Paul Robustelli, Ph.D. **Assistant Professor of Chemistry**
Paul.J.Robustelli@Dartmouth.edu **Dartmouth College**

Professional Experience

- **Dartmouth College (Jan 2020–Present)**
  - Assistant Professor of Chemistry
  - Member, Neukom Faculty Cluster of Computational Science
  - Member, Department of Biochemistry and Cell Biology
- **D.E. Shaw Research (2013-2019)**
  Scientist
  - Developing Improved Physical Models for the Accurate Simulation of both Folded and Disordered Protein States
  - Elucidating Dynamic Binding Modes of Small Molecules with Intrinsically Disordered Proteins and Rationally Designing Tighter Binders
- **Columbia University Medical Center (2011-2013)**
  NSF Postdoctoral Research Fellow
  - Mentor: Arthur G. Palmer III
  - Studying the Role of Conformational Dynamics in Protein Function with NMR Spectroscopy and Molecular Simulations
- **University of Cambridge, Department of Chemistry (2006-2011)**
  Graduate Research Assistant
  - Mentor: Michele Vendruscolo
  - Development and Application of Novel Computational Methods for Protein Structure Determination from NMR Chemical Shifts
- **Pomona College, Department of Chemistry (2004-2006)**
  Undergraduate Research Assistant
  - Mentor: Wayne E. Steinmetz
  - Determination of the Structure and Conformational Dynamics of Tricothecene Mycotoxins with NMR Spectroscopy and Molecular Modeling

Education

- **University of Cambridge** - Ph.D. in Chemistry (2010)
  - Dissertation Title: Protein Structure Determination from NMR Chemical Shifts
  - Supervisor: Michele Vendruscolo
- **Pomona College** - B.A. in Chemistry with Minor in Mathematics (2006)
  - Dissertation Title: Determination of the Solution-Phase Structures and Dynamics of the Tricothecene Mycotoxins Verrucarin A and Roridin A

Manuscript Preprints Under Review:

1. Molecular basis of small-molecule binding to a-synuclein, P Robustelli, Ibanez-de-Opakua A, Campbell-Bezat C, Giordanetto F, Becker S, Zweckstette Mr, Pan AC, Shaw DE, *bioRxiv* (2021) https://doi.org/10.1101/2021.01.22.426549

Peer Reviewed Publications (Total: 18, Total Citations: 2222, h-index: 16)
Google Scholar Page: https://scholar.google.com/citations?user=2Fr4owoAAAAJ&hl=en

1. Quantifying the Relationship between Conformational Dynamics and Enzymatic Activity in Ribonuclease HI Homologues, J Martin, P Robustelli, AG Palmer III, *Biochemistry* (2020)

2. The Mechanism of Coupled Folding-Upon-Binding of An Intrinsically Disordered Protein, P Robustelli, S Piana, DE Shaw, *Journal of the American Chemical Society* (2020)

3. Development of a Force Field for the Simulation of Single-Chain Proteins and Protein-Protein Complexes. S Piana*, P Robustelli*, D Tan, S Chen, DE Shaw (*=equal contributions), *Journal of Chemical Theory and Computation*, 16, 4, 2494-2507 (2020)

4. Developing a Molecular Dynamics Force Field for Both Folded and Disordered Protein States, P Robustelli, S Piana, DE Shaw, *Proceedings of the National Academy of Sciences*, p.201800690 (2018)

5. Water Dispersion Interactions Strongly Influence Simulated Structural Properties of Disordered Protein States, S Piana, A Donchev, P Robustelli, DE Shaw, *Journal of Physical Chemistry B,* 119 (16), 5113-5123 (2015)

6. Functional implications of large backbone amplitude motions of the glycoprotein 130-binding epitope of interleukin-6, R Bobby, P Robustelli, AV Kralicek, M Mobli, GF King, J Grötzinger, AJ Dingley, *FEBS Journal,* 281(10), 2471-83 (2014

7. Conformational Dynamics of the Partially Disordered Yeast Transcription Factor GCN4, P Robustelli, N Trbovic, RA Friesner, AG Palmer III, *Journal of Chemical Theory and Computation*, 9(11), 5190–5200 (2013)

8. Thermal Adaption of Conformational Dynamics in Ribonuclease H, KA Stafford, P Robustelli, AG Palmer III, *PLoS Computational Biology*, 9(10), e1003218 (2013)

9. Structure of an Intermediate State in Protein Folding and Aggregation, P Neudecker, P Robustelli, A Cavalli, P Walsh, P Lundstrom, A Zarrine-Afsar, S Sharpe, M Vendruscolo, LE Kay, *Science*, 336, 362-366 (2012)

10. Interpreting Protein Structural Dynamics from NMR Chemical Shifts, P Robustelli, KA Stafford, AG Palmer III, *Journal of the American Chemical Society*, 134, 6365-6374 (2012)

11. Characterization of the Conformational Equilibrium Between the Two Major Substates of RNase A using NMR chemical shifts, C Camilloni, P Robustelli, A De Simone, A Cavalli, M Vendruscolo, *Journal of the American Chemical Society*, 134, 3968-3971 (2012)

12. Effects of the Known Pathogenic Mutations on the Aggregation Pathway of the Amyloidogenic Peptide of Apolipoprotein A-I, S Raimondi, F Guglielmi, S Giorgetti, S Di Gaetano, A Arciello, DM Monti, A Relini, D Nichino, SM Doglia, A Natalello, P Pucci, P Mangione, L Obici, G Merlini, M Stoppini, P Robustelli, GG Tartaglia, M Vendruscolo, CM Dobson, R Piccoli, V Bellotti, *Journal of Molecular Biology*, 407(3), 465-76 (2011)

13. Using NMR Chemical Shifts as Structural Restraints in Molecular Dynamics Simulations of Proteins, P Robustelli, KJ Kohlhoff, A Cavalli, M Vendrusculo, *Structure*, 18, 1-11 (2010)

14. Fast and Accurate Predictions of Protein NMR Chemical Shifts from Interatomic Distance, KJ Kohlhoff, P Robustelli, A Cavalli, X Salvatella, M Vendruscolo, *Journal of the American Chemical Society,* 131 (39), 13894-13895 (2009)

15. Folding of Small Proteins with Chemical Shift Restrained Monte Carlo Simulations without the use of Molecular Fragment Replacement or Structural Homology, P Robustelli, A Cavalli, CM Dobson, M Vendruscolo, X Salvatella, *Journal of Physical Chemistry B,* 113 (22), 7890-7896 (2009)

16. Determination of Protein Structures in the Solid State from NMR Chemical Shifts, P Robustelli, A Cavalli, M Vendruscolo, *Structure*, 16, 1764-1769 (2008)

17. Structure and Conformational Dynamics of Tricothecene Mycotoxins, WE Steinmetz, P Robustelli, E Edens, D Heineman, *Journal of Natural Products*, 71 (4), 589-594 (2008)

18. A Molecular switch based on a biologically important redox reaction, P Yan, MW Holman, P Robustelli, A Chowdhury, FI Ishak, DM Adams, *Journal of Physical Chemistry B*, 109, 130-137 (2005)

Funding Awarded

- NIH Maximizing Investigators Research Award (MIRA) – NIH#13214730 (2021-2026) - PI
  - "Characterizing the binding mechanisms of castration-resistant prostate cancer therapeutics to the intrinsically disordered N-terminal domain of the Androgen Receptor"
  - Total Award: $1,250,000 (Direct Costs) / $1,979,921 (Total Costs)
- National Research Council/Pittsburgh Supercomputing Center Anton2 Supercomputing Grant - MCB200087P (2020) - PI
  - "Characterizing the binding mechanisms of castration-resistant prostate cancer therapeutics to the intrinsically disordered N-terminal domain of the Androgen Receptor"
  - Total Award: 460,000 MD Simulation Units
- Burke Research Initiation Award, Dartmouth College (2020-2022) – PI
  - Total Award: $30,000
- National Science Foundation Postdoctoral Research Fellowship - NSF#1002684 (2010-2012) – PI
  - Total Award: $123,000
- National Science Foundation Graduate Research Fellowship - NSF#0938784 (2006-2010)
  - Total Award: $124,500 ($41,500 accepted)
- Gates Cambridge Scholarship (2006-2009)
  - Total Award: $250,000

Oral Conference Presentations

- "How Do Small Molecule Drugs Bind Intrinsically Disordered Proteins?"
  Intrinsically Disordered Proteins Telluride Science Research Center Workshop (2021)
- "Molecular Recognition Mechanisms of Intrinsically Disordered Proteins"
  Open Source Software for Enhanced-Sampling Simulations, Lugano, Switzerland, (2019)
- "Molecular Recognition Mechanisms of Intrinsically Disordered Proteins"
  Biomolecules and Nanostructures, Pomlewo, Poland (2019)
- "Improved Physical Models Enable the Investigation of Molecular Recognition in Intrinsically Disordered Proteins at Atomistic Resolution" - Biophysical Society Meeting, Baltimore, MD, USA (2019)
  Biophysical Society Meeting, Baltimore, MD, USA (2019)
- "Improved Physical Models Enable the Investigation of Molecular Recognition in Intrinsically Disordered Proteins at Atomistic Resolution"
  Computational Biophysics at the Molecular and Mesoscales, Quy Nhon, Vietnam (2018)
- "Improved Physical Models Enable the Investigation of Molecular Recognition in Intrinsically Disordered Proteins at Atomistic Resolution"
  Protein Society Meeting, Boston, MA, USA (2018)

- "An Improved Force Field Enables the Elucidation of the Fundamental Biophysical Interactions of Intrinsically Disordered Proteins"
  CECAM Workshop: Disordered Protein Segments, Paris, France (2017)
- "Developing Force Fields for the Accurate Simulation of Both Ordered and Disordered Protein States"
  Conformational Ensembles from Experimental Data and Computer Simulations, Berlin, Germany (2017)
- "Developing Force Fields for the Accurate Simulation of Both Ordered and Disordered Protein States"
  Biophysical Society Meeting, New Orleans, LA, USA (2017)
- "Developing Force Fields that More Accurately Describe the Structural Properties of Ordered and Disordered Protein States"
  Experimental Nuclear Magnetic Resonance Conference, Asilomar, CA, USA (2015)
- "Tuning the Conformational Dynamics and Enzymatic Activity of Ribonuclease H"
  Frontiers of Structural Biology Keystone Symposia, Snowbird, UT, USA (2014)
- "Atomistic Descriptions of Protein Dynamics on Multiple Timescales from NMR Chemical Shifts"
  Computational Aspects - Biomolecular NMR Gordon Research Conference, West Dover, VT, USA (2013)
- "Atomistic Descriptions of Protein Dynamics on Multiple Timescales from NMR Chemical Shifts"
  ISMAR Meeting, Rio De Janiero, Brazil (2013)
- "Dynamically Averaged NMR Chemical Shifts Provide Atomistic Descriptions of Protein Motions"
  Protein Society Meeting, Boston, MA, USA (2011)
- "Direct Utilization of Chemical Shift Restraints in Protein Structure Calculations"
  Protein Society Meeting, Boston, MA, USA (2009)

Selected Invited Seminars

(As Dartmouth PI)

- "Characterizing dynamic and disordered proteins with molecular simulations and NMR spectroscopy"
  Roivant Sciences (2021)
- "Molecular Recognition Mechanisms of Intrinsically Disordered Proteins"
  IDP Seminars, Virtual Seminar Series, IDPseminars.com, (2020)
- "Molecular Recognition Mechanisms of Intrinsically Disordered Proteins"
  Dewpoint Therapeutics, Boston, MA, (2020)
- "Molecular Recognition Mechanisms of Intrinsically Disordered Proteins"
  University College of London, Thomas Young Centre Seminar Series, London, UK, (2019)
- Molecular Recognition Mechanisms of Intrinsically Disordered Proteins"
  University of Cambridge, Centre for Misfolding Diseases, Cambridge, UK, (2019)
- "Molecular Recognition Mechanisms of Intrinsically Disordered Proteins"
  Institute for Research in Biomedicine, Chemistry & Structural Biology, Barcelona, Spain, (2019)
- "Molecular Recognition Mechanisms of Intrinsically Disordered Proteins"
  Sanofi R&D, Paris, France, (2019)
- "Molecular Recognition Mechanisms of Intrinsically Disordered Proteins"
  Institut Pasteur, Department of Structural Biology and Chemistry, Paris, France, (2019)

(Prior to Dartmouth)

- "Molecular Recognition Mechanisms of Intrinsically Disordered Proteins"
  ETH Zürich, Department of Chemistry and Applied Bioscience, Zurich, Switzerland, (2019)

- "Molecular Recognition Mechanisms of Intrinsically Disordered Proteins"
  University of Copenhagen, Department of Biology, Copenhagen, Denmark, (2019)
- "Molecular Recognition Mechanisms of Intrinsically Disordered Proteins"
  Memorial Sloan Kettering Cancer Center, New York, NY, USA (2019)
- "Molecular Recognition Mechanisms of Intrinsically Disordered Proteins"
  CUNY ASRC/City College of New York, Biochemistry, Biophysics & Biodesign Seminar Series, New York, NY, USA (2019)

Teaching Experience

- **Dartmouth College, Honors General Chemistry (CHEM.010)**
  Lecture & Laboratory
  Topics: Quantum Mechanics, Bonding, Thermodynamics, Kinetics, Equilibria & Electrochemistry
- **Dartmouth College, Physical Chemistry II (CHEM.076)**
  Lecture & Laboratory
  Topics: Quantum Mechanics, Molecular Spectroscopy, Kinetics, & Statistical Thermodynamics
- **Dartmouth College, Graduate Research Colloquium in Computational & Theoretical Chemistry (CHEM.265)**
  Discussion of papers from the theoretical and computational chemistry literature
- **Dartmouth College, Computational Methods in Chemistry & Biophysics (CHEM101.6)**
  Project-based graduate course taught through a jupyter notebook / google collab interface.
  Topics: Quantum calculations, Molecular Dynamics simulations, Protein Dynamics, Protein Folding, Polymer Simulations & Enhanced Sampling Methods
- **Columbia University, Advanced Biophysical Chemistry (Guest Instructor)**
  -Lectures and Computational Exercises on Protein Structure and Dynamics from NMR Spectroscopy and Theory and Applications of Molecular Dynamics Simulations.
- **New York Structural Biology Center / City College of New York, Graduate Protein NMR Spectroscopy (Guest Instructor)**
  - Special Topics Lectures: "Protein Structure and Dynamics from NMR Chemical Shifts"
- **New York Academy of Sciences Afterschool Science, Technology, Engineering, and Mathematics Mentoring Program**
  - 12-lesson mathematics and science outreach curriculum to a 6th grade class '

Mentoring Experience

- **Dartmouth College**
  PhD Students
  - Jiaqi Zhu (2019 - Present), Kaushik Borthakur (2020 - Present) Thomas Sisk (2021 - Present)

  Undergraduate Students
  - Vaishnavi Katragadda (2021), Vaani Gupta (2021), Maeen Arslan (2021) Sarah Chong (2020)

Selected Awards and Honors

- 2021 - Invited Speaker, *Intrinsically Disordered Proteins: Telluride Science Research Center Workshop*, CO, USA
- 2021 - Open Science Fellow & Scientific Consultant, Roivant Sciences
- 2020 - Member of Scientific Advisory Board & Scientific Consultant, Dewpoint Therapeutics
- 2020 - Member, Department of Biochemistry and Cell Biology, Dartmouth College, Hanover, NH
- 2020 - Member, Neukom Academic Cluster in Computational Science, Dartmouth College, Hanover, NH
- 2019 - Invited Speaker, *Biomolecules and Nanostructures*, Pomlewo, Poland
- 2019 - Invited Speaker, *Computational Biophysics at the Molecular and Mesoscales*, Quy Nhon, Vietnam
- 2019 - Member, Editorial Board, *Frontiers in Molecular Biosciences*
- 2017 - Invited Speaker, *CECAM Workshop: Disordered Protein Segments*, Paris, France
- 2011-2013 - NSF Postdoctoral Research Fellowship
- 2009-2011 - NSF Graduate Research Fellowship
- 2006-2009 - Gates Cambridge Scholarship
- 2006 - Member, Phi Beta Kappa
- 2005 - Barry M. Goldwater Scholarship
- 2005 - Member, Sigma Xi
- 2005 - Arnold and Mabel Beckman Scholarship
- 2005 - Achievement Rewards for College Scientists Foundation Scholarship (2005)

Professional Service

- Reviewer For: *Elife*, *Nature Communications, Science Advances, Journal of the American Chemical Society, Journal of Chemical Theory and Computation, PLoS Computational Biology, Biochemistry*, *Biophysical Society*, *Structure*, *Journal of Physical Chemistry B, Communications Biology, Journal of Chemical Information and Modeling, Physical Chemistry Chemical Physics, Proteins: Structure, Function, and Bioinformatics, Journal of Biomolecular NMR, Life, Frontiers in Molecular Biosciences, Communications Biology*
- Professional Memberships: Protein Society, Biophysical Society, American Chemical Society
- Reviewer for Swiss National Super Computing Centre (CSCS) Grants
- Faculty Liaison for Dartmouth Chemistry Graduate Student Committee