Alexander Benjamin Barnes: CV and Major Scientific Achievements

1. Personal information

Family name, First name:	Barnes, Alexander Benjamin
Researcher unique identifier(s):	ORCID: 0000-0003-3748-8508, Research ID: D-5354-2009, Google Scholar ID: Alexander Barnes
Date of birth:	May 1, 1981
Nationality:	United States of America
URL for website:	http://pages.wustl.edu/barneslab

2. Education

2011 Massachusetts Institute of Technology, PhD Physical Chemistry.
Thesis Title: "High-Resolution High-Frequency Dynamic Nuclear Polarization for Biomolecular Solid State NMR"
2003 Whitman College, B.A. Chemistry with Honors.

3. Employment history including current position

Since 09/2019 Professor, Department of Chemistry and Applied Biosciences, Swiss Federal Institute of Technology in Zürich (ETH Zürich), Switzerland
2019 Associate Professor, Department of Chemistry, Washington University in St. Louis, USA
2013 Assistant Professor, Department of Chemistry, Washington University in St. Louis, USA
2011-2013 Post-doctoral Research Scientist, Department of Chemistry, Stanford University, USA
Advisor: Lynette Cegelski
2011 Post-doctoral Research Scientist, Plasma Science and Fusion Center and Department of Chemistry, Massachusetts Institute of Technology, USA. Advisors: Richard J. Temkin and Robert G. Griffin
2004-2011 Graduate Research and Teaching Assistant, Department of Chemistry, Massachusetts Institute of Technology, USA. Advisor: Robert G. Griffin
2004 Post-baccalaureate Research Assistant, Institute for Physical Chemistry, Münster University, Germany. Advisor: Hellmut Eckert
2002-2003 Undergraduate Research Assistant, Department of Chemistry, Washington University in St. Louis, USA. Advisor: Sophia E. Hayes

4. Institutional responsibilities

2016-2019 NMR and EPR facility committee, Department of Chemistry, Washington University in St. Louis, USA
2015-2019 Co-chair of St. Louis NMR discussion group (ACS-funded lecture series with national recognition)
2014-2019 Steering committee: Biochemistry, Biophysics and Structural Biology, WU School of Medicine, USA
2014-2019 Machine shop committee (Chair), Department of Chemistry, Washington University in St. Louis, USA
2013-2019 Admission committee, Department of Chemistry, Washington University in St. Louis, USA
2013-2019 Website committee, Department of Chemistry, Washington University in St. Louis, USA

5. Approved and completed research projects

- Magnetic Resonance Technology for In-cell NMR Structural Determination of HIV Latency Reversal Agents (Camille Dreyfus Teacher-Scholar Award, Dreyfus Foundation, 05/01/18-08/31/2019, 75,000 USD)
- CAREER: Structural Biology in a Cellular Context with High-sensitivity NMR (NSF, NSF 1553577 PI: Barnes, PI, 08/01/16-08/31/2019, 690,578 USD)
- High-Sensitivity NMR at Room Temperature for Molecular Structure and Dynamics (NIH, 1DP2OD021207-01, PI: Barnes, 09/30/15-08/31/2019, 2,230,000 USD)
- Administrative Supplement for Alzheimer's Disease and Related Dementias/ADRD (NIH, supplement to DP2, 1DP2OD021207-01, Barnes, PI, 09/30/18-08/31/2019, 389,494 USD)
- STTR Phase 1: Probe for High Field DNP at Room Temperature (NSF, NSF 1521314, PI: Sirigiri, PI, 07/01/15-06/30/16, 89,978 USD
- Novel NMR and EPR Technology for Surface Characterization of Biomass (SEAS Collaboration Initiation Grant, Internal Award, PIs: Barnes/Foston, 6/1/15-7/30/16, 7,500 USD)
- 1000-fold Sensitivity Enhancement and Organelle Contrast of In-cell NMR (Washington University Molecular Imaging Center, 15-021M, PI: Barnes, 5/22/15 – 3/30/16, 10,000 USD)

6. Supervision of junior researchers at graduate and postgraduate level

2017-2019: 3 postgraduate researchers: Dr. Erika Sesti, Dr. Thomas M. Osborn Popp (since July 2019), Dr. Sarah A. Overall (since June 2019)

2013-2019: 7 PhD students. Researchers mostly involved in DNP NMR technology development: Dr. Faith Scott, Dr. Brice Albert, Dr. Edward Saliba, Dr. Pin-Hui Chen, Dr. Chukun Gao, Mr. Nicholas Alaniva, Ms. Lauren Price

7. Teaching activities

- Spring 2014-18: Thermodynamics (Chemistry 402), Washington University in St. Louis, St. Louis MO, USA. Hours Lectured: 170; Student Evaluations: Teaching rated 6.1 out of 7.0 (average over 5 years)
- Fall 2016: Electron Paramagnetic Resonance and Dynamic Nuclear Polarization (Chemistry 5762), Washington University in St. Louis, St. Louis MO, USA. Hours Lectured: 39; Student Evaluations: Teaching rated 4.6 out of 5.0
- Fall 2014, 2015, 2017: Freshman Seminar in Chemical Sciences (Chemistry 181), Washington University in St. Louis, St. Louis MO, USA. Course instructor (2015, 2017), Hours Lectured: 5; Student Evaluations: Teaching rated 6.6 out of 7.0

8. Memberships in panels, boards, etc., and individual scientific reviewing activities

2018 Scientific review committee for NIH. CSR-ZRG1 CVRS-H 50 R Special Emphasis Panel

2018 Scientific reviewer for ACS Petroleum Research Fund

2017 Scientific review committee for NSF. MRI-CHE

2017 Scientific review committee for NIH. ZRG1 IMST-L (10) B Small Business: Bioanalytical Chemistry, BioPhysics and Assay Development

2013-2019 Reviewer for manuscripts submitted to: Journal of the American Chemical Society, Angewante Chemie, Journal of Magnetic Resonance, Journal of Physical Chemistry, Journal of Physical Chemistry Letters, Journal of Chemical Physics, Magnetic Resonance in Chemistry, Solid State Nuclear Magnetic Resonance, Concepts in Magnetic Resonance

2016-2019 NMR and EPR facility committee, Department of Chemistry

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2014-2019 Steering committee: Biochemistry, Biophysics and Structural Biology, WU School of Medicine

2014-2019 Machine shop committee (chair), Department of Chemistry

2013-2019 Admission committee, Department of Chemistry

2013-2019 Website committee, Department of Chemistry

9. Active memberships in scientific societies, fellowships in renowned academies

- International Society of Magnetic Resonance (ISMAR)
- American Association for the Advancement of Science (AAAS)
- American Chemical Society (ACS)
- Institute of Electrical and Electronic Engineers (IEEE)

11. Prizes, awards, fellowships

2019 Varian Young Investigator Award

2018 Leadership and Entrepreneurial Acceleration Program (LEAP) Award

2017 Camille Dreyfus Teacher-Scholar Award

2016 NSF CAREER Award

2015 NIH Director's New Innovator Award, 2015

2011 Postdoctoral Fellowship, Center for Molecular Analysis and Design at Stanford University, 2011

2005 NSF Graduate Research Fellowship, 2005

Major scientific achievements in the past five years

Over the last five years, I have overseen the design and implementation of a novel magic angle spinning (MAS) dynamic nuclear polarization (DNP) spectrometer capable of performing: 1) the first electron decoupling experiments using chirped microwave pulses; 2) the first cryogenic MAS DNP experiments at 4.2 Kelvin; 3) the first MAS-DNP within intact human cells; and 4) the first MAS experiments using spherical rotors. I have also employed conventional solid-state NMR (without DNP) to reveal multiple conformations of bryostatin bound to the C1b regulatory domain of PKC. I therefore have the necessary expertise and have assembled an expert scientific team to deliver important improvements in MAS DNP technology. Currently, DNP experiments employ continuous wave (CW) microwave irradiation, which has major disadvantages compared to pulsed approaches. Our new microwave and magnetic resonance instrumentation allow us to generate pulsed microwaves for DNP while cooling samples to <6 K by employing spherical rotors for MAS. Our previous experiments on bryostatin/PKC required one year of signal averaging without DNP; our signal enhancements allow us to record the same datasets in only a few hours.

1. Frequency-agile gyrotrons as microwave sources for DNP-NMR:

Dynamic nuclear polarization (DNP) improves NMR sensitivity by orders of magnitude by transferring polarization from electron to nuclear spins. Although discovered in the 1950s, the application of DNP to magnetic fields suitable for high-resolution NMR and structural biology has been hindered by a lack of high-power microwave sources in the 140-460 GHz frequency band. To fill this technological gap, my research has focused on the design and implementation of new microwave technology. Specifically, I have overseen the design and implementation of a high-power frequency-agile 198 GHz gyrotron, which we have used to perform electron decoupling with chirped microwave pulses. I now have an extensive track record in this area. Our frequency-agile gyrotrons are critical to implementing pulsed DNP with MAS-NMR for application to biological systems; for instance, time-domain DNP will provide higher DNP enhancements in biological membranes and in cells.

2. Spherical rotors for magic angle spinning (MAS) for magnetic resonance:

For the last 60 years, MAS-NMR samples have typically been packed in hollow, cylindrical sample containers with turbine inserts to supply drive propulsion. Scaling cylindrical rotors to micron sizes to access spinning frequencies >150 kHz is difficult. Cylinders are also difficult to insert and eject from stators within magnet bores. Furthermore, cryogenic MAS of cylinders requires substantial quantities of cryogens, especially for DNP experiments. Cylindrical rotors surrounded by solenoids also complicate microwave coupling strategies aiming to maximize electron spin Rabi frequencies for electron decoupling and pulsed DNP. To overcome these limitations, I have introduced spheres for MAS, successfully demonstrating MAS-NMR spectroscopy of samples packed within spherical rotors spinning stably at the magic angle. Spherical rotors have distinct advantages over cylindrical rotors. For example, in our current implementation, spherical rotors contain cylindrical sample chambers and equatorial turbine grooves cut into the rotor surface. Ensuring that the mass distribution of high-density zirconia is distant from the spinning axis achieves a large moment of inertia and improves spinning stability. Converting the zirconia rotor body into a turbine, rather than relying on turbine inserts, delivers an exceedingly robust drive platform with high torque.

These spheres also have superior mechanical strength to cylindrical rotors because the rotor wall can be strengthened selectively at sites of high centrifugal stress.

3. Cryogenic MAS-NMR and DNP probe technology:

MAS-NMR experiments must currently be conducted at cryogenic temperatures (<100 K) to achieve significant NMR signal enhancements from DNP. Cryogenic temperatures increase electronic and nuclear relaxation times, improving the efficiency of DNP whilst also increasing the overall spin polarization due to Boltzmann statistics. We performed the first MAS DNP experiments with sample temperatures <6 K, achieving ~200-fold DNP enhancements and, when multiplied by the 42x gain in sensitivity from the cryogenic temperatures, we achieved >8000-times NMR sensitivity gains. This translates into a 8000_2 = 64 million times faster signal averaging, such that our year-long experiments on bryostatin bound to PKC could be accomplished within hours.

4. Electron decoupling and DNP method development:

A detailed understanding of the theoretical basis of DNP is required to interpret DNP data and improve DNP methodology. I characterized the deleterious effects of adding DNP paramagnetic agents on NMR and introduced electron decoupling to improve DNP spectra. Together, theoretical DNP treatments and NMR spin physics yield a complete understanding of the inter-nuclear interactions that ultimately deliver extremely high-precision 3D biomolecular structures, as I demonstrated on peptides. The details of how electron spins interact with incoming microwave power are an important aspect of understanding DNP experiments and can best be understood by adopting a rigorous approach to determine the propagation and intensity of microwaves together with theoretical spin-physics calculation packages.

5. In-cell NMR, solid-state NMR of bryostatin, and DNP-NMR of membrane proteins:

In conventional (non-DNP) NMR experiments, I demonstrated that bryostatin adopts multiple conformations while bound to the C1b regulatory domain of PKC. Isotopic ^{19}F, ^{2}H, and ^{13}C sites incorporated into bryostatin allowed us to measure very high-quality, long-range distances with rotational echo double resonance (REDOR) NMR. I previously employed MAS DNP-NMR to determine molecular structures within membranes including bacteriorhodopsin and the M2 influenza protein.