Supplementary information

Efficient sampling of high-dimensional free energy landscapes using adaptive reinforced dynamics

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Supplementary Information for Efficient sampling of high-dimensional free energy landscapes using adaptive reinforced dynamics

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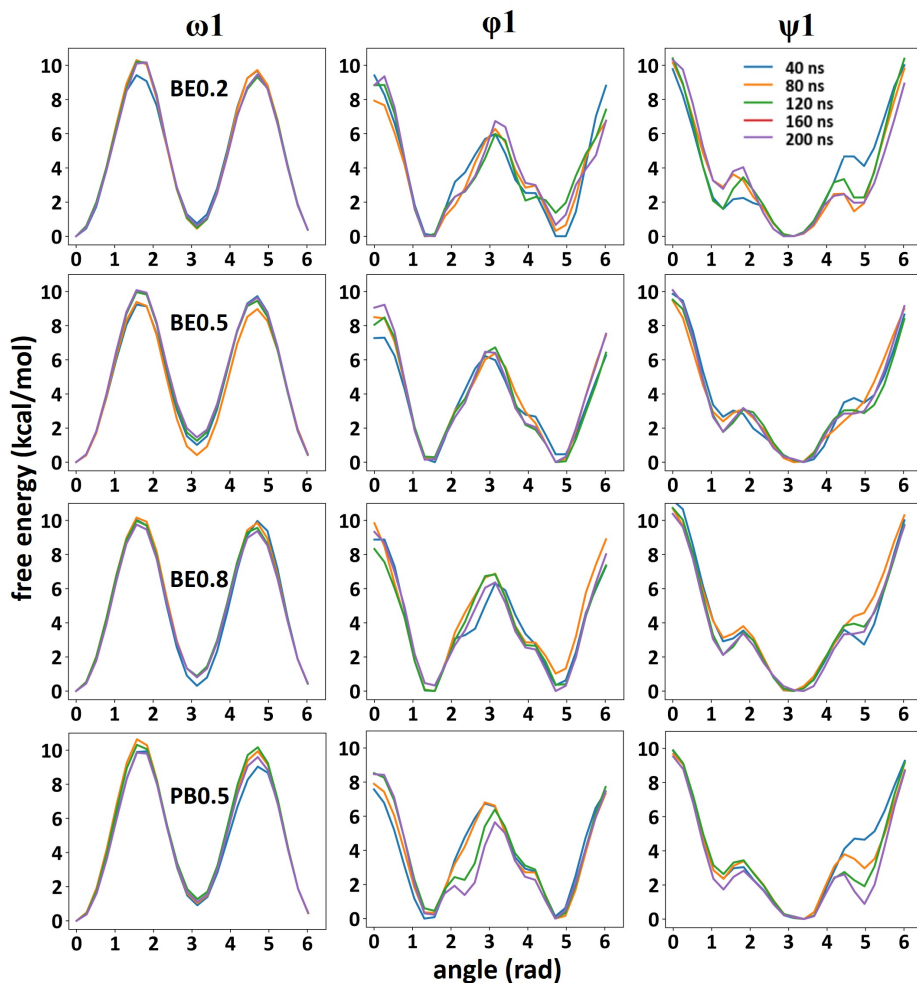[*]Electronic address: `linfeng.zhang.zlf@gmail.com`

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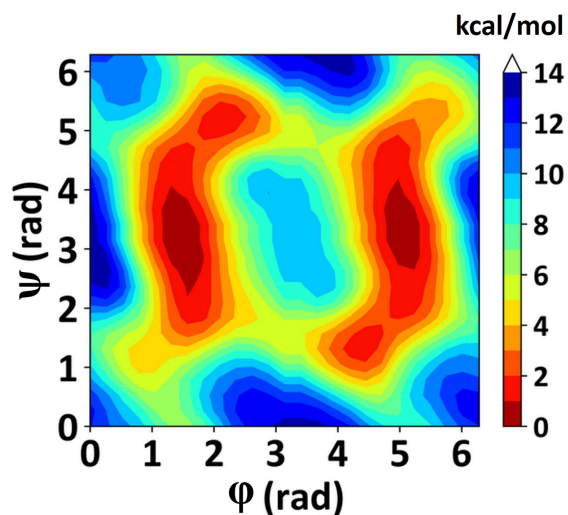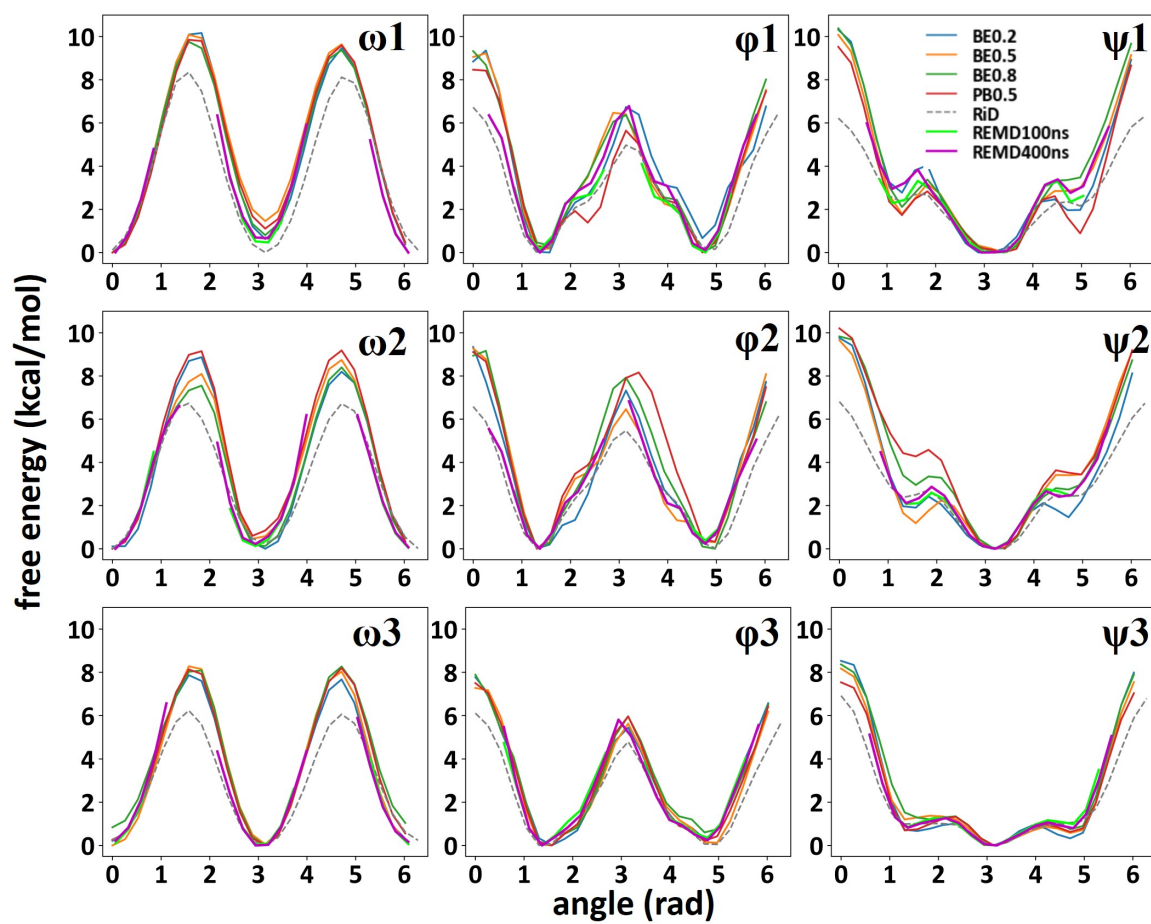
Supplementary Figure 1: The free energy of s1pe projected on ϕ and ψ.
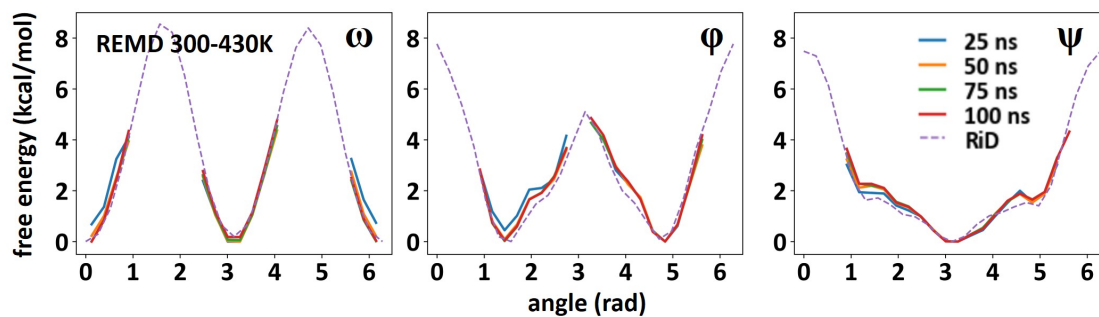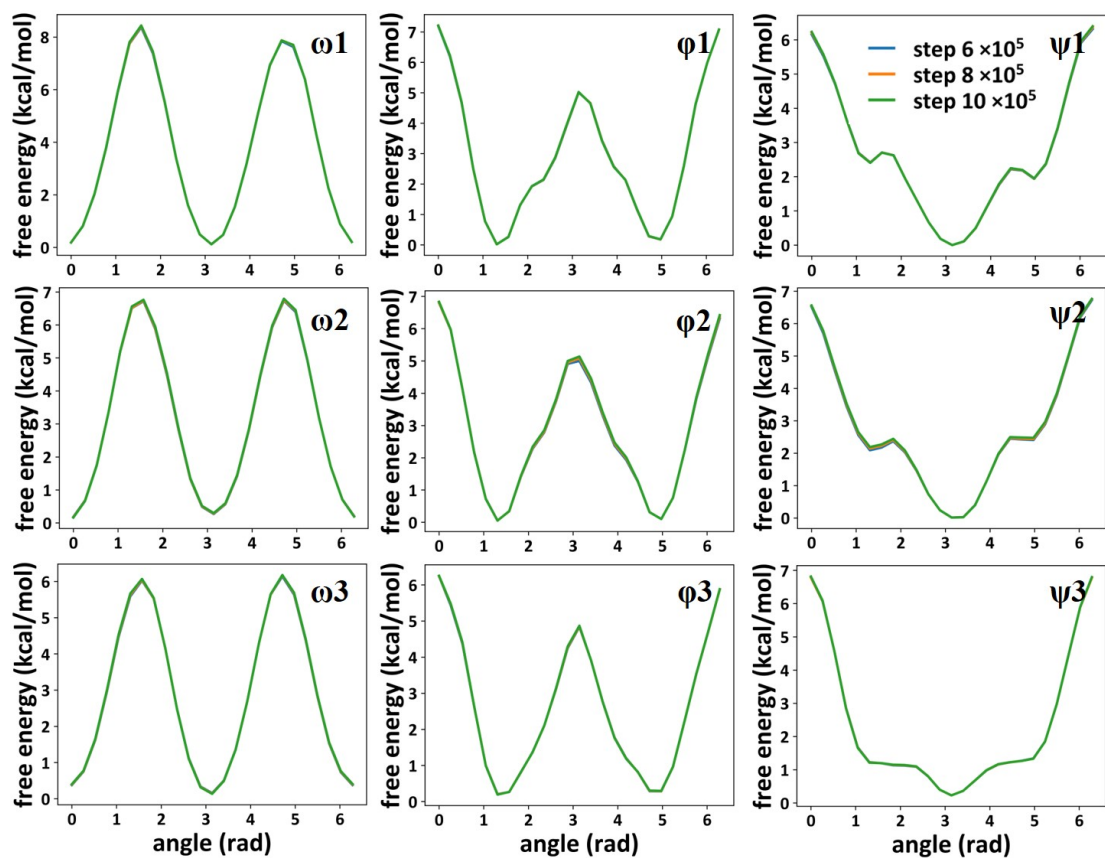

Supplementary Figure 2: Assessing the convergence of the free energy curve of each angle of the peptoid s1pe derived from REMD trajectory at 300K.
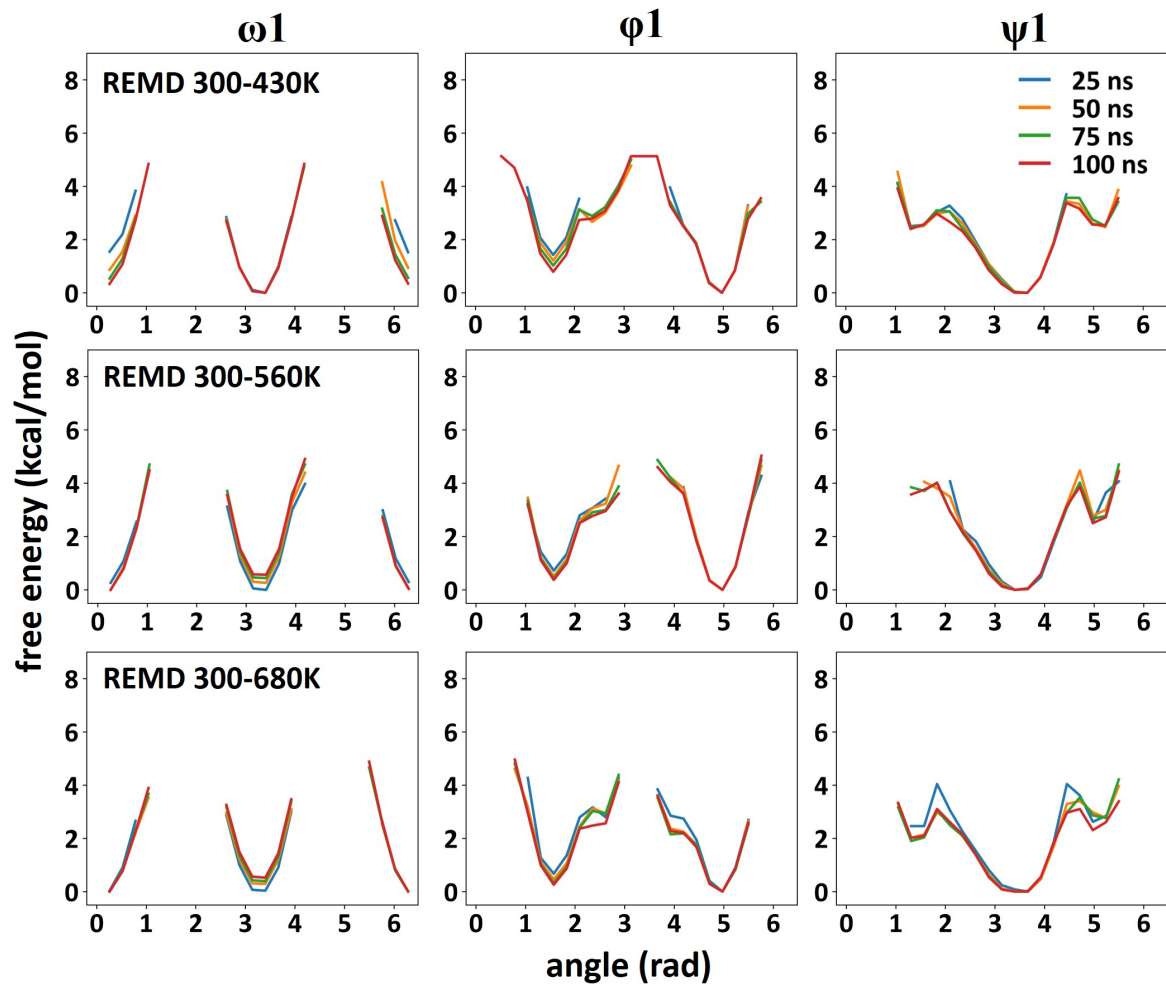
Supplementary Figure 3: Assessing the convergence of different metadynamics simulations of peptoid trimer (s1pe)3. Free energy curves of first three angles of the peptoid trimer (s1pe)3 derived from different metadynamics trajectories. Three bias-exchange metadynamics (BE-MetaD) simulations are conducted. Among them, the parameters of BE0.2 derived from plumID:19.059 are [PACE=1000 HEIGHT=0.2 SIGMA=0.17 GRID_MIN=-pi GRID_MAX=pi BIASFACTOR=10.0 TEMP=300]. The parameters of BE0.5 derived from plumID:21.014 are [PACE=500 HEIGHT=0.5 SIGMA=0.015 SIGMA_MAX=0.6 SIGMA_MIN=0.03 ADAPTIVE=GEOM GRID_MIN=-pi GRID_MAX=pi BIASFACTOR=10.0 TEMP=300]. The parameters of BE0.8 are [PACE=500 HEIGHT=0.8 SIGMA=0.25 GRID_MIN=-pi GRID_MAX=pi BIASFACTOR=10.0 TEMP=300]. One parallel-bias metadynamics (PBMetaD) simulation is conducted and its parameters derived from plumID:21.014 are [PACE=500 HEIGHT=0.5 SIGMA=0.015 SIGMA_MAX=0.6 SIGMA_MIN=0.03 ADAPTIVE=GEOM GRID_MIN=-pi GRID_MAX=pi BIASFACTOR=10.0 TEMP=300], named PB0.5.

Supplementary Figure 4: The comparison of the free energy curve of each angle of the peptoid trimer (s1pe)3 derived from different metadynamics, adaptive RiD and REMD 300-680K of 100ns with REMD 300-680K of 400ns.

Supplementary Figure 5: Assessing the convergence of MCMC simulations of (s1pe)$_3$. The high-dimensional FES used in MCMC simulations is from 140th iteration of adaptive RiD.

Supplementary Figure 6: Assessing the convergence of different REMD simulations of peptoid trimer (s1pe)3. Free energy curves of first three angles of the peptoid trimer (s1pe)3 derived from different REMD trajectories at 300K.
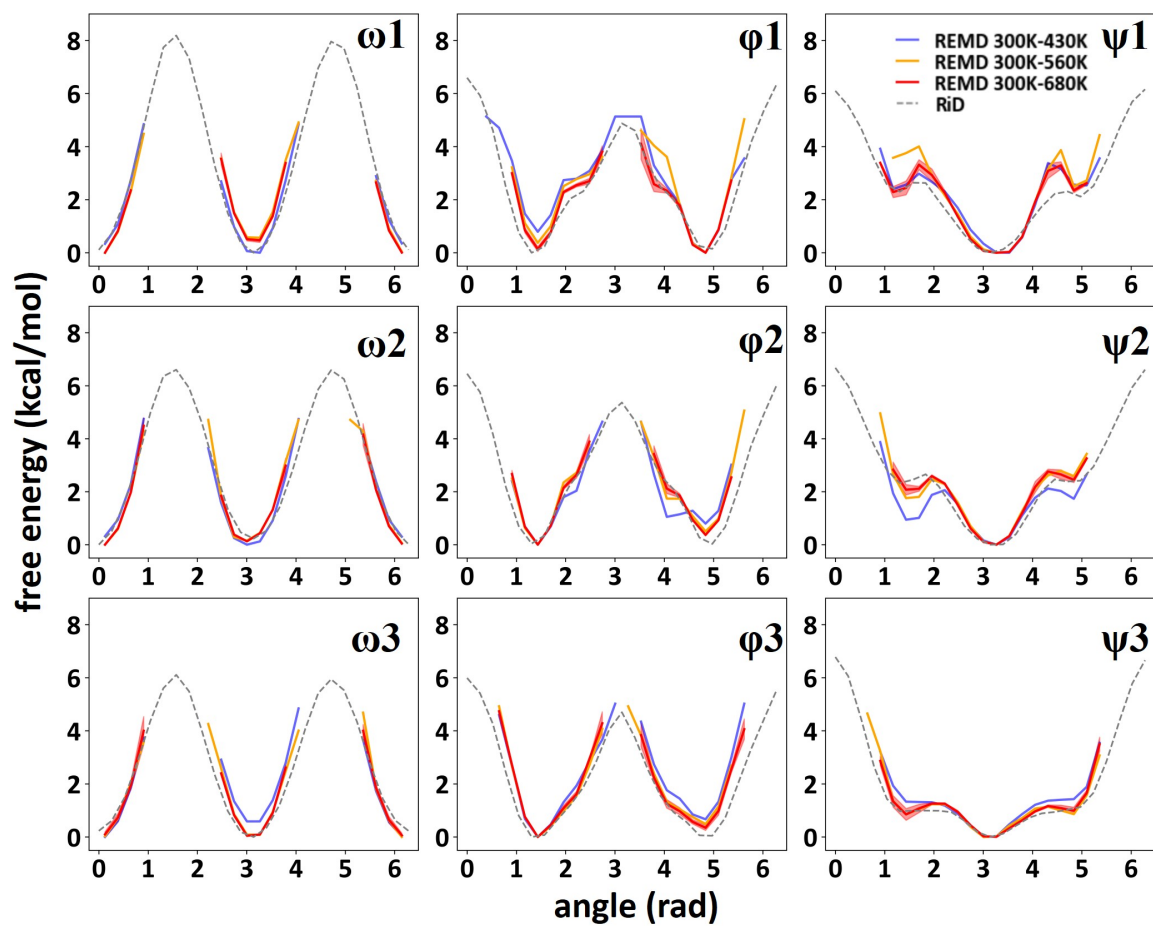
Supplementary Figure 7: The comparison of the free energy curve of each angle of the peptoid trimer (s1pe)3 derived from different REMD trajectories at 300K and RiD. The error bar of the red line is calculated from three independent simulations.
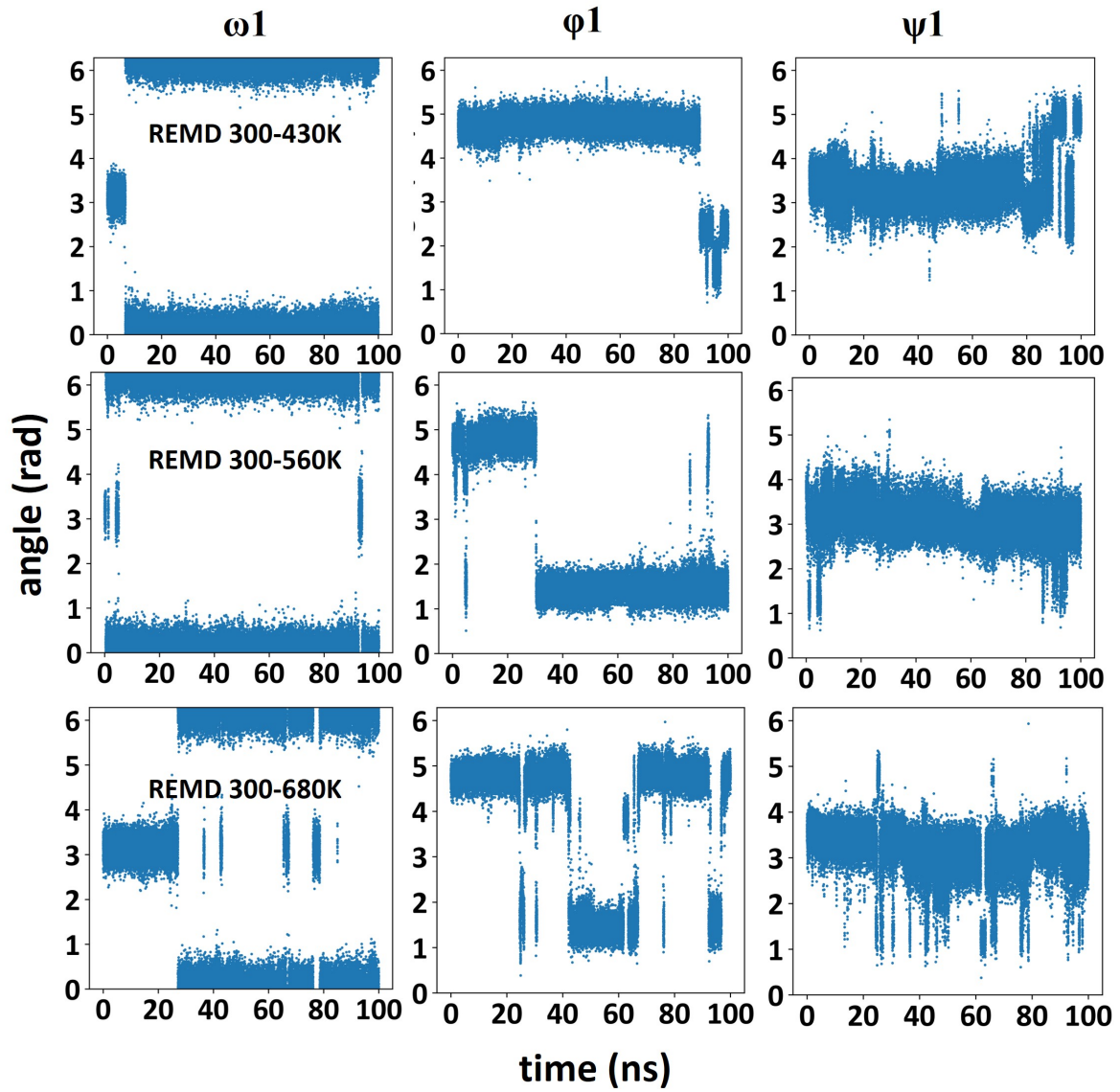
Supplementary Figure 8: Blue dots represent the torsion angles ω_1, ϕ_1 and ψ_1 of the peptoid trimer (s1pe)3 as a function of the simulation time of different REMD simulations.

Supplementary TABLE 1: The comparison of the number of transitions of torsion angles ω (Cα, C, N, Cα) and ϕ (C, N, Cα, C) of s1pe between adaptive RiD and original RiD.

walker	ω_{aRiD}	ϕ_{aRiD}	ω_{RiD}	ϕ_{RiD}
000	2	34	1	3
001	4	45	3	9
002	4	29	3	8
003	3	37	1	11
004	4	22	3	15
005	6	24	0	13
006	7	27	1	6
007	2	31	1	10
008	5	29	3	18
009	3	16	3	10
010	4	38	2	28
011	3	25	1	8
total	47	357	22	139

Supplementary TABLE 2: The number of transitions of six torsion angles ω_1, ω_2, ω_3, ϕ_1, ϕ_2, ϕ_3 of (s1pe)3 in adaptive RiD.

walker	ω_1	ω_2	ω_3	ϕ_1	ϕ_2	ϕ_3
000	9	1	3	35	6	12
001	15	1	1	13	6	36
002	38	8	7	11	10	41
003	27	3	5	9	1	48
004	33	2	1	17	12	18
005	31	7	7	8	6	46
006	11	1	3	12	0	25
007	14	4	3	12	3	35
008	12	2	5	10	1	28
009	18	4	4	7	3	29
010	20	3	10	22	5	44
011	19	11	8	10	1	31
total	247	47	57	166	54	393

Supplementary TABLE 3: The deviation of the reconstructed free-energy (kcal/mol) of REMD 300-680K of 100ns, BEMetaD, PBMetaD and adaptive RiD from the reference, REMD 300-680K of 400ns.

methods	ω_1	ϕ_1	ψ_1	ω_2	ϕ_2	ψ_2	ω_3	ϕ_3	ψ_3	average
REMD100ns	0.1185	0.3841	0.3697	0.1498	0.0971	0.1233	0.1212	0.2252	0.1474	0.1929
BE0.2	1.0602	1.2210	0.7910	1.3004	0.9046	0.6460	0.7650	0.6148	0.6713	0.8860
BE0.5	1.1686	1.0603	0.6663	1.0742	1.0752	0.5910	0.9383	0.7722	0.5952	0.8824
BE0.8	0.9640	0.9357	0.7015	1.0658	1.3056	0.8811	1.0833	0.7544	0.7624	0.9393
PB0.5	1.1003	1.1909	1.0549	1.2253	1.6884	1.2703	0.9484	0.6509	0.5353	1.0738
RiD	1.1501	1.1430	0.9483	1.0240	0.8184	0.6552	0.8730	0.9347	0.6006	0.9053

Supplementary TABLE 4: The total number of transitions of six torsion angles ω_1, ω_2, ω_3, ϕ_1, ϕ_2, ϕ_3 of (s1pe)3 in different REMD simulations.

Temperature range	ω_1	ω_2	ω_3	ϕ_1	ϕ_2	ϕ_3
REMD 300-430K	25	34	26	43	46	12
REMD 300-560K	635	311	357	680	221	1273
REMD 300-680K	2817	1362	1699	1992	713	3548

Supplementary TABLE 5: The comparison of transition rate (number/μs) of chignolin among BEMetaD, PBMetaD and adaptive RiD. RMSD with respect to a reference folded state of chignolin are smoothed using 3-ns-width windows.

methods	folding rate	unfolding rate
BE0.2	3.24	0.93
BE0.5	2.31	0.46
BE0.8	4.63	0.46
PB0.5	**5.56**	3.24
RiD	4.30	**4.30**