3D Gaussian Splatting for Volume Reconstruction in Cryo-EM

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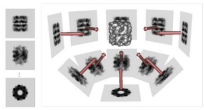
Motivation

- Accurate structural maps are fundamental to the study of molecular functions: *"Structure determines function."*
- Cryogenic electron microscopy provides 2D images, capturing the electrostatic potential of biomolecules.
- This introduces a complex inverse problem to reconstruct these discrete images into a high-resolution 3D structure.



"Cryo-electron microscopy (cryo-EM)" by Greg Pintilie, [https://people.csail.mit.edu/gdp/cryoem.html]

$$Y_i = P_{\phi_i} V_i + \eta_i$$

2D Images ← Projection — 3D Volume ← Noise

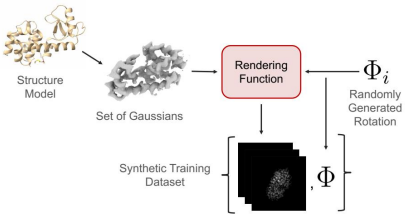
?

- This work adapts 3D Gaussian Splatting [1] from other domains to improve cryo-EM volume reconstruction, seeking enhanced resolution and computational efficiency.

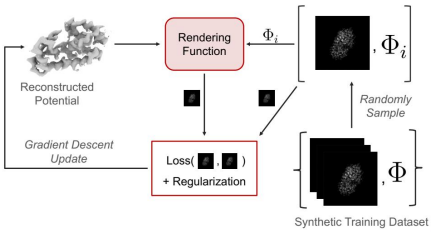
3D Gaussian Splatting

Model potential $V : \mathbb{R} \to \mathbb{R}^3$ as sum of Gaussians: $V(\boldsymbol{r}) = \sum_k \mathcal{N}(\boldsymbol{r}, \boldsymbol{\mu}_k, \Sigma_k)$

Synthetic Dataset Generation:



Reconstruction:



Related Work

Cryo-EM

- Many modern reconstruction approaches, like CryoAI [2] and CryoDRGN [3], make use of neural networks to represent electrostatic potentials. Training these networks can be computationally costly.
- Common techniques leverage the Fourier slice theorem in the Fourier domain for efficiency, thereby sacrificing interpretability of certain operations.

3D Scene Reconstruction

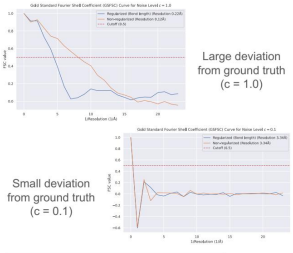
- Neural Radiance Fields (NeRFs, [4]) are a powerful technique to render complex 3D scenes with high fidelity from a neural representation.
- 3D Gaussian Splatting [1] replaces the neural representation by a set of Gaussians to significantly cut down training times compared to NeRFs.

Can strengths of 3D Gaussian Splatting be harnessed for cryo-EM reconstruction?

References

[1] Kerbl et al. "3D Gaussian Splatting for Real-Time Radiance Field Rendering", ACM Transactions on Graphics (SIGGRAPH Conference Proceedings), Volume 42, Number 4, July 2023
[2] Levy et al. "CryoAI: Amortized Inference of Poses for Ab Initio Reconstruction of 3D Molecular Volumes from Real Cryo-EM Images", European Conference on Computer Vision, 2022.
[3] Zhong et al. "CryoDRGN: reconstruction of heterogeneous cryo-EM structures using neural networks", Nature Methods, Volume 18, 2021
[4] Mildenhall et al. "NeRF: Representing Scenes as Neural Radiance Fields for View Synthesis", Communications of the ACM, Volume 65, Number 1, 2022

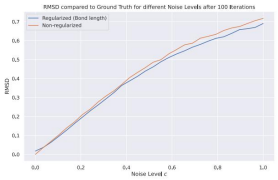
Experimental Results



Large deviation from ground truth (c = 1.0)

Small deviation from ground truth (c = 0.1)

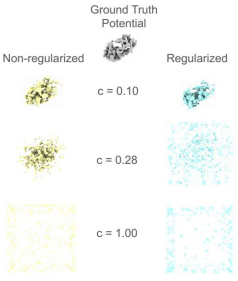
GSFSC:
1. Construct two separate electron density maps from halves of the dataset.
2. Compute the correlation between these maps across different frequencies to assess resolution.



Initialize potential as $\theta^0 \leftarrow \theta^* + c\varepsilon$

where $\varepsilon \sim N(0,1)$

Ground Truth Potential — Added Gaussian noise scaled by a factor c



How accurately does the model converge back to the actual ground truth when starting from a potential ground truth with added noise?