ProtPainter: Draw or Drag Protein via Topology-guided Diffusion

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Abstract

Recent advances in protein backbone generation have achieved promising results under structural, functional, or physical constraints. However, existing methods lack the flexibility for precise topology control, limiting navigation of the backbone space. We present **ProtPainter**, a diffusion-based approach for generating protein backbones conditioned on 3D curves. ProtPainter follows a two-stage process: curve-based sketching and sketch-guided backbone generation. For the first stage, we propose **CurveEncoder**, which predicts secondary structure annotations from a curve to parametrize sketch generation. For the second stage, the sketch guides the generative process in Denoising Diffusion Probabilistic Modeling (DDPM) to generate backbones. During this process, we further introduce a fusion scheduling scheme, Helix-Gating, to control the scaling factors. To evaluate, we propose the first benchmark for topology-conditioned protein generation, introducing Protein Restoration Task and a new metric, self-consistency Topology Fitness (scTF). Experiments demonstrate ProtPainter's ability to generate topology-fit (scTF $>$ 0.8) and designable (scTM $>$ 0.5) backbones, with drawing and dragging tasks showcasing its flexibility and versatility.

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