Non-coding RNA (ncRNA) molecules play critical roles in cellular life. Many ncRNAs fold into specific structures in order to perform their biological functions. Some of the ncRNAs, such as riboswitches, can even fold into alternative structural conformations in order to participate in different biological processes. In addition, these ncRNAs can transit dynamically between different functional structures along folding pathways on their energy landscapes. These alternative functional structures are usually energetically favored and are stable in their local energy landscapes. Moreover, conformational transitions between any pair of alternate structures usually involve high energy barriers, such that RNAs can become kinetically trapped by these stable and local optimal structures.

We have proposed a suite of computational approaches for ncRNA analysis and novel ncRNA detection through studying folding pathways, alternative structures and energy landscapes associated with conformational transitions of ncRNAs. First, we developed an approach, RNAEAPath, which can predict low-barrier folding pathways between two conformational structures of a single RNA molecule. Using RNAEAPath, we can analyze folding pathways between ncRNA's functional structures, and therefore study the mechanism behind ncRNA's functional transitions from a thermodynamic perspective. Second, we introduced an approach, RNASLOpt, for finding all the stable and local optimal structures on the energy landscape of a single ncRNA molecule. We can use the generated stable and local optimal structures to represent the ncRNA's energy landscape in a compact manner. In addition, we applied RNASLOpt to several known riboswitches and predicted their alternate functional structures accurately. Third, we integrated a comparative approach with RNASLOpt, and developed RNAConSLOpt, which can find all the consensus stable and local optimal structures that are conserved among a set of homologous ncRNAs. We can use RNAConSLOpt to predict alternate functional structures for ncRNA families. Finally, we have proposed a pipeline making use of RNAConSLOpt to computationally discover novel riboswitches in bacteria genomes. An application of the proposed pipeline to a set of bacteria in Bacillus genus results in the re-discovery of many known riboswitches, and the detection of several novel riboswitch candidates.

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The public is welcome to attend.