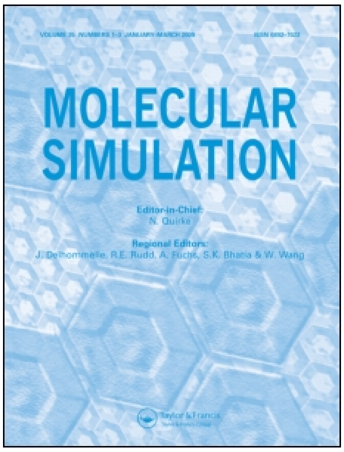

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Molecular dynamic studies of the compatibility of some cellulose derivatives with selected ionic liquids

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Molecular dynamic studies of the compatibility of some cellulose derivatives with selected ionic liquids

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Molecular dynamics techniques were used to study oligomers that mimic cellulose and various derivatives in the amorphous phase, including cellulose (C), methyl cellulose (MC), hydroxypropyl cellulose (HPC), and carboxymethyl cellulose (CMC). Densities and solubility parameters were determined for a series of oligomers with increasing chain length. Both properties were found to change linearly with the degree of polymerization (from monomers to dodecamers). Extrapolated predictions of the densities (g/cm^3) for long chain polymers are: C, 1.42; MC, 1.33; HPC, 1.30; and CMC, 1.42. Computed values for the solubility parameter (MPa$^{1/2}$) are: C, 25.39; MC, 21.43; HPC, 21.70; and CMC, 24.35. We also evaluated the sensitivity of the solubility parameter to changes in the calculated density and found the dependence to be significant. The calculated solubility parameters were evaluated against experimental and other theoretical values as well as against selected ionic liquids comprised of cations in the imidazolium family and the chloride and trifluoroacetate anions.

Keywords: Cellulose; Ionic liquid; Density; Solubility parameter; Simulation; COMPASS

1. Introduction

Mutual compatibility of polymers and solvents is one of the important issues of materials engineering not only in the polymer industry but also for pharmaceuticals, where drug delivery and release is closely related to the properties of the individual components. In simple terms, "like dissolves like," a principle that can be quantified through the Hildebrand solubility parameter, which is defined as the square root of the cohesive energy density. The basic concept has been further refined by Hansen [1], who introduced individual terms related to the van der Waals dispersion forces, dipole interaction and hydrogen bonding. The total solubility parameters and the individual contributions are determined experimentally from intrinsic viscosity measurements and, for polymers, from swelling measurements.

Cellulose and its derivatives are widely used in the pharmaceutical, food, plant, oil and other industries. It is a biorenewable material for which further expansion of the large industrial application is somewhat hindered by the unusual and expensive solvents and harsh processing conditions [2] that are often required to solubilize it. Chemically, cellulose is a homopolysaccharide composed of β-D-glucopyranose units which are linked together by (1 → 4)-glucosidic bonds. Strong intramolecular and intermolecular hydrogen bonding is a major contributing factor to the strength of wood and other plant matter based upon cellulose. The same strong bonds are the root cause of its difficult solubilization. Ionic liquids may offer an attractive environment-friendly and economical alternative for the chemical and physical processing of cellulose which could have a significant impact on utilizing its full potential as a renewable raw material in special areas such as polymer manufacturing.

Ionic liquids are often referred to as "green" solvents. Recently, a discussion has emerged among green chemists about the possible global and local interpretation of "greenness" of chemical processes in general and solvents in particular [3–4]. Nevertheless, when compared to the harsh conditions required currently to solubilize cellulose, ionic liquids still can be considered as "green" alternatives. One of the greatest advantages of ionic liquids is their remarkable versatility: with different combinations of cations and anions, approximately 10^{18} different ionic liquids are possible [5]. The great flexibility and desirably low environmental impact suggests that task-specific ionic liquids with pre determined physical

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and chemical properties may hold great promise for future applications. In spite of the obvious interest in this area, only a few ionic liquids have been characterized even by such basic properties as density, conductivity, melting point and so on. *In silico* experiments with predictive power can greatly facilitate the implementation of ionic liquids in industrial applications.

Molecular modeling has been demonstrated to be a useful tool in the characterization of many different types of chemical systems, including bulk materials. Many properties can be computed with an accuracy which is comparable to experimental capabilities [6]. Simulation of properties is especially important for systems that are challenging to study experimentally due to their limited solubility in common solvents. In some other cases, the experiment itself may be difficult due either to sensitivity to sample preparation or to ambiguities in the interpretation of the results. When the system consists of a relatively small number of atoms, both traditional *ab initio* and density functional methods can be employed. In the case of sugar molecules and disaccharides, a number of studies have been carried out to develop force field methods [7] to be used in molecular dynamics simulations while studying the conformations of cellulose and its interactions with water and other molecules [8–16].

Computer simulations of ionic liquids have largely focused on the development of force field parameters specific to an ionic liquid or an ionic liquid family [17–23]. In addition to simulation of structural, dynamical, electric and thermodynamic properties of several pure ionic liquids [24–26], the solvation of small solutes in ionic liquids has also been investigated [27–31]. Compatibility of ionic liquids and cellulose derivatives has not been explored extensively with molecular theory: the current work is intended to draw attention to this area.

2. Methodology

All of the calculations described in this work employed the Discover simulation engine as implemented in the Materials Studio® suite of programs by Accelrys. The COMPASS Force Field was used throughout for cellulose mimicking oligomers because it has been specifically optimized to yield accurate cohesive properties for a great variety of molecules [6] and since it has been successfully applied in the computation of solubility parameters for rigid chain polymers [32]. COMPASS assigned partial charges were used throughout since exploratory calculations on small oligomers showed only mild changes when charges derived from density functional calculations were employed. In order to test the accuracy of the approach for cellulose, some common solvents with structural similarity to the polysaccharide repeat units were also investigated using the same force field.

Densities are well known experimentally for common solvents and many polymers but they are largely unknown for oligomers with a small degree of polymerization. In order to calculate these densities, each cellulose mimicking oligomer was built using the Polymer Builder module in Materials Studio® and its structure minimized (without an extensive conformer search) using Discover. Taking the structure in the optimal geometry, at least five copies of a 3D periodic amorphous cubic box were constructed (usually in the 16–18 A size range, containing about 650–750 atoms). The 3D periodic boxes were then equilibrated for 20 ps under NPT conditions (number of atoms, pressure and temperature were kept constant at $p = 1$ atm and $T = 298$ K using velocity scaling as thermostat and the Berendsen method as barostat). In the production run, a 100 ps NPT molecular dynamics simulation was executed while sampling the conformer space at 5000 fs intervals (using the Andersen thermostat). Atom based summation was used throughout for the non-bonding interactions. The resulting average density for each simulation was then recorded for statistical analysis.

The protocol to calculate the solubility parameters was somewhat similar. Using the same geometry optimized oligomer molecule, five copies of a cubic amorphous box were created at the average density (calculated as described above). The system was equilibrated for 20 ps at 298 K in an NVT simulation (constant number of atoms, volume and temperature, velocity scaling), followed by a 100 ps production run (Andersen thermostat). The conformer space was sampled at 5000 fs intervals. Cohesive energy densities and solubility parameters were then evaluated for these trajectories.

3. Results and discussion

3.1 Validation studies

In order to assess the accuracy of the simulations and the COMPASS force field in these calculations, two organic solvents were studied first. Glycerol was chosen because it is a polyol, in common with the building blocks of cellulose; 2-methanol-tetrahydropyran (THPMeOH) was chosen because its ring structure is analogous to the repeat unit of cellulose. The calculated densities and solubility parameters are presented in table 1 along with the experimental values.

It can be seen from table 1 that both the room temperature density and the solubility parameter of glycol are in good agreement with experimental findings. For the

Table 1. Calculated room temperature densities and solubility parameters of selected organic solvents with structural similarity to the cellulose repeat unit along with experimental values.

	Density (g/cm^3)		*Solubility parameter (MPa$^{1/2}$)*	
	*Expt**	*Calc*	*Expt**	*Calc†*
Glycerol	1.258	1.243	36.2	35.2
THPMeOH	1.021	1.093	22	23.5

* Taken from [33]. † Calculated at the experimental density.

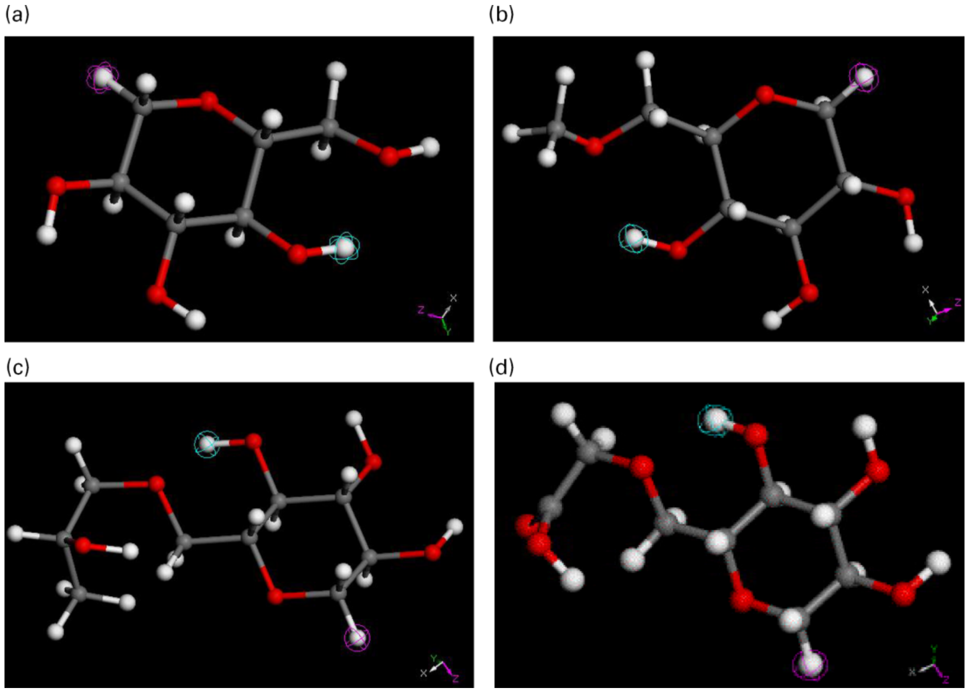

Figure 1. Repeat units of C (a), MC (b), HPC (c) and CMC (d) with the head and tail atoms marked.

pyran derivative, the density is somewhat overestimated in these calculations, while the solubility parameter is reproduced with a good accuracy.

3.2 Density of cellulose mimicking oligomers

The cellulose derivatives chosen for these studies were cellulose itself (C), methyl cellulose (MC), hydroxypropyl cellulose (HPC), and carboxymethyl cellulose (CMC). The repeat units are shown in figure 1.

In order to explore the dependence of the calculated density on the polymer length, a series of oligomers with increasing degree of polymerization was created for each cellulose derivative. The results for cellulose are presented in table 2.

It can be seen from the table that the density increases with increasing degree of polymerization up to the tetramer, remains unchanged up to the hexamer and starts to slowly decrease for the longer chain lengths. In this format, it is challenging to extrapolate to the behavior of very long polymer chains and therefore, instead of the degree of polymerization, the inverse of the molar mass was chosen as independent variable. The results for cellulose and the three derivatives are shown in figure 2.

Figure 2 shows that in general, the density decreases with increasing inverse molar mass (increases with the degree of polymerization). The dependence is more or less linear with the longest oligomer (dodecamer in these calculations) lying below the straight line. Earlier work for poly(ethylene oxide) [34] found linear dependence of density on the inverse of molar mass for a series of oligomers, with a somewhat tighter fit than the current calculations. A possible explanation for this might be the length of the molecular dynamics runs: if the cellulose polymer chain is much less flexible than poly(ethylene oxide), there may not be sufficient time for the system to relax into the optimal, tight packing density from the unfavorable geometry of the initial amorphous packing. (In test runs, molecular dynamics calculations with the simulation time increased up to 500 ps failed to introduce any noticeable change in the density.)

Nevertheless, the straight line fit allows an extrapolation for the intercept with the *y* axis which is the equivalent of the simulated density of polymers of very large molar

Table 2. Molecular formulas, molar masses and calculated room temperature densities of cellulose mimicking oligomers with increasing degree of polymerisation.

	Cellulose mimicking oligomers, C							
Degree of polymerisation	1	2	3	4	5	6	8	12
Density (g/cm^3)	1.36	1.38	1.4	1.42	1.42	1.42	1.41	1.39
Molecular formula	$C_6H_{12}O_5$	$C_{12}H_{22}O_{10}$	$C_{18}H_{32}O_{15}$	$C_{24}H_{42}O_{20}$	$C_{30}H_{52}O_{25}$	$C_{36}H_{62}O_{30}$	$C_{48}H_{82}O_{40}$	$C_{48}H_{122}O_{60}$
Molar mass (g/mol)	164	325	489	653	813	981	1299	1948

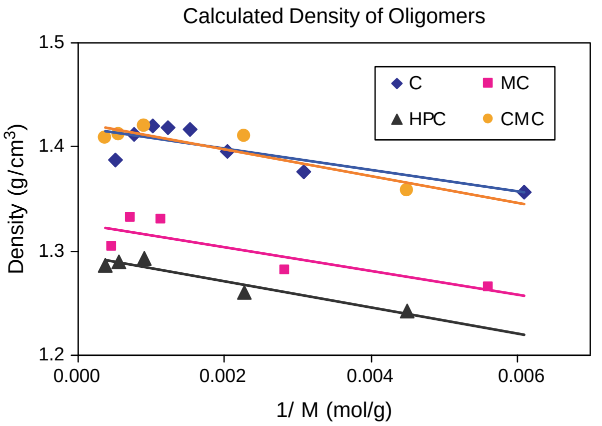

Figure 2. The density of a series of cellulose mimicking oligomers as a function of the inverse of the molar mass.

masses (infinite, in principle). The extrapolated density values are listed in table 3 along with the values of R^2 to show the accuracy of the fit.

Experimental values for the density of cellulose are often reported as ranges rather than as single numbers. There are two reasons for this: native cellulose is a mixture of crystalline and amorphous sections and it is almost always hydrated to a certain degree. Our simulations included no water and thus represent a limiting value, and simulations were performed for the amorphous phase only. Crystalline cellulose has two polymorphs with densities of 1.582 and 1.599 g/cm^3 [35]. Very recently, it was shown that the true density is lower (between 1.40 and 1.47 g/cm^3 for water concentrations of ~2–9%) [35]. This indicates that the density of anhydrous amorphous cellulose must be even lower. Mazeau and Heux [36] used the PCFF force field to model both the crystalline and amorphous phases of cellulose and calculated 1.3762 g/cm^3 as average density. Our value of 1.42 g/cm^3 is somewhat higher than that but it is still within the range of 1.28–1.44 g/cm^3 which was offered in Ref. [36] as expected for amorphous systems. Chen *et al.* [37] tested three different force fields in their simulations for the amorphous phase of cellulose and found that the PCFF force field yielded density of 1.385 g/cm^3 was the closest to the reported literature value of 1.48 g/cm^3 [38]. Choi *et al.* [39] studied hydroxyethyl cellulose and HPC in the amorphous phase using the Dreiding II force field. In their paper, they refer to measured film densities of 1.10 g/cm^3 for HPC (obtained from Aqualon). Our calculated value of 1.30 g/cm^3 is higher than this measured value.

Table 3. Extrapolated values for room temperature densities to high molar mass polymers for cellulose and some of its derivatives along with the accuracy of the straight line fit.

Cellulose derivative	*C*	*MC*	*HPC*	*CMC*
Density (g/cm^3)	1.42	1.33	1.3	1.42
R^2	0.65	0.73	0.92	0.79

It is worthwhile to point out that when a non-linear (second order polynomial) fit to the points in figure 2 is performed, the extrapolated densities are somewhat lower than those presented in table 3. Densities are lowered by about 6% for cellulose itself and 2–3% for the derivatives. Since the accuracy of the density calculations has an impact on the calculated solubility parameters (as it will be shown later), the uncertainties of densities will carry over to those calculations as well.

3.3 Solubility parameters for a series of oligomers

As described in the methodology section, solubility parameters were calculated for each oligomer at its calculated average density. In order to explore the sensitivity of the results to the accuracy of the density calculations, solubility parameters were also calculated at 10% above and below the average density for the case of the octamer of the cellulose repeat unit. The results are shown in figure 3.

The sensitivity analysis shows that a 10% change in density results in a significant change in the solubility parameter (around 2.5 MPa$^{1/2}$ in this case). This observation emphasizes the need for accurate values for the density of oligomers in theoretical calculations aimed to predict solubility parameters.

The dependence of the solubility parameter on the degree of polymerization was also evaluated. The effect is significantly larger than the result of changes in the density only by itself as shown in figure 4.

The dependence of the solubility parameter on the inverse of molar mass is linear with a good accuracy. Longer chain lengths result in lower values and the range of change is about 6 MPa$^{1/2}$ for all four cellulose derivatives studied here. Extrapolation allows us to estimate the values for very high molar masses, results that are summarized in table 4 along with the accuracy of the linear fit.

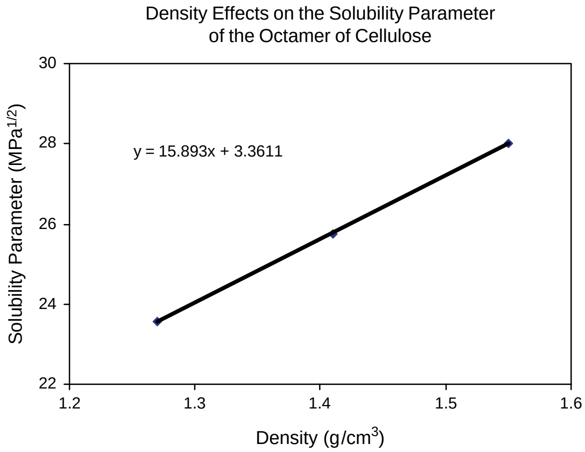

Figure 3. Solubility parameters of the eight repeat unit oligomer mimicking cellulose as obtained at the average simulated density as well as 10% higher and lower densities.

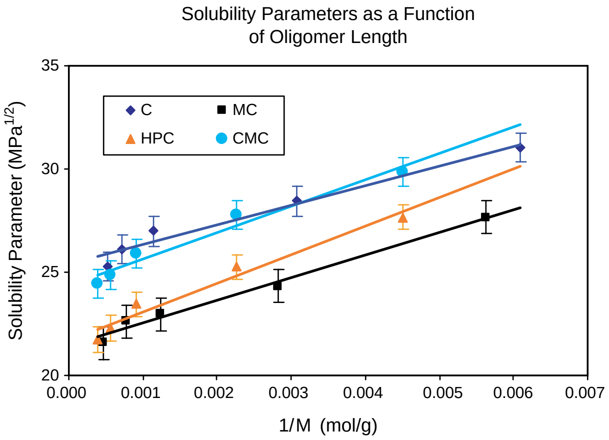

Figure 4. Solubility parameters of oligomers mimicking cellulose and its derivatives as a function of the inverse molar mass.

MC has the lowest and cellulose itself has the highest calculated solubility parameter in this series and the span is about 4 MPa$^{1/2}$. Choi and coworkers [39] recently estimated the solubility parameters of hydroxyethyl and hydroxypropyl cellulose using the Dreiding II force field. They investigated two forms of HPC, one is analogous to our system and the other one was fully substituted. They obtained values of 23.7 and 22.1 MPa$^{1/2}$ for the two variants, respectively, which is only moderately higher than our calculated value of 21.7 MPa$^{1/2}$. Our result for HPC also agrees reasonably well with the experimental value of 23.9 MPa$^{1/2}$ as determined by Archer for fully substituted HPC [40]. Chen and coworkers [37] simulated cellulose in the amorphous phase and predicted a solubility parameter of 19.0 MPa$^{1/2}$. Our calculated value is somewhat higher and compares less favorably with the literature values of 18.4–20.5 MPa$^{1/2}$ reported for rayon fibers [41]. At the same time, Mazeau *et al.* [36] reported a calculated solubility parameter of 68 (J/cm^3)$^{1/2}$ for the amorphous phase of cellulose and also concluded that the solubility parameters of the two crystalline phases are only slightly higher. The solubility parameter of microcrystalline cellulose has been investigated by several authors using mechanical calculations [42–45], surface free energies [46–48] and inverse gas chromatography [49]. With the exception of the last method, all values are in the range of 23.6–27.7 MPa$^{1/2}$ (IGC yields a higher value, 39.3 MPa$^{1/2}$, which was attributed [42] to the sample preparation required by the method). Roberts and Rowe [42] proposed 25.7 MPa$^{1/2}$ as indicative of the typical material used in processing. In the backdrop of these experimental values and the finding of [36] that the solubility parameter of the amorphous phase is only about 4% less than that of the crystalline phases, our calculated value of 25.4 MPa$^{1/2}$ appears to be very reasonable. The variations within the experimental and calculated values underline the difficulty of accurate determination of solubility parameters for cellulose and its derivatives both experimentally and theoretically.

Table 4. Extrapolated values for room temperature solubility parameters to high molar mass polymers for some derivatives of cellulose along with the accuracy of the straight line fit.

Cellulose derivative	*C*	*MC*	*HPC*	*CMC*
Solubility parameter (MPa$^{1/2}$)	25.39	21.43	21.7	24.35
R^2	0.9687	0.9847	0.9674	0.9641

3.4 *Ionic liquid calculations*

In order to assess the compatibility of cellulose and its derivatives with selected imidazolium based ionic liquids, we performed solubility parameter calculations for those systems as well. Force field calculations have been successfully applied in the simulation of charged systems [50–54] while the COMPASS force field has not been explicitly validated for cohesive energy calculations in such systems. To explore its performance for ionic liquids containing cations of the imidazolium family and some anions, we carried out density and cohesive energy calculations for 1-R-3-methylimidazolium (R = ethyl: emim, R = butyl: bmim, and R = hexyl: C$_6$mim) using chloride and trifluoroacetate as counterions. The details of these calculations are described in detail elsewhere [55], only a brief summary is provided here to draw certain conclusions. First, it must be pointed out that COMPASS assigned partial charges performed poorly for the calculation of the density of these ionic liquids. Instead, electrostatic potential derived charges were used in all simulations, as determined from gradient corrected density functional calculations using the PW91 functional and double numeric polarized basis sets. In general, calculated densities for a variety of ionic liquids were found to be in agreement with experimental values. For example, the density of bmim–CF$_3$COO was calculated as 1.24 g/cm^3 while the experimental density is 1.22 g/cm^3 [56]. The calculated solubility parameters are summarized in table 5 for compatibility considerations.

The predicted values of the solubility parameters for these ionic liquids are much higher than those of any of the cellulose derivatives in this study. It was found experimentally [2] that imidazolium based ionic liquids are only able to dissolve cellulose after repeated microwave heating and agitation. It would require further simulation studies to determine how to mimic these

Table 5. Calculated solubility parameters of ionic liquids comprised of the 1-R-3-methylimidazolium cation (emim: R-ethyl, bmim: R = butyl and C$_6$: R = hexyl) and two different anions.

Cation	*Anion*	*Solubility parameter(MPa$^{1/2}$)*
[emim]	CI–	55.86
	CF3COO–	54.58
[bmim]	CI–	50.26
	CF3COO–	49.79
[C6mim]	CI–	46.77
	CF3COO–	45.26

experimental conditions since temperature effects have not been included so far. Solvent engineering, i.e. finding a suitable ionic liquid among a very large number of candidates for dissolving a given cellulose derivative requires exploiting variability in solubility parameters. We found only a limited variation in this small sampling of anions, while there was a larger sensitivity to the carbon chain length of the cations. Based on the results obtained here, it appears that the calculated solubility parameters have only limited use in the prediction of compatibility of cellulose derivatives and ionic liquids.

4. Conclusions

The commercially available COMPASS force field as implemented in Materials Studio by Accelrys performed well in the simulation of densities and solubility parameters of small molecules structurally related to the building blocks of some cellulose derivatives. A series of oligomers of increasing degree of polymerization mimicking the amorphous phase of cellulose and its derivatives offered some insight into the dependence of these properties on polymer chain length. Extrapolation to high molar mass polymers was performed by linear fit. Solubility parameters for longer oligomers were significantly lower than those of the monomer in all cases, while changes in the density exhibited only moderate dependence on the degree of polymerization. The calculated densities and solubility parameters, in most cases, agreed well with other calculated and experimental values where those were available. For imidazolium based ionic liquids, density simulations yielded results in good agreement with experiments, but further verification of the COMPASS force field for the calculation of cohesive energies of polyelectrolytes is needed before simulations can reliably be used to assess compatibility of these solvents with organic polymers.

5. Future work

One of the unexpected outcomes of the investigations was the surprisingly small change in the calculated solubility parameters upon derivatization of cellulose, which is performed precisely to increase solubility. Future studies in this area will improve the theoretical model used by including higher degrees of substitution, structural polydispersity, and the effect of moisture. Since the room temperature solubility parameter was found to be unsatisfactory to assess compatibility with ionic liquids, other means, such as energy of mixing and interaction energy between layers will also be explored along with an extension of the investigations to higher temperatures. Also, some exploratory calculations will be performed to explore some kinetic aspects of the dissolution of cellulose in ionic liquids.

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