

RNA Structure modeling





• Primary structure

5' aaaaagcaaaaatgtgatcttgcttgtaaatacaattttgagaggttaataaattacaagtagtgcta tttttgtatttag gttagctatttagctttacgttccagg atgcctagtg gcagccccac aatatccagg aagccctctctgcggttttt 3'











Three canonical base pairs : « A » helices



A wealth of non canonical base pairs : Bulges, 3D contacts Specific shape

Some examples of tertiary motifs





A structured bulge





- Secondary structure modeling is a limiting step
- Structure modeling software (Mfold, RNAfold ...) are based on :
 - Thermodynamic experimental data have defined a free energy for a bp in a given context (nearest neighbour theory)
 - Probability (Boltzmann statistics)
- Such modeling is often inexact if the RNA is over > 50(ish) nucleotide long
 - Thermodynamic model is incomplete
 - Does not predict non canonical base pairs pseudoknots
 - Does not take into account folding kinetics
 - A single RNA may adopt several foldings
- Yields several models how to choose?

Generating folding constraints



Goal: Experimentally define nucleotides that are in single strand conformation

- Single stand RNAse : T1, A, S1 etc ...
- Small molecules: DMS, CMCT, SHAPE reagents







Is this enough?





Not predicting the tertiary structure impairs the 2D prediction

Multiple probes





Use a multiprobing approach to improve modeling





















Developpement of a new model that takes into account all the probing results

Currently validating the approach on a « benchmark » RNA

Detecting the tertiary structure





We are currently developping approaches to predict pseudoknots using such data

Combining Probing and NGS





Naive probing of multiple mutants







Integrative approach to model RNA structure at the atomic level







Base pairing (kissing complex) between loop IIId (HCV IRES) and ES7 (18S rRNA) favours the 40S recruitment, and is required for an efficient translation

IRES structure and structural rearrangment





IRES footprinting on the18S rRNA





Fitting the atoms in the envelop





Coordinates from Hashem et al. 2013

Model by Benoit Masquida

3D model of the IRES-40S





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