BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: McElheny, Daniel John

eRA COMMONS USER NAME: DMCELHENY

POSITION TITLE: Director of NMR Laboratory (University of Illinois at Chicago)

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

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Illinois State University	B.S.	08/1993	Chemistry
Illinois State University	M.S.	01/1996	Chemistry
University of Illinois at Chicago	Ph.D.	01/2001	Chemistry
The Scripps Research Institute		11/2004	Molecular Biology
The University of Chicago		06/2006	Molecular Biology

A. Personal Statement

Extensive solution, solid and liquid crystalline NMR characterization expertise. Large molecule assignment and structural analysis through 3D NMR methods. Expert at automating experimental routines for binding analysis. Residual dipolar coupling, Model-free, relaxation dispersion, and DOSY experience.

Small molecule characterization through standard HMQC, H2BC, HMBC, NOESY *etc*. Implementation of novel pure shift 1D and 2D experiments. Pulse sequence development and usage of adiabatic/non-adiabatic shaped pulse implementation through custom written in-house programs.

Proficient at molecular modeling, structure computation and in silico binding analysis. Expert level usage of AMBER, Rosetta and CYANA. Recently submitted an invited publication to Methods in Molecular Biology regarding amyloid beta fibril structure determination through use of SSNMR and CYANA/AMBER refinement.
Proficient at C, C++, Perl, Tcl/Tk, Python, HTML, shell scripting, and the Linux/Unix environments. Developed custom written code for automating analysis of binding assays, relaxation experiments and structural interpretation in C++.

B. Positions and Honors

2001- Fellow, Peter E. Wright (PI), The Scripps Research Institute
2004- Research Associate, Shohei Koide (PI), University of Chicago
2006- Director, NMR Facilities at the University of Illinois at Chicago

C. Contributions to Science

1. **Methods development and NMR study of aramide polymers and glasses.** During my Ph.D. graduate study I was very fortunate to be advised by Dr. Lucio Frydman who is a world leader in the field of NMR in both solids and currently MRI methods. During these years the students (including myself) were involved in building three spectrometers and many probes; an endeavor which certainly helps to bolster ones understanding of Magnetic Resonance. One novel probe design included a so called “dynamic director” probe which allows the aligned liquid crystal to be reoriented mechanically with a motor during data acquisition. From this, insight into the liquid crystals ordering and distribution could be determined at the atomic level. The unique probe design and spectrometer also allowed for additional rheology studies to be performed.

   The Frydman lab also developed the novel MQMAS NMR method during this time for studying quadrupolar nuclei. This experiment has revolutionized the field of NMR in applications towards ceramics and glasses for nuclei such as 23Na, 11B, and many other spin-half quadrupolar nuclei. The MQMAS experiment is now an indispensable routine method for SSNMR and is used by many labs throughout the world.

   a. The Influence of Monomer Structures on the Order of Aramide Polymers: An NMR Analysis. McElheny D, Frydman V, Zhou M, Frydman L. *The Journal of Physical Chemistry. B.* 1999; 103(44):9505.

   b. McElheny D, DeVita E, Frydman L. Heteronuclear local field NMR spectroscopy under fast magic-angle sample spinning conditions. *Journal of magnetic resonance* (San Diego, Calif. : 1997). 2000; 143(2):321-8. PMID: 10729258

   c. McElheny D, Zhou M, Frydman L. Two-dimensional dynamic-director (13)C NMR of liquid crystals. *Journal of magnetic resonance* (San Diego, Calif. : 1997). 2001; 148(2):436-41. PMID: 11237650

   d. McElheny D, Frydman V, Frydman L. A solid-state 13C NMR analysis of molecular dynamics in aramide polymers. *Solid state nuclear magnetic resonance*. 2006; 29(1-3):132-41. PMID: 16199142

2. **Free energy landscape of DHFR.** During my postdoctoral study in the laboratory of Dr. Peter Wright at the TSRI I learned to use liquid state NMR methods for studying the structure and dynamics of proteins. During this time we were able to characterize the dynamic behavior of the remarkable system of DHFR throughout its catalytic cycle whereby leading to a publication in the journal *Science*. My contribution involved helping to implement modern pulse sequences and playing a role in the development of in-house data fitting program (GLOVE) for the generated relaxation data. I also prepared the samples for NMR analysis.

   a. Boehr DD, McElheny D, Dyson HJ, Wright PE. The dynamic energy landscape of dihydrofolate reductase catalysis. *Science* (New York, N.Y.). 2006; 313(5793):1638-42. PMID: 16973882

   b. Boehr DD, McElheny D, Dyson HJ, Wright PE. Millisecond timescale fluctuations in dihydrofolate reductase are exquisitely sensitive to the bound ligands. *Proceedings of the National Academy of Sciences of the United States of America*. 2010; 107(4):1373-8. PMID: 20080605, PMCID: PMC2824364

   c. McElheny D, Schnell JR, Lansing JC, Dyson HJ, Wright PE. Defining the role of active-site loop fluctuations in dihydrofolate reductase catalysis. *Proceedings of the National Academy of Sciences of the United States of America*. 2005; 102(14):5032-7. PMID: 15795383, PMCID: PMC556001

   d. Venkitakrishnan RP, Zaborowski E, McElheny D, Benkovic SJ, Dyson HJ, Wright PE. Conformational changes in the active site loops of dihydrofolate reductase during the catalytic cycle. *Biochemistry*. 2004; 43(51):16046-55. PMID: 15609999

3. **Solid state NMR reveals the structure Amyloid-beta 1-42**. Over the past decade or so I've been collaborating with Dr. Yoshitaka Ishii in the study of amyloid fibrils. SSNMR is a powerful method for studying amyloid at atomic resolution. Dr. Ishii and his group were the first to acquire NMR distance and torsion angle restraints for the extremely important system Amyloid-beta 42, a suspected pathogen in Alzheimers disease. My role was to help in incorporating the restraints into the molecular modeling programs CYANA and AMBER for structural determination. This effort led to the discovery of the unique fold of Aβ42 and its local structural elements which were previously unknown.

    a. Xiao Y, Ma B, McElheny D, Parthasarathy S, Long F, Hoshi M, Nussinov R, Ishii Y. Aβ(1-42) fibril structure illuminates self-recognition and replication of amyloid in Alzheimer's disease. *Nature structural & molecular biology*. 2015; 22(6):499-505. NIHMSID: NIHMS665499 PMID: 25938662, PMCID: PMC4476499

    b. Xiao Y, McElheny D, Hoshi M, Ishii Y. Solid-State NMR Studies of Amyloid Materials: A Protocol to Define an Atomic Model of Aβ(1-42) in Amyloid Fibrils. *Methods in molecular biology* (Clifton, N.J.). 2018; 1777:407-428. PMID: 29744851

    c. Parthasarathy S, Yoo B, McElheny D, Tay W, Ishii Y. Capturing a reactive state of amyloid aggregates: NMR-based characterization of copper-bound Alzheimer disease amyloid β-fibrils in a redox cycle. *The Journal of biological chemistry.* 2014; 289(14):9998-10010. PMID: 24523414, PMCID: PMC3975043

    d. Parthasarathy S, Long F, Miller Y, Xiao Y, McElheny D, Thurber K, Ma B, Nussinov R, Ishii Y. Molecular-level examination of Cu2+ binding structure for amyloid fibrils of 40-residue Alzheimer's β by solid-state NMR spectroscopy. *Journal of the American Chemical Society*. 2011; 133(10):3390-400. NIHMSID: NIHMS275468 PMID: 21341665, PMCID: PMC3074258

D. Additional Information: Research Support and/or Scholastic Performance

National Research Service Award – National Institute of Health
1 F32 GM68380-29 Wright(Sponsor) 6/1/03 – 5/31/05
"Structural Fluctuations in the Catalytic Cycle of DHFR"
NMR study of the structure and dynamics of DHFR throughout its catalytic cycle. We were able to correlate how active site loop motions on the millisecond timescale play an important part in the kinetic behavior of DHFR. The work resulted in several publications including a seminal paper in the journal "*Science*".