

## Topological structure determination of RNA using small angle X-ray scattering

Although RNAs play a critical role in all cellular processes, the elucidation of their 3D structures is a daunting task. Naked RNAs are difficult to crystallize, and NMR spectroscopy is generally limited to small RNA fragments. As there is little apparent correlation between RNA primary sequences and three-dimensional folding, the usefulness of a pure computational structure prediction approach is also limited. Currently, general methods for high throughput topological structure determination of RNAs, guided by some experimental data are lacking. We present here a novel method (RS3D) that can assimilate the RNA secondary structure information, SAXS data, and any readily available tertiary contact information to determine the topological fold of RNA. Starting from an open conformation that satisfies the secondary structure information in a glob model, where each glob represents a specific nucleotide, the algorithm carries out natural hierarchical moves evident from the structural composition of RNAs. Every new move is guided towards satisfying the SAXS data fit, secondary structure constraints, and any additional long-range interaction information. The best-ranked glob models are then converted to explicit all-atom coordinates and refined against the SAXS data and solvent accessibility data (if available) under the constraints of robust force fields using the Xplor-NIH program. Our method is benchmarked with a variety of RNA folding architectures currently present in the structure database. Furthermore, we demonstrate the applicability and feasibility of the program to derive low resolution topological structures of relatively large multi-domain RNAs.

Yuba Bhandari	USA	National Cancer Institute
Linxin Fan	USA	National Cancer Institute
Xianyang Fang	China	Tsinghua University, China
George Zaki	USA	National Cancer Institute
Eric Stahlberg	USA	National Cancer Institute
Wei Jiang	USA	Argonne National Laboratory
Charles Schwieters	USA	NIH
Jason Stagno	USA	National Cancer Institute
Yun-Xing Wang	USA	National Cancer Institute