

ERC-funded postdoctoral position to use NMR and integrated structural biology to describe highly dynamic viral replication assemblies (SARS-CoV-2, Measles, Influenza)

Blackledge Lab (Protein Dynamics and Flexibility by NMR) Institute of Structural Biology, Grenoble, France.

We are seeking highly motivated post-doctoral researchers to exploit and/or develop NMR spectroscopic approaches to study the functional modes of highly dynamic assemblies involved in the replication of pathogenic RNA viruses, in particular SARS-CoV-2.

Project description:

Despite major advances made over the last decade both in cryo-electron microscopy and in protein structure prediction, a significant fraction of all proteomes remains beyond the reach of static structure determination due to their highly dynamic or disordered nature. NMR spectroscopy is the only tool capable of describing such systems at atomic resolution.

The molecular mechanisms regulating the functional modes of intrinsically disordered proteins (IDPs) remain poorly understood. In our group we use NMR spectroscopy to describe the conformational dynamics of highly disordered assemblies as a function of their environment (dilute, crowded, phase separated or *in cellulo*) and to map their molecular interaction trajectories, both in time and space.

The successful candidate will join a multi-disciplinary team investigating the physical role of highly dynamic proteins involved in viral replication, in particular SARS-CoV-2, the virus responsible for the COVID-19 pandemic, influenza virus and measles. The project lies at the interface of biology, chemistry and physics and will combine state-of-the-art NMR spectroscopy with MD simulation (atomic and coarse grained), fluorescence spectroscopy and imaging, X-ray crystallography, cryo-electron microscopy and small angle scattering.

Profile(s):

We are looking for candidates who are interested in applying physico-chemical approaches to resolve fascinating biological problems. Candidates should have a PhD in biophysics or biomolecular NMR-related subject.

Interested candidates should send a cv, motivation letter and the names of two referees to martin.blackledge@ibs.fr or write to martin.blackledge@ibs.fr for more details.

Grenoble: Capital of the French Alps, Grenoble is a world-renowned scientific hub with a strong international flavour. It is a pleasant city, situated at the foot of three mountain ranges offering many possibilities for cultural, outdoor and sporting activities throughout the year. Grenoble is close to the French riviera, Italy and Switzerland and is served by international and national airports and a high-speed rail network <http://www.ibs.fr/jobs/about-grenoble/>

Facilities: The IBS is situated on the European Photon and Neutron ([EPN](#)) campus together with its European partners, the [EMBL](#) (European Molecular Biology Laboratory), the [ESRF](#) (European Synchrotron Radiation Facility), and the [ILL](#) (Institute Laue-Langevin). This unique site provides access to state of the art equipment to analyze biological systems at different scales of resolution. The EPN site, and the Grenoble scientific community in general represents a true hub of integrated structural and dynamic biology.

The IBS itself provides a lively international working environment with state-of-the-art NMR facilities, including 950, 850, 700 and 600MHz NMR spectrometers with both liquid-state cryoprobes and state-of-the-art solid-state technology, dedicated wet-lab facilities for cloning, expression and purification of proteins and state-of-the-art imaging facilities. Access to

biophysical platforms is facilitated via the Integrated Structural Biology Grenoble (ISBG) platform (<http://www.isbg.fr/spip.php?lang=en>).

Blackledge research group:

<http://www.ibs.fr/groups/protein-dynamics-and-flexibility/?lang=en>

Recent publications giving examples of the type of work we do in this field

<https://scholar.google.com/citations?user=m7f8QWQAAAAJ&hl=en>

The intrinsically disordered SARS-CoV-2 nucleoprotein in dynamic complex with its viral partner nsp3a. Bessa LM, Guseva S, Camacho-Zarco AR, Salvi N, Mariño Perez L, Maurin D, Botova M, Malki A, Nanao M, Jensen MR, Ruigrok R, Blackledge M* *Science Advances* 8, eabm4034 (2022).

Molecular basis of host-adaptation interactions between influenza virus polymerase PB2 subunit and ANP32A Camacho-Zarco AR, Kalayil S, Maurin D, Salvi N, Delaforge E, Milles S, Jensen MR, Hart DJ, Cusack S, Blackledge M* *Nature communications* 11, 1-12 (2020)

Measles virus nucleo- and phosphoproteins form liquid-like phase-separated compartments that promote nucleocapsid assembly. Guseva, Milles, Jensen, Salvi, Kleman, Maurin, Ruigrok, Blackledge M* *Science Advances* eaaz7095 (2020)

A unified description of intrinsically disordered protein dynamics under physiological conditions using NMR spectroscopy. Adamski, Salvi, Magnat, Milles, Jensen, Abyzov, Moreau, Blackledge* *J Am Chem Soc*, 141, 17817-17829 (2019)

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 R,* Blackledge M* *Science Advances*, 4, eaat7778 (2018)

Analytical Description of NMR Relaxation Highlights Correlated Dynamics in Intrinsically Disordered Proteins. Salvi, Abyzov, Blackledge. *Angew Chem Int Ed Engl*. 5614020-14024 (2017)

Identification of Dynamic Modes in an Intrinsically Disordered Protein using Temperature Dependent NMR Relaxation. Abyzov, A., Salvi, N., Schneider, R., Maurin, D., Ruigrok R, Jensen MR, Blackledge M* *J Am Chem Soc*, 138, 6240–6251 (2016)

Visualizing the molecular recognition trajectory of an intrinsically disordered protein using multinuclear relaxation dispersion NMR. Schneider R, Maurin D, Communie G, Kragelj J, Hansen F, Ruigrok R, Jensen M, Blackledge M* *J Am Chem Soc* 137, 1220 (2015)

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*. 163, 734 (2015)

Direct observation of hierarchical protein dynamics. Lewandowski J, Halse M, Blackledge M*, Emsley L* *Science* 348, 578 (2015)

Large Scale Conformational Dynamics Control H5N1 Influenza Polymerase PB2 Binding to Importin α . Delaforge, Milles, Bouvignies, Bouvier, Boivin, Salvi, Maurin, Martel, Round, Lemke, Jensen, Hart, Blackledge *J Am Chem Soc* 137,15122 (2015)