

# SE(3) diffusion model with application to protein backbone generation

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# Outline

Background

Preliminaries and Notation

Method

Experiment

Discussion

# Background

- **Generative Modeling:** The  $N - C_\alpha - C$  atoms for each residue are described as a **frame**[\[1\]](#)[\[2\]](#)[\[3\]](#)[\[4\]](#). The backbone structure with  $N$  residues (frames) is represented as an element of  $SE(3)^N$ .

- Rotation matrix  $r$ .

$$u_1 = v_1, \quad u_2 = v_2 - \text{Proj}_{u_1}(v_2) = v_2 - \frac{\langle v_2, u_1 \rangle}{\langle u_1, u_1 \rangle} u_1$$

$$e_1 = \frac{v_1}{\|v_1\|}, \quad e_2 = \frac{v_2}{\|v_2\|}, \quad e_3 = e_1 \times e_2$$

$$r = [e_1 \quad e_2 \quad e_3]$$

- Translation  $x$  (the  $C_\alpha$  coordinate).

$$\Rightarrow T = (r, x) \in SE(3), \quad \text{Decoupled}$$

- Torsion angle  $\psi$ .

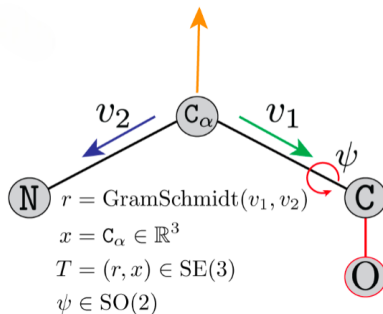


Figure 1: A frame for each residue.

# Background

- ▶ **Diffusion modeling** has been extended to Riemannian manifolds like  $SE(3)$ [\[5\]](#)[\[6\]](#).
  - Lack tractable training procedures.
  - Fail to effectively incorporate geometric invariances.
- ▶ **SOTA** at that time: RFdiffusion[\[7\]](#).
  - Rely on a heuristic denoising loss.
  - Require pretraining on protein structure prediction.

Motivated by the above...

# Contributions

Propose a theory and methodology for **SE(3) diffusion models** applied to **protein backbone generation without pretraining**.

- ▶ Develop a diffusion process on  $SE(3)^N$ .
- ▶ Implement an  $SE(3)$ -invariant diffusion model for protein backbones.
- ▶ FrameDiff generates diverse, designable, and novel protein monomers up to 500 residues.
- ▶ FrameDiff achieves in-silico designability rates, second only to RFdiffusion[7], a pretrained model with 4x more parameters.

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# Preliminaries and Notation

## ► Backbone Parameterization

Following the AlphaFold2 (AF2)<sup>[1]</sup> approach,  $N$  residues (frames) are mapped from fixed coordinates  $\mathbf{N}^*, \mathbf{C}_\alpha^*, \mathbf{C}^*, \mathbf{O}^* \in \mathbb{R}^3$ , with  $\mathbf{C}_\alpha^*$  at  $(0, 0, 0)$ .

**Each coordinate reflects idealized bond angles and lengths from experimental data.**

For residue  $n$ :

$$[\mathbf{N}_n, \mathbf{C}_n, (\mathbf{C}_\alpha)_n] = T_n \cdot [\mathbf{N}^*, \mathbf{C}^*, \mathbf{C}_\alpha^*]$$

where  $T_n = [r_n, x_n] \in \text{SE}(3)$ ,  $r_n \in \text{SO}(3)$  is a  $3 \times 3$  rotation matrix, and  $x_n \in \mathbb{R}^3$ . For any  $v \in \mathbb{R}^3$ ,  $T_n \cdot v = r_n v + x_n$ .  $\mathbf{T} = [T_1, \dots, T_N] \in \text{SE}(3)^N$  is the full transformation.

$\mathbf{O}_n$  rotates around the bond between  $\mathbf{C}_n$  and  $(\mathbf{C}_\alpha)_n$  with angle  $\psi_n$ .

# Preliminaries and Notation

## ► Diffusion Modeling on Manifolds

Based on the Riemannian score-based generative model[6], where  $X^{(0)} \sim p_0$  is supported on a Riemannian manifold  $\mathcal{M}$ . A  $\mathcal{M}$ -valued forward process  $(X^{(t)})_{t \geq 0}$  evolves from  $p_0$  towards the invariant density  $p_{\text{inv}}(x) \propto e^{-U(x)}$ , following:

$$d\mathbf{X}(t) = -\frac{1}{2} \nabla U(\mathbf{X}(t)) dt + d\mathbf{B}_{\mathcal{M}}^{(t)}, \quad \mathbf{X}^{(0)} \sim p_0,$$

where  $\mathbf{B}_{\mathcal{M}}^{(t)}$  is Brownian motion on  $\mathcal{M}$ . The time-reversed process is described by:

## Proposition 1 (Time-reversal)[6]

For  $T_F > 0$ , with  $\overleftarrow{X}(0) \stackrel{d}{=} X(T_F)$ ,

$$d\overleftarrow{\mathbf{X}}(t) = \left\{ \frac{1}{2} \nabla U(\overleftarrow{\mathbf{X}}(t)) + \nabla \log p_{T_F-t}(\overleftarrow{\mathbf{X}}(t)) \right\} dt + d\mathbf{B}_{\mathcal{M}}^{(t)},$$

where  $p_t$  is the density of  $\overleftarrow{\mathbf{X}}^{(t)}$ . Under mild assumptions,  $\overleftarrow{\mathbf{X}}(t) \stackrel{d}{=} \mathbf{X}(T_F - t)$ .



# Preliminaries and Notation

## ► Riemannian Gradients and Brownian Motion

### ■ Tangent Space and Gradients:

Riemannian gradients  $\nabla U(x)$  and  $\nabla \log p_t(x)$  are in the tangent space  $T_x\mathcal{M}$  at  $x$ , with an inner product  $\langle \cdot, \cdot \rangle_{\mathcal{M}}$ .

### ■ Brownian Motion and Laplace-Beltrami:

Brownian motion on  $\mathcal{M}$  follows the Laplace-Beltrami operator  $\Delta_{\mathcal{M}}$  and evolves via:

$$\frac{\partial \pi_t}{\partial t} = \frac{1}{2} \Delta_{\mathcal{M}} \pi_t.$$

## ► Denoising Score Matching:

DSM approximates the Stein score  $\nabla \log p_t$  with a score network  $s_{\theta}(t, \cdot)$ . The DSM loss is:

$$\mathcal{L}(\theta) = \mathbb{E} \left[ \lambda_t \|\nabla \log p_{t|0}(\mathbf{X}^{(t)} | \mathbf{X}^{(0)}) - s_{\theta}(t, \mathbf{X}^{(t)})\|^2 \right],$$

where  $p_{t|0}$  is the conditional density of  $\mathbf{X}^{(t)}$  given  $\mathbf{X}^{(0)}$ , and  $\lambda_t$  is a weighting factor.

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# Method Overview

## ► Theoretical Part:

- **Step 1:** Define a forward diffusion process on  $SE(3)$ .
- **Step 2:** Derive DSM training on compact Lie groups, using  $SO(3)$  as an example.
- **Step 3:** Ensure  $SE(3)$  invariance, with  $SE(3)^N$  data distribution invariant to global rotations and translations.

## ► Practical Part:

- **Step 1:** Propose FrameDiff which learns the score using frame and torsion predictions.
- **Step 2:** Training losses.
- **Step 3:** Sampling procedure.

# Theoretical Part Step 1: Forward diffusion on $SE(3)$

To define a canonical forward diffusion on  $SE(3)^N$ .

- **Choose an inner product on  $SE(3)$  to define a Brownian motion.**

Derive from the canonical inner products for  $SO(3)$  and  $\mathbb{R}^3$

$$\langle u, v \rangle_{\mathfrak{so}(3)} = \frac{\text{Tr}(uv^\top)}{2} \quad \text{and} \quad \langle x, y \rangle_{\mathbb{R}^3} = \sum_{i=1}^3 x_i y_i,$$

Under an appropriate choice of inner product,  $SE(3)$  can be identified with  $SO(3) \times \mathbb{R}^3$  from a Riemannian point of view.

# Theoretical Part Step 1: Forward diffusion on $\text{SE}(3)$

## Proposition 2 (Metric on $\text{SE}(3)$ )

For any  $T \in \text{SE}(3)$  and  $(a, x), (a', x') \in T_T \text{SE}(3)$  we define

$$\langle (a, x), (a', x') \rangle_{\text{SE}(3)} = \langle a, a' \rangle_{\text{SO}(3)} + \langle x, x' \rangle_{\mathbb{R}^3}.$$

We have:

(a) for any  $f \in C^\infty(\text{SE}(3))$  and  $T = (r, x) \in \text{SE}(3)$ ,

$$\nabla_T f(T) = (\nabla_r f(r, x), \nabla_x f(r, x)),$$

(b) for any  $f \in C^\infty(\text{SE}(3))$  and  $T = (r, x) \in \text{SE}(3)$ ,

$$\Delta_{\text{SE}(3)} f(T) = \Delta_{\text{SO}(3)} f(r, x) + \Delta_{\mathbb{R}^3} f(r, x),$$

(c) for any  $t > 0$ ,  $B_{\text{SE}(3)}^{(t)} = [B_{\text{SO}(3)}^{(t)}, B_{\mathbb{R}^3}^{(t)}]$  with independent  $B_{\text{SO}(3)}^{(t)}$  and  $B_{\mathbb{R}^3}^{(t)}$ .

## Theoretical Part Step 1: Forward diffusion on $\text{SE}(3)$

The metric in **Proposition 2** allows to treat  $\text{SO}(3)$  and  $\mathbb{R}^3$  forward processes independently (conditionally on  $\mathbf{T}(0)$ ). The associated forward process  $(\mathbf{T}^{(t)})_{t \geq 0} = (\mathbf{R}^{(t)}, \mathbf{X}^{(t)})_{t \geq 0}$  is given by

$$d\mathbf{T}^{(t)} = \left[ 0, -\frac{1}{2}\mathbf{X}^{(t)} \right] dt + \left[ d\mathbf{B}_{\text{SO}(3)}^{(t)}, d\mathbf{B}_{\mathbb{R}^3}^{(t)} \right].$$

Thus, we have

$$\nabla_{\mathbf{T}^{(t)}} \log p_{t|0}(\mathbf{T}^{(t)} | \mathbf{T}^{(0)}) = \left( \nabla_{\mathbf{R}^{(t)}} \log p_{t|0}(\mathbf{R}^{(t)} | \mathbf{R}^{(0)}), \nabla_{\mathbf{X}^{(t)}} \log p_{t|0}(\mathbf{X}^{(t)} | \mathbf{X}^{(0)}) \right)$$

$\Rightarrow$  **Denoising score matching on  $\text{SO}(3)$  and  $\mathbb{R}^3$  separately.**

## Theoretical Part Step 2: Denoising score matching on $\text{SE}(3)$

### ► Denoising score matching on $\text{SO}(3)$ .

The forward process  $(\mathbf{R}^{(t)})_{t \geq 0}$  is simply the Brownian motion on  $\text{SO}(3)$ , and  $p_{t|0}$  is defined by the heat kernel.

### Proposition 3 (Brownian motion on compact Lie groups)

Assume that  $\mathcal{M}$  is a compact Lie group, where for any  $\ell \in \mathbb{N}$   $\chi_\ell$  is the character associated with the irreducible unitary representation of dimension  $d_\ell$ . Then  $\chi_\ell : \mathcal{M} \rightarrow \mathbb{R}$  is an eigenvector of  $\Delta$  and there exists  $\lambda_\ell \geq 0$  such that  $\Delta \chi_\ell = -\lambda_\ell \chi_\ell$ . In addition, we have for any  $t > 0$  and  $x^{(0)}, x^{(t)} \in \mathcal{M}$ ,

$$p_{t|0}(x^{(t)}|x^{(0)}) = \sum_{\ell \in \mathbb{N}} d_\ell e^{-\lambda_\ell t/2} \chi_\ell \left( \left( x^{(0)} \right)^{-1} x^{(t)} \right).$$

## Theoretical Part Step 2: Denoising score matching on $\text{SE}(3)$

### Proposition 4 (Brownian motion on $\text{SO}(3)$ ))

For any  $t \geq 0$  and  $r^{(0)}, r^{(t)} \in \text{SO}(3)$ , we have that  $p_{t|0}(r^{(t)}|r^{(0)}) = \text{IGSO}_3(r^{(t)}, r^{(0)}, t)$  given by  $\text{IGSO}_3(r^{(t)}, r^{(0)}, t) = f(\omega(r^{(0)\top} r^{(t)}), t)$ , where  $\omega(r)$  is the rotation angle in radians for any  $r \in \text{SO}(3)$ —in the axis-angle representation—and

$$f(\omega, t) = \sum_{\ell \in \mathbb{N}} (2\ell + 1) e^{-\ell(\ell+1)t/2} \frac{\sin((\ell + 1/2)\omega)}{\sin(\omega/2)}.$$

Accurate values of the Brownian density can easily be obtained by **truncating** the series and it allows computation of the conditional score required by the DSM loss.



## Theoretical Part Step 2: Denoising score matching on $\text{SE}(3)$

### Proposition 5 (Score on $\text{SO}(3)$ )

For  $t > 0$ ,  $r^{(0)}, r^{(t)} \in \text{SO}(3)$ , we have

$$\nabla \log p_{t|0}(r^{(t)}|r^{(0)}) = \frac{r^{(t)}}{\omega^{(t)}} \log \left\{ r^{(0,t)} \right\} \frac{\partial \omega f(\omega^{(t)}, t)}{f(\omega^{(t)}, t)},$$

with  $r^{(0,t)} = r^{(0)} r^{(t)}$ ,  $\omega^{(t)} = \omega(r^{(0,t)})$  and  $\log$  the inverse of the exponential on  $\text{SO}(3)$ , i.e., the matrix logarithm.

► **Denoising score matching on  $\mathbb{R}^3$ .**

$p_{t|0}(x^{(t)}|x^{(0)}) = \mathcal{N}(x^{(t)}; e^{-t/2}x^{(0)}, (1 - e^{-t})I_3)$  and the corresponding conditional score is

$$\nabla \log p_{t|0}(x^{(t)}|x^{(0)}) = (1 - e^{-t})^{-1}(e^{-t/2}x^{(0)} - x^{(t)}).$$

## Theoretical Part Step 3: $\text{SE}(3)$ Invariance via Centered $\text{SE}(3)^N$

No output of an  $\text{SE}(3)^N$  diffusion model can be  $\text{SE}(3)$  invariant, as no probability measure on  $\mathbb{R}^{3N}$  is  $\mathbb{R}^3$ -invariant.

### ► From $\text{SE}(3)$ to $\text{SO}(3)$ Invariance:

- Construct an invariant measure on  $\text{SE}(3)^N$  by fixing the center of mass, i.e.,  
$$\sum_{n=1}^N x_n = 0.$$
- This defines a subgroup  $\text{SE}(3)_0^N$ , with elements  $[(r_1, x_1), \dots, (r_N, x_N)]$ .
- $\text{SE}(3)_0^N$  remains a Lie group, with  $\text{SO}(3)$  as a subgroup of  $\text{SE}(3)_0^N$ .

### Proposition 6 (Disintegration of measures on $\text{SE}(3)^N$ )

Under mild assumptions, for every  $\text{SE}(3)$ -invariant measure  $\mu$  on  $\text{SE}(3)^N$ , there exist an  $\text{SO}(3)$ -invariant probability measure on  $\text{SE}(3)_0^N$  and  $\mu$  proportional to the Lebesgue measure on  $\mathbb{R}^3$  such that

$$d\mu(\{(r_i, x_i)\}_{i=1}^N) = d\mu\left(\frac{1}{N} \sum_{i=1}^N x_i\right) \times d\eta\left((r_1, x_1 - \frac{1}{N} \sum_{i=1}^N x_i), \dots, (r_N, x_N - \frac{1}{N} \sum_{i=1}^N x_i)\right).$$

## Theoretical Part Step 3: $\text{SE}(3)$ Invariance via Centered $\text{SE}(3)^N$

In order to define a  $\text{SE}(3)$ -invariant measure on  $\text{SE}(3)^N$  one needs only to **define an  $\text{SO}(3)$  invariant measure on  $\text{SO}(3)_0^N$** .

► **Diffusion models on  $\text{SE}(3)_0^N$ -Forward:**

$$d\mathbf{T}^{(t)} = \left[ 0, -\frac{1}{2}\mathbf{X}^{(t)} \right] dt + \left[ d\mathbf{B}_{\text{SO}(3)}^{(t)}, d\mathbf{B}_{\mathbb{R}^3}^{(t)} \right] \text{ (page 13)}$$

$\Downarrow$

$$d\mathbf{T}^{(t)} = \left[ 0, -\frac{1}{2}\mathbf{P}\mathbf{X}^{(t)} \right] dt + \left[ d\mathbf{B}_{\text{SO}(3)^N}^{(t)}, \mathbf{P}d\mathbf{B}_{\mathbb{R}^{3N}}^{(t)} \right],$$

$\mathbf{P} \in \mathbb{R}^{3N \times 3N}$  is the projection matrix removing the center of mass  $\frac{1}{N} \sum_{n=1}^N \mathbf{x}_n$ .

## Theoretical Part Step 3: $\text{SE}(3)$ Invariance via Centered $\text{SE}(3)^N$

► Diffusion models on  $\text{SE}(3)_0^N$ -Backward:

$$d\overleftarrow{\mathbf{X}}^{(t)} = \left\{ \frac{1}{2} \nabla U(\overleftarrow{\mathbf{X}}^{(t)}) + \nabla \log p_{T_{F-t}}(\overleftarrow{\mathbf{X}}^{(t)}) \right\} dt + d\mathbf{B}_{\mathcal{M}}^{(t)} \text{ (page 8)}$$

$\Downarrow$

$$d\overleftarrow{\mathbf{R}}^{(t)} = \nabla_r \log p_{T_{F-t}}(\overleftarrow{\mathbf{T}}^{(t)}) dt + d\mathbf{B}_{SO(3)^N}^{(t)},$$

$$d\overleftarrow{\mathbf{X}}^{(t)} = \mathbf{P} \left\{ \frac{1}{2} \overleftarrow{\mathbf{X}}^{(t)} + \nabla_x \log p_{T_{F-t}}(\overleftarrow{\mathbf{T}}^{(t)}) \right\} dt + \mathbf{P} d\mathbf{B}_{\mathbb{R}^{3N}}^{(t)}.$$

# Theoretical Part Step 3: SE(3) Invariance via Centered SE(3)<sup>N</sup>

## Proposition 7 (G-invariance and SDEs)

Let  $G$  be a Lie group and  $H$  a subgroup of  $G$ . If (a)  $X(0) \sim p_0$  for an  $H$ -invariant distribution  $p_0$  and (b)  $dX(t) = b(t, X(t))dt + \Sigma^{1/2}dB(t)$  for bounded,  $H$ -equivariant coefficients  $b$  and  $\Sigma$  satisfying  $b \circ L_h = dL_h(b)$  and  $\Sigma dL_h(\cdot) = dL_h(\Sigma)$ , and where  $B(t)$  is a Brownian motion associated with a left-invariant metric. Then for every  $t \geq 0$

- (a) the distribution  $p_t$  of  $X(t)$  is  $H$ -invariant, and
- (b) its score  $\nabla_x \log p_t(X(t))$  is  $H$ -equivariant.

## Corollary

Suppose  $\{T^{(0)}\}_{t \geq 0}$  has SO(3) invariant initial distribution  $p_0$  and evolves according to forward equation. Then for every  $t \in (0, T_F)$ ,  $\nabla \log p_{T_F-t}(\tilde{T}(t))$  is SO(3) equivariant, and the distribution of  $(\mathbf{R}(t), \mathbf{X}(t))$  implied by backward equation is SO(3)-invariant.

# Practical Part Step 1: Framework of FrameDiff

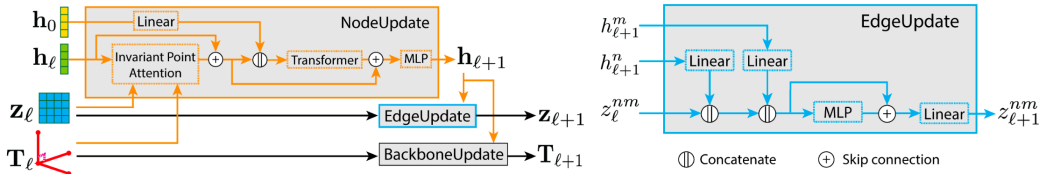


Figure 2: Framework of FrameDiff

$$(\hat{T}^{(0)}, \hat{\psi}) = \text{FramePred}(\hat{T}(t), t, \theta), \quad \hat{T}^{(0)} = (\hat{R}^{(0)}, \hat{X}^{(0)})$$

$$\nabla_{T^{(t)}} \log p_{t_0} \left( T^{(t)} \mid \hat{T}^{(0)} \right) = \left\{ \left( s_\theta^r(t, T^{(t)})_n, s_\theta^x(t, T^{(t)})_n \right) \right\}_{n=1}^N$$

$$s_\theta^r(t, T^{(t)})_n = \nabla_{R_n^{(t)}} \log p_{t_0} \left( R_n^{(t)} \mid \hat{R}_n^{(0)} \right), \quad s_\theta^x(t, T^{(t)})_n = \nabla_{X_n^{(t)}} \log p_{t_0} \left( X_n^{(t)} \mid \hat{X}_n^{(0)} \right)$$

## Practical Part Step 2: Training losses

### ► DSM losses

$$\mathcal{L}(\theta) = \mathbb{E} \left[ \lambda_t \|\nabla \log p_{t|0}(\mathbf{X}^{(t)} | \mathbf{X}^{(0)}) - s_\theta(t, \mathbf{X}^{(t)})\|^2 \right],$$

where  $\lambda_t^r = \frac{1}{\mathbb{E}} \|\nabla \log p_{t|0}(R_n^{(t)} | R^{(0)})\|_{\mathfrak{so}(3)}^2$ ,  $\lambda_t^x = \frac{1-e^{-t}}{e^{-t/2}}$  and  $\mathcal{L}_{\text{dsm}} = \mathcal{L}_{\text{dsm}}^r + \mathcal{L}_{\text{dsm}}^x$ .

### ► Auxiliary losses

$$\mathcal{L}_{\text{bb}} = \frac{1}{4N} \sum_{n=1}^N \sum_{a \in \Omega} \|a_n^{(0)} - \hat{a}_n^{(0)}\|^2.$$

$$\mathcal{L}_{2D} = \frac{1}{Z} \sum_{n,m=1}^N \sum_{a,b \in \Omega} \mathbf{1}\{d_{ab}^{nm} < 0.6\} \|d_{ab}^{nm} - \hat{d}_{ab}^{nm}\|^2$$

$$Z = \left( \sum_{n,m=1}^N \sum_{a,b \in \Omega} \mathbf{1}\{d_{ab}^{nm} < 0.6\} \right) - N.$$

$$\Rightarrow \mathcal{L} = \mathcal{L}_{\text{dsm}} + w \cdot \mathbf{1} \left\{ t \leq \frac{T_F}{4} \right\} (\mathcal{L}_{\text{bb}} + \mathcal{L}_{2D})$$

## Practical Part Step 3: Sampling procedure

- ▶ Utilize the Euler–Maruyama discretization of backward equation as a geodesic random walk.
- ▶ Sampling involves  $Z_n^x$  and  $Z_n^r$  from Gaussian distributions in tangent spaces of  $X_n^{(t)}$  and  $R_n^{(t)}$ , respectively.
- ▶ For rotations,  $\delta_i$  from  $N(0, 1)$  for orthonormal basis vectors of Lie algebra  $so(3)$  used to form  $Z_n^r = R_n^{(t)} \sum_{i=1}^3 \delta_i e_i$ , rotating into the tangent space as  $T_{R_n^{(t)}} N(0, \text{Id})$ .

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**Algorithm 1** FrameDiff sampling of protein backbones

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**Require:**  $\theta, N, T_F, N_{\text{steps}}, \zeta, \epsilon$

```
1:  $\gamma = (1 - \epsilon)/N_{\text{steps}}$ 
2: # Sample from invariant density
3:  $\mathbf{T}^{(T_F)} \sim P_{\#p_{\text{inv}}}^{\text{SE}(3)^N}$ 
4: for  $t = T_F, T_F - \gamma, T_F - 2\gamma, \dots, \epsilon$  do
5:    $\hat{\mathbf{T}}^{(0)}, _- = \text{FramePred}(\mathbf{T}^{(t)}, t; \theta)$ 
6:    $\{(s_{\theta,n}^r, s_{\theta,n}^x)\}_{n=1}^N = \nabla_{\mathbf{T}^{(t)}} \log p_{t|0}(\mathbf{T}^{(t)} \mid \hat{\mathbf{T}}^{(0)})$ 
7:   for  $(R_n^{(t)}, X_n^{(t)}) = T_1^{(t)}, \dots, T_N^{(t)}$  do
8:     # Translation tangent Gaussian
9:      $Z_n^x \sim \mathcal{N}(0, \text{Id}_3)$ 
10:     $W_n^x = P\gamma[\frac{1}{2}X_n^{(t)} + s_{\theta,n}^x] + \zeta\sqrt{\gamma}Z_n^x$ 
11:    # Remove center of mass
12:     $W_n^x = PW_n^x$ 
13:    # Rotation tangent Gaussian
14:     $Z_n^r \sim \mathcal{TN}_{R_n^{(t)}}(0, \text{Id})$ 
15:    # Euler–Maruyama step on tangent space
16:     $W_n^r = \gamma s_{\theta,n}^r + \zeta\sqrt{\gamma}Z_n^r$ 
17:     $T_n^{(t-\gamma)} = \exp_{T_n^{(t)}} \{(W_n^r, W_n^x)\}$ 
18:  end for
19: end for
20: Return:  $\text{FramePred}(\mathbf{T}^{(\epsilon)}, \epsilon; \theta)$ 
```

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# Outline

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Method

**Experiment**

Discussion

# Experiment

20312 backbones taken from the Protein Data Bank (PDB). Our model comprises 17.4 million parameters and was trained for one week on two A100 Nvidia GPUs.

- ▶ **Designability:** TM-score (**scTM**, higher is better) and C RMSD (**scRMSD**, lower is better).
- ▶ **Diversity:** The proportion of unique clusters: (number of clusters) / (number of samples).
- ▶ **Novelty:** Search for similar structures and report the highest TM-scores of samples to any chain in PDB, which they refer to as **pdbTM**.

# Experiment

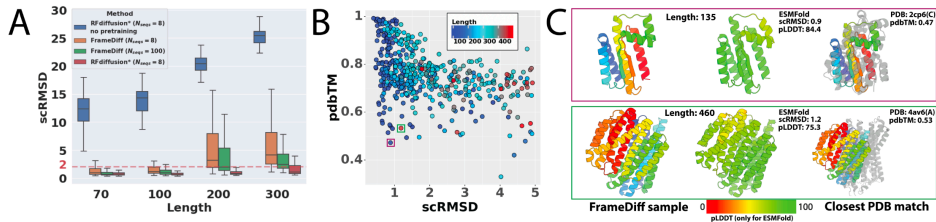


Table 1. FrameDiff sample metrics.

NOISE SCALE $\zeta$	1.0	0.5	0.1	0.1	0.1
$N_{\text{STEPS}}$	500	500	500	500	100
$N_{\text{SEQ}}$	8	8	8	100	8
$> 0.5 \text{ sCTM} (\uparrow)$	49%	74%	75%	84%	74%
$< 2\text{\AA} \text{ sCRMSD} (\uparrow)$	11%	23%	28%	40%	24%
DIVERSITY ( $\uparrow$ )	0.75	0.56	0.53	0.54	0.55

Table 2. FrameDiff ablations.

$> 0.5 \text{ sCTM} (\uparrow)$	SELF COND.	$\mathcal{L}_{2D}$	$\mathcal{L}_{bb}$	$\mathcal{L}_{dsm}$	$\mathcal{L}_F$
49%	✓	✓	✓	✓	
39%	✓	✓	✓		✓
42%		✓	✓	✓	
22%			✓	✓	
16%				✓	
0%	✓	✓	✓		

# Outline

Background

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Method

Experiment

Discussion

# Discussion

Translation and quaternion are decoupled in this line of work[\[1\]](#)[\[2\]](#)[\[3\]](#)[\[4\]](#).

- ▶ Independent treatment of rotations and translations assumes that the stochastic properties of these processes are uniform and independent across all dimensions and scenarios, this assumptions may be wild.
- ▶ In many physical and real-world systems, rotations and translations are not entirely independent; they can influence each other.
- ▶ "dual quaternions" can represent rotation and translation at the same time. Building SDE or flow matching (more popular last year) on dual quaternion manifold is interesting and meaningful.

Thank you!

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