

Decoding dynamic biomolecular interactions by NMR and integrative structural biology - from RNA binding to structure-based drug discovery

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Abstract

My lab employs integrative structural biology approaches to unravel the molecular mechanisms linked to the assembly and molecular functions of protein complexes in RNA processing and signaling. Solution NMR-spectroscopy and SAXS/SANS provide unique information on functionally important dynamics and are combined with structural information from X-ray crystallography and electron microscopy. Together these data provide unique information for defining domain or subunit arrangements in multidomain proteins and protein complexes. We also combine solution structural biology and FRET to characterize dynamic conformations and populations shifts of these interactions. Examples will be presented that highlight the role of conformational dynamics, binding avidity and cooperativity, and population shifts in protein-RNA and protein-protein recognition.

We also use integrative approaches in structure-based drug discovery targeting neglected diseases. A recent example where we identified a novel target and small molecule inhibitors of an essential protein-protein interaction in trypanosome parasites will be discussed.