Andrew L. Lee, Ph.D.

Assistant Professor
University of North Carolina at Chapel Hill
Division of Medicinal Chemistry and Natural Products
School of Pharmacy
310 Beard Hall, CB# 7360
Chapel Hill, NC 27599-7360

Phone: (919)-966-7821
Fax: (919)-843-5150
drewlee@unc.edu

Personal

Born, March 24, 1967

Residence:	2490 Lamont Norwood Rd. Pittsboro, NC 27312
Phone:	(919)-918-3865

Education

1996	Ph.D., Chemistry	University of California, Berkeley
1989	B.A., Chemistry	Pomona College

Professional Experience

March, 2001-	Assistant Professor*	University of North Carolina at Chapel Hill School of Pharmacy, Division of Medicinal Chemistry and Natural Products (*primary appointment)
March, 2001-	Assistant Professor	University of North Carolina at Chapel Hill Department of Biochemistry and Biophysics
1996-2000	Postdoctoral Fellow	University of Pennsylvania/SUNY Buffalo Department of Biochemistry and Biophysics *Advisor: Dr. A. Joshua Wand*
1990-1996	Graduate Student	University of California, Berkeley Department of Chemistry *Advisor: Dr. David E. Wemmer*

Honors

2001 American Association of Colleges of Pharmacy (AACP) New Investigator Program Award

1997 NIH Individual National Research Service Award: State University of New York at Buffalo/University of Pennsylvania.

Bibliography

Unpublished Refereed Papers/Articles (*corresponding author)

Hu, H., Clarkson, M.W., Lee, A.L., and Hermans, J.* Correlation of Order Parameters of Protein Side-Chain Methyl Groups from NMR Spin Relaxation Experiments and Long MD Simulations. *J. Am. Chem. Soc.* (in preparation).

Fuentes, E.J., Der, C.J., and Lee, A.L.* Ligand-Dependent Dynamics and Intramolecular Signaling in a PDZ Domain. *J. Mol. Biol.* (to be accepted with minor revisions).

Published Refereed Papers/Articles (*corresponding author)

Hu, H., Clarkson, M.W., Hermans, J., and Lee, A.L.* Increased Rigidity of Eglin c at Acidic pH: Evidence from NMR Spin-Relaxation and MD Simulations. *Biochemistry* (in press).

Prabhu, N.V., Lee, A.L., Wand, A.J., and Sharp, K.A.* Dynamics and Entropy of a Calmodulin-Peptide Complex Studied by NMR and Molecular Dynamics. *Biochemistry* (2003), 42, 562-570.

Lee, A.L., Sharp, K.A., Kranz, J.K., Song, X., and Wand, A.J.* Temperature Dependence of the Internal Dynamics of a Calmodulin-Peptide Complex. *Biochemistry* (2002), 41, 13814-13825.

Walsh, S.T.R., Lee, A.L., DeGrado, W.F., and Wand, A.J.* Backbone and Side-Chain Dynamics of a *De novo* Designed Three-Helix Bundle Protein Studied by ^{15}N, ^{13}C, and ^{2}H NMR Relaxation Methods. *Biochemistry* (2001), 40, 9560-9569.

Flynn, P.F., Urbauer, R.J.B., Zhang, H., Lee, A.L., and Wand, A.J.* Main Chain and Side Chain Dynamics of a Heme Protein: ^{15}N and ^{2}H NMR Relaxation Studies of *R. capsulatus* Ferrocytochrome c2. *Biochemistry* (2001), 40, 6559-6569.

Lee, A.L. and Wand, A.J.* Microscopic Origins of Entropy, Heat Capacity and the Apparent Glass Transition in Proteins: The Internal Dynamics of a Calmodulin-Peptide Complex. *Nature* (2001), 411, 501-504.

Lee, A.L. and Wand, A.J.* NMR Spectroscopy for Monitoring Molecular Dynamics in Solution. *Encyc. Life Sci.* (www.els.com).

Lee, A.L., Kinnear, S.A., and Wand, A.J.* Redistribution and Loss of Side-Chain Entropy Upon Formation of a Calmodulin-Peptide Complex. *Nat. Struct. Biol.* (2000) 7, 72-77.

Volkman, B.F., Wilkens, S.J., Lee, A.L., Xia, B., Westler, W.W., Beger, R., and Markley, J.L.* Redox-dependent Magnetic Alignment of *Clostridium pasteurianum* Rubredoxin: Measurement of Magnetic Susceptibility Anisotropy and Prediction of Pseudocontact Shift Contributions. *J. Am. Chem. Soc.* (1999) 121, 4677-4683.

Lee, A.L., Flynn, P.F., and Wand, A.J.* Comparison of ^{2}H and ^{13}C Relaxation Techniques for the Study of Protein Methyl Group Dynamics in Solution. *J. Am. Chem. Soc.* (1999) 121, 2891-2902.

Lee, A.L. and Wand, A.J.* Assessing Potential Bias in the Determination of Rotational Correlation Times of Proteins by NMR Relaxation. *J. Biomol. NMR* (1999) 13, 101-112.

Lee, A.L., Urbauer, J.L., and Wand, A.J.* Improved Labeling Strategy for ^{13}C Relaxation Measurements of Methyl Groups in Proteins. *J. Biomol. NMR* (1997) 9, 437-440.

Lee, A.L., Volkman, B.F., Robertson, S.A., Rudner, D.Z., Barbash, D.A., Cline, T.W., Kanaar, R., Rio, D.C., and Wemmer, D.E.* Chemical Shift Mapping of the RNA-Binding Interface of the Multiple-RBD Protein Sex-lethal. *Biochemistry* (1997) 36, 14306-14317.

Kanaar, R., Lee, A.L., Rudner, D.Z., Wemmer, D.E. , and Rio, D.C.* Interaction of the Sex-lethal RNA Binding Domains with RNA. *EMBO J.* (1995) 14, 4530-4539.

Lee, A.L., Kanaar, R., Rio, D.C., and Wemmer, D.E.* Resonance Assignments and Solution Structure of the Second RNA-Binding Domain of Sex-Lethal Determined by Multidimensional Heteronuclear Magnetic Resonance. *Biochemistry* (1994) 33, 13775-13786.

Oliphant, N., Lee, A., and Bernath, P.F.* Fourier Transform Emission Spectroscopy of the Jet-Cooled CCN Free Radical. *J. Chem. Phys.* (1990) 92, 2244-2247.

Invited Seminars

Apr. 26, 2003. "New Insights into Protein Energetics and Dynamics from a PDZ-Ligand Interaction". 117th North Carolina-ACS Sectional Conference. Chapel Hill, NC.

Feb. 9, 2003. "Dynamic Response of a PDZ Domain Protein to Peptide Binding" (presented by postdoctoral fellow Ernesto J. Fuentes). Keystone Symposium, Membrane Proteins and Frontiers in NMR. Taos, NM.

Nov. 16, 2002. "Dissections of Protein Flexibility from Experimental and Theoretical Methods". 4th Biannual Triangle Biophysics Symposium: Physics & Computation on Protein Structure. Chapel Hill, NC.

Apr. 25, 2001. "Dynamic Motions in a Calmodulin-Peptide Complex Determined by NMR Relaxation Measurements". UNC Department of Chemistry.

Apr. 21, 2001. "Temperature Dependence of Dynamics in a Calmodulin Complex: Viewing the Glass Transition with Solution NMR". 116th North Carolina-ACS Sectional Conference. Raleigh, NC.

Posters

Apr. 26, 2003. "Side-chain and Backbone Dynamics of a Free and Peptide Bound PDZ Domain". 117th North Carolina-ACS Sectional Conference. Chapel Hill, NC.

Apr. 26, 2003. "Dynamic Effects of Large-To-Small Mutations in Eglin c Extend to Non-Adjacent Side Chains". 117th North Carolina-ACS Sectional Conference. Chapel Hill, NC.

Mar. 23, 2003. "Dynamic Response of a PDZ Domain Protein to Peptide Binding". The Seventh Hopkins Folding Meeting. Berkeley Springs, WV.

Mar. 23, 2003. "Acid-Induced Rigidification of Eglin c at low pH: Evidence from NMR Spin-Relaxation Experiments and MD Simulations". The Seventh Hopkins Folding Meeting. Berkeley Springs, WV.

Feb. 8, 2003. "Side-chain and Backbone Dynamics of a Free and Peptide Bound PDZ Domain". Keystone Symposium, Membrane Proteins and Frontiers in NMR. Taos, NM.

Teaching Experience

2001-present (fall)	Lectures in PHCY 52 (Biochemistry I) 5 75 min. lectures, 2 recitations. Topics include amino acids, protein structure, protein structure/function relationships, antibody structure, protein-drug interactions.
2001-present (spring)	Lectures in MedChem 168 (Concepts of Drug Discovery and Design) Number of lectures has increased to 6 in spring of 2003. Topics include nucleic acid structure, nucleic acid-drug interactions, protein structure and drug

	interactions, introduction to multi-dimensional NMR spectroscopy, NMR-based drug screening.
2002-present (fall, spring)	Course coordinator, MedChem 361 (Graduate student seminar) Advise ~10 student seminars each semester. Teach basic principles of scientific speaking to a group of 25-30 graduate students. Advise students on an individual basis for talk organization, construction, and topic selection. I also provide feedback after their presentation has been given.
2003 (spring)	1 Lecture in MedChem 276 (Macromolecular Modeling). Protein structure determination by NMR.

Grants

Pending

2004-2008 "Energetics and Dynamics in Protein Recognition"
NSF Research Proposal, # 0344354, $551,000 (direct costs) requested
Submitted July 10, 2003.
PI: Lee, A.

2003 "Acquisition of a 700 MHz NMR Spectrometer and Cryoprobe"
NIH equipment grant, $500,000 requested
Submitted March 20, 2003. Priority score 153.
PI: Campbell, S.

2003-2008 "Coupling Networks and Side-Chain Dynamics in Proteins"
NIH R01 GM066009-01A1, $1,250,000 (direct costs) requested
Submitted February, 2003. Priority score 166.
PI: Lee, A.

Funded

2002 "Dynamic Motions and Energetic Couplings in Proteins"
Pharmacy Foundation of North Carolina, $5000
PI: Lee, A.

2001-2003 "Structural Studies and Molecular Interactions of a BRCT Domain from Human DNA Polymerase μ"
American Association of Colleges of Pharmacy
PI: Lee, A., New Investigator Program, $10,000

Not funded

2002 "Dynamics and Propagation in Proteins"
NSF Research Proposal, # 0235391
PI: Lee, A.

2002 "Acquisition of a 600 MHz NMR Spectrometer"
NIH Shared Instrumentation Equipment Grant, 1 S10 RR017844-01
$500,000 requested
PI: Lee, A.

2002 "Side-Chain Dynamics and Coupling Networks in Proteins"
NIH R01 GM066009-01
PI: Lee, A.

2002 Fellowship for Science and Engineering (UNC nominee)
The David and Lucile Packard Foundation
PI: Lee, A.

2001 "Type G" New Investigator Award
American Chemical Society Petroleum Research Fund
PI: Lee, A.

Professional Service

To Discipline

- Peer review for academic journals and funding agencies:
  Proteins: Structure, Function, Genetics (2001)
  Protein Science (2003)
  NSF equipment grant (2002)

- Active participant in Triangle Magnetic Resonance (TriMR) Discussion Group

Within UNC-Chapel Hill

- Graduate Student Thesis Committees
  In my research group:
  Michael Clarkson (Biochemistry & Biophysics)
  Emilie Lopes-Fernandes (Medicinal Chemistry)

  From other research groups:
  Suzanne Thorp (Medicinal Chemistry)
  Jacque Legere (Medicinal Chemistry)
  Richard Durham (Medicinal Chemistry)
  Hao Hu (Biochemistry & Biophysics)
  Stephanie Nick (Biochemistry & Biophysics)
  Carrie Stentz (Biochemistry & Biophysics) - Chair
  Fang Yi (Biochemistry & Biophysics)
  Julie Bryant (Chemistry)

- School of Pharmacy Dean Search Committee
- School of Pharmacy IT Committee
- Biophysics Training Program Administrative Board
- Biochemistry Graduate Student Written Report Committee
  Graded 20 rotation reports during 2001-2003

- Co-founder/Organizer of NMR Enthusiasts' Group
- Supervisor of the School of Pharmacy NMR Facility
  Oversee maintenance, user training, and billing of the 300 MHz NMR spectrometer. Assist in design of new Kerr Hall facility and installation of 500 MHz NMR spectrometer.

- School of Medicine NMR Advisory Committee
- Hosted Seminar Speakers
  Oct. 31, 2002 - Robert London (NIEHS)
  Apr. 10, 2003 - Clifford Robinson (University of Delaware)

Lab Personnel

Michael W. Clarkson	4th year graduate student (Biochemistry)
Emilie Lopes-Fernandes	2nd year graduate student (MCNP)
Ernesto J. Fuentes	Postdoctoral Fellow
Steven Gilmore	Research Technician

Research Statement

Laboratory research forms the center of my scholarly activities. The lab currently consists of two graduate students, one postdoctoral fellow, and one research technician. My group's research interests are in the areas of protein structure, dynamics, and energetics, and how these relate to protein function and evolution. NMR spectroscopy is our primary tool for characterizing proteins, structurally and dynamically, at atomic resolution. We are currently pursuing publications and major grants for three projects. In the first project, we are using a small serine protease inhibitor, eglin c (8 kDa), as a model protein for investigating the link between coupled motions and cooperative energetics in the native state. Our findings should have implications for understanding the physical basis of long-range communication and the effect of non-additive contributions to protein stability. In the second project, motional dynamics in a human PDZ domain from protein tyrosine phosphatase-1E (hPTP-1E) are being correlated with evolutionarily conserved communication pathways shared by the PDZ domain family as a whole. The immediate impact of this work will be significant insofar as the human proteome alone contains over 400 PDZ domains, many of which are involved in signaling and synaptic complexes. The characterizations are being carried out in the context of bound peptide ligand, and should therefore lead to a deeper understanding of protein-ligand interactions. In the third project, we are investigating the structural and dynamic properties of the 3C protease from poliovirus, a member of the picornaviral family. How these properties contribute to proteolytic catalysis and drug binding should lead to a greater understanding of these processes in enzymes. We are also interested in how mutations affect 3C behavior as a

model system for viral proteases. This is expected to have implications with regard to the development of drug resistance though this mechanism.

In addition, we are developing other structural biology projects in collaboration with various labs on campus. My aim is to have a variety of projects in the lab that stress complimentary ideas and approaches. For example, we are already using experimental and theoretical approaches to address the general problem of protein dynamics.

My research efforts are not only critical to the research itself, but also to scientific development of the students and postdoctoral fellow(s) in the lab, my service to the UNC and outside communities, and to my development as an effective teacher at the professional and graduate levels. Discoveries in research and related scholarly activities fuel the learning process in general, thereby facilitating teaching and additional research.

Teaching Statement

Teaching is the defining activity of the academic. Not only is it important for the simple passage of information, but it can have a profound effect on students' careers and life paths. It also is the most effective means by which the teacher organizes his thoughts and thereby shapes his career path as well. For these reasons, I take my teaching responsibilities very seriously.

I teach in a variety of ways. First, I teach biochemistry in a didactic setting to the pharmacy professional students. Even though I have not yet developed what I feel will be my most effective teaching practices and style, I feel that I have gained considerable experience and confidence teaching at this level and now know how to prepare my lectures and problem sets. I look forward to being course coordinator for PHCY 52 and enhancing both the continuity in the course and the students' appreciation for it's relevance to drug therapy. Second, I teach in graduate level courses. This provides an opportunity for me to lecture at a more advanced level in a more intimate and interactive setting. It is also an opportunity for the graduate students to get a glimpse of how I think about ongoing science research. Third, I teach and train students in my lab on an individual basis. I realize that each student has a different personality and different strengths and weaknesses. I find that it's most effective to treat them differently, based on their idiosyncracies, which is challenging and satisfying at the same time. I feel that I have much to offer to students in my lab, not only in terms of scientific knowledge, but also in helping them develop an approach to solving problems and doing science in general. I insist that they formally discuss their results with the group in our group meetings. This forces them to think about their results and sharpens their speaking skills.

I believe that effective teaching is inherently difficult, but worthy of much effort. After two-and-a-half years at UNC, I feel that I have become more effective, particularly through improving my lecture preparation and a better knowledge of what is possible to get across to the students.