

Project title: Deciphering multivalent interactions in dynamic bio-heteropolymers using single molecule fluorescence and nuclear magnetic resonance spectroscopy

Group: Protein Dynamics and Flexibility

Supervisor: Sigrid Milles
+33 4 57 42 87 50
sigrid.milles@ibs.fr

Keywords: Intrinsically disordered proteins, single molecule fluorescence spectroscopy, nuclear magnetic resonance spectroscopy, endocytosis

Project description:

Intrinsically disordered proteins (IDP) are proteins without a stable three-dimensional structure. Frequently described with polymer physics approaches, these proteins are very dynamic and can easily adapt to interactions with different partner proteins. Such interactions are often vital and achieved using short linear motifs, i.e. short stretches of amino acids within the IDP. An exemplary system for the presence of IDPs and a high concentration of linear motifs is the clathrin mediated endocytosis machinery of the eukaryotic cell, the major mechanism by which the cell takes up nutrients, signaling molecules, but also pathogens. The molecular mechanism of such interactions, especially when multiple motifs act in concert, is however only poorly understood particularly since the dynamic and flexible nature of IDPs makes them a very challenging object to study.

The candidate will use single molecule fluorescence spectroscopy and nuclear magnetic resonance spectroscopy, which together are very powerful to address such dynamic protein system. This project is interdisciplinary and, in addition to spectroscopy, involves biochemistry and chemical biology approaches, instrumentation on a custom fluorescence setup as well as programming, depending on the interest of the candidate.

Key publications:

An ultraweak interaction in the intrinsically disordered replication machinery is essential for measles virus function. Milles S, Jensen MR, Lazert C, Guseva S, Ivashchenko S, Communie G, Maurin D, Gerlier D, Ruigrok RWH, Blackledge M., Sci Adv. 2018

Plasticity of an ultrafast interaction between nucleoporins and nuclear transport receptors. Milles S, Mercadante D, Aramburu IV, Jensen MR, Banterle N, Koehler C, Tyagi S, Clarke J, Shammas SL, Blackledge M, Gräter F, Lemke EA., Cell. 2015

Click strategies for single-molecule protein fluorescence. Milles S, Tyagi S, Banterle N, Koehler C, VanDelinder V, Plass T, Neal AP, Lemke EA., J Am Chem Soc. 2012

Single molecule study of the intrinsically disordered FG-repeat nucleoporin 153. Milles S, Lemke EA., Biophys J. 2011