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RNA druggability assessment

Job summary

Job ID:	4lvv-demo
Date:	2026-05-11 20:51 UTC
Sequence length:	89 nt
Conformers:	5
Pockets detected:	20 (across all frames)
Clusters:	7 (4 passing persistence floor)
Top-3 surfaced:	3
RhoFold pLDDT (mean):	81.805

Sequence:

GGAGAGUAGAUGAUUCGCGUUAAGUGUGUGUGAAUGGGAUGUCGUCACACAACGAAGCGAGAGCGCGGUGAAUCAUUGCA
UCCGCUCCA

Top-3 candidate druggable pockets

#1 Cluster 1 (geometric rank #1) — STRICT (50%)

Persistence:
0.80 (4 of 5 frames)
Geometric score (ranking):
5.600 = persistence × n_residues_intersected (0.80 × 7)
Mean druggability (metadata, not ranking):
0.026 -- fpocket protein-trained score, see Methods
Median druggability:
0.000
Max druggability:
0.104
Centroid (A):
6.26 -1.99 -0.64
Residues (union):
7, 8, 9, 35, 36, 38, 39, 40, 41, 42, 43, 44, 78, 79
Residues (intersection):
8, 35, 42, 43, 44, 78, 79
Binding-site overlap (benchmark):
8/16 residues (50%) - strict (>=50% of binding-site residues)

#2 Cluster 3 (geometric rank #2) — NEAR (44%)

Persistence:
0.80 (4 of 5 frames)
Geometric score (ranking):
5.600 = persistence × n_residues_intersected (0.80 × 7)
Mean druggability (metadata, not ranking):
0.418 -- fpocket protein-trained score, see Methods
Median druggability:
0.510
Max druggability:
0.619
Centroid (A):
6.12 0.06 -7.76
Residues (union):
7, 34, 35, 36, 38, 39, 40, 41, 42, 44, 79, 80, 81
Residues (intersection):
35, 36, 38, 39, 40, 41, 79
Binding-site overlap (benchmark):
7/16 residues (44%) - near (>=30% of binding-site residues)

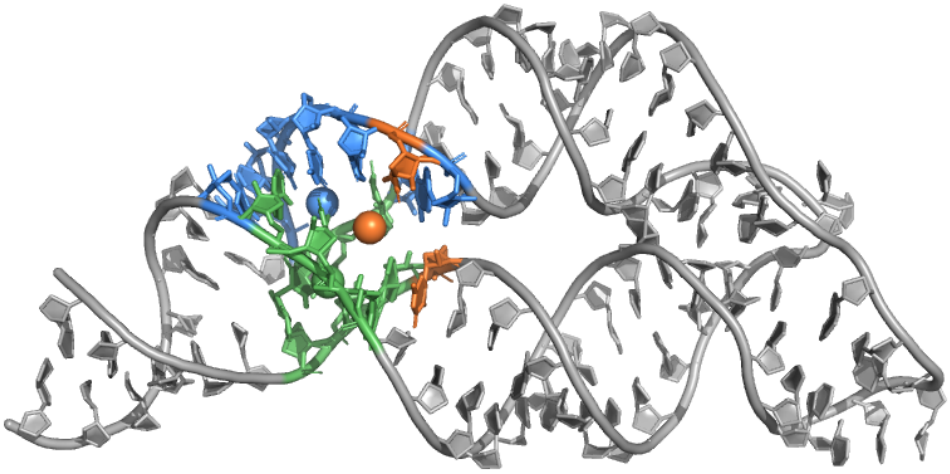
#3 Cluster 2 (geometric rank #3) — NEAR (38%)

Persistence:
0.80 (4 of 5 frames)
Geometric score (ranking):
4.800 = persistence × n_residues_intersected (0.80 × 6)
Mean druggability (metadata, not ranking):
0.002 -- fpocket protein-trained score, see Methods
Median druggability:
0.000
Max druggability:
0.006

Centroid (A):
0.75 0.68 -0.91
Residues (union):
6, 7, 8, 35, 36, 78, 79, 80
Residues (intersection):
6, 7, 8, 36, 78, 79
Binding-site overlap (benchmark):
6/16 residues (38%) - near (>=30% of binding-site residues)

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 1; #2 = cluster 3; #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.