Computational modeling of RNA 3D structures and RNA-protein complexes, with the use of experimental data

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Ribonucleic acid (RNA) molecules are master regulators of cells. They are involved in many molecular processes: they transmit genetic information, sense cellular signals and communicate responses, and even catalyze chemical reactions. RNA function and in particular its ability to interact with other molecules such as proteins, is encoded in the sequence. Understanding how RNAs and RNA-protein complexes carry out their biological roles requires detailed knowledge of the RNA structure.

Due to limitations in experimental structure determination, complete high-resolution structures are available for a tiny fraction of all the known RNA molecules crucial for numerous fundamental cellular processes. <1% of RCSB entries represent RNA structures, and only around 3% of RNA families available in the Rfam database have at least one experimentally determined structure. This relative paucity of information compared to what is available for proteins also makes computational RNA 3D structure prediction much less successful. Currently, purely computational RNA 3D structure prediction is limited to sequences shorter than 100 nt.

I will present strategies for computational modeling of RNA and RNA-protein complex structures that utilize SimRNA, a suite of methods developed in my laboratory, which use coarse-grained representations of molecules, rely on the Monte Carlo method for sampling the conformational space, and employ statistical potentials to approximate the energy and identify conformations that correspond to biologically relevant structures. In particular, I will discuss the use of computational approaches for RNA structure determination based on low-resolution experimental data, including low-resolution crystallographic electron density maps and cryo-EM maps.

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Keywords: RNA, RNA-protein, modeling, crystallography, cryo-EM