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RNA druggability assessment

Job summary

Job ID:	2hoj-demo
Date:	2026-05-11 21:14 UTC
Sequence length:	83 nt
Conformers:	5
Pockets detected:	22 (across all frames)
Clusters:	13 (5 passing persistence floor)
Top-3 surfaced:	3
RhoFold pLDDT (mean):	75.381

Sequence:

GCGACUCGGGGUGCCCUUCUGCGUGAAGGCUGAGAAAUACCCGUAUCACCUGAUCUGGAUAAUGCCAGCGUAGGGAAGUC
GCA

Top-3 candidate druggable pockets

#1 Cluster 1 (geometric rank #1) — STRICT (53%)

Persistence:
1.00 (5 of 5 frames)
Geometric score (ranking):
7.000 = persistence × n_residues_intersected (1.00 × 7)
Mean druggability (metadata, not ranking):
0.222 -- fpocket protein-trained score, see Methods
Median druggability:
0.144
Max druggability:
0.630
Centroid (A):
4.76 -11.59 7.46
Residues (union):
11, 12, 31, 32, 34, 35, 37, 50, 64, 65
Residues (intersection):
11, 12, 31, 32, 34, 35, 65
Binding-site overlap (benchmark):
9/17 residues (53%) - strict (>=50% of binding-site residues)

#2 Cluster 9 (geometric rank #2) — NEAR (47%)

Persistence:
0.60 (3 of 5 frames)
Geometric score (ranking):
3.600 = persistence × n_residues_intersected (0.60 × 6)
Mean druggability (metadata, not ranking):
0.065 -- fpocket protein-trained score, see Methods
Median druggability:
0.058
Max druggability:
0.111
Centroid (A):
13.85 -6.08 6.50
Residues (union):
50, 51, 52, 53, 64, 66, 67, 68, 69, 70
Residues (intersection):
50, 51, 52, 64, 67, 68
Binding-site overlap (benchmark):
8/17 residues (47%) - near (>=30% of binding-site residues)

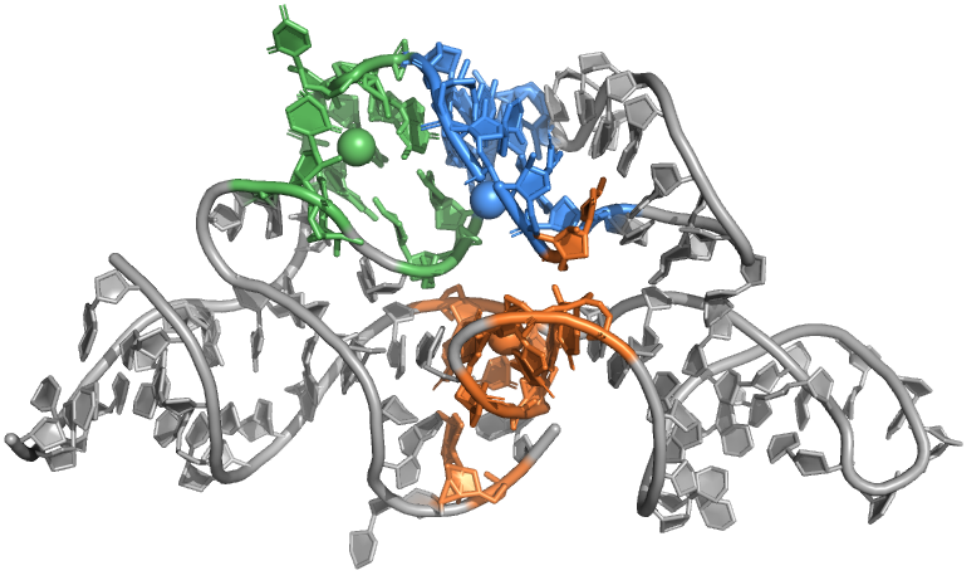
#3 Cluster 4 (geometric rank #3) — NONE (18%)

Persistence:
0.40 (2 of 5 frames)
Geometric score (ranking):
3.200 = persistence × n_residues_intersected (0.40 × 8)
Mean druggability (metadata, not ranking):
0.001 -- fpocket protein-trained score, see Methods
Median druggability:
0.001
Max druggability:
0.001

Centroid (A):
13.64 3.40 0.76
Residues (union):
46, 47, 49, 50, 70, 71, 72, 73, 74
Residues (intersection):
46, 47, 49, 50, 70, 71, 72, 73
Binding-site overlap (benchmark):
3/17 residues (18%) - 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 1; #2 = cluster 9; #3 = cluster 4.



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.