

Recalibrating Replica Exchange Solute Tempering for Sampling Disordered Proteins Yumeng Zhang and Jianhan Chen



Enhanced Sampling



• Exchange a pair of replicas from *m* to *n*:

$$\begin{pmatrix} x_m^{[i]} &\equiv (q^{[i]}, p^{[i]})_m \to x_m^{[j]'} &\equiv (q^{[j]}, p^{[j]'})_n \\ x_n^{[j]} &\equiv (q^{[j]}, p^{[j]})_n \to x_n^{[i]'} &\equiv (q^{[i]}, p^{[i]'})_n \end{cases}$$

• The transition probability:

$$\frac{w(X \to X')}{w(X' \to X)} = \exp(-X)$$

$$\Delta \equiv [\beta_n - \beta_m] (E(q^{[i]}) - E(q^{[j]}))$$

 $A = \min \{1, \exp(-\Delta)\}$

• Limitation:

Replicas needed with the degrees of freedom of the target system.

$$N_{rep} \propto O(f^{1/2})$$

***** Rational of REST

• Only scale the selected "solute" portion of the original Hamiltonian. • Requires much fewer numbers of replicas for covering the same temperature range compared to the traditional REX.



***** Rational of REST3

- Adjusting can help approxim sample II conforma in REST protocol, compared samplings under un
- high temperatu

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• **Replica Exchange Solute Tempering and REST2**



• Develop REST3 protocol for IDP samplings

$E_m^{REST3}(X) = \beta_m E_{pp} + \beta_m E_{pp}$	$\frac{B'_m E_{pw}}{E_{ww}} + \frac{E_{ww}}{X}$
$\beta_m^{pw'} = \lambda_{\gamma}$	$\boldsymbol{\beta}_{m}^{pw}$

• β_m^{pw} is independent from β_m^{pp} . • $\beta_m^{pw} / \beta_m^{pw}$ is important for IDP samplings.

T			$\Gamma = \mathcal{O}$			
$\beta \beta_m^{pw}$	reps	Temp (K)	β_m^{pp} REST2	β_m^{pw} REST2	$\beta_m^{pw'}$ REST3	Scaling (λ)
	0	298	1	1	1	-
nately OP	1	308	0.966	0.983	0.983	-
	2	319	0.933	0.966	0.966	-
	3	330	0.902	0.950	0.950	-
itions	4	342	0.871	0.933	0.938	1.005 x
	5	354	0.841	0.917	0.926	1.010 x
	6	366	0.813	0.902	0.915	1.015 x
	7	379	0.785	0.886	0.904	1.020 x
l to	8	392	0.759	0.871	0.823	1.025 x
S	9	406	0.733	0.856	0.882	1.030 x
	10	420	0.708	0.841	0.871	1.035 x
ures.	11	435	0.684	0.827	0.860	1.040 x
	12	450	0.661	0.813	0.850	1.045 x
	13	466	0.639	0.799	0.839	1.050 x
	14	483	0.617	0.785	0.829	1.055 x
	15	500	0.596	0.772	0.818	1.060 x





***** High T collapse hinders the efficiency.





• Re
[1] Prod 27.1020
[2] J. P.
[3] <i>J</i> . <i>C</i> [4] <i>Biod</i>





• **REST3 vs. REST2 (Preliminary Data)**



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- diffusion rate.

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0 0.75 1.00 1.25 1.50 1.75 2.00 2.25 Rg (nm)

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