REGULAR ARTICLE

CL&P: A generic and systematic force field for ionic liquids modeling

José N. Canongia Lopes · Agílio A. H. Pádua

Abstract In this account, we review the process that led to the development of one of the most widely used force fields in the area of ionic liquids modeling, analyze its subsequent expansions and alternative models, and consider future routes of improvement to overcome present limitations. This includes the description and discussion of (1) the rationale behind the generic and systematic character of the Canongia Lopes & Padua (CL&P) force field, namely its built-in specifications of internal consistency, transferability, and compatibility; (2) the families of ionic liquids that have been (and continue to be) parameterized over the years and those that are the most challenging both in theoretical and applied terms; (3) the steps that lead to a correct parameterization of each type of ion and its homologous family, with special emphasis on the correct modeling of their flexibility and charge distribution; (4) the validation processes of the CL&P and other force fields; and finally (5) the compromises that have to be attained when choosing between generic or specific force fields, coarse-grain or atomistic models, and polarizable or non-polarizable methods. The application of the CL&P and other force fields to the study of ionic liquids using quantum- and statistical-mechanics methods has led to the discovery and analysis of the unique nature of their liquid phases, that is, the notion that ionic liquids are nano-segregated fluids with structural and dynamic heterogeneities at the nanoscopic scale. This successful contribution of theoretical chemistry to the field of ionic liquids will also serve as a guide throughout the ensuing discussion.

Keywords Ionic liquids · Force field · Molecular dynamics simulations

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1 Introduction

Molecular modeling and simulation include computational techniques developed within the frameworks of quantum or statistical mechanics that are able to analyze the links between the macroscopic behavior of matter and its characteristics at a molecular level. Modeling and simulation studies are traditionally used either as predictive or interpretative research instruments but in the case of ionic liquids—a relatively recent research front—they have also assumed the role of exploratory tools leading to some discoveries that were only later corroborated by experimental evidence. For instance, one of the first works dealing with the recognition of ionic liquids as nano-segregated fluids

originated from molecular dynamics (MD) studies [1], reported in the sequence of the development of a systematic force field for ionic liquids [2, 3]. In other words, the knowledge about the physical chemistry of ionic liquids is rapidly advancing through the interplay between experiments, theory, and modeling, each providing challenges, guidelines, and checks to the others.

Molecular modeling at the level of an atomistic description starts with the definition of a suitable force field capable of describing the intra- and inter-molecular interactions taking place between the different units that constitute the systems to be studied.

At the beginning of the century, the number of force field models capable of describing ionic liquids was very limited and fragmented, with only a few ionic liquids studied in an almost case-by-case basis [4–7]. When Canongia Lopes and Padua developed and introduced their force field [2, 3] (CL&P) their main objective was to provide a systematic and transferable model that could be generalized to describe entire families of ionic liquids.

In order to meet that objective and to take into account the "modular" nature of ionic liquids—substances constituted exclusively of cations and anions where a myriad of feasible ionic combinations are possible—three basic specifications were built into the model: internal consistency, transferability, and compatibility (Fig. 1). In fact these three requirements reflect the intrinsic nature of ionic liquids: internal consistency is needed because unlike molecular substances ionic liquids are composed by anions and cations that can be viewed as discrete units but whose interactions should be modeled in a consistent way; transferability is useful because cations or anions are often members of homologous families of compounds and can also be replaced by other cations or anions—a process called metathesis

that plays a pivotal role in the synthesis of new ionic liquids; and finally, compatibility is necessary because the cations (and sometimes the anions) include organic moieties that can be modeled by other well-established force fields.

Presently, the CL&P force field describes twelve families of ions that compose the most important classes of ionic liquids: four cation families—alkylimidazolia, alkylpyridinia, alkylphosphonia, and alkylammonia—including polyalkylated, cyclic, and/or functionalized derivatives, and eight anion families/individual ions—halogens, triflate, bis(sulfonyl)imide, and its derivatives, alkylsulfates, alkylsulfonates, phosphate derivatives, dicyanamide, and nitrate. The different classes of ions are summarized in Table 1, and their parameterization is given as supplementary information to this article.

Moreover, the overall underlying rationale was that, since ionic liquids were a new field of study and these compounds exist in enormous variety, it made more sense to have a more general, though eventually less precise model, instead of a more meticulous model that would represent just one, specific ionic liquid. This somewhat flexible approach proved to be quite successful—nowadays, the CL&P force field is one of the most widely used parameterizations for the molecular simulation of ionic liquids: the five articles that presently describe the force field (2 in 2004, 2006, 2008, and 2010) [2, 3, 8–11] have collected up to date more than 450 citations between them. Most of these studies centered on the prediction of thermophysical and structural properties with various degrees of success (see Sect. 4). Earlier works centered on bulk properties, whereas more recent developments (from 2008 onwards) moved to areas as diverse as surface properties or systems under nonequilibrium conditions. The main conclusion that can be drawn from this wealth of results is that as the problems
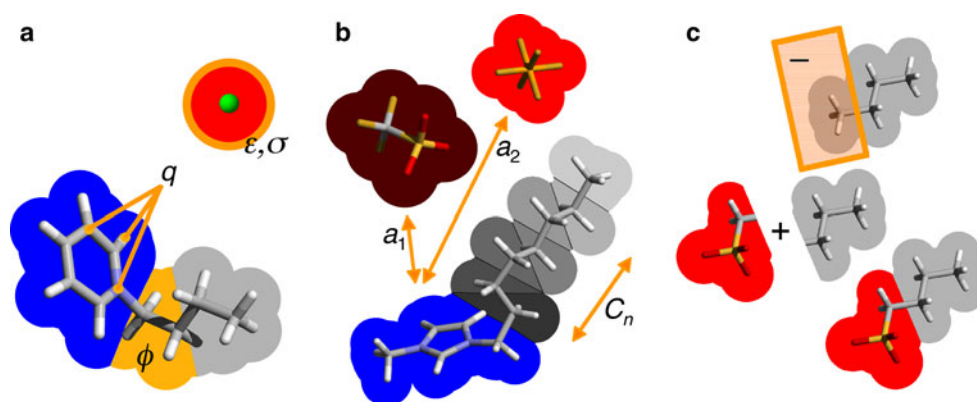
Fig. 1 The three built-in specifications of the CL&P force field: **a** Internal consistency: anions and cations are parameterized with the same force field functional form, with special attention given to the parameterization of atomic partial point charges (q), the flexibility (dihedral angles, ϕ) of the ions, and the adequacy of the repulsive and dispersive forces (ε, σ); **b** transferability: force field parameters are valid within the same homologous family (for instance ions with different alkyl side chain lengths, C_n). They also allow the possibility of ion interchange (a_1, a_2) to yield different ionic liquids; **c** Compatibility: molecular residues and moieties are taken directly from well-established force fields ($-$). Simple rules are established to join seamlessly neutral molecules into an existing ion ($+$)

Table 1 Summary list of ionic liquid ions modeled by the CL&P force field (end of 2010)

Cations		Anions	
Imidazolium		Chloride, Bromide [2,3,9]	Cl^- Br^-
…1,3-dialkyl [2,3]		Triflate [8]	$CF_3SO_3^-$
…1-alkyl [9]		Bis(sulfonyl)imide	
…1,2,3-trialkyl [10]		…bis(trifluoromethyl) [8]	$(CF_3SO_2)_2N^-$
…functionalized [10,11]		…bis(fluoro) [11]	$(FSO_2)_2N^-$
		…bis(perfluoroalkyl) [11]	$(C_nF_{2n+1}SO_2)_2N^-$
N-alkylpyridinium [9]		Alkylsulfates [10]	$C_nH_{2n+1}SO_4^-$
Ammonium		Alkylsulfonates [10]	$C_nH_{2n+1}SO_3^-$
…Tri-, tetra-alkyl [8]		Phosphate	
…N,N-pyrrolidinium [8]		…hexafluoro [2,3,8]	PF_6^-
		…trifluorotrifluoroalkyl [11]	$PF_3(C_nF_{2n+1})_3^-$
Tetralkylphosphonium [9]		Nitrate [2,3,8], Dicyanamide [9]	NO_3^- $N(CN)_2^-$

become more complex (surface vs. bulk conditions, equilibrium vs. transport properties, specific vs. non-specific interactions), the use of the CL&P becomes more difficult. Most of its proposed and undergoing refinements stem from the need of adapting the generic character of the CL&P force field to particular problems/systems without the loss of its inherent internal consistency.

Finally, it must be stressed that ionic liquids are complex fluids that present structural and dynamic heterogeneities at the microscopic scale. These persistent structures of nanometer size [1] mean that ionic liquids can be chemically functionalized for potential applications or to render them more environmentally friendly but without severely modifying their defining physico-chemical properties, such as their low volatility or liquid range. This concept is at the origin of task-specific ionic liquids, [12] or designer solvents. Exploring impact of these modification in chemical structure of the ions on the physico-chemical properties is an important goal of molecular simulation studies; therefore, the possibility of easily representing these task-specific ionic liquids in a force field is an interesting feature, fully within the design spirit based on generality, transferability, and compatibility of the CL&P force field. Several examples have already been published of ionic liquid structures designed for a particular application, such as capture of CO_2 [11], enhanced biodegradability [10, 13], or modification of interface properties [14].

2 Development

Ionic liquids share parts of their molecular architectures with molecules that have been parameterized by existing force field frameworks (AMBER [15], OPLS [16, 17], CHARMM [18], etc.), for example, imidazole rings are present in the amino acid histidine. However, ionic liquids have one essential difference: they are composed of ions, and although they may be built by similar structural groups, the distributions of electrostatic charge will be specific. In order to represent correctly the structure and interactions of these new compounds, the sets of parameters that determine charge distributions and conformations (at the least) had to be developed for this class of substances.

The CL&P model was built based on the OPLS-AA functional form [16, 17] (Fig. 2) which means that, technically, it is easy to combine any molecule or residue already defined in the OPLS-AA database with the structures developed for ionic liquids. Compared to other generalist force fields, special attention was devoted in OPLS-AA to the simulation of liquid-state thermodynamic properties, which made this simple and widely used force field an obvious choice for the implementation of an extension to model ionic liquids.

At the time the CL&P force field was proposed, many of the existing ionic liquid models were built by borrowing parameters from different, not always compatible, sources. For instance, it was common to see parameterizations of the cation and of the anion using information from different force fields [4, 6, 7]. In the development of the CL&P force field, in order to respect internal consistency, electronic structure calculations were used extensively to provide essential data for the development of an internally consistent parameter set. This included not only the determination of parameters absent from the OPLS-AA database but, most importantly, the critical re-evaluation of all required terms.

$$\underbrace{\overbrace{\sum_{ij}^{\text{bonds}} \frac{k_{r,ij}}{2}(r_{ij} - r_{0,ij})^2}^{\text{stretch}} + \overbrace{\sum_{ijk}^{\text{angles}} \frac{k_{\theta,ijk}}{2}(\theta_{ijk} - \theta_{0,ijk})^2}^{\text{bend}}}_{}$$

a

b

$$+ \overbrace{\sum_{ijkl}^{\text{dihedrals}} \sum_{m=1}^{4} \frac{V_{m,ijkl}}{2}[1 + (-1)^m \cos(m\,\varphi_{ijkl})]}^{\text{torsion}}$$

bonded

c

intramolecular

inter-molecular

$$+ \overbrace{\sum_{i}^{\text{atoms}} \sum_{j \neq i} \left\{ 4\epsilon_{ij}\left[\left(\frac{\sigma_{ij}}{r_{ij}}\right)^{12} - \left(\frac{\sigma_{ij}}{r_{ij}}\right)^{6}\right] + \frac{1}{4\pi\epsilon_0}\frac{q_i q_j}{r_{ij}} \right\}}^{\text{Lennard Jones + Coulomb}}$$

non-bonded

Fig. 2 Schematic representation of the different atom–atom interactions parameterized by the CL&P force field functional for ionic liquids. The three paragraph letters correspond to the sections where each type of interaction is discussed

While developing the CL&P model, two features became the most significant in terms of the (re)-parameterization of the force field: the characterization of the flexibility of the ions (through the torsion energy profiles associated with the different dihedral angles) and the atomic point-charge distributions. Basically, the functional form of the potential energy in the CL&P force field consists of non-bonded and bonded interactions (Fig. 2). The former are repulsive, dispersive, and electrostatic interactions and are represented by Lennard-Jones and Coulomb terms, while the latter are related to the covalent-bond stretching, valence-angle bending, and dihedral angle torsions (internal rotations and flexions), within a given molecular backbone. Because the CL&P is based on the OPLS-AA framework, a large part of the Lennard-Jones, bond, and angle parameters could be transferred without major modifications. This is not surprising (or inconsistent) since many ionic liquids are derived from (neutral) molecules that are contained in the OPLS-AA database (originally developed for organic compounds and residues that are part of biologically relevant molecules like the DNA bases or amino acids). Nevertheless, this sort of compatibility leaves out two of the most important features of many of the ions that compose ionic liquids, viz their asymmetrical charge distribution and their particular conformational flexibility. As it was stressed above, these are parameterized by the atomic point charges,

responsible for modeling the electrostatic field around each ion, and by the parameters associated with the torsions around the dihedral angles, which must reproduce the correct conformational landscape of the ions. These will be discussed in the following Sects. 2.2 and 2.3. First—in Sect. 2.1—we will address the issue of transferring bond and angle parameters.

2.1 Stretching and bending: geometry optimization

Most often than not molecular geometry parameters can be reliably obtained from relatively low-level ab initio or DFT calculations (HF, B3LYP) using simple basis sets (for instance 6-31G) describing a single molecule or ion.

As an example, one can take the ubiquitous cations of the 1-alkyl-3-methylimidazilium family ($[C_n\text{mim}]^+$, Fig. 3): several models [2, 3, 5, 6] used similar methods to estimate the parameters describing the imidazolium ring and the published results are comparable with experimental data obtained by diffraction studies [19, 20], as shown in Table 2. Two conclusions can be drawn directly from the table: i) the ring geometry is not strongly affected by the environment of the imidazolium molecule since the ring geometry in two completely different crystals, $[C_2\text{mim}]$ $[\text{VOCl}_4]$ [19] and $[C_{12}\text{mim}][\text{PF}_6]$ [20], is comparable between them and similar to the quantum calculation values for the isolated imidazolium cation; and ii) the distortion of the ring caused by different alkyl substituents is so small that the use of a symmetrical ring geometry as in a (symmetrical) $C_1\text{mim}^+$ cation represents a good approximation.

Therefore, the first step in obtaining the CL&P force field parameterization for a new type of ion has been its geometry optimization using HF ab initio calculations and the comparison of the obtained structural data (bond lengths and angles) with relevant published diffraction and other electronic structure results. Most bond and angle parameters have been taken from or based on the OPLS-AA and AMBER force fields [15–17] without any modification. However, whenever significant differences were found between our ab initio geometries and reported OPLS-AA or AMBER parameters, notably in equilibrium distances and angles, we have proposed new values.

Fig. 3 Nomenclature of 1-alkyl-3-methyl-imidazolium, $[C_n\text{ mim}]^+$

Table 2 Comparison between experimental x-ray (XR) geometries and single-molecule ab initio (AI) calculations for the imidazolium ring contained in different 1-alky-3-methylimidazolium ions

	$[C_2mim]^+$ XR[a] [19]	$[C_{12}mim]^+$ XR[b] [20]	$[C_2mim]^+$ AI [5]	$[C_2mim]^+$ AI [6]	$[C_2mim]^+$ AI [3]
Bonds (pm)[c]					
N_A–C_R	131.1 (4)	132.2(3)	–	131.4	131.5
	131.1 (4)	132.6(3)		131.5	
N_A–C_W	135.7 (5)	137.3(3)	–	137.8	137.8
	136.0 (6)	137.4(3)		137.8	
C_W–C_W	133.4 (8)	133.4(8)	–	134.2	134.1
N_A–C_1	145.2 (4)	146.8(3)	–	146.6	146.6
	146.8 (4)	147.7(3)		147.8	
C_1–C_E	150.0 (9)	–	–	152.0	–
Angles (°)[c]					
N_A–C_R–N_A	109.6 (3)	–	109.8	109.9	109.8
N_A–C_W–C_W	107.1 (3)	–	108.1	107.0	107.1
	107.6 (4)		108.0	107.2	
C_W–N_A–C_R	108.0 (3)	–	106.9	107.9	108.0
	107.6 (2)		106.8	108.0	
C_W–N_A–C_1	125.9 (3)	–	–	125.6	125.6
	125.2 (3)			125.9	
C_R–N_A–C_1	126.5 (3)	–	–	126.4	126.3
	125.4 (3)			126.1	

[a] $[C_2mim][VOCL_4]$ crystal

[b] $[C_{12}mim][PF_6]$ crystal

[c] Double entries refer to bond lengths and angles on the alkyl and methyl side of the imidazoilum ring, respectively

For instance, and taking again as an example the imidazolium ring, we have established that the use of imidazole bond distances and angles (present in the OPLS-AA database) to model the imidazolium ring of an alkylimidazolium cation can lead to an inaccurate parameterization: unlike the imidazolium ring, the imidazole ring residue is not symmetrical and the distortions of the structure around the carbon connected to the two (non-equivalent) nitrogen atoms are noticeable.

As far as the force constants of the stretching and bending modes are concerned, most of the corresponding parameters could be obtained from the AMBER and OPLS-AA force fields without modification. When these were not available, we have estimated them using normal-mode analyses on the optimized ab initio geometries or (as a last resource) the empirical correlation suggested by Halgren [21]. The main departure from the OPLS-AA force field regards our use of constrained bond lengths for all stretching modes involving hydrogen atoms and constrained 180° angles for ions like dicyanamide [9]—these allow longer simulation time steps (2 fs) to be used in the molecular dynamics simulations. Otherwise, all ions have been modeled as flexible structures (from the stretching and bending points of view). Even the hexafluorophosphate and nitrate anions that were parameterized as rigid ions in the first article describing the CL&P force field [2, 3] have been re-parameterized as flexible ions in subsequent versions [8, 9].

2.2 Torsion: potential energy profiles

The dihedral functions in OPLS-AA, expressed by a cosine series (Fig. 2), must not render the full potential energy related to the torsion around a given covalent bond (the same is true in other force field specifications). This is because non-bonded interactions, that is, Lennard-Jones and Coulombic terms, also act between sites within the same molecule connected by three or more bonds. In OPLS-AA, such non-bonded intramolecular interactions are described by the same parameters used in intermolecular interactions, scaled by a factor of 0.5 in the case of atoms situated exactly 3 bonds apart. These non-bonded (steric/electrostatic) effects account for a part, sometimes predominant, of the torsion energy profile. Thus, the task of fitting force field parameters to torsion energies is particular and specific, in the sense that the non-bonded interactions (Lennard-Jones and coulombic) that contribute to the torsional energy profiles must be accounted for. The significance of these non-bonded contributions is not easily estimated a priori [22]. Therefore, contrary to the cases of bond lengths and valence angles for which parameters can be taken from established force fields without major concerns, the torsion energy profiles depend on the cosine series (cf. Fig. 2) but also on the intermolecular features of the model. Therefore, it is fundamentally inconsistent to take parameters for torsion energies from the literature and then calculate electrostatic charge distributions or modify

existing terms of the non-bonded interactions. If this is done, then the model will likely not be able to reproduce conformations in a satisfactory manner. In other words, it is not correct to transpose the parameters of the cosine series between different ions: these should be readjusted on a case-by-case basis to attain agreement with the non-bonded part.

In ionic liquids, only the parts of the ions whose atomic point charges did not suffer substantial re-parameterization (see Sect. 2.3) or whose constrains were dominated by bonded interactions had their torsion parameters taken directly from the AMBER/OPLA-AA force fields [15–17]. These include the parameterization of alkyl chains sufficiently removed from the high charge-density parts ("polar head-groups") of the ions or the proper/improper dihedral angles used to define planar, aromatic rings. All other torsion parameters (specially, those modeling the dihedral angles between polar and non-polar parts, rings and their alkyl side chains, or "conjugate" dihedral angles) were defined with the aid of torsion energy profiles calculated ab initio.

There are several methods to attain internal consistency between the conformational and intermolecular terms. A stepwise approach was chosen [16, 17, 23] in which the model is built up in such a way that the parameters for a given dihedral angle are invariant for any molecular structure within the same homologous series in which that dihedral term may occur, and without loss of accuracy in representing the conformational features of each particular ion. Other strategies exist in which a set of parameters is obtained for each ion individually, but here generality and transferability are lost [24]. The conformational landscapes in the CL&P force field reproduce electronic structure calculations at the post-HF MP2 theoretical level using relatively extended basis sets, cc-pVTZ(-f) [2, 3, 8–11, 23]. These are schematized in Fig. 4.

For a given dihedral, the parameters of the cosine series have been fitted to the difference between the a) total torsion energy profile calculated ab initio, and b) the

torsion energy profile corresponding to the non-bonded contribution (Fig. 4a, b). In the former case (1) the profiles have been obtained using geometry optimizations at the RHF/6-31G(d) level followed by single-point energy calculation at the MP2/cc-pVTZ(-f) level of configurations
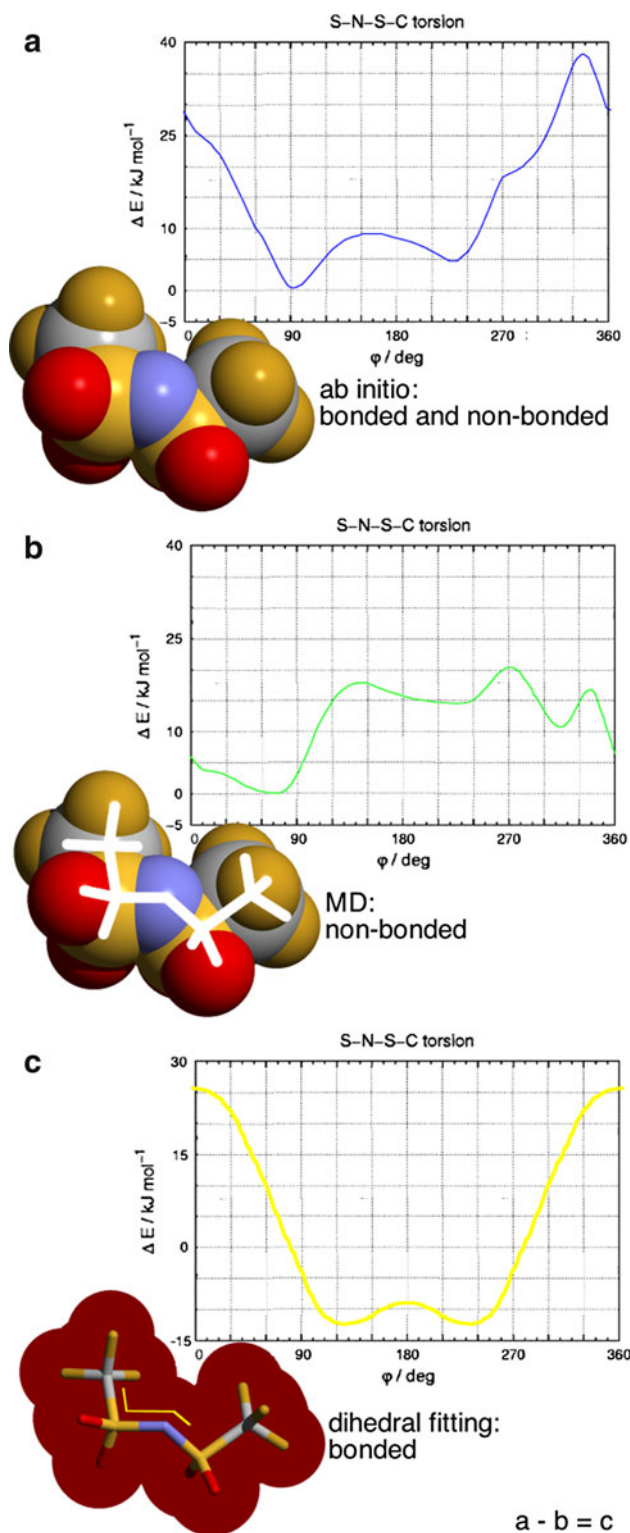
Fig. 4 The parameterization of the S–N-S–C dihedral angle of the bis(trifluoromethylsulfonyl)imide anion, [Ntf$_2$]$^-$, using **a** the total torsion energy profile calculated ab initio, **b** the non-bonded component of the energy profile using molecular dynamics simulations with null dihedral angle parameters, and **c** the fitting of the difference between **a** and **b** to yield the required parameters. It must be stressed that the [Ntf$_2$]$^-$ anion has two interdependent *dihedral angles* around the central imide group that are particularly difficult to parameterize. However, the difference of the two highly asymmetrical profiles given by **a** and **b** yields the symmetrical profile (**c**), proofing that the irregularity of the total torsion profile stems from non-bonded interactions and the soundness of the method used to parameterize this type of dihedral angles. Further validation was also possible using spectroscopic data related to two most stable conformations of this anion [25]

constrained at a fixed value of the dihedral angle under scrutiny. These have been followed by (2) molecular dynamics runs under similar constraint conditions and with the parameters of the selected dihedral cosine series set to zero. Finally, the correct parameterization can be checked by running MD simulations with the full torsion parameterization and evaluating the difference between the obtained results and the total torsion energy profiles calculated ab initio.

2.3 Non-bonded parameters

The OPLS-AA/AMBER models [15–17] both comprise repulsion-dispersion terms represented by a 12–6 Lennard-Jones potential function and an electrostatic term represented by partial charges located at each interaction site of the molecule.

Most of the Lennard-Jones parameters for each type of atom were taken from the OPLS-AA parameter set [16, 17]. The interactions between atoms of different type (cross parameters) have been parameterized using geometric-mean Lorentz-Berthelot mixing rules. The parameters for the halogen and nitrate anions have been obtained by fitting their Born–Mayer potentials developed for crystalline and molten salts [2, 3] to the Lennard-Jones function. It is important to stress that the resulting Lennard-Jones parameters of these inorganic anions are quite different from those usually employed for chlorine or nitrate groups bonded to organic molecules or from those obtained for chloride or nitrate anions in aqueous solutions. The differences are apparent if we take for instance the interaction diameter of the chloride ion/chlorine atom, σ_{Cl}, in the three situations: 3.77 Å in molten salts/ionic crystals [2, 3, 26], around 3.5 Å in organic chlorine atoms [4, 15–17] and around 4.4 Å in aqueous solution [15].

The coulomb parameters describing the electrostatic forces acting on each ion are also determined using calculations of the electron density at the MP2 theoretical level and using sufficiently large basis sets (cc-pVTZ(-f)). The point charges placed at the center of each atom of the ion are then calculated from the electron density using an electrostatic surface potential methodology (CHelpG), in which the values of the atomic charges are optimized to reproduce the electrostatic field generated by the molecule. The most stable conformation obtained by geometry optimization of the isolated ion is generally taken as the reference but, in ions with multiple stable conformers, several ab initio calculations were performed, and an averaging process was implemented to define the charges in each atom. Since one of the objectives of the present force field is the possibility of parameter transfer within families of ionic liquids, the point charges attributed to the various molecular residues were subjected to different degrees of

approximation to find general trends that could then be applied along an entire series of analogous ionic liquids, without the need to perform quantum calculations and parameter fitting procedures for each ion within a family. These approximations include: (1) the charges on equivalent atoms are the same (for instance, the three hydrogen atoms of a methyl group will have averaged-out point-charges obtained from the ab initio data; (2) symmetrical or slightly asymmetrical rings exhibit similar charges on the "symmetrical" atoms (for instance, cf. Fig. 3, the C4 and C5 atoms of imidazolium ions or the ortho atoms of pyridinium ions); (3) the length of alkyl side chains does not affect the charge distribution on the high charge-density parts of the ions; (4) the charge distribution on carbon and hydrogen atoms situated in alkyl side chains three bonds removed from the high charge-density parts of the ion are given the corresponding OPLS-AA values for alkanes [16]; v) the charge in the atoms that establish the connection between the high charge-density parts of the ion and its alkyl side chains is adjusted empirically in order to respect the total charge of the ion (for instance, cf. Fig. 3, C_E in $[C_2 \text{ mim}]^+$ and C_2 in $[C_n \text{ mim}]^+$ with $n > 2$). Interestingly, these "junction" atoms exhibit the same charge in different families of ionic liquids [9, 10] (for instance both in 1-alkyl-3-methylimidazolium and in N-alkylpyridinium cations).

3 Validation

The CL&P model has permitted the access to the molecular properties of ionic liquids through computer simulation "virtual experiments". Before these results could be fully explored, it was necessary to validate the force field parameters by comparing experimental results to the in silico measurements. Ionic liquids have a non-measurable vapor pressure at room temperature conditions or indeed for the larger part of their liquid temperature range. This means that the traditional way to validate a molecular force field, to be used within the framework of statistical mechanics calculations in condensed phases, was somehow curtailed at the time the model was introduced. The validation procedure had to rely exclusively on volumetric data available for some selected ionic liquids [2, 3, 8–11]. This is not a comfortable situation, since it is better to have at least one property related to the length scale of the ions (volumetric data) and at least one related to the energy scale (such as the heat of vaporization). However, and since the force field had been built in a systematic way, it was possible to test it against series of homologous ionic liquids, by predicting their densities both in the liquid and in the solid states and comparing the results with experimental data (liquid density and X-ray diffraction data).

It must be stressed that in the case of solid state data, not only the volumetric data per se were validated but also the parameters defining the crystalline unit cells (in some cases simulations started with a spurious initial crystalline structure were allowed to evolve and equilibrate to the correct crystalline structure [2, 3]).

After the discovery that ionic liquids could be vaporized at moderately high temperature (around 550 K) and reduced pressure (around 500 Pa) [27], new experimental data related to their liquid–vapor equilibrium, and thus cohesive energy, became available, and it was possible to test the performance of the CL&P force field against different estimations of the enthalpy of vaporization of 1-alkyl-3-methylimidazolium bis(trifluoromethylsulfonyl) imide ionic liquids. Although the uncertainties both in the simulation and experimental results are still big at this stage due to the extremely difficult nature of the experiments and constraints imposed on the simulation methods (poor statistics of the simulation of an isolated ionic pair in the gas phase), it was possible to conclude that for this particular family of ionic liquids, the enthalpies of vaporization at room temperature are in the 120–160 kJ/mol range (with MD over-predicting the experimental results by 15–30%) [28]. It must be stressed that the use of the model is in all cases (density and calorimetric estimations) purely predictive, which means that deviations of a few percentage points in the case of density and a few tens of percentage points in the case of the enthalpies of vaporization are in fact quite reasonable.

Validation with another property related to the energy scale (surface tension data would be an obvious choice) proved unfeasible due to the lack of reliable experimental data and also to the large uncertainty associated with the results obtainable by MD simulation. However, very recent results have shown that it is possible to estimate correct surface tension values using the CL&P force field if sufficiently long simulation times are employed [29].

4 Past, present, and future developments

In order to improve transferability, the parameterization of ionic liquids in the CL&P force field was not meant be too specific because the objective was to deal with families of similar compounds that could be combined with different counter-ions. Homologous series may be expressed in the cation, such as in alkylmidazoliums, or in the anion, such as alkylsulfates. Force field parameterization was concentrated on parts of the molecules that were common to an entire family of ions, and strategies were adopted to add specific molecular residues or functional groups. Moreover, the anions and cations were modeled independently, meaning that an ionic liquid can be assembled from any available cation–anion combination (as illustrated in Fig. 1). This transferability implies different sorts of approximation. For example, it does not account for the possibility of charge-transfer effects between ions, an issue that was thoroughly discussed at different stages of force field development and that may not be very significant in condensed phases, where each ion has a large coordination number of neighbors of opposite charge. Also, polarization of electron clouds is not taken into account explicitly, although it was included a posteriori through a number of refinement schemes (see below). Inclusion of explicit polarization accelerates the microscopic dynamics obtained with the models but has little effect on the estimation of equilibrium or structural properties (cf. below).

Most force field parameterizations that appeared at approximately the same time of the CL&P model included either united-atom (UA) or all-atom (AA) descriptions based on extensions of well-established force fields like CHARMM [18], AMBER [15], or OPLS [16, 17] with extra parameters obtained from quantum calculations. As examples, we can cite the work based on the UA force field of Ed Maggin and co-workers [4] used to predict gas solubilities [30], the structure and dynamics studies by Mauro Ribeiro using his own UA force field [31], or the introduction by Maggin and co-workers of a new AA version of their own force field, used to predict the solubility of CO_2 in imidazolium-based ionic liquids [32]. These examples reflect a shift from united-atom models to all-atom models, attempts to encompass whole families of ionic liquids (breaking with the past tradition of modeling ionic liquids on a one-to-one basis), and some extra care in incorporating into the model some degree of flexibility (the description of the torsion movements of the ions are attempted in some cases). These advances show in fact a general convergence between the different approaches to force field development, in agreement with the basic postulates behind the development of CL&P (Fig. 1). At that time, a model based on force matching to Car-Parinello molecular dynamics simulation of ionic liquids was also introduced [33], but poor rendering of dispersion forces and the extremely small size and time scales of these simulations are major difficulties when treating ionic liquids and their slow dynamics.

More recent developments witnessed the emergence of the modeling of ionic liquid plus molecular solvent systems. In terms of force field development, this means that the premises of transferability/compatibility claimed by most models have to be valid not only between the ions of the ionic liquid but also between those ions and molecular (neutral) species. All-atom models based on traditional force fields (CHARMM [18], AMBER [15], or OPLS [16, 17]) have a clear advantage in addressing this problem since most of the neutral species are already parameterized

within those force fields. Examples of ionic liquid mixtures and solutions studied by MD include: fluid-phase equilibria based on MD simulations using the CL&P force field [34, 35]; the discussion of solvation effects in ionic liquids [36] using MD results obtained using a CHARMM-based rigid force field [37]; the analysis of ionic liquid–solute interactions [38] and the analysis of the interplay between solvation and nanostructure [33], both based on the CL&P force field [2, 3, 8–11]; interpretations of large-angle X-ray scattering experimental data [39] using derived versions of the CL&P force field [2, 3]; Monte Carlo computations [40] of pure and binary gas isotherms in ionic liquids using parameters form the Maggin force field [41] to model the cations and the CL&P force field to model the bistriflamide anion [8]; or studies of the solvation of toluene in different ionic liquids in order to interpret their specific catalytic capabilities [42] using the CL&P force field [2, 3, 8].

In the latest years, ionic liquid modeling witnessed a further shift from bulk conditions to non-equilibrium or interfacial settings, and many of the newer models include polarization explicitly. Examples include the discussion of the interfacial structure of ionic liquids using x-ray reflectometry studies aided by a self-consistent mean field theory (SCMFT) model and MD simulations using a polarizable force field based on AMBER parameterizations [43]; the characterization of ionic liquids that can be used as electrolytes for batteries and super-capacitors (including the correct description of the transport of lithium ions in an ionic liquid media) using a polarizable, transferable, and quantum-chemistry-based force field denominated as Atomistic Polarizable Potential for Liquids, Electrolytes, & Polymers (APPLE&P) [44, 45]; the study of different properties of ionic liquids such as interfacial structure, self-diffusion, and viscosity using coarse-grain models, namely the effective force coarse-graining (EF-CG) method [46]; the analysis of ionic liquids under non-equilibrium conditions such as high electric fields [47] using an AMBER-based all-atom force field [5] and the EF-CG coarse-grained [46] force field; studies related to the structure of the electrochemical interface between a graphite surface and an ionic liquid using an all-atom AMBER-based force field [48]; the determination of self-diffusion coefficients in a series of ionic liquids using an adapted and extended version of the CL&P force field [49]; or, the estimation of different non-equilibrium properties of amino-functionalized ionic liquids using an all-atom AMBER-based force field [50].

Due to the complexity of ionic liquid phases, both in structural and dynamic terms, and the wide range of space and time scales that have to be considered in order to capture the behavior of these fluids, multi-scale approaches are a promising route. Here, information obtained at a more detailed level is used to impose consistency when building a coarser model. The levels of description that can be connected in this way are electronic structure calculations, atomistic force fields, and coarse-grained models [51].

These developments have been complemented by other new contributions in terms of force field refinement given by Ludwig and co-workers [52] and Siehl [53]. The latter author introduced the possibility of modeling charge transfer between ions as a way to account for polarization effects in ionic liquids and their solutions; the former authors produced a refined version of the CL&P force field [2, 3, 8], capable of taking into account the specific interactions between the acidic hydrogen atoms of dialkylimidazolium cations and different anions. All these contributions represent valid routes to the development of force fields that are fine-tuned to certain classes of ionic liquids, where problems such as polarizability, charge transfer, hydrogen bonding, or the occurrence of specific interactions may hinder the use of more general models.

The development and use of different types of force field for ionic liquids can be summarized as follows: Different force fields with different degrees of resolution from coarse-grain to atomistic models have emerged in the past decade. All-atom models have been the most popular due to their general character and the straightforward way in which they can be integrated with vast force field parameter sets for common molecules. United-atom models (halfway between all-atom and coarse-grain models) are loosing popularity, with most simulations being run at the atomistic or coarse-grain levels. The latter type of models are specially suitable for non-equilibrium conditions but sometimes lack the detail necessary to the correct description of specific interactions, a situation that is particularly relevant in the case of mixtures of ionic liquids with molecular solvents. Quantum mechanical simulation methods represent the ultimate models in terms of "resolution" but are costly in terms of computing time and were only applied to a few systems.

On the other hand, in order to improve transferability (see Fig. 1), the parameterization of ionic liquids in systematic atomistic force fields like CL&P was not meant be too specific because the objective was to model families of homologous ions that could be combined with different counter-ions. This meant that, on one hand, the parameterization was concentrated on parts of the ions that defined entire homologous series and, on the other hand, that the anions and cations were parameterized independently. This sort of transferability implies different types of approximation. For example, it does not account for the possibility of charge-transfer effects between different ions (the charges are usually obtained ab initio from isolated ions). In the condensed phase where each ion is surrounded by neighbors of opposite charge such effect does not have a profound impact in terms of structure but will certainly

play a role in terms of the intensity of possible specific interactions between ions and the formation of (transient) ion pairs. [52] Also, polarization of electron clouds is not taken into account explicitly, although was included a posteriori through a number of refinement schemes [43–45]. Inclusion of explicit polarization accelerates the microscopic dynamics obtained with the models but has little effect on the estimation of equilibrium or overall structural properties [54]. On the other hand, local structural effects or specific interactions can be affected by the modeling or not of polarizability effects. [55, 56].

The introduction of these two types of correction/approximation (charge-tranfer and polarization methods) represent two major routes to the refinement of systematic (either atomistic or coarse grained) models. In fact the two types of approximation/correction have been somewhat merged into a single procedure [54] that tries to account for the lack of polarizability effects in the CL&P by using an ad-hoc correction factor applicable to all parameterized point charges that mimics a charge-transfer process between ions. The resulting anions and cations—with overall charges around (-0.8 to -0.9) and ($+0.8$ to $+0.9$), respectively—interact via subdued electrostatic interactions which in turn lead to a better description of the available enthalpy of vaporization and volumetric data, faster dynamics and (possibly) a less stringent separation between polar and non-polar domains (nano-segregation) of the ionic liquids [57, 58]. The task of using this kind of procedure in a systematic and coherent way (it is for instance questionable the application of the correction factor to the charges of the alkyl side chains that are not subjected to noticeable polarizability effects) is one of the challenges to be addressed in future developments of the CL&P force field.

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