

Quotient-Space Diffusion Models

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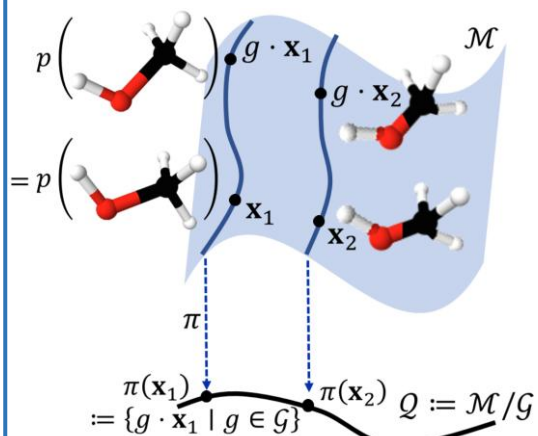
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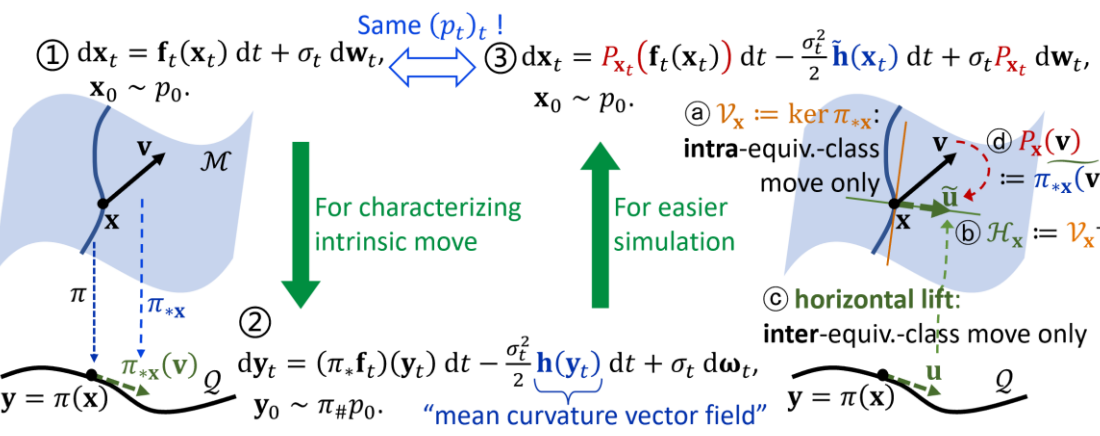
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Describing Group Symmetry on the Quotient Space



Quotient-Space Diffusion Process and Simulation in the Original Space



Results: Molecular Structure Generation

Datasets	Methods	Recall				Precision			
		Coverage ↑ mean	median	AMR ↓ mean	median	Coverage ↑ mean	median	AMR ↓ mean	median
GEOM-QM9 (Positive samples are within 0.5 Å RMSD.)	CGCF	69.47	96.15	0.425	0.374	38.20	33.33	0.711	0.695
	GeoDiff	76.50	100.00	0.297	0.229	50.00	33.50	1.524	0.510
	GeoMol	91.50	100.00	0.225	0.193	87.60	100.00	0.270	0.241
	Torsional Diff.	92.80	100.00	0.178	0.147	92.70	100.00	0.221	0.195
	MCF	95.0	100.00	0.103	0.044	93.7	100.00	0.119	0.055
GEOM-DRUGS (Positive samples are within 0.75 Å RMSD.)	ET-Flow(SO(3))	95.98	100.00	0.076	0.030	92.10	100.00	0.110	0.047
	+ Geodiff alignment	95.71	100.00	0.085	0.040	95.20	100.00	0.098	0.050
	+ AF3 alignment	92.67	100.00	0.131	0.070	84.38	100.00	0.205	0.146
	+ Quotient-space diffusion	96.40	100.00	0.069	0.024	93.30	100.00	0.096	0.036
	GeoDiff	42.10	37.80	0.835	0.809	24.90	14.50	1.136	1.090
GEOM-DRUGS (Positive samples are within 0.75 Å RMSD.)	GeoMol	44.60	41.40	0.875	0.834	43.00	36.40	0.928	0.841
	Torsional Diff.	72.70	80.00	0.582	0.565	55.20	56.90	0.778	0.729
	MCF - S (13M)	79.4	87.5	0.512	0.492	57.4	57.6	0.761	0.715
	MCF - B (62M)	84.0	91.5	0.427	0.402	64.0	66.2	0.667	0.605
	MCF - L (242M)	84.7	92.2	0.390	0.247	66.8	71.3	0.618	0.530
	ET-Flow (8.3M)	79.53	84.57	0.452	0.419	74.38	81.04	0.541	0.470
	+ reproduction	78.94	84.24	0.489	0.472	66.24	70.42	0.651	0.595
	+ Quotient-space diffusion	79.86	85.71	0.459	0.433	72.70	79.63	0.565	0.501
	ET-Flow(SO(3)) (9.1M)	78.18	83.33	0.480	0.459	67.27	71.15	0.637	0.567
	+ reproduction	74.91	80.90	0.541	0.515	60.33	62.71	0.724	0.665
	+ Geodiff alignment	75.11	80.74	0.545	0.526	59.58	60.48	0.734	0.678
+ AF3 alignment	71.66	76.09	0.572	0.570	52.21	50.00	0.828	0.793	
+ Quotient-space diffusion	78.50	84.20	0.477	0.455	67.35	71.42	0.635	0.563	

Quotient-Space Diffusion Model on the Shape Space $Q = \mathbb{R}^{3N}/SE(3)$

$Q = \mathbb{R}_{CoM}^{3N}/SO(3)$: for zero-CoM $\mathbf{x} = [\vec{x}^{(n)}]_n$ and zero-momentum $\mathbf{v} = [\vec{v}^{(n)}]_n$,

$P_{\mathbf{x}}(\mathbf{v}) = [\vec{v}^{(n)} - \mathbf{K}(\mathbf{x})^{-1} (\sum_{n'=1}^N \vec{x}^{(n')} \times \vec{v}^{(n')}) \times \vec{x}^{(n)}]_n$ removes total/rigid-body angular momentum (only deformation),

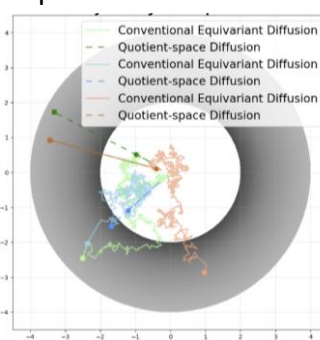
$\vec{h}(\mathbf{x}) = [(\mathbf{K}(\mathbf{x})^{-1} - \text{tr}(\mathbf{K}(\mathbf{x})^{-1}) \mathbf{I}) \vec{x}^{(n)}]_n$,

where $\mathbf{K}(\mathbf{x}) := \sum_{n=1}^N \|\vec{x}^{(n)}\|^2 \mathbf{I} - \sum_{n=1}^N \vec{x}^{(n)} \vec{x}^{(n)\top}$.

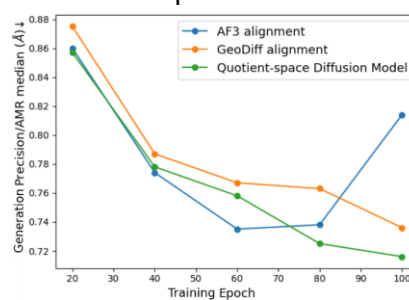
v.s. Alignment-based methods: $\mathcal{A}_{\mathbf{y}}(\mathbf{x}) := \text{argmin}_{\mathbf{x}' \in \{g \cdot \mathbf{x} | g \in G\}} d(\mathbf{x}', \mathbf{y})$

Training strategy for D_θ	Optimal solution of D_θ	Reduction of learning difficulty		Sampling compatibility
		Removal of equivalent DoFs	Removal of variance on equivalent DoFs	
Conventional loss $\mathbb{E} \ D_\theta(\mathbf{x}_t, t) - \mathbf{x}_1\ ^2$	$\mathbb{E}[\mathbf{x}_1 \mathbf{x}_t]$	✗	✗	✓
GeoDiff alignment loss $\mathbb{E} \ D_\theta(\mathbf{x}_t, t) - \mathcal{A}_{\mathbf{x}_t}(\mathbf{x}_1)\ ^2$	$\mathbb{E}[\mathcal{A}_{\mathbf{x}_t}(\mathbf{x}_1) \mathbf{x}_t]$	✗	✓	✗
AF3 alignment loss $\mathbb{E} \ D_\theta(\mathbf{x}_t, t) - \mathcal{A}_{D_\theta(\mathbf{x}_t, t)}(\mathbf{x}_1)\ ^2$	$g \cdot \mathbb{E}[\mathcal{A}_{\mathbf{x}_t}(\mathbf{x}_1) \mathbf{x}_t]$ for arbitrary $g \in G$	✓	✓	✗
quotient-space diffusion loss $\mathbb{E} \ P_{\mathbf{x}_t}(D_\theta(\mathbf{x}_t, t) - \mathbf{x}_1)\ ^2$	$\mathbb{E}[P_{\mathbf{x}_t}(\mathbf{x}_1) \mathbf{x}_t] + \mathbf{v}^\nu$ for arbitrary $\mathbf{v}^\nu \in \text{Ker}(P_{\mathbf{x}_t})$	✓	✓	✓

Sampling: no intra-equiv.-class movement!



Training: $\mathbb{E} \|P_{\mathbf{x}_t}(D_{\theta,t}(\mathbf{x}_t) - \mathbf{x}_1)\|^2 \rightarrow$ no need to learn anything on the equiv. class!



Results: Protein Structure Generation

Settings	Methods	Designability (%) [†]	FPSD vs.		fS		fJSD vs.	
			PDB↓	AFDB↓	(C/A/T)↑	PDB↓	AFDB↓	
Representative References	FrameDiff	65.4	194.2	258.1	2.46/5.78/23.35	1.04	1.42	
	FoldFlow (base)	96.6	601.5	566.2	1.06/1.79/9.72	3.18	3.10	
	FoldFlow (stoc.)	97.0	543.6	520.4	1.21/2.09/11.59	3.69	2.71	
	FoldFlow (OT)	97.2	431.4	414.1	1.35/3.10/13.62	2.90	2.32	
	FrameFlow	88.6	129.9	159.9	2.52/5.88/27.00	0.68	0.91	
	ESM3	22.0	933.9	855.4	3.19/6.71/17.73	1.53	0.98	
	Chroma	74.8	189.0	184.1	2.34/4.95/18.15	1.00	1.08	
	RFDiffusion	94.4	253.7	252.4	2.25/5.06/19.83	1.21	1.13	
	Proteus	94.2	225.7	226.2	2.26/5.46/16.22	1.41	1.37	
	Genie2	95.2	350.0	313.8	1.55/3.66/11.65	2.21	1.70	
SDE Sampling	Proteina $\mathcal{M}_{fS}^{\text{align}}$, $\gamma = 0.35$	96.0	386.5	378.2	1.77/4.97/17.78	2.17	1.73	
	+ Quotient-space diffusion	97.6	274.7	277.1	2.24/6.69/20.99	1.68	1.55	
	Proteina $\mathcal{M}_{fS}^{\text{align}}$, $\gamma = 0.45$	92.2	332.9	320.4	1.83/5.01/20.22	1.93	1.49	
	+ Quotient-space diffusion	92.6	244.5	246.3	2.24/6.68/23.47	1.43	1.28	
ODE Sampling	Proteina $\mathcal{M}_{fS}^{\text{align}}$, $\gamma = 0.50$	89.2	306.2	290.8	1.86/4.92/21.15	1.81	1.36	
	+ Quotient-space diffusion	90.2	228.0	228.7	2.25/6.59/25.24	1.32	1.17	
ODE Sampling	Proteina \mathcal{M}_{fS}	19.6	85.4	21.4	2.51/5.65/27.35	0.59	0.09	
	Proteina $\mathcal{M}_{fS}^{\text{align}}$	13.8	83.2	21.9	2.45/5.63/31.76	0.58	0.12	
	+ AF3 alignment	3.8	229.0	82.4	2.18/4.30/14.28	1.35	0.36	
	+ Quotient-space diffusion	15.6	69.9	17.6	2.57/6.40/32.14	0.41	0.11	