

## **Postdoctoral position: Protein disorder in RNA-protein interactions: from dynamic structures to pathology**

**Jeschke group (EPR Spectroscopy). ETH Zurich, Zurich, Switzerland.**

### **Project description:**

In a Sinergia project funded by Swiss National Science Foundation, we address structure and functional relevance of intrinsically disordered protein domains (IDDs) of RNA-binding proteins. This includes liquid-liquid phase separation phenomena, which underlie formation of transient membraneless organelles, such as stress granules. We collaborate with the groups of Ben Schuler (University of Zurich, single-molecule FRET), Frédéric Allain (ETH Zurich, NMR), and Magdalini Polymenidou (University of Zurich, cell and tissue biology, superresolution microscopy).

Our part of the project uses continuous-wave EPR, Overhauser DNP measurements of water accessibility, and distance distribution measurements by double electron electron resonance (DEER) for obtaining information on structure and dynamics of (IDDs) in the dispersed and condensed state at ambient temperature and after fast freezing. We generate ensemble models by integrating information from EPR, NMR, small-angle scattering techniques and, potentially, FRET.

The successful candidate will design and develop spectroscopically orthogonal spin labelling methodology, use DEER and NMR paramagnetic relaxation enhancement (PRE) measurements to gather restraints for integrative structure modelling, and will be involved in further development of our modelling approach.

### **Profile:**

The candidate is either an NMR spectroscopist with experience in biochemistry and biophysics, who is interested in EPR spectroscopy or an EPR spectroscopist with interest in biological applications and in NMR. Candidates should have a PhD in chemistry, biochemistry, or biophysics.

**Interested candidates should send a C.V., motivation letter and the names of two referees to [gjeschke@ethz.ch](mailto:gjeschke@ethz.ch). Deadline 15th May 2022.**

**Facilities and Competence:** We are situated at the Hönggerberg campus of ETH Zurich, in easy commuting distance to the city campus of ETH and to the Irchel campus of University of Zurich. For this project, we have a share in wet-lab facilities and NMR spectrometers of the Allain group in the Department of Biology of ETH.

Our group operates fully equipped commercial pulsed EPR spectrometers at X-, Q-, and W-band frequency and home-built spectrometers at S-, X-, and Q-band frequencies, among them two unique ultra-wideband home-built spectrometers at X- and Q-band frequencies. We develop the protein ensemble modelling package MMMx (<https://mmm.x.info>) that uses distance distribution information for specifying ensemble width.

### **Jeschke group:**

<https://epr.ethz.ch/>

## Relevant publications of the group

G. Jeschke, L. Esteban-Hofer, *Methods in Enzymology*, in press, doi: 10.1016/bs.mie.2022.02.010 (2022) Integrative ensemble modeling of proteins and their complexes with distance distribution restraints

I. Ritsch, L. Esteban-Hofer, E. Lehmann, L. Emmanouilidis, M. Yulikov, F. H.-T. Allain, G. Jeschke, *Frontiers in Molecular Biosciences* 8, 636599. doi: 10.3389/fmolb.2021.636599 (2021) Characterization of Weak Protein Domain Structure by Spin-Label Distance Distributions.

L. Emmanouilidis, L. Esteban-Hofer, F. F. Damberger, T. deVries, C. K. X. Nguyen, L. Fabregas Ibanez, S. Mergenthal, E. Klotzsch, M. Yulikov, F. H.-T. Allain, *Nature Chemical Biology* 17, 608-614 doi: 10.1038/s41589-021-00752-3 (2021) NMR and EPR reveal a compaction of the RNA-binding protein FUS upon droplet formation

G. Jeschke, *Protein. Sci.* 30, 125-135 doi: 10.1002/pro.3965 (2021) MMM: Integrative ensemble modeling and ensemble analysis

G. Masliah, C. Maris, S. L. Konig, M. Yulikov, F. Aeschmann, A. L. Malinowska, J. Mabile, J. Weiler, A. Holla, J. Hunziker, N. Meisner-Kober, B. Schuler, G. Jeschke, F. H. Allain, *EMBO J.* 37, UNSP e97089 (2018), Structural basis of siRNA recognition by TRBP double-stranded RNA binding domains

G. Jeschke, *Emerging Topics in Life Science*, 2, 9-18, doi: 10.1042/ETLS20170143 (2018) The contribution of modern EPR to structural biology

C. Gmeiner, G. Dorn, F. H. T. Allain, G. Jeschke, M. Yulikov, *Phys. Chem. Chem. Phys.* 19, 28360-28380 (2017) Spin labelling for integrative structure modelling: a case study of the polypyrimidine-tract binding protein 1 domains in complexes with short RNAs

G. Jeschke, *Proteins* 84, 544-560 (2016), Ensemble models of proteins and protein domains based on distance distribution restraints

O. Duss, M. Yulikov, F. H.-T. Allain, G. Jeschke, *Methods in Enzymology*, 558, 279-331 (2015) Combining NMR and EPR to Determine Structures of Large RNAs and Protein–RNA Complexes in Solution

O. Duss, E. Michel, M. Yulikov, M. Schubert, G. Jeschke, F. H.-T. Allain *Nature*, 509, 588-592. (2014) Structural basis of the non-coding RNA RsmZ acting as protein sponge