BIOGRAPHICAL SKETCH

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NAME: Zilm, Kurt W.

eRA COMMONS USER NAME (agency login): zilmku

POSITION TITLE: Professor of Chemistry

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
University of Utah, Salt Lake City, Utah	BS	06/1976	Chemistry
University of Utah, Salt Lake City, Utah	PHD	06/1981	Physical Chemistry
University of California, Berkeley, California	Postdoctoral Fellow	07/1983	Chemical Physics

A. PERSONAL STATEMENT

My laboratory has been developing solid state NMR methods and instrumentation over 34 years for all sorts of applications in chemistry, material science and biophysics. In the past decade we have primarily focused on techniques for determining elements of protein structure in macromolecular complexes and for probing questions related to their physical chemistry. We pioneered the use of uniform ^{13}C enriched samples in fast magic angle spinning solid state protein NMR, development of high field ^{1}H detected MAS solids NMR suitable for studying proteins, and the use of extensive deuteration with fast magic angle spinning to achieve high resolution $^{1}H/^{15}N$ spectra of microcrystalline proteins. Current research in the laboratory is split between two principal thrusts. The first is development of microliter scale dynamic nuclear polarization instrumentation using diode based millimeter wave frequency sources, which we believe will make DNP a much more applicable and accessible technique in biophysics. The second thrust involves solid state NMR investigations of prion protein in two different disease systems. In collaboration with the Supattapone lab at Dartmouth, we are determining the structural differences between infectious and non-infectious isoforms of recombinant PrP^{Sc}. With the Strittmatter lab at the Yale medical school we are working on solid state NMR structure elucidation of the complex of Aβ-oligomers and PrP^{C} that is implicated in Alzheimer's disease. These collaborative projects provide exceptional training opportunities for graduate students through the combination of exposure to instrument and methods development in my laboratory, protein biophysics, and an immersion into the structural biology of these two very important disease systems in the laboratories of our medical school collaborators.

1. Paulson EK, Morcombe CR, Gaponenko V, Dancheck B, Byrd RA, et al. High-sensitivity observation of dipolar exchange and NOEs between exchangeable protons in proteins by 3D solid-state NMR spectroscopy. J Am Chem Soc. 2003 Nov 26;125(47):14222-3. PubMed PMID: 14624539.
2. Paulson EK, Morcombe CR, Gaponenko V, Dancheck B, Byrd RA, et al. Sensitive high resolution inverse detection NMR spectroscopy of proteins in the solid state. J Am Chem Soc. 2003 Dec 24;125(51):15831-6. PubMed PMID: 14677974.
3. Zurawel AA, Walsh DJ, Fortier SM, Chidawanyika T, Sengupta S, et al. Prion nucleation site unmasked by transient interaction with phospholipid cofactor. Biochemistry. 2014 Jan 14;53(1):68-76. PubMed PMID: 24328062; PubMed Central PMCID: PMC3953128.

B. POSITIONS AND HONORS

Positions and Employment

1983 - 1988 Assistant Professor of Chemistry, Yale University, New Haven, CT
1988 - 1993 Associate Professor of Chemistry, Yale University, New Haven, CT
1993 - Professor of Chemistry, Yale University, New Haven, CT

Other Experience and Professional Memberships

1997 - 2010	Board member, Technical Advisory Council, Nova Chemicals
2001	review panel member, Canada Foundation for Innovation
2002	panel member, NIH shared instrumentation SEP for NCRR
2002	panel review member, NSF major chemical instrumentation
2003	Chair, Gordon Conference on Magnetic Resonance in Chemistry and Physics
2003	ad hoc member, NIH BBCB study section
2003	site visit team member, NIH NIBIB
2005	ad-hoc member, NIH macromolecular structure-function special study section
2005 - 2017	Chair, Rocky Mountain Conference on Analytical Chemistry and Spectroscopy
2006	Chair, Experimental NMR Conference
2006	Chair, NIH S10 shared instrumentation study section
2008	invited workshop participant, NSF workshop on instrument development
2009	member, NIH S10 shared instrumentation study section
2012-	ad hoc member, NIH EBIT study section
2015	NSF/NIH/DOE invited participant, "Ultrahigh Field NMR and MRI: Science at a Crossroads",
2015	NSF Centers for Chemical Innovation review panelist, Arlington, VA, February 2016.
2016	MIT-Harvard Center for Magnetic Resonance advisory committee
2016	NIH BTRR P41 site visit review panelist.

Honors

1976	ERDA Energy Traineeship, University of Utah
1978	Eastman Kodak award for graduate research, University of Utah
1982	IBM postdoctoral fellowship, University of California, Berkeley
1983	Dreyfus award for newly appointed faculty in chemistry, Camille and Henry Dreyfus Foundation
1986	Bituminous Coal Research Inc. - R.A. Glenn Award, ACS Division of Fuel Chemistry
1986	Morse Faculty Fellowhip, Yale University
1987	Franz-Vogt Prize, Justis-Liebig University, Giessen, FDR
1987	IR-100 Award for patented design of a zero field NMR spectrometer, Ind. Res. Magazine
1988	Dreyfus Teacher Scholar award, Camille and Henry Dreyfus Foundation
1991	Milton Harris Associate Professor of Chemistry, Yale University
2006	Elected Fellow, American Association for the Advancement of Science
2008	Fellow, International Union of Pure and Applied Chemists
2009	Robert Vaughan Lecturer, Rocky Mountain Conference on Analytical Chemistry
2012	Seton Elm-Ivy Award, Yale University
2014	Elected, Connecticut Academy of Sciences
2017	Laukien Award, Experimental NMR Conference

C. Contribution to Science

1. My earliest work involved application of high resolution solid state NMR to the study of naturally occurring organic matter including fossil kerogens, soil, gallstones and surface adsorbed species on supported metal catalysts. These studies were all pioneering efforts that for the first time identified the key organic structural components of these materials. In addition my group developed widely used spectral editing techniques for simplifying the complex spectra of such materials.

    a. Zilm KW, Pugmire RJ, Larter SR, Allan J, Grant DM. C-13 CP-MAS Spectroscopy of Coal Macerals. Fuel (London, England). 1981; 60(8):717-722.
    b. Wilson MA, Pugmire RJ, Zilm KW, Koh KM, Heng S, et al. Cross-Polarization C-13-NMR Spectroscopy With Magic Angle Spinning Characterizes Organic-Matter in Whole Soils. Nature. 1981; 294(5842):648-650.
    c. Zilm KW, Bonneviot L, Hamilton DM, Webb GG, Haller GL. C-13 NMR-Studies of CO Adsorbed On Supported Platinum And Palladium Catalysts Using Magic Angle Sample Spinning. Journal of Physical Chemistry. A. 1990; 94(4):1463-1472.

d. Wu XL, Burns ST, Zilm KW. Spectral Editing in CPMAS NMR - Generating Subspectra Based on Proton Multiplicities. Journal of Magnetic Resonance. Series A. 1994; 111(1):29-36.

2. The second major theme in my research career applied solid state NMR to characterize unusual bonding arrangements in small molecules by solid state NMR, including the combination of solid state NMR and matrix isolation techniques. These studies determined the orientation of ^{13}C shielding tensors in classic bonding environments, provided the first NMR spectra of matrix isolated reactive intermediates, and characterized unusual main group bonding arrangements.
   a. Zilm KW, Grant DM. C-13 Dipolar Spectroscopy of Small Organic-Molecules in Argon Matrices. Journal of the American Chemical Society. 1981; 103(11):2913-2922.
   b. Zilm KW, Merrill RA, Greenberg MM, Berson JA. The 1st Magic Angle Spinning NMR-Spectrum of a Captive Intermediate - Direct Observation of a Singlet Ground-State Biradical, 3,4-Dimethylenefuran. Journal of the American Chemical Society. 1987; 109(5):1567-1569.
   c. Zilm KW, Merrill RA, Webb GG, Greenberg MM, Berson JA. Two-Dimensional Solid-State NMR of a Captive Intermediate - Structure of The Radical Centers In 3,4-Dimethylenethiophene. Journal of the American Chemical Society. 1989; 111(4):1533-1535.
   d. Zilm KW, Lawless GA, Merrill RM, Millar JM, Webb GG. Nature of the Tin-Tin Double-Bond As Studied By Solid-State and Solution Nuclear-Magnetic-Resonance. Journal of the American Chemical Society. 1987; 109(23):7236-7238.

3. Transition metal polyhydrides have some of the most unexpected bonding and dynamics. My research group provided the first measurements of H-H distances in transition metal dihydrogen complexes and measured the dihydrogen ligand rotation barrier by solid state NMR. We also discovered and theoretically explained nuclear exchange couplings in transition metal polyhydrides. This latter phenomenon is the only coherent nuclear tunneling to ever have been observed in fluid phase at ambient temperatures. This work fundamentally changed the way inorganic chemists view transition metal hydrides.

   a. Zilm KW, Merrill RA, Kummer MW, Kubas GJ. Characterization of Transition-Metal Molecular Hydrogen Complexes By Solid-State Proton NMR. J Am Chem Soc. 1986 Nov 1;108(24):7837-9. PubMed PMID: 22283298.
   b. Zilm KW, Heinekey DM, Millar JM, Payne NG, Demou P. Proton Proton-Exchange Couplings in Transition-Metal Polyhydrides. Journal of the American Chemical Society. 1989; 111(8):3088-3089.
   c. Inati SJ, Zilm KW. Spin Correlations and Symmetrization in the Nuclear Magnetic Resonance of Molecular Systems with Tunneling. Phys Rev Lett. 1992 Jun 1;68(22):3273-3276. PubMed PMID: 10045660.

4. The development of superconducting magnets with fields in excess of 17 T revolutionized the use of solid state NMR in structural biology. My group was the first to recognize this potential, and was central in development of the instrumentation needed for high resolution MAS NMR of proteins and the first applications to assignment of spectra of uniformly ^{13}C enriched proteins. This work inspired a whole generation of solid state NMR applications to biochemical systems.
   a. Martin RW, Paulson EK, Zilm KW. Design of a Triple Resonance Magic Angle Sample Spinning Probe for High Field Solid State Nuclear Magnetic Resonance. The Review of scientific instruments. 2003; 74(6):3045-3061.
   b. Morcombe CR, Zilm KW. Chemical Shift Referencing in MAS Solid State NMR. J Magn Reson. 2003 Jun;162(2):479-86. PubMed PMID: 12810033.
   c. Martin RW, Zilm KW. Preparation of Protein Nanocrystals and Their Characterization by Solid State NMR. J Magn Reson. 2003 Nov;165(1):162-74. PubMed PMID: 14568526.
   d. McDermott A, Polenova T, Bockmann A, Zilm KW, Paulson EK, et al. Partial NMR Assignments for Uniformly (^{13}C, ^{15}N)-Enriched BPTI in the Solid State. J Biomol NMR. 2000 Mar;16(3):209-19. PubMed PMID: 10805127.

5. Solid state NMR of proteins obtained from heavily deuterated samples was pioneered by my lab, and has proven especially fruitful. We developed key methods including proton detection methods for 2D and 3D NMR of solid proteins used widely in the field. In addition we have used isotope labeling to modulate NMR relaxation times, and are developing ways to use such phenomena to determine long internuclear distances.
   a. Paulson EK, Morcombe CR, Gaponenko V, Dancheck B, Byrd RA, et al. High-Sensitivity Observation of Dipolar Exchange and NOEs Between Exchangeable Protons in Proteins By 3D Solid-State NMR Spectroscopy. J Am Chem Soc. 2003 Nov 26;125(47):14222-3. PubMed PMID: 14624539.
   b. Paulson EK, Morcombe CR, Gaponenko V, Dancheck B, Byrd RA, et al. Sensitive High Resolution Inverse Detection NMR Spectroscopy of Proteins in the Solid State. J Am Chem Soc. 2003 Dec 24;125(51):15831-6. PubMed PMID: 14677974.
   c. Morcombe CR, Gaponenko V, Byrd RA, Zilm KW. Diluting Abundant Spins by Isotope Edited Radio Frequency Field Assisted Diffusion. J Am Chem Soc. 2004 Jun 16;126(23):7196-7. PubMed PMID: 15186155.
   d. Fry EA, Sengupta S, Phan VC, Kuang S, Zilm KW. CSA-Enabled Spin Diffusion Leads to MAS Rate-Dependent T_1s at High Field. J Am Chem Soc. 2011 Feb 9;133(5):1156-8. PubMed PMID: 21207992.

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/kurt.zilm.1/bibliography/47423758/public/?sort=date&direction=ascending

D. RESEARCH SUPPORT

Ongoing Research Support

CHE-1413096, National Science Foundation Zilm, Kurt (PI) 2014/09/01-2017/08/31
Physical Chemistry of Macromolecules as Probed by High Resolution Solid State NMR
Development of new high resolution solid state NMR techniques such as microliter dynamic nuclear polarization. These methods are being applied to probe water and backbone dynamics in proteins, and obtain structural constraints from NMR relaxation measurements.
Role: PI

R01 AG034924-06A1, NIH Strittmatter, Stephen (PI) 06/01/16-05/31/21
Mechanisms of A-Beta Oligomer Induced Synapase Dysfunction in Alzheimer's Disease
The goal in this project is to determine the molecular basis of A-Beta oligomer toxicity leading to Alzheimer's disease. Our portion of the project is to determine the structure of the PrP^C protein in the PrP-A-Beta oligomer complex, and to obtain insights into the molecular arrangement of the A-Beta oligomers using a variety of sold state NMR methods.
Role: Co-PI

1R56NS094576-01A1, NIH Zilm, Kurt (co-PI) 08/01/2017-08/01/2018
Structural Mechanism of Mammalian Prion Infectivity
This is a joint award with the Supattapone group at Dartmouth. The goals of this research are to identify the structural differences between infectious $PrP^{Sc}$and non-infectious PrP^{Sc} using soild state NMR methods.
Role: Co-PI

Completed Research Support

None