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RNA druggability assessment

Job summary

Job ID:	2gdi-demo
Date:	2026-05-06 09:38 UTC
Sequence length:	78 nt
Conformers:	5
Pockets detected:	30 (across all frames)
Clusters:	12 (8 passing persistence floor)
Top-3 surfaced:	3
RhoFold pLDDT (mean):	0.729

Sequence:

GACUCGGGGUGCCCUUCUGCGUGAAGGCUGAGAAAUACCCGUAUCACCUGAUCUGGAUAAUGCCAGCGUAGGGAAGUU

Top-3 candidate druggable pockets

#1 Cluster 0 (geometric rank #1)

STRICT (71%)

Persistence:
1.00 (5 of 5 frames)
Geometric score (ranking):
5.000 = persistence × n_residues_intersected (1.00 × 5)
Mean druggability (metadata, not ranking):
0.015 -- fpocket protein-trained score, see Methods
Median druggability:
0.016
Max druggability:
0.029
Centroid (A):
-9.57 0.21 0.55
Residues (union):
9, 10, 29, 30, 32, 33, 47, 62, 63, 64
Residues (intersection):
9, 10, 30, 32, 33
Binding-site overlap (benchmark):
10/14 residues (71%) - strict (>=50% of binding-site residues)

#2 Cluster 8 (geometric rank #2)

NONE (29%)

Persistence:
0.40 (2 of 5 frames)
Geometric score (ranking):
4.400 = persistence × n_residues_intersected (0.40 × 11)
Mean druggability (metadata, not ranking):
0.010 -- fpocket protein-trained score, see Methods
Median druggability:
0.010
Max druggability:
0.018
Centroid (A):
-9.22 9.51 -0.36
Residues (union):
11, 12, 13, 27, 28, 29, 33, 57, 58, 59, 60, 61, 62, 63
Residues (intersection):
11, 12, 28, 29, 33, 57, 58, 60, 61, 62, 63
Binding-site overlap (benchmark):
4/14 residues (29%) - neither strict nor near

#3 Cluster 2 (geometric rank #3)

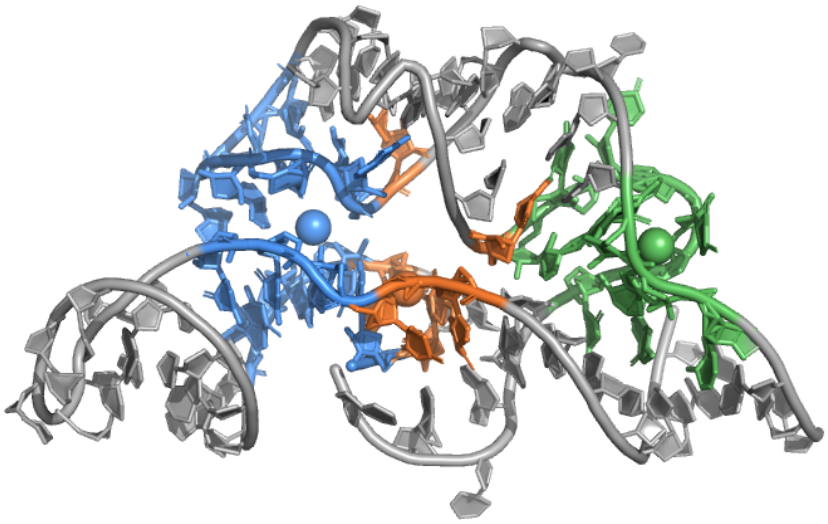
NONE (0%)

Persistence:
0.80 (4 of 5 frames)
Geometric score (ranking):
4.000 = persistence × n_residues_intersected (0.80 × 5)
Mean druggability (metadata, not ranking):
0.539 -- fpocket protein-trained score, see Methods
Median druggability:
0.468
Max druggability:
0.892

Centroid (A):
3.65 -16.21 -1.40
Residues (union):
40, 41, 42, 43, 44, 45, 46, 73, 74, 75
Residues (intersection):
41, 42, 43, 73, 74
Binding-site overlap (benchmark):
0/14 residues (0%) - neither strict nor near

Predicted structure with top-3 pockets

Cartoon backbone, gray. Top-3 pocket residues highlighted (orange / azure / green = ranks 1 / 2 / 3). Centroid spheres shown at the geometric centre of each cluster's Kabsch-aligned member centres. Legend: #1 = cluster 0; #2 = cluster 8; #3 = cluster 2.



Methods

v0.2 ranks candidate pockets by structural persistence across the conformational ensemble, weighted by binding-residue stability (score = persistence x n_residues_intersected). This replaces the v0.1 ranker, which used fpocket's druggability score as the primary ranking signal. fpocket's druggability score is the output of a logistic regression trained on protein druggable-vs-non-druggable cavities; its dominant feature is normalised against a protein hydrophobic-density range that does not transfer to RNA cavities. On validated RNA benchmark targets the protein-trained classifier consistently scored the actual binding-site cluster near zero while assigning non-binding cavities scores in the 0.1-0.7 range. The geometric ranker recovers the binding-site cluster at rank-1 on 3 of 4 v0.1 retro benchmark targets vs 0 of 4 with the previous ranker. fpocket's druggability score is still computed and reported per cluster as metadata; druggability assessment itself is left to the customer's medicinal chemistry workflow.

Structures are predicted using RhoFold+ (Apache 2.0). Conformational ensemble generated by anisotropic network model (ANM) normal-mode sampling on the C3' backbone, perturbing along the 10 lowest-frequency collective modes (ProDy, BSD-3). Pockets detected per conformer using fpocket (MIT) with RNA-tuned alpha-sphere and clustering parameters (min radius 3.0 A, max 5.7 A, min alpha-spheres 35, clustering distance 1.65 A). Pockets are clustered across the ensemble after Kabsch-aligning frames to the reference. Persistence is the fraction of frames a cluster is detected in; binding-residue stability is the count of residues contacted by the cluster in every member frame. Clusters with persistence below the configured floor are excluded from the customer-visible top-3.

For targets with diverse-tail evolutionary representation (sequences with at least one homolog at <77% identity, or a non-trivial fraction of homologs in the 70-80% identity band), an MSA-aware structure prediction path is available as an opt-in mode. This empirical screening criterion is calibrated on a benchmark of seven RNA targets and will be refined as more targets accumulate. Single-sequence prediction is the default for all other targets.

Results are computational predictions. Experimental validation is required before use in drug development or clinical applications.

Binding-mode caveat

Pipeline detects cleft-shaped binding pockets. Groove-binding modes and shallow surface-deformation binding may be missed. Contact us if your target's binding mode is groove-mediated.