## **Supplementary Information for**

### Thermodynamic anatomy of micelle-small molecule coacervation

Fengxiang Zhou,<sup>1,2</sup> Mingyue Lu,<sup>1,2</sup> and Lingxiang Jiang<sup>1,2\*</sup>

- <sup>1</sup>South China Advanced Institute for Soft Matter Science and Technology (AISMST), State Key Laboratory of Pulp and Paper Engineering, School of Emergent Soft Matter, South China University of Technology, Guangzhou 510640, China
- <sup>2</sup> Guangdong Provincial Key Laboratory of Functional and Intelligent Hybrid Materials and Devices, Guangdong Basic Research Center of Excellence for Energy & Information Polymer Materials, South China University of Technology, Guangzhou 510640, China

\* Correspondence to: jianglx@scut.edu.cn

#### Atomistic reference simulations

All-atom reference molecular dynamics (MD) simulations were performed using the Optimized Potentials for Liquid Simulations-All Atom (OPLS-AA) force field and the TIP3P water model<sup>1</sup> to derive key topological parameters for coarse-grained (CG) model development. Atomistic topology parameters were obtained from LigParGen with the 1.14\*CM1A-LBCC charge model<sup>2-4</sup>. A single parameterized molecule was initially placed in a cubic box of 5.0 nm length and fully solvated. Appropriate counterions (Na<sup>+</sup> or Br<sup>-</sup>) were added to ensure charge neutrality of the system. The box size was rescaled during simulations to maintain isotropic pressure coupling. The system was equilibrated for 50 ns using the Berendsen thermostat ( $\tau_T = 0.2$  ps) at 300 K and the Berendsen barostat ( $\tau_P = 0.5$  ps) at 1 bar. Production runs lasted 200 ns with the Nosé-Hoover thermostat ( $\tau_T = 0.5$  ps) and the Parrinello–Rahman barostat ( $\tau_P = 1.0$  ps). Lennard-Jones interactions were treated with a truncated potential, and electrostatics were calculated using the particle-mesh Ewald (PME) method. Lennard-Jones and electrostatic interactions are subject to 1.2 nm cutoffs. The neighbor list was updated every 10 steps, and the time step was set to 2 fs.

#### The force-field validation of the CG model.

The topological potentials between the CG beads were optimized through single-chain solution simulations using the parameters outlined in the section B, except for the box size, which was set to 5 nm. Iterative refinements ensured that the CG model accurately reproduced the key topological features of the atomistic (AA) reference simulations. These features include consistent distributions of bond lengths, and dihedral angles (Fig. S1). The Connolly surface method visually evaluates the consistency of molecular volumes between the AA and CG models (Fig. S2), showing that the atomistic moiety is, on average, captured quite accurately by the CG model.







Figure S1. Distributions of AA and CG bond and dihedral angles at 300 K for CA<sup>+</sup> (a) and MC<sup>4-</sup> (bc). The encoding rules for each subgraph title are defined as follows: "b" denotes a bond, "c" denotes a constraint, "dih" denotes a dihedral angle, the subscript indicates the sequence order, and "i-j" specifies the bond or constraint connecting the i-th and j-th beads.



Figure S2. Connolly surface for the CA<sup>+</sup> (a) and MC<sup>4-</sup> (b). AA in gray, CG in magenta.

# The optimal topological potentials.

	Dead number	Reference value	Force constant
	Dead number	(nm or °)	kJ/(mol• nm) or kJ/(mol•rad <sup>2</sup> )
CA <sup>+</sup>	1-2	0.404	10000
	2-3	0.47	1250
	+ 3-4	0.47	1250
	1-2-3	170.0	15.0
	2-3-4	180.0	25.0
	1-8	0.303	25000
	2-8	0.299	25000
	1-9	0.303	25000
	5-9	0.299	25000
	6-10	0.299	25000
	7-10	0.303	25000
	3-11	0.299	25000
	7-11	0.303	25000
	2-3	0.220	*
	2-5	0.465	*
MC	4- 2-6	0.514	*
IVIC	3-6	0.465	*
	5-6	0.220	*
	2-3-5-6	180	200
	8-5-6-3	0	200
	1-8-2-5	0	200
	9-2-3-6	0	200
	1-9-5-2	0	200
	10-3-2-5	0	200
	7-10-6-3	0	200
	11-6-5-2	0	200
	7-11-3-6	0	200

Table S1. Topology parameters. Asterisks indicate constraints.



Figure S3. Histogram of umbrella sampling for ion pairing (a) and coalescence (b) stages.



Figure S4. Charge neutrality is maintained within the coacervate phase.



Figure S5. Potential of mean force profiles for CA<sup>+</sup> micelle fusion in the absence of MC<sup>4-</sup>.



Figure S6. Temperature dependence of the free energy.



Figure S7. The cutoff for defining hydration water (a) and adsorbed counterions (b) was identified at the first minima in the radial distribution functions for ions and water, and for complexed charged units and counterions.

#### Reference

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