Multi-scale framework for predicting α-cyclodextrin assembly on polyethylene glycol axles - Supplementary Information

Cameron D. Smith,[a] Chenfeng Ke*[b] and Wenlin Zhang*[a]

[a] *Department of Chemistry, Dartmouth College, Hanover, New Hampshire 03755, United States. E-mail: wenlin.zhang@dartmouth.edu*

[b] *Department of Chemistry, Washington University in St. Louis, One Brookings Drive, St. Louis, MO 63130, United States. E-mail: cke@wustl.edu*

A1.1 Umbrella sampling harmonic potentials

The harmonic biasing potential for each sampling window was chosen to ensure sufficient overlap in neighboring sampling windows. A harmonic potential of 200 kJ mol^{-1} nm^{-2} was used to retain the radial displacement (ζ_r) in all windows for all small molecules.

Configurations were taken from -1.4 nm to 1.4 nm at a minimum of every 0.1 nm along the threading axis. A negative displacement indicates the small molecule COM is on the primary face side, relative to the COM of the αCD. Some small molecules required additional windows to sufficiently sample the threading free energy surface and they are given in Table A1. A harmonic potential of 2000 kJ mol^{-1} nm^{-2} was used for every umbrella window along the threading axis (ζ_x) unless stated in Table A1.

	2000 kJ mol^{-1} nm^{-2}	4000 kJ mol^{-1} nm^{-2}	8000 kJ mol^{-1} nm^{-2}
Dimethoxyethane	-	-	-
Diethylene glycol	-	-	-
Tetraethylene glycol	-	-	-
Diethyl-L-tartrate	-0.15	-	-
1,6-Hexanediol	-	-	-
1,7-Heptanediol	-	-	-
Benzene	-0.05	-	-
Hydroquinone	-0.05	-	-
1,4-Difluorobenzene	-0.05	-	-
1,4-Dichlorobenzene	-0.05	-	-
1,4-Dibromobenzene	-0.05	-	-
m-Xylene	-	-	-0.1, -0.05, 0.0, 0.05, 0.1
p-Xylene	-0.05	-	-
Cyclohexane	-	-0.2, -0.15, -0.1	-0.05, -0.025, 0.0, 0.05, 0.1
Norbornene	-	-0.3	-0.2, -0.15, -0.1, -0.05, 0.0, 0.05, 0.1, 0.15, 0.2

Table A1: Additional harmonic potentials used for the umbrella sampling of α-cyclodextrin and small molecule.

A2.2 Justification of ΔG_R

The one-dimensional potential of mean force of tetraethylene glycol provided the estimated value for $\Delta G_R = -8$ kT for the kMC. We simulated the assembly of PSRs with ΔG_R values of -6 kT, -8 kT, and -10 kT, using a system representative of PEG_{1k} and αCD at initial concentrations of 1 mM and 50 mM, respectively.

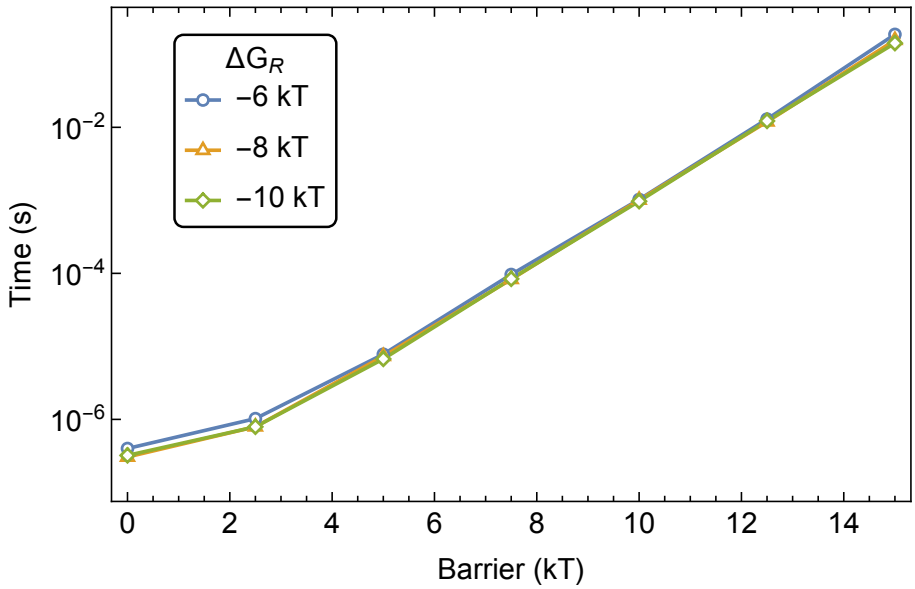

Figure A1: Mean first passage times (MFPT) for the formation aggregates consisting of 10 CD along the backbone of bifunctionalized PEG_{1k}.

Figure A1 shows the MFPT for the formation of an aggregate of 10 αCDs on the two-end functionalized PEG backbone is almost identical for each value of ΔG_R. The lack of sensitivity to the value of ΔG_R is attributed to the comparatively low barrier for hopping along the backbone, at 4.4 kT, which results in a higher probability for a threaded αCDs to diffuse into the polymer rather than dethread. Once there is an imposed barrier on the end group from functionalization, the probability for dethreading drops exponentially and the chain ends essentially represent a reflective boundary for the diffusion of threaded αCDs. We therefore use -8 kT as the value for ΔG_R in our study.

A3.3 Tabulated MFPT data

Barrier (kT)	Aggregate MFPT and standard error (s)			Samples
	10 αCD	18 αCD	40 αCD	
0.0	$(1.748 \pm 0.045) \times 10^{-6}$	$(5.704 \pm 0.097) \times 10^{-6}$	$(5.934 \pm 0.467) \times 10^{-4}$	200
5.0	$(2.179 \pm 0.062) \times 10^{-6}$	$(1.031 \pm 0.023) \times 10^{-5}$	$(6.261 \pm 0.443) \times 10^{-4}$	200
10.0	$(2.099 \pm 0.060) \times 10^{-6}$	$(1.139 \pm 0.025) \times 10^{-5}$	$(6.543 \pm 0.434) \times 10^{-4}$	200
15.0	$(2.174 \pm 0.098) \times 10^{-6}$	$(1.193 \pm 0.032) \times 10^{-5}$	$(6.663 \pm 0.565) \times 10^{-4}$	100
20.0	$(2.000 \pm 0.083) \times 10^{-6}$	$(1.188 \pm 0.036) \times 10^{-5}$	$(6.986 \pm 0.741) \times 10^{-4}$	100
25.0	$(1.995 \pm 0.087) \times 10^{-6}$	$(1.160 \pm 0.043) \times 10^{-5}$	$(7.162 \pm 0.521) \times 10^{-4}$	100
30.0	$(2.192 \pm 0.103) \times 10^{-6}$	$(1.229 \pm 0.040) \times 10^{-5}$	$(6.377 \pm 0.717) \times 10^{-4}$	100

Table A2: MFPT data for monofunctionalized PEG_{5k} and αCD at 1 mM and 50 mM, respectively.

Barrier (kT)	Aggregate MFPT and standard error (s)			Samples
	10 αCD	18 αCD	40 αCD	
2.5	$(3.860 \pm 0.075) \times 10^{-6}$	$(9.828 \pm 0.171) \times 10^{-6}$	$(7.177 \pm 0.463) \times 10^{-4}$	200
5.0	$(1.916 \pm 0.032) \times 10^{-5}$	$(4.827 \pm 0.082) \times 10^{-5}$	$(1.012 \pm 0.055) \times 10^{-3}$	200
7.5	$(1.581 \pm 0.025) \times 10^{-4}$	$(3.862 \pm 0.056) \times 10^{-4}$	$(3.697 \pm 0.146) \times 10^{-3}$	200
10.0	$(1.479 \pm 0.024) \times 10^{-3}$	$(3.726 \pm 0.050) \times 10^{-3}$	$(2.392 \pm 0.067) \times 10^{-2}$	200
12.5	$(1.414 \pm 0.046) \times 10^{-2}$	$(3.713 \pm 0.107) \times 10^{-2}$	$(2.080 \pm 0.058) \times 10^{-1}$	50
15.0	$(1.459 \pm 0.128) \times 10^{-1}$	$(3.558 \pm 0.222) \times 10^{-1}$	1.838 ± 0.144	10

Table A3: MFPT data for bifunctionalized PEG_{5k} and αCD at 1 mM and 50 mM, respectively.

Barrier (kT)	Aggregate MFPT and standard error (s)			Samples
	10 αCD	18 αCD	40 αCD	
0.0	$(1.477 \pm 0.038) \times 10^{-6}$	$(4.794 \pm 0.075) \times 10^{-6}$	$(2.396 \pm 0.170) \times 10^{-4}$	200
2.5	$(2.566 \pm 0.054) \times 10^{-6}$	$(7.016 \pm 0.123) \times 10^{-6}$	$(2.586 \pm 0.154) \times 10^{-4}$	200
5.0	$(1.161 \pm 0.017) \times 10^{-5}$	$(2.741 \pm 0.045) \times 10^{-5}$	$(3.359 \pm 0.179) \times 10^{-4}$	200
7.5	$(8.808 \pm 0.130) \times 10^{-5}$	$(2.130 \pm 0.030) \times 10^{-4}$	$(1.596 \pm 0.051) \times 10^{-3}$	200
10.0	$(7.966 \pm 0.133) \times 10^{-4}$	$(1.954 \pm 0.028) \times 10^{-3}$	$(1.153 \pm 0.028) \times 10^{-2}$	200
12.5	$(7.729 \pm 0.274) \times 10^{-3}$	$(1.973 \pm 0.051) \times 10^{-2}$	$(1.108 \pm 0.052) \times 10^{-1}$	50
15.0	$(8.113 \pm 0.793) \times 10^{-2}$	$(2.002 \pm 0.148) \times 10^{-1}$	1.083 ± 0.054	10

Table A4: MFPT data for bifunctionalized PEG_{5k} and αCD at 2 mM and 100 mM, respectively.

Barrier (kT)	Aggregate MFPT and standard error (s)	Samples
	10 αCD	
0.0	$(3.055 \pm 0.115) \times 10^{-7}$	100
2.5	$(7.928 \pm 0.282) \times 10^{-7}$	100
5.0	$(7.312 \pm 0.318) \times 10^{-6}$	100
7.5	$(8.287 \pm 0.313) \times 10^{-5}$	100
10.0	$(1.011 \pm 0.055) \times 10^{-3}$	50
12.5	$(1.191 \pm 0.069) \times 10^{-2}$	50
15.0	$(1.560 \pm 0.099) \times 10^{-1}$	30

Table A5: MFPT data for bifunctionalized PEG_{1k} and αCD at 1 mM and 50 mM, respectively.