

Andrew L. Lee, Ph.D.

Professor

Division of Chemical Biology and Medicinal Chemistry

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Joint Professor:

Department of Biochemistry and Biophysics

School of Medicine

EDUCATION

B.A. , Chemistry	Pomona College	1989
Ph.D. , Chemistry	University of California, Berkeley	1996
Postdoctoral Fellow	University of Pennsylvania/SUNY Buffalo	1996-2000

PROFESSIONAL EXPERIENCE

Professor (2013-present)	Division of Chemical Biology and Medicinal Chemistry, UNC Eshelman School of Pharmacy, University of North Carolina at Chapel Hill
Associate Professor ('07-'13)	Division of Chemical Biology and Medicinal Chemistry, Eshelman School of Pharmacy, University of North Carolina at Chapel Hill
Assistant Professor ('01-'07)	Division of Medicinal Chemistry and Natural Products, School of Pharmacy, University of North Carolina at Chapel Hill
Joint Professor (2001-present)	Department of Biochemistry and Biophysics, University of North Carolina at Chapel Hill

RESEARCH INTERESTS

Protein structure, dynamics, and allostery; NMR spectroscopy; NMR spin relaxation; the relation of flexibility in proteins and their structural ensembles to protein and enzyme function; protein-ligand and protein-drug interactions and their relationship with protein dynamics; timescales of motions in proteins; protein biophysics; structure and dynamics of thymidylate synthase; molecular dynamics simulations and protein bioinformatics. PDZ domain function and intramolecular signaling mechanisms as they relate to ligand binding; the relationship between dynamic motions and allosteric communication within protein structures.

TEACHING EXPERIENCE

Pharmacy Bridging Course (PHCY 500), Biochemistry module

2015-present (Fall) Lecturer on protein structure and function, enzyme kinetics.
Course director 2015-2016
PharmD course in UNC Eshelman School of Pharmacy

Biochemistry I (PHCY 421)

2001-2014 (Fall) Lecturer on protein structure and function, enzyme
kinetics, energy metabolism, nitrogen metabolism.
Course director 2003-2014
PharmD course in UNC Eshelman School of Pharmacy.

Concepts of Drug Discovery and Design (MEDC 833)

2001-present (Spring) Lecturer on NMR spectroscopy applications to macromolecules.
Graduate course in School of Pharmacy.

HONORS AND AFFILIATIONS

2016 Faculty of 1000 (F1000.com), Structural Biology (Macromolecule-Ligand Interactions)
2015 Teaching "Worthy of Recognition" Award, Pharmacy Bridging Course (Biochemistry module,
Fall)
2014 Teaching "Worthy of Recognition" Award, Pharmaceutical Biochemistry I (Fall)
2013 Invited speaker, 27th Annual Symposium of the Protein Society (2013). Chaired session on
"Functional Dynamics".
2011 NIH study section (MSFE), ad hoc member.
2010 NIH study section (special emphasis panel for S10 NMR shared instrumentation)
2009 NIH study section (MSFB), ad hoc member
2006 Academic Excellence in Teaching Award (UNC School of Pharmacy)
2006 Junior Faculty IBM Fund Award
2002 Associate Membership for UNC Lineberger Comprehensive Cancer Center (School of
Medicine)
2001 American Association of Colleges of Pharmacy (AACP) New Investigator Program Award
2001 Faculty member of the Molecular and Cellular Biophysics Training Program at UNC Chapel Hill
1997 NIH Individual National Research Service Award: State University of New York at
Buffalo/University of Pennsylvania.

PUBLICATIONS

*corresponding author

1. Sapienza PJ and Lee AL*, Widespread perturbation of function, structure, and dynamics by a conservative single atom substitution in thymidylate synthase, *Biochemistry* (2016), 55, 5702-5713.
2. Falk BT, Sapienza PJ, and Lee AL*, Chemical shift imprint of intersubunit communication in a symmetric homodimer, *Proc. Natl. Acad. Sci. U.S.A.* (2016), 113, 9533-9538. (Commentary in same issue, pp. 9407-9409)

3. Sapienza PJ, Li L, Williams T, Lee AL, and Carter C*, An ancestral tryptophanyl-tRNA synthetase precursor achieves high catalytic rate enhancement without ordered ground-state tertiary structures, *ACS Chem Biol* (2016), 11, 1661-1668.
4. Francis K, Sapienza PJ, Lee AL, and Kohen A*, The effect of the protein mass modulation on human dihydrofolate reductase, *Biochemistry* (2016), 55, 1100-1106.
5. Sapienza PJ, Falk BT, and Lee AL*, Bacterial thymidylate synthase binds two molecules of substrate and cofactor without cooperativity, *JACS* (2015), 137, 14260-14263.
6. Lee AL*, Contrasting roles of dynamics in protein allostery: NMR and structural studies of CheY and the third PDZ domain from PSD-95, *Biophysical Reviews* (2015), 7, 217-226.
7. Sapienza PJ and Lee AL*, Backbone and ILV methyl resonance assignments of E. coli thymidylate synthase bound to cofactor and a nucleotide analog, *Biomolecular NMR Assignments* (2014), 8, 195-199.
8. Petit CM and Lee AL*, Monitoring Side-Chain Dynamics of Proteins Using ^2H Relaxation, *Methods in Molecular Biology* (2014), 1084, 3-27.
9. McDonald LR, Whitley MJ, Boyer JA, and Lee AL*, Colocalization of fast and slow timescale dynamics in the allosteric signaling protein CheY, *J. Mol. Biol.* (2013), 425, 2372-2381.
10. Wang Z, Sapienza PJ, Abeysinghe T, Luzum C, Lee AL, Finer-Moore JS, Stroud RM, Kohen A, Mg^{2+} binds to the surface of thymidylate synthase and affects hydride transfer at the interior active site, *J. Am. Chem. Soc.* (2013), 135, 7583-7592.
11. Zhang J, Lewis SM, Kuhlman B, and Lee AL*, Supertertiary structure of the MAGUK core from PSD-95, *Structure* (2013), 21, 402-413.
12. Lee AL*. Dynamics and allostery (chapter), *Encyclopedia of Biophysics*, Roberts GCK (Ed.), Springer (2013).
13. McDonald LR, Boyer JA, and Lee AL*, Segmental motions, not a two-state concerted switch, underlie allostery in CheY, *Structure* (2012), 20, 1363-1373. **(Selected by Faculty of 1000)**
14. Mauldin RV, Sapienza PJ, Petit CM, and Lee AL*, Structure and dynamics of the G121V dihydrofolate reductase mutant: lessons from a transition-state inhibitor complex, *PLoS ONE* (2012), 7(3), e33252.
15. Carroll MJ, Mauldin RV, Gromova AV, Singleton SF, Collins EJ, and Lee AL*, Evidence for dynamics in proteins as a mechanism for ligand dissociation, *Nat. Chem. Biol.* (2012), 8, 246-252. **(Selected by Faculty of 1000)**
16. Zhang J, Petit CM, King DS, and Lee AL*, Phosphorylation of a PDZ domain extension modulates binding affinity and interdomain interactions in PSD-95, *J. Biol. Chem.* (2011), 286, 41776-41785.
17. Carroll MJ, Gromova AV, Miller KR, Tang H, Wang XS, Tripathy A, Singleton SF, Collins EJ, and Lee AL*, Direct detection of structurally resolved dynamics in a multi-conformation receptor-ligand complex, *J. Am. Chem. Soc.* (2011), 133, 6422-6428. **(Selected by Faculty of 1000)**
18. Whitley MJ and Lee AL*, Exploring the role of structure and dynamics in the function of chymotrypsin inhibitor 2, *PROTEINS: Structure, Function, and Bioinformatics* (2011), 79, 916-24.
19. Sapienza PJ, Mauldin RV, and Lee AL*, Multi-timescale dynamics study of FKBP12 along the rapamycin and mTOR binding coordinate, *J. Mol. Biol.* (2011), 405, 378-394.
20. Zhang J, Sapienza PJ, Ke H, Chang A, Hengel SR, Wang H, Phillips GN, and Lee AL*, Crystallographic and NMR evaluation of the impact of peptide binding to the second PDZ domain of PTP1E. *Biochemistry* (2010), 49, 9280-9291.
21. Sapienza PJ and Lee AL*, Using NMR to study fast dynamics in proteins: methods and applications, *Curr. Op. Pharmacol.* (2010), 10, 723-730.
22. Boyer JA, Clay CJ, Luce KS, Edgell MH, Lee AL*, Detection of native-state non-additivity in double mutant cycles via hydrogen exchange, *J. Am. Chem. Soc.* (2010), 132, 8010-8019.
23. Mauldin RV and Lee AL*, NMR study of the role of M42 in the solution dynamics of *E. coli*

- dihydrofolate reductase. *Biochemistry* (2010), 49, 1606-15.
24. Petit CM, Zhang J, Sapienza PJ, Fuentes EJ, and Lee AL*, Hidden dynamic allostery in a PDZ domain, *Proc. Natl. Acad. Sci. U.S.A.* (2009), 106, 18249-18254.
 25. Law AB, Fuentes EJ, and Lee AL*, Conservation of side-chain dynamics within a protein family, *J. Am. Chem. Soc.* (2009), 131, 6322-23.
 26. Mauldin RV, Carroll MJ, and Lee AL*, Dynamic dysfunction in dihydrofolate reductase results from antifolate drug binding: modulation of dynamics within a structural state, *Structure* (2009), 17, 386-394. **(Selected by Faculty of 1000)**
 27. Whitley MJ* and Lee AL*, Frameworks for understanding long-range intra-protein communication, *Current Protein and Peptide Science* (2009), 10, 116-127.
 28. Whitley MJ, Zhang J, and Lee AL*, Hydrophobic core mutations in CI2 globally perturb fast side-chain dynamics similarly without regard to position, *Biochemistry* (2008), 47, 8566-8576.
 29. Boyer JA and Lee AL*, Monitoring aromatic ps-ns dynamics in proteins via ¹³C relaxation: Expanding perturbation mapping of the rigidifying core mutation, V54A, in eglin c, *Biochemistry* (2008), 47, 4876-4886.
 30. DeRose EF, Clarkson MW, Gilmore SA, Galban CJ, Tripathy A, Havener JM, Mueller GA, Ramsden DA, London RE, and Lee AL*, The solution structure of polymerase μ 's BRCT domain reveals an element essential for its role in nonhomologous end joining, *Biochemistry* (2007), 46, 12100-12110.
 31. Fuentes EJ, Gilmore SA, Mauldin RV, and Lee AL*, Evaluation of energetic and dynamic coupling networks in a PDZ domain protein, *Journal of Molecular Biology* (2006), 364, 337-351.
 32. Clarkson MW, Gilmore SA, Edgell MH, and Lee AL*, Dynamic coupling and allosteric behavior in a non-allosteric protein, *Biochemistry* (2006), 45, 7693-7699. **(Selected by Faculty of 1000)**
 33. Igumenova TI, Lee AL, and Wand AJ, Backbone and side chain dynamics of mutant calmodulin-peptide complexes, *Biochemistry* (2005), 44, 12627-12639. **(Selected by Faculty of 1000)**
 34. Hu H, Hermans J, and Lee AL*, Relating side-chain mobility in proteins to rotameric transitions: Insights from molecular dynamics simulations and NMR, *J. Biomol. NMR* (2005), 32, 151-162.
 35. Partch CL, Clarkson MW, Ozgur S, Lee AL, and Sancar A, Role of structural plasticity in signal transduction of the cryptochrome blue-light photoreceptor, *Biochemistry* (2005) 44, 3795-3805.
 36. Clarkson MW and Lee AL*, Long-range dynamic effects of point mutations propagate through side chains in the serine protease inhibitor eglin c, *Biochemistry* (2004) 43, 12448-12458.
 37. Ohnishi S, Lee AL, Edgell MH, and Shortle D, Direct demonstration of structural similarity between native and denatured eglin c, *Biochemistry* (2004) 43, 4064-4070.
 38. Fuentes EJ, Der CJ, and Lee AL*, Ligand-dependent dynamics and intramolecular signaling in a PDZ Domain, *J. Mol. Biol.* (2004), 335, 1105-1115. **(Selected by Faculty of 1000)**
 39. Hu H, Clarkson MW, Hermans J, and Lee AL*, Increased rigidity of eglin c at acidic pH: Evidence from NMR spin-relaxation and MD simulations, *Biochemistry* (2003), 42, 13856-13868.
 40. Prabhu NV, Lee AL, Wand AJ, and Sharp KA, Dynamics and entropy of a calmodulin-peptide complex studied by NMR and molecular dynamics, *Biochemistry* (2003), 42, 562-570.
 41. Lee AL, Sharp KA, Kranz JK, Song X, and Wand AJ, Temperature dependence of the internal dynamics of a calmodulin-peptide complex, *Biochemistry* (2002), 41, 13814-13825.
 42. Walsh STR, Lee AL, DeGrado WF, and Wand AJ, Backbone and side-chain dynamics of a *de novo* designed three-helix bundle protein studied by ¹⁵N, ¹³C, and ²H NMR relaxation methods, *Biochemistry* (2001), 40, 9560-9569.
 43. Flynn PF, Urbauer RJB, Zhang H, Lee AL, and Wand AJ, Main chain and side chain dynamics of a heme protein: ¹⁵N and ²H NMR relaxation studies of *R. capsulatus* ferrocyclochrome c2, *Biochemistry* (2001), 40, 6559-6569.
 44. Lee AL and Wand AJ, 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.

45. Lee AL and Wand AJ, NMR spectroscopy for monitoring molecular dynamics in solution, *Encyc. Life Sci.* (www.els.net).
46. Lee AL, Kinnear SA, and Wand AJ, Redistribution and loss of side-chain entropy upon formation of a calmodulin-peptide complex, *Nat. Struct. Biol.* (2000) 7, 72-77.
47. Volkman BF, Wilkens SJ, Lee AL, Xia B, Westler WW, Beger R, and Markley JL, 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.
48. Lee AL, Flynn PF, and Wand AJ, Comparison of ^2H and ^{13}C relaxation techniques for the study of protein methyl group dynamics in solution, *J. Am. Chem. Soc.* (1999) 121, 2891-2902.
49. Lee AL and Wand AJ, Assessing potential bias in the determination of rotational correlation times of proteins by NMR relaxation, *J. Biomol. NMR* (1999) 13, 101-112.
50. Lee AL, Urbauer JL, and Wand, AJ, Improved labeling strategy for ^{13}C relaxation measurements of methyl groups in proteins, *J. Biomol. NMR* (1997) 9, 437-440.
51. Lee AL, Volkman BF, Robertson SA, Rudner DZ, Barbash DA, Cline TW, Kanaar R, Rio DC, and Wemmer DE, Chemical shift mapping of the RNA-binding interface of the multiple-RBD protein sex-lethal, *Biochemistry* (1997) 36, 14306-14317.
52. Kanaar R, Lee AL, Rudner DZ, Wemmer DE, and Rio DC, Interaction of the sex-lethal RNA binding domains with RNA, *EMBO J.* (1995) 14, 4530-4539.
53. Lee AL, Kanaar R, Rio DC, and Wemmer DE, 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.
54. Oliphant N, Lee A, and Bernath PF, Fourier transform emission spectroscopy of the jet-cooled CCN free radical, *J. Chem. Phys.* (1990) 92, 2244-2247.