Solid-State NMR for Molecular Science

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Keywords Solid State NMR, Biomolecules, Developments

In order to elucidate functions of molecules, characterization of the molecule is the first step. There are varieties of important molecules which are insoluble to any solvents and functional at amorphous state. Solid-state NMR enables to obtain variety of information at atomic resolution without damages of molecules and significant restrictions. Thus solid-state NMR is one of the essential tools for the characterization of those molecules.

We have been working on methodology and hardware developments of solid-state NMR and their applications for structural biology and material science. We study characterization of membrane proteins and peptides, organic materials, natural products and synthetic polymers. Characterizations of those molecules based on solid-state NMR are under investigations through corroborations with several research groups.

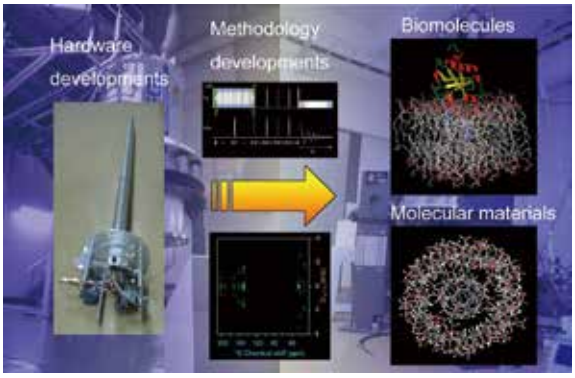

Figure 1. Outline of our studies.

Selected Publications

- J. Hu, R. Fu, K. Nishimura, L. Zhang, H. X. Zhou, D. D. Busath, V. Vijayvergiya and T. A. Cross, "Histidines, Heart of the Hydrogen Ion Channel from Influenza A Virus: Toward an Understanding of Conductance and Proton Selectivity," *Proc. Natl. Acad. Sci. U.S.A.* **103**, 6865–6870 (2006).
- K. Nishimura and A. Naito, "Remarkable Reduction of RF Power by ATANSEMA and DATANSEMA Separated Local Field in Solid-State NMR Spectroscopy," *Chem. Phys. Lett.* **419**, 120–124 (2006).
- N. Uekama, T. Aoki, T. Maruoka, S. Kurisu, A. Hatakeyama, S. Yamaguchi, M. Okada, H. Yagisawa, K. Nishimura and S. Tuzi, "Influence of Membrane Curvature on the Structure of the Membrane-Associated Pleckstrin Homology Domain of Phospholipase C-δ1," *Biochim. Biophys. Acta, Biomembr.* **1788**, 2575–2583 (2009).
- T. Iijima and K. Nishimura, "^{2}H Quadrupolar Carr-Purcell-Meiboom-Gill NMR for Paramagnetic Solids," *Chem. Phys. Lett.* **514**, 181–186 (2011).
- K. Yazawa, F. Suzuki, Y. Nishiyama, T. Ohata, A. Aoki, K. Nishimura, H. Kaji and T. Asakura, "Determination of Accurate ^{1}H Positions of Alanine Tripeptide with Anti-Parallel and Parallel β-Sheet Structures by High Resolution ^{1}H Solid State NMR and GIPAW Chemical Shift Calculation," *Chem. Commun.* **48**, 11199–11201 (2012).
- M. Tanio and K. Nishimura, "Intramolecular Allosteric Interaction in the Phospholipase C-δ1 Pleckstrin Homology Domain," *Biochim. Biophys. Acta, Proteins Proteomics* **1834**, 1034–1043 (2013).

1. Characterization of Organic Materials Based on Solid-State NMR through Observation of Natural Abundant Isotopes

There are so many organic materials which are insoluble to organic solvents. Solid-state NMR is one of the powerful tools to characterize such molecules. For small organic molecules and polymers consisting of repeated local structures, ^{1}H and ^{13}C solid-state NMR spectra through observation of natural abundant isotopes retain reasonable spectral sensitivities. Thus various types of 2D ^{1}H-^{13}C hetero-nuclear correlation experiments can be performed. By combining with spectral-editing techniques, signal assignments for ^{1}H and ^{13}C nuclei may be achieved. In the following, we show some collaboration works for characterization of organic materials achieved by those techniques.

Dr. Higashibayashi and co-works in IMS discovered a new phenomenon in which N-N linked bicarbazole and tetramethylbiacridine derivatives undergo electron transfer disproportionation by acid stimuli. In order to elucidate molecular structure of N-N linked bicarbazole molecules at neutral condition in solid state, signal assignments of ^{1}H and ^{13}C nuclei for the molecule were successfully carried out based on the two types of 2D ^{1}H-^{13}C hetero-nuclear correlation experiments together with several spectral-editing techniques. The aromatic back born carbons exhibited two sets of signals that suggest either mixture of two different conformations or asymmetric local conformations respect to the symmetric axis of the molecule. Finally, the closed state of the molecules in solid state was successfully proved through the signal assignments.[1)]

Dr. Ito and co-workers successfully developed formal aryne/carbon monoxide copolymerization using [2.2.1.] oxabicyclic alkenes as aryne equivalents. For insoluble fractions in individual reaction step was evaluated by observing ^{13}C solid-state NMR spectra. All of ^{13}C signals were successfully assigned based on the several spectral editing techniques in solid-state NMR at individual reaction steps.[2)]

We are also collaborating with several other research groups for characterization of natural products and synthetic polymers and *etc.*, based on solid state NMR. Currently, new types of correlation experiments for such organic molecules without isotope enrichments are also under investigated.

2. Intermolecular Packing in *B. mori* Silk Fibroin Revealed by Solid-State NMR[3)]

We have been collaborated with Prof. Asakura's group during couple of years for characterization of silk model peptides using solid-state NMR. The group has been suggested that crystalline *Bombyx mori* silk in silk II form (the silk after spinning) is intrinsically heterogeneous anti-parallel β-sheets.

In this study, full assignments of high resolution ^{1}H solid state NMR spectra for model peptide (Alanine-Glycine)15 peptide was successfully obtained using ultra high speed magic angle spinning (MAS) probe under ultra high field 920 MHz spectrometer in IMS. Distinct heterogeneity was observed for both ^{1}H and ^{13}C spectra for the AG(15) peptide. A new model containing two different packing arrangement of anti-parallel β-sheets was proposed based on obtained results. Through the energetically minimized structure using CASTEP, chemical shifts for ^{1}H, ^{13}C and ^{15}N nuclei were calculated. The obtained new model structure was supported by both calculated and experimentally observed chemical shifts for those nuclei in addition to the ^{1}H-^{1}H proximities obtained through the analyses of 2D ^{1}H-double quantum MAS experiments. Thus intermolecular packing of *B. mori* silk fibroin has been solved in this study.

3. Selective Observation of ^{2}H Quadrupole Interaction by Two Dimensional Solid-State NMR in Paramagnetic Compounds[4)]

A simple 2D solid-state NMR correlation experiments exhibiting ^{2}H quadrupolar interaction in indirect dimension for paramagnetic compounds was developed. The method is based on a quadupole-echo sequence inserted with π pulses where the pulse spaces are incremented an asymmetric fashion with use of strong rf field pulses. Quadrupolar interaction can be analyzed by projected quadrupole spectrum in the indirect dimension of 2D spectrum obtained by this technique through the simulation of the quadrupole-echo sequence without considering the effect of the paramagnetic shift.

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