Annotated tertiary interaction motifs in RNA structures

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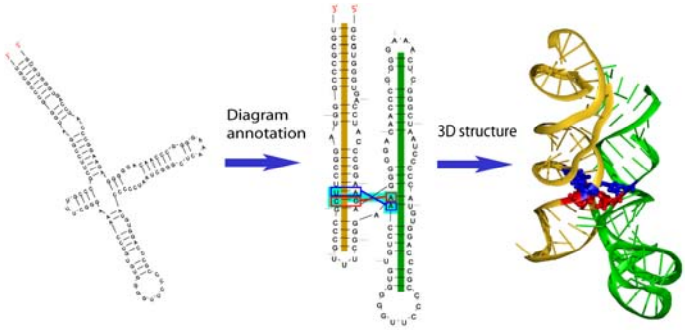
Introduction

- RNA folding is recognized as hierarchical[1,2]: an RNA sequence forms secondary structural elements (helices and single strands), followed by recurrent tertiary interactions, and then it folds into a native structure.
- RNA tertiary motifs are recurrent interactions connecting between secondary structural elements.
- Understanding the role of RNA tertiary motifs in RNA folding will help to understand RNA 3D prediction.

Objective

- Compile a non-redundant dataset.
- Annotate tertiary interaction motifs.
- Perform analysis over the diagrams produced.
- Propose tertiary constraints for the purpose of RNA 3D prediction.



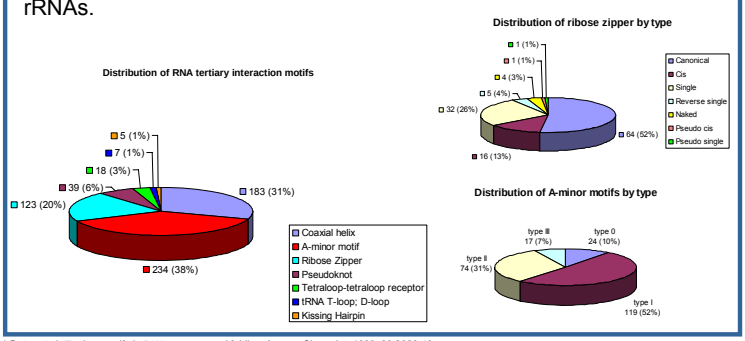
Methods

- Compiled a dataset containing 54 high-resolution (≤ 3.0 Å) RNA crystal structures.
- Selected seven RNA tertiary motifs: coaxial helix[2], A-minor[4] motif, ribose zipper[6], tetraloop-tetraloop receptor[2], pseudoknot[1], kissing hairpin[1], and tRNA D-loop:T-loop[1].
- Searched RNA tertiary motifs via different computer programs:

RNA tertiary motif	Software used for annotation
Coaxial helices	3DNA[3], RNAVIEW[7]
A-minor	FR3D[5]
Ribose zipper	RZparser[6], FR3D
Tetraloop-tetraloop receptor	FR3D
Pseudoknot	RNAVIEW
Kissing hairpin	RNAVIEW
tRNA D-loop: T-loop	RNAVIEW

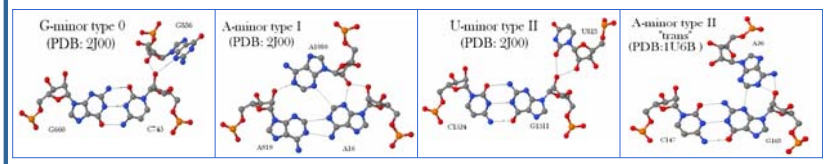
Analysis

For 54 high-resolution RNA structures, 602 RNA tertiary interactions were found. Most of these 3D interactions occur in the 16S and 23S rRNAs.

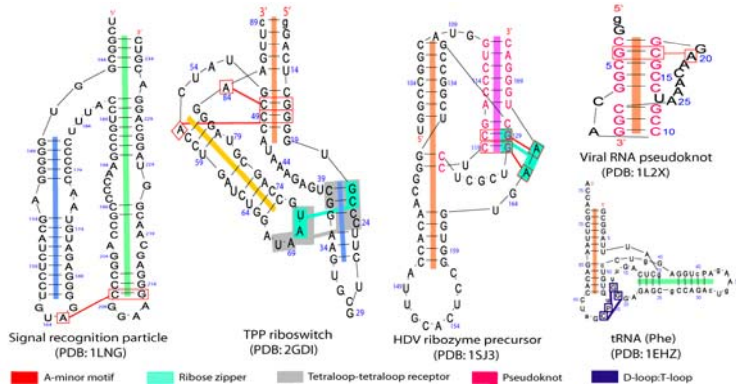


1 Batey et al. *Tertiary motifs in RNA structure and folding*. Angew. Chem. Int. 1999; 38:2326-43.
2 Hendrix et al *RNA structural motifs: building blocks of a modular biomolecule*. Q. Rev. Biophys. 2005; 38(3):221-43.
3 Lu and Olson. *3DNA: a software package for the analysis, rebuilding and visualization of three-dimensional nucleic acid structures*. NAR 2002; 31(17), 5108-21.
4 Nissen et al *RNA tertiary interactions in the large ribosomal subunit: the A-minor motif*. PNAS USA. 2001; 98(9):4899-903.
5 Sarver et al *FR3D: finding local and composite recurrent structural motifs in RNA 3D structures*. J. Math. Biol. 2007.
6 Tamura and Holbrook. *Sequence and structural conservation in RNA ribose zippers*. J. Mol. Biol. 2002; 320(3), 455-74.
7 Yang et al *Tools for the automatic identification and classification of RNA base pairs*. NAR 2003; 31(13), 3450-60.

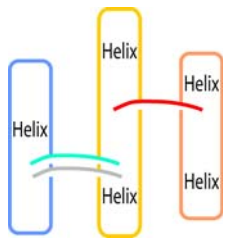
A-minor motifs are diverse



Annotated RNA diagrams

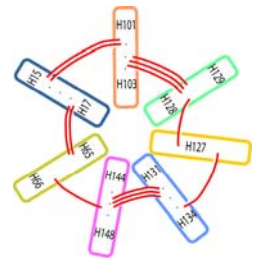


Coaxial helices involved in long-range interactions form "composite" motifs



TPP riboswitch (PDB: 2GDI)

Groups of helices are often connected together by long-range interactions in a linear fashion or (less often) as a cycle.



23S rRNA fragment (PDB: 1VQO)

Findings

- Pseudoknots and A-minor motifs are related: 23 (59%) out of the 39 pseudoknots are observed with A-minor (87% type I, 26% type II, 8% type 0, and 21% both type I and II).
- A-minor motifs are involved in long-range helix-helix interactions: 60-70% of the A-minor in rRNA.
- Most junctions contain at least one coaxial helix: 74 (84%) out of the 88 junctions are observed with coaxial helices. Junctions with no coaxial helices occur only at the 16S and 23S rRNA, where a number of long range interactions between helices are strongly present.
- Search with FR3D showed multiloop-multiloop receptors with discrepancy[5] numbers ranging from 0.39 to 0.67, from the traditional tetraloop-tetraloop receptor.

Conclusions

- Tertiary interaction annotations allow the identification of "composite" motifs.
- Exhaustive search of A-minor motifs reveals diversity of interaction.
- A-minor motifs interact both locally and globally.
- Both pseudoknots and coaxial helices are correlated with A-minor motifs and can be part of "composite" motifs.
- RNA junctions have a high probability to contain at least one coaxial helix.
- For large RNAs, strong long-range interactions can prevent coaxial helices from forming.

Acknowledgements

The work was supported by the Human Frontier Science Program (HFSP) and by a joint NSF/NIGMS initiative in Mathematical Biology (DMS-0201160). The authors would like to thank Hin Hark Gan for valuable comments.