# Coarse-Grained Molecular Dynamics Simulations of Photoswitchable Assembly and Disassembly

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# **Supplementary Information**

Supplementary information for this article include the simulation details with both AA and CG models, four figures, and the GROMACS topology files for host and guest molecules in the CG model.

AA Molecular Dynamics Simulations. The all-atom molecular dynamics simulations were based on our previously built force field for AzoC10 and  $\alpha$ -CD.<sup>1</sup> A pre-assembled spherical micellar structure was generated with the PACKMOL program.<sup>2</sup> For *cis*-AzoC10, the micellar structure was built from 70 *cis*-AzoC10 surfactant monomers by constraining the N<sup>+</sup> atom of the pyridinium head group outside a sphere of 2.4 nm and one of N atoms, the one closer to the head group, of the azobenzene moiety inside a concentric sphere of radius 0.5 nm. The spherical micelle structure built from 50 *trans*-AzoC10 surfactants was generated by constraining N<sup>+</sup> inside a sphere of radius 0.4 nm, and one of N atoms, the one closer to the head group, of the azobenzene moiety algorithm were performed for *cis*- and *trans*-AzoC10 systems to minimize the distances between the surfactants and to ensure that no water molecules existing inside the micelle structure in the starting configuration. After minimization, the micellar structures were solvated by roughly 108000 pre-equilibrated SPC<sup>3</sup> water molecules to render the box length twice the diameter of the micelle (~ 15.0 nm) and to avoid interactions of the periodic images of the micelle with itself. To neutralize the system, one bromide ion per AzoC10 molecule was added. The classical Newton's equations of motion were integrated at a time step of 1 fs using the leapfrog Verlet algorithm.<sup>4</sup> The reciprocal space sum of electrostatic interactions was calculated by the particle mesh Ewald (PME) method,<sup>5.6</sup> and the direct space sum was evaluated with a cutoff distance of 1.0 nm. Each system was simulated for 10 ns to relax the micelle structures and to reach an equilibrium, with configurations stored every 1 ps for analysis. No constraints were applied in the simulations, and the pre-assembled micelles were found stable in water.

**CG Molecular Dynamics Simulations.** The coarse-grained molecular dynamics simulations were performed with the modified MARTINI force field.<sup>7</sup> To better validate the CG model, the number of surfactants, ions and the cubic box size in the CG simulations are the same as in the AA simulations. The pre-assembled spherical micelle structures of *cis*-AzoC10 and *trans*-AzoC10 were generated with the PACKMOL program.<sup>2</sup> The 70 *cis*-AzoC10 spherical micelle was generated by constraining the N0 bead of the azobenzene moiety to an inner sphere of radius 0.5 nm, and the SQ0 bead in the head group to a concentric outer sphere of radius 2.4 nm. For the pre-assembled 50 *trans*-AzoC10 micelle, the N0 beads of the azobenzene moiety were constrained inside an inner sphere of radius 0.4 nm, and the SQ0 beads of the head group were constrained outside a concentric sphere of 2.3 nm. The micellar structures were solvated in a pre-equilibrated cubic box of 26945 CG water particles with roughly 15 nm on each side. The counterions were also added to neutralize

the system. All the simulations with the CG model were performed in the *NPT* ensemble (T = 300 K and P = 1 bar) by Berendsen coupling<sup>8</sup> with the relaxation times of 0.3 and 1.3 ps respectively. The cutoff for nonbonded interactions was set to be 1.2 nm with the standard shift functions of the GROMACS packacge,<sup>9</sup> where the Lennard-Jones potential was shifted from 0.9 to 1.2 nm and the electrostatic potential was shifted from 0 to 1.2 nm mimicing the effects of a distance-dependent screening.<sup>7</sup>

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#### Comparison for *a*-CD between AA and CG Models

 $\alpha$ -CD has a hydrophobic cavity and a hydrophilic exterior. In order to validate the CG model and reveal the behavior of  $\alpha$ -CDs in aqueous solution, we performed MD simulations with both AA and CG models. The starting configurations were generated by randomly solvating 40  $\alpha$ -CDs in a cubic box with the side length of 15 nm. The total amount of water molecules was close to 10800. The simulation time was 10 ns for the AA model and 200 ns for the CG model, and the final configurations of  $\alpha$ -CDs were shown in Figure S1. It is clear that the isolated and clusterized  $\alpha$ -CDs co-exist in either case, but the driving forces for the clusterization are different. In the AA model, the intermolecular H-bonds formed between the hydroxyl groups of  $\alpha$ -CDs and the water molecules are the major diving force for the clusterization. Besides, orientations of the primary and secondary rims of the clusterized  $\alpha$ -CDs and the number of H-bonds formed are not fixed. As for the isolated  $\alpha$ -CD, nearly every hydroxyl group forms H-bonds with water molecules. During the 10 ns AA MD simulations, we found that once  $\alpha$ -CDs clusterize, they will not separate from each other again in the reachable simulation time. In the CG model, since the hydrogen atoms are neglected for their small size and light weight, the information of H-bonds is lost. But small clusters of  $\alpha$ -CDs also showed up as in the AA model. Due to different polarities of the beads representing the primary and secondary rims and the middle part of  $\alpha$ -CDs, the hydrophilic and hydrophobic beads arrange alternatively in the CG model. Thus, the hydrophobic interactions exist for CG  $\alpha$ -CDs in aqueous solution. The main driving force for the clusterization in CG simulations is the reduction of the hydrophobic area exposed to water.  $\alpha$ -CDs in most clusters arrange shoulder by shoulder, but the orientation of the primary and secondary rims of  $\alpha$ -CDs is not fixed. In a word, although the CG model of  $\alpha$ -CD does not contain all the information of the atomistic  $\alpha$ -CD, their aggregation behaviors in aqueous solution are similar. Therefore, it is feasible to use the CG model to study the assembly and disassembly between  $\alpha$ -CD and AzoC10 in aqueous solution.



**Fig. S1** Comparison of the final configuration of  $\alpha$ -CDs in aqueous solution between the AA (left) and CG (right) models. The hydrogen atoms in the AA model and the water molecules in both

models were not shown for clarity.



Fig. S2 Time evolution of the number of monomers, the number of clusters, and the average size of clusters in the aggregation of *trans*-AzoC10 with N = 500, 1000, 1500 and 2000, respectively.



**Fig. S3** The largest micelles formed by (a) *cis*-AzoC10 which is disk-like and (b) *trans*-AzoC10 which is worm-like. The left panel is the side view of micelles, and the right panel is the cross-sectional view of micelles.



**Fig. S4** A worm-like micelle formed with *cis*-AzoC10/ $\alpha$ -CD.

**Topology Files.** The itp files contain important force field information with respect to *cis*-AzoC10, *trans*-AzoC10 and  $\alpha$ -CD molecules. Precisely, itp files provide intramolecular bond, angle, dihedral parameters, and partial charges on each CG site. In addition, the type of each bead is specified so that the non-bonded Lennard-Jones parameters can be read directly from the MARTINI force field library.

- cis-AzoC10\_CG.itp Gromacs topology file with the modified force field parameters for cis-AzoC10.
- (2) *trans*-AzoC10\_CG.itp Gromacs topology file with the modified force field parameters for *trans*-AzoC10.
- (3)  $\alpha$ -CD\_CG.itp Gromacs topology file with the modified force field parameters for  $\alpha$ -CD.

(1) cis-AzoC10\_CG.itp

1

[ moleculetype ] ; molname nrexcl cis-AzoC10\_CG

[ atoms ]

;	id	type	resnr	residu	atom	cgnr	charge
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	2	SC4	1	CIS	R2	2	0.0000
	3	SC4	1	CIS	R3	3	0.0000
	4	N0	1	CIS	DN	4	0.0000
	5	SC4	1	CIS	R4	5	0.0000
	6	SC4	1	CIS	R5	6	0.0000
	7	SC4	1	CIS	RO	7	0.0000
	8	C1	1	CIS	C1A	8	0.0000
	9	C2	1	CIS	C2A	9	0.0000
	10	C1	1	CIS	C3A	10	0.0000
	11	SQ0	1	CIS	RN	11	1.0000
	12	SC3	1	CIS	R6	12	0.0000
	13	SC3	1	CIS	R7	13	0.0000
	14	Qa	1	CIS	Br	14	-1.000

[bonds]

;	i	j	funct	length	force.c.
	1	2	1	0.270	30000
	1	3	1	0.270	30000
	2	3	1	0.270	30000
	3	4	1	0.200	1250
	4	6	1	0.250	1250
	6	5	1	0.270	30000
	6	7	1	0.270	30000
	5	7	1	0.270	30000
	7	8	1	0.360	1250
	8	9	1	0.470	1250
	9	10	1	0.470	1250
	10	11	1	0.300	1250
	11	12	1	0.27	30000
	11	13	1	0.27	30000
	11	14	1	0.34	1250
	12	13	1	0.27	30000

#### [ angles ]

;	i	j	k	funct	angle	force.c.
	1	3	4	2	160.0	25.0
	2	3	4	2	140.0	25.0

3	4	6	1	120.0	10.0
4	6	5	2	100.0	25.0
4	6	7	2	150.0	25.0
5	7	8	2	180.0	25.0
6	7	8	2	180.0	25.0
7	8	9	2	180.0	25.0
8	9	10	2	180.0	25.0
9	10	11	2	180.0	25.0
10	1	1 12	2	180.0	25.0
10	1	1 13	2	180.0	25.0
10	1	1 14	2	180.0	25.0

# (2) trans-AzoC10\_CG.itp

[ moleculetype ]

; molname nrexcl

*trans*-AzoC10\_CG 1

### [ atoms ]

; id	type	resnr	residu	atom	cgnr	charge
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2	SC4	1	TRA	R2	2	0.0000
3	SC4	1	TRA	R3	3	0.0000
4	N0	1	TRA	DN	4	0.0000
5	SC4	1	TRA	R4	5	0.0000
6	SC4	1	TRA	R5	6	0.0000
7	SC4	1	TRA	RO	7	0.0000
8	C1	1	TRA	C1A	8	0.0000
9	C2	1	TRA	C2A	9	0.0000
10	C1	1	TRA	C3A	10	0.0000
11	SQ0	1	TRA	RN	11	1.0000
12	SC3	1	TRA	R6	12	0.0000
13	SC3	1	TRA	R7	13	0.0000
14	Qa	1	TRA	Br	14	-1.000

#### [bonds]

;	i	j	funct	length	force.c.
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	2	3	1	0.270	30000
	3	4	1	0.180	1250
	4	6	1	0.220	1250
	6	5	1	0.270	30000
	6	7	1	0.270	30000
	5	7	1	0.270	30000

7	8	1	0.360	1250
8	9	1	0.470	1250
9	10	1	0.470	1250
10	11	1	0.300	1250
11	12	1	0.27	30000
11	13	1	0.27	30000
11	14	1	0.34	1250
12	13	1	0.27	30000

### [angles]

;	i	j	k	funct	angle	force.c.
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	2	3	4	2	150.0	35.0
	3	4	б	1	180.0	30.0
	4	6	5	2	150.0	35.0
	4	6	7	2	150.0	35.0
	5	7	8	2	180.0	25.0
	6	7	8	2	180.0	25.0
	7	8	9	2	180.0	25.0
	8	9	10	2	180.0	25.0
	9	10	) 11	2	180.0	25.0
	10	1	1 12	2	180.0	25.0
	10	1	1 13	2	180.0	25.0
	10		11 14	2	180.0	25.0

## (3) $\alpha$ -CD\_CG.itp

[ moleculetype ] ; molname nrexcl α-CD\_CG 1

## [ atoms ]

1 4						
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P4	1	4GA	O2	2	0.0000	34.0148
6 P1	1	4GA	C6	2	0.0000	44.0534
N0	1	4GA	C4	3	0.0000	84.0748
P4	1	4GA	O2	3	0.0000	34.0148
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P4	1	4GA	O2	4	0.0000	34.0148
P1	1	4GA	C6	4	0.0000	44.0534
N0	1	4GA	C4	5	0.0000	84.0748
P4	1	4GA	O2	5	0.0000	34.0148
	type       N0       P4       P1       N0       P4	type resnr   N0 1   P4 1   P1 1   P4 1	I   type   reshr   reshdu     N0   1   4GA     P4   1   4GA     P1   1   4GA     P1   1   4GA     P1   1   4GA     P4   1   4GA     P4   1   4GA     P4   1   4GA     P4   1   4GA     P1   1   4GA     P4   1   4GA     P4   1   4GA     P4   1   4GA     P1   1   4GA     P4   1   4GA     P4   1   4GA     P4   1   4GA     P4   1   4GA     P1   1   4GA     P1   1   4GA     P1   1   4GA     P1   1   4GA     P4   1   4GA     P4   1   4GA     P4   1   4GA	I   type   reshr   reshu   atom     N0   1   4GA   C4     P4   1   4GA   O2     P1   1   4GA   C6     N0   1   4GA   C6     N0   1   4GA   C4     P4   1   4GA   C4     P4   1   4GA   C4     P4   1   4GA   C2     P1   1   4GA   C4     P4   1   4GA   C2     P1   1   4GA   C6     N0   1   4GA   C4     P4   1   4GA   C4     P4   1   4GA   C4     P4   1   4GA   C4	ItypereshrreshuatomcgnrN014GAC41P414GAO21P114GAC61N014GAC42P414GAO22P414GAC62N014GAC62N014GAC43P414GAO23P114GAC63N014GAC44P414GAO24P414GAC64N014GAC64N014GAC45P414GAO25	type     reshr     reshu     atom     cgnr     charge       N0     1     4GA     C4     1     0.0000       P4     1     4GA     O2     1     0.0000       P1     1     4GA     C6     1     0.0000       P1     1     4GA     C6     1     0.0000       N0     1     4GA     C4     2     0.0000       P4     1     4GA     O2     2     0.0000       P4     1     4GA     O2     2     0.0000       N0     1     4GA     C6     2     0.0000       N0     1     4GA     C4     3     0.0000       P4     1     4GA     O2     3     0.0000       P1     1     4GA     C4     4     0.0000       P4     1     4GA     O2     4     0.0000       P4     1     4GA     C6     4     0.0000       P1     1<

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