Ribosome folding and function: from RNA base pairs to protein delivery

Abstract: The ribosome is the macromolecular machine responsible for the production of proteins in all living system. The molecular components include dozens of proteins, located primarily on the surface of the massive assembly, and long pieces of RNA that perform the primary biological functions — decoding the genetic information presented by messenger RNA and catalyzing the formation of peptide bonds. While there are now myriad high-resolution structures detailing the precise location of every atom within a ribosome, the RNA displays a bewildering complexity that overwhelms our abilities to comprehend its three-dimensional organization. The RNA strands contain thousands of nucleotides that associate with one another through various edge-to-edge and stacked associations of the planar bases. Except for the small fragments of RNA tied to specific biological function, much of our current understanding of ribosome organization focuses on the locations of specific three-dimensional features within the conventional secondary structure, i.e., the planar representation of RNA depicting the identities of the canonical, base-paired double-helical stretches and the intervening loops of single-stranded RNA. The many known ribosome structures also reveal spatial details about various local folding motifs. Despite the accumulated knowledge, understanding how the molecular components fit together remains an open question. Our group has begun to attack this problem by taking advantage of the multi-scale structural information collected with in-house software designed to streamline the analysis and annotation of RNA structures (1-2). The results serve as a starting point for multi-scale investigations of RNA folding, including the connections between different modes of base pairing and various 3D structural motifs (3-6). We are trying to make sense of the overall folding of ribosomal RNA using distance matrices, i.e., two-dimensional grids that depict the interactions of sequentially distant residues, and other geometric descriptors of three-dimensional structure, such as the curved, cylindrical pathways described by the global axes of long coaxially stacked helices and loops. We are also exploring previously unrecognized structural motifs within the ribosome, including a large, asymmetric internal loop located at the very end of the tunnel that protects and slowly delivers the newly synthesized protein chain to the ribosome exterior.

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