# GOLD: Geometric Optimized Latent Diffusion for Structure-Aware RNA Inverse Folding

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**Paper: https://arxiv.org/abs/2610.22992**
**Code: https://github.com/darkflash03/GOLD**

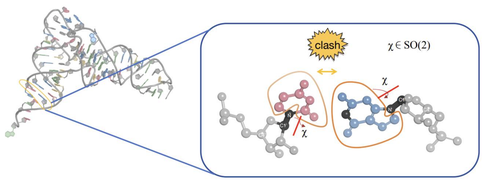
## Insight & Motivation

- Existing RNA inverse folding models condition on a 3D backbone, yet generate nucleotide sequences only.
- Missing side-chain orientation allows steric clashes and locally invalid 3D geometries.
- GOLD co-generates nucleotide identity and continuous side-chain torsion.

**Core insight: Couple sequence identity and side-chain geometry in a shared latent space.**

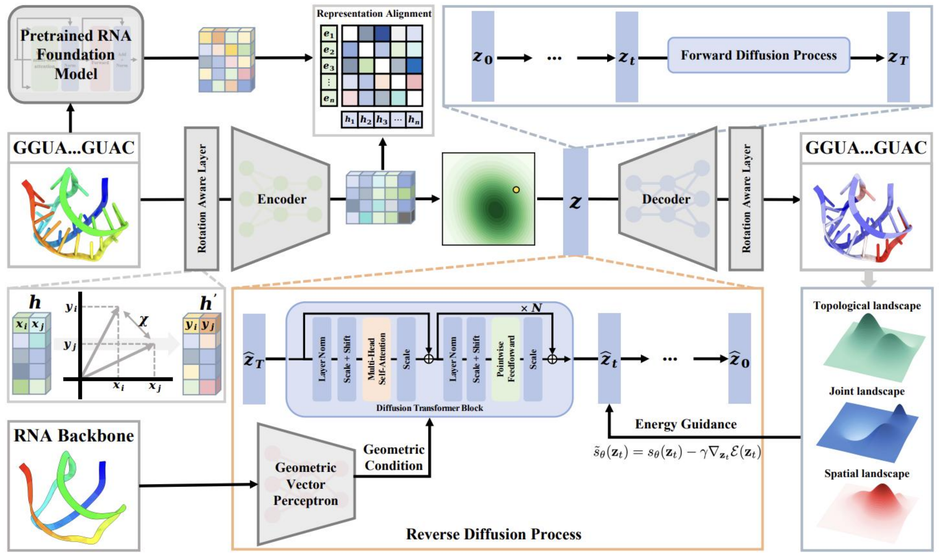
## Preliminaries

### Geometric representation of RNA




- A rigid nucleobase rotates around the glycosidic bond.
- The key continuous degree of freedom is the glycosidic torsion angle.
- Fixed backbone and torsion enable differentiable reconstruction of 3D side-chains.

## Method: GOLD




### (1) GeoVAE: unified latent manifold

SO(2)-aware fusion encodes discrete sequences and continuous side-chain torsion linto one atent manifold.

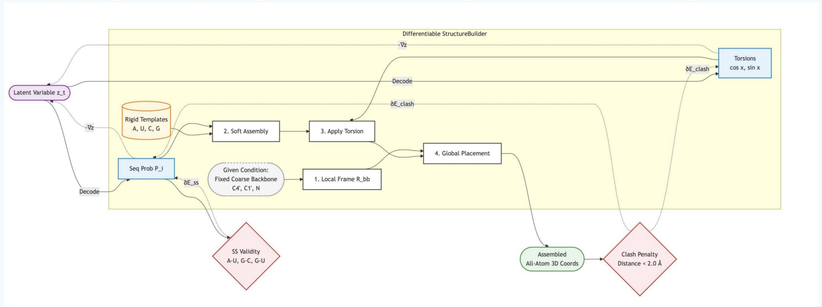
Sequence, torsion, and coordinate reconstruction losses enforce geometric consistency; RNA-FM aligns sequence representations.

### (2) Backbone-conditioned latent diffusion

A GVP encoder extracts 3D backbone geometry; a latent DiT learns the conditional RNA design distribution.

### (3) Training-free dual guidance

Decode soft sequence probabilities and torsion, assemble 3D side-chains, and backpropagate 2D pairing and 3D clash energies to steer denoising.




## Main Results

| Method | Seq Recovery (↑) | SS Recovery (↑) | RMSD (Å, ↓) | |
|---|---|---|---|---|
| | | | RhoFold | AlphaFold3 |
| **GOLD Benchmark (In-Distribution)** | | | | |
| PiFold | $0.4123 \pm 0.0354$ | $0.6184 \pm 0.0648$ | $17.26 \pm 3.56$ | $18.73 \pm 4.27$ |
| RDesign | $0.4430 \pm 0.0326$ | $0.6751 \pm 0.1106$ | $14.65 \pm 4.36$ | $15.12 \pm 3.85$ |
| gRNAde | $0.5453 \pm 0.0873$ | $0.6450 \pm 0.1183$ | $15.38 \pm 4.84$ | $16.10 \pm 4.37$ |
| RiboDiffusion | $0.5148 \pm 0.0574$ | $0.6948 \pm 0.0846$ | $13.07 \pm 3.19$ | $13.89 \pm 3.92$ |
| SOLD | $0.5843 \pm 0.0635$ | $0.7366 \pm 0.0983$ | $12.61 \pm 2.79$ | $13.65 \pm 4.06$ |
| **GOLD (Base)** | $0.6249 \pm 0.0283$ | $0.7785 \pm 0.0782$ | $11.99 \pm 2.84$ | $13.26 \pm 4.34$ |
| **GOLD (Dual-Guided)** | $\mathbf{0.6380 \pm 0.0292}$ | $\mathbf{0.8186 \pm 0.0724}$ | $\mathbf{10.65 \pm 2.63}$ | $\mathbf{12.31 \pm 3.63}$ |
| **CASP15 (Out-of-Distribution)** | | | | |
| PiFold | $0.3156 \pm 0.0362$ | $0.3407 \pm 0.0564$ | $36.23 \pm 4.94$ | $35.43 \pm 6.72$ |
| RDesign | $0.3640 \pm 0.0305$ | $0.4250 \pm 0.0568$ | $33.18 \pm 4.86$ | $38.42 \pm 5.86$ |
| gRNAde | $0.5161 \pm 0.0204$ | $0.4266 \pm 0.0478$ | $33.89 \pm 5.53$ | $39.23 \pm 5.39$ |
| RiboDiffusion | $0.4959 \pm 0.0265$ | $0.6134 \pm 0.0505$ | $31.14 \pm 3.57$ | $30.74 \pm 4.28$ |
| SOLD | $0.5877 \pm 0.0106$ | $0.6367 \pm 0.0481$ | $28.87 \pm 3.23$ | $27.74 \pm 4.04$ |
| **GOLD (Base)** | $0.6187 \pm 0.0246$ | $0.6521 \pm 0.0484$ | $28.32 \pm 3.76$ | $27.17 \pm 4.74$ |
| **GOLD (Dual-Guided)** | $\mathbf{0.6624 \pm 0.0308}$ | $\mathbf{0.7089 \pm 0.0427}$ | $\mathbf{27.64 \pm 3.57}$ | $\mathbf{26.18 \pm 3.93}$ |

GOLD (Base) improves over SOLD; dual guidance adds gains on both benchmarks.

## Ablations

Table 5: Ablation study on the training-free Guidance mechanism.

| Guidance Setup | Weights | | Seq Recovery (↑) | SS Validity (↑) | Clash Score (↓) |
|---|---|---|---|---|---|
| | $\omega_{ss}$ | $\omega_{clash}$ | | | |
| Base (No Guidance) | 0.0 | 0.0 | 0.6249 | 0.9040 | 4.51 |
| SS Guidance Only | 1.0 | 0.0 | 0.6267 | 0.9343 | 4.32 |
| | 2.0 | 0.0 | 0.6264 | 0.9356 | 4.43 |
| | 3.0 | 0.0 | 0.6268 | **0.9382** | 4.38 |
| Clash Guidance Only | 0.0 | 0.05 | 0.6362 | 0.9012 | 3.11 |
| | 0.0 | 0.1 | 0.6378 | 0.9028 | 2.76 |
| | 0.0 | 0.5 | 0.6353 | 0.9061 | **2.28** |
| | 0.0 | 1.0 | 0.6269 | 0.8938 | 2.77 |
| **Dual-Guidance** | **1.0** | **0.1** | **0.6380** | 0.9290 | 2.67 |

## Case Studies

