Research on analytical methods in nuclear magnetic resonance (NMR)

Daisuke KUWAHARA Laboratory

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Summary of Research

Large-Scale, High Functionality, and Costly Instruments at the Coordinated Center for UEC Research Facilities

Associate Professor Kuwahara, our laboratory director, is also an administrator at the Coordinated Center for UEC Research Facilities. Here we will provide a brief introduction to the center.

The center was founded to collectively manage the many large and costly research instruments installed at the center for research in the physical sciences. These instruments fall into two major groups: surface and interfacial structure analysis systems and chemical structure analysis systems.

Of the instruments in the surface and interfacial structure analysis group, the electron microscopes are the most important. The center currently operates a 200-kV thermal electron emission transmission electron microscope (TEM), a 200-kV field emission TEM, a field emission scanning electron microscope (SEM), and a scanning electron microscope for analyzing variations in crystal orientation.

For investigations of the surfaces of solid bodies, the center operates an X-ray photoelectron spectroscope and ultra-vacuum scanning tunneling and atomic force microscopes.

The key instruments in the chemical structure analysis group are the NMR system and mass spectrometers, including two Fourier Transform NMR spectrometers (300 MHz, 500 MHz), and three types of mass spectrometer: a tandem mass spectrometer, a double-focusing mass spectrometer, and a MALDI-TOF mass spectrometer.

The center features an impressive lineup of X-ray analysis instruments crucial for structural analysis in both physics and chemistry, including a 4-axis single crystal X-ray diffractometer, small area X-ray stress measurement apparatus, CCD single-crystal X-ray diffractometer, and a powder X-ray diffractometer (for simultaneous differential scanning calorimetry).

The center operates more than 20 other large-scale analysis and measuring instruments, including a superconducting quantum interference device (SQUID) and electron spin resonance (ESR) spectrometer.

The center operates in own liquid helium recovery and recycling system, allowing recovery, liquefaction, and reuse of the helium used on campus.

Observing Substances with NMR

The appointment of Associate Professor Kuwahara as administrator at the Coordinated Center for UEC Research Facilities is closely tied to his research theme—“Studies on NMR”—which involves fundamental studies of analytical methods and methodologies for “observing” substances in greater detail with NMR.

His first topic of interest is high-resolution ultrasonic radiation in solid-state NMR. In these studies, ultrasonic waves are incident upon a solid sample immersed in solution to enable NMR signal observations and to obtain NMR spectra almost as clearly defined as for liquids.

When small molecules are dissolved in solutions, high-speed isotropic motion in the solution cancels out the various interactions, producing NMR spectra of extremely high resolution. NMR spectra of such clarity are not possible for molecules of large molecular weights, such as proteins and organic molecules, since they do not move fast enough for their interactions to cancel out. For this reason, the identification and structural analysis of samples of large molecular weight substances has been less successful. This problem is known as the 30K molecular weight boundary.

Various procedures developed to observe proteins and organic molecules in the solid

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NMR, nuclear magnetic resonance of solids, electron spin resonance

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state focus on specific local structures but not the whole of the molecule. While fairly successful in elucidating the structures of these molecules, most methods involve sophisticated and specialized techniques such as isotopic substitution in the sample, leaving many issues to be resolved before we can establish an NMR measurement technique for solid samples in the original state.

A secondary theme is the development of analytical methods in NMR that will allow structural analysis of proteins in the solid state and requires no prior sample preparation.

Advantages

One of the Few Laboratories in Japan Pursuing Research on Analytical Methods

We are among the few laboratories in Japan specializing in the analytical methods and methodologies for observing substances with NMR. While Japan has relatively few researchers focusing specifically on the development of NMR methodologies and techniques, they can be found in abundance in the western academic world. (To date, four have been awarded the Nobel Prize for their findings.)

The development of better analytical methods will allow observations of the previously unobservable or of materials and phenomena in greater detail, providing scientists with a powerful tool for research in the physical sciences.

One of our greatest advantages is that we have at our disposal various research instruments for this fascinating genre of research on the investigation and development of analytical methods and methodologies.

Future Prospects

Our Ultimate Goal: Observing a Single Molecule

A frontline theme in NMR spectrometry around the globe for the past 20 years has been observing molecules of large molecular weights, such as proteins and organic molecules, at higher resolution.

Although crystal structures can be observed with an X-ray diffractometer, XRD observations require the synthesis of single crystals, a major difficulty with proteins. Scientists have begun looking for ways to observe proteins with NMR that does not require single crystals. Additionally, X-ray observations sometimes result in sample destruction, thus analysis by NMR analytical methods may be regarded as relatively sample-friendly.

Our laboratory has made various efforts to sharpen the broad NMR spectrum obtained for the substances mentioned above, including shaking samples placed in a solution at high speed to induce Brownian motion.

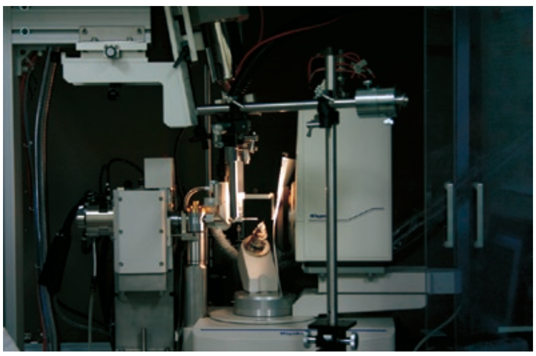
Improving NMR signal intensity is another research theme. Among NMR's weaknesses is weak signal intensity relative to other spectrometric methods. We are currently exploring a method whereby NMR information is superimposed on ESR signals. This technique requires molecules to have unpaired electrons. As long as this condition is satisfied, the method is theoretically possible and appears feasible for practical implementation.

Our hope is that the development of such methods, even if real-world implementation lies some distance in the future, will ultimately enable scientists to observe single molecules and molecular surfaces.

Superconducting Fourier transform NMR system (300 MHz)


200-kV thermal electron emission transmission electron microscope


Ultra-vacuum scanning tunneling microscope


CCD single-crystal X-ray diffractometer