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Computational methods for comparing and integrating multiple probing assays to predict RNA secondary structure

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1-Introduction
- RNA is key to understand many biological processes.
- RNA maintains a stable tertiary structure.
- The determination of the structure allows understanding its operating mechanism.
- We study the 444nt long VIH1 Gag-IRES.

RNA Structure determination
- 3D structure can be resolved experimentally \{remains expensive and time-consuming\}.
- Computational methods allow to have accurate secondary structure predictions (PPV \approx 75\%). Less accurate predictions for long RNA.
- \textit{+} Experimental Data [Chemical\text{\textbackslash SHAPE} \text{\textbackslash Enzymatic}] improve predictions.

3-Results

Optimal centroid structures from 140 [8000 structures]

2-Material & Methods

2-1 Experimental data

SHAPE-Map experiments

High Throughput Sequencing

SHAPE reactivity calculation

Boltzmann probability to observe a structure $S$:

$$ P(S) = \frac{e^{-U(S)}}{Z} $$

with $Z$ the partition function:

$$ Z = \sum_{S} e^{-U(S)} $$

V-Enzymatic cleavage targets paired nucleotides. Cleavage reveals unpaired nucleotides.

2-2 Sampling/Clustering workflow

Data processing

Structure sampling

Set of ensemble structures

Clustering[Affinity propagation]

Optimal clusters?

Coherence Diversity Stability

Maximization \textarrow{\rightarrow} Pareto Frontier

Optimal Centroid Structures

References


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