

Visual exploration of the functional consequence of structure and structure change in RNA ensembles

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Motivation: A majority of ribonucleic acid (RNA) molecules adopt multiple conformations. The ensemble of possible RNA conformations can be sampled using Boltzmann suboptimal sampling. Visualization of the relationships between structures in an ensemble is key to understanding the effects of mutation or environment on RNA folding, stability and function. Current visualization methods are often useful for visualizing RNA structure and base pairing probability, but do not sufficiently explore the functional consequence of structure and structure change in an ensemble. Therefore, a robust method for visualizing the sampled suboptimal structures of RNAs remains a contemporary challenge in the field.

Method: We have developed a method that creates a stable map of conformational space for a given RNA and its mutants. We explore the most diverse conformational space for this map and generate structures using established sampling algorithms. Using vector representation based on nested structure patterns, we project clusters of structures from the map into two dimensions using non-metric multi-dimensional scaling. Individual RNA ensembles are visualized in this space by fluctuating the size of the structure clusters in a bubble plot.

Results: In combination with ultra-high throughput experimental methods for structural determination, we used this visualization method to explore differences in RNA ensembles. We visualized how mutations and changes in environment could lead to shifts in the structural ensemble that may alter function. Ultimately, we aim to determine how changing structural elements lead to differences in RNA function, and to establish what are biologically important features for structure change.