Supporting Information:

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Table S1: Non-bonded interaction parameters (σ and ϵ) for ionic liquids CG bead types and other CG bead types from *ProMPT*.

	TQ0		TQa		TC6h		TC5h	
	σ	ϵ	σ	ϵ	σ	ϵ	σ	ϵ
POL	0.61	4.50	0.38	5.00	0.39	1.55	0.39	1.36
PP5	0.61	5.32	0.38	5.32	0.40	1.67	0.40	1.67
APP5	0.61	5.32	0.38	5.32	0.40	1.67	0.40	1.67
PNda	0.61	4.22	0.38	5.32	0.40	2.43	0.40	2.16
PAC1	0.61	2.30	0.38	2.30	0.40	1.67	0.40	1.85
PN0	0.61	3.72	0.38	3.72	0.40	2.43	0.40	2.16
PNa	0.61	4.22	0.38	4.22	0.40	2.43	0.40	2.16
N0	0.61	4.00	0.38	4.00	0.40	2.43	0.40	2.16
C1	0.61	2.30	0.38	2.30	0.40	1.67	0.40	1.85
C3	0.61	2.70	0.38	2.70	0.40	2.11	0.40	2.11
SC6	0.40	2.43	0.40	2.43	0.37	2.11	0.37	2.11
AR*	0.61	2.30	0.38	2.30	0.37	1.75	0.37	1.75
APR*	0.61	2.02	0.38	2.02	0.37	1.75	0.37	1.75
Qd*	0.61	2.30	0.38	4.00	0.40	2.43	0.40	2.16
Qa	0.61	2.30	0.38	3.50	0.40	2.43	0.40	2.16
TQa	0.49	2.30	0.38	3.50	0.40	2.43	0.40	2.16
TQ0	0.61	3.50	0.49	2.30	0.40	2.43	0.40	2.16
TC6h	0.40	2.43	0.40	2.43	0.34	2.02	0.34	1.77
TC5h	0.40	2.16	0.40	2.16	0.34	1.77	0.34	1.77

Simulation setup to validate [Chol][Cl] coarse-grained (CG) model

Coarse-grained simulations of 25wt% [Chol][Cl]: 50 choline and chloride beads were placed in a simulation box of 4nm^3. The box was solvated with 278 Martini polarizable water model.[1] The final production run is a 10ns NPT simulation with a timestep of 10 femtoseconds. Temperatures were fixed at 300K using the Nose-Hoover thermostat with a time constant of 1 picosecond. Pressure was maintained at 1 atm using the Parrinello-Rahman barostat with isotropic pressure coupling. A relative dielectric constant of 2.5 was used. Electrostatics were computed using Particle Mesh Ewald[2,2] with a cutoff of 1.6 nm. Nos$\tilde{e}$-Hoover thermostat is used to maintain the system at the desired temperature[3] and the LINCS algorithm was used to evaluate constraints.[4] Neighborlist was updated every 10 steps.

Atomistic simulations of 25wt% [Chol][Cl]: Amber99sb[5] was used to simulate 25wt%[Chol][Cl] systems. A 4nm^3 box was solvated with 1113 TIP3P water and 50 choline and chloride molecules. A timestep of 0.5 femtosecond was used to run a NVT simulation for 100 picoseconds, followed by an NPT simulation of 10ns. Temperature was maintained at 300K using the V-rescale algorithm.[6] Pressure was maintained at 1atm using the Parrinello-Rahman barostat with isotropic pressure coupling. Electrostatics were computed using the PME algorithm[2] and constraints were handled using the LINCS algorithm.[4]

Validation of [Chol][Cl] coarse-grained model

The density in the CG simulations of 25wt% [Chol][Cl] is 916.3 $\pm$ 8 kg/m^3, while in the atomistic simulations, it is 1052.6 $\pm$ 24 kg/m^3. Our experimentally measured density stands at 1036.2 kg/m^3. To evaluate electrostatic properties, we computed the dielectric constant for both CG and atomistic simulations. The dielectric constant for CG simulations is 47.3 $\pm$ 2.8, whereas for atomistic simulations, it is 56.1 $\pm$ 2.7. Figure S1 depicts the comparison of the radial distribution function (RDF) between atomistic and CG simulations.

It is important to note that we expect to observe shifts in the peaks of the RDFs between CG and atomistic systems. In CG simulations, we condense four water molecules into a single site, while the choline CG mapping comprises only two beads, each representing multiple atoms. Additionally, chloride ions are modeled as hydrated ions. Nevertheless, we are capturing the general trend in the peak locations of the different RDFs.

The RDF first peak between the oxygen of choline and water of the atomistic system corresponds to the first coordination shell of water molecules, which our CG model cannot precisely capture since we aggregate four water molecules into a single CG bead. However, we do accurately represent the other coordination shells.

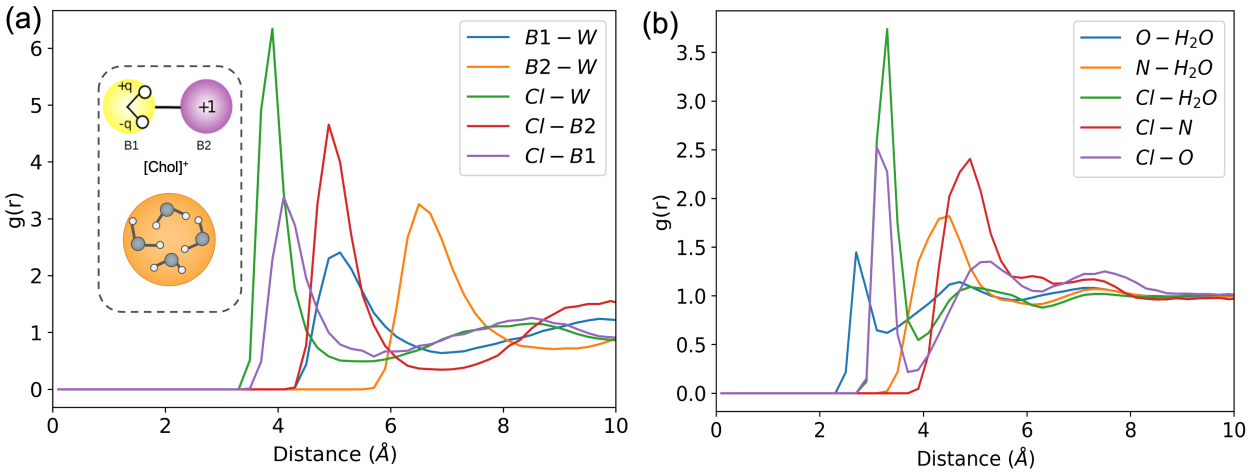

Figure S1: Radial distribution function of 25wt%[Chol][Cl] for different groups, for coarse-grained (a) and atomistic (b) simulations.

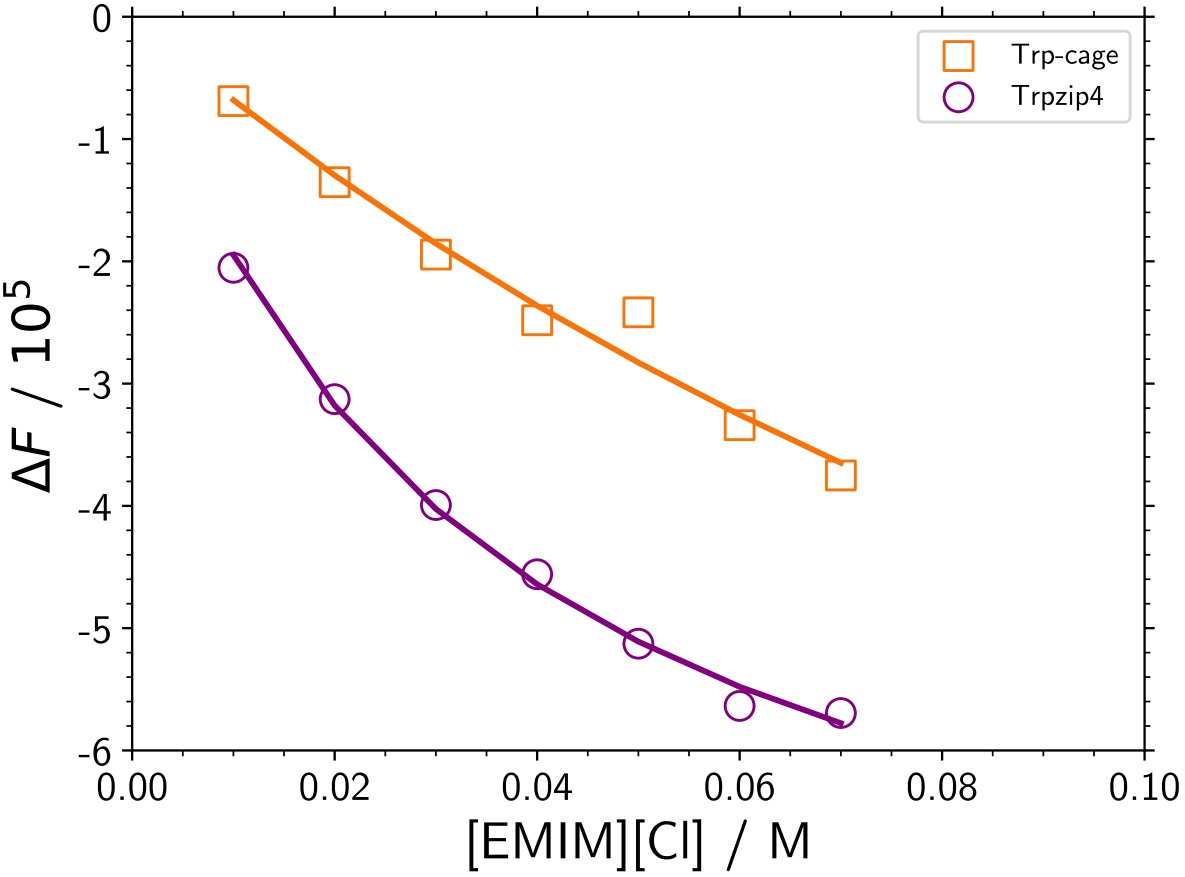

Figure S2: Change in Trp fluorescence intensity with [EMIM][Cl] concentration. Curves are nonlinear regression fits, from which binding constants are obtained.

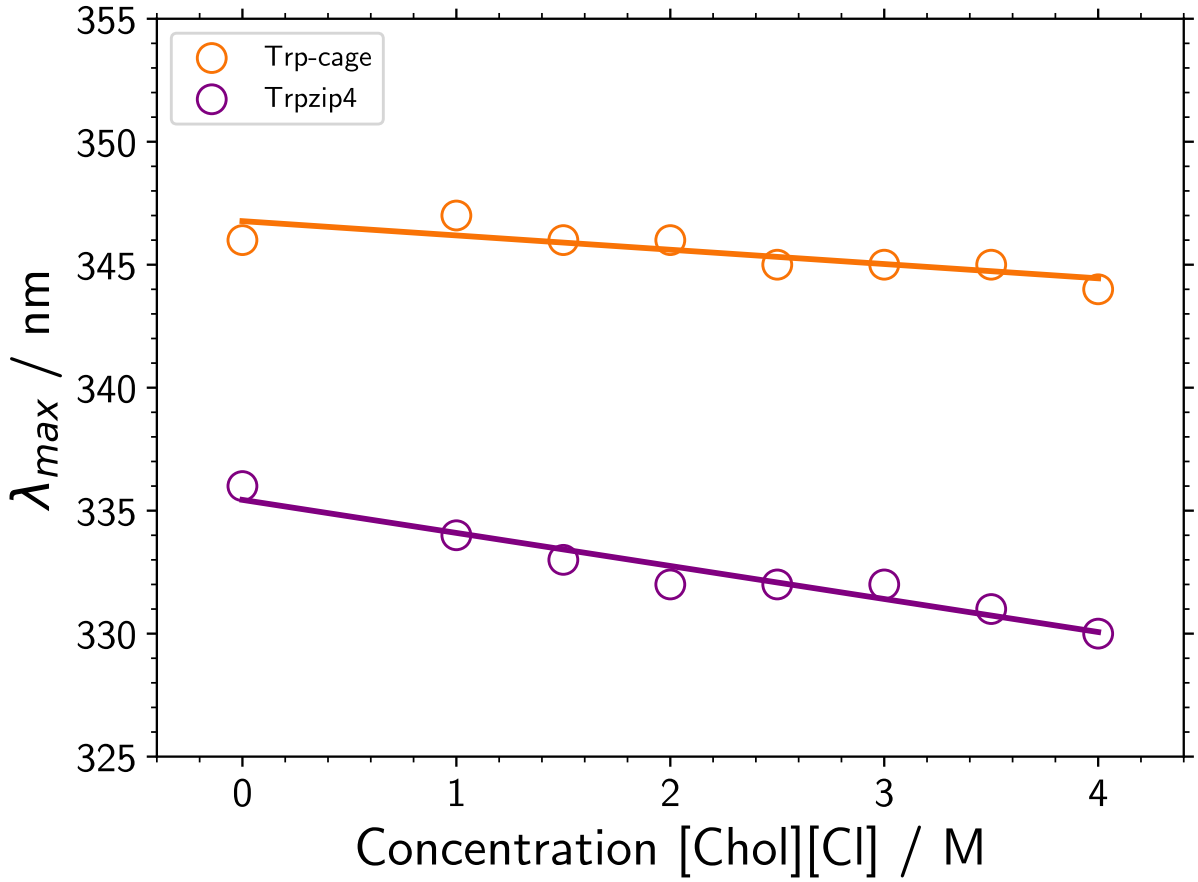

Figure S3: The maximum emission wavelength for various concentrations of [Chol][Cl].

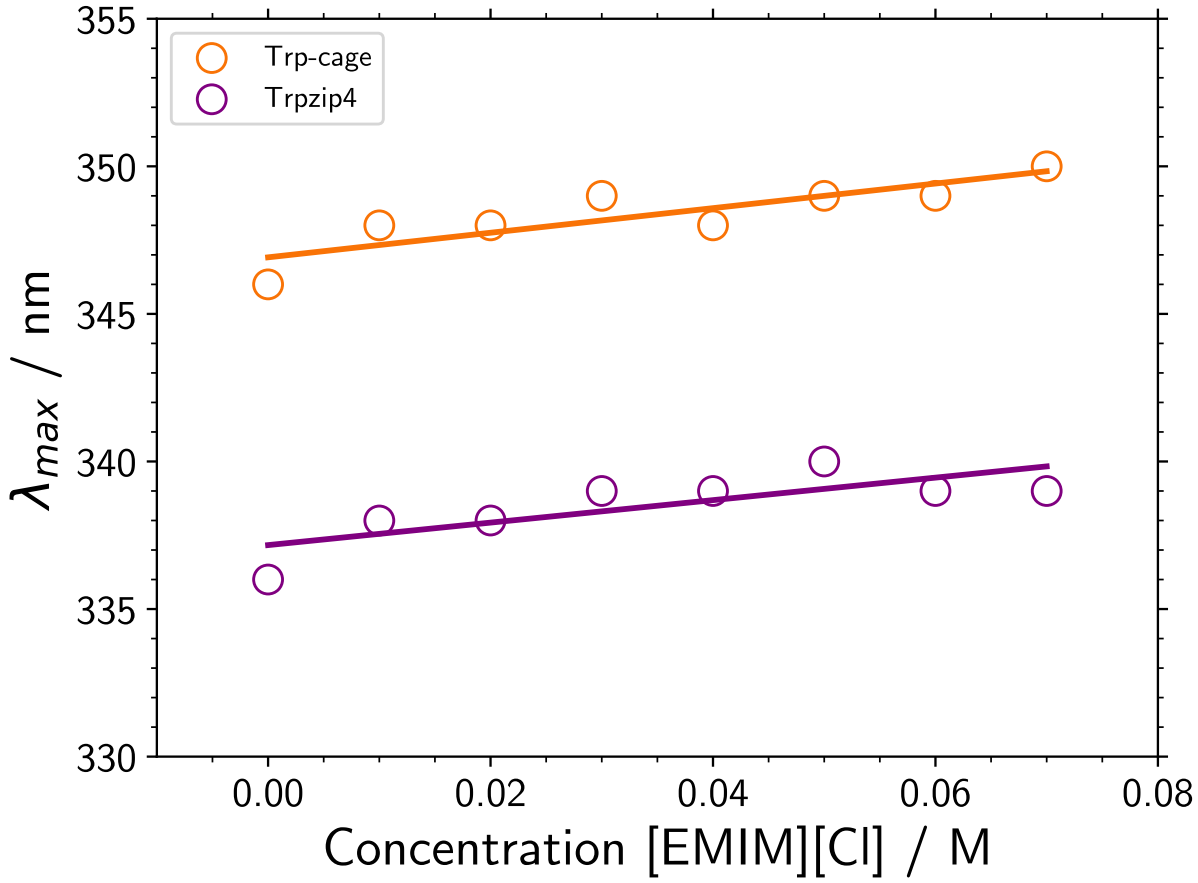

Figure S4: The maximum emission wavelength for various concentrations of [EMIM][Cl].

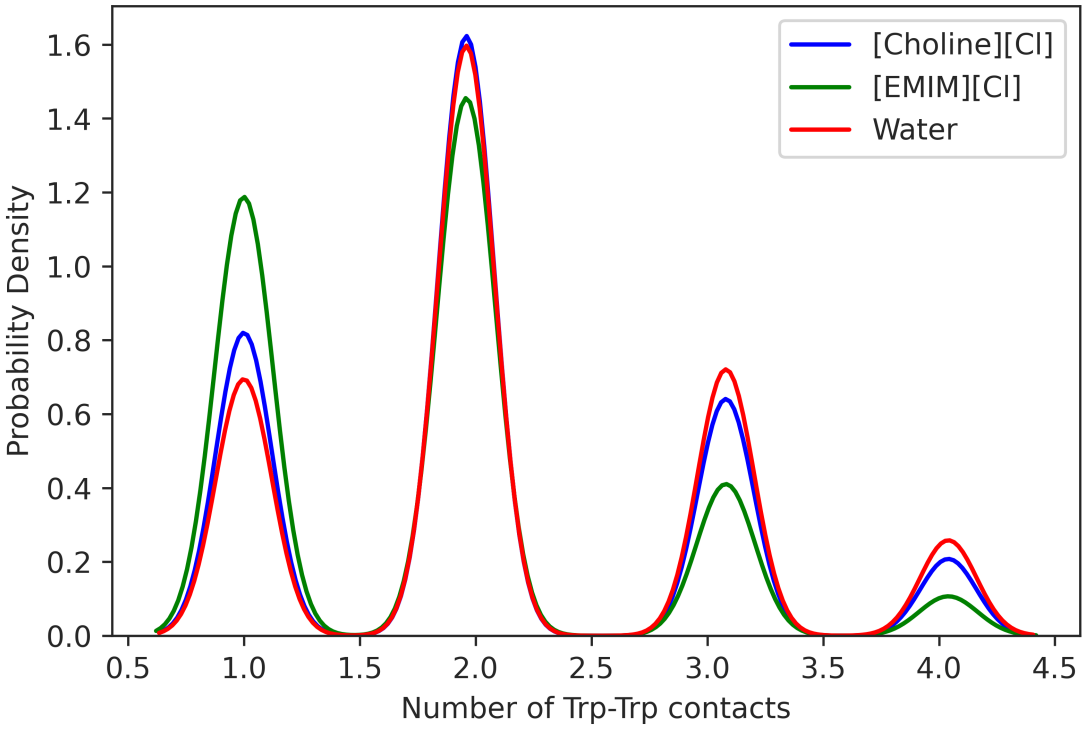

Figure S5: Distribution of the number of Trp-Trp contacts in Trpzip4 in the folded basin at 350K.

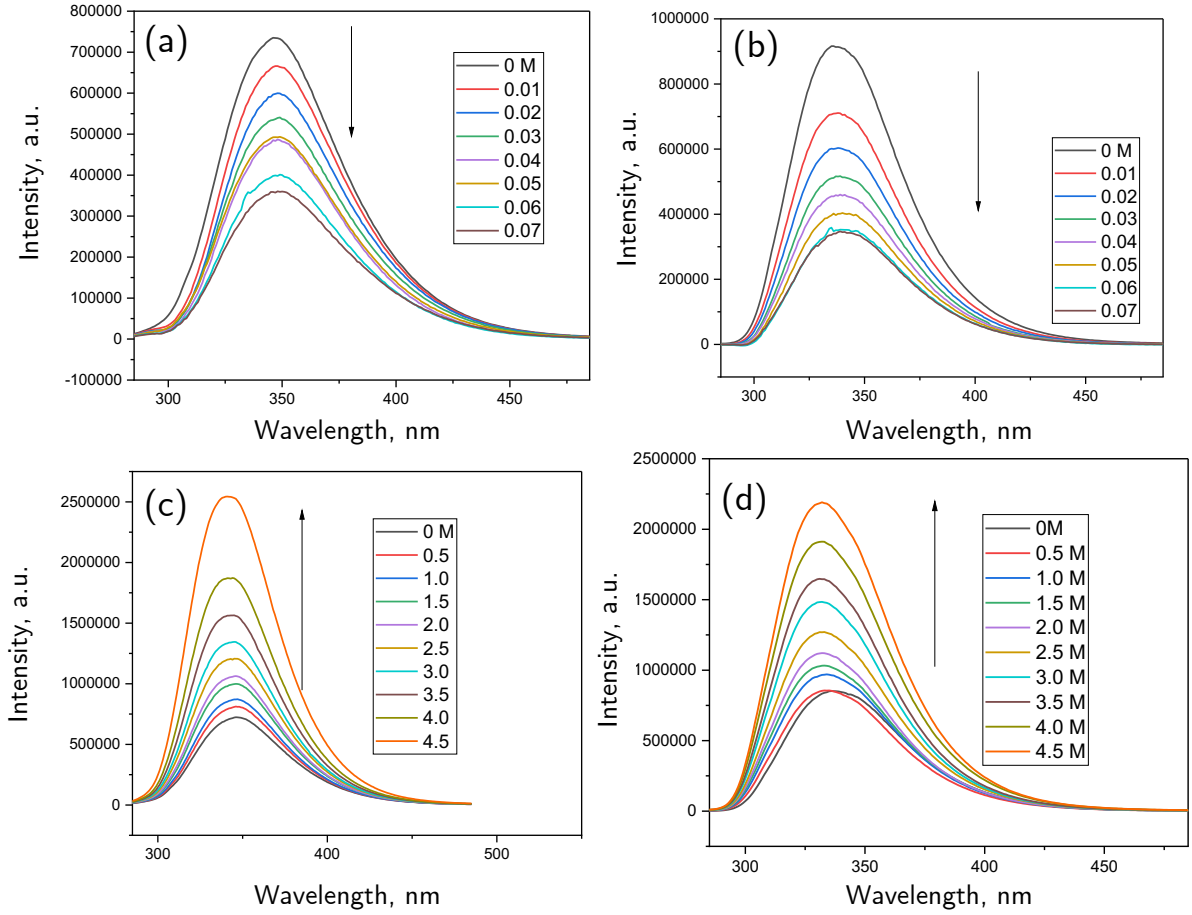

Figure S6: Steady-state fluorescence emission spectra from Trp residues. (a) [EMIM][Cl] added to Trp-cage; (b) [EMIM][Cl] added to Trpzip4; (c) [Chol][Cl] added to Trp-cage; (d) [Chol][Cl] added to Trpzip4.

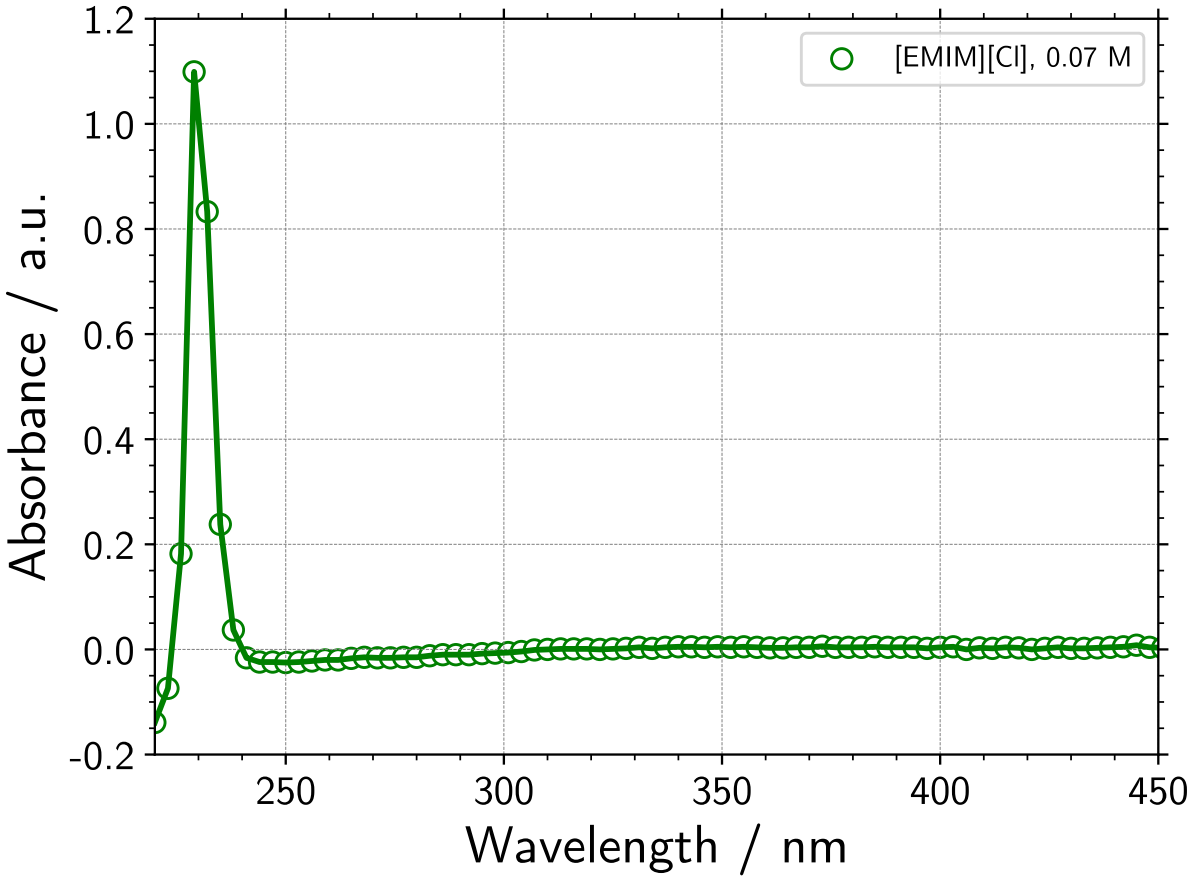

Figure S7: The absorbance spectra of [EMIM][Cl] were acquired using a Nanodrop ND-1000 spectrophotometer, employing a path length of 1 mm. Water served as the reference for background subtraction. The concentration tested here (0.07 M) matches the highest concentration employed in the fluorescence quenching experiments. Notably, the only signal detected lies within the far-UV region, specifically below 240 nm, consistent with the findings of Marszall *et al.*[7]

References

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