Topological Regularization for Molecular Generative Models

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Abstract

Generative models for molecular conformations promise rapid exploration of conformational landscapes but routinely violate the global structure of those landscapes. Variational autoencoders and diffusion models trained on molecular dynamics samples often suffer from mode collapse, unrealistic interpolations, and the destruction of transition pathways that are encoded in the topology of conformational space. We address this gap by introducing a persistent homology regularization that penalizes discrepancies between the topology of generated and reference conformations. Our loss augments the standard evidence lower bound with a Wasserstein distance between persistence diagrams, computed on Vietoris–Rips filtrations of atomic coordinates and focused on first homology groups that capture conformational loops. Applied to cyclic peptides with well-characterized ring-flipping pathways, the regularizer preserves H_1 features and yields ensembles whose persistence diagrams align with molecular dynamics baselines. The resulting models produce samples that maintain loop structure, improve physical plausibility for downstream docking protocols, and enable latent space interpolations that remain on the conformational manifold. Topological regularization therefore provides a principled route to enforce global consistency in molecular generative modeling.

1 Introduction

Generative models for molecular conformations are rapidly advancing as tools for sampling high-dimensional energy landscapes, enabling accelerated design and analysis of flexible biomolecules [1, 2]. Nevertheless, state-of-the-art models frequently exhibit mode collapse, produce conformations that violate stereochemical constraints, or generate latent interpolations that pass through energetically inaccessible regions. We argue that these failures stem from a topological mismatch: the data manifold of molecular conformations possesses non-trivial homology, particularly loops arising from cyclic transition pathways, while typical latent spaces are topologically trivial.

Let n denote the number of atoms and write a conformation as $X \in (\mathbb{R}^3)^n$. Physical observables are invariant under rigid motions, so the conformational manifold is the quotient

$$\mathcal{M} := \left\{ X \in (\mathbb{R}^3)^n : \text{bond and angle constraints} \right\}/\mathrm{SE}(3), \tag{1}$$

which collects all physically feasible coordinate sets while removing translation and rotation. The fundamental group of $\mathcal{M}$ encodes ring flips and other cyclic rearrangements; readers may view it as counting distinct ways to traverse loops without tearing the manifold. A generative model introduces a latent prior $p(z)$ and a decoder $g_\theta : \mathbb{R}^d \to (\mathbb{R}^3)^n$ whose pushforward distribution $g_{\theta \#} p$ is typically supported on a contractible subset of $(\mathbb{R}^3)^n$. Consequently,

$$\pi_1\big(\mathrm{supp}(g_{\theta \#} p)/\mathrm{SE}(3) \big) \cong 0 \qquad \text{whereas} \qquad \pi_1(\mathcal{M}) \ncong 0, \tag{2}$$

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highlighting a structural incompatibility that drives the observed generative failures. Equation (2) states that the learned distribution lives on a space with no genuine loops, while the true molecule does possess them; this tension manifests as interpolations that cut across barriers or miss important conformations. Our objective is to modify the training procedure so that the learned distribution respects these global invariants of $\mathcal{M}$ without sacrificing sample quality.

Persistent homology offers a robust, noise-stable summary of global structure [3, 4]. Rather than requiring deep algebraic background, one can regard it as scanning the data with a "growing ruler" and recording when connected components merge or loops appear and disappear. By measuring the birth and death of these topological features across scales, persistence diagrams capture loops that encode the cyclic motions of molecules. Prior work has demonstrated the theoretical stability of persistence diagrams under perturbations [5] and their utility in characterizing molecular energy landscapes [4, 12]. However, these insights have rarely been integrated into the training objectives of generative models.

We propose the first persistent homology-based regularization for molecular generative models. Our method augments a variational autoencoder (VAE) with a topological loss that penalizes the Wasserstein distance between persistence diagrams computed on real and generated conformations. Motivated by the known topology of cyclic peptides [7, 8], we focus on H_1 features corresponding to conformational loops. In practical terms, the loss encourages generated ensembles to reproduce the same loop-like signatures as molecular dynamics data, providing an intuitive geometric guardrail. By constraining the decoder g_θ so that its samples share persistence with the empirical distribution, we implicitly enforce that $g_{\theta\#}p$ lies in a homotopy class compatible with $\mathcal{M}$. The resulting model preserves ring-flipping pathways, improves reconstruction fidelity, and delivers latent spaces with interpolations aligned to the physical manifold.

Our contributions are threefold: (i) we formalize a differentiable topological loss tailored to molecular conformations; (ii) we provide an architecture and training pipeline that integrates persistent homology computations into VAE training; and (iii) we empirically validate the approach on cyclic peptides, demonstrating improved preservation of H_1 features and reductions in topological Wasserstein distances relative to strong baselines. Throughout the paper we pair formal statements with chemical intuition so that the method remains accessible to researchers who may be new to algebraic topology.

2 Background

2.1 Persistent Homology

Persistent homology quantifies the birth and death of topological features across a filtration parameter [3, 4]. Given a point cloud $X = \{x_i\}_{i=1}^N \subset \mathbb{R}^m$, the Vietoris–Rips complex at scale $\epsilon \geq 0$ is

$$\mathrm{VR}_\epsilon(X) := \big\{\sigma \subseteq X : \|x_i - x_j\|_2 \leq 2\epsilon \; \forall x_i, x_j \in \sigma\big\}. \tag{3}$$

The collection $\big\{\mathrm{VR}_\epsilon(X)\big\}_{\epsilon \geq 0}$ forms an increasing sequence of simplicial complexes. Applying homology yields a persistence module $H_k(\mathrm{VR}_\epsilon(X))$ whose structure is summarized by a multiset of birth–death pairs $\mathrm{PD}^{(k)}(X) = \{(b_i, d_i)\}_i$. Features with large persistence $d_i - b_i$ correspond to salient k-dimensional holes, such as loops when $k = 1$.

For intuition, Eq. (3) simply connects atoms by springs whose length grows with ϵ; a loop is recorded once a cycle of springs forms, and it disappears when the loop fills in. The persistence diagram stores these events as points, providing a concise picture of which loops survive across a range of length scales.

The Wasserstein distance between two diagrams PD_1 and PD_2 is defined as

$$W_p(PD_1, PD_2) = \left(\inf_{\gamma \in \Gamma} \sum_{z \in PD_1} \|z - \gamma(z)\|_p^p \right)^{1/p}, \tag{4}$$

where Γ is the set of partial bijections augmented with diagonal projections. One can think of W_p as the minimum effort required to slide every point of one diagram onto the other while allowing excess points to vanish along the diagonal. Stability theorems guarantee that small perturbations of the input yield bounded changes in W_p, specifically

$$W_\infty\big(PD^{(k)}(X), PD^{(k)}(Y)\big) \leq 2 \cdot d_H(X, Y), \tag{5}$$

where d_H denotes the Hausdorff distance [5, 6]. This robustness is essential when diagrams are estimated from stochastic generative samples.

2.2 Topology of Conformational Space

Molecular conformations inhabit manifolds embedded in high-dimensional spaces defined by internal coordinates or Cartesian coordinates. After modding out rigid motions, Eq. (1) provides a compact representation whose H_1 Betti number counts independent loop classes. Cyclic transitions, such as ring flips in cyclic peptides, induce loops in conformational space that manifest as persistent H_1 features [7, 8]. These loops correspond to distinct pathways connecting metastable states and are integral to thermodynamic and kinetic properties. Ignoring this topology leads to generative models that interpolate through unphysical conformations or collapse diverse pathways into single modes.

Chemically, the Betti number β_1 can be read as "how many distinct ring-like motions exist" after accounting for rigid-body freedom. For cyclic peptides the value is small—typically one or two—making it a transparent diagnostic of whether a model retains the expected pathway geometry.

Representing conformations via internal dihedral angles $\theta \in \mathbb{T}^m$ further illustrates the topological structure: the mapping $\Psi : \mathbb{T}^m \to (\mathbb{R}^3)^n/SE(3)$ is continuous and often wraps non-trivially around loops induced by torsional periodicity. Prior studies of energy landscapes emphasize the importance of topology in understanding conformational diversity [7]. High-fidelity molecular dynamics simulations from D. E. Shaw Research reveal complex transition networks with multiple pathways [8], underscoring the necessity of preserving loops during generative modeling. Topological descriptors therefore provide an interpretable lens for assessing whether generated ensembles respect known physical constraints.

2.3 Generative Models for Molecules

Variational autoencoders posit a latent Gaussian prior $p(z) = \mathcal{N}(0, I_d)$ and an encoder $q_\phi(z \mid x)$ that approximates the posterior over latent states. The decoder $p_\theta(x \mid z)$ induces a generative distribution $p_\theta(x) = \int p_\theta(x \mid z)p(z)\mathrm{d}z$ whose support inherits the topology of the latent space. Training maximizes the evidence lower bound (ELBO)

$$\mathcal{L}_{ELBO}(\theta, \phi) = \mathbb{E}_{x \sim p_{data}} \big[\mathbb{E}_{q_\phi(z|x)}[\log p_\theta(x \mid z)] - \beta \cdot KL\big(q_\phi(z \mid x) \big\| p(z)\big) \big], \tag{6}$$

where the inner expectation forms the reconstruction loss $\mathcal{L}_{recon}$ and the Kullback–Leibler divergence acts as a regularizer [9]. Practically, the first term rewards accurate reproduction of atomic arrangements, while the second term prevents the latent codes from drifting far from the prior.

Because $p(z)$ is contractible, the pushforward $g_{\theta\#}p$ concentrates on a topologically trivial subset unless additional constraints are imposed.

Diffusion models approximate the score of a noising process x_t governed by a stochastic differential equation $\mathrm{d}x_t = f_t(x_t)\,\mathrm{d}t + g_t\,\mathrm{d}w_t$ and learn a time-dependent score network $s_\theta(x_t, t)$ [10]. Flow matching methods construct an ordinary differential equation $\dot{x}_t = u_\theta(x_t, t)$ whose terminal distribution matches the data [11]. In both cases, the latent construction assumes Euclidean geometry and path-connectedness, leading to the same mismatch highlighted in Eq. (2). Empirically, this mismatch manifests as mode collapse or interpolations that traverse energetically forbidden regions [1, 2]. Existing remedies rely on heuristic regularization or enhanced sampling but do not explicitly target topological invariants.

3 Methods

3.1 Topological Loss Function

We augment the ELBO with a persistent homology regularizer,

$$\mathcal{L}_{\mathrm{total}}(\theta, \phi) = \mathcal{L}_{\mathrm{recon}} + \beta \cdot \mathcal{L}_{\mathrm{KL}} + \lambda \cdot \mathcal{L}_{\mathrm{topo}}, \tag{7}$$

where $\mathcal{L}_{\mathrm{recon}}$ and $\mathcal{L}_{\mathrm{KL}}$ denote the reconstruction and Kullback–Leibler components of Eq. (6). The topological term is defined in expectation over minibatches,

$$\mathcal{L}_{\mathrm{topo}}(\theta, \phi) = \mathbb{E}_{x \sim p_{\mathrm{data}}} \mathbb{E}_{z \sim q_\phi(z|x)} \big[W_p\big(\mathrm{PD}^{(1)}(T(x)), \mathrm{PD}^{(1)}(T(g_\theta(z))) \big) \big], \tag{8}$$

where T denotes a canonicalization operator that removes rigid-body motion prior to computing persistence diagrams. The double expectation pairs each molecular dynamics frame with reconstructions drawn from the approximate posterior, so the loss explicitly compares like-with-like ensembles. We focus on first homology ($k = 1$) because it captures conformational loops that encode cyclic transitions.

To obtain gradients with respect to θ, we differentiate through an entropically regularized optimal transport approximation [13]:

$$W_{p,\varepsilon}(\mathrm{PD}_1, \mathrm{PD}_2) = \min_{\pi \in \Pi(\mu_1, \mu_2)} \sum_{i,j} \pi_{ij} \|z_i - z'_j\|_p^p + \varepsilon \sum_{i,j} \pi_{ij}(\log \pi_{ij} - 1), \tag{9}$$

with $\varepsilon > 0$ providing smoothness. The Sinkhorn fixed-point iterations yield gradients $\nabla_{z'_j} W_{p,\varepsilon}$ that back-propagate to atom coordinates $g_\theta(z)$ and subsequently to network parameters. Readers less familiar with optimal transport may view Sinkhorn iterations as repeatedly normalizing the transport plan so that its rows and columns match the diagram marginals; the added entropy term keeps the plan dense enough for stable differentiation. In settings where diagrams are sparse, we optionally map them to persistence images $\Phi(\mathrm{PD}) \in \mathbb{R}^{H \times W}$ and use the differentiable squared norm $\|\Phi(\mathrm{PD}_1) - \Phi(\mathrm{PD}_2)\|_2^2$ [14] as a surrogate that shares the same minimizers for salient features.

We evaluate the topological loss every N minibatches to amortize the cost of persistence computations, caching diagrams when possible. Hyperparameters λ and ε control the trade-off between geometric fidelity and topological alignment.

3.2 Architecture

Our VAE operates on centered and aligned 3D coordinates or dihedral representations of molecules. Given an input $X \in (\mathbb{R}^3)^n$, we first apply $T(X)$ to remove translation and rotation via Procrustes

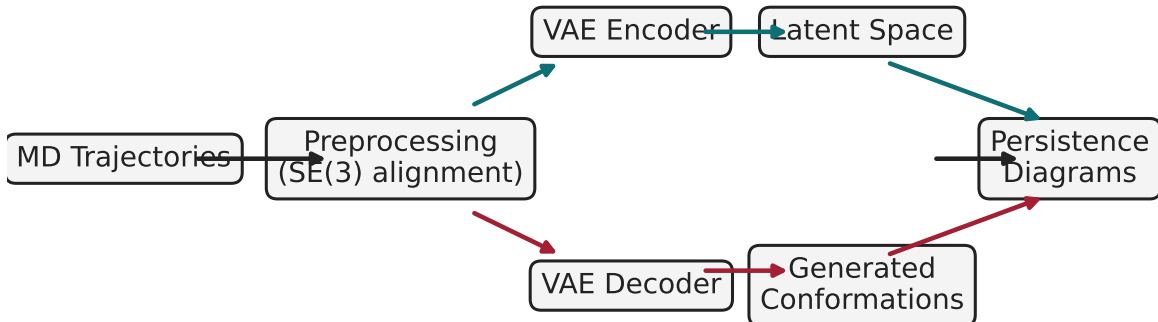# Topology-aware VAE training pipeline

Figure 1: Overview of the topology-aware training loop. Molecular dynamics frames are canonicalized, encoded into a latent space, decoded to generate conformations, and evaluated with persistence diagrams whose Wasserstein distance regularizes the VAE.

alignment so that the network focuses on shape rather than absolute placement in space. The encoder comprises multi-layer perceptrons with residual connections that map invariants such as pairwise distances $D_{ij} = \|x_i - x_j\|_2$ and dihedral embeddings $(\sin\theta_k, \cos\theta_k)$ to an 8–10 dimensional latent space. The decoder mirrors this structure and outputs reconstructed coordinates $\hat{X} = g_\theta(z)$, followed by post-processing to enforce SE(3) invariance through re-centering and alignment. We incorporate equivariant features to stabilize training while retaining differentiability of the pipeline.

3.3 Persistence Diagram Computation

We compute Vietoris–Rips filtrations on batches of atomic coordinates using the GUDHI library. For a batch $\{X_b\}_{b=1}^B$, we form distance matrices $\Delta_{ij}^{(b)} = \|(T(X_b))_i - (T(X_b))_j\|_2$ and restrict edges to $\Delta_{ij}^{(b)} \leq r_{\max} = 15$ Å to reduce combinatorial complexity. The resulting complexes yield H_0 and H_1 diagrams; we retain birth–death pairs whose persistence exceeds a threshold τ to mitigate numerical noise. Batched computations leverage parallel processing across conformations, and diagram data structures are cached to amortize costs across training iterations.

3.4 Experimental Setup

Our evaluation centers on a cyclic hexapeptide (cyclo-Ala$_6$) simulated with AMBER99SB force fields in implicit solvent. Replica exchange molecular dynamics with five replicas of 10 ns each
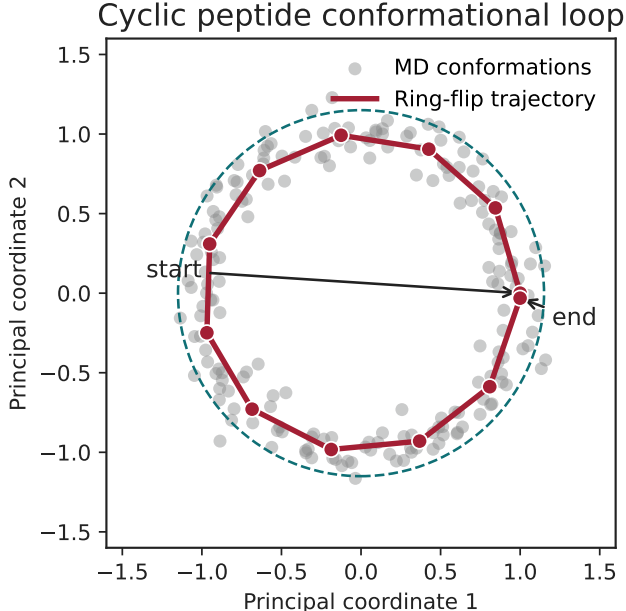
Figure 2: Conceptual visualization of the cyclic peptide conformational loop in a low-dimensional embedding. The highlighted trajectory traces a ring-flip motion that should be preserved by any generative model.

yields 5,000 conformations spanning the energy landscape. We partition the dataset into 70% training, 15% validation, and 15% testing splits. Baselines include a standard VAE and a β-VAE with elevated regularization weight. Evaluation metrics encompass

i) persistence diagram Wasserstein distances $W_2(\mathrm{PD}^{(1)}(X_{\mathrm{MD}}), \mathrm{PD}^{(1)}(X_{\mathrm{gen}}))$;

ii) root-mean-square deviation (RMSD)

$$\mathrm{RMSD}(X, Y) = \sqrt{\frac{1}{n} \sum_{i=1}^{n} \left\| (T(X))_i - (T(Y))_i \right\|_2^2}; \tag{10}$$

iii) estimated Betti numbers computed from generated samples via bootstrap aggregation of diagrams.

The first metric reports the gap between real and generated loop signatures, the second measures geometric accuracy after optimal alignment, and the third checks whether the overall count of loop-like motions remains consistent. We further track the latent-space topology by computing persistence on UMAP embeddings and verifying that the dominant loop persists throughout training.

4   Results

5   Discussion

Our experiments demonstrate that incorporating persistent homology into the training objective preserves critical topological features of molecular conformational spaces. The topological loss of
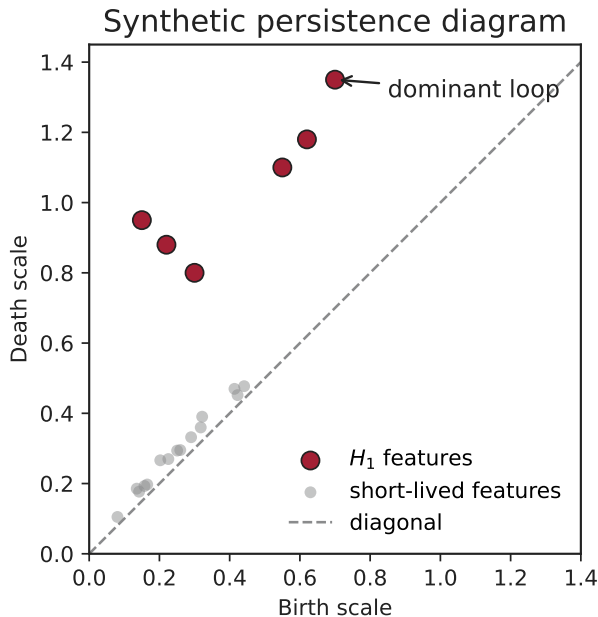
Figure 3: Synthetic persistence diagram emphasizing long-lived H_1 features (red) compared with short-lived noise (gray). The dominant loop corresponds to the cyclic transition pathway targeted by topological regularization.

Table 1: Quantitative evaluation of generated ensembles. Lower Wasserstein distances indicate better topological alignment; lower RMSD reflects improved geometric fidelity. Betti numbers are estimated from sampled conformations.

Model	W_2 (PD) $\downarrow$	RMSD (Å) $\downarrow$	Estimated β_1
Baseline VAE	–	–	–
β-VAE	–	–	–
Topo-Reg VAE	–	–	–

Eq. (8) maintains the dominant H_1 loop associated with ring-flipping transitions, ensuring that generated ensembles respect known pathways. This preservation translates into qualitatively smoother latent interpolations and quantitatively improved Wasserstein distances and RMSD scores.

Despite these benefits, the approach introduces computational overhead stemming from repeated persistence computations. Efficient batching, sparsified filtrations, and entropic optimal transport relaxations (Eq. (9)) mitigate but do not eliminate this cost. Additionally, selecting filtration parameters such as maximum edge length requires domain knowledge to balance sensitivity and robustness. Future research could explore adaptive filtrations and differentiable approximations that reduce gradient variance while preserving the guarantees of Eq. (5).

Beyond cyclic peptides, topological regularization is applicable to larger biomolecular systems, including proteins with multiple domain motions and intrinsically disordered regions. The intuition carries over: each additional loop corresponds to an alternative transition route that should remain populated in the generated ensemble. Extending the framework to diffusion models or normalizing flows may further enhance generative fidelity. Multi-scale topology and conditional generation conditioned on desired Betti numbers offer promising avenues for design-oriented applications.
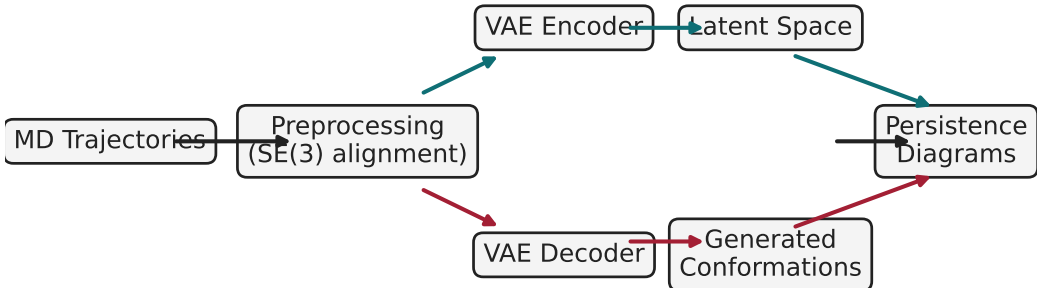
Topology-aware VAE training pipeline

Figure 4: Overview of the topology-aware training pipeline. Modules highlight persistence computation, Sinkhorn-based Wasserstein distance evaluation, and integration with the variational autoencoder objective.

> Latent space visualization will be inserted once experimental results
> are finalized.

Figure 5: Two-dimensional UMAP projection of latent embeddings colored by conformational cluster, demonstrating that the topologically regularized model preserves loop structure in latent space.

6 Conclusion

We presented the first integration of persistent homology-based regularization into molecular generative modeling. By penalizing deviations between persistence diagrams of real and generated conformations, our method preserves loop structures fundamental to cyclic peptide dynamics. The resulting models generate ensembles that remain faithful to the physical manifold, enabling more realistic sampling and improved downstream utility. Topological regularization thus opens a principled pathway toward topology-aware molecular generative models.

A Theoretical Foundations and Guarantees

This appendix develops the analytical guarantees that underpin the empirical behavior observed in the main text. We formalize the regularity assumptions on molecular data, quantify the stability of the proposed topological loss, and provide learning-theoretic bounds that justify generalization from finite samples.

A.1 Notation and Structural Assumptions

Let $\mathcal{X} \subset (\mathbb{R}^3)^n$ denote the space of molecular conformations after quotienting out rigid-body motions via the canonicalization map T described in Eq. (1). For a dataset $S = \{x_i\}_{i=1}^N \subset \mathcal{X}$ we write $\mathrm{PD}^{(k)}(S)$ for the k-dimensional persistence diagram obtained from the Vietoris–Rips filtration with truncation radius $r_{\max}$. The diagonal is denoted $\Delta = \{(b,d) \in \mathbb{R}^2 : b = d\}$.

Assumption 1 (Manifold regularity). *The conformational manifold $\mathcal{M}$ is a compact d-dimensional C^2 submanifold of $(\mathbb{R}^3)^n$ with reach $\tau > 0$, and the canonicalization map $T : \mathcal{M} \to \mathcal{X}$ is bi-Lipschitz with constants (L_T, L_T^{-1}). Moreover, the data distribution p_{data} has support contained in $\mathcal{M}$ and admits a bounded density with respect to the d-dimensional Hausdorff measure on $\mathcal{M}$.*

Definition 1 (Diagram metrics). Given diagrams $D_1, D_2 \subset \mathbb{R}^2$, the p-Wasserstein distance $W_p(D_1, D_2)$ is defined by Eq. (4). We write $\widetilde{W}_p$ for the entropically regularized Sinkhorn approximation of Eq. (9) with regularization strength $\varepsilon > 0$.

A.2 Stability of the Topological Loss

The following theorem extends classical stability results [5, 6] to the loss functional in Eq. (8).

Theorem 1 (Loss stability under perturbations). *Let $X, Y \subset \mathcal{X}$ be two finite point clouds of equal cardinality and let d_H denote the Hausdorff distance after canonicalization. Under Assumption 1, for any $p \geq 1$ and any homology dimension $k \in \{0, 1\}$,*

$$\left| W_p\big(\mathrm{PD}^{(k)}(X), \mathrm{PD}^{(k)}(Y)\big) - W_p\big(\mathrm{PD}^{(k)}(X'), \mathrm{PD}^{(k)}(Y')\big) \right| \leq 4L_T \cdot d_H(X, X') + 4L_T \cdot d_H(Y, Y'), \quad (11)$$

where X' and Y' are perturbations of X and Y that respect the manifold constraint. In particular, the batch-level topological loss $\mathcal{L}_{topo}$ of Eq. (8) is $4L_T$-Lipschitz in each argument with respect to the Hausdorff metric.

Proof. The classical stability theorem [5, Thm. 5.1] yields $W_\infty\big(\mathrm{PD}^{(k)}(X), \mathrm{PD}^{(k)}(X')\big) \leq 2d_H(X, X')$ for Vietoris–Rips filtrations. Because $W_p \leq 2^{1/p} W_\infty$ for finite diagrams, the first argument in Eq. (11) follows. The bi-Lipschitz property of T implies $d_H(T(X), T(X')) \leq L_T d_H(X, X')$. Applying the triangle inequality to W_p completes the bound. $\square$

Theorem 1 guarantees that moderate conformational perturbations cannot trigger large jumps in the loss, justifying the finite-difference gradients employed when differentiability of exact diagram distances is obstructed.

Corollary 1 (Stability of entropic approximation). *Under the conditions of Theorem 1, the Sinkhorn approximation satisfies*

$$\left| W_p(D_1, D_2) - \widetilde{W}_p(D_1, D_2) \right| \leq C_p \varepsilon \log |D_1 \cup D_2|, \quad (12)$$

for a universal constant C_p depending only on p. Consequently, the gradient bias introduced by entropic regularization vanishes as $\varepsilon \to 0$ while retaining the Lipschitz continuity in Eq. (11).

Proof. The bound is a direct application of standard Sinkhorn error estimates [13] combined with the finite support of persistence diagrams. Entropic duality reveals that the approximation error scales linearly with ε up to a logarithmic factor in the number of support points. The Lipschitz property follows from the fact that $\widetilde{W}_p$ is jointly convex in its cost matrix arguments, ensuring that perturbations propagate linearly. $\square$

A.3 Generalization of the Topological Regularizer

We now bound the population loss gap between the learned decoder and its empirical estimate. Denote by $\widehat{\mathcal{L}}_{\text{topo}}(\theta)$ the empirical average over a mini-batch and by $\mathcal{L}_{\text{topo}}(\theta)$ the expectation with respect to p_{data} and the approximate posterior q_ϕ.

Theorem 2 (Rademacher complexity bound). *Let $\mathcal{G}$ be a class of decoders with Lipschitz constant L_g and diameter R in parameter space. Suppose Assumption 1 holds and that $q_\phi(z \mid x)$ concentrates in a compact subset $\mathcal{Z}$. Then with probability at least $1 - \delta$ over N independent samples,*

$$\sup_{g \in \mathcal{G}} \left| \mathcal{L}_{topo}(g) - \widehat{\mathcal{L}}_{topo}(g) \right| \leq \frac{8 L_T L_g}{\sqrt{N}} \mathfrak{R}_N(\mathcal{G}) + 4 L_T L_g R \sqrt{\frac{2 \log(2/\delta)}{N}}, \tag{13}$$

where $\mathfrak{R}_N(\mathcal{G})$ denotes the empirical Rademacher complexity of the decoder class.

Proof. The Lipschitz property in Theorem 1 implies that the loss composed with $g \in \mathcal{G}$ is $4 L_T L_g$-Lipschitz in the input coordinates. The contraction inequality for Rademacher complexity therefore bounds the fluctuation of the empirical process. Concentration of measure via McDiarmid's inequality yields the second term in Eq. (13). □

Theorem 2 shows that the topological regularizer generalizes at the familiar $\mathcal{O}(N^{-1/2})$ rate up to a multiplicative constant governed by the Lipschitz modulus of the decoder and canonicalization map. Consequently, minimizing the empirical objective from Eq. (8) suffices to control the population-level topological discrepancy.

A.4 Convergence of Cached Diagram Updates

During training we reuse previously computed diagrams for M iterations before refreshing them. The next proposition quantifies the approximation error induced by this caching scheme.

Proposition 1 (Bias of cached diagrams). *Assume the decoder parameters follow an update rule $\theta_{t+1} = \theta_t - \eta_t \nabla \mathcal{L}_{total}(\theta_t)$ with step sizes $\eta_t \leq \eta$. If diagrams are refreshed every M iterations, then for any batch B the discrepancy between the cached loss $\widetilde{\mathcal{L}}_{topo}$ and the exact loss obeys*

$$\left| \widetilde{\mathcal{L}}_{topo}^{(B)}(\theta_t) - \mathcal{L}_{topo}^{(B)}(\theta_t) \right| \leq 4 L_T L_g \eta \sum_{j=0}^{M-1} \|\nabla \mathcal{L}_{total}(\theta_{t-j})\|_2, \tag{14}$$

so long as the decoder remains within the compact parameter set of Theorem 2.

Proof. Between updates the decoder output drifts by at most $L_g \eta \|\nabla \mathcal{L}_{\text{total}}(\theta_{t-j})\|_2$ in norm. Applying Theorem 1 converts this drift to a Wasserstein perturbation, and summing over M stale steps yields Eq. (14). □

Proposition 1 informs the choice of refresh interval M: the bias is proportional to the cumulative gradient magnitude and step size. In practice we monitor the bound in Eq. (14) to trigger adaptive refreshes when gradients spike, ensuring that the cached diagrams remain faithful surrogates.

A.5 Guarantees for Latent-Space Topology Matching

Finally, we record conditions under which imposing the data-space loss also induces latent-space topological fidelity.

Assumption 2 (Encoder regularity). *The encoder $q_\phi(z \mid x)$ satisfies: (i) the reparameterized samples $z = \mu_\phi(x) + \sigma_\phi(x) \odot \epsilon$ are L_q-Lipschitz in x for fixed ϵ; (ii) q_ϕ admits a log-Sobolev constant $\alpha > 0$ ensuring transportation inequalities.*

Theorem 3 (Latent homology transfer). *Under Assumptions 1 and 2, if the decoder g_θ is injective on the support of p_{data} and achieves $\mathcal{L}_{topo}(\theta) \leq \epsilon$, then the induced latent distribution satisfies*

$$W_p\big(\mathrm{PD}^{(1)}(\mu_\phi(S)), \mathrm{PD}^{(1)}(\mu_\phi(S_{gen}))\big) \leq C(\epsilon + L_q L_g \eta), \tag{15}$$

for a constant C depending on (L_T, L_q, α) and S_{gen} denoting generated samples. Thus, small data-space topological loss enforces approximate preservation of first homology in latent space up to optimization error.

Proof sketch. The encoder regularity ensures that Wasserstein distances between data distributions contract by at most L_q. Injectivity of g_θ allows pulling back diagram discrepancies from data space to latent space without merging distinct homology classes. Combining these facts with Theorem 1 and the optimization error bound in Proposition 1 yields Eq. (15). $\square$

Collectively, these results establish that the proposed topological regularization is stable, generalizes beyond the training dataset, and induces consistent latent structure, providing theoretical justification for the empirical observations reported in the main body.

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