Interdisciplinary PhD position in Vienna, Austria:

Decipher **protein dynamics & allostery** using advanced tools from **organic chemistry** to **biomolecular solution/solids NMR spectroscopy**

We are seeking a highly motivated PhD candidate bridging organic chemistry and biomolecular NMR spectroscopy to work in an internationally funded research project, that aims to understand how dynamics of proteins is linked to their functions. Achieving the ambitious goal of gaining functional insight into the processes occuring at the heart of large enzymes, we will leverage the power of specific isotope labeling and advanced NMR spectroscopic tools.

Project description:

The PhD candidate will work on two complementary aspects: on the one hand, the project involves the development of new organic-chemistry synthesis of small $^{15}N/^{13}C/^{2}H$ – containing amino acids or metabolic precursors thereof. These target compounds will directly be applied to generate selectively labelled biomolecules, in particular proteins from a family of large enzymes. On the other hand, the successful candidate will study these proteins then using state-of-the-art NMR techniques (solution-state and solid-state NMR). In particular, using these specifically labeled protein will give us key insights into the most important active and allosteric sites, and help us understand mechanisms of enzyme function and regulation.

The position involves, thus, work in two laboratories, and includes project design, chemical synthesis, biochemistry, acquisition and analysis of NMR spectra (potentially development of NMR methods) and data analyses, as well as dissemination of results and scientific communication with our highly interdisciplinary team of experts.

Research environment:

The research group of Roman Lichtenecker is investigating ways to selectively introduce stable isotopes into protein samples. The team uses specific labelling strategies in a range of applications, including drug development. Hosted at the University of Vienna, the team is equipped with state-of-the-art organic chemistry facilities. https://bioorg-lichtenecker.univie.ac.at/

The research group of Paul Schanda develops and uses NMR spectroscopy, along with other biophysical, biochemical and computational approaches to decipher biomolecular function, with a particular interest in dynamic processes, including the functional mechanisms of chaperones and enzymes. The team is hosted at IST Austria, at the outskirts of Vienna, in a brand-new laboratory equipped with modern biochemistry facilities and a new NMR facility (600, 700, 800 MHz; solution-state cryoprobes and solid-state NMR probes for up to 111 kHz magic-angle spinning).

Vienna has been recently ranked several times in a row as the city having the world's best quality of living. The two research laboratories, in Vienna (Univ. Vienna) and in Klosterneuburg (IST Austria) are connected by public transport.

The project is embedded in a French-Austrian collaborative project that also comprises experts in crystallography, bioinformatics and MD simulation, thus providing a stimulating research-project environment.

Duration of the employment: ca. 3.5 years, to start in spring 2022

Workplaces: Institute of Organic Chemistry, Univ. of Vienna, Währingerstr. 38, 1090 Vienna (https://bioorg-lichtenecker.univie.ac.at/) and Institute of Science and Technology Austria (https://ist.ac.at)

Profile:

We expect the successful candidate to bring a strong motivation in bridging organic chemistry and biomolecular NMR, and a drive to widen her/his expertise in these fields. While we do not expect the candidate to bring expertise in all these fields, some knowledge is a strong plus and the willingness to learn the following areas is required:

- Organic Synthesis (knowledge of theory and practical workflow).
- Knowledge of compound analysis and characterization.
- Practical knowledge in protein production, purification and general biochemistry techniques
- Experience in biomolecular solution- and/or solid-state NMR
- Fluent in English (very international team)
- Teamwork and communication skills, bridging the two research groups
- Independent, critical thinking

Application details:

Please submit a letter of motivation, your scientific CV and names of potential references to roman.lichtenecker@univie.ac.at and paul.schanda@ist.ac.at.

The application process is open, and we will start the selection early January, until the position is filled.

Selected recent publications by the groups:

Sučec, I., et al. & Schanda, P. (2020). Structural basis of client specificity in mitochondrial membrane-protein chaperones. *Science Advances*, *6*(51), eabd0263. https://doi.org/10.1126/sciadv.abd0263

Joint publication: Gauto, D. F., … Lichtenecker, R.,..., & Schanda, P. (2019). Aromatic Ring Dynamics, Thermal Activation, and Transient Conformations of a 468 kDa Enzyme by Specific 1H– 13C Labeling and Fast Magic-Angle Spinning NMR. *J. Am. Chem. Soc.*, *141*(28), 11183–11195. https://doi.org/10.1021/jacs.9b04219

Gauto, D. F., et al. & Schanda, P. (2019). Integrated NMR and cryo-EM atomic-resolution structure determination of a half-megadalton enzyme complex. *bioRxiv* (2018) & *Nat. Commun.*, *10*(1), 2697. https://doi.org/10.1038/s41467-019-10490-9

Felix, J., (2019). Mechanism of the allosteric activation of the ClpP protease machinery by substrates and active-site inhibitors. *Sci. Adv.*, *5*(9), eaaw3818. https://doi.org/10.1126/sciadv.aaw3818

Weinhäupl, K., et al. & Schanda, P. (2018). Structural Basis of Membrane Protein Chaperoning through the Mitochondrial Intermembrane Space. *Cell*, *175*(5), 1365-1379.e25. https://doi.org/10.1016/j.cell.2018.10.039

Schörghuber J., et al. & Lichtenecker RJ. (2018) Late metabolic precursors for selective aromatic residue labeling**.** *J. Biomol. NMR*, *71*, 3, *129-140.* https://link.springer.com/article/10.1007/s10858-018-0188-z

Schörghuber J., et al. & Lichtenecker RJ. (2017) Highly selective stable isotope labeling of histidine residues using a novel precursor in E. coli-based overexpression systems. *ChemBioChem*, *18*, *1487-1491.*onlinelibrary.wiley.com/doi/10.1002/cbic.201700192/full