

## Postdoc on protein LLPS :

### Understanding the transition to amyloids through protein and water dynamics

Liquid-liquid phase separation (LLPS) of biological macromolecules can create so-called membraneless organelles where the protein is locally overconcentrated. LLPS can also have a pathological activity by promoting amyloid aggregation, which is involved in several neurodegenerative diseases. Yet, the basic properties of the proteins under LLPS have been scarcely characterized, and the processes leading LLPS to partake in functional or pathological activities are unknown. Of particular interest is how hydration water of proteins modulate their assembly and transition toward pathogenic amyloids. The aim of this project is to understand how water and protein dynamics is perturbed by LLPS and enable the formation of amyloid assemblies. In particular, we will study the medically important intrinsically disordered proteins tau and alpha-synuclein.

In this project, the candidate will fully map the liquid-to-solid transition occurring when tau and a-synuclein LLPS age. This aging process is highly dependent on the experimental conditions and represent the tilting point between functional and pathological LLPS. The goal of the project is to characterize the protein and hydration dynamics during this aging process. The candidate will combine multiple biophysical methods including fluorescence, electron paramagnetic resonance (EPR) spectroscopy and overhauser dynamic nuclear polarization (ODNP). The project will be in strong collaboration with two american teams (Santa Barbara and Boston) performing simulations as well as a team at ILL (Grenoble, France) performing neutron scattering experiments. Travels to these locations are planned during this postdoctoral experience.

We are looking for a highly motivated candidate seeking to expend their research experience. The ideal candidate will have a strong understanding of protein liquid-liquid phase separation and a good background in biophysical methods. An interest in water science is essential as well. This is a great opportunity to embrace a multidisciplinary project combining biochemistry, biophysics and physical chemistry. The successful candidate will be independent and thrive in a small and synergetic team.

The position will take place at the CBMN Laboratory (UMR5248) in the team of Y. Fichou ([www.fichou-lab.cnrs.fr](http://www.fichou-lab.cnrs.fr)), located at the European Institute of Chemistry and Biology (IECB) near Bordeaux. The IECB is a multidisciplinary institute at the interface of biology and chemistry, and is equipped with several platforms (biochemistry, bacteriology, crystallography, NMR, cryo-electron microscopy) that will be accessible during the postdoctoral project. The project is in collaboration with Prof. Shea at UC Santa Barbara, Prof. Straub at Boston Univ. and Prof. Weik in Grenoble.

Please reach out to Yann Fichou ([y.fichou@iecb.u-bordeaux.fr](mailto:y.fichou@iecb.u-bordeaux.fr)) for any query.