Supporting Information

Epitope mapping of imidazolium cation in ionic liquid-protein interactions unveils the balance between hydrophobicity and electrostatics towards protein destabilisation

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STD-NMR experiments

Figure S1 – Top – STD NMR spectrum of 5 mM [C₄dmim][Cl] with 50 μM human HSA and relative STD NMR intensities in percentage; Bottom – Reference spectrum (off resonance) with resonance assignments.

Figure S2 – Top – STD NMR spectrum of 5 mM [C₃Omim][Cl] with 50 μM human HSA and relative STD NMR intensities in percentage; Bottom – Reference spectrum (off resonance) with resonance assignments. H2 exchanges with D₂O over time and therefore its STD response can not be accurately determined.
**Figure S3** – Top – STD NMR spectrum of 5 mM [C_2OHmim][Cl] with 50 μM human HSA and relative STD NMR intensities in percentage; Bottom – Reference spectrum (off resonance) with resonance assignments.

**Figure S4** – Top – STD NMR spectrum of 5 mM [C_4mim][dca] with 50 μM human HSA and relative STD NMR intensities in percentage; Bottom – Reference spectrum (off resonance) with resonance assignments. H2 exchanges with D_2O over time and therefore its STD response can not be accurately determined.
Figure S5 – Top – STD NMR spectrum of 5 mM [C₃mim][dca] with 50 μM human HSA and relative STD NMR intensities in percentage; Bottom – Reference spectrum (off resonance) with resonance assignments. H₂ exchanges with D₂O over time and therefore its STD response can not be accurately determined.

Figure S6 – Top – STD NMR spectrum of 5 mM [C₅Omim][Cl] with 50 μM human HSA and relative STD NMR intensities in percentage; Bottom – Reference spectrum (off resonance) with resonance assignments.
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**Figure S8** – Top – STD NMR spectrum of 2.5 mM [C$_2$ mim][Cl] and [C$_4$ mim][Cl] with 50 µM human HSA and relative STD NMR intensities in percentage; Bottom – Reference spectrum (off resonance) with resonance assignments.
Figure S9 – Effect of HSA addition on the $^{35}\text{Cl}$ resonance of a sample containing 5 mM $[\text{C}_2\text{mim}][\text{Cl}]$ in D$_2$O (500 µL). Increased HSA concentration was achieved through the addition of small volumes of 50 µM HSA, 5 mM $[\text{C}_2\text{mim}][\text{Cl}]$ to maintain the total concentration of chlorine constant. From bottom to top: volumes added in µL (HSA concentration in µM): 0 (0), 10 (0.98), 20 (1.92), 30 (2.83), 50 (4.55), 75 (6.52), 100 (8.33), 150 (11.54), 225 (15.52), 300 (18.75), and 360 (20.93). Top spectrum: 50 µM HSA, 5 mM $[\text{C}_2\text{mim}][\text{Cl}]$. 
Figure S10 – Effect of HSA addition on the $^{35}\text{Cl}$ resonance of a sample containing 5 mM [C$_4$ mim][Cl] in D$_2$O (500 μL). Increased HSA concentration was achieved through the addition of small volumes of 50 μM HSA, 5 mM [C$_4$ mim][Cl] to maintain the total concentration of chlorine constant. From bottom to top: volumes added in μL (HSA concentration in μM): 0 (0), 10 (0.98), 20 (1.92), 30 (2.83), 50 (4.55), 100 (8.33), 150 (11.54), 225 (15.52), 300 (18.75), and 385 (21.75). Top spectrum: 50 μM HSA, 5 mM [C$_4$ mim][Cl].
Figure S11 – Effect of HSA addition on the $^{35}$Cl resonance of a sample containing 5 mM [C$_4$dmim][Cl] in D$_2$O (500 µL). Increased HSA concentration was achieved through the addition of small volumes of 50 µM HSA, 5 mM [C$_4$dmim][Cl] to maintain the total concentration of chlorine constant. From bottom to top: volumes added in µL (HSA concentration in µM): 0 (0), 10 (0.98), 20 (1.92), 30 (2.83), 50 (4.55), 75 (6.52), 100 (8.33), 150 (11.54), 225 (15.52), 300 (18.75), and 360 (20.93). Top spectrum: 50 µM HSA, 5 mM [C$_4$dmim][Cl].
**Figure S12** – Effect of HSA addition on the $^{35}$Cl resonance of a sample containing 5 mM [C$_3$Oim][Cl] in D$_2$O (500 μL). Increased HSA concentration was achieved through the addition of small volumes of 50 μM HSA, 5 mM [C$_3$Oim][Cl] to maintain the total concentration of chlorine constant. From bottom to top: volumes added in μL (HSA concentration in μM): 0 (0), 10 (0.98), 20 (1.92), 30 (2.83), 50 (4.55), 75 (6.52), 100 (8.33), 150 (11.54), 225 (15.52), 300 (18.75), and 360 (20.93). Top spectrum: 50 μM HSA, 5 mM [C$_3$Oim][Cl].
Figure S13 – Effect of HSA addition on the $^{35}$Cl resonance of a sample containing 5 mM [C$_2$OHmim][Cl] in D$_2$O (500 µL). Increased HSA concentration was achieved through the addition of small volumes of 50 µM HSA, 5 mM [C$_3$Omim][Cl] to maintain the total concentration of chlorine constant. From bottom to top: volumes added in µL (HSA concentration in µM): 0 (0), 10 (0.98), 20 (1.92), 30 (2.83), 50 (4.55), 75 (6.52), 100 (8.33), 150 (11.54), 225 (15.52), 300 (18.75), and 360 (20.93). Top spectrum: 50 µM HSA, 5 mM [C$_2$OHmim][Cl].
Table S1 - NMR determined self-diffusion coefficient of HDO in IL solutions with different HSA concentrations

<table>
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<th>0 µM HSA (×10⁻⁹ m²/s)</th>
<th>21.75 µM (×10⁻⁹ m²/s)</th>
<th>50 µM (×10⁻⁹ m²/s)</th>
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<td>[C₄mim][Cl]</td>
<td>1.68 ± 0.01</td>
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<td>[C₂OHmim][Cl]</td>
<td>1.69 ± 0.01</td>
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