origin of the cloud point observed for most non-ionic surfactants, and more rarely for ionic surfactants, is generally attributed to micellar growth and attractive interactions resulting in micellar branching.\textsuperscript{39,42,53–57} A similar phase transition mechanism to that obtained in Fig. 5 was observed for the tetrabutylphosphonium trifluoroacetate ([P4444][CF3CO2])–water system, with the IL molecules forming microemulsions despite no surfactants being present in the system.\textsuperscript{12,14} The size of the microemulsion droplet swelled exponentially with increasing solution temperature; the final aggregate size was found to depend on the system’s IL concentration.

4.4. Temperature effect in ABS formation – the role of the water network

The temperature response of the [P4444]Cl-based system is further studied by CG simulations. Due to the limitation of the MARTINI model to discriminate between ions of the same charge, only simulations of the ABS containing NaCl are here considered. Whilst counterion effects are determinant drivers of micellar aggregation, the more static nature of concentrated bi-continuous systems suggests that the conclusions presented below for ABS may also apply to AcABS. Six simulations in rectangular boxes for a fixed number of [P4444]Cl components (500) and varying NaCl concentrations (0 to 965 components) were performed, with the simulation details and snapshots of the final simulation provided in Table 1 (systems (5) to (9)) and Fig. S6 of the ESI† respectively. Above 20 wt% [P4444]Cl the NaCl/[P4444]Cl/H2O binodal is practically vertical. This implies that for the IL concentration range studied in systems (5) to (9) (31 to 40 wt%) at 298 K, all systems undergo phase demixing for [NaCl] = 5 wt%.\textsuperscript{17}

The monophasic nature of the binary [P4444]Cl/H2O system (5) is identifiable from the simulation results presented in Fig. 6A. The density profile along the z-axis confirms that both the IL and water molecules are fully dispersed throughout the box. Water channels within the IL network are clearly identifiable in Fig. 6A. Following the formation of a bi-continuous phase, the water molecules are ‘trapped’ within the sponge-like network of water channels containing the more polar components present in the system, namely the chloride and sodium ions. Addition of 8 wt% NaCl (system (9)) results in a sharp phase separation into an IL-rich phase and a salt-rich phase, Fig. 6B.

The greater entropy of hydration of NaCl compared to [P4444]\textsuperscript{+} forces the migration of water molecules from the IL–water interface towards the bulk to preferentially solvate the inorganic salt, as evidenced by the decreasing RDF intensity of the water molecules around the [P4444]\textsuperscript{+} head (Fig. S7, ESI†) and the corresponding reduction in the water coordination number (Table S1, ESI†). The dehydration of the interfaces raises the interfacial tension of the cavity, thereby promoting inter IL interaction with an additional entropic contribution from the expelled water as shown in Fig. 7. This ultimately results in enhanced segregation and a lower free energy of solvation of [P4444]Cl with increasing NaCl addition. The solvent accessible surface area (ASA) of the different systems presented in Fig. 7 was obtained using the inbuilt Gromacs ‘sasa’ tool, which is linked to the free energy of solvation according to eqn (1):

\[
\Delta G_{\text{Solv}} = \sum_i \sigma_i \text{ASA}_i \tag{1}
\]

Fig. 6 Simulation snapshots and corresponding density profiles along the z-axis of 500 component [P4444]Cl aqueous systems at 298 K containing (A) no NaCl (system (5)) and (B) 965 NaCl (system (9)). Tail atoms are shown in green, head atoms in purple, chloride ions in black, sodium ions in orange and water in blue. The origin of the density profile corresponds to the top of the simulation box shown on the left.

Fig. 7 Effect of the NaCl concentration observed in the 500 [P4444]Cl component CG systems on the total solvent accessible surface area of [P4444]Cl over 2 \(\mu\)s simulation time and at 298 K.
where ASA, is the accessible surface area of atom $i$, and $\sigma_i$ is the solvation parameter of atom $i$, i.e., the contribution to the free energy of solvation of atom $i$ per surface unit area. Dehydration of the hydrophobic moieties of the $[P_{44414}]^+$ cation, which includes the apolar butyl chains of the phosphonium head, is entropically favoured and promotes interactions between $[P_{44414}]Cl$ aggregates. The greater segregation with increasing NaCl concentration was visually assigned to the contraction in the diameter of the water channels within the IL bi-continuous network. However, this effect is not linear in the simulation as little variation is observed for NaCl concentrations in the monophasic domain of the phase diagram ($\leq 5$ wt% NaCl). Above 5 wt% NaCl a sharp decrease in both $\Delta G_{\text{solv}}$ and the solvent accessible surface area is obtained, corresponding to the transition to a biphasic regime. Although Fig. 6B clearly indicates that phase separation has occurred, water can still be found within the IL-rich phase as experimentally expected in ABS.

The transition from monophasic to biphasic with temperature for a given NaCl (2 wt%) and $[P_{44414}]Cl$ concentration (38 wt%) was studied using an annealing simulation from room temperature to 348 K. The cloud point of the ABS at the composition of system (6) is of 320 K. Starting from an equilibrated system at 298 K, it was annealed to 398 K to speed up the dynamics prior to cooling to 348 K and equilibrating for 2 $\mu$s. The simulation results are presented in Fig. 8. Similarly to the behaviour shown in Fig. 6A, the monophasic regime in Fig. 8A is characterised by the presence of easily identifiable water channels within the IL network (which is itself more condensed due to the presence of 2 wt% NaCl) at approximately 10 nm along the z-axis. Raising the temperature 28 K above the cloud point temperature results in the expulsion of water molecules from the larger water channels as shown by the decrease in the partial water density at 10 nm along the z-axis in Fig. 8B and ultimately its disappearance in Fig. 8C after 2 $\mu$s holding. This is consistent with experimental results which indicated the gradual dehydration of the $[P_{44414}]Cl$-rich phase in AcABS with increasing temperature. Although the more mobile water present in the larger channels of the bi-continuous network is pushed out to the salt-rich phase during phase separation, the water molecules present in the smaller nano-scaled water domains in the IL-rich phase remain. These smaller water domains are limited in mobility as a minimal amount of water molecules are required to solvate the chloride anions required to maintain the electroneutrality of the IL-rich phase. The thermomorphic behaviour of phosphonium-based ILs therefore proceeds via increased attractive forces between the apolar moieties of the cations. This contraction of the IL domain in aqueous solution results in the expulsion of water molecules, firstly from the mesoscale water channels and after from the smaller nano-scaled domains.

4.5. Counterion effect – AcABS vs. ABS

An additional consideration is the role of the hydronium cation ($[H_3O]^+$) as it is well known that micellar aggregation is affected by the nature of counter ions in solution. To understand the molecular scale mechanism driving the aggregation in the studied AcABS, the behaviour of the HCl/$[P_{44414}]Cl/H_2O$ system is analysed using AA-MD simulations and compared with the equivalent NaCl-based ABS. Simulation details and snapshots of the final simulation are provided in Table 1 and Fig. 9 and 10, respectively. The behaviour of $[P_{44414}]^+$ cations in aqueous solution in the absence of additives is that typical of a surfactant with the formation of spherical micelles containing 20 to 35 $[P_{44414}]^+$ ions (Fig. S2, ESI†). The addition of a small amount of NaCl or HCl to this system (200 components) has a different effect on the organization of $[P_{44414}]^+$. The presence of NaCl (i) causes an increase in the size of the micelles to approximately 50 $[P_{44414}]^+$ ions; and (ii) compacts the micelles thereby increasing their sphericity (Fig. 9). In contrast, the addition of HCl has no noticeable impact on micelle growth. Whilst the size and number of the micelles remain unchanged, $[H_3O]^+$ appears to act by allowing increased interactions between neighbouring micelles, resulting in the formation of micelle clusters (Fig. 10).
The dissimilarities between micelle aggregation in ABS (NaCl) and AcABS (HCl) is thus attributed to the difference in Na\(^+\) and \([\text{H}_3\text{O}]^+\) interactions with \([\text{P}44414]^+\) due to the nature of \([\text{H}_3\text{O}]^+\). Fig. S8 (ESI†) shows the micelle density profile for systems (2) and (3) depicting the Na\(^+\) and \([\text{H}_3\text{O}]^+\) distribution around the micelle surface. Fig. 11 focuses on the Na\(^+\) and \([\text{H}_3\text{O}]^+\) distribution by comparing the standardised density profile (\(r/r_0\) with \(r_0\) being the density of NaCl or HCl, respectively) of both distributions. Fig. 11 shows how the amphiphilic nature of the hydronium ion allows for a greater degree of interaction with the \([\text{P}44414]^+\) micelle surface. To further ascertain the extent of ion-interaction between \([\text{H}_3\text{O}]^+\) or Na\(^+\) and the \([\text{P}44414]^+\) micelle surface, the coordination number (CN) of \([\text{P}44414]^+\) with \([\text{H}_3\text{O}]^+\) and Na\(^+\) as function of distance, using the central phosphorus atom (P) as a reference point, was computed and compared to that of the NaCl system – cf. Fig. S9A (ESI†). The CN of P-Na\(^+\) indicates that the sodium cation is well solvated and resides away from the micelle interface (>1 nm). In contrast, a distinct shoulder is found in the CN of P-[\text{H}_3\text{O}]^+ starting at ~0.7 nm; calculations indicate a CN of 0.2 once the 2nd \([\text{P}44414]^+\) hydration shell is reached at 0.8 nm. This behaviour is consistent with the reported accumulation of hydronium cations at the air–water interface, which is well correlated with cation adsorption behaviour at hydrophobic surfaces.\(^{41,61,62}\) This is also reflected in the spatial distribution function (SDF) of \(\text{H}_2\text{O}, \text{Cl}^–\) and \([\text{H}_3\text{O}]^+\) around a \([\text{P}44414]^+\) cation (Fig. S9B, ESI†). Fig. S9B (ESI†) shows the presence of a small amount of \([\text{H}_3\text{O}]^+\) (red surface) in the second hydration shell of the \([\text{P}44414]^+\) polar head with the chloride anion (blue surface) present in the first hydration sphere shielding the cation–cation charge repulsion. This greater interaction between \([\text{P}44414]^+\) and \([\text{H}_3\text{O}]^+\) results in a decrease of the hydrophobic effect and results in the low salting-out potential of HCl compared to conventional inorganic salts.

4.6. Proposed mechanism of phase separation in AcABS

To summarize, the LCST mechanism of bulky quaternary phosphonium and ammonium ILs directly stems from the shielded nature of the cationic electrostatic charge conferred by the presence of large alkyl moieties around the charge centre. The relatively apolar solvent accessible surface area of such ILs leads to self-assembly primarily driven by dispersive forces and entropic effects, resulting in a greater propensity for self-organisation of the cations with temperature and ultimately yielding enhanced phase separation. This is in marked contrast to smaller quaternary ammonium and phosphonium ILs in which electrostatic forces dominate. Furthermore, the LCST transition in AcABS was shown to be dynamic and non-linear, dependent on multiple factors including the IL concentration and the IL phase existing in solution at a given acid to IL ratio, namely a micellar or bi-continuous regime. The presence of a bi-continuous phase above \([\text{P}44414]\text{Cl}\geq 40\text{ wt%}\) has a pronounced effect on the thermal-responsiveness of AcABS due to the rigidity of the IL phase. In this regime, phase separation with increasing temperature is achieved through contraction of the water channels within the bi-continuous network and the expulsion of the water to the acid-rich phase. A second factor in concentrated AcABS is the availability of water molecules to adequately solvate all solutes present. In the micellar regime,
HCl promotes additional structuring of aqueous \([\text{P}_{44414}\text{Cl}]^{-}\) solutions not through micelle growth or fusion, but rather by increasing micelle–micelle interactions. The \([\text{H}_3\text{O}]^{+}\) acts as an ‘adhesive’ between individual micelles by further screening the electrostatic repulsion between the head groups of the IL cation. A schematic diagram summarizing the mechanism driving the LCST formation of the HCl/\([\text{P}_{44414}\text{Cl}]^{-}/\text{H}_2\text{O}\) system is provided in Fig. 12 based on the reported results.

5. Conclusions

The experimental and simulation results presented in this work highlight the thermo-responsive nature of \([\text{P}_{44414}\text{Cl}]^{-}\)-based systems, allowing for the reversible phase transition and separation induced by changes in temperature. An apolar accessible micelle surface appears to be a strong pre-requisite for AcABS formation as this prevents electrostatic forces from dominating the aggregation. The remarkable responsiveness of AcABS expands the potential applicability of such systems. The phase transition temperature can be tuned for a specific application by judicious selection of the acid and IL concentration, thereby allowing for the ‘one-pot’ separation of value-added compounds. The LCST mechanism of AcABS was found to differ from that of conventional ABS based on inorganic salts because of the greater interaction of the hydronium cation with the micelle surface. The presence of \([\text{H}_3\text{O}]^{+}\) promotes greater micelle–micelle interaction due to the formation of ion-channels between each respective micelle, reducing their mutual electrostatic repulsion and favouring aggregation. Finally, the new transferrable CG model for \([\text{P}_{44414}\text{Cl}]^{-}\) developed could successfully capture the shielded nature of the cationic charge and reproduce the aqueous aggregation of \([\text{P}_{44414}\text{Cl}]^{-}\) for a wide range of IL concentrations and NaCl concentrations.

Conflicts of interest

There are no conflicts to declare.

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