GCP-VQVAE: A Geometry-Complete Language for Protein 3D Structure

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Abstract

Protein structure tokenization provides a discrete interface between 3D geometry and modern learning systems, with applications in reconstruction, retrieval, and generative modeling. However, existing protein structure tokenizers are still not sufficiently accurate, robust to structural perturbations, or efficient enough for real-world use, and the field still lacks a fully open, end-to-end method that combines these properties with transparent reproducibility for the community. In this work, we introduce GCP-VQVAE, a fully open discrete protein structure tokenizer built around a chirality-aware, SE(3)-equivariant GCPNet encoder. Our design is motivated by the hypothesis that stronger geometry-aware continuous representations provide a better substrate for discrete structure tokenization.

Trained on monomer protein backbone structures from the AlphaFold Protein Structure Database, GCP-VQVAE delivers the strongest reconstruction performance among the open-source baselines evaluated in this work. For example, it attains 0.5293 Å RMSD on CASP15, reducing error by 38.5% relative to the strongest prior open baseline (AIDO), and 0.8193 Å RMSD on a zero-shot benchmark of 1,938 newly deposited experimental structures, a 59.2% improvement over the same baseline. In addition, the Large and Lite variants are approximately 408× and 530× faster SOTA, respectively, while remaining robust to structural perturbations such as rigid-body rotations and other input corruptions. To the best of our knowledge, this is the first protein structure tokenizer to release the full training pipeline, datasets, model weights, and implementation details, providing a fully transparent and reproducible foundation for the community to build on.

1 Introduction

Protein structure tokenization seeks to convert three-dimensional protein geometry into a discrete language that can interface naturally with modern learning systems. Such a representation is attractive because it can support accurate reconstruction, compact storage, efficient retrieval, and, potentially, multimodal sequence–structure modeling (Kim et al., 2023; Van Kempen et al., 2024; Hsieh et al., 2025). More broadly, discrete structural codes offer a way to bridge the continuous geometric nature of protein backbones with the scalable modeling tools that have proved effective in language, vision, and other domains (Ruff et al., 2022; Kilgore et al., 2025; Weissenow & Rost, 2025).

Despite recent progress in protein generative modeling and structure-aware representation learning, effective tokenization of protein 3D structure remains an open problem (Draizen et al., 2024; Lu et al., 2025; Yuan et al., 2025b). Existing approaches still face several practical limitations: reconstruction accuracy is often insufficient for high-fidelity use, robustness to structural perturbations remains underexplored, and inference efficiency can be prohibitive for real-world deployment. At the same time, many protein structure tokenizers are closed-source or only partially released, which limits reproducibility and makes rigorous comparison difficult for the broader research community (Gao et al., 2024c; Hayes et al., 2025). As a result, the field still lacks a fully open, end-to-end protein structure tokenizer that is accurate, robust, efficient, and easy to reproduce.

A central question in protein structure tokenization is how to encode geometric information before discretization. Since token quality ultimately depends on the quality of the underlying continuous representation, a natural

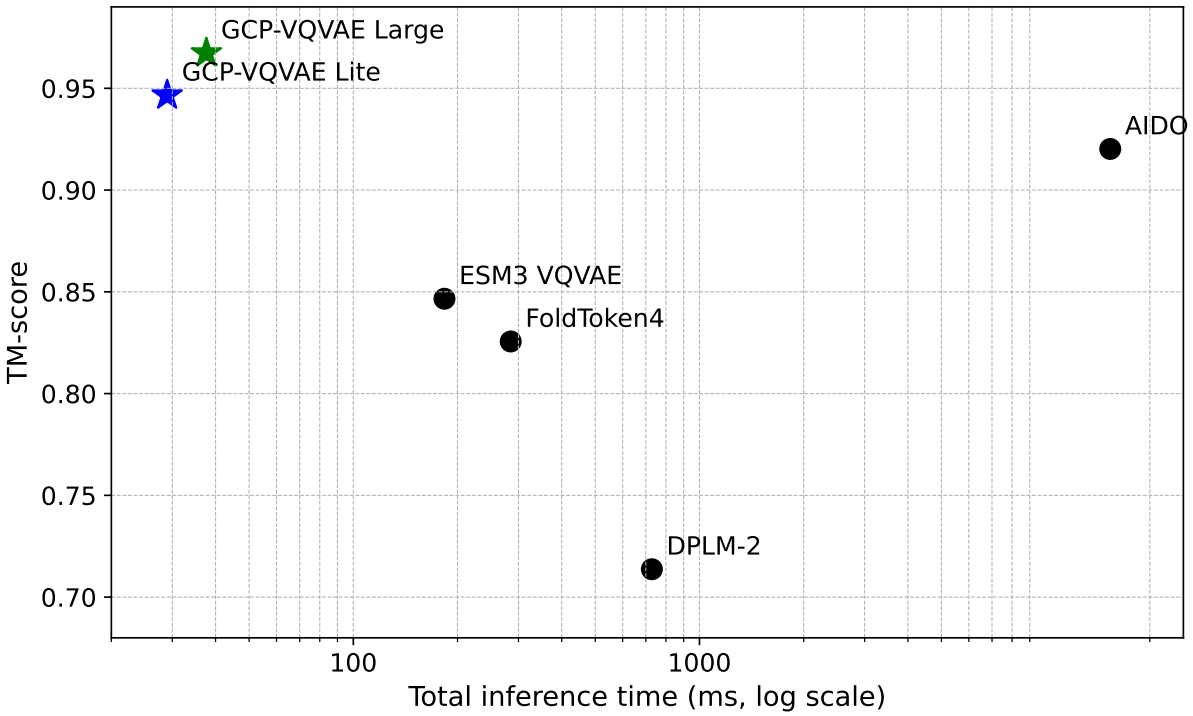
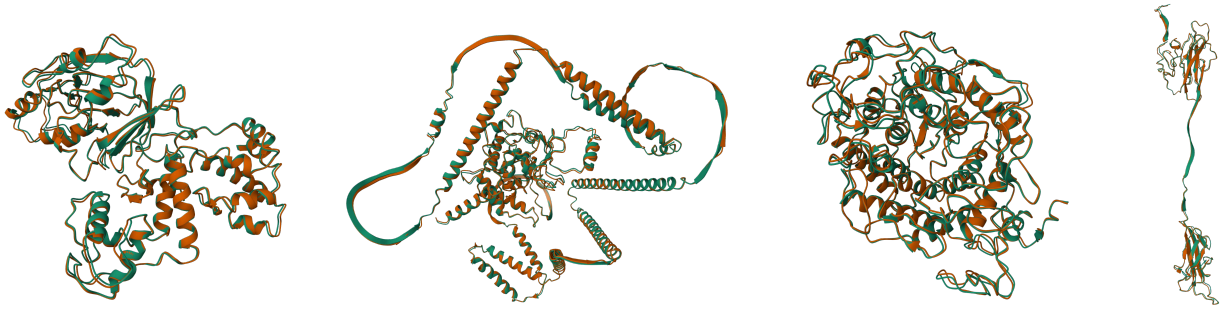


Figure 1: **Speed–quality trade-off for discrete protein structure tokenizers.** We plot total end-to-end inference time against TM-score on the zero-shot benchmark for sequence length 1024.

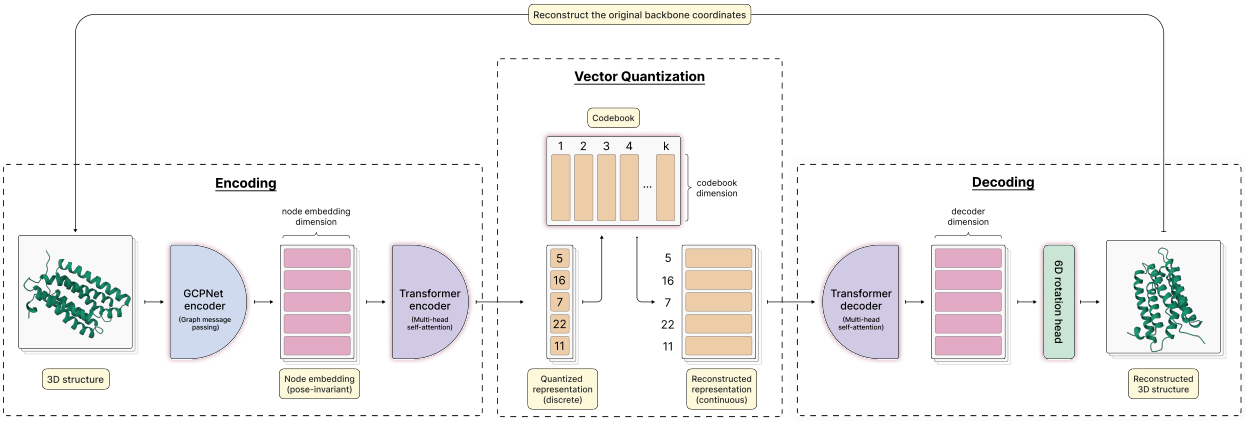
design principle is to begin with a strong geometry-aware encoder and then learn a discrete codebook over its representations. Motivated by this view, we build on GCPNet, a geometry-complete SE(3)-equivariant graph neural network that preserves directional and chiral information through local edge frames (Morehead & Cheng, 2024b). Prior work has shown that this class of architecture is highly effective for protein structure representation learning, suggesting that stronger continuous geometric representations may provide a better substrate for discrete structure tokenization. In this work, we therefore adopt a chirality-aware GCPNet encoder as the front-end of our tokenizer and pair it with vector quantization and transformer-based decoding for protein backbone reconstruction.

Our goal is not to propose a new geometric encoder from scratch, but to develop a fully open and transparent protein structure tokenizer that is strong enough to serve as a practical foundation for future research. To this end, we train GCP-VQVAE at scale on monomer protein backbones from the AlphaFold Protein Structure Database and evaluate it across standard external benchmarks, newly deposited experimental structures, robustness tests under structural perturbations, and inference-efficiency comparisons. This framing allows us to study whether a geometry-complete, chirality-aware encoder can improve discrete protein structure tokenization in practice, while also providing the community with a reproducible system whose data, models, and evaluation pipeline are openly available.

Contributions. (1) We introduce GCP-VQVAE, a fully open protein structure tokenizer that couples a chirality-aware, geometry-complete GCPNet encoder with vector quantization and transformer-based backbone reconstruction. (2) We scale training to 24M monomer structures from the AlphaFold Protein Structure Database and conduct extensive evaluation across CAMEO2024, CASP14/15/16, and a zero-shot benchmark of newly deposited experimental structures. (3) GCP-VQVAE achieves the strongest reconstruction performance among the open-source baselines considered in this work, including 0.8193 Å backbone RMSD and 0.9673 TM-score on the zero-shot benchmark, while consistently outperforming prior open-source methods on unseen proteins. (4) We evaluate practical deployment properties of GCP-VQVAE through end-to-end



(A) **Superposition of GCP-VQVAE Large reconstructions (orange) with native structures (green) for four long, held-out backbone coordinates of proteins.** Left→right: T1079 (CASP14; 482 residues; TM-score 0.9909; RMSD 0.7533 Å), T2272S8 (CASP16; 818 residues; TM-score 0.9967; RMSD 0.5639 Å), T1157s1-D1 (CASP15; 661 residues; TM-score 0.9920; RMSD 0.8172 Å), and 8BQU, chain A (CAMEO2024; 298 residues; TM-score 0.9764; RMSD 0.9981 Å).



(B) **GCP-VQVAE overview.** A protein backbone (N–C_α–C) is first encoded by a SE(3)-equivariant GCPNet that preserves orientation and chirality. A transformer encoder produces latents that are vector-quantized into a sequence of code indices from a 4 096-entry codebook (e.g., 5, 16, 7, 22, 11), yielding pose-invariant discrete tokens. For reconstruction, the indices are de-quantized to continuous embeddings and passed to a transformer decoder equipped with a 6-D rotation head, which predicts rigid updates to recover the original backbone coordinates.

Figure 2: Qualitative reconstructions (A) and an overview of the GCP-VQVAE architecture (B).

inference latency across sequence lengths and reconstruction robustness under structural perturbations and partial-structure inputs. (5) Following Yuan et al. (2025b), we assess the quality of the learned continuous protein structure representations using probes of varying complexity to study how readily task-relevant information can be extracted for downstream supervised tasks. (6) We release the full training pipeline, datasets, model weights, and implementation details to provide a transparent and reproducible benchmark for the community.

2 Related Work

An early and influential approach to casting protein 3D structure as a discrete language is FoldSeek van Kempen et al. (2022), which learns a 20-state 3Di alphabet with a VQ-VAE trained for evolutionary conservation and encodes structures as token sequences for ultra-fast k-mer–based local/global alignment. Building on the notion of a discrete structural language—but targeting generative reconstruction rather than search—the FoldToken series (Gao et al., 2025; 2024a;b;c) develops a VQ-VAE–style tokenizer and decoder: FoldToken introduces a SoftCVQ fold language with joint sequence–structure generation; FoldToken2 stabilizes quantization and extends to multi-chain settings; FoldToken3 mitigates gradient/class-space issues to reach

256-token compression with minimal loss; and FoldToken4 unifies cross-scale consistency and hierarchies in a single model, reducing redundant multi-scale training and code storage.

Yuan et al. (2025b) introduces AminoAseed codebook reparameterization plus Pareto-optimal K×D sizing, proposes structtokenbench—a fine-grained evaluation suite—and diagnoses codebook under-utilization in VQVAE PSTs. Concurrently, Gaujac et al. (2024) tokenizes protein backbones with a VQ autoencoder (codebooks 4k–64k); its main open-source limitation is that it does not support sequences shorter than 50 or longer than 512 amino acids.

ESM-3 (Hayes et al., 2025) couples its multimodal transformer with a VQVAE structure tokenizer that discretizes local 3D geometry into structure tokens; structure, sequence, and function are jointly trained under a masked-token objective. The tokenizer uses an SE(3)-aware module within the encoder, and ESM-3 employs a 4 096-code structure codebook (plus special tokens) for downstream generation and masked reconstruction.

Across prior structure tokenizers, neither openness nor accuracy are yet satisfactory. The FoldToken line spans four variants, but to our knowledge, only FoldToken-4 offers a partial open release, without the strongest checkpoints, limiting reproducibility (Gao et al., 2024c). ESM-3 exposes an internal VQ-VAE tokenizer, yet public artifacts lack fully documented training/evaluation procedures and best weights, making directly comparable reconstruction benchmarking difficult (Hayes et al., 2025). The open VQ autoencoder of Gaujac et al. (2024) supports a restricted length window (e.g., ∼50–512 residues), precluding fair assessment on long chains where reconstruction accuracy degradation is most evident. Finally, FoldSeek's learned 3Di alphabet targets ultra-fast structure search and does not provide a generative decoder from discrete codes back to coordinates, so reconstruction fidelity cannot be evaluated (van Kempen et al., 2022). Consequently, the community still lacks a fully open, end-to-end tokenizer with released best weights and source codes that attains high reconstruction accuracy on *unseen* proteins.

3 GCP-VQVAE Architecture

Our design starts from the hypothesis that high-quality protein structure tokenization depends critically on the quality of the underlying geometric representation. Rather than proposing a new graph encoder from scratch, we build on GCPNet, a geometry-complete SE(3)-equivariant architecture whose original work showed strong protein-structure representation learning performance and explicit preservation of directional and chiral information. We therefore use GCPNet as a principled front-end for structure tokenization, with the expectation that better continuous geometric representations should yield better discrete structural codes. The resulting model couples (i) a geometry-complete SE(3)-equivariant GCPNet encoder that maps protein backbone coordinates (N–C_α–C) to per-residue embeddings, with (ii) a transformer-based VQVAE that discretizes these embeddings into pose-invariant code indices and reconstructs the backbone in 3D. In this work, our primary question is whether this encoder choice improves structure tokenization quality, which we evaluate mainly through reconstruction fidelity and robustness to structural corruption. An overview is shown in Figure 2B; full architectural details are provided in Appendix A.

3.1 GCPNet Encoder

We adopt GCPNet (Morehead & Cheng, 2024b) as the geometric front-end because it performs scalar–vector message passing while explicitly preserving orientation and chirality via local edge frames, yielding SE(3)-equivariant backbone representations. Our motivation is that a stronger geometry-aware continuous representation should provide a better substrate for vector quantization and, in turn, for protein structure tokenization. We use the final node embeddings as the continuous input sequence to the VQVAE (Appendix A.1).

3.2 VQVAE

The VQVAE follows the standard *encoder* → *vector quantization* → *decoder* pipeline: a transformer encoder produces latent vectors $\mathbf{z}$, which are mapped to the nearest codebook entry $\mathbf{e}_k$ (discrete index k), and a transformer decoder maps the de-quantized embeddings back to structure. To generate coordinates, the

Table 1: **Dataset and benchmark statistics.** Training data is deduplicated at 100% sequence identity against all validation/test splits and external benchmarks (CAMEO2024, CASP14–16). We also include a zero-shot set of 1 938 newly deposited experimental monomer chains (PDB, 2024–2025).

Split	Source	Selection criterion	# Samples
Training (Large)	AFDB ∩ UniRef50	Uniform random sample from ∼42M pool	24 000 000
Training (Lite)	AFDB	Cluster representatives (`afdb_rep_v4`)	2 200 000
Validation	From Tests A/B/C	2k random per test (A,B,C) merged	6 000
Test set A	PDB DB	cross-referenced AF pLDDT ≤ 70; len ≥ 25; < 25 consecutive missing residues; dedup	31 112
Test set B	AFDB	97 species; ∼2.5k/species; len ≥ 25; dedup	17 353
Test set C	PDB DB	under-represented taxonomies in SwissProt; pLDDT ≥ 95; < 25 consecutive missing residues; dedup	31 867
Zero-shot (experimental)	PDB DB	recent experimental monomers (2024–2025); len 25–2048; dedup; $< 50\%$ seq id vs train	1 938
CAMEO2024	CAMEO	-	574
CASP14	CASP	-	33
CASP15	CASP	-	45
CASP16	AF3 predictions	-	104

decoder is equipped with a 6D rotation head (Zhou et al., 2019) that predicts rigid updates and applies them to a fixed local backbone template (Appendix A.2).

3.3 Training objective

We supervise reconstruction with a weighted sum of pose-invariant geometric losses. We first align the ground-truth backbone to the prediction using Kabsch alignment (proper rotation + translation; no reflections), and then compute an aligned MSE term, a backbone distance-matrix loss, and a pose-invariant *relative* direction/orientation loss. The latter matches internal backbone directions and plane normals by comparing their pairwise dot products, and is therefore invariant to global rigid transformations:

$$\mathcal{L}_{\text{rec}} \;=\; \lambda_{\text{mse}}\,\mathcal{L}_{\text{MSE}} + \lambda_{\text{dist}}\,\mathcal{L}_{\text{dist}} + \lambda_{\text{dir}}\,\mathcal{L}_{\text{dir}}. \tag{1}$$

The full objective adds standard VQ codebook and commitment losses (Van Den Oord et al., 2017), regularized to encourage diverse code usage and orthogonality:

$$\mathcal{L} = \mathcal{L}_{\text{rec}} + \mathcal{L}_{\text{code}} + \lambda_{\text{commit}}(\,\mathcal{L}_{\text{commit}} + \lambda_{\text{orth}}\,\mathcal{L}_{\text{orth}}), \tag{2}$$

with implementation details deferred to Appendix A.2.

4 Dataset

We began with the latest release of UniRef50 (Consortium, 2019) [1], which clusters protein sequences at 50% identity and thus offers a natural, non-redundant scaffold for large-scale structure modeling. For every UniRef50 entry with a corresponding model in the AlphaFold Database (AFDB; Varadi et al. (2022)), we downloaded the per-protein structure (PDB format at collection time). Limiting to UniRef50 reduces near-duplicate leakage by ensuring that homologs within clusters do not exceed 50% identity. After parsing and splitting multi-chain records into individual chains, this procedure yielded approximately 42M single-chain PDB samples.

From this AFDB ∩ UniRef50 pool, we drew a uniform random sample of 24M single-chain structures to form the training set. This down-sampling keeps training throughput tractable while preserving the global distribution of lengths, folds, and taxa present in the full pool. To support our lightweight model variant, we also employed the `afdb_rep_v4` dataset (Jamasb et al., 2024), which contains approximately 2.2 million cluster-representative structures, serving as a data-efficient alternative to the full training corpus.

We evaluate on three held-out test suites capturing complementary shifts (see Table 1): *A* low-confidence AF2 SwissProt models, *B* species-diverse (97-species) taxonomic shift, and *C* high-confidence structures from under-represented taxa. All suites are per-chain, length-filtered, deduplicated, and NaN-aware; a balanced validation set of 6 000 chains (2k per suite) is sampled disjointly. Full curation criteria, thresholds, and counts are provided in Appendix B .

[1] March 2024 release.

To probe generalization to genuinely new structures, we assembled a zero-shot suite from *recently deposited experimental* monomeric chains in the PDB (calendar years 2024–2025). Multi-chain entries were split into per-chain backbones, chains shorter than 25 residues or longer than 2 048 residues were discarded, and we retained entries even when they contained missing coordinates (`NaN`) to reflect typical experimental gaps, yielding 76 503 pdbs in total. We deduplicated using structural clustering with FoldSeek `easy-cluster` (alignment type 2, tmscore threshold 0.80, cov-mode 0, lddt-threshold 0.65), retaining one representative per cluster. This resulted in 10 689 clusters (van Kempen et al., 2022). For leakage control, each representative was compared with foldseek `easy-search` against (i) the AFDB ∩ UniRef50 set used for our GCP-VQVAE Large model training and (ii) the `afdb_rep_v4` (Barrio-Hernandez et al., 2023) representative set used to pre-train the GCPNet encoder in ProteinWorkshop (Jamasb et al., 2024) and training the GCP-VQVAE Lite model. We *excluded* any candidate with $\geq 50\%$ structure similarity to any chain in those sources; the resulting zero-shot set comprises 1 938 monomer chains.

Independent benchmarks. In addition to the internal splits, we evaluate on community benchmarks to facilitate comparison with prior work: CAMEO2024 (Robin et al., 2021; Leemann et al., 2023), CASP14 (Kryshtafovych et al., 2021), CASP15 (Kryshtafovych et al., 2023), and AlphaFold3 (Abramson et al., 2024) predictions for CASP16 (Yuan et al., 2025a) targets. Each benchmark is processed with the same per-chain extraction and deduplication pipeline and is used strictly for out-of-distribution evaluation.

Table 1 summarizes the composition and selection criteria of all splits. Counts after converting multi-chain inputs into per-chain samples. Also, all samples are truncated to a maximum of 2 048 amino acids in length.

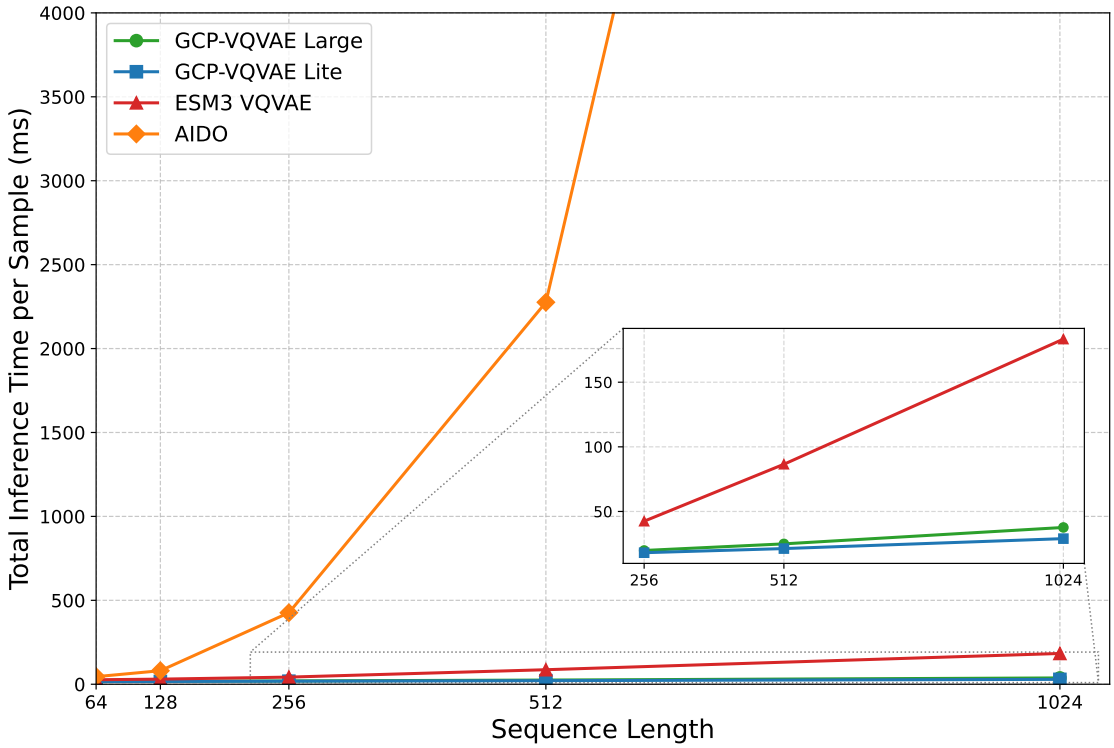


Figure 3: **End-to-end inference time per protein (ms) as a function of sequence length for GCP-VQVAE (Large/Lite) and top-performing open baselines (ESM3 VQVAE, AIDO).** The inset highlights the long-sequence regime (256–1024 residues).

5 Experiments

In this section, optimization is used with AdamW (Loshchilov, 2017) and a cosine-annealed learning-rate schedule with warm-up steps (Loshchilov & Hutter, 2016). Experiments were implemented in PyTorch 2.7 (Ansel et al., 2024) [2] with mixed-precision (BF16) training (Kalamkar et al., 2019; Micikevicius et al., 2017) on four nodes of NVIDIA 8 × A100 GPUs. For the GCPNet encoder, we initialized from the ProteinWorkshop checkpoint (Jamasb et al., 2024). Both light and large GCP-VQVAE configurations and exact hyperparameter values are listed in Appendix C; Table 9 and 10.

For the GCP-VQVAE Lite variant, we employed the `afdb_rep_v4` dataset from the ProteinWorkshop benchmark (Jamasb et al., 2024), which consists of approximately 2.27 million representative AlphaFold structures. This roughly 10-fold reduction in training data relative to our primary model allows us to demonstrate the architectural efficiency and robust performance of GCP-VQVAE even under significantly reduced computational budgets.

Table 2: **Reconstruction comparison with the available open-source structure tokenizer methods.** FoldToken-4, AminoAseed, and DPLM-2 use 256, 512, and 8 192 vocab sizes, respectively. Other methods use 4 096 vocab size. The Structure Tokenizer of Gaujac et al. (2024) only supports sequences of length 50–512. For AIDO, sequences longer than 1 024 are omitted due to OOM.

Dataset	**Metric**	**GCP-VQVAE Large (Ours)**	**GCP-VQVAE Lite (Ours)**	**AIDO** (Zhang et al., 2024)	**ESM-3 VQVAE** (Hayes et al., 2025)	**DPLM-2 VQVAE** (Wang et al., 2024b)	**FoldToken 4** (Gao et al., 2024c)	(Gaujac et al., 2024)	**AminoAseed** (Yuan et al., 2025b)
CASP14	TM-score ↑	**0.9890**	0.9751	0.9831	0.9734	0.9056	0.8989	0.8940	0.3951
	RMSD ↓	**0.5431**	0.8435	0.6587	1.0968	2.0896	2.0027	1.8913	14.6739
CASP15	TM-score ↑	**0.9884**	0.9665	0.9660	0.9418	0.8268	0.9136	0.7911	0.3831
	RMSD ↓	**0.5293**	0.9219	0.8611	1.3407	6.3826	1.6856	8.5592	18.5827
CASP16	TM-score ↑	**0.9857**	0.9757	0.8805	0.9103	0.7852	0.8211	0.8345	0.3433
	RMSD ↓	**0.7567**	1.0614	4.9773	4.4918	14.1934	5.4115	6.9375	25.9508
CAMEO2024	TM-score ↑	**0.9918**	0.9794	0.9851	0.9736	0.9243	0.9346	0.9114	0.4632
	RMSD ↓	**0.4377**	0.7401	0.5867	1.0156	1.941	1.4069	2.1726	12.6203
Zero-Shot	TM-score ↑	**0.9673**	0.9466	0.9202	0.8466	0.7137	0.8256	0.7662	0.4155
	RMSD ↓	**0.8193**	1.1152	2.0105	6.5075	12.2182	4.5465	10.4405	19.2612
Average	TM-score ↑	**0.9844**	0.9687	0.9470	0.9291	0.8311	0.8788	0.8394	0.4000
	RMSD ↓	**0.6172**	0.9364	1.8189	2.8905	7.3650	3.0106	6.0002	18.2178

Training of the large model proceeded in two stages on the same training split. In Stage 1, sequences are truncated to 512 residues. In Stage 2, the maximum length is increased to 1 280 residues. In Stage 2, we also introduce a simple `NaN`-masking augmentation to handle missing coordinates; implementation details are provided in Appendix C (Figure 6). At the end of Stage 2 training, on the validation set, the model attains MAE 0.2239, RMSD 0.4281, GDT-TS 0.9856, and TM-score 0.9889 with 100% codebook utilization. Similarly, the training of the lite model proceeded by one stage only with 1 280 residues. On the validation set, the model attains MAE 0.3961, RMSD 0.5707, GDT-TS 0.9327, and TM-score 0.9741 with 100% codebook utilization. Per-test-set result of the large model appears in Table 3.

Table 3: Evaluating GCP-VQVAE large on the predefined test sets.

Method	**Test set A**	**Test set B**	**Test set C**
RMSD ↓	0.5124	0.4027	0.4787
TM-score ↑	0.9823	0.9951	0.9885

Figure 3 compares end-to-end inference latency across sequence lengths measured on a Nvidia A6000 Ada GPU, showing that GCP-VQVAE scales efficiently to long proteins relative to open baselines; full benchmarking details are provided in Appendix C.2.

To quantify the contribution of each decoder reconstruction term, we performed a small ablation study over the aligned MSE ($\mathcal{L}_{\text{MSE}}$), distance-matrix ($\mathcal{L}_{\text{dist}}$), and direction/orientation ($\mathcal{L}_{\text{dir}}$) losses. All ablations were trained with the GCP-VQVAE Lite architecture on 100k randomly sampled training structures for 32 epochs, using a maximum sequence length of 512 residues. Table 4 reports reconstruction quality under different loss combinations.

[2] We built the VQVAE components extensively by using the x-transformers and vector-quantize-pytorch libraries.

Table 4: Ablation of reconstruction losses and their impact on backbone reconstruction quality.

Reconstruction losses			Metrics		
$\mathcal{L}_{\text{MSE}}$	$\mathcal{L}_{\text{dist}}$	$\mathcal{L}_{\text{dir}}$	RMSD ↓	TM-score ↑	GDT-TS ↑
✓	✓	✓	1.1071	0.8968	0.8071
✓	✓	✗	1.1851	0.8786	0.7789
✓	✗	✓	1.2718	0.8686	0.7307
✓	✗	✗	1.5227	0.8082	0.6421
✗	✓	✓	14.3828	0.1106	0.0144

We compared against open-source structure tokenizers. Among them, in practice, ESM-3 does not provide documented usage or official evaluation scripts for its VQ-VAE; we therefore reproduced its evaluation using the publicly released weights and their GitHub codebase. The original FoldToken-4 evaluation repository was prohibitively slow, so we re-implemented it, yielding a $\sim$20$\times$ speed-up with negligible loss in reconstruction rate. For all other baselines, we relied on the officially released implementations and corresponding checkpoints. See Table 2 for aggregate metrics; Figure 5 visualizes the full RMSD error across test sets.

We examined how reconstruction error varies with sequence length on the validation set (Appendix C; Figure 7). Errors increase only mildly with length, indicating stable accuracy up to 1 280 residues with only a slight variance rise for very long chains. On the zero-shot set we obtain mean RMSD 0.8193 Å and TM-score 0.9673 (Table 2), with group-wise trends summarized in Table 5; extended zero-shot analyses (Figure 9 to 15) appear in Appendix C.1.

We additionally evaluate reconstruction robustness under coordinate perturbations and partial-structure inputs, reporting ΔRMSD degradation relative to clean reconstructions in Appendix C.3.

Table 5: **Metrics by structure group on the zero-shot dataset with respect to the GCP-VQVAE Large.** Groups are defined by secondary-structure composition thresholds and are not mutually exclusive. Thresholds of each group are described in Appendix B

Group	Count	RMSD ↓	TM-score ↑
All rows	1938	0.8193	0.9673
A (mainly α)	776	0.7537	0.9707
B (mainly β)	309	0.7635	0.9762
AB (mixed)	71	0.6166	0.9878
D (coil-rich/disordered)	552	0.9476	0.9498
No-NaN residues	1231	0.6179	0.9755
Has-NaN residues ($\geq$1)	707	1.1699	0.9531

5.1 Codebook Evaluation

Table 6: Comprehensive codebook analysis comparing structure tokenization methods on the zero-shot test set.

			Unigram Statistics			Zipf Fit		Conditional Stats			Mutual Info (bits)	
Model	**Vocab**	**Util. ↑**	H_1	PPL	Usage	Slope (b)	R^2	$H(Z_t\|Z_{t-1})$	$H(Z_t\|Z_{t-2}, Z_{t-1})$	Tri PPL	$I(Z_t; Z_{t+1})$	$I(Z_t; Z_{t+4})$
GCP-VQVAE (Lite)	4096	99.8%	9.266	615.8	15.1%	−1.390	0.954	7.309	2.095	4.27	1.958	1.954
GCP-VQVAE (Large)	4096	**100%**	11.326	2567.6	62.7%	−0.804	0.844	7.247	0.232	1.17	4.082	4.104
ESM3 VQVAE	4096	95.2%	11.269	2467.0	60.2%	−0.750	0.665	6.924	0.549	1.46	4.346	4.359
AIDO	512	**100%**	8.967	500.3	97.7%	−0.197	0.744	8.310	1.316	2.49	0.656	0.732
DPLM-2	8192	94.7%	12.250	4872.3	62.8%	−0.987	0.647	6.341	0.215	1.16	5.910	5.905
FoldToken	256	**100%**	7.649	200.7	78.4%	−0.696	0.735	3.731	3.313	9.94	3.916	2.097
(Gaujac et al., 2024)	4096	58.8%	10.700	1662.9	69.1%	−0.991	0.553	7.149	0.280	1.21	3.548	3.670

We analyzed the distribution and informational properties of the learned discrete codes on the zero-shot test set (Table 6). GCP-VQVAE demonstrates superior codebook efficiency, achieving 100% utilization of its vocabulary. In terms of structural grammar, the Large model exhibits a transition from high unigram entropy ($H_1 = 11.3$ bits) to extremely low conditional trigram entropy (≈ 0.23 bits). This sharp drop implies that the model has learned a highly structured *syntax* for protein coordinates, where local dependencies (likely corresponding to secondary structure constraints) make token sequences highly predictable locally, similar to DPLM-2 and ESM3 models.

Geometrically, the reconstructed backbone dihedrals closely imitate the original distribution, validating the decoder's precision. However, the observation (Appendix Figure 17) that individual top codes often span multiple Ramachandran regions suggests that tokens are not uniquely tied to narrow geometries but cover broader conformational modes, likely relying on sequence context for disambiguation (Appendix C.5). This interpretation is also supported by the codebook statistics in Table 6, whose entropy and mutual-information trends indicate that token usage is structured and context-dependent rather than purely local.

5.2 Representation Evaluation

Beyond coordinate reconstruction, we evaluate the semantic quality of the learned latent space using PST benchmark (Yuan et al., 2025b). Following PST, we extract continuous (de-quantized) embeddings from our codebook and assess how well they support downstream prediction under frozen encoder settings. Since the measured utility of a representation can depend on the capacity of the evaluation head, we report results in Table 8 using three probe families: the PST-standard two-layer MLP, a stronger four-layer MLP probe, and a lightweight context-aware probe consisting of a single transformer block with the same MLP dimension.

Table 8 indicates that, under the PST-standard probe, our continuous embeddings capture non-trivial functional and physicochemical signals but remain behind sequence- and function-trained baselines on several functional-site tasks, particularly on harder SupFam splits. Notably, increasing probe expressiveness substantially narrows this gap: both the deeper MLP and the single-block transformer yield large gains, and the transformer probe produces the strongest overall results for both model sizes. This suggests that a significant portion of the task-relevant information is present in the learned latent space but is more readily extracted when the evaluation head can perform limited contextual aggregation across residues. Interestingly, despite weaker reconstruction fidelity, the Lite variant can match or slightly exceed the Large model under stronger probes, further supporting the view that reconstruction accuracy and downstream extractability are not strictly coupled.

For unsupervised conformational benchmarks (Table 7), our model achieves the best Apo–Holo correlations among the compared structure tokenizers, highlighting that the learned representations capture meaningful structural variation across conformational states. This suggests that our representation is particularly well-suited for applications demanding fine-grained structural discrimination rather than broad functional categorization. On fold-switching, our results remain competitive but trail the strongest baseline.

Table 7: Performance on unsupervised Apo Holo and Fold Switching benchmarks.

Model	**Apo Holo**		**Fold Switching**	
	PCC% ↑	**Spearman's ρ% ↑**	**PCC% ↑**	**Spearman's ρ% ↑**
ProteinMPNN	35.80	45.22	51.46	55.91
MIF	35.82	43.55	54.48	59.27
FoldSeek	34.79	43.03	51.88	56.54
ProTokens	43.32	54.05	61.20	65.90
ESM3	39.76	50.97	57.12	62.23
VanillaVQ	39.62	50.61	56.51	61.51
AIDO	43.02	54.25	<u>61.59</u>	66.11
AminoAseed	42.47	54.88	**65.61**	**75.89**
Our model (lite)	<u>48.56</u>	<u>59.33</u>	61.11	<u>73.94</u>
Our model (large)	**48.16**	**59.84**	59.63	72.33

6 Discussion and Future Work

GCP-VQVAE delivers consistently high-fidelity reconstruction across diverse benchmark suites, with sub-angstrom error on standard external evaluations and similarly strong behavior on our internal splits (Figure 2A). Relative to the strongest prior open baseline, it substantially improves reconstruction quality while also offering a dramatically better speed–accuracy trade-off: compared with AIDO (Zhang et al., 2024), GCP-VQVAE reduces reconstruction error by a large margin on challenging unseen-protein evaluations and accelerates

Table 8: **Protein Structure Tokenization benchmark across supervised Functional Site Prediction tasks.** We report the two additional probes in parentheses (four-layer MLP, single-block transformer).

		VQ-VAE-based PST						Ours	
Task	**Split**	**Fold Seek**	**Pro Tokens**	**VanillaVQ**	**AIDO**	**ESM3**	**AminoAseed**	**Our Model (Large)**	**Our Model (Lite)**
Functional Site Prediction (AUROC% ↑)									
BindInt	Fold	53.18	44.66	47.25	44.66	44.30	47.11	52.61 (50.26, 52.78)	49.43 (49.0, **55.03**)
	SupFam	46.20	86.05	86.71	84.21	**90.77**	90.53	58.04 (70.61, 80.67)	62.27 (70.27, 80.77)
BindBio	Fold	52.37	58.47	62.02	65.50	62.84	65.73	75.05 (92.74, 84.01)	80.93 (**94.61**, 91.74)
	SupFam	52.41	60.47	62.92	66.70	65.22	68.30	75.64 (93.4, 86.62)	81.72 (**94.08**, 90.08)
BindShake	Org	53.40	59.82	67.04	69.28	66.10	69.61	66.97 (67.96, **72.71**)	66.34 (67.11, 68.08)
CatInt	Fold	53.43	58.16	58.89	57.30	61.09	**62.19**	55.92 (53.15, 60.67)	54.36 (55.49, 58.09)
	SupFam	51.41	83.85	85.00	81.94	89.82	**91.91**	63.22 (73.43, 84)	62.24 (68.88, 85.18)
CatBio	Fold	56.37	56.14	67.58	73.72	65.33	65.95	67.12 (79.66, 71.64)	67.25 (**92.28**, 86.11)
	SupFam	53.78	64.05	70.92	78.66	74.65	87.59	73.77 (89.64, 86.95)	75.57 (**95.72**, 93.38)
Con	Fold	49.26	56.23	56.98	56.64	55.22	57.23	52.64 (53.29, **62.97**)	51.15 (51.56, 61.52)
	SupFam	51.39	74.33	74.60	73.79	80.53	**86.60**	61.31 (68.84, 84.05)	58.66 (65.23, 85.79)
Rep	Fold	47.70	**77.25**	75.99	77.69	74.70	74.97	51.19 (50.95, 66.19)	52.04 (52.79, 61.22)
	SupFam	52.53	78.90	82.09	78.08	82.36	84.57	54.17 (65.26, 85.77)	56.5 (54.65, **85.94**)
Ept	Fold	54.52	54.69	59.28	60.26	**63.69**	62.16	54.24 (54.21, 58.19)	53.05 (54.63, 56.89)
	SupFam	50.56	67.52	67.24	72.30	61.97	**72.02**	55.91 (58.03, 66.31)	56.13 (58.25, 64.09)
Average AUROC%		51.90	65.37	68.30	69.38	69.24	72.43	61.19 (68.09, 73.57)	61.84 (68.3, **74.92**)
Physicochemical Property Prediction (Spearman's ρ% ↑)									
FlexRMSF	Fold	15.35	13.81	44.22	33.15	44.53	**44.63**	18.05 (20.04, 24.37)	24.71 (29.08, 23.79)
	SupFam	11.99	7.62	39.08	26.93	39.68	**40.99**	20.37 (21.21, 38.89)	25.67 (28.03, 30.52)
FlexBFactor	Fold	4.17	6.67	22.32	18.88	23.60	21.30	13.66 (14.88, 18.87)	16.95 (15.79, **26.22**)
	SupFam	6.97	5.47	23.73	19.31	**25.80**	21.76	15.85 (15.4, 11.87)	17.52 (17.82, 20.38)
FlexNEQ	Fold	5.71	12.98	35.95	16.41	45.08	**49.64**	15.41 (17.13, 17.37)	18.68 (21.43, 18.95)
	SupFam	2.60	12.50	35.61	16.17	45.43	**50.15**	16.31 (18.33, 16.82)	21.51 (24.22, 23.48)
Average Spearman's ρ%		7.80	9.84	33.49	21.81	37.35	**38.08**	16.61 (17.89, 21.36)	20.84 (22.73, 23.89)

inference by over two orders of magnitude for both the Large and Lite variants. These gains are achieved while maintaining robustness to structural perturbations and corrupted inputs (Appendix Figure 16).

On the zero-shot benchmark of newly deposited experimental monomers, the model continues to generalize strongly beyond the training distribution. Our analysis suggests that performance degradation is driven primarily by missing-coordinate burden, and secondarily by sequence length, which is consistent with the trends observed on the validation set (Appendix Figures 10, 11, and 9). Consistent with this interpretation, proteins without missing residues are reconstructed more accurately than those containing gaps (Table 5).

Comparing reconstruction and representation trends across tokenizers (Tables 2 and 8), we observe that high reconstruction accuracy does not necessarily imply superior downstream representation quality. For example, AminoAseed exhibits strong downstream performance yet very poor reconstruction, whereas our Large model achieves state-of-the-art reconstruction while the Lite model can yield stronger supervised transfer under richer probes. This highlights that reconstruction fidelity and downstream extractability are partially decoupled objectives, and that probe-based evaluation provides a complementary view of representation quality beyond reconstruction metrics alone.

Taken together, these results position GCP-VQVAE as a high-accuracy, fully open structure tokenizer that is both robust under distribution shift and practically usable at scale. Beyond reconstruction, our codebook analysis indicates that the learned tokens form a structured and highly utilized geometric vocabulary (Table 6), supporting the view that GCP-VQVAE learns a coherent "syntax" for protein backbones. Moreover, the Ramachandran analysis (Figure 17) suggests that individual tokens can span multiple local conformational regions rather than mapping to a single narrowly defined geometry, indicating that codes represent broader structural modes whose precise realization is resolved by context during decoding. We next highlight practical applications enabled by this geometry-complete discrete language.

Several avenues look promising to explore: scaling GCP-VQVAE tokenization to multi-chain complexes, enriching tokens with side-chain information, and evaluating GenAI-friendliness of this new language to unify sequence and structure generation via autoregressive protein language models (PLM).

Finally, for the proposed GCP-VQVAE architecture, we have described its applications of it in Appendix D.

7 Limitations

Backbone-only discretization. Our tokenizer operates solely on backbone coordinates (N–C_α–C) and does not incorporate side-chain geometry into the discrete vocabulary. While this design enables stable training and high-fidelity backbone reconstruction, it omits chemically informative details such as rotamer states, functional group orientation, and local packing interactions that are often critical for binding and catalysis.

Reconstruction–representation gap. Although GCP-VQVAE achieves strong reconstruction accuracy, representation transfer on supervised functional benchmarks is comparatively lower, indicating that reconstruction fidelity alone does not ensure that downstream-relevant information is easily extractable from the learned embeddings. Notably, this gap narrows substantially when using more expressive yet lightweight probes (e.g., a deeper MLP or a single-block transformer), indicating that a meaningful fraction of task-relevant signal is present but may require limited contextual aggregation to decode.

Monomer-only scope. We train and evaluate GCP-VQVAE exclusively on single-chain proteins and do not explicitly support multi-chain tokenization. As a result, the learned discrete language does not capture inter-chain geometry or interface-driven constraints that arise in complexes, limiting direct applicability to settings where quaternary structure plays a central functional role.

8 Conclusion

In this work, we have introduced GCP-VQVAE, a state-of-the-art open-source protein structure tokenizer. GCP-VQVAE offers improved structure reconstruction quality and generalization compared to prior methods, which could enable new (sequence and structure-based) predictive and generative modeling applications in future work.

Impact Statement

This work advances machine learning methods for protein 3D structure tokenization and representation learning. By enabling accurate, open-source discretization and reconstruction of protein backbones, it may support downstream applications in protein analysis and design, including biomedical research. As with other generative or representation models for biomolecules, potential risks include misuse for harmful design intents or overreliance on model outputs beyond their validated scope. However, we do not foresee specific societal harms unique to this contribution beyond those already associated with progress in protein modeling.

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A Methods

The proposed architecture leverages two main parts: (1) a GCPNet encoder to encode backbone coordinates into embeddings, and (2) a transformer-based VQVAE, which discretizes backbone embeddings and then converts them back into 3D coordinates.

A.1 GCPNet Encoder

GCPNet (Morehead & Cheng, 2024b) extends the scalar–vector message-passing philosophy of GVP-GNN to a geometry-complete, SE(3)-equivariant encoder. Every atom i in a molecular graph $G = (V, E)$ carries scalars $s_i \in \mathbb{R}^{d_s}$ and row-wise vectors $\mathbf{v}_i \in \mathbb{R}^{d_v \times 3}$ that rotate as $\mathbf{v}_i \mapsto R\mathbf{v}_i$ under $g = (R, \mathbf{t}) \in \mathrm{SE}(3)$, while each edge (i, j) stores analogous features $\big(s_{ij}, \mathbf{v}_{ij}\big)$ and the relative displacement $\mathbf{r}_{ij} = \mathbf{x}_j - \mathbf{x}_i$. Before any update, the model attaches to every edge a right-handed orthonormal frame $F_{ij} = [\mathbf{a}_{ij}, \mathbf{b}_{ij}, \mathbf{c}_{ij}] \in \mathrm{SO}(3)$ with $\mathbf{a}_{ij} = \mathbf{r}_{ij}/\|\mathbf{r}_{ij}\|$; this frame supplies a reference for chirality and orientation that GVP-GNN lacks.

The core computation is a Geometry-Complete Perceptron (GCP) micro-step that first down-scales the vectors and then projects them into the local frame to extract nine orientation-aware features. Denoting $\mathbf{z}_{ij} = W_d \mathbf{v}_{ij}$ and $\mathrm{vec}(\cdot)$ the row-wise vectorization, the joint update mixes the old scalars with their orientation signatures (the frame-projected vectors and their norms) and gates the vectors through a learnable row-wise gate to preserve equivariance; ϕ_s is an MLP and σ denotes a learnable gating function that need not be a fixed sigmoid (Equation 3).

$$\big(s_{ij}, \mathbf{v}_{ij}\big) \;\mapsto\; \Big(\phi_s\big[s_{ij}, \|\mathbf{z}_{ij}\|_2, \mathrm{vec}(\mathbf{z}_{ij} F_{ij}^{\top})\big],\; \sigma\big(W_g s_{ij}\big) \odot W_v \mathbf{z}_{ij}\Big) \tag{3}$$

In the node update, the orientation features are averaged over neighbors. A sequence of such micro-steps, wrapped by a residual shortcut, forms a GCPConv edge block. After aggregating messages $m_i = \sum_{j \in \mathcal{N}(i)} \mathrm{GCPConv}(i, j)$, a gated scalar–vector MLP updates the node features, and stacking L layers yields an invariant backbone. When tasks require coordinates, each layer appends an equivariant displacement head whose output is a learned 3-dimensional vector; this vector is added residually to $\mathbf{x}_i$ and re-centered to ensure translation invariance, enabling force or trajectory prediction without breaking equivariance.

$$\mathbf{x}_i \;\leftarrow\; \mathbf{x}_i + \mathbf{f}_i\,, \qquad \mathbf{f}_i = \mathrm{MLP}_{\mathrm{disp}}(m_i) \tag{4}$$

Equations 3 and 4 commute with every rigid motion, making the encoder strictly SE(3)-equivariant, while projection through F_{ij} preserves the complete set of edge orientations so that the latent remains *geometry-complete* at any depth. Eliminating the frame ($F_{ij} = I$), replacing the orientation features by $\|\mathbf{v}_{ij}\|_2$, and dropping the coordinate head restores a frame-free, E(3)-equivariant network akin to GVP-GNN—thereby isolating the contributions responsible for our empirical gains. Because GCPNet keeps directional and chiral cues that GVP-GNN discards, it supports optional equivariant coordinate updates for force or dynamics prediction and attains improved performance across invariant (e.g., binding affinity; Morehead & Cheng (2024b)), equivariant (e.g., force regression; Morehead & Cheng (2024b)), and coordinate-generative (e.g., molecular diffusion; Morehead & Cheng (2024a)) tasks with only modest extra computation.

A.2 VQVAE

The transformer–based VQVAE employed in this work is organized into the classical three-stage pipeline of *encoder*, *vector-quantization*, and *decoder*. The encoder processes the given embeddings into a sequence of latent vectors, the quantizer discretizes these latents, and the decoder reconstructs the original signal from the resulting code indices.

Both stacks adopt a lightweight pre-layer-normalized transformer that integrates several recent efficiency upgrades: (i) Pre-LayerNorm places the LayerNorm before each sub-block (Xiong et al., 2020), which keeps activations in a well-behaved range throughout the network, reduces gradient-scale drift, and therefore allows training with larger learning rates and much milder warm-up schedules; (ii) separately normalizes query and

key vectors before computing attention logits (Henry et al., 2020). This prevents overly large dot-products, stabilizes attention distributions, and mitigates softmax saturation, especially in low-resource or small-batch training scenarios; (iii) Grouped-Query Attention shares key–value projections across groups of query heads (Ainslie et al., 2023), reducing both memory and compute without harming quality; (iv) Rotary Positional Embeddings (RoPE) inject relative-position information by applying position-dependent planar rotations to each query–key pair (Su et al., 2024), letting the model generalize to much longer sequences with virtually no extra computational cost; (v) We remove bias terms from projection and feed-forward layers, an established simplification that has negligible effect on accuracy while trimming a fraction of parameters and FLOPs.

In the architecture, the vector quantization layer provides the discrete bottleneck between the aforementioned encoder and decoder. While fixed quantizers such as finite scalar quantization (FSQ) (Mentzer et al., 2023) can simplify optimization and offer strong rate–distortion behavior, our target application emphasizes a discrete *representation* that can serve as a reusable interface for both reconstruction and downstream generative modeling. Learned VQ codebooks provide an explicit set of trainable embeddings whose geometry and usage statistics can be shaped by objectives beyond pixel/coordinate reconstruction, which is important when tokens are later modeled by autoregressive or masked-token transformers.

This design choice is supported by recent findings in visual tokenization: tokenizers that improve *semantic* fidelity (e.g., by distilling from strong understanding encoders) yield better generation quality, indicating that learned discrete spaces can capture information that is directly useful for generative modeling (Wang et al., 2024a). Furthermore, work on the compression–generation trade-off shows that stronger generation can emerge from token spaces that are intentionally easier for a stage-2 model to learn, motivating tokenizer training recipes that go beyond pure reconstruction (Ramanujan et al., 2024). Recent studies demonstrated that the VQ-based tokenizers are scalable and can reach full (100%) codebook utilization and avoid classic collapse/under-use pathologies (Chang et al., 2025). Given that our training achieves near-complete codebook utilization on validation, we retain learnable VQ rather than switching to a fixed quantizer, preserving the ability to incorporate auxiliary semantic constraints into the token space when needed.

Before training starts, we run k-means on the encoder outputs of the first mini-batch to seed the codebook as displayed in Equation 5, where $Z^{(0)} \subset \mathbb{R}^d$ are the features, K the codebook size, and T the number of Lloyd iterations. Empirically, this step mitigates early code collapse and improves utilization when K is large.

$$E^{(0)} = \mathrm{KMEANS}\big(Z^{(0)}, K, T\big), \tag{5}$$

Given an encoder vector $\mathbf{z} \in \mathbb{R}^d$, quantization proceeds by nearest-neighbor lookup, Equation 6, which is identical to the vanilla VQ rule.

$$k = \arg\min_j \big\|\mathbf{z} - \mathbf{e}_j\big\|_2^2, \qquad \mathbf{z}_q = \mathbf{e}_k, \tag{6}$$

To transmit gradients through this non-differentiable operation, instead of using the straight-through estimate (STE) introduced in Van Den Oord et al. (2017), we adopt the rotation trick (Fifty et al., 2024). During back-propagation, the Jacobian is replaced by Equation 7, where R is the shortest-arc rotation aligning the unit vectors $\hat{\mathbf{z}}$ and $\hat{\mathbf{e}}_k$. This modification embeds both angular and magnitude mismatch into the back-propagated signal, yielding faster convergence and richer code usage in practice.

$$\mathbf{J}_k = \frac{\|\mathbf{e}_k\|}{\|\mathbf{z}\|}\, R\big(\hat{\mathbf{z}} \to \hat{\mathbf{e}}_k\big), \tag{7}$$

The codebook updates and the encoder commitment follow the standard VQ losses (Equation 8), with β balancing the commitment pressure.

$$\mathcal{L}_{\text{code}} = \|\mathrm{sg}[\mathbf{z}] - \mathbf{e}_k\|_2^2, \qquad \mathcal{L}_{\text{commit}} = \beta\, \|\mathbf{z} - \mathrm{sg}[\mathbf{e}_k]\|_2^2, \tag{8}$$

To encourage diverse and well-separated embeddings, we regularize the codebook with the Frobenius norm (Equation 9) weighted by λ_{orth}. This orthogonality constraint spreads codes over the hypersphere and curbs under-utilization, which is a common failure mode in large books.

$$\mathcal{L}_{\text{orth}} = \left\| E^\top E - I_K \right\|_F^2, \tag{9}$$

To translate the decoder's abstract embeddings into a physically meaningful 3D structure, we utilize a 6D rotation head on top of the decoder. This module's primary purpose is to provide a stable and continuous parameterization of 3D rotations and translations, which is crucial for effective training of deep neural networks. This approach, notably used in AlphaFold2 and supported by the findings of Zhou et al. (2019) on rotation representations, avoids the well-known issues of Gimbal lock in Euler angles and the double-cover ambiguity of quaternions.

Intuitively, the head operates by predicting an intermediate representation for each residue, comprising two 3D direction vectors and a translation. The direction vectors are deterministically converted into a stable rotation matrix via the Gram-Schmidt process, while the translation is scaled by a hyper-parameter, α, to an arbitrary range (e.g., Å). This resulting rigid transformation acts as an update, which is composed with the residue's running pose. The final backbone coordinates are then generated by applying this new, refined pose to a fixed local atomic template ($\mathbf{X}^{\text{local}}$). This iterative process ensures the structure is built in a geometrically consistent and equivariant manner, with the full operational details provided in Algorithm 1.

The decoder is supervised with a weighted sum of three geometric objectives. Building on the loss terms defined in Algorithm 2 (distance, direction and aligned MSE) and the Kabsch alignment returned by Algorithm 3, we supervise the decoder with the weighted sum of Equation 1 as the reconstruction part (L_{rec}) of the final loss. We emphasize that Kabsch alignment removes only global pose (proper rigid motion with $\det(R) = +1$), while the distance and direction losses are defined on internal geometric relations and remain invariant to any global SE(3) transform.

$$\mathcal{L}_{\text{rec}} \;=\; \lambda_{\text{mse}}\,\mathcal{L}_{\text{MSE}} + \lambda_{\text{dist}}\,\mathcal{L}_{\text{dist}} + \lambda_{\text{dir}}\,\mathcal{L}_{\text{dir}}, \tag{10}$$

Here, $\mathcal{L}_{\text{MSE}}$ is the mean-squared error between predicted and native backbones after Kabsch alignment, $\mathcal{L}_{\text{dist}}$ penalises deviations in the $3L \times 3L$ backbone distance matrix (clamped at 5 Å^2), and $\mathcal{L}_{\text{dir}}$ measures squared differences of pairwise dot-product tensors over the six orientation vectors per residue (clamped at 20). Finally, the overall objective optimized for each iteration is demonstrated in Equation 2 where $\mathcal{L}_{\text{rec}}$ is the decoder reconstruction.

$$\mathcal{L} = \mathcal{L}_{\text{rec}} + \mathcal{L}_{\text{code}} + \lambda_{\text{commit}}(\,\mathcal{L}_{\text{commit}} + \lambda_{\text{orth}}\,\mathcal{L}_{\text{orth}}), \tag{11}$$

Algorithms 1–3 define the decoder head, geometric losses, and alignment used in training. Given per-residue embeddings, the 6D head projects to two direction vectors and a translation, constructs a proper rotation via Gram–Schmidt, composes this rigid update with the running pose, and applies it to a fixed (N–C_α–C) template to produce backbone coordinates. Reconstruction is supervised by the weighted sum in Equation 1: (i) aligned MSE after optimal Kabsch alignment, (ii) a clamped backbone distance-matrix loss, and (iii) a clamped pairwise orientation (direction) loss built from six backbone vectors per residue.

Algorithm 1 Pseudocode for 6D rotation-based structure prediction

```
def dim6rot_structure_head(h: Tensor[N, d],
                           g_initial: Tuple[Tensor[N,3,3], Tensor[N,3,1]],
                           alpha: float = 1.0):
    """
    Predicts backbone coordinates from embeddings using a 6D rotation representation.
    This process is vectorized over N residues.

    h: [N, d] float32          -- input embeddings for N residues
    g_initial: (R_0, t_0)      -- initial SE(3) pose (running transformation)
    alpha: float               -- translation scaling hyper-parameter
    """
    # Define a fixed local reference frame for backbone atoms (N, C_alpha, C)
    X_local = torch.tensor(...) # Shape: [3, 3]

    # 1) Project embeddings to unconstrained translations and direction vectors
    # This represents the internal FFN and projection layers.
    h_ffn = LayerNorm(GELU(Linear(h)))
    # W_rigid projects h_ffn to 9 dimensions for t_tilde, a, and b
    rigid_proj = Linear(h_ffn) # Output shape: [N, 9]
    t_tilde, a, b = torch.split(rigid_proj, 3, dim=-1)

    # 2) Create rotation R_i via Gram-Schmidt orthonormalization
    a_hat = a / torch.norm(a, dim=-1, keepdim=True)
    c = torch.cross(a_hat, b, dim=-1)
    c_hat = c / torch.norm(c, dim=-1, keepdim=True)
    b_hat = torch.cross(c_hat, a_hat, dim=-1)

    # Stack column vectors to form the rotation matrix R
    R = torch.stack([a_hat, b_hat, c_hat], dim=-1) # Shape: [N, 3, 3]

    # 3) Scale the translation vector
    t = t_tilde * alpha # Shape: [N, 3]

    # 4) Form the local rigid body update g = (R, t) and compose it
    #    with the running pose g_initial = (R_0, t_0)
    R_0, t_0 = g_initial
    R_new = R_0 @ R
    t_new = (R_0 @ t.unsqueeze(-1)) + t_0

    # 5) Apply the new pose g_new to the local template to get final coordinates
    # Unsqueeze t_new for broadcasting over the 3 atoms in X_local
    X_pred = (R_new @ X_local.T).transpose(-1, -2) + t_new.transpose(-1, -2)

    return X_pred, (R_new, t_new) # Return coords and the updated pose
```

Algorithm 2 Pseudocode for backbone *distance*, *direction* and *MSE* losses

```
def compute_backbone_vectors(coords: Tensor[L, 3, 3]) -> Tensor[L, 6, 3]:
    """
    coords[..., 0/1/2] = (N, CA, C) atom positions for each residue.
    Returns six normalised vectors per residue:
        1)  N → CA            4)  -n_CA    (binormal of NCA plane)
        2)  CA → C            5)   n_N     (binormal of CN_prev-N plane)
        3)  C  → N_{i+1}      6)   n_C     (binormal of CA C N_{i+1} plane)
    """
    # bond vectors ------------------------------------------------------------
    v1 = coords[:, 1] - coords[:, 0]            # N → CA
    v2 = coords[:, 2] - coords[:, 1]            # CA → C
    v3 = pad_end(coords[1:, 0] - coords[:-1, 2])     # C → N_{i+1}
    v4 = -torch.cross(v1, v2)                   # -n_CA
    v5 = torch.cross(v3, v1)                    #  n_N
    v6 = torch.cross(v2, v3)                    #  n_C

    V = torch.stack([v1, v2, v3, v4, v5, v6], dim=1)
    return F.normalize(V, dim=-1)               # shape = [L, 6, 3]


def backbone_distance_loss(x_pred, x_true, mask):
    """
    x_pred/x_true : [L, 3, 3]  predicted & native backbone coords
    mask          : [L]        boolean, valid residues
    """
    P = x_pred[mask, :3].reshape(-1, 9)         # flatten 3 atoms → 9-D point
    T = x_true[mask, :3].reshape(-1, 9)

    D_pred = pairwise_l2(P, P)                  # (N, N) distance matrix
    D_true = pairwise_l2(T, T)

    diff   = (D_pred - D_true).pow(2).clamp(max=25.)
    return diff.mean()


def backbone_direction_loss(x_pred, x_true, mask):
    """
    Uses six orientation vectors per residue as returned by
    `compute_backbone_vectors`.
    """
    V_pred = compute_backbone_vectors(x_pred[mask, :3])
    V_true = compute_backbone_vectors(x_true[mask, :3])

    # Pairwise dot-product tensors:  S_{ij}^{kl} = v_i^{(k)} · v_j^{(l)}
    S_pred = torch.einsum('ikd,jld->ijkl', V_pred, V_pred)
    S_true = torch.einsum('ikd,jld->ijkl', V_true, V_true)

    diff   = (S_pred - S_true).pow(2).clamp(max=20.)
    return diff.mean()


def aligned_mse_loss(x_pred, x_true, mask):
    """
    Mean-squared error after optimal rigid alignment
    (Kabsch) between predicted and native backbone coords.

    Args
    ----
    x_pred : Tensor[L, 3, 3]   # predicted (N, CA, C)
    x_true : Tensor[L, 3, 3]   # ground truth
    mask   : BoolTensor[L]     # valid residues
    """
    # 1) select masked residues and flatten atoms ------------- #
    P = x_pred[mask].reshape(-1, 3)   # (3N, 3)
    T = x_true[mask].reshape(-1, 3)   # (3N, 3)

    # 2) best-fit rotation / translation via Kabsch ------------ #
    R, t = kabsch(P, T)               # R ∈ SO(3), t ∈ ℝ^3
    T_aln = (T @ R.T) + t             # align native coords

    # 3) mean-squared error ---------------------------------- #
    mse = ((P - T_aln).pow(2)).mean()
    return mse
```

Algorithm 3 Pseudocode for rigid alignment via Kabsch

```
def kabsch_align(A: Tensor[N, 3],
                 B: Tensor[N, 3],
                 allow_reflections : bool = False):
    """
    Optimal rigid alignment (rotation R, translation t) of
    point cloud A onto reference cloud B.

    A, B : [N, 3] float32  -- corresponding coordinates
    """
    # 1) centre the clouds --------------------------------- #
    centroid_A = A.mean(0);  centroid_B = B.mean(0)
    AA = A - centroid_A      # centred source
    BB = B - centroid_B      # centred target

    # 2) SVD of covariance -------------------------------- #
    H = AA.T @ BB                            # 3x3
    U, _, Vh = torch.linalg.svd(H)           # H = U S Vh

    # 3) ensure proper rotation (det = +1) ----------------- #
    if not allow_reflections and torch.det(Vh.T @ U.T) < 0:
        Vh[-1, :] *= -1

    R = Vh.T @ U.T                           # rotation
    t = centroid_B - R @ centroid_A          # translation

    return (R @ A.T).T + t                  # aligned A
```

B Datasets

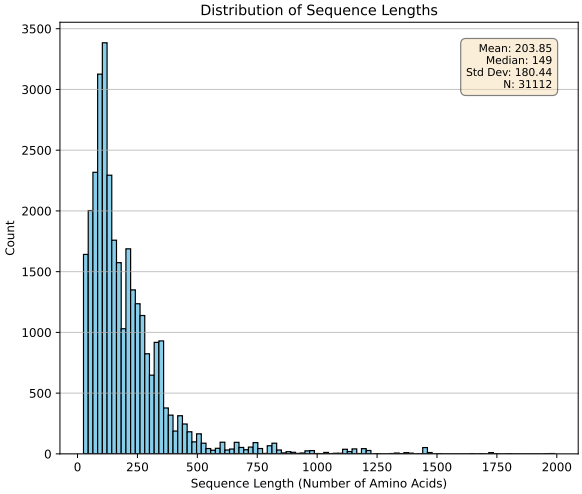
Test A (low-confidence) evaluates robustness under structural uncertainty using a curated subset of AlphaFold2 (AF2) models for SwissProt proteins. We enumerated all AF2-predicted structures available for SwissProt entries in AFDB and retained only those with average pLDDT ≤ 70 (AFDB's 0–100 scale), discarding higher-confidence models. The surviving records were *cross-referenced* against the PDB to annotate the presence of experimental structures for the same proteins. Multimer entries were decomposed into per-chain monomer samples, after which we removed chains shorter than 25 amino acids and retained only chains with fewer than 25 consecutive missing residues. A final deduplication step produced 33 112 single-chain samples for Test A.

Test B (species-diverse, taxonomic shift) assesses generalization under distributional shift in species rather than structure confidence. We assembled a broad species roster (expanded to 100 and finalized at 97 species) and targeted roughly 2 500 proteins per species from AFDB without pLDDT filtering to reflect natural variability, dropping species with fewer than 1 000 available structures. After aggregation, per-chain conversion, and deduplication, this suite comprised 19 353 single-chain samples.

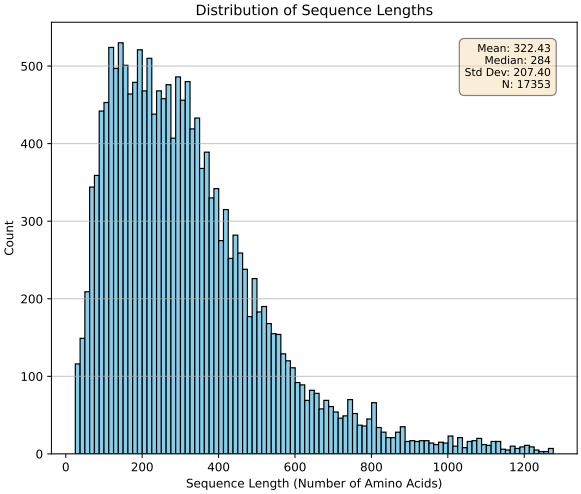
Test C (high-confidence, under-represented taxa) measures performance on high-confidence structures from taxa under-represented in SwissProt. We selected species with low SwissProt coverage and required high average pLDDT (> 95). The selected taxonomies were cross-referenced against the PDB to find the presence of experimental structures for the proteins from those species. Applying the same preprocessing and deduplication as Test A above yielded 33 867 single-chain samples.

To obtain a balanced validation set independent of training, we first constructed three targeted hold-out suites and then set aside a fixed 2 000 randomly sampled chains from each to form a combined 6 000-chain validation set; the remaining examples constitute Test sets A, B, and C, respectively. The distribution of length sequences in the test sets is displayed in Figure 4.

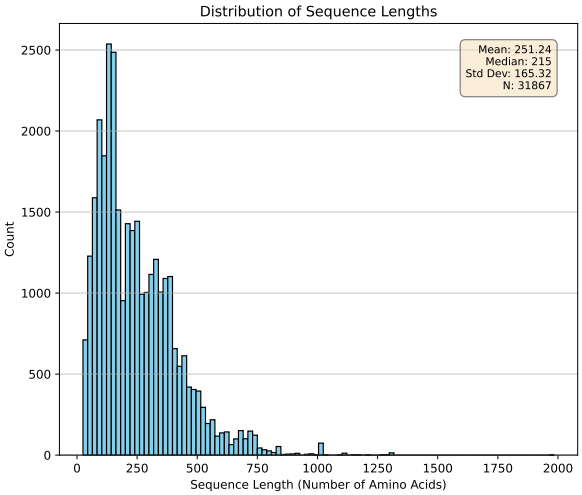
From the zero-shot set, we defined interpretable structural subsets based on each protein's secondary-structure composition. Coil-rich (D) includes sequences with at least 60% coil/disordered content. Mainly α (A) requires an α-helical fraction of at least 45% and an $\alpha - \beta$ difference of at least 15 percentage points; mainly β (B) requires a β-strand fraction of at least 25% and a $\beta - \alpha$ difference of at least 10 points. Balanced (AB) captures mixed folds with $\alpha \geq 25\%$, $\beta \geq 15\%$, and $|\alpha - \beta| \leq 10$ points. We also report two data-quality



(a) Test set A



(b) Test set B



(c) Test set C

Figure 4: **Distribution of sequence lengths in the three test sets.** The majority of samples have sequence length $< 1\,280$ amino acids.

subsets: sequences with no missing residues and sequences with at least one missing residue. Groups are defined independently (i.e., they may overlap).

C Experiments

This subsection compiles all experimental assets: Table 9 lists the full optimization schedule and training hyperparameters for the Lite and Stages 1–2 of the Large model; Table 10 specifies the exact model configuration (GCPNet, VQ, and Transformer stacks). Figure 5 reports RMSD error distributions on the zero-shot dataset across methods; Figure 6 shows qualitative robustness to contiguous missing-residue segments from benchmark structures; Figure 7 plots sequence length versus reconstruction RMSD with a least-squares fit on the validation set; Figure 8 visualizes the highest-RMSD (worst-case) examples per benchmark suite. Metrics use backbone atoms (C_α) after Kabsch alignment, and statistics are over the full, unfiltered test sets.

We set the coefficients λ (Equation 1) by monitoring the per-term gradient norms and equalizing their contribution to shared parameters. This gradient-norm balancing prevents any single term (e.g., direction or distance) from dominating updates and yields stable, faster convergence.

Following the structure-tokenizer configuration in ESM-3 (Hayes et al., 2025), we adopt a 4 096-token codebook and select the code embedding dimension to balance reconstruction fidelity and utilization. In particular, the Lite model uses a 128-dim codebook embedding, while the Large model increases this to 256 to better utilize the larger decoder capacity and improve representational bandwidth through the discrete bottleneck. In preliminary sweeps, increasing the code embedding dimension beyond 256 tended to reduce effective codebook utilization, so we use 256 as a practical upper bound in our setting.

Throughout all experiments, sequences longer than the model's input window are truncated to the first L residues (Stage 1: $L = 512$, Stage 2: $L = 1\,280$), and all metrics are computed on the truncated region.

Table 9: Training hyperparameters for Large (Stages 1 & 2) and Lite models.

Hyperparameter	**Large (Stage 1)**	**Large (Stage 2)**	**Lite**
Optimizer type	AdamW	AdamW	AdamW
β_1	0.9	0.9	0.9
β_2	0.98	0.98	0.98
ϵ	10^{-7}	10^{-7}	10^{-7}
Weight decay	10^{-3}	10^{-3}	10^{-2}
Gradient clipping (max L_2 norm)	1.0	1.0	1.0
Gradient accumulation	1	1	1
8-bit parameters	✗	✓	✓
Batch size (per GPU)	16	4	16
Learning-rate strategy	Cosine annealing	Cosine annealing	Cosine annealing
Base learning-rate	$1e-4$	$5e-5$	$1e-4$
Min learning-rate	$1e{-}6$	$1e{-}6$	$1e{-}6$
Warm-up steps	16 000	16 000	4 096
Total steps	375 000	1 500 000	284 000
MSE coefficient (λ_{MSE})	1×10^{-3}	5×10^{-3}	1×10^{-3}
Backbone distance coefficient (λ_{dist})	10^{-2}	10^{-2}	10^{-2}
Backbone direction coefficient (λ_{dir})	5×10^{-2}	5×10^{-2}	5×10^{-2}

Table 10: Configurations of GCP-VQVAE architectures (Large Stages 1 & 2, and Lite).

Hyperparameter	**Large (Stage 1)**	**Large (Stage 2)**	**Lite**
GCPNet Encoder			
Initialization	(Jamasb et al., 2024)	Stage 1	(Jamasb et al., 2024)
Input dim (node scalars h)	6	6	6
Input dim (node vectors χ)	3	3	3
Input dim (edge scalars e)	8	8	8
Input dim (edge vectors ξ)	1	1	1
Hidden dim (node scalars h)	128	128	128
Hidden dim (node vectors χ)	16	16	16
Hidden dim (edge scalars e)	32	32	32
Hidden dim (edge vectors ξ)	4	4	4
Number of layers	6	6	6
SE(3) equivariance	✓	✓	✓
Vector Quantization			
Initialization	Random	Stage 1	Random
Hidden dimension	256	256	128
Vocab size	4 096	4 096	4 096
EMA Decay	0.99	0.995	0.99
Threshold EMA dead code	2	2	2
Commitment weight (λ_{commit})	0.5	0.25	0.25
Orthogonal reg weight (λ_{orth})	10	10	10
Orthogonal reg max codes	512	512	512
Orthogonal reg active codes only	✓	✓	✓
Rotation trick	✓	✓	✓
KMeans initialization	✓	✓	✓
KMeans iteration	10	10	10
Transformer Encoder			
Initialization	Random	Stage 1	Random
Hidden dimension	1024	1024	1024
FF Multiplier	4×	4×	4×
Blocks	12	12	8
Query heads	12	12	8
Key-value heads	3	3	2
Positional encoding	RoPE	RoPE	RoPE
Query-key norm	✓	✓	✓
Pre-norm	✓	✓	✓
Transformer Decoder			
Initialization	Random	Stage 1	Random
Hidden dimension	1024	1024	1024
FF Multiplier	4×	4×	4×
Blocks	16	16	12
Query heads	16	16	8
Key-value heads	1	1	2
Positional encoding	RoPE	RoPE	RoPE
Query-key norm	✓	✓	✓
Pre-norm	✓	✓	✓

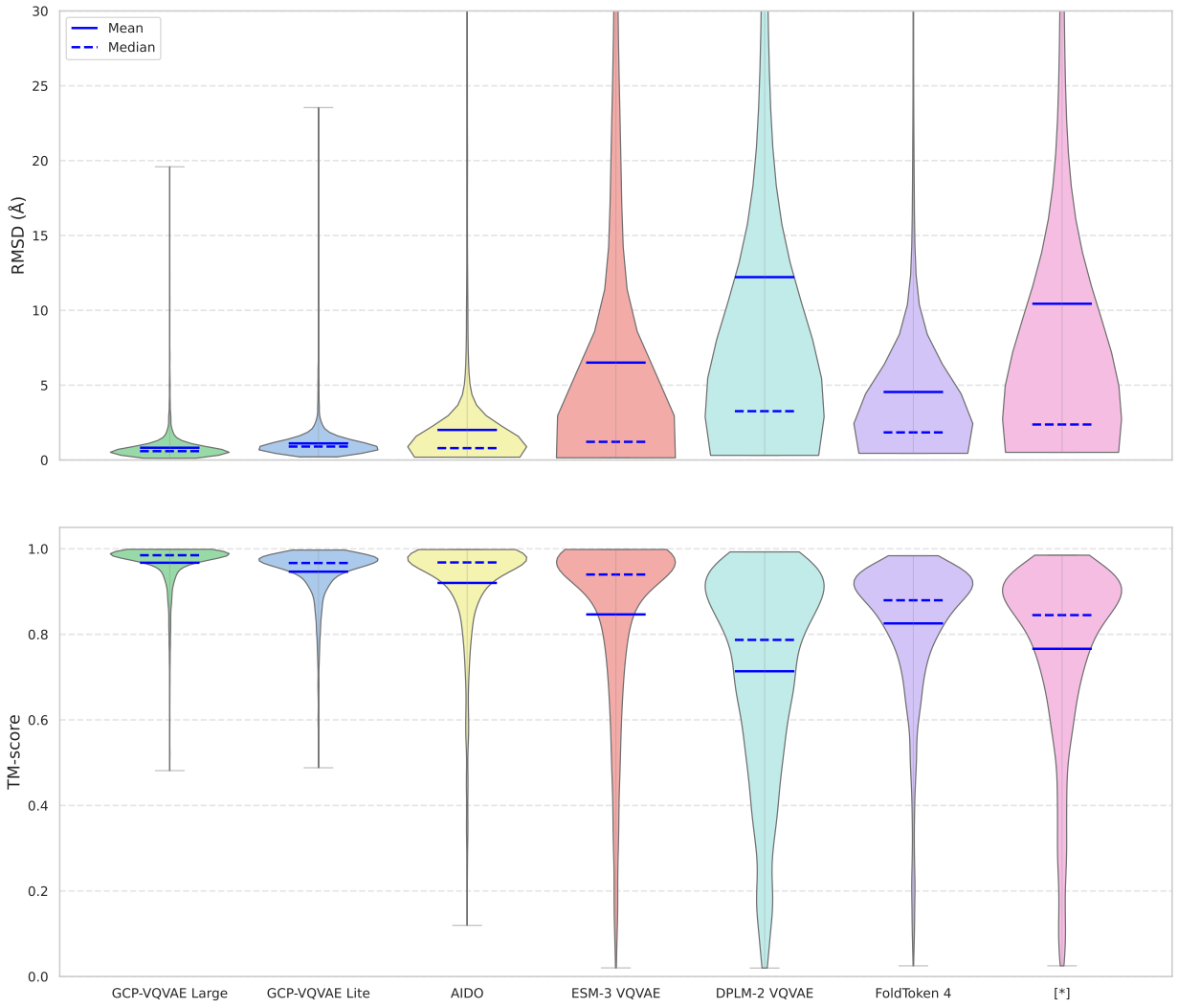


Figure 5: **RMSD (Å) and TM-score error distributions on the zero-shot dataset.** Gaujac et al. (2024) is shown as [∗]. For Gaujac et al. (2024), samples outside its supported length range (50–512 residues) are excluded; other methods use the full sets.

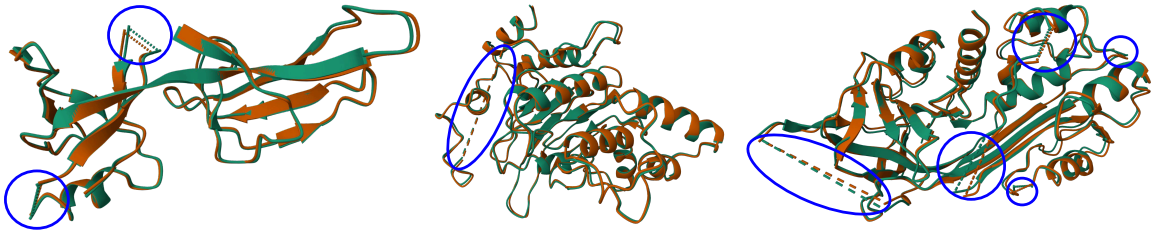


Figure 6: **Superposition of GCP-VQVAE reconstructions (orange) with native backbones (green) for three proteins drawn from our external benchmark suites.** Blue circles mark contiguous missing-residue segments (dashed guides span regions without deposited atoms); the model tracks the native structure outside the gaps.

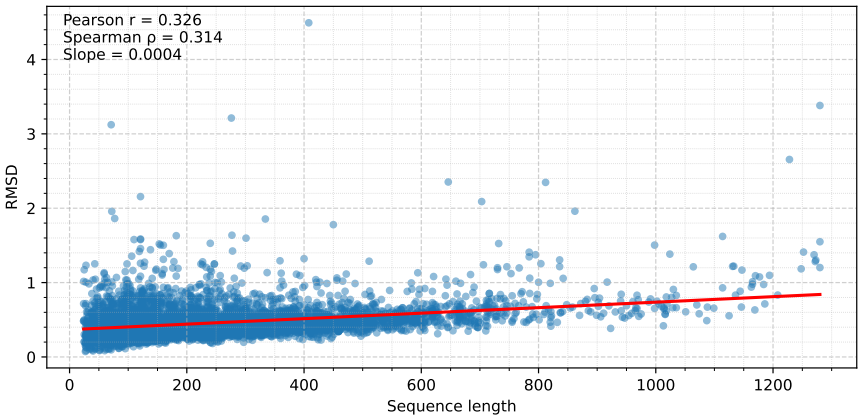


Figure 7: **Sequence length vs. reconstruction error (validation set).** Each point is one protein; the red line is a least-squares fit. The dependence on length is modest (Pearson $r = 0.326$, Spearman $\rho = 0.314$) with a small slope of $\approx 4 \times 10^{-4}$ Å/residue (~ 0.4 Å per 1k residues).

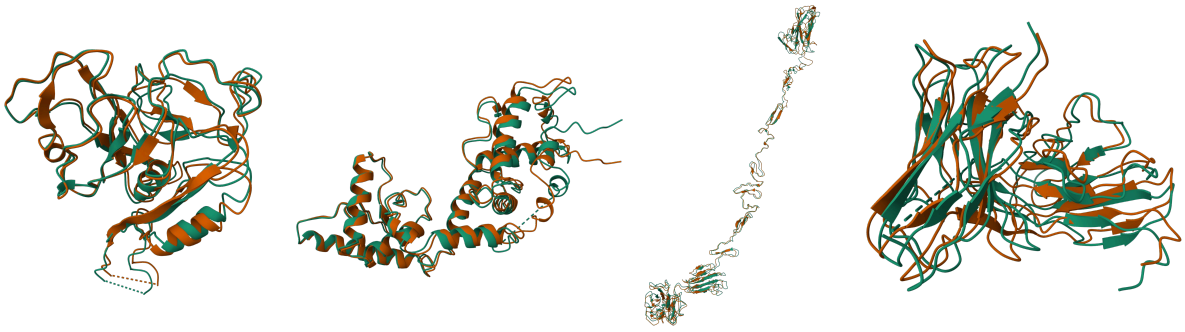


Figure 8: **Superposition of GCP-VQVAE (orange) and native backbones (green) for the highest–backbone-RMSD example in each suite.** Left → right: CASP14, CASP15, CASP16, CAMEO2024.

C.1 Zero-Shot Performance

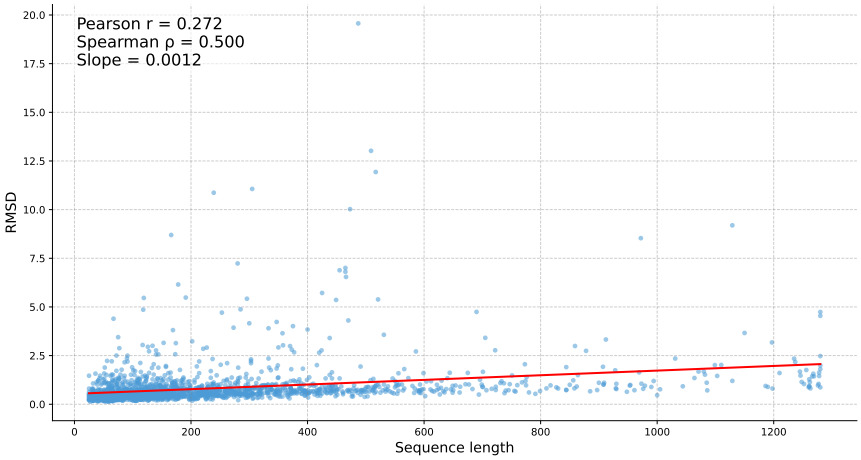


Figure 9: **RMSD as a function of sequence length (number of amino acids) on the zero-shot set.** Each dot is one protein. The red line is an ordinary-least-squares (OLS) fit; the panel reports Pearson r, Spearman ρ, and the fitted slope (RMSD units per residue).

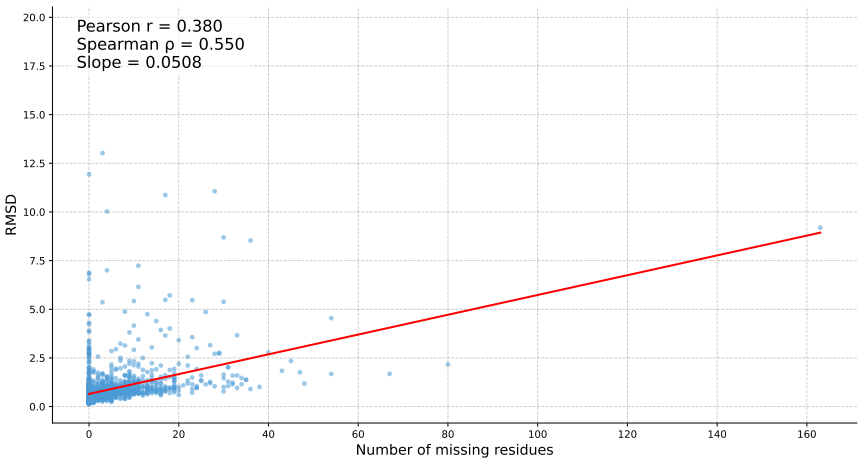


Figure 10: **RMSD as a function of the number of missing residues on the zero-shot set.** Points show individual proteins; the red line is an OLS fit. The panel reports Pearson r, Spearman ρ, and the fitted slope (RMSD units per missing residue).

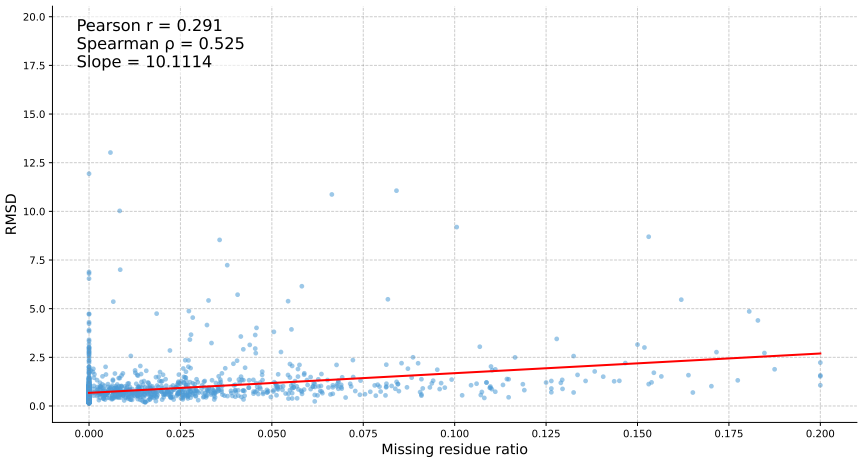


Figure 11: **RMSD as a function of the missing-residue ratio on the zero-shot set.** The red line is an OLS fit; the panel reports Pearson r, Spearman ρ, and the fitted slope (RMSD units per unit fraction; 1.0=100%).

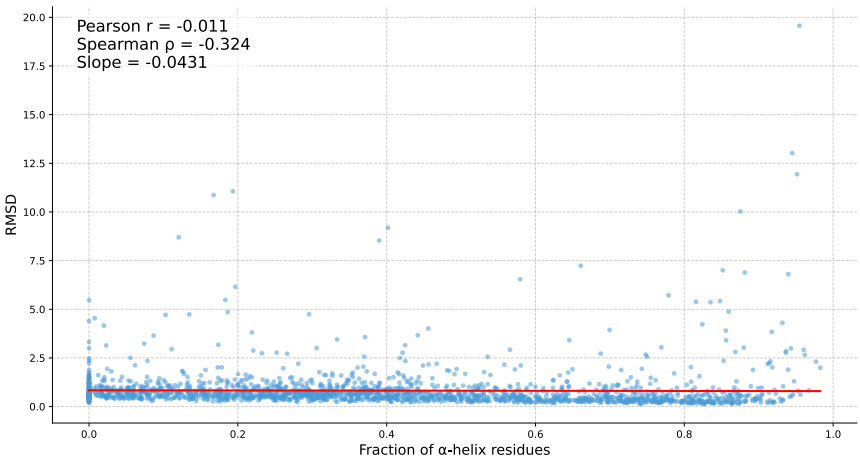


Figure 12: **RMSD as a function of the fraction of α-helix residues on the zero-shot set.** The red line indicates an OLS fit. The panel reports Pearson r, Spearman ρ, and the fitted slope (RMSD units per unit fraction; 1.0=100%).

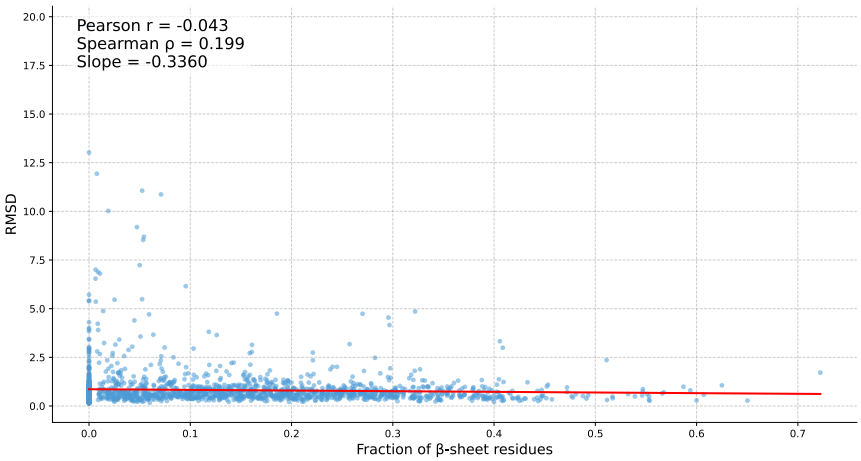


Figure 13: **RMSD as a function of the fraction of β-sheet residues on the zero-shot set.** The red line indicates an OLS fit. The panel reports Pearson r, Spearman ρ, and the fitted slope (RMSD units per unit fraction; 1.0=100%).

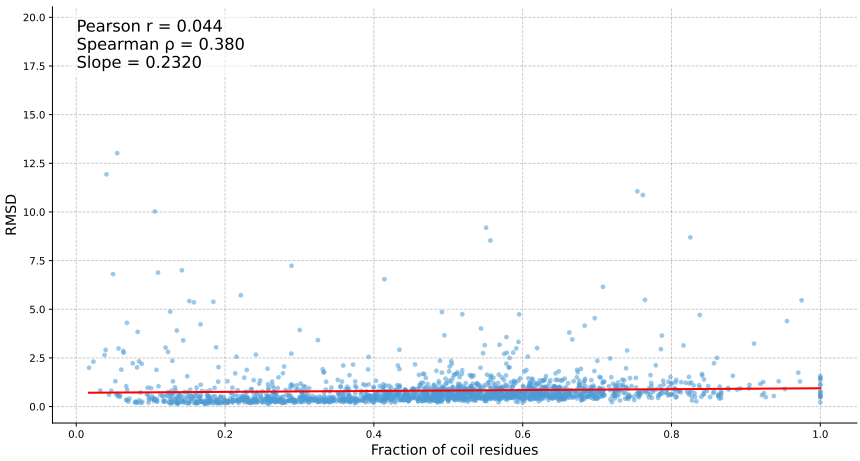


Figure 14: **RMSD as a function of the fraction of coil residues on the zero-shot set.** The red line indicates an OLS fit. The panel reports Pearson r, Spearman ρ, and the fitted slope (RMSD units per unit fraction; 1.0=100%).

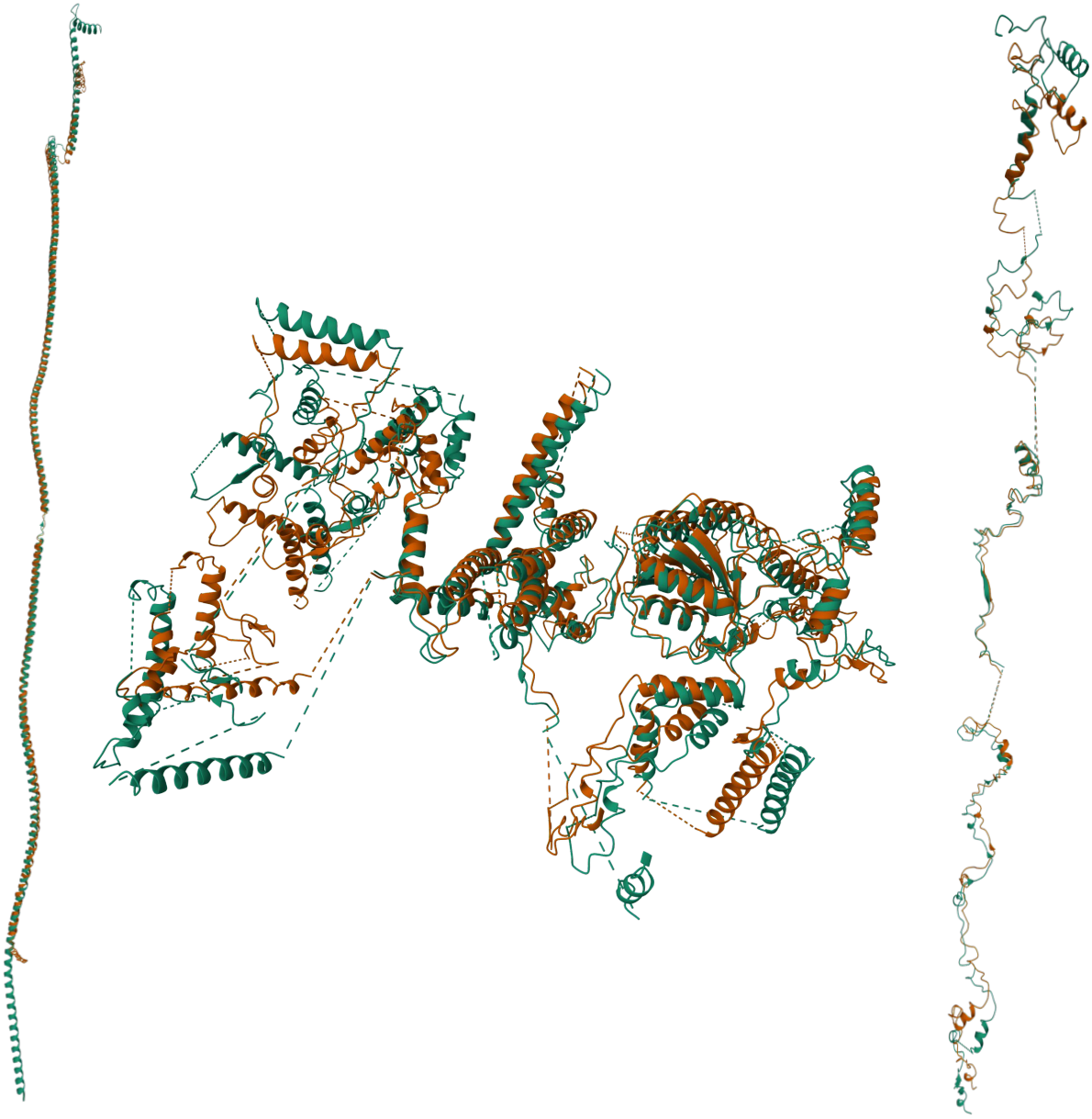


Figure 15: **Worst zero-shot reconstructions (orange: GCP-VQVAE Large; green: native).** Left: RMSD 19.568 Å, TM-score 0.691, length 487, NaN residues 0. Middle: RMSD 9.1924 Å, TM-score 0.7442, length 1129, NaN residues 163. Right: RMSD 11.0627 Å, TM-score 0.4755, length 305, NaN residues 28. The middle and right cases exhibit an extreme number of `NaN` residues introduced by our current `NaN`-handling/augmentation pipeline, which forces the model to contend with long masked segments and degrades reconstruction accuracy; improving the `NaN` strategy (e.g., capping gap ratio, better segmentation, and length-aware masking) should mitigate this failure mode.

C.2 Inference Speed Benchmarking

We benchmark inference latency for our GCP-VQVAE variants (Large and Lite) alongside top-performing open baselines, ESM3 VQVAE and AIDO StructureTokenizer, across sequence lengths ranging from 32 to 1 024 residues. We report the mean wall-clock runtime per protein (in milliseconds) for (i) the encoding pass (backbone coordinates → discrete tokens), (ii) the decoding pass (tokens → reconstructed coordinates), and

(iii) end-to-end inference. Benchmarks are conducted on a single Nvidia A6000 Ada 48GB GPU via bf16, using maximum feasible batch sizes (128 for GCP and ESM3; 4 for AIDO, reduced to 1 at $L = 1\,024$ due to VRAM constraints). Table 11 summarizes the resulting compute profiles, revealing distinct scaling behaviors: While ESM3 is competitive for short sequences, GCP-VQVAE Lite is the fastest method across *all* evaluated sequence lengths, achieving up to ∼6× lower end-to-end latency than ESM3 and ∼500× lower latency than AIDO at 1 024 residues.

Table 11: **Inference latency (ms) for structure tokenization (encoder) and reconstruction (decoder) across different sequence lengths.** Total denotes end-to-end time (encode + decode) per protein.

Seq. Len.	GCP-VQVAE Large			GCP-VQVAE Lite			ESM3 VQVAE			AIDO		
	Enc ↓	Dec ↓	Total ↓	Enc ↓	Dec ↓	Total ↓	Enc ↓	Dec ↓	Total ↓	Enc ↓	Dec ↓	Total ↓
32	15.53	0.17	15.70	15.21	0.10	**15.31**	3.98	21.70	25.68	7.35	39.34	46.68
64	15.93	0.45	16.38	15.46	0.20	**15.67**	4.90	21.81	26.71	6.89	38.29	45.18
128	16.51	1.20	17.71	15.79	0.69	**16.48**	8.60	21.87	30.46	7.37	73.22	80.59
256	17.18	2.63	19.82	16.39	1.69	**18.08**	16.92	25.54	42.46	16.57	409.51	426.08
512	19.60	5.34	24.93	17.78	3.51	**21.28**	34.16	52.36	86.52	35.01	2240.84	2275.86
1024	25.15	12.47	37.63	21.46	7.52	**28.99**	70.96	112.40	183.36	65.52	15303.70	15369.22

C.3 Reconstruction Robustness to Structural Noise

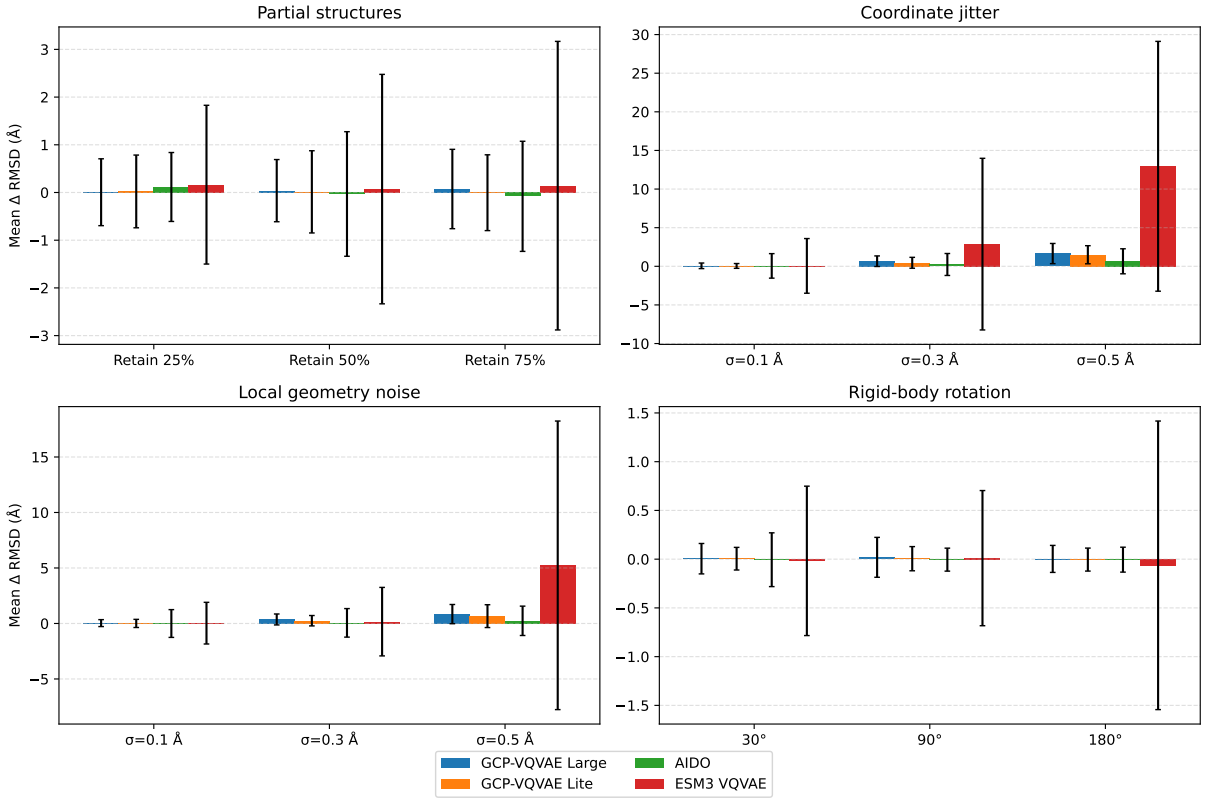


Figure 16: **Reconstruction robustness to structural noise and input corruption.** We report mean ± std ΔRMSD (in Å) over 500 zero-shot proteins, where ΔRMSD = RMSD(noisy reconstruction, clean input) − RMSD(clean reconstruction, clean input), computed on C_α atoms after Kabsch alignment. We evaluate four perturbation families: (top-left) partial structures via contiguous truncation (retain 25/50/75% of residues), (top-right) global coordinate jitter with Gaussian noise $\mathcal{N}(0, \sigma^2)$ applied to all backbone atoms, (bottom-left) local geometry noise by perturbing N/C/O around fixed C_α positions, and (bottom-right) rigid-body rotations of the full backbone. Lower values indicate higher robustness, and rigid-body rotations act as a sanity check where degradation should remain near zero under pose-invariant tokenization.

To assess robustness beyond `NaN`-masking, we stress-test reconstruction under controlled perturbations of the input backbone coordinates (N, C_α, C, O). For each structure, we first compute a clean baseline reconstruction, then apply a noise transformation to the input coordinates, re-tokenize and reconstruct, and measure the reconstruction degradation as ΔRMSD relative to the clean baseline. Concretely, we report ΔRMSD = RMSD(noisy reconstruction, clean input) − RMSD(clean reconstruction, clean input), where RMSD is computed on C_α atoms after Kabsch alignment.

We evaluate four perturbation families: (i) partial-structure truncation by keeping only a contiguous segment of the chain, (ii) global coordinate jitter via i.i.d. Gaussian noise applied to all backbone atoms, (iii) local geometry noise by jittering N/C/O around fixed C_α positions, and (iv) rigid-body rotations. Experiments are run on 500 randomly sampled proteins from our zero-shot PDB 2024–2025 set, truncated to 1024 residues prior to noise injection, and in figure 16, we report mean ± std ΔRMSD across samples for GCP-VQVAE (Large/Lite) and representative open baselines (ESM3 VQVAE, AIDO).

C.4 Representation Evaluation

We note that the remote homology tasks are omitted from the reported results due to data and label missing and inconsistencies. Integrating our custom GCP-VQVAE architecture with the official PST benchmark codebase (Yuan et al., 2025b) was not a straightforward task, as the original framework does not natively support external VQ-VAE models without significant modification. Consequently, we were required to re-implement the evaluation pipeline for each specific task. This extensive re-engineering introduced potential uncertainties regarding the alignment between our embeddings and the regression targets.

C.5 Codebook Evaluation

To investigate the relationship between learned VQ codebook tokens and protein backbone geometry, we performed a Ramachandran plot analysis on a zero-shot test set (Figure 17) comprising 1 938 protein structures not seen during training. For each protein, we passed the original backbone coordinates through the GCPNet encoder and vector quantizer to obtain per-residue VQ code assignments, then decoded these quantized representations to reconstruct the backbone coordinates. We computed backbone dihedral angles ϕ and ψ for both original and reconstructed structures using standard geometric formulas based on the N, Cα, and C atomic positions of consecutive residues.

Each residue was plotted in Ramachandran space and colored according to its assigned VQ code index. For visualization clarity, we highlighted the top-30 most frequent codes with distinct colors while displaying remaining codes in gray. We included reference boxes indicating canonical secondary structure regions: the α-helix region ($\phi \in [-90°, -30°]$, $\psi \in [-70°, -15°]$) and the β-sheet region ($\phi \in [-160°, -80°]$, $\psi \in [90°, 180°]$). These boundaries represent simplified rectangular approximations of sterically allowed regions based on standard Ramachandran conventions.

We analyzed both the Lite and Large model variants across a total of 447 784 residue-level data points. The comparison between original and reconstructed structure distributions allows us to assess whether the quantization bottleneck preserves local backbone geometry, while the comparison between model variants reveals differences in codebook utilization and conformational specificity (Table 12).

Table 12: **Top-10 most frequent codebook tokens and their usage percentages on the zero-shot test set.** We omit the AminoAseed report due to poor reconstruction results.

Rank	GCP-VQVAE Lite		GCP-VQVAE Large		ESM3		AIDO		DPLM-2		FoldToken		(Gaujac et al., 2024)	
	Code	%	Code	%	Code	%	Code	%	Code	%	Code	%	Code	%
1	1181	2.96	2324	0.65	588	0.88	490	0.36	2234	0.31	182	1.88	2541	0.44
2	2431	2.37	1666	0.58	264	0.67	431	0.33	2235	0.30	211	1.68	2542	0.38
3	3862	2.10	732	0.49	2056	0.58	284	0.33	2362	0.28	51	1.47	815	0.31
4	2337	1.83	2391	0.48	3961	0.52	435	0.31	2490	0.24	105	1.38	2556	0.25
5	3340	1.73	3436	0.47	1476	0.49	347	0.30	2363	0.24	112	1.33	799	0.21
6	3874	1.57	1064	0.45	1197	0.49	272	0.30	2107	0.21	11	1.29	4048	0.20
7	1497	1.57	2440	0.44	3101	0.48	113	0.30	2491	0.20	230	1.23	3808	0.19
8	1800	1.16	1772	0.43	987	0.48	334	0.30	2299	0.20	251	1.22	3792	0.19
9	4026	1.13	4046	0.42	3954	0.47	132	0.30	3258	0.19	195	1.14	2023	0.19
10	3792	1.11	3766	0.36	2082	0.45	404	0.30	2106	0.19	38	1.08	3776	0.19
Top-10 Total	—	**17.53**	—	**4.77**	—	**5.51**	—	**3.13**	—	**2.36**	—	**13.70**	—	**2.55**

To quantitatively assess the information content and utilization of the learned VQ codebook, we computed the following information-theoretic metrics on the discrete token sequences $Z = (z_1, z_2, \ldots, z_L)$ generated by the encoder:

Unigram Statistics. We measure codebook utilization using unigram entropy $H_1 = -\sum p(z) \log_2 p(z)$ and perplexity $\text{PPL} = 2^{H_1}$. Perplexity represents the effective vocabulary size; an ideal uniform codebook would have $\text{PPL} = |K| = 4\,096$ ($H_1 = 12$ bits). We report *Effective Usage* as $\text{PPL}/|K|$.

Zipf Distribution Fit. Natural languages typically follow Zipf's law, where the frequency of the r-th most common token scales as $f(r) \propto r^{-b}$. We fit a linear regression to the log-log rank-frequency plot and report the slope b and coefficient of determination R^2. A slope near -1 with high R^2 indicates natural language-like power-law scaling.

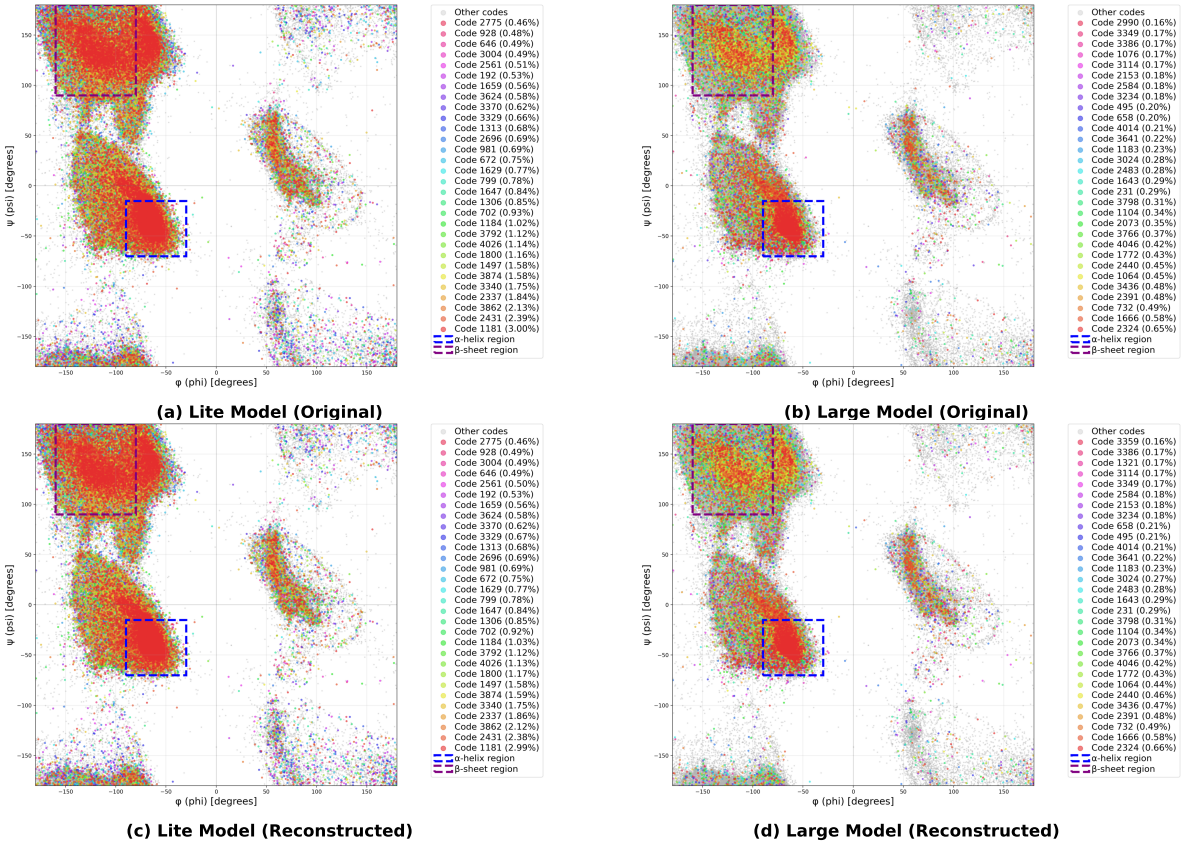


Figure 17: **Ramachandran plot analysis of VQ codes on a zero-shot test set, colored by the top-30 most frequent codes with respect to the reconstructed and original coordinates.** Dashed boxes indicate α-helix (blue) and β-sheet (purple) regions. **(a-b)** Lite model. **(c-d)** Large model. The top row shows original coordinates; the bottom row shows reconstructed coordinates.

Conditional Statistics. To evaluate sequential structure, we compute conditional entropies $H(Z_t|Z_{t-1})$ (bigram) and $H(Z_t|Z_{t-2}, Z_{t-1})$ (trigram). Lower conditional entropy indicates higher predictability given context. We report the *Trigram Perplexity* (Tri PPL $= 2^{H(Z_t|Z_{t-2},Z_{t-1})}$), which quantifies the effective branching factor of the sequence given a two-token history.

Mutual Information. We measure long-range dependencies using mutual information $I(Z_t; Z_{t+\Delta}) = H(Z_t) - H(Z_t|Z_{t+\Delta})$ at various lags $\Delta \in \{1, 4\}$. Higher mutual information indicates that tokens carry significant predictive information about future states in the sequence.

C.6 Major Issues in Performance Analysis

During our evaluation pipeline development, we identified a critical issue affecting TM-score calculations for experimental PDB structures. Unlike computationally predicted structures that typically use sequential residue numbering starting from 1, experimental PDB files from sources such as CASP and CAMEO often contain non-standard residue indices reflecting the original crystallographic or NMR data (e.g., residues numbered 23–97 instead of 1–75). Additionally, experimental structures frequently contain missing residues due to unresolved electron density or flexible loop regions, creating gaps in the residue numbering sequence (e.g., residues 1–45, 52–120) that further complicate alignment. In the first release of the manuscript, when VQ-VAE reconstruction scripts saved decoded structures with default 1-indexed sequential residue numbering while comparing against original PDBs with their native non-sequential numbering, the TM-align algorithm failed to correctly pair corresponding residues, resulting in artificially low TM-scores despite near-identical

atomic coordinates. For instance, a structure with actual Cα-RMSD of 0.30 Å was incorrectly reported as having TM-score of 0.10 due to this mismatch. We corrected this by preserving the original residue indices when writing reconstructed PDB files and applying Kabsch alignment before evaluation, ensuring consistent residue numbering between original and reconstructed structures for accurate metric computation.

D Applications

For the proposed GCP-VQVAE architecture, we see the following applications:

Structure compression. Using a 4 096-entry codebook yields about $\sim 24\times$ compression of backbone coordinates for a 512-residue monomer (Appendix D.1). Given our low RMSDs of $\sim$ 0.4–0.8 Å (Table 2), this is a practical lossy backbone codec. Further gains are possible by (i) allowing a single code to represent short residue spans (e.g., 2–4 amino acids), reducing the token rate while the decoder expands span-tokens to per-residue poses, and/or (ii) increasing the codebook size (e.g., 8k–64k) to lower per-token quantization error so that fewer tokens are needed at a target distortion. These options trade bitrate against utilization and latency, and remain compatible with our VQ training approach.

Structure comparison. Our discrete geometry language converts backbones into high-resolution token strings that can be indexed (Altschul et al., 1990; Ma et al., 2002) and aligned with dynamic programming over a learned substitution matrix between codes. Compared to fixed 3Di alphabets as in FoldSeek, a learned 4 096-code vocabulary; optionally make it with side-chain–aware, captures finer local shape and orientation, enabling more accurate substructure and whole-chain comparisons.

Downstream 3D learning representation. De-quantized code embeddings yield continuous, structure-aware features that can serve as a compact intermediate representation for a range of downstream 3D learning tasks (Yuan et al., 2025b). In practice, these embeddings can be used as fixed inputs for supervised residue-level prediction (e.g., functional site annotation), physicochemical property regression, and unsupervised conformational analysis, providing a reusable structural featurization that bridges discrete token sequences and continuous geometric learning. This interface enables transferring geometric information from a high-fidelity tokenizer into lightweight task-specific heads, and supports applications such as structure-aware retrieval, clustering, and structure-conditioned modeling without operating directly on raw coordinates.

Generative modeling. Because our structure representation is discrete and pose-invariant, it slots directly into autoregressive PLM pre-training: tokens can be interleaved with amino-acid symbols, letting us exploit next-token scaling laws observed in autoregressive Large Language Models (LLM) (Kaplan et al., 2020). This unifies sequence and structure in a single model, enabling controllable generation via simple conditioning; e.g., sequence-given-structure and structure-given-sequence modes. Structure tokens serve as an explicit geometric prior for PLMs (Hayes et al., 2025; Su et al., 2023), potentially enabling more control over protein design. Moreover, the same machinery supports higher-throughput structure prediction from sequence by first predicting structural tokens and then mapping them to backbones with GCP-VQVAE's decoder (Pourmirzaei et al., 2025; Lu et al., 2024; Chen et al., 2024).

D.1 Compression calculation

Each residue is encoded by one code from a 4 096-entry book, i.e., $\log_2(4096) = 12$ bits $= 1.5$ bytes/residue. For $L = 512$ residues, the token stream is $512 \times 1.5 = 768$ bytes. Raw backbone coordinates (N, C_α, C) stored as 32-bit floats require 3 atoms $\times$ 3 coords $\times$ 4 bytes $= 36$ bytes/residue, i.e., $36 \times 512 = 18{,}432$ bytes. If we include a tiny global pose header (e.g., rotation+translation) of ≈ 36 bytes, the coded footprint is $768 + 36 = 804$ bytes. Thus the compression ratio is $18\,432/804 \approx 22.9\times$ (approximately $24\times$ if the pose header is omitted). This estimate concerns backbone only; metadata and format containerization add negligible overhead relative to the raw-float baseline.

E LLM Usage

In this manuscript, we used large language models only for copy-editing: improving grammar, clarity, and style of author-written text.