Towards a robust conformational description of intrinsic protein disorder using nuclear magnetic resonance spectroscopy

Martin Blackledge, Guillaume Communie, Elise Delaforge, Paul Guerry, Jie-Rong Huang, Malene Ringkjobing Jensen, Jaka Kragelj, Damien Maurin, Luca Mollica, Valery Ozenne and Robert Schneider

Institut de Biologie Structurale, Grenoble, France

Protein plasticity enables conformational changes that are essential for biological function. Intrinsically disordered proteins (IDPs) represent extreme examples where flexibility plays a determining role. The development of meaningful descriptions of the behaviour of IDPs is a key challenge for contemporary structural biology. Explicit molecular ensembles representing a dynamic equilibrium of rapidly interconverting conformers are gradually becoming established as appropriate descriptors to determine protein conformational disorder. 1 Due to the available degrees of freedom, the identification of accurate protein conformational ensembles requires the development of robust approaches to determine the significance and uniqueness of any proposed equilibrium. I will present novel approaches to determine local and long-range structural behaviour in IDPs from NMR and SAXS. I will describe their application to active sites in viral proteins that fold upon binding. 2 The conformational behaviour of these proteins will be studied in their physiological context, 3 and the timescale and kinetics of important conformational transitions will be characterized at atomic resolution.