Figures

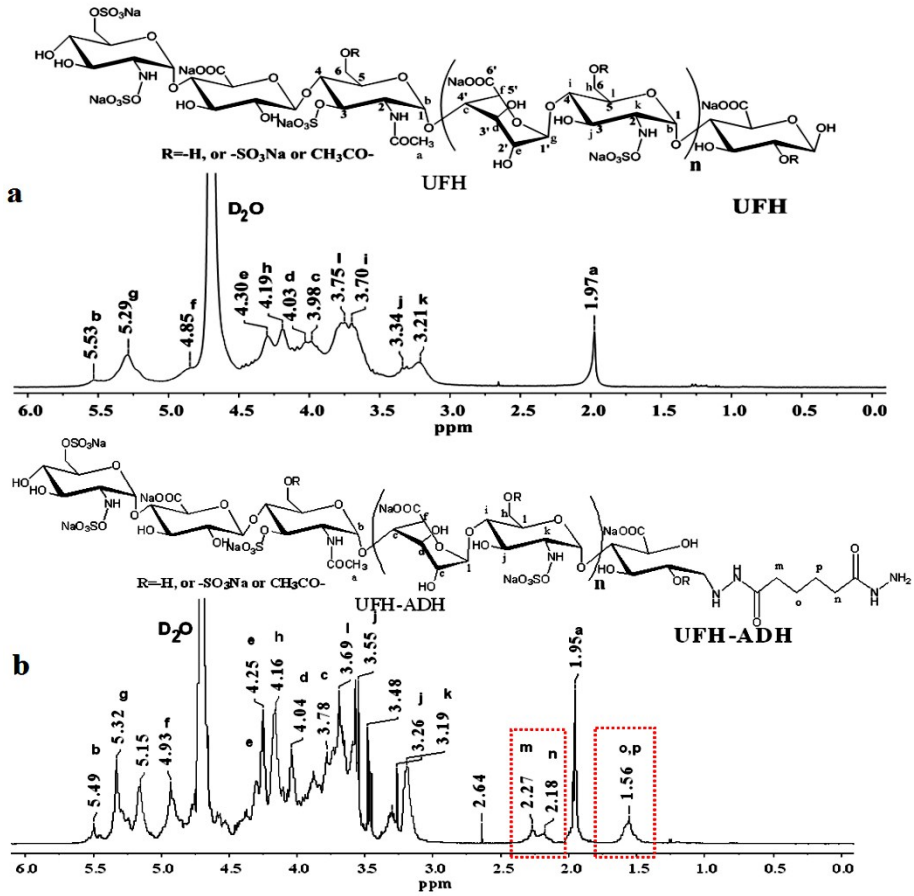

Fig. S1 ^{1}HNMR spectra of (a) UFH and (b) UFH-ADH.

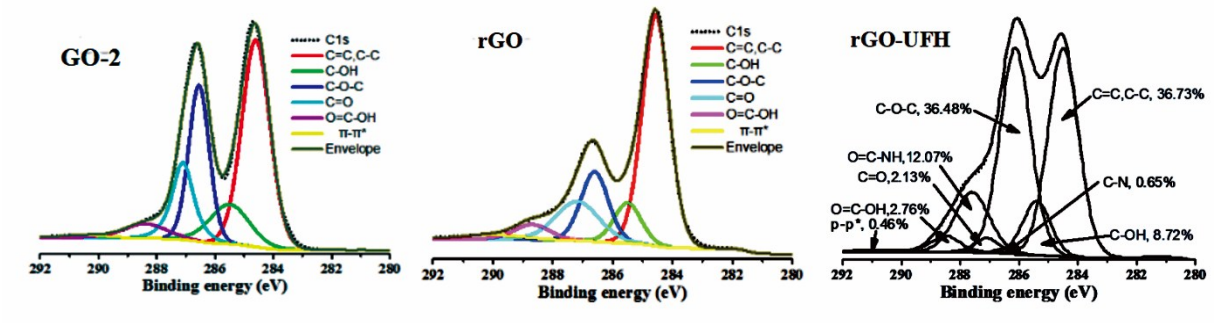

Fig. S2 High-resolution core-level C 1s XPS spectra for GO-2, rGO and rGO-UFH.

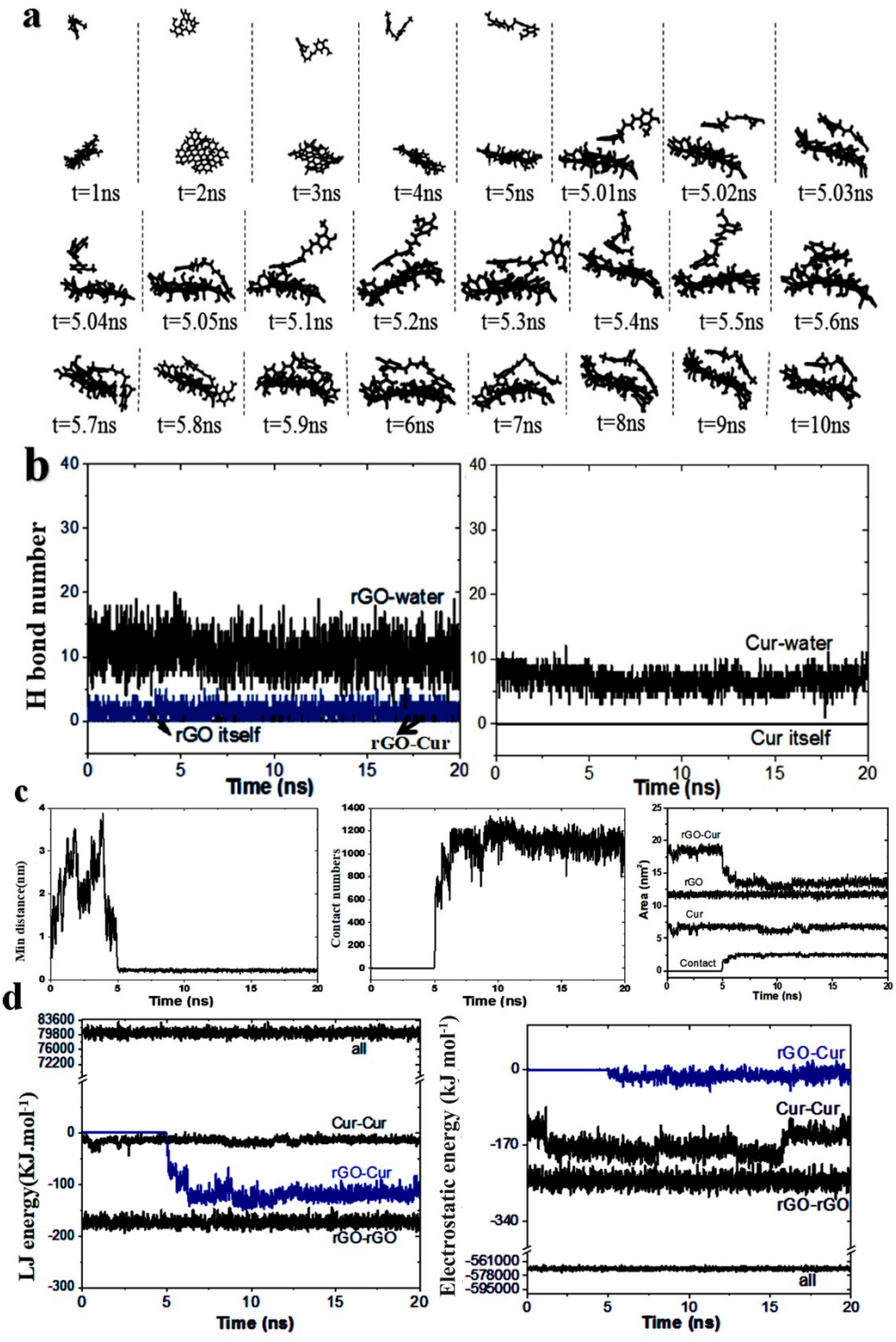

Fig. S3 MD simulation for interaction analysis of rGO-Cur complexes. (a) Trajectory analysis showing the adsorption process of Cur onto rGO surface. (b) Hydrogen numbers between rGO-water, rGO-rGO, rGO-Cur (left); Cur-water and Cur-Cur (right). (c) The minimum distance between Cur and rGO (left); the contact number when atomic distance between rGO and Cur was less than 0.6nm (middle); the SASA and contact area change between Cur and rGO (right). (d)The energy contribution during adsorption of Cur onto rGO: LJ energy (left) and electrostatic energy (right).

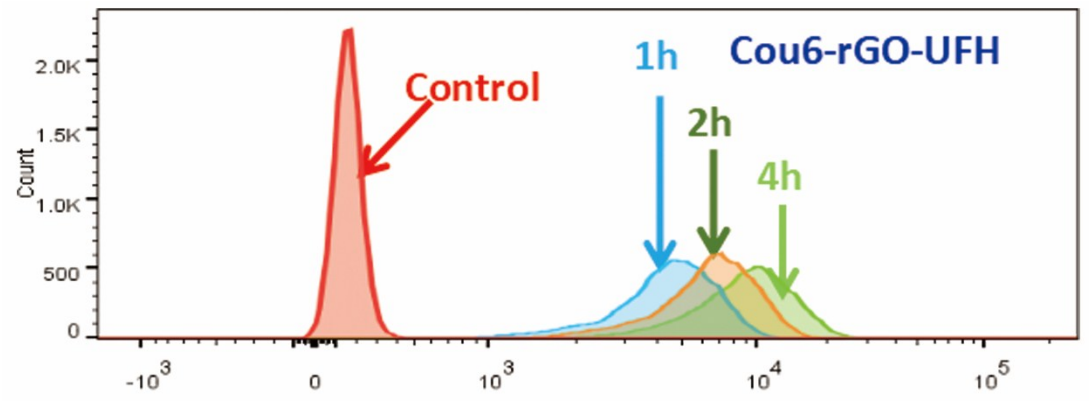

Fig. S4 Flow cytometry analysis for Cou6 loaded rGO-UFH nanocomposites on MCF-7 cells after incubation for 1, 2 and 4h.

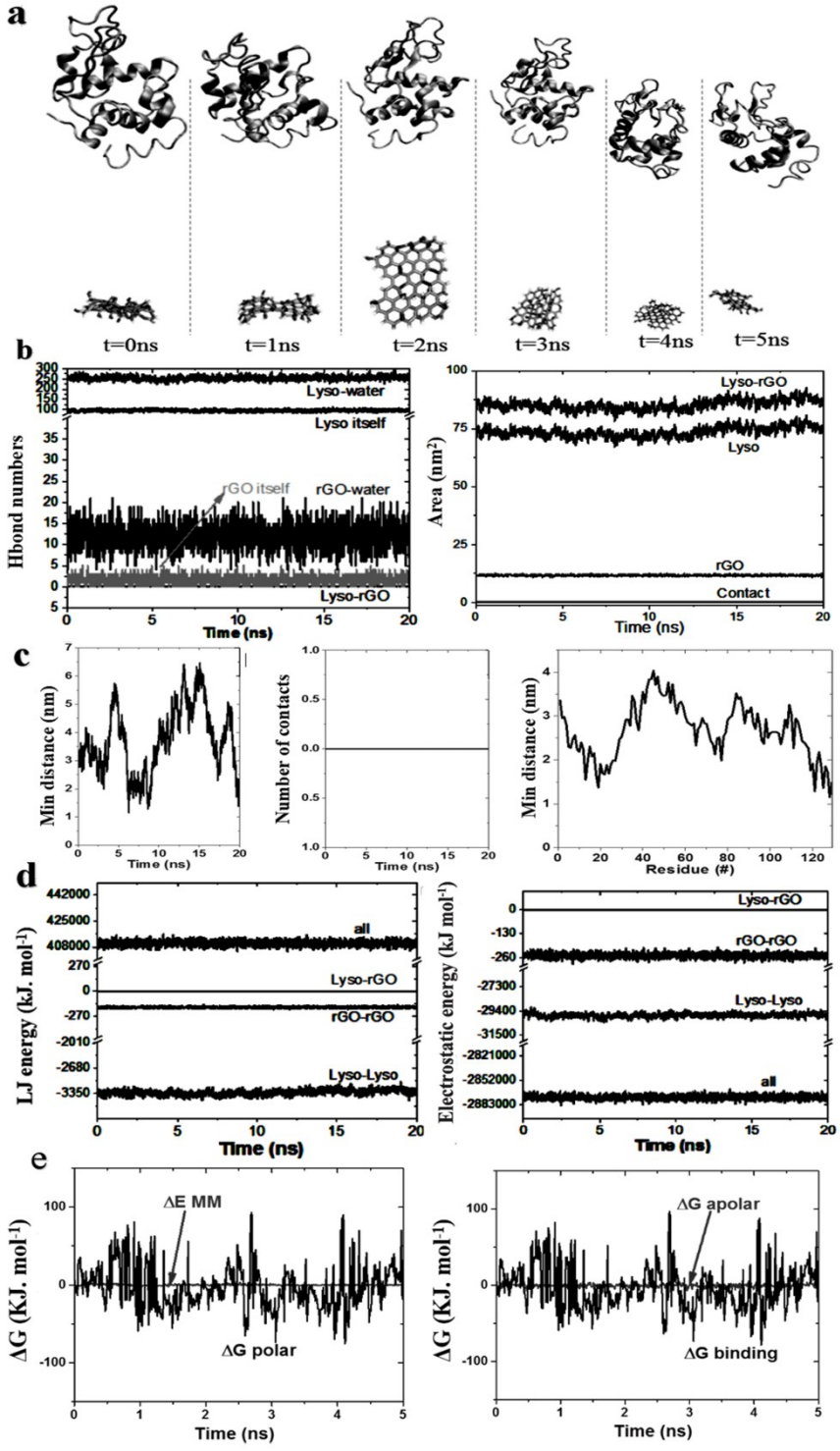

Fig. S5 MD simulation for interaction analysis of rGO-Lyso complexes. (a) Trajectory analysis of rGO-Lyso complex in the first 5ns. (b) The hydrogen numbers between rGO-water, rGO-rGO, rGO-Lyso, Lyso-water and Lyso-Lyso (left); the SASA and contact area change between Lyso and rGO (right). (c) The minimum distance between Lyso and rGO (left); the contact number when atomic distance between rGO and Lyso was less than 0.6nm (middle); the minimum distance between amino acid residues of Lyso and rGO. (d) The energy contribution during adsorption of Lyso on rGO: LJ energy (left) and electrostatic energy (right). (e) Interaction energy decomposition of ΔE_{MM} and ΔG_{polar} (left); ΔG_{apolar} and $\Delta G_{binding}$ (right).

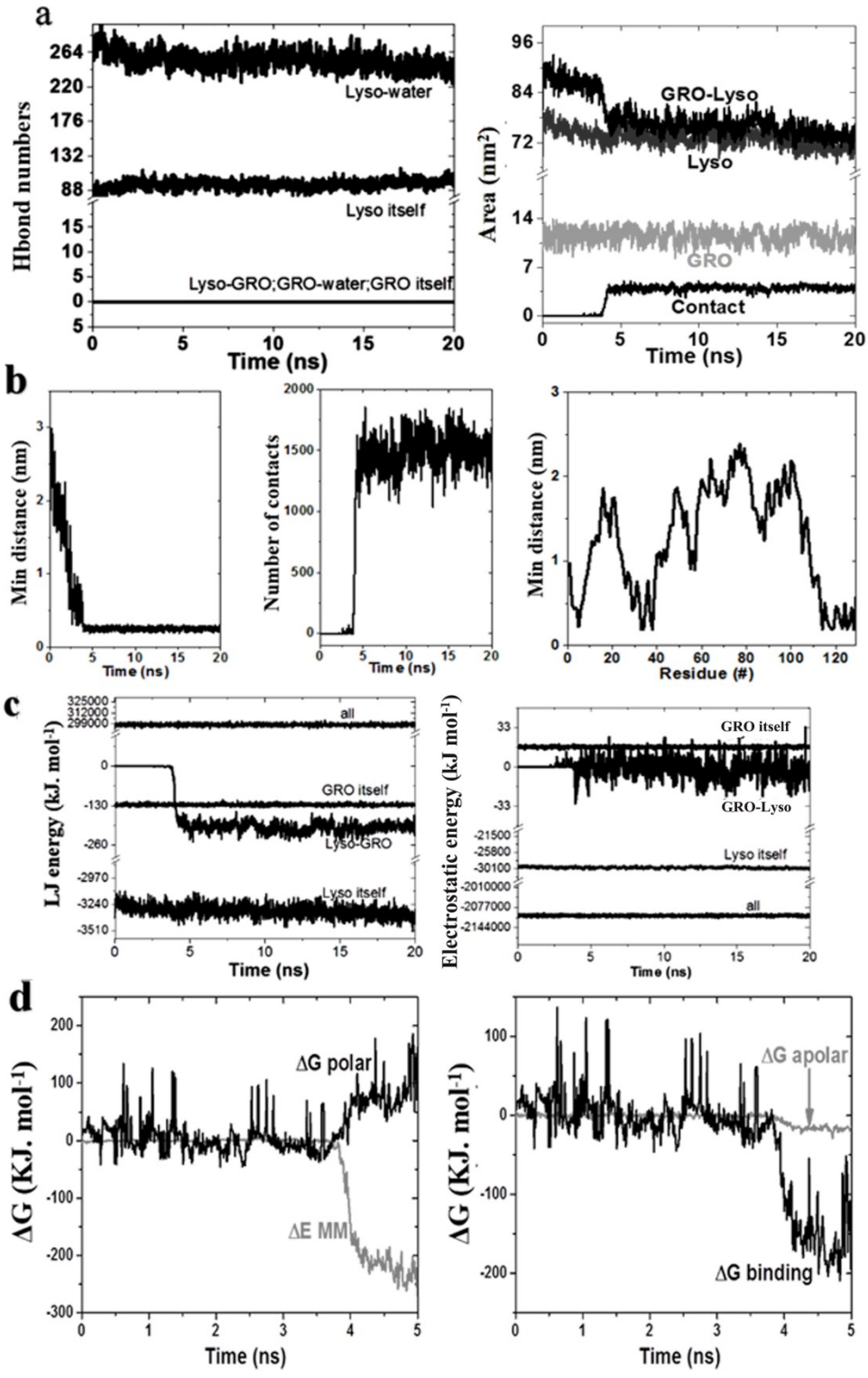

Fig. S6 MD simulation for interaction analysis of GRO-Lyso complexes. (a) The hydrogen numbers between GRO-water, GRO-GRO, GRO-Lyso, Lyso-water and Lyso-Lyso (left); the SASA and contact area change between Lyso and GRO (right). (b) The minimum distance between Lyso and GRO (left); the contact number when atomic distance between GRO and Lyso was less than 0.6 nm (middle); the minimum distance between amino acid residues of Lyso and GRO (right). (c) The energy contribution during adsorption of Lyso on GRO: LJ energy (left) and electrostatic energy (right). (d) Interaction energy decomposition of ΔE_{MM} and ΔG_{polar} (left); ΔG_{apolar} and $\Delta G_{binding}$ (right).

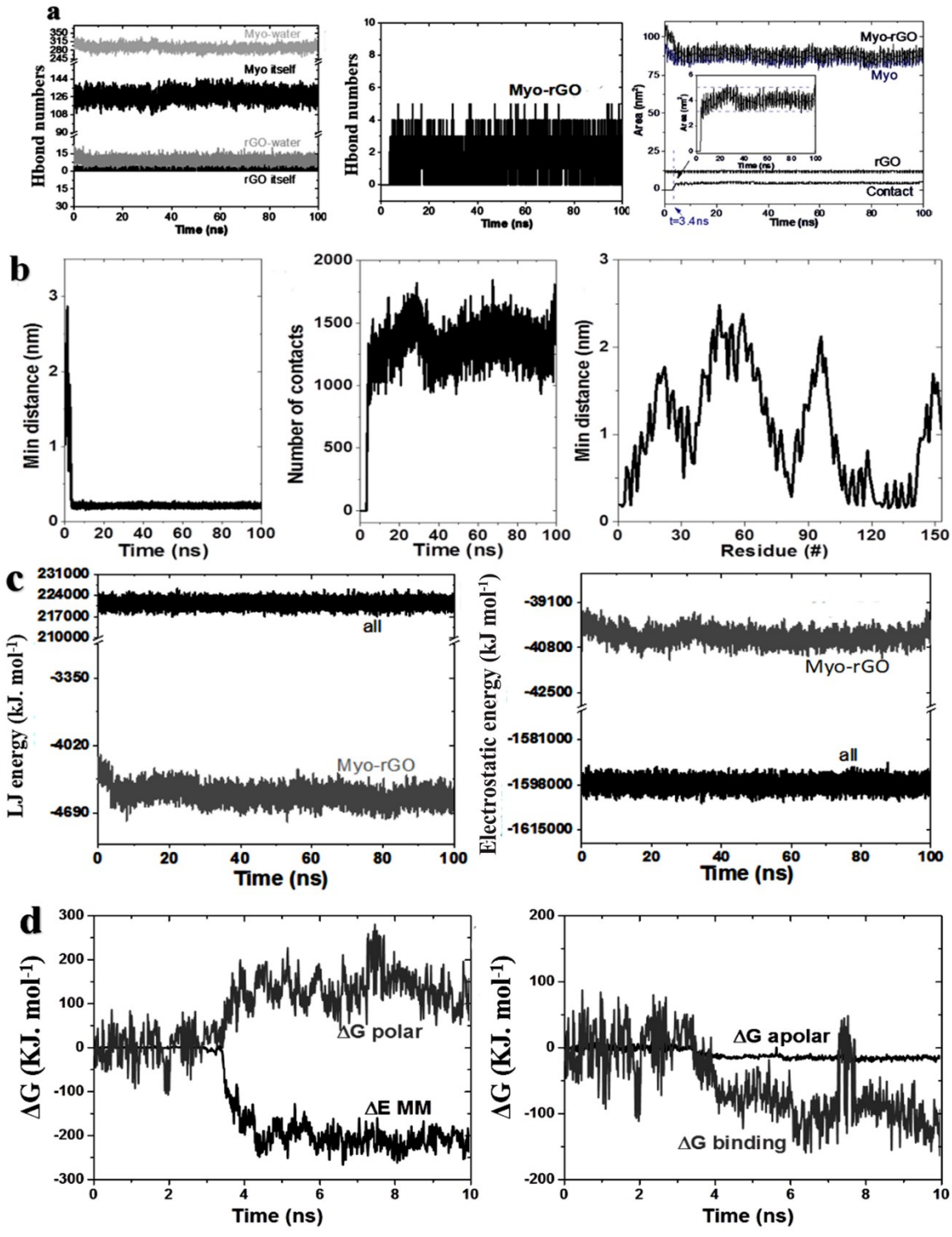

Fig. S7 MD simulation for interaction analysis of rGO-Myo (without heme) complexes. (a) The hydrogen numbers between rGO-water, rGO-rGO, Myo-water, Myo-Myo (left) and rGO-Myo (middle); the SASA and contact area change between Myo and rGO (right). (b) The minimum distance between Myo and rGO (left); the contact number when atomic distance between rGO and Myo was less than 0.6nm (middle); the minimum distance between amino acid residues of Myo and rGO. (c)The energy contribution during adsorption of Myo on rGO: LJ energy (left) and electrostatic energy (right). (d) Interaction energy decomposition of ΔE_{MM} and ΔG_{polar} (left); ΔG_{apolar} and $\Delta G_{binding}$ (right).

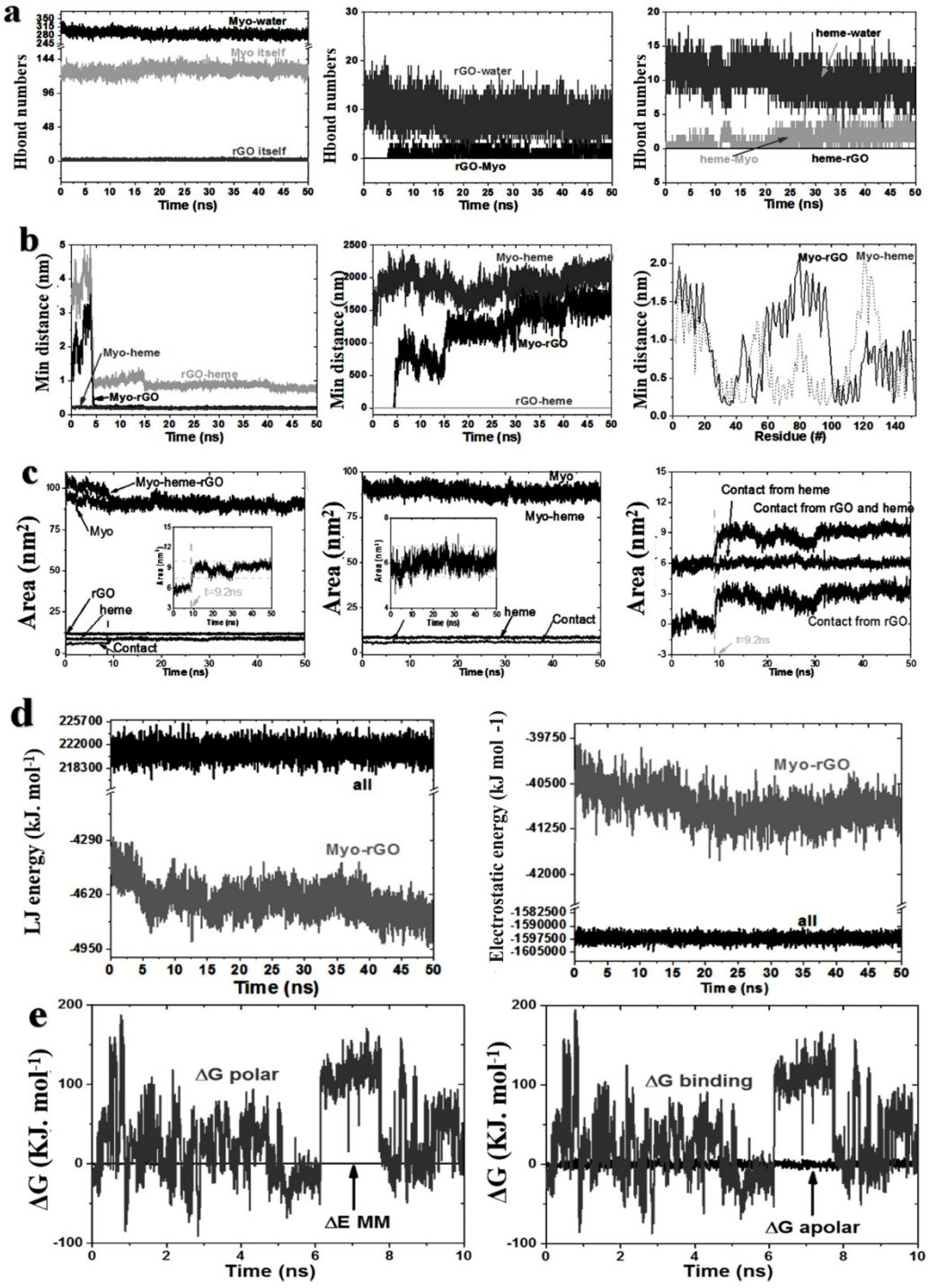

Fig. S8 MD simulation for interaction analysis of rGO-Myo-heme complexes. (a) The hydrogen numbers between rGO-water, rGO-rGO, Myo-water (left); rGO-water and rGO-Myo (middle); heme-water, rGO-heme and Myo-heme (right). (b) The minimum distance of Myo-rGO, Myo-heme and rGO-heme (left); the contact number when atomic distance of complexs (Myo-rGO, Myo-heme and rGO-heme) was less than 0.6nm (middle); the minimum distance between amino acid residues of Myo and rGO/heme (right). (c) The SASA among Myo, heme and rGO, and the total contact area (left); the SASA and contact area between Myo and heme (middle); the contact area between Myo and rGO (right). (d) The energy contribution during adsorption of Myo on rGO: LJ energy (left) and electrostatic energy (right). (e) Interaction energy decomposition of ΔE_{MM} and ΔG_{polar} (left); ΔG_{apolar} and $\Delta G_{binding}$ (right).

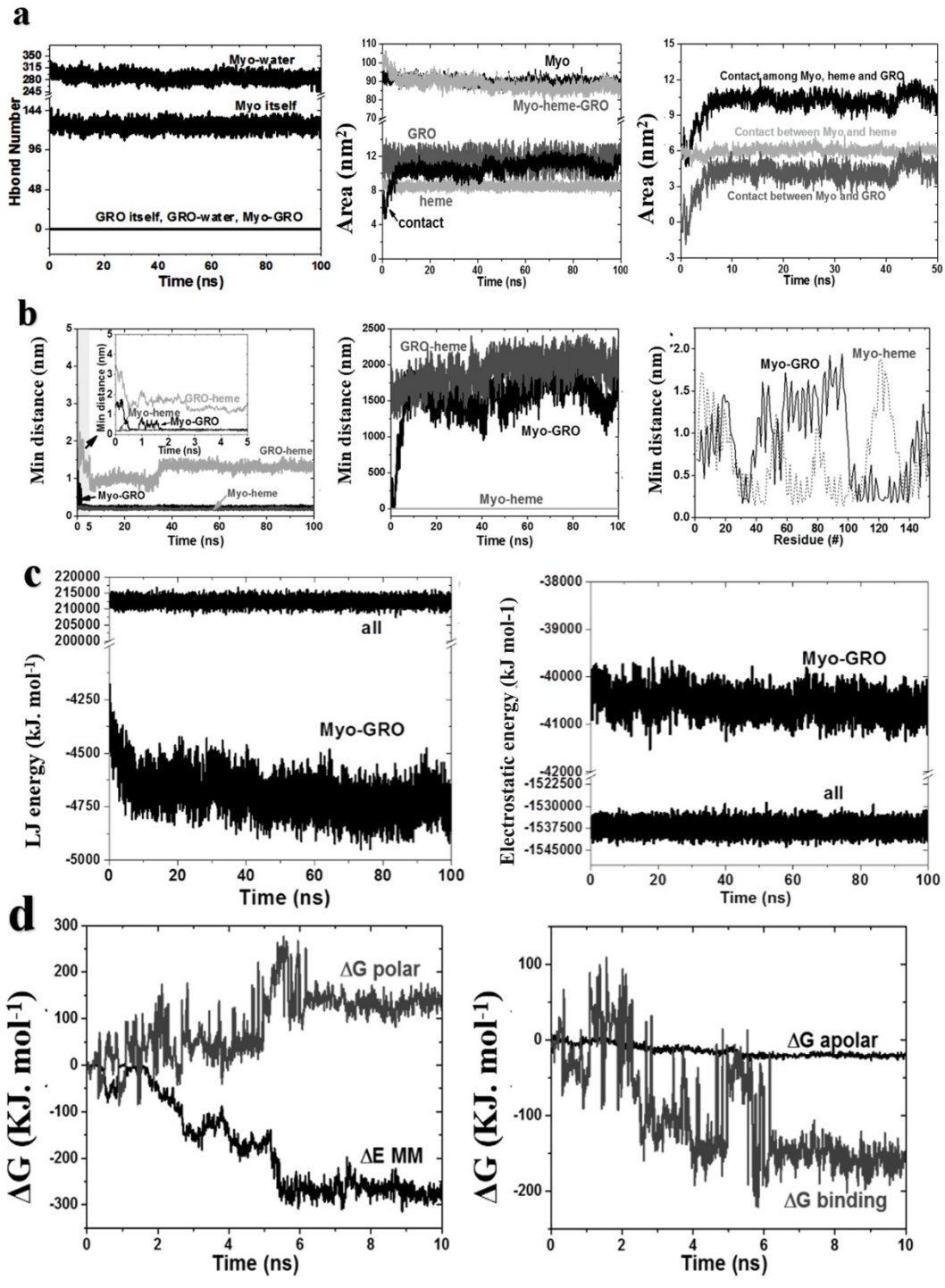

Fig. S9 MD simulation for interaction analysis of GRO-Myo-heme complexes. (a) The hydrogen numbers between GRO-water, GRO-GRO, Myo-water, GRO-water and GRO-Myo (left); The SASA among Myo, heme and GRO (middle); the contact area between Myo and GRO, Myo and heme, the total contact area (right). (b) The minimum distance of Myo-GRO, Myo-heme and GRO-heme (left); the contact number when atomic distance of complexs (Myo-GRO, Myo-heme and GRO-heme) was less than 0.6nm (middle); the minimum distance between amino acid residues of Myo and GRO/heme (right). (c)The energy contribution during adsorption of Myo on GRO: LJ energy (left) and electrostatic energy (right). (d) Interaction energy decomposition of ΔE_{MM} and ΔG_{polar} (left); ΔG_{apolar} and $\Delta G_{binding}$ (right).

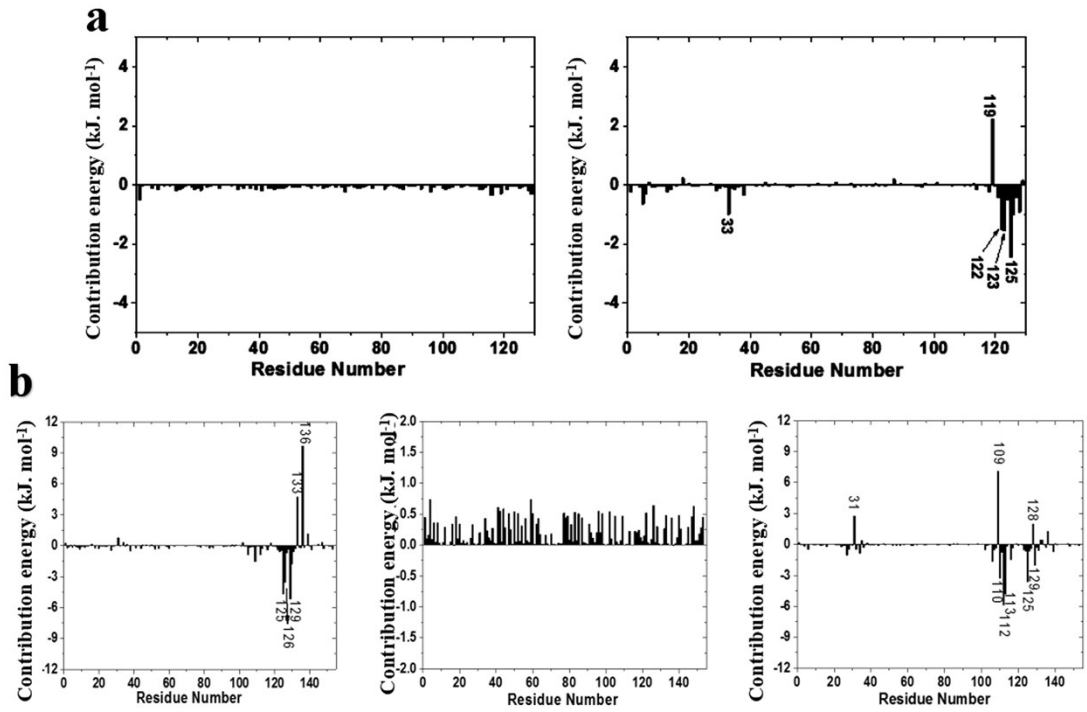

Fig. S10 Energy contribution of residues for binding between: (a) Lyso and rGO (left); Lyso and GRO (right) and (b) rGO and Myo without heme (left); rGO and Myo with heme (middle); GRO and Myo with heme (right).

Tables

Table 1 Factors and levels of central composite design-response surface methods

Factors	Levels				
	-1.414	-1	0	1	1.414
X_1 (mg·mL^{-1})	0.500	1.01	2.25	3.49	4.00
X_2 (mL)	0.200	0.259	0.400	0.541	0.600

Table 2 The results of central composite design-response surface methods

No	X_1	X_2	DL(%)	EE(%)
1	1.01	0.259	21.95	86.02
2	3.48	0.259	40.71	60.93
3	1.01	0.541	11.33	18.70
4	3.48	0.541	37.84	25.87
5	0.5	0.2	10.77	96.59
6	4	0.4	53.70	57.98
7	2.25	0.2	34.81	94.91
8	2.25	0.6	14.30	9.89
9	2.25	0.4	31.33	40.55
10	2.25	0.4	30.98	39.89
11	2.25	0.4	30.63	39.24
12	2.25	0.4	31.33	40.55
13	2.25	0.4	31.75	41.36

Table 3 MD simulation parameters of interaction between rGO/GRO and Myo / Lyso.

Parameters	rGO-Myo (no heme)	rGO-Myo (with heme)	GRO-Myo (with heme)	rGO-Lyo	GRO-Lyo
Total simulation time / adsortion time (ns / ns)	100 / 3.4	50 / 10	100 / 1	No adsorption in 20 ns	20 / 3.9
Hydrogen bond numbers	1 ~ 5 (3.4 ~ 100 ns)	1 ~ 5 (rGO-Myo, 5 ~ 50 ns); 1 ~ 6 (Myo-heme, 0 ~ 50 ns); 0 (rGO-heme).	0	0	0
Minimum distance between two molecules (nm)	~ 0.25 (3.4 ns)	<0.3 (rGO-Myo, 5 ~ 50 ns); <0.3 (Myo-heme, 0 ~ 50 ns); 0.8 ~ 1.1 (rGO-heme, 5 ~ 50 ns).	<0.3 (GRO-Myo, < 1 ns); <0.3 (Myo-heme, 0 ~ 50 ns); 0.8nm ~ 1.4 (GRO-heme, 1 ~ 50 ns)	~ 1.1 nm (6 ns)	~ 0.25 (3.9 ns)
Contact numbers (atomic distances of two molecules <0.6 nm)	1000 ~ 1750 (3.4 ~ 100 ns)	500 ~ 1100 (rGO-Myo, 5 ~ 14 ns), 1000 ~ 1500 (rGO-Myo, 15 ~ 30 ns), 1300 ~ 2000 (rGO-Myo, 30 ~ 50 ns); 1500 ~ 2300 (Myo-heme); 0 (rGO-heme).	1000 ~ 2000 (GRO-Myo, 3 ~ 50 ns); 0 (GRO-heme).	0	1200 ~ 1500 (3.9 ~ 20 ns)
Reduced solvable area (nm^2)	6.4 ~ 10 (3.4 ~ 100 ns)	4.6 ~ 6.8 (9.2 ns ~ 50 ns)	7 ~ 12 (5.5 ~ 100 ns)	0	7 ~ 8.4 (3.9 ~ 20 ns)
Proportion of contact area in rGO area	55.17% ~ 86.21% (3.4 ~ 100 ns)	40% ~ 59.2% (rGO-Myo, 9.2ns ~ 50 ns)	56% ~ 100% (GRO-Myo, 5.5 ~ 100 ns)	0	56% ~ 67.2% (3.9 ~ 20 ns)
LJ energy change ($KJ.mol^{-1}$)	~ −410 (0 ~ 3.4 ns)	~ −450 (0 ~ 50 ns)	~ −450 (0 ~ 100 ns)	−0.0004 (0 ~ 6 ns)	~ −200 (3.9 ~ 20 ns)
Electrostatic energy change ($KJ.mol^{-1}$)	~ −800 (0 ~ 3.4 ns)	~ −800 (0 ~ 50 ns)	0	0.0015 (0 ~ 6 ns)	~ ± 20 (3.9 ~ 20 ns)
ΔE_{MM} ($KJ.mol^{-1}$)	~ −200 (3.4 ~ 10 ns)	0	~ −280 (0 ~ 10 ns)	0	~ −260 (3.9 ~ 5 ns)
ΔG_{polar}($KJ.mol^{-1}$)	~ −110 (3.4 ~ 10 ns)	−20 (5 ns); −125 (6 ns); 0 (7.5 ns); +50 (9.2 ns)	~ +150 (0 ~ 10 ns)	±100 (0 ~ 5 ns)	~ +75 (3.9 ~ 5 ns)
ΔG_{apolar} ($KJ.mol^{-1}$)	~ −17 (3.4 ~ 10 ns)	0	~ −20 (0 ~ 10 ns)	0	~ −15 (3.9 ~ 5 ns)
$\Delta G_{binding}$ ($KJ.mol^{-1}$)	~ −100 (3.4 ~ 10 ns)	Similar with ΔG_{polar}	~ −150 (0 ~ 10 ns)	~ ±100 (0 ~ 5 ns)	−100 ~ −200 (3.9 ~ 5 ns)
Contributed amino acid residues to adsorption	Positive: Ala-125, Asp-126 and glycine (Gly)-129; Negative: lysine (Lys)-133 and glutamic acid (Glu)-136.	weak	Positive: Ala-110, Ile-112, histidine (His)-113, Ala-125 and Gly-129. Negative: Arg-31, Glu-109 and glutamine (Gln)-128.	weak	Positive: Tyr-33, Ala-122, Trp-123 and Arg-125 Negative: Asp-119