1 Ablation on different window size (A2/Reviewer RhsB & A5/Reviewer i74U)

Window size	GPU Hours	Log Likelihood	KL Divergence	Max Energy
2 (default)	2.5	1505.6 ± 0.45	164.93	245.05 ± 0.02
1	2	1393.79 ± 0.51	290.27	822.82 ± 0.1
4	4	1545.82 ± 0.48	137.75	260.5 ± 0.04

Table 1: Performance of Doob's Seq2Seq with different window sizes on Alanine Dipeptide.

2 Discretized KLD Objective (Global Response)

2.1 Extended Experiments with new KLD Objective

ALDP				
Method	**GPU Hours**	**Log Likelihood**	**KL Divergence**	**Max Energy**
TPS-DPS	12	1562.79 ±9.39	-0.25	26.44 ±16.07
Doob's Lagrangian	0.65	1446.26 ±0.51	224.93	730.66 ±0.04
+ fixed attention (Doob's Seq2Seq)	2.5	1505.6 ±0.45	164.93	245.05 ±0.02
KLD Objective	0.2	1541.6 ±0.41	128	679.66 ±0.02
+ fixed attention (KLD-SeqSeq)	0.5	1628.25 ±0.38	41.2	203.87 ±0.03
Chignolin				
Method	**GPU Hours**	**Log Likelihood**	**KL Divergence**	**Max Energy**
TPS-DPS	6.5	7906.05 ± 51.71	3.05	466.96 ± 204.91
Doob's Lagrangian	2.5	9289.54 ± 1.19	1235.23	3828.38 ± 0.1
+ fixed attention (Doob's Seq2Seq)	12	9898.07 ± 0.28	626.9	1858.75 ± 0.07
KLD Objective	0.2	9137.65 ±2.34	322.61	1272.72 ±0.46
+ fixed attention (KLD-SeqSeq)	1	10369.86 ±1.46	184.43	308.98 ±0.23

Table 2: **Alanine Dipeptide and Chignolin results.** Across all metrics, discretized KL divergence objective shows comparable or superior performance to Doob's Lagrangian objective at a much lower computational cost, demonstrating its effectiveness. Additionally, incorporating an attention mechanism reliably enhances performance, as evidenced by the improvements in Doob's Seq2Seq and KLD-Seq2Seq against its non-attention counterparts. All methods are trained and evaluated in vacuum, and metrics are calculated on 64 sampled paths.

2.2 Scaling Experiments on Fast Folding Proteins

TRP-Cage				
Method	**GPU Hours**	**Log Likelihood**	**KL Divergence**	**Max Energy**
TPS-DPS	9	19193.62 ±218.24	4.57	1159.35 ±210.71
Doob's Lagrangian	3.5	17967 ±10.08	8265.17	13124 ±4.19
KLD-Seq2Seq	1	25794.02 ±1.29	372	628.96 ±0.5
BBA				
Method	**GPU Hours**	**Log Likelihood**	**KL Divergence**	**Max Energy**
TPS-DPS	13	32127 ±780.83	9.66	971.62 ±224.74
Doob's Lagrangian	4.5	30045.22 ±1.09	6354.38	39615.68 ±0.7
KLD-Seq2Seq	1.5	44796.67 ±1.73	561.95	901.66 ±0.16

Table 3: **TRP-Cage and BBA results.** To further assess the scalability and efficiency of our method, we extend our experiments to fast-folding proteins with up to 30 amino acids. KLD-Seq2Seq continues to provide highly efficient training, requiring only a fraction of the computational cost compared to other methods while remaining competitive. Doob's Lagrangian fails to scale to bigger systems, yielding unrealistic max energy and high KL divergence. All methods are trained and evaluated in vacuum, and metrics are calculated on 64 sampled paths.

3 Extended result with Internal Coordinate (A4/Reviewer oxap)

ALDP			
Method	**Log Likelihood**	**KL Divergence**	**Max Energy**
Doob's Lagrangian (Internal)	1647.88 ±0.28	23.87	-16.9 ±0.02
+ temperature annealing	1651.23 ±0.35	22.4	-17.1 ±0.02
+ fixed attention (Doob's Seq2Seq)	1626 ±0.2	22.0	-17.26 ±0.18
Chignolin			
Method	**Log Likelihood**	**KL Divergence**	**Max Energy**
Doob's Lagrangian (Internal)	10169 ±0.37	355	1754 ±0.09
+ temperature annealing	10234.31 ±0.4	291.24	724.98 ±0.07
+ fixed attention (Doob's Seq2Seq)	10194.93 ±0.15	276.14	402.81 ±0.04

Table 4: Ablation Studies on Internal Coordinate.

4 Effects of simulation environment (A8/Reviewer oxap)

Method	**Train**	**Evaluate**	**Log Likelihood**	**KL Divergence**	**Max Energy**
TPS-DPS	Solvent	Solvent	8124.53 ± 2518.24	4.64	-914 ± 138.36
	Vacuum	Vacuum	7906.05 ± 51.71	3.05	466.96 ± 204.91
	Vacuum	Solvent	7812.95 ± 47.89	3.29	-541.59 ± 184.78
Doob's Seq2Seq	Vacuum	Vacuum	9898.07 ± 0.28	626.9	1858.75 ± 0.07
	Vacuum	Solvent	9826.04 ± 0.45	698.2	902.18 ±0.1

Table 5: **Effects of training and evaluation environments on Chignolin transition paths**. This table examines how training and evaluation in different environments affect model performance. The results show that when evaluating a model in different environments (e.g., vacuum vs. solvent), log-likelihood and KL divergence remain relatively consistent, indicating robustness in model evaluation, whereas max energy is more sensitive to the solvent conditions. Comparing TPS-DPS models trained in solvent and vacuum, we observe differences, but training in vacuum remains a valid approach: log-likelihood and KL divergence are within reasonable ranges, and while max energy differs, it remains physically interpretable. Therefore, while a vacuum-trained model may not recover the exact same transition path distribution as a solvent-trained one, we conclude that it still produces meaningful transition paths. Due to DMFF not supporting implicit solvent, our experiments are currently limited to vacuum conditions; future work will include experiments with explicit solvent training for a more comprehensive studies.