# Laboratory for Molecular Biophysics

## Institute for Protein Research


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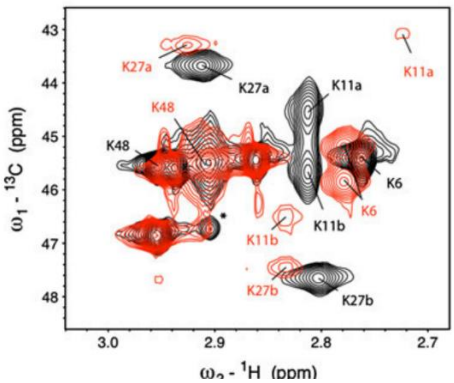
Within our bodies, energy and information conversions occur via protein-protein interactions; dysfunction of these processes disrupts biological networks, causing disease. Our research employs solution-state and solid-state NMR spectroscopy, focusing on membrane proteins and those forming liquid-liquid phase separation and amyloid aggregates. We investigate their physiological and pathological functions from a structural perspective, while developing novel instrumentation and methodologies utilizing spin hyperpolarization.



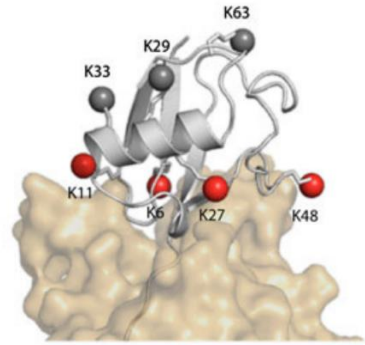




Fig. 1 Two-dimensional NMR spectra showing protein-protein interactions and the interaction between protein ubiquitin and YUH revealed by NMR.

We mainly focus on structural analysis and intermolecular interactions, particularly in signal transduction proteins and molecular motor machinery. By investigating changes in protein dynamics upon interaction, we aim to elucidate their correlation between protein structural dynamics and their biological functions. We also conduct drug discovery research targeting proteins such as antibodies and membrane proteins, and develop new lead compounds. Furthermore, since the methodologies required for these NMR studies are still evolving, we are also developing new NMR analytical methods.

### Structure and function analysis of proteins by solid-state NMR

Solid-state NMR enables analysis of systems challenging for solution NMR, X-ray crystallography, and cryo-electron microscopy due to insolubility, non-crystallinity, or polydispersity. These include protein aggregates (amyloid fibrils) associated with neurodegenerative disorders and G protein-coupled receptors (GPCRs), which constitute 30% of drug targets. Higher-order structures and conformational equilibria influenced by cellular environments and lipid membranes are not genetically encoded and require experimental determination. We are developing technologies for direct structural and interaction analyses within cells. Additionally, we are developing ultra-sensitive solid-state NMR instrumentation utilizing dynamic nuclear polarization (DNP). These methodologies extend beyond biological applications to collaborative research with domestic and international companies in chemical, materials, and pharmaceutical sectors.

### Structure and function analysis of proteins by solution NMR

NMR is a powerful technique that enables atomic resolution analysis of protein structures, dynamics, and interactions within cellular environments, making it valuable for understanding the biological functions of proteins.

### Research Topics

1. Atomic resolution analysis of protein function and structure in cells
2. Structural and functional analysis of amyloid proteins
3. Structural analysis of membrane proteins for signal transduction
4. Development of NMR structural analysis based on selective isotope labeling
5. Analysis of protein structure and conformational change using paramagnetic probe molecules
6. Development of protein-drug interaction analysis using $^{19}$F-NMR
7. Development of ultra-sensitive NMR using spin hyper-polarization techniques and its application to biological systems


Figure 2 Ultra-highly sensitive DNP-NMR spectrometer. A superconducting magnet (left) and a terahertz-wave light source, a gyrotron (right), are used to observe NMR at cryogenic temperatures.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