Determining the structural ensembles of disordered RNA and proteins using an integrated approach

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Much of the proteome and transcriptome lacks secondary and tertiary structure but still maintains important function. Not conforming to a single well-defined structure affords macromolecules greater flexibility, as seen for instance in the nuclear pore complex, histone tails, and noncoding RNA scaffolds. Multivalent, dynamic interactions between disordered proteins and RNA are also critical toward the formation of phase separated biomolecular condensates, which have been shown to have critical roles in cellular physiology.

Despite the emerging importance of disordered macromolecules, our structural understanding of them lags behind functional characterizations. This is due largely to their structural parameters existing as a broad distribution rather than a single state, precluding the use of crystallography and electron microscopy in many cases.

This study employs small-angle X-ray scattering in conjunction with molecular dynamics and ensemble optimization approaches tailored toward flexible nucleic acids and proteins. With this integrated approach we investigate the structural ensembles of highly flexible single-stranded RNA model constructs, as well as a physiological intrinsically disordered protein. In addition to characterizing the structures of these disordered macromolecules, a goal of this work is to examine interactions between them in order to monitor the formation of biomolecular condensates at the molecular level.