Electronic Supplementary Material (ESI) for Physical Chemistry Chemical Physics.

Electronic Supplementary Information for Dual Mechanism of Ionic Liquid-Induced Protein Unfolding

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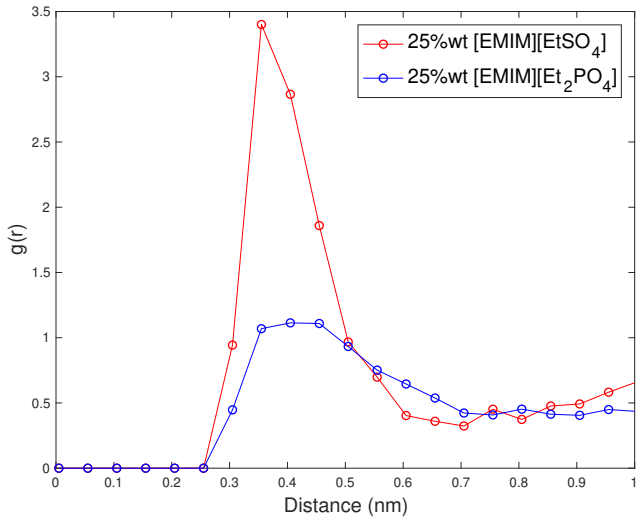

Figure S1: RDF between CR atom of TRP62 and Cδ2 or Cϵ2 atom of $[EMIM]^+$ for 25 wt% [EMIM][$EtSO_4$] (red) and 25 wt% [EMIM][Et_2PO_4] (blue).

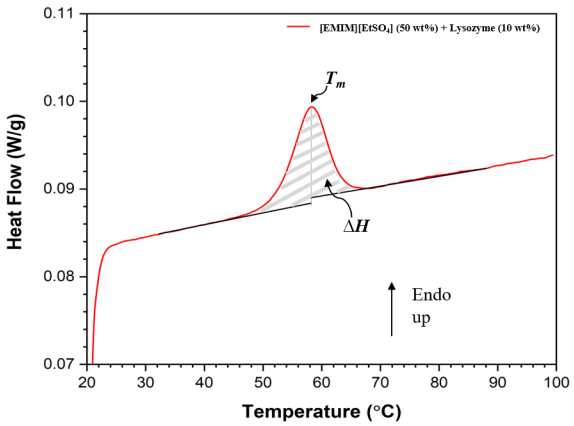

Figure S2: Representative endotherm for lysozyme in IL-water mixture.

Three properties were calculated to validate the force field for [EMIM][Et_2PO_4] taken from the LigParGen server[1], which were density, specific heat capacity, and surface tension. The density for neat [EMIM][Et_2PO_4] at 300 K was calculated to be 1123.51±5.26257 kg/m^3 and at 333 K was calculated to be 1100.88±6.24452 kg/m^3. The experimental values are 1140.0 kg/m^3 and 1111.1 kg/m^3 at 298.15 K and 333.15 K[2], respectively. The specific heat capacity calculated for neat [EMIM][Et_2PO_4] was 1.8017 J/(g*K) at 300 K while the experimental value is 2.0457 J/(g*K). The surface tension was calculated to be 56 mN/m for neat [EMIM][Et_2PO_4] at 300 K, which is higher than the experimental value of 35.88 mN/m at 298.15 K[2]. It is reported that the surface tension is generally overestimated in simulation at ambient temperatures so we also calculated the surface tension at 333 K to validate the precision of force field on dynamical properties. The surface tension at 333 K was calculated to be 38 mN/m. The experimental value at 333.15 K for surface tension is 33.88 mN/m, which is close to the value determined from simulation.

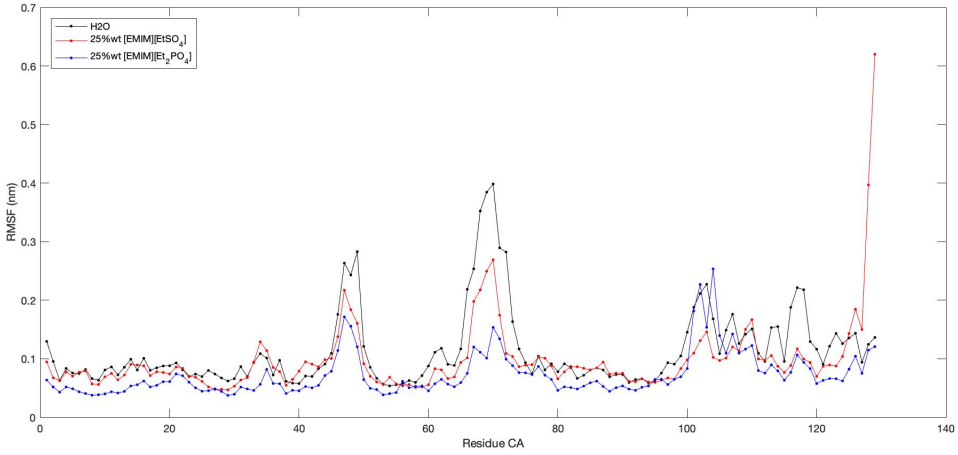

Figure S3: RMSF of lysozyme Cα atoms in nm, where black represents water, red represents 25 wt% [EMIM][$EtSO_4$], and blue represents 25 wt% [EMIM][Et_2PO_4].

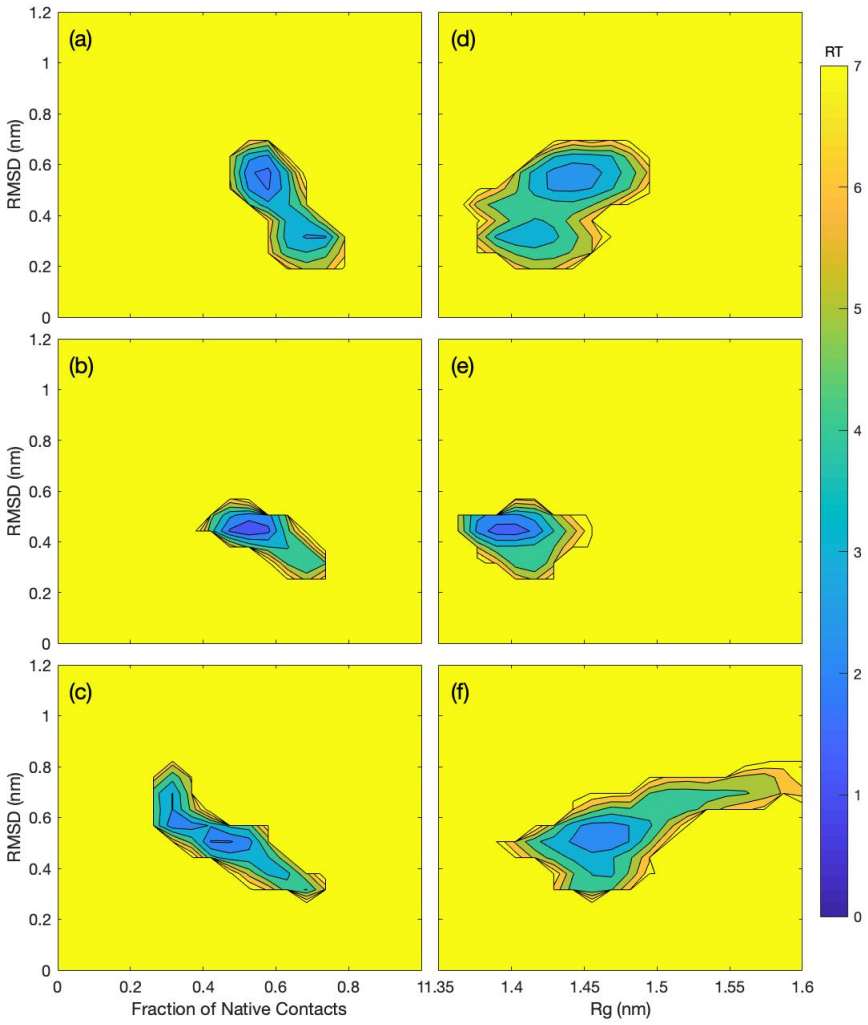

Figure S4: Potential mean force plot at 370 K, where the reaction coordinates used for the left column are RMSD and fraction of native contacts and the reaction coordinates used for the right column are RMSD and R_g. (a) and (d) are water system, (b) and (e) are 25 wt% [EMIM][$EtSO_4$] system, and (c) and (f) are 25 wt% [EMIM][Et_2PO_4] system. Potential mean force is in RT unit.

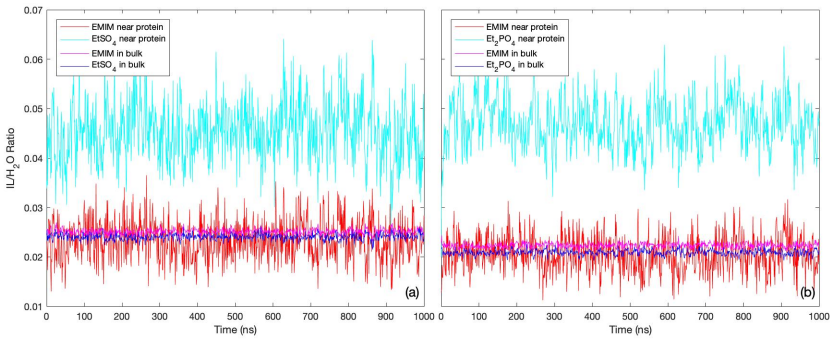

Figure S5: Ratio of ILs to H_2O near lysozyme and in bulk in (a) 25 wt% [EMIM][$EtSO_4$] and (b) 25 wt% [EMIM][Et_2PO_4] at 300 K.

References

[1] L. S. Dodda, I. Cabeza de Vaca, J. Tirado-Rives and W. L. Jorgensen, *Nucleic acids research*, 2017, **45**, W331–W336.

[2] J.-y. Wang, F.-Y. Zhao, R.-j. Liu and Y.-q. Hu, *The Journal of Chemical Thermodynamics*, 2011, **43**, 47–50.