Electronic Supplementary Material (ESI) for RSC Advances.

Supplementary information for

Dual responsive PMEEECL-PAE block copolymers: a computational self-assembly and doxorubicin uptake study

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Table S1: Details of simulation systems for all-atom (AA) and coarse-grained (CG) simulations.

System	AA/CG	Production time (ns)	Simulation box size (nm^3)	Temperature (K)
$PMEEECL_{20}$-PAE_5 in water box	AA	50	245	285, 290, 295, 300, 305, 310, 315, 320, 325, 330, 335
$PMEEECL_{20}$-PAE_{10} in water box	AA	50	310	285, 290, 295, 300, 305, 310, 315, 320, 325, 330, 335
$PMEEECL_{20}$-PAE_{15} in water box	AA	50	382	285, 290, 295, 300, 305, 310, 315, 320, 325, 330, 335
$PMEEECL_2$-PAE_2 in water box	AA	10	90	300
$PMEEECL_2$-PAE_2 in water box	CG	300	12350	300
$PMEEECL_{20}$-PAE_5 in water box	CG	600	32768	300, 305, 310, 315, 320, 325, 330
$PMEEECL_{20}$-PAE_{10} in water box	CG	600	33076	300
$PMEEECL_{20}$-PAE_{15} in water box	CG	600	33560	300
DOX in water Box	AA	10	60	300
DOX in water Box	CG	300	11148	300
DOX 1wt% of $PMEEECL_{20}$-PAE_5 in water box	CG	640	31300	300
DOX 5wt% of $PMEEECL_{20}$-PAE_5 in water box	CG	640	31357	300
DOX 10wt% of $PMEEECL_{20}$-PAE_5 in water box	CG	640	31381	300

Table S2. Flory-Huggins interaction parameters χ_{ij} used in the SCF computations.

i	j	χ_{ij}	i	j	χ_{ij}
W	A	0.51	A	I^+	0
W	B	1.8	B	C	0.5
W	C	3.5	B	I^-	0
W	I^-	0	B	I^+	0
W	I^+	0	C	I^-	0
A	B	0.4	C	I^+	0
A	C	0.8	I^+	I^-	0
A	I^-	0			

Table S3: All-atom MD simulations results for the radius of gyration (R_g) for both the hydrophilic (PMEEECL) and hydrophobic (PAE) parts of $PMEEECL_{20}$-PAE_M block copolymer with M = 5, 10, and 15 for various temperatures from 285 K to 335 K.

	R_g (Å)					
	$PMEEECL_{20}$-PAE_5		$PMEEECL_{20}$-PAE_{10}		$PMEEECL_{20}$-PAE_{15}	
T (K)	PMEEECL	PAE	PMEEECL	PAE	PMEEECL	PAE
285	24.2 ± 0.6	19.3 ± 0.6	24.4 ± 0.2	32.1 ± 0.5	26.2 ± 0.2	40 ± 0.6
290	21.9 ± 0.9	18.6 ± 0.6	22.8 ± 0.5	37 ± 0.4	25.6 ± 0.5	45.4 ± 0.9
295	20.2 ± 0.4	17.7 ± 0.8	24.9 ± 0.3	30 ± 0.5	27.2 ± 0.4	34.5 ± 0.6
300	22 ± 1	17 ± 1	23.8 ± 0.6	34.2 ± 0.7	21.3 ± 0.5	45.3 ± 0.5
305	24.4 ± 0.3	16.4 ± 0.5	16.2 ± 0.3	38.5 ± 0.4	19.7 ± 0.6	47.2 ± 0.3
310	22.2 ± 0.3	18.8 ± 0.2	17.4 ± 0.4	34.2 ± 0.6	19 ± 0.2	44.5 ± 0.4
315	16.2 ± 0.3	15.1 ± 0.5	17.1 ± 0.5	34 ± 2	22.4 ± 0.3	38.9 ± 0.6
320	15 ± 1	19 ± 1	19.8 ± 0.2	29.6 ± 0.3	19.5 ± 0.3	52 ± 0.9
325	17 ± 2	17.3 ± 0.3	17.9 ± 0.6	36.4 ± 0.3	20 ± 0.4	38.1 ± 0.5
330	15.1 ± 0.3	16.5 ± 0.6	16.1 ± 0.4	38.4 ± 0.5	20.7 ± 0.5	41.7 ± 0.4
335	17.3 ± 0.4	19.1 ± 0.3	17.3 ± 0.5	36.2 ± 0.8	20.2 ± 0.4	43.4 ± 0.5

Table S4: Estimated coil-to-globule transition temperature (T_{cg}) of PMEEECL in PMEEECL$_{20}$-PAE$_M$ block copolymers with M = 0, 5, 10, and 15 as a function of hydrophilic mass fraction from fitting equation 1 to simulations data in Fig. 1a and Table S3. For M = 0 the T_{cg} is excerpted from [24].

PMEEECL$_{20}$-PAE$_M$

M	Hydrophilic mass fraction (f)	T_{cg} (K)
0	1	318 ± 2.5
5	0.697	312 ± 2.5
10	0.563	302 ± 2.5
15	0.463	298 ± 2.5

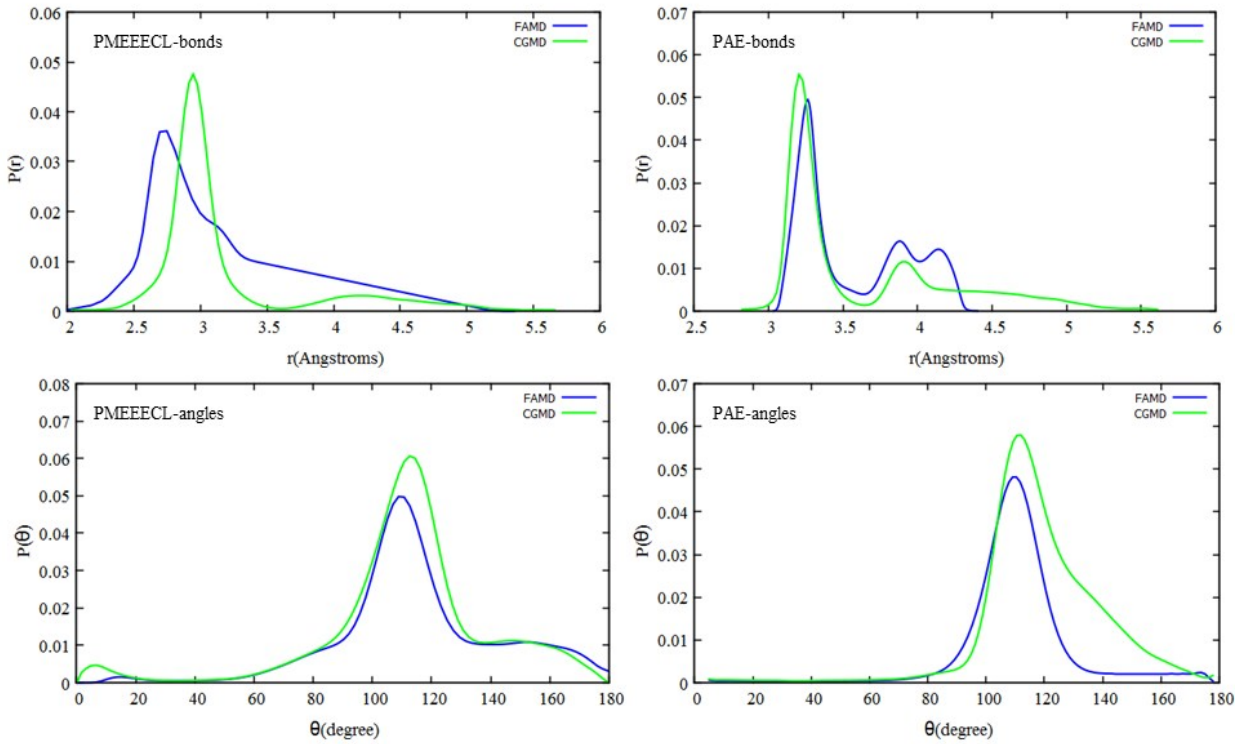

FIG. S1: Bond and angle distributions P(r) and P(θ) of PMEEECL and PAE for all-atom MD simulations and MARTINI CG force field simulations.

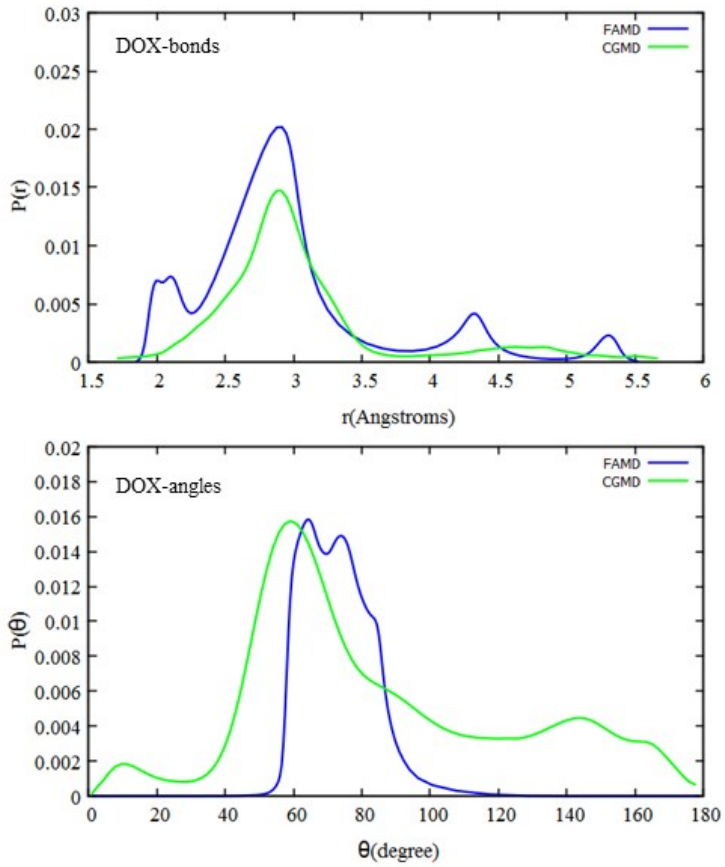

FIG. S2: Bond and angle distributions P(r) and P(θ) of DOX for all-atom MD simulations and MARTINI CG force field simulations.

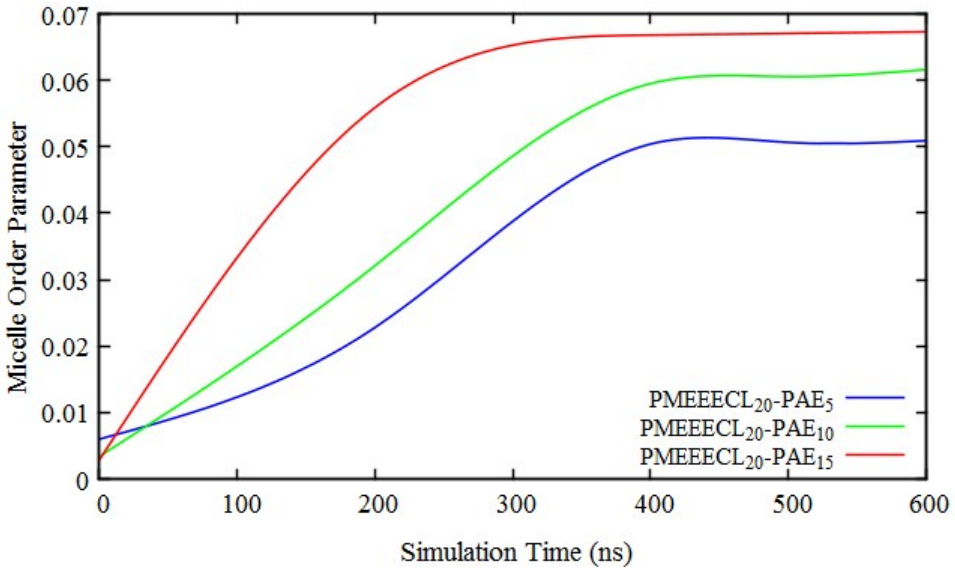

FIG. S3: Micelle order parameter as a function of simulation time.

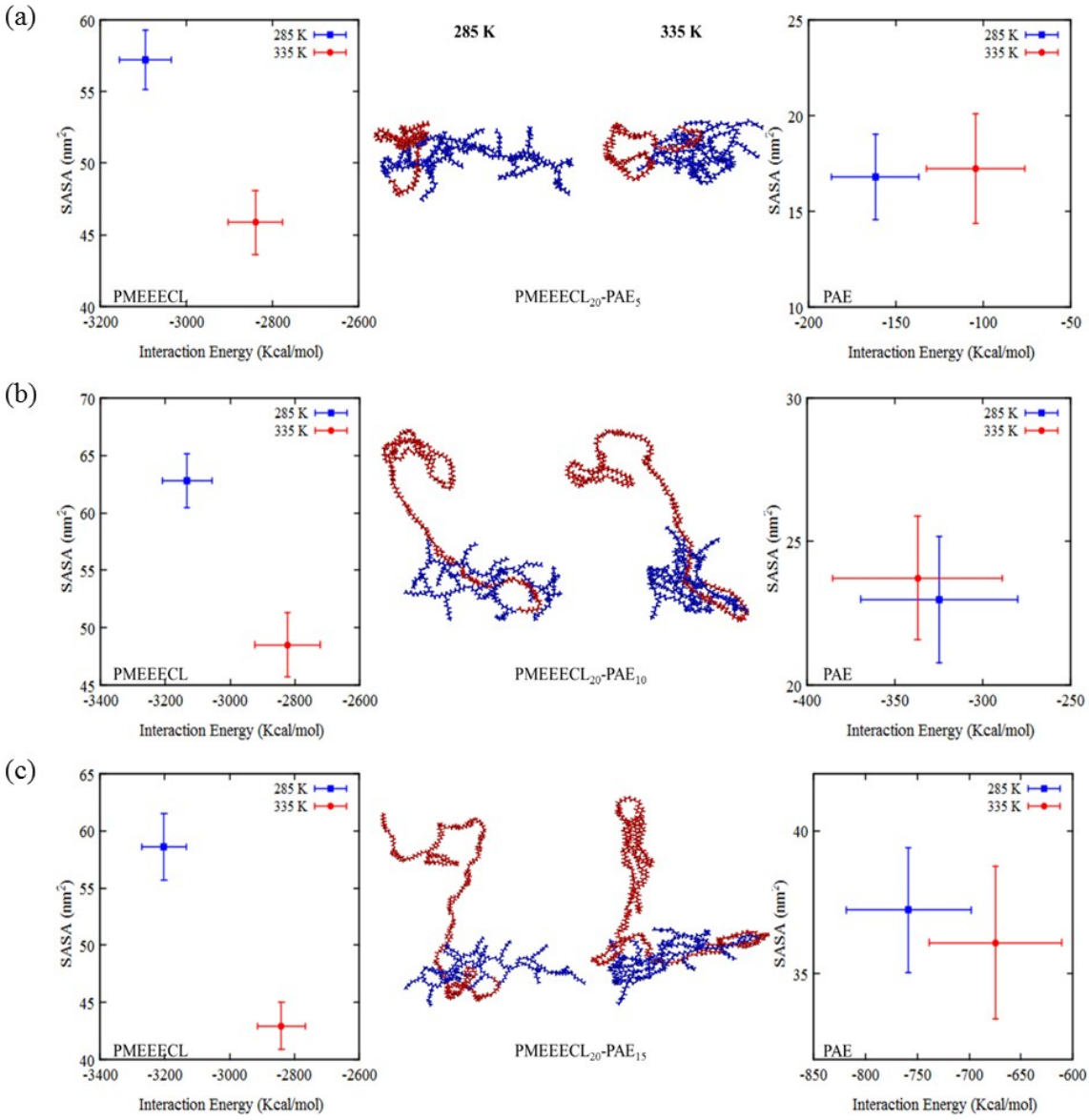

Figure S4: Solvent accessible surface area (SASA) as a function of non-bonded interaction energy of PMEEECL and PAE in addition to PMEEECL-PAE snapshot at 285 K and 335 K for a) $PMEEECL_{20}$-PAE_5, b) $PMEEECL_{20}$-PAE_{10}, and c) $PMEEECL_{20}$-PAE_{15}. Blue and red chains in snapshots are the PMEEECL and PAE blocks, respectively.

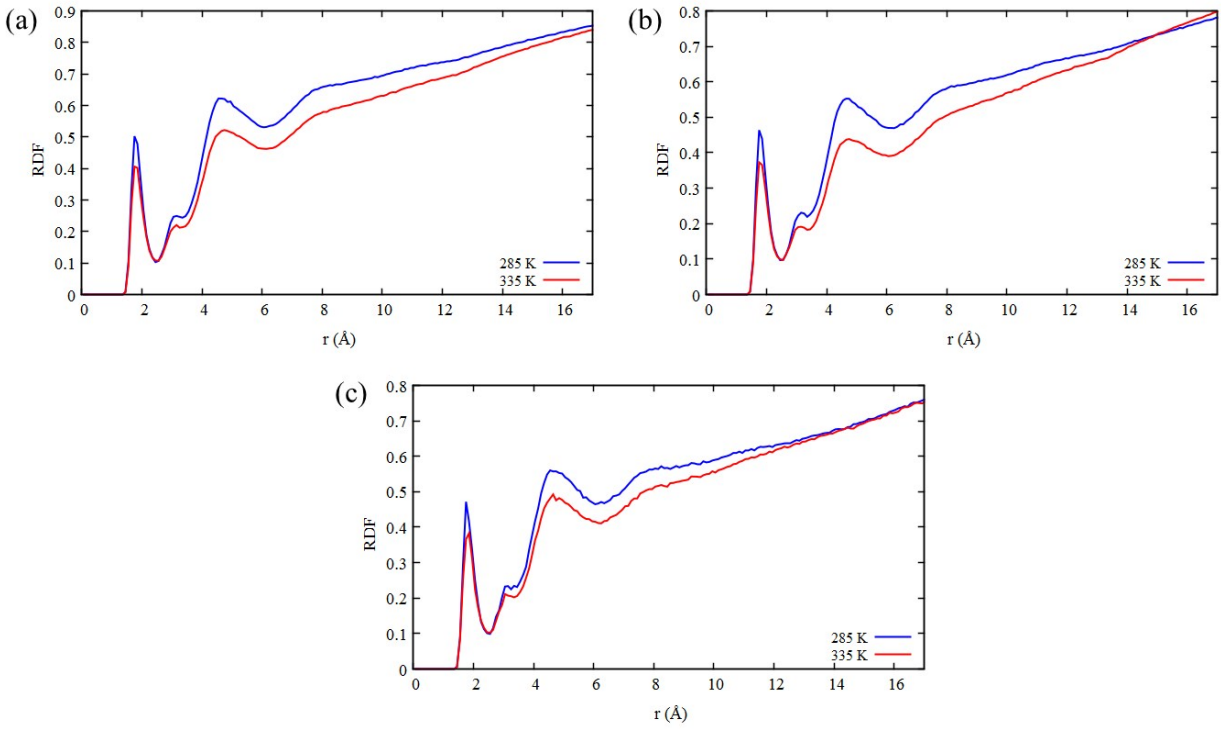

Figure S5: Radial distribution function (RDF) between hydrogen of water molecules and oxygen of PMEEECL at 285 K and 335 K for a) $PMEEECL_{20}$-PAE_5, b) $PMEEECL_{20}$-PAE_{10}, and c) $PMEEECL_{20}$-PAE_{15}.

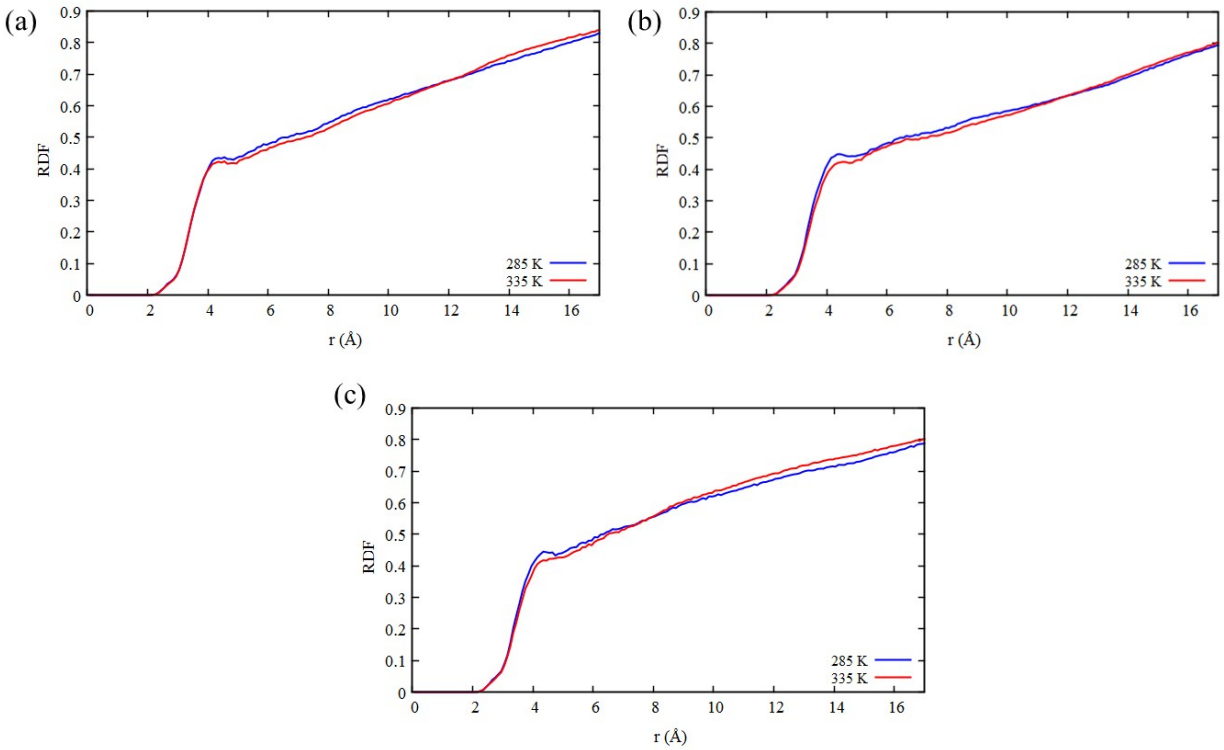

FIG. S6: Radial distribution function (RDF) between PAE monomer and water molecules at 285 K and 335 K.

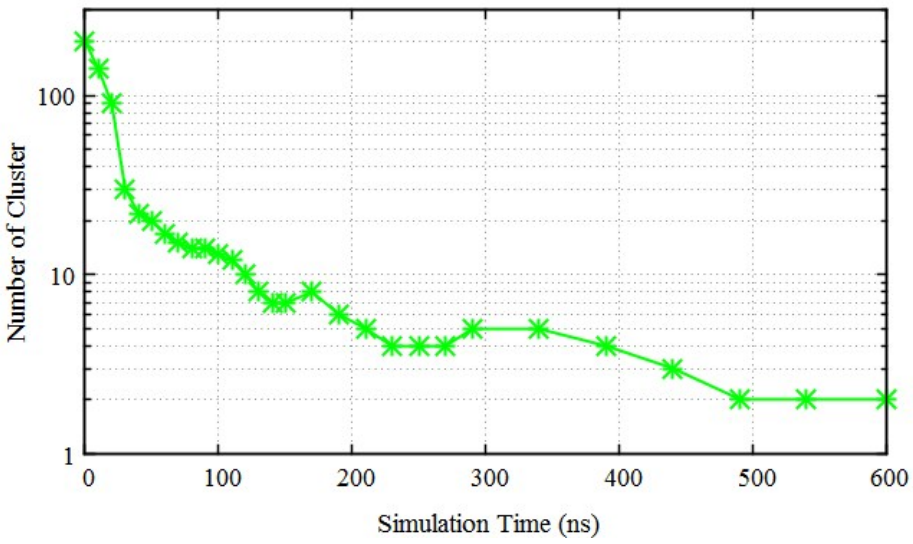

FIG. S7: Number of clusters as a function of simulation time for spherical micelles composed of $PMEEECL_{20}$-PAE_5.

Response to temperature by CG simulations

As the PMEEECL beads are the thermoresponsive part of $PMEEECL_{20}$-PAE_5 amphiphilic block copolymer and based on the Fig. 1a there are 4 different types of beads needed to mimic the PMEEECL block and consequently the RDF of these beads and water ones are calculated and plotted in Fig. S8. For all beads of PMEEECL there is an observable reduction for the affinity of them and water beads by increasing temperature and the transition temperature could be observable around 315 K, which is in consistent with all-atom MD simulations for $PMEEECL_{20}$-PAE_5 amphiphilic block copolymer.

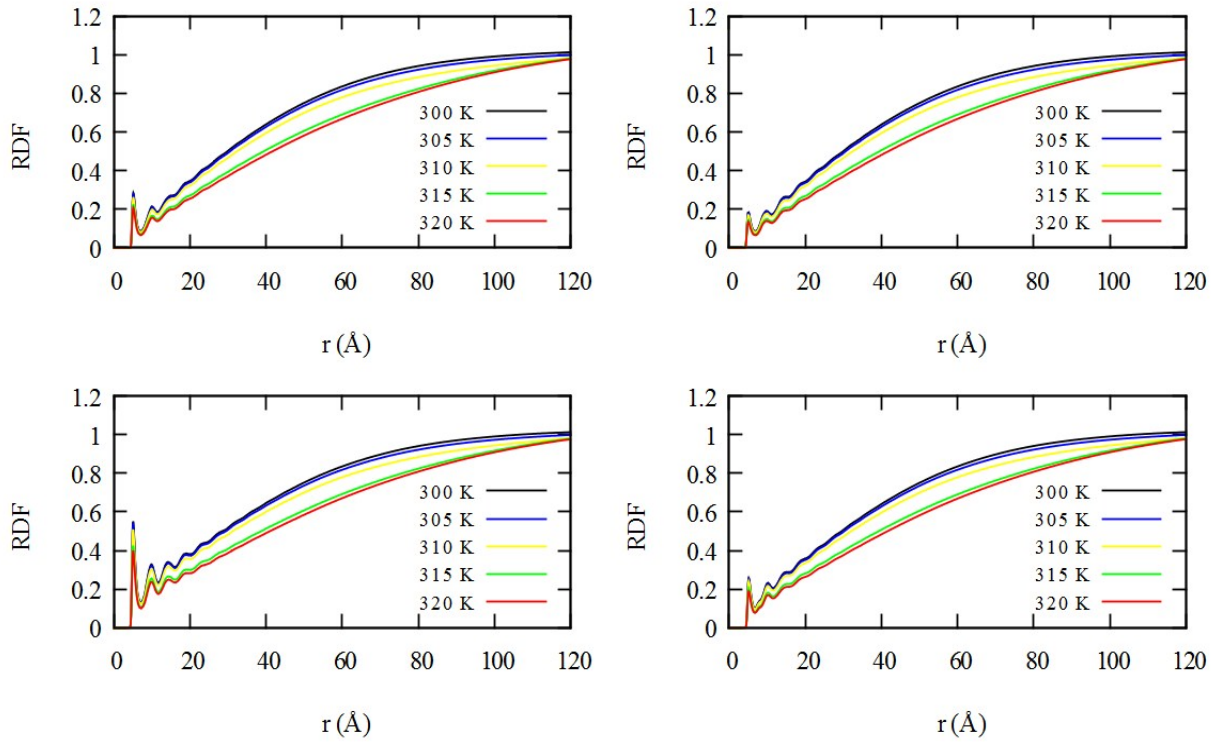

Figure S8: The RDF between the centers of mass of four different beads of PMEEECL block and water beads as a function of temperature.