Yet another definition of a long-range RNA tertiary motif

Eugene Baulin
Laboratory of Bioinformatics and Protein Engineering (prof. Janusz M. Bujnicki)
International Institute of Molecular and Cell Biology in Warsaw

Benasque, 18 August 2022

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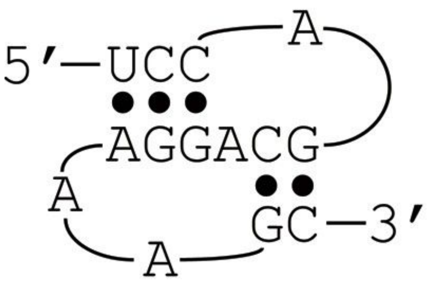
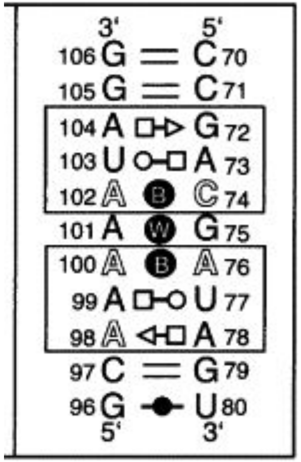
RNA tertiary structure

2D ≤ X ≤ 3D

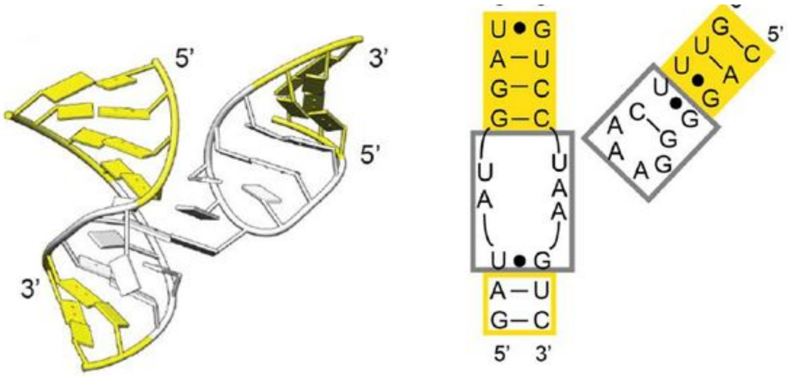
2D ≤ X ≤ **2.5D**

2.5D ≤ X ≤ 3D





- Pseudoknots
- “Nested” non-canonical interactions

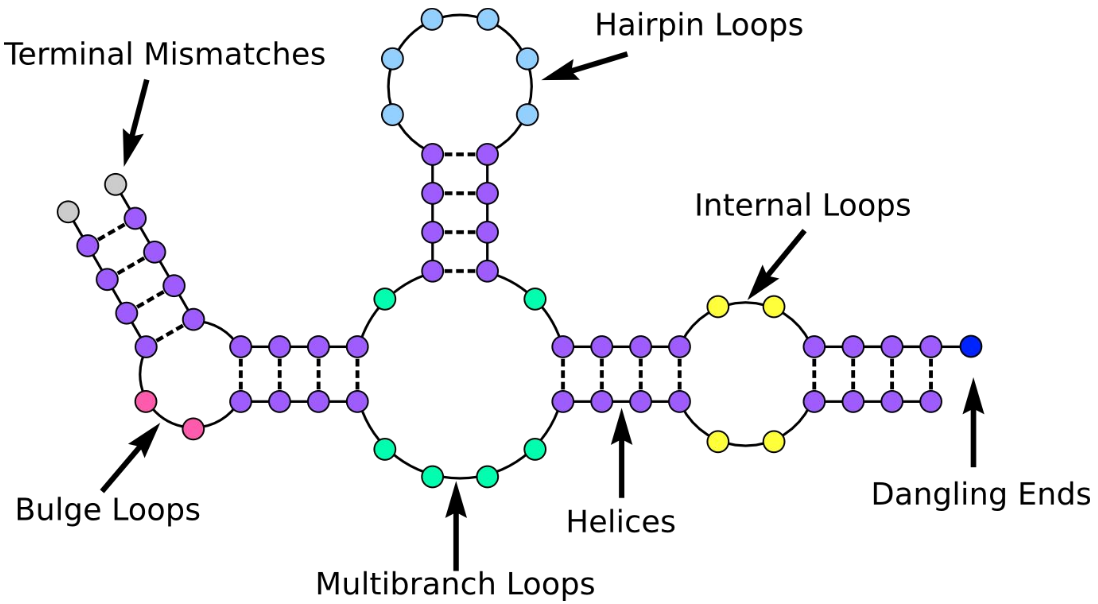


GAAA/11nt

Local tertiary motifs

2D ≤ X ≤ 3D

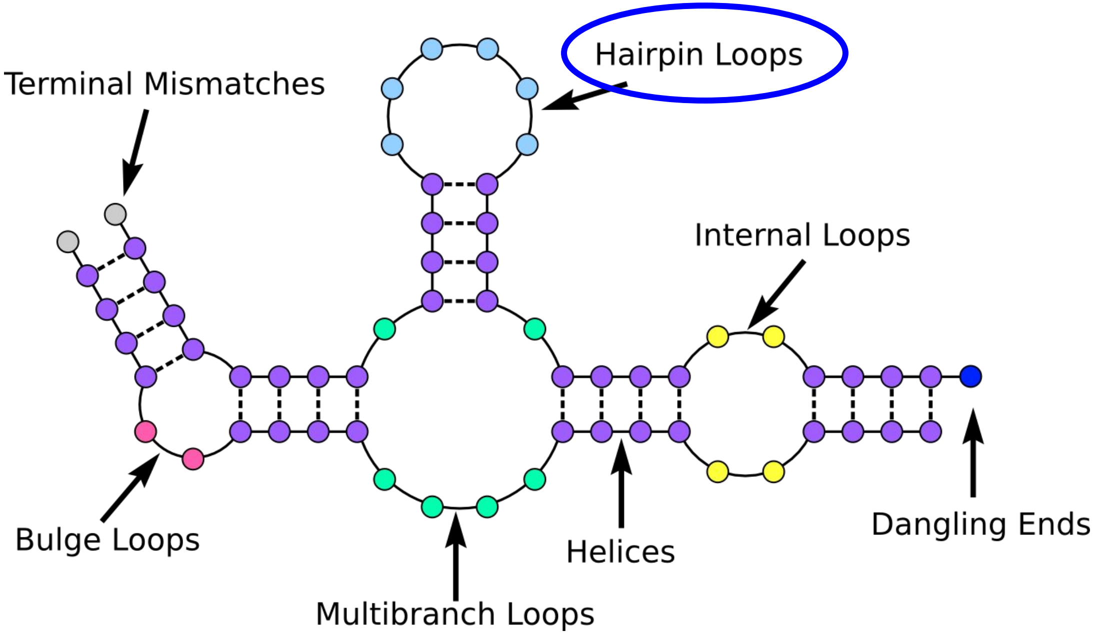
2D ≤ X ≤ **2.5D**

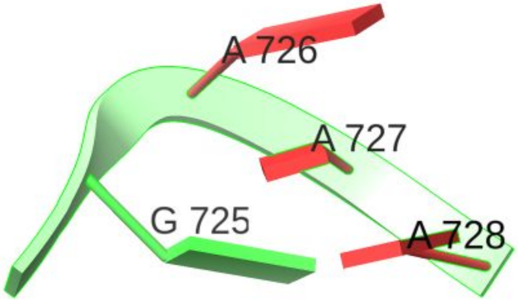


Local tertiary motifs

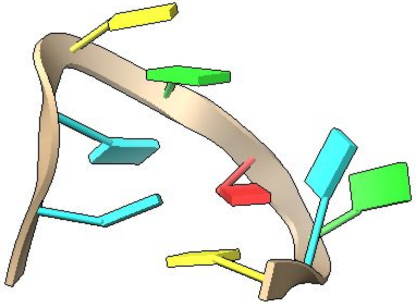
2D ≤ X ≤ 3D

2D ≤ X ≤ **2.5D**





GAAA tetraloop

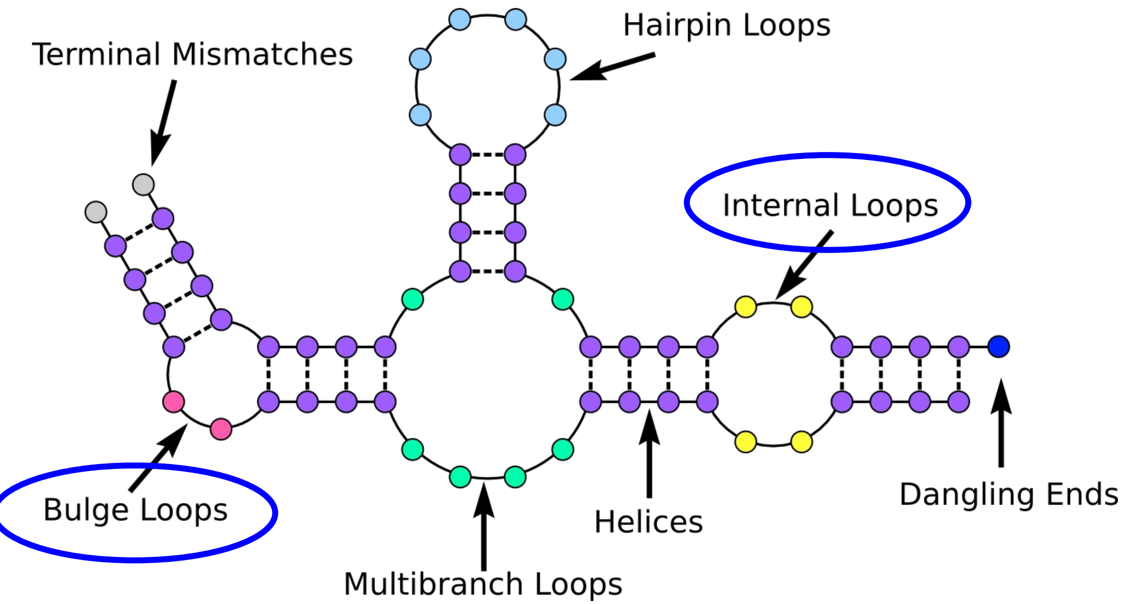


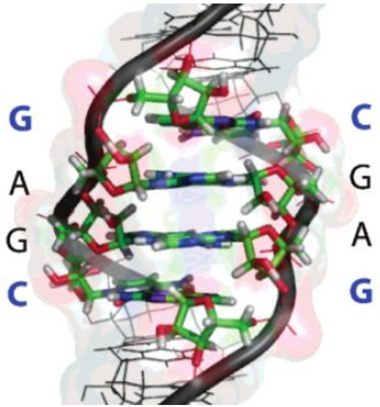
T-loop

Local tertiary motifs

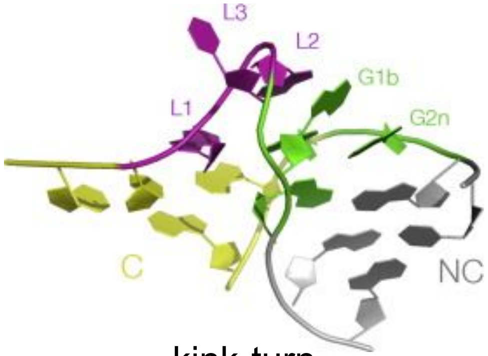
2D ≤ X ≤ 3D

2D ≤ X ≤ **2.5D**





tandem-sheared-GA

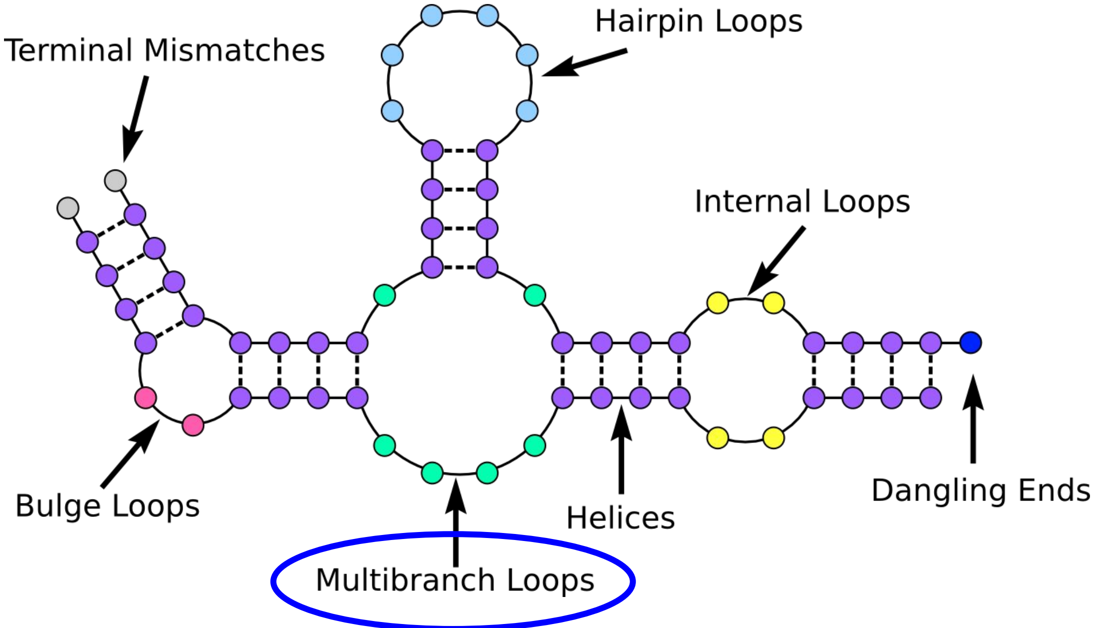


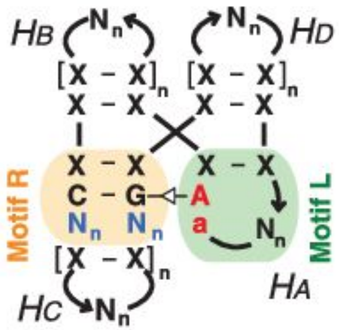
kink-turn

Local tertiary motifs

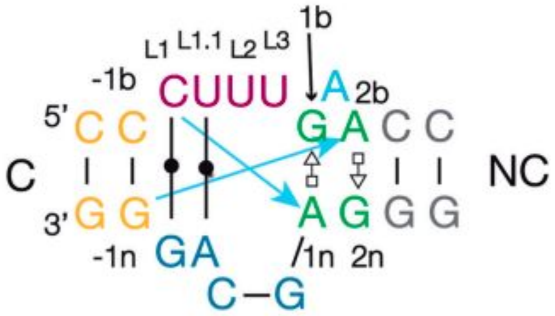
2D ≤ X ≤ 3D

2D ≤ X ≤ **2.5D**





A-minor junction



k-junction

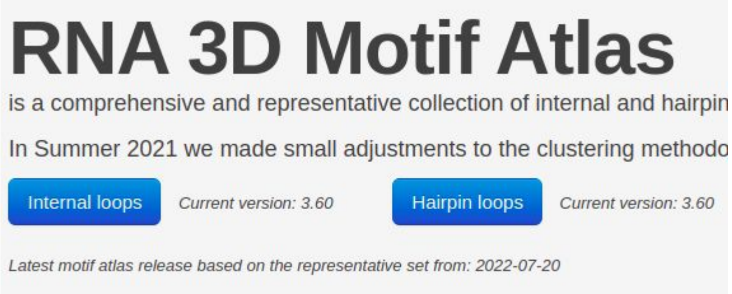
Local tertiary motifs

2D ≤ X ≤ 3D

2D ≤ X ≤ **2.5D**

RNA CoSSMos
Characterization of Secondary Structure Motifs

RNA Bricks



RNA 3D Motif Atlas

is a comprehensive and representative collection of internal and hairpin

In Summer 2021 we made small adjustments to the clustering methodo

Current version: 3.60

Current version: 3.60

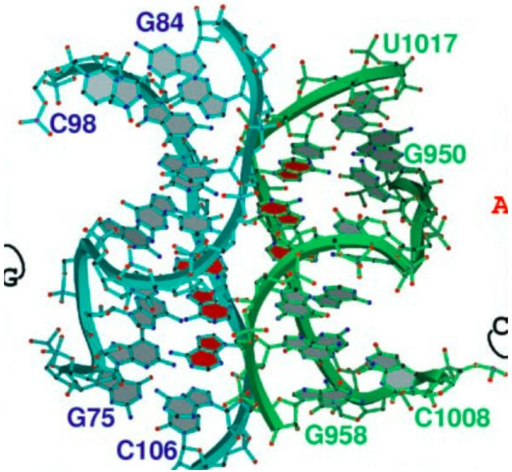
Latest motif atlas release based on the representative set from: 2022-07-20

RNAJunction
A database of RNA junction and kissing loop structures

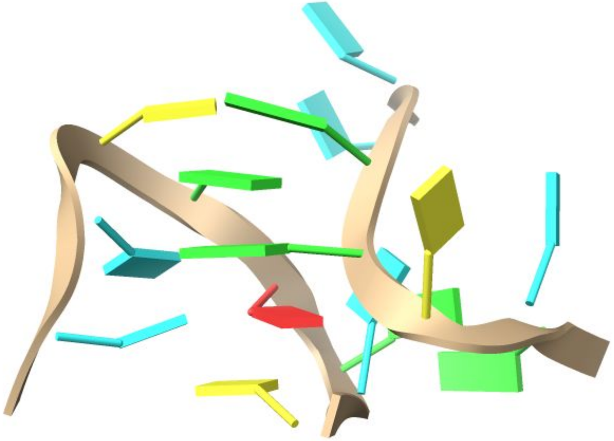
Long-range tertiary motifs

2D ≤ X ≤ 3D

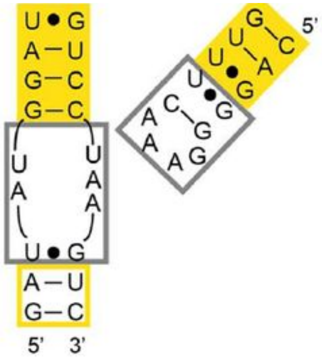
2.5D ≤ X ≤ 3D



A-patch



D-loop/T-loop



GAAA/11nt

Long-range tertiary motifs

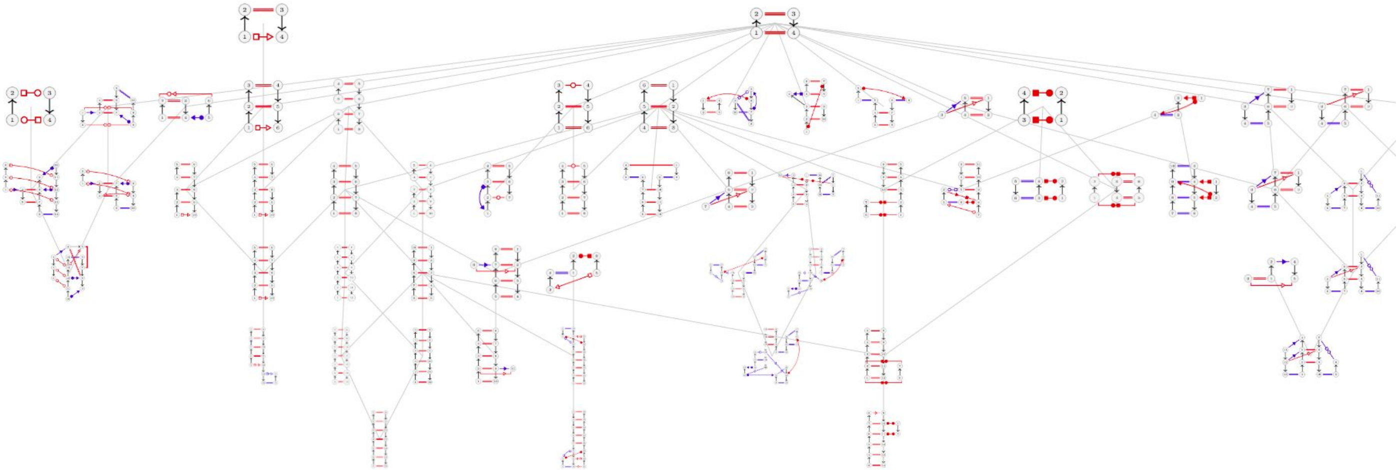
2D ≤ X ≤ 3D

2.5D ≤ X ≤ 3D

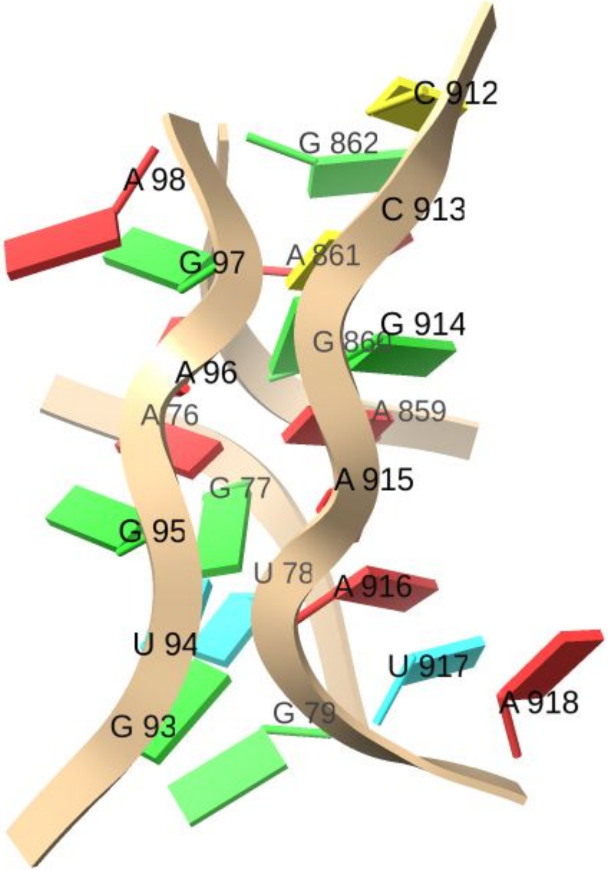
Distant SSEs RINs

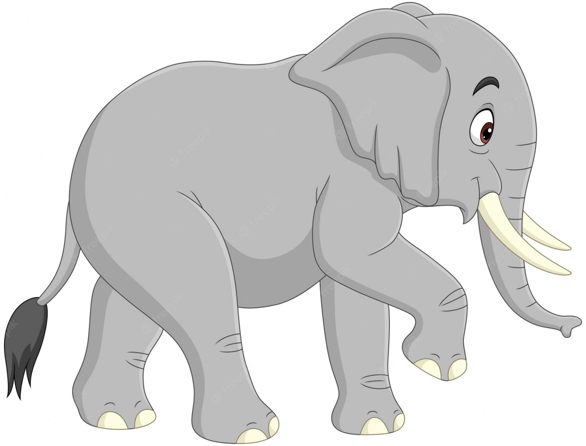
Pseudoknot mesh
A-minor mesh
A-minor type I
A-minor type I/II
trans-W-C/H mesh
Ribose zipper
GNRA
A-rich loop

CaRNAval
Homepage



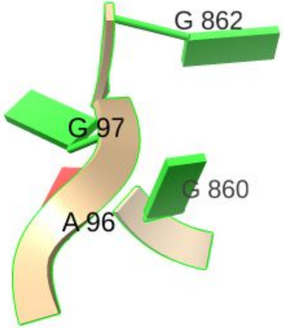
Double symmetrical A-patch (23S-5S rRNA)

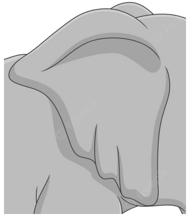




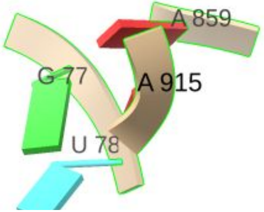
Double symmetrical A-patch (23S-5S rRNA)

```
7M4Y|1|B|A|96   ntSS  7M4Y|1|A|G|860
7M4Y|1|B|G|97    1BPh 7M4Y|1|A|G|862
```

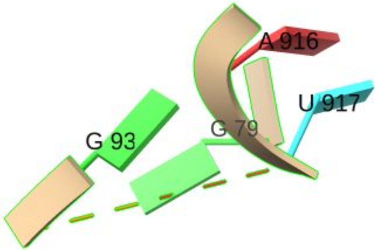


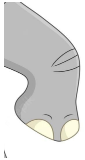


```
7M4Y|1|A|A|915   2BR  7M4Y|1|B|U|78
7M4Y|1|B|G|77   ntSS  7M4Y|1|A|A|915
7M4Y|1|B|G|77   ncSS  7M4Y|1|A|A|859
```



```
7M4Y|1|A|A|916   2BPh 7M4Y|1|B|G|79
7M4Y|1|B|G|93   n1BPh 7M4Y|1|A|U|917
7M4Y|1|B|G|93    3BR  7M4Y|1|A|A|916
```

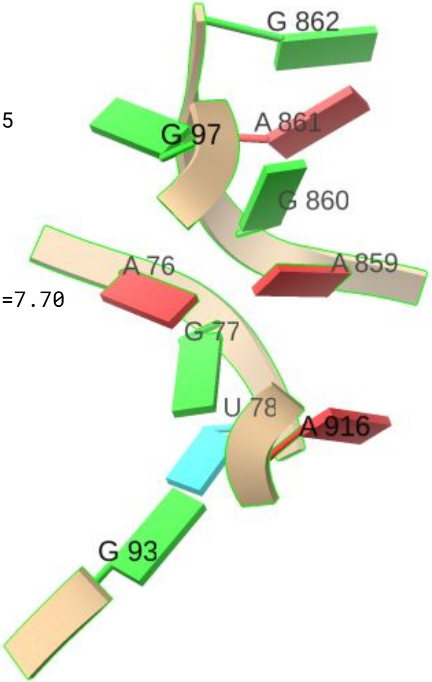




http://rna.bgsu.edu/rna3dhub/pdb/7M4Y/interactions/fr3d/all

Double symmetrical A-patch (23S-5S rRNA)

```
1..A.A.859.    1..B.G.77.     interBase-angle=66 H-bonds[2]: "O2'(hydroxyl)-O3'[3.06],N3-O2'(hydroxyl)[2.60]" min-baseDist=4.83
1..A.G.860.    1..B.A.76.     interBase-angle=65 H-bonds[2]: "O3'-O2'(hydroxyl)[2.97],O2'(hydroxyl)-N3[3.04]" min-baseDist=5.75
1..A.G.860.    1..B.G.97.     interBase-angle=71 H-bonds[1]: "N2(amino)-O4'[3.50]" min-baseDist=5.19
1..A.A.861.    1..B.G.97.     interBase-angle=74 H-bonds[2]: "O3'-N2(amino)[3.32],O2'(hydroxyl)-O2'(hydroxyl)[2.74]"
min-baseDist=6.52
1..A.G.862.    1..B.G.97.     interBase-angle=78 H-bonds[1]: "OP1-N2(amino)[3.43]" min-baseDist=7.69
1..A.A.916.    1..B.G.77.     interBase-angle=65 H-bonds[1]: "O4'-N2(amino)[3.18]" min-baseDist=4.60
1..A.A.916.    1..B.U.78.     interBase-angle=67 H-bonds[3]:
"O2'(hydroxyl)-O2'(hydroxyl)[3.03],O2'(hydroxyl)-O2(carbonyl)[3.48],N3-O2'(hydroxyl)[2.57]" min-baseDist=5.70
1..A.A.916.    1..B.G.93.     interBase-angle=69 H-bonds[1]: "O2'(hydroxyl)-N2(amino)[2.94]" min-baseDist=6.55
1..A.G.862.     OP1-hbonds[2]: "N2@1..B.G.97.[3.43]"
nts=4 AGAG 1..A.A.859.,1..A.G.860.,1..B.A.76.,1..B.G.77. (ribose zipper)
```

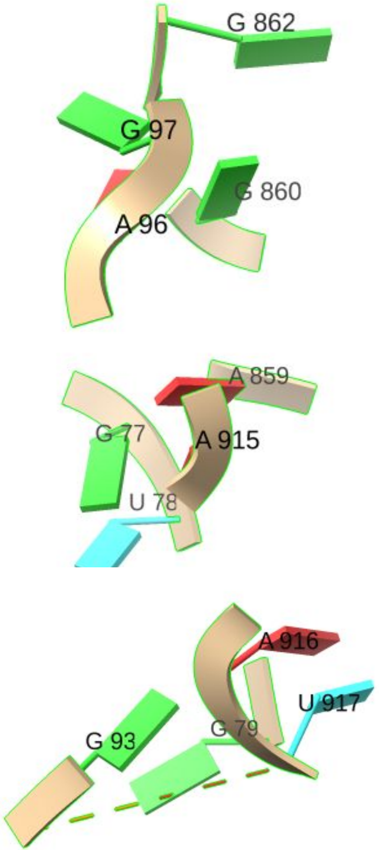


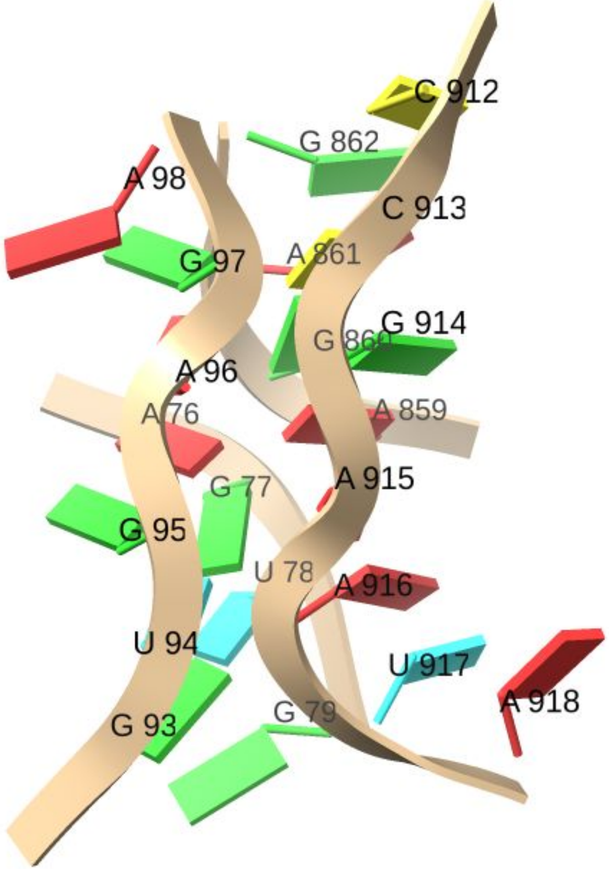
```
1..A.G.914.    1..B.A.96.     interBase-angle=60 H-bonds[1]: "O2'(hydroxyl)-O2'(hydroxyl)[3.28]" min-baseDist=7.70
```

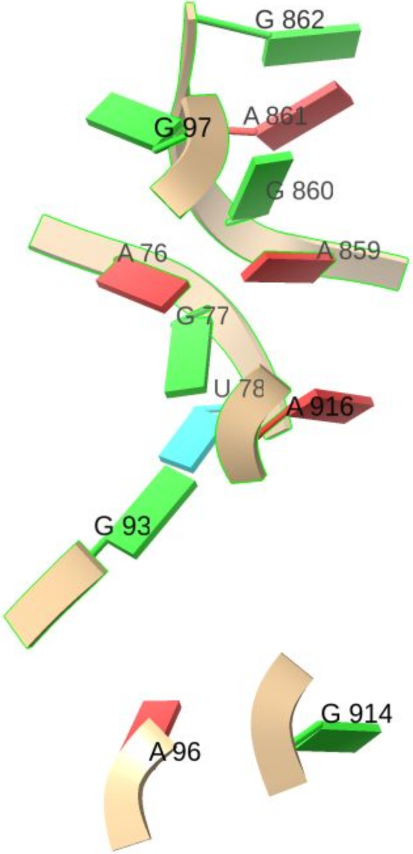
0 A-minors!!

http://forum.x3dna.org/rna-structures/ (DSSR, version 2.0)

And what about the “consensus”?



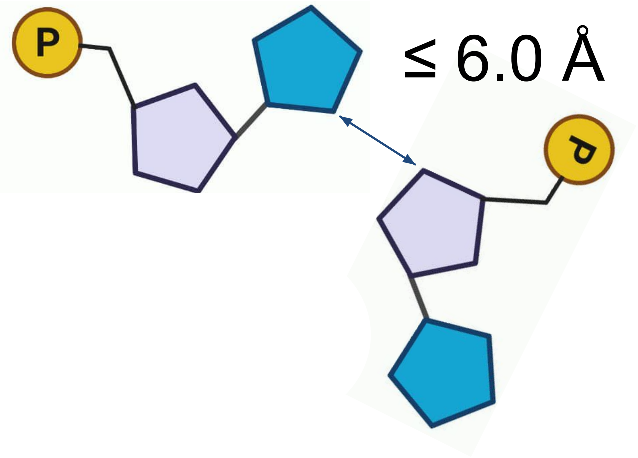


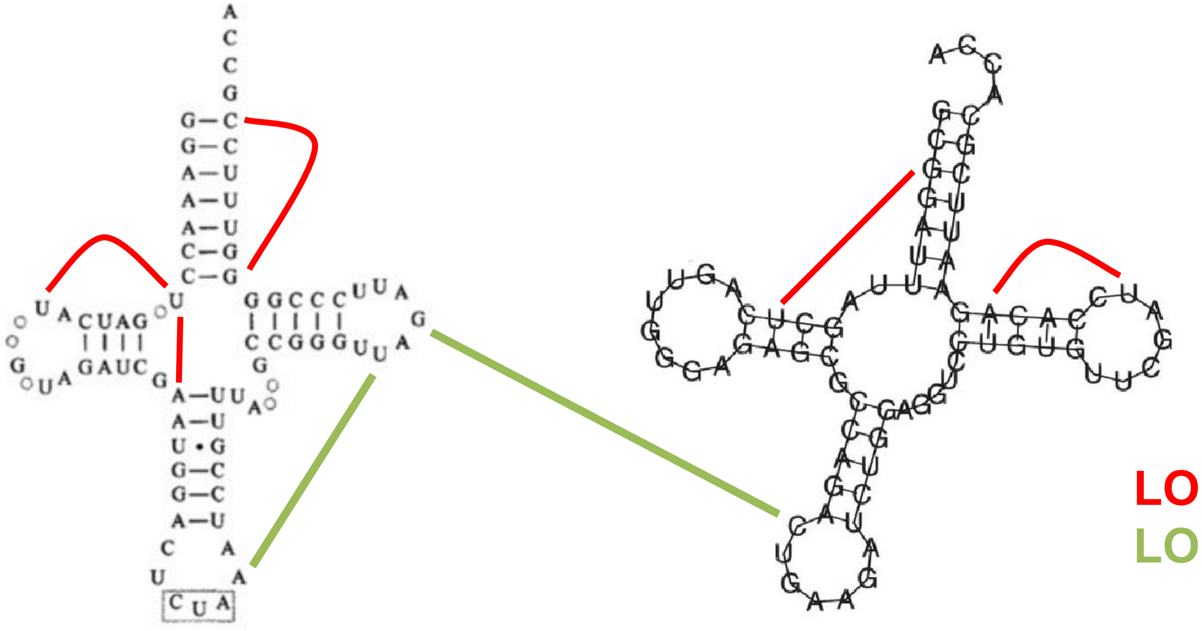


Long-range (LR) residue-residue pairs

BGSU NR-list, 4.0Å cutoff -> one chain per Rfam family

-> 97 RNA chains -> 70 chains with at least one LR pair





LOCAL

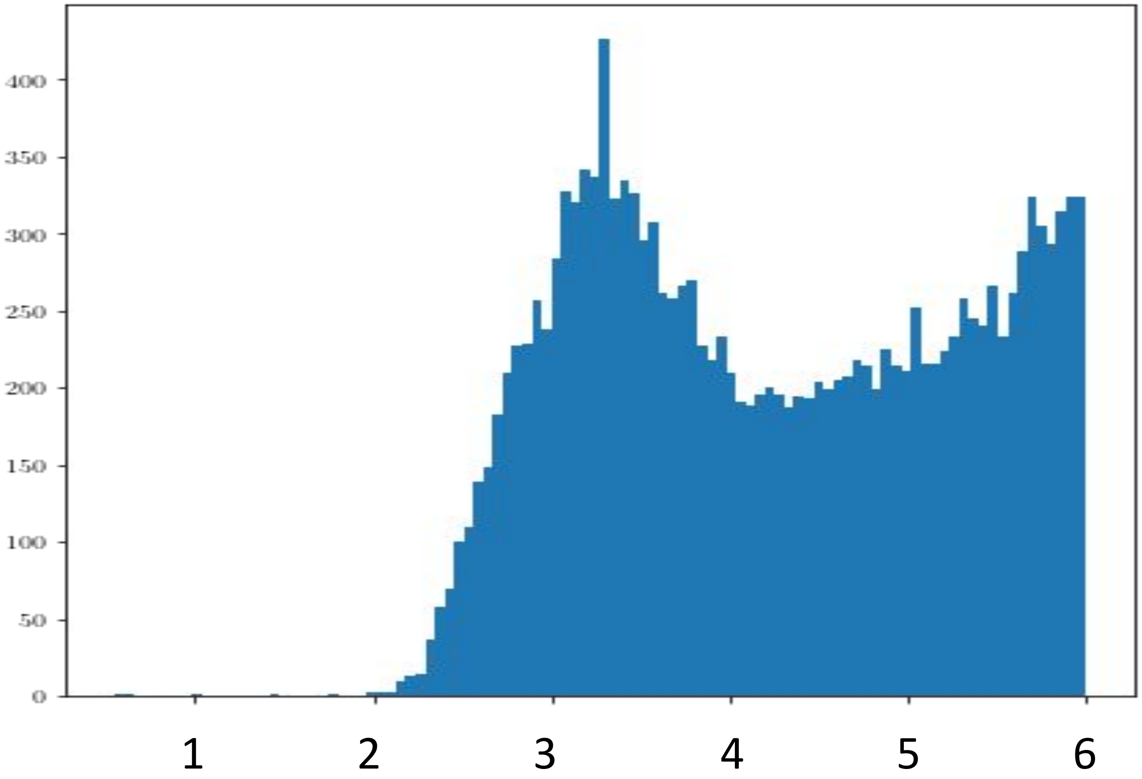
LONG-RANGE

Long-range (LR) residue-residue pairs

OVERALL	Stem	Loop	Total	Total %
A	550 (19.5%)	**2269 (80.5%)**	2819	26.30%
G	**2118 (61.2%)**	1340 (38.8%)	3458	32.30%
C	**1733 (69.3%)**	769 (30.7%)	2502	23.40%
U	840 (43.4%)	**1095 (56.6%)**	1935	18.00%
Total	5241 (48.9%)	5473 (51.1%)	10714	100%

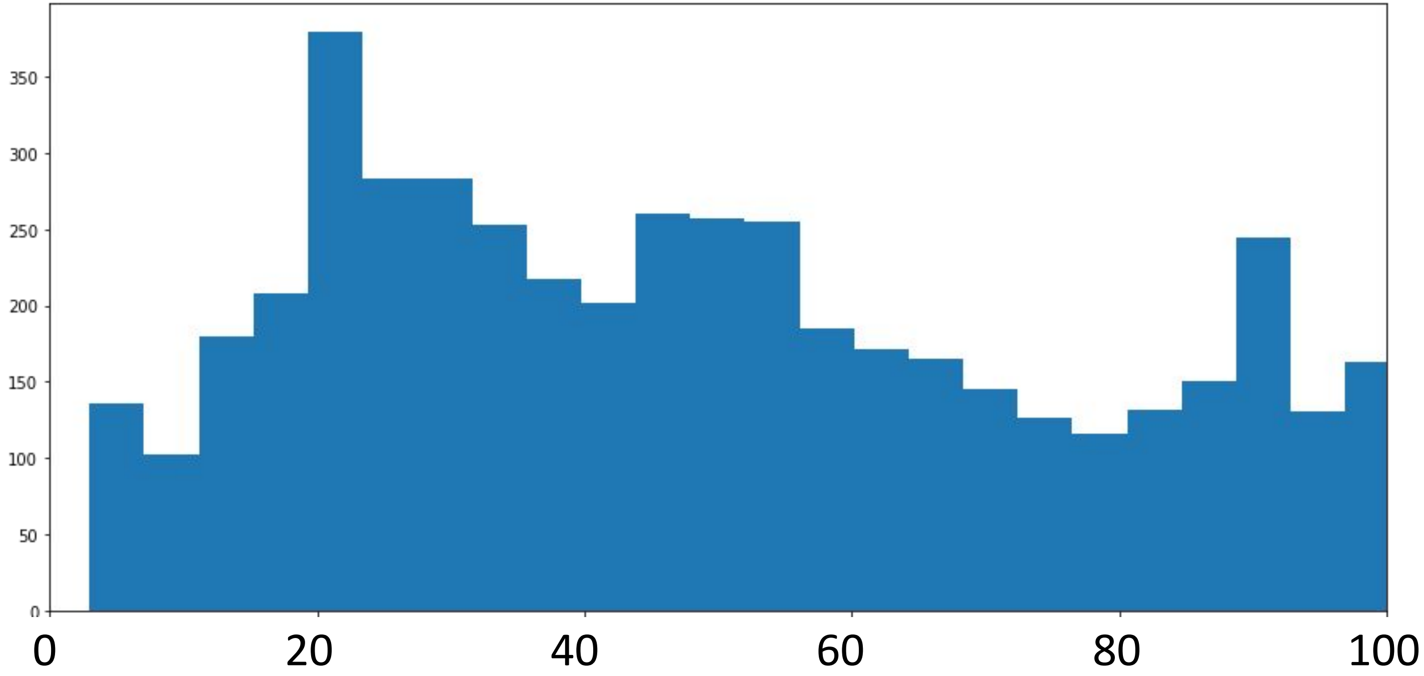
Long-range (LR) residue-residue pairs

Closest atom-atom pair distance (in angstroms)

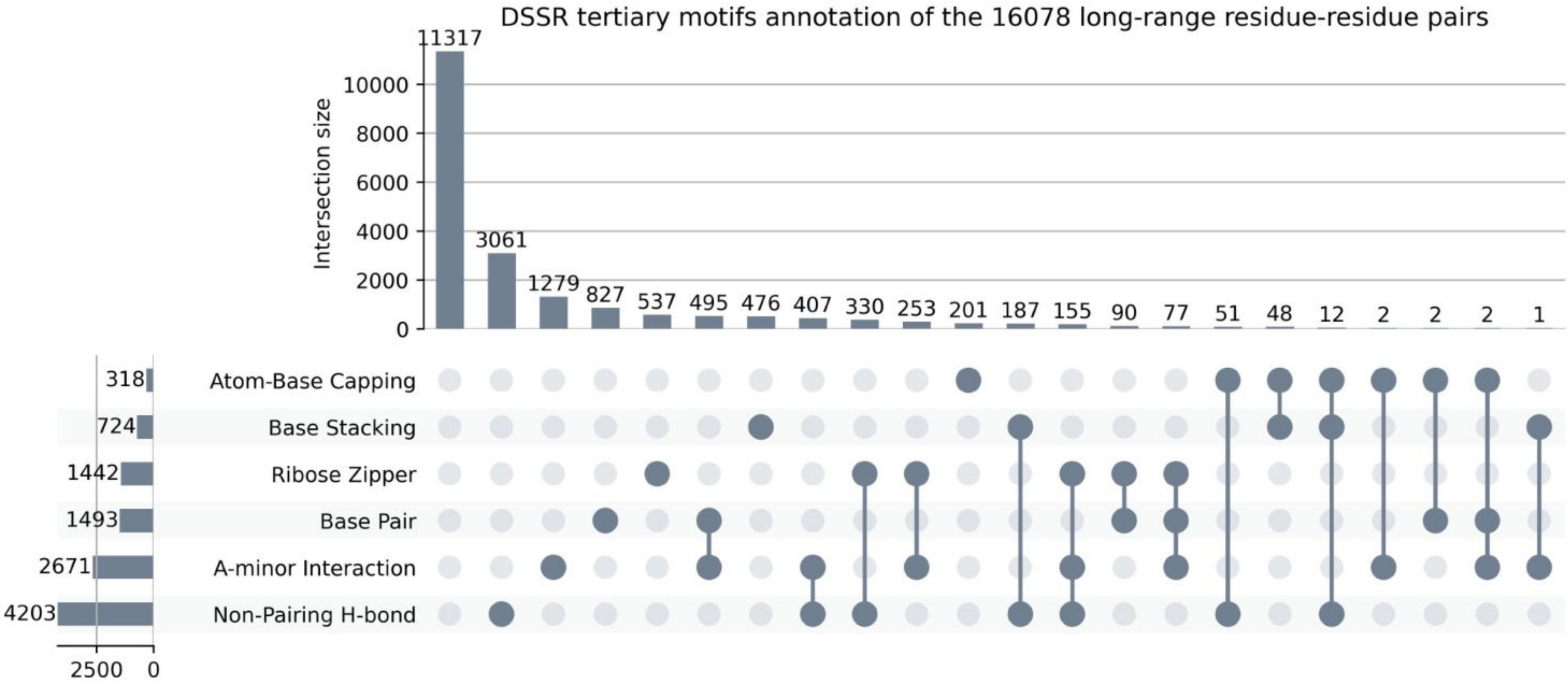


Long-range (LR) residue-residue pairs

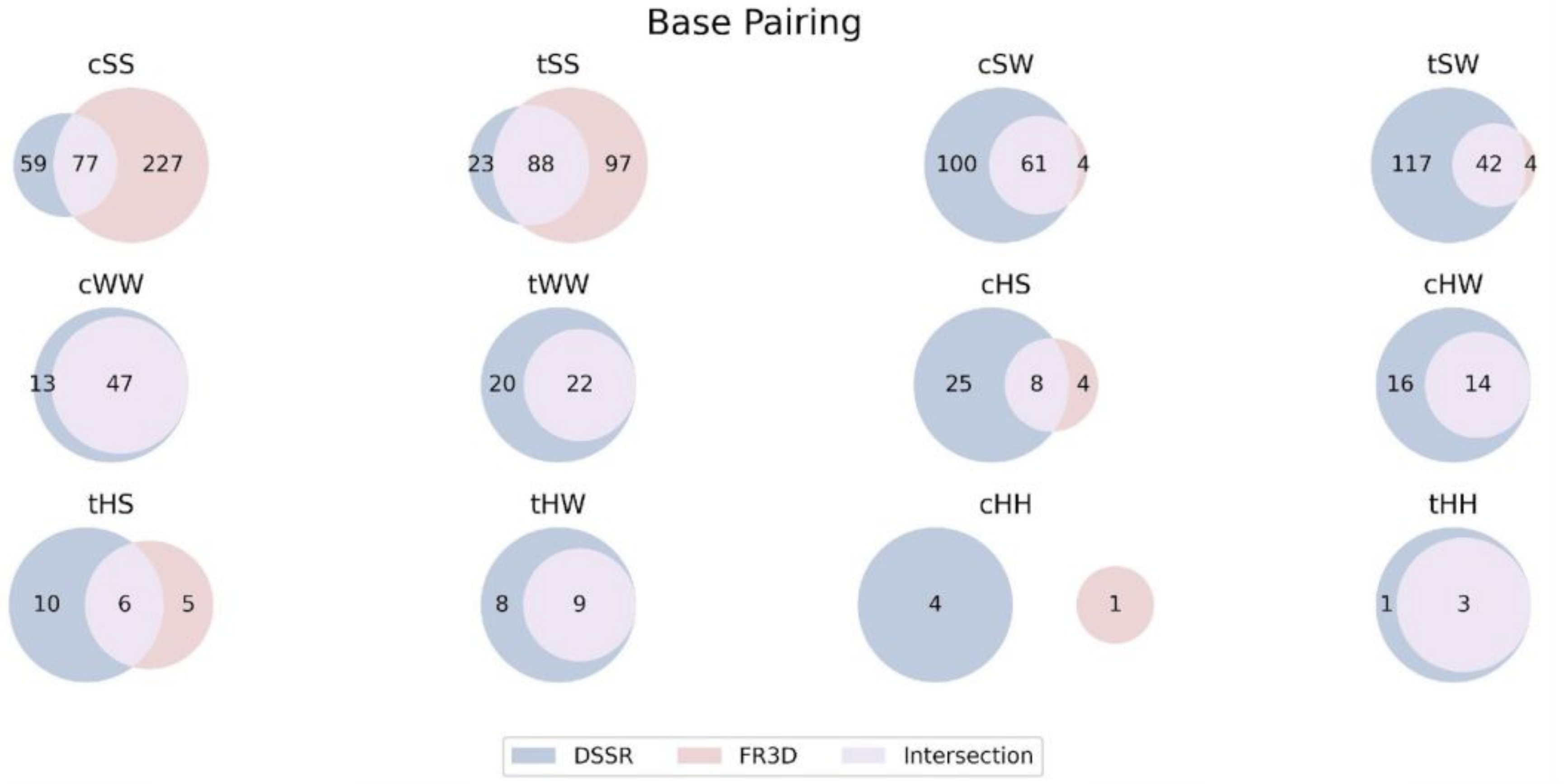
Sequence distance (in residues, cut at 100, median = 200, mean = 500)



Long-range (LR) residue-residue pairs

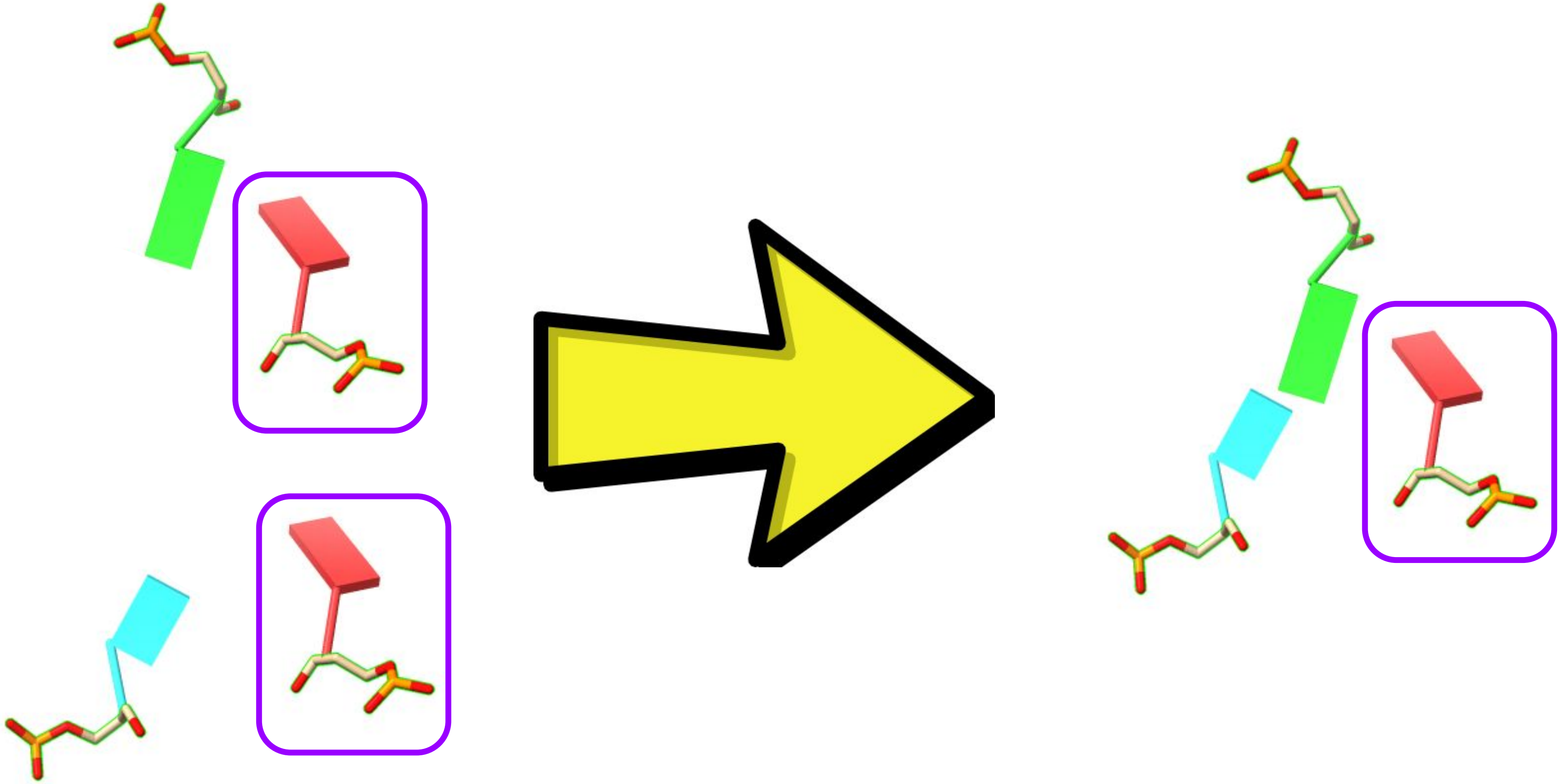

DSSR tertiary motifs annotation of the 16078 long-range residue-residue pairs

Long-range (LR) residue-residue pairs

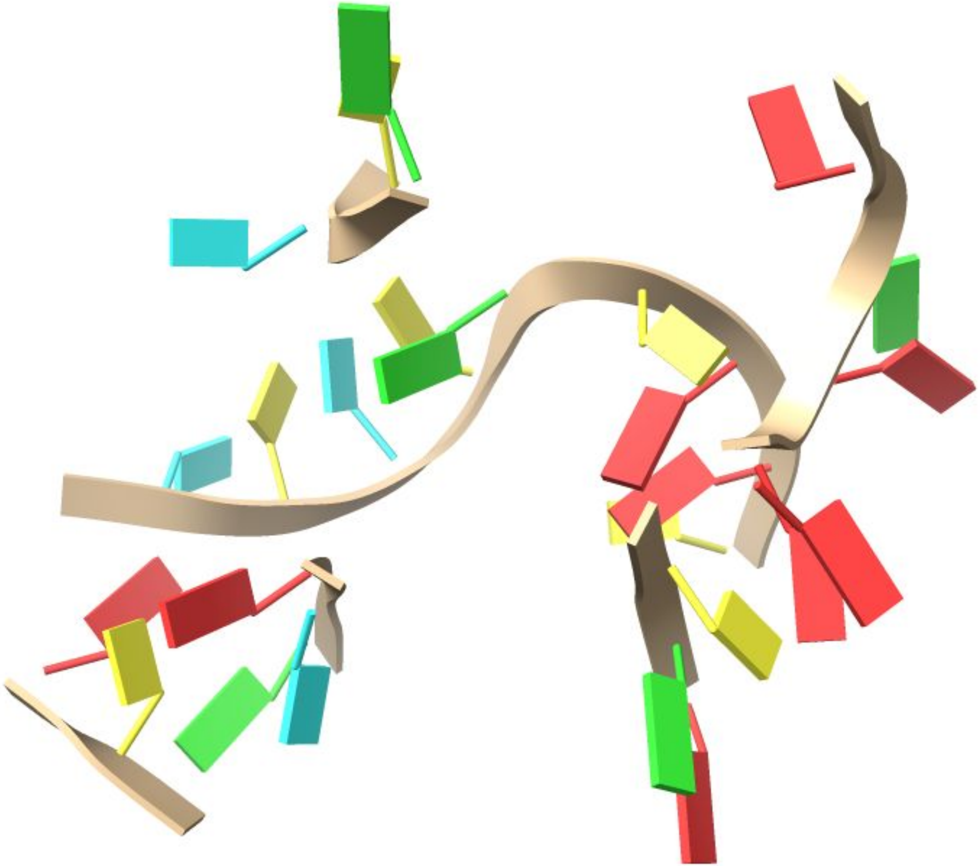


How to assemble LR modules?

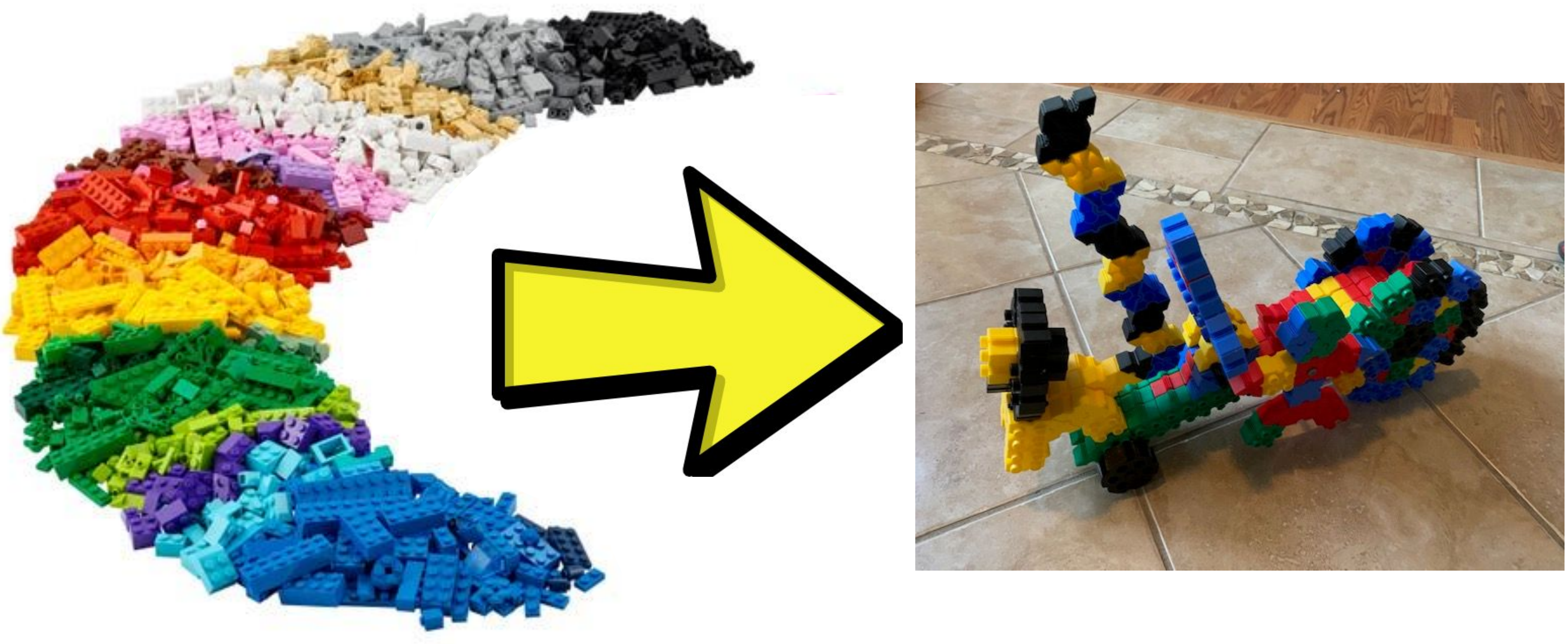
Glue pairs together?



Glue pairs together?

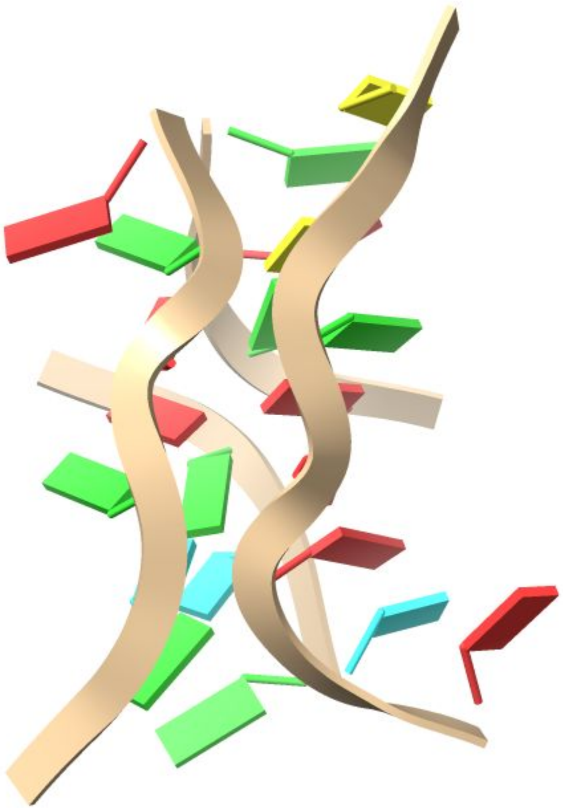


Glue pairs together?

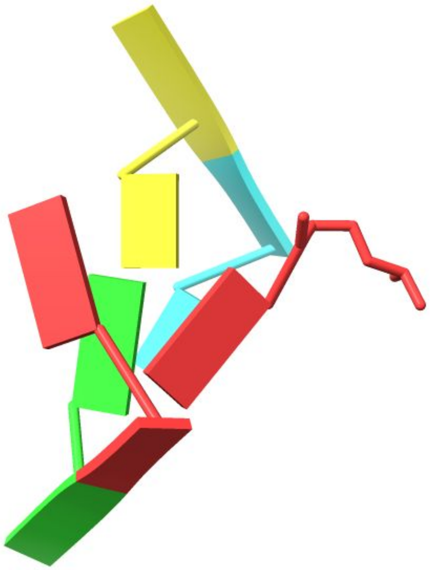


Another simple solution worked!

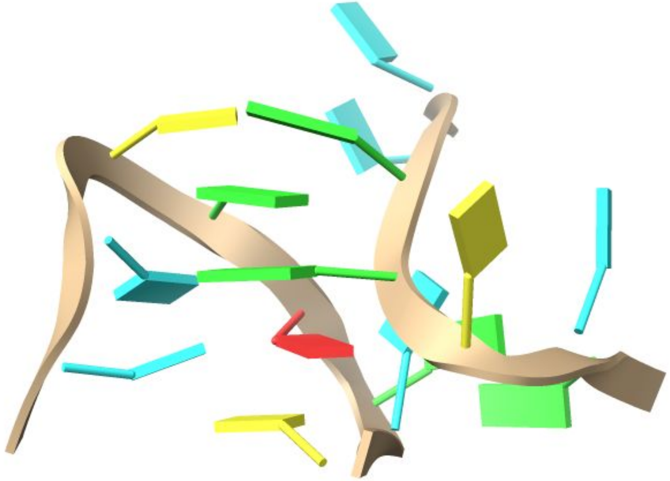
Double A-patch



Type-I A-minor

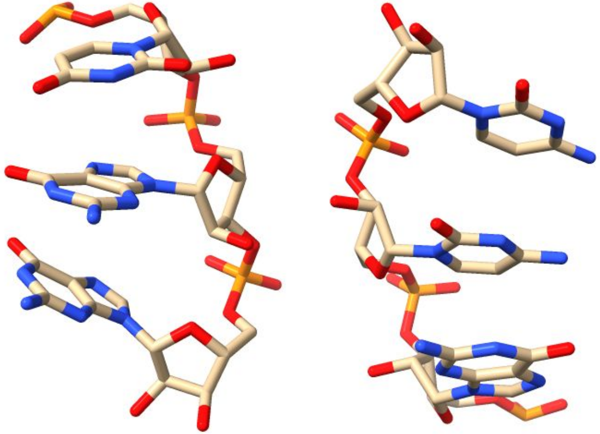


D-loop/T-loop interaction

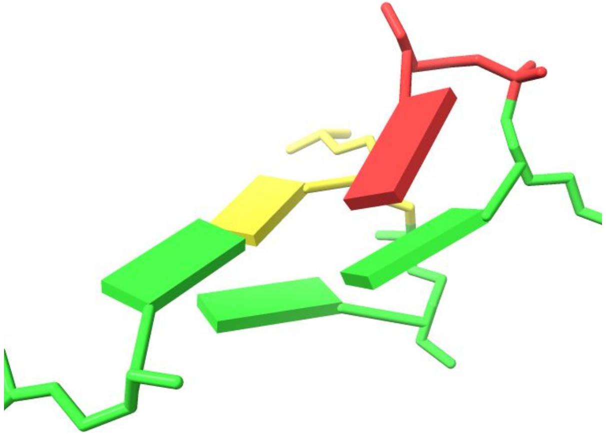


Another simple solution worked!

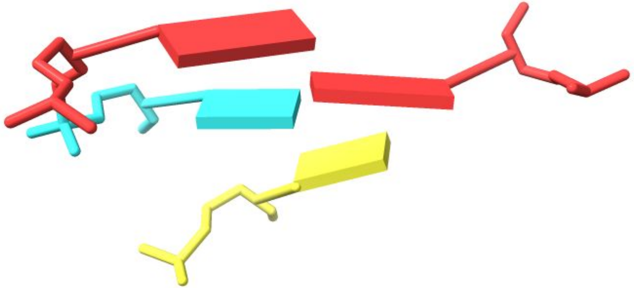
Ribose-zipper



Type-I/II
A-minor motif
(GA-variant)

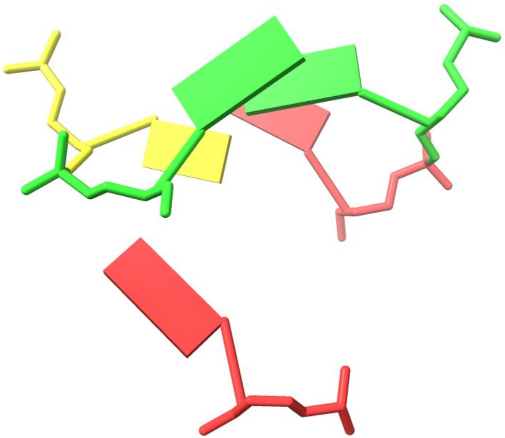


Cross-strand stack

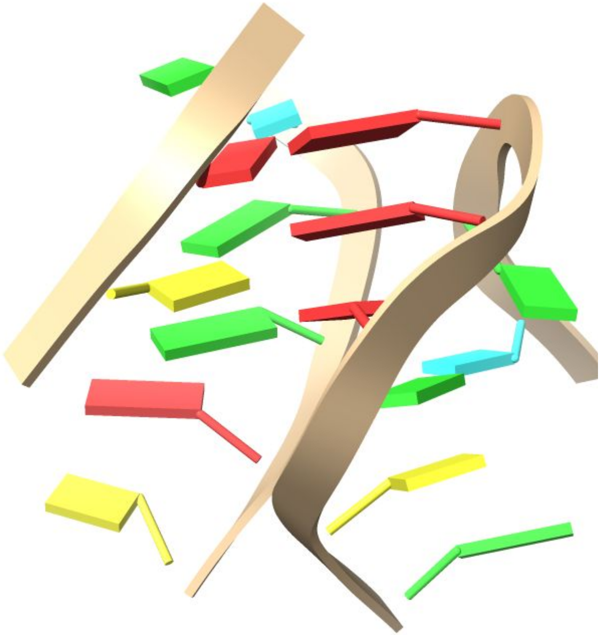


Another simple solution worked!

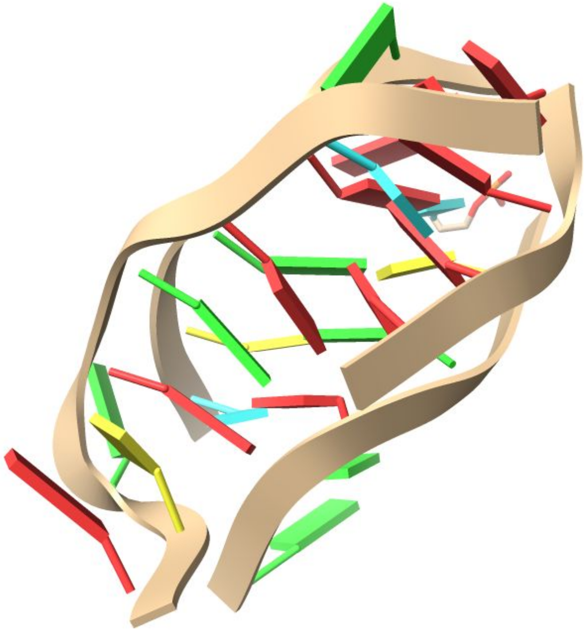
Non-canonical
A-minor



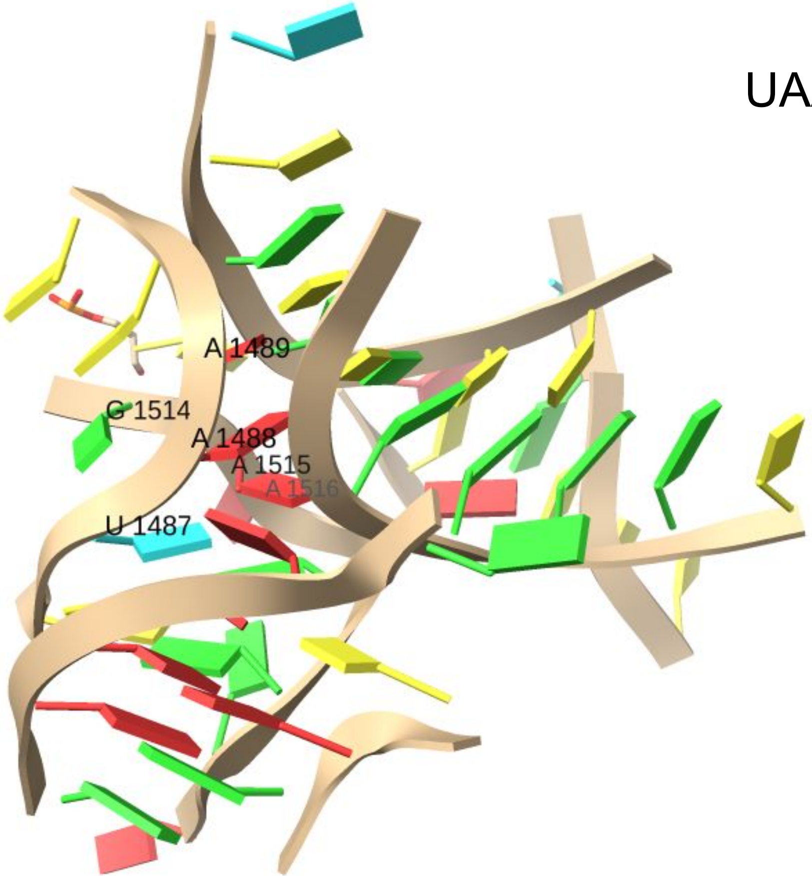
GAAA-tetraloop/receptor



A-patch of length 6



Context!



UAA/GAN internal loop

Better moment for contact annotations

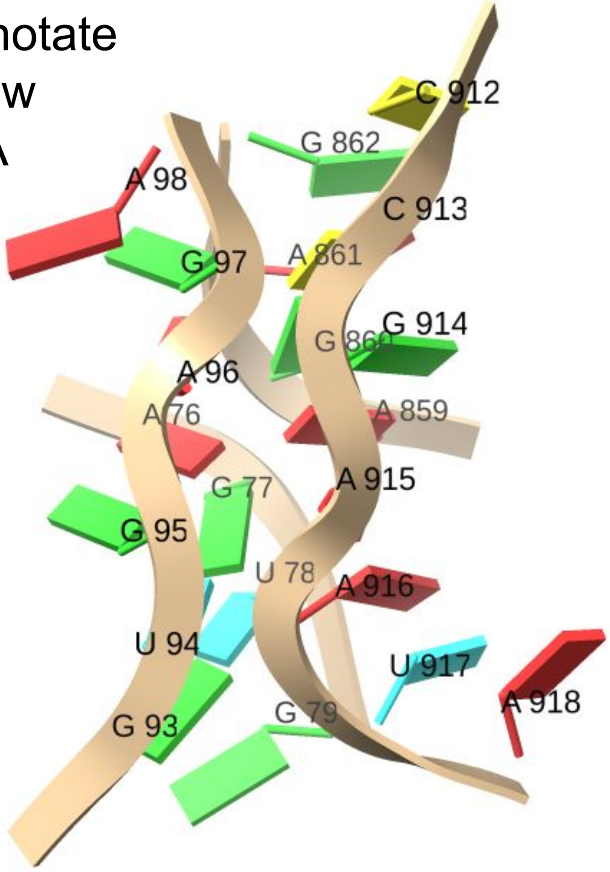
```
7M4Y|1|B|A|96   ntSS  7M4Y|1|A|G|860
7M4Y|1|B|G|97    1BPh 7M4Y|1|A|G|862

7M4Y|1|A|A|915   2BR  7M4Y|1|B|U|78
7M4Y|1|B|G|77   ntSS  7M4Y|1|A|A|915
7M4Y|1|B|G|77   ncSS  7M4Y|1|A|A|859

7M4Y|1|A|A|916   2BPh 7M4Y|1|B|G|79
7M4Y|1|B|G|93   n1BPh 7M4Y|1|A|U|917
7M4Y|1|B|G|93    3BR  7M4Y|1|A|A|916
```

FR3D

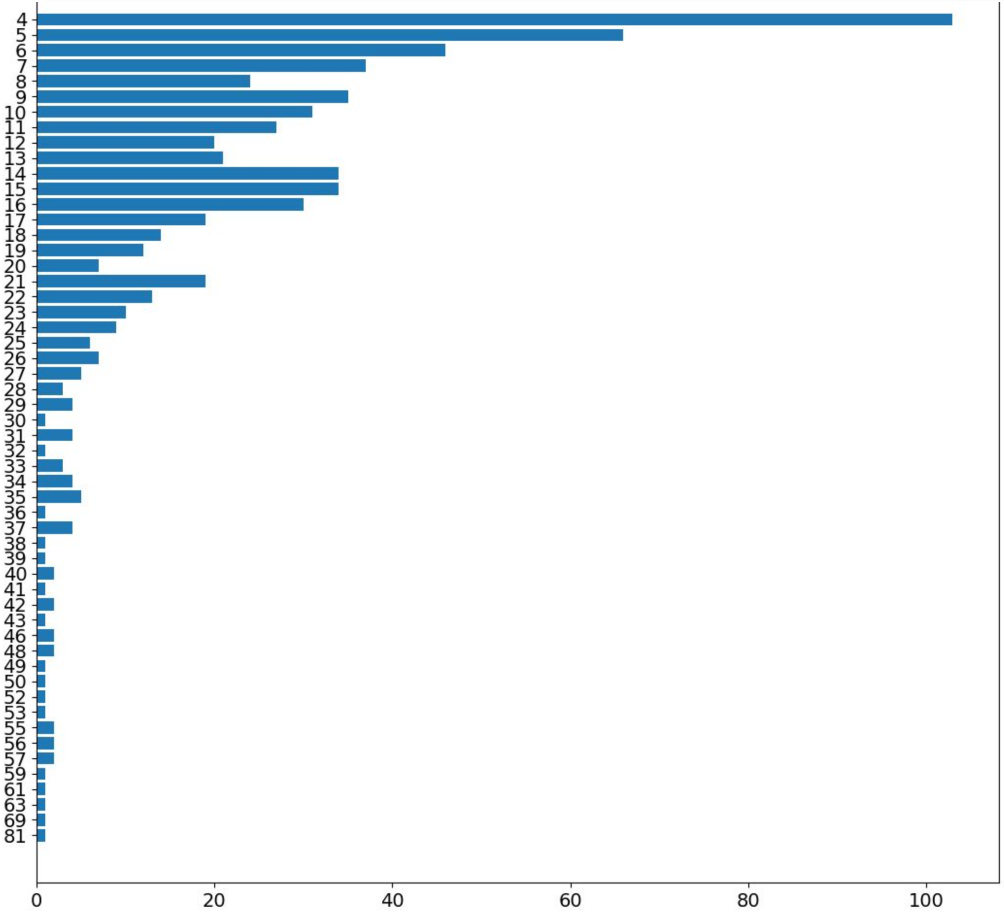
```
1..A.A.859.    1..B.G.77.     interBase-angle=66 H-bonds[2]:
"O2'(hydroxyl)-O3'[3.06],N3-O2'(hydroxyl)[2.60]" min-baseDist=4.83
1..A.G.860.    1..B.A.76.     interBase-angle=65 H-bonds[2]:
"O3'-O2'(hydroxyl)[2.97],O2'(hydroxyl)-N3[3.04]" min-baseDist=5.75
1..A.G.860.    1..B.G.97.     interBase-angle=71 H-bonds[1]:
"N2(amino)-O4'[3.50]" min-baseDist=5.19
1..A.A.861.    1..B.G.97.     interBase-angle=74 H-bonds[2]:
"O3'-N2(amino)[3.32],O2'(hydroxyl)-O2'(hydroxyl)[2.74]" min-baseDist=6.52
1..A.G.862.    1..B.G.97.     interBase-angle=78 H-bonds[1]:
"OP1-N2(amino)[3.43]" min-baseDist=7.69
1..A.A.916.    1..B.G.77.     interBase-angle=65 H-bonds[1]:
"O4'-N2(amino)[3.18]" min-baseDist=4.60
1..A.A.916.    1..B.U.78.     interBase-angle=67 H-bonds[3]:
"O2'(hydroxyl)-O2'(hydroxyl)[3.03],O2'(hydroxyl)-O2(carbonyl)[3.48],
N3-O2'(hydroxyl)[2.57]" min-baseDist=5.70
1..A.A.916.    1..B.G.93.     interBase-angle=69 H-bonds[1]:
"O2'(hydroxyl)-N2(amino)[2.94]" min-baseDist=6.55
1..A.G.862.    OP1-hbonds[2]: "N2@1..B.G.97.[3.43]"
nts=4 AGAG 1..A.A.859.,1..A.G.860.,1..B.A.76.,1..B.G.77. (ribose zipper)

1..A.G.914.    1..B.A.96.     interBase-angle=60 H-bonds[1]:
"O2'(hydroxyl)-O2'(hydroxyl)[3.28]" min-baseDist=7.70
```

DSSR

+ MC-Annotate
+ RNAView
+ ClaRNA



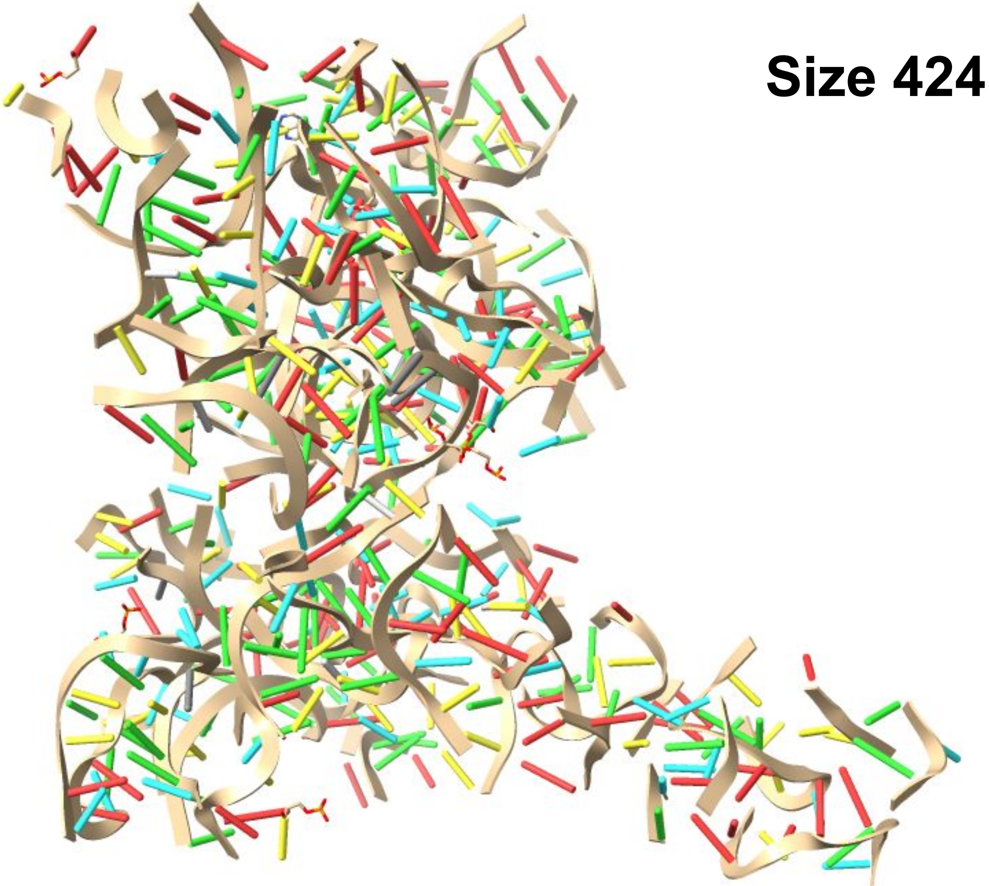
Well, to some extent…



Size 2 = ~400
Size 3 = ~200

Size ~100 = 3
Size ~500 = 3

Well, to some extent…



Size 424 (LSU rRNA)

Summary

- We suggest a new approach to long-range RNA tertiary module annotation

- The method does not rely on any interaction type

- How to go from modules to motifs?

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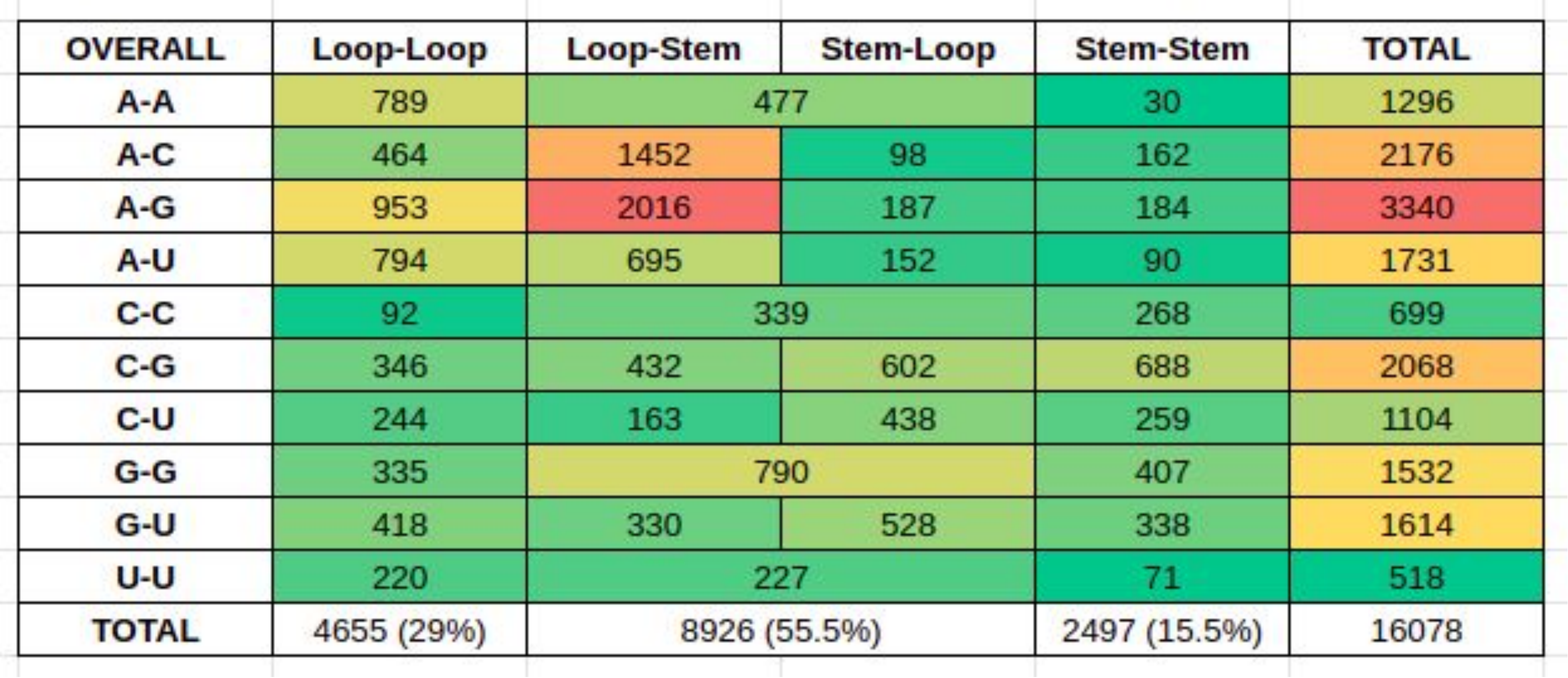
Thank you!

Long-range (LR) residue-residue pairs



OVERALL	Loop-Loop	Loop-Stem	Stem-Loop	Stem-Stem	TOTAL
A-A	789	477		30	1296
A-C	464	1452	98	162	2176
A-G	953	2016	187	184	3340
A-U	794	695	152	90	1731
C-C	92	339		268	699
C-G	346	432	602	688	2068
C-U	244	163	438	259	1104
G-G	335	790		407	1532
G-U	418	330	528	338	1614
U-U	220	227		71	518
TOTAL	4655 (29%)	8926 (55.5%)		2497 (15.5%)	16078