

Paul J. Sapienza, Ph.D.

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University of North Carolina at Chapel Hill
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EDUCATION

Ph.D., Molecular Biology	University of Pittsburgh	2005
B.S., Biology	James Madison University	1998

PROFESSIONAL EXPERIENCE

Research Assistant Professor	University of North Carolina at Chapel Hill Division of Chemical Biology and Natural Products Eshelman School of Pharmacy Appointment: 2011-present
Postdoctoral Fellow	University of North Carolina at Chapel Hill 2006-2011
Postdoctoral Fellow	University of Pittsburgh 2005

RESEARCH INTERESTS

Protein structure; thermodynamics of macromolecular binding processes; enzyme catalysis; protein dynamics; NMR spectroscopy; allostery.

TEACHING EXPERIENCE

Lecturer for Computational Biology (Biosci1540; *upper level undergraduate course*). Topics included introductions to experimental macromolecular structure determination and using Visual Molecular Dynamics (VMD) software. (2002-2005)

Teaching assistant for Biophysical Chemistry recitation and laboratory (Biosci 1470; *upper level undergraduate course*). Topics included x-ray crystallography, measurement of protein stability, and thermodynamics of protein ligand interactions using isothermal titration calorimetry. (2002)

Teaching assistant for Macromolecular Structure and Function recitation (Biosci 1819; *upper level undergraduate course*). Topics included rudiments of protein and DNA structure, thermodynamics of protein folding and protein-DNA interactions. (1999&2000)

HONORS AND AWARDS

Innovator, Eshelman Institute of Innovation (2019)
Faculty of 1000 (F1000.com), Structural Biology (Macromolecule-Ligand Interactions) (2016)
University of Pittsburgh Nominee for Microfilms International Dissertation Award (2005)
Andrew Mellon Predoctoral Research Fellowship (2002)
Stanton C. Crawford Award for excellence in teaching (2000)

INVITED PRESENTATIONS

1. Carolina NMR Symposium (Kannapolis, NC), "Functional Dynamics in Thymidylate Synthase", November 6, 2014.
2. Gibbs Conference on Biological Thermodynamics (Carbondale, IL), "Inter-Active Site Communication Mediated by the Dimer Interface Beta-Sheet in the Half-the-Sites Enzyme, Thymidylate Synthase", September 25, 2017.

PUBLICATIONS

1. **Sapienza PJ***, Currie MM, Lancaster NM, Li K, Aubé J, Goldfarb D, Cloer EW, Major MB, Lee AL. Visualizing an Allosteric Intermediate Using CuAAC Stabilization of an NMR Mixed Labeled Dimer. *ACS Chem Biol*. 2021 Dec 17;16(12):2766-2775.
2. **Sapienza, PJ***, Popov, KI, Mowrey, DD, Falk, BT, Dokholyan, NV, Lee, AL, Inter-Active Site Communication Mediated by the Dimer Interface Beta-Sheet in the Half-the-Sites Enzyme, Thymidylate Synthase. *Biochemistry*. 2019 Jul 30;58(30):3302-3313.
3. Bonin JP, **Sapienza PJ**, Wilkerson E, Goldfarb D, Wang L, Herring L, Chen X, Major MB, Lee AL. Positive Cooperativity in Substrate Binding by Human Thymidylate Synthase. *Biophys J*. 2019 Sep 17;117(6):1074-1084.
4. Ranasinghe C, Pagano P, **Sapienza PJ**, Lee AL, Kohen A, Cheatum CM. Isotopic Labeling of Formate Dehydrogenase Perturbs the Protein Dynamics. *J Phys Chem B*. 2019 Dec 12;123(49):10403-10409.
5. Lee AL, **Sapienza PJ**. Thermodynamic and NMR Assessment of Ligand Cooperativity and Intersubunit Communication in Symmetric Dimers: Application to Thymidylate Synthase. *Front Mol Biosci*. 2018 May 25;5:47.
6. Ranasinghe C, Guo Q, **Sapienza PJ**, Lee AL, Quinn DM, Cheatum CM, Kohen A. Protein Mass Effects on Formate Dehydrogenase. *Journal of the American Chemical Society*. 2017; 139(48):17405-17413.

7. Law AB, **Sapienza PJ**, Zhang J, Zuo X, Petit CM. Native State Volume Fluctuations in Proteins as a Mechanism for Dynamic Allostery. *J Am Chem Soc.* 2017, Jan 17. doi: 10.1021/jacs.6b12058.
8. **Sapienza PJ**, Lee AL. Widespread Perturbation of Function, Structure, and Dynamics by a Conservative Single-Atom Substitution in Thymidylate Synthase. *Biochemistry.* 2016, 55, 5702-5713.
9. Falk BT, **Sapienza PJ**, Lee AL. Chemical shift imprint of intersubunit communication in a symmetric homodimer. *Proc Natl Acad Sci U S A.* 2016, 113:9533-8.
10. **Sapienza PJ**, Li L, Williams T, Lee AL, Carter CW Jr. An Ancestral Tryptophanyl-tRNA Synthetase Precursor Achieves High Catalytic Rate Enhancement without Ordered Ground-State Tertiary Structures. *ACS Chem Biol.* 2016, 11, 1661-8.
11. Francis, F, **Sapienza, PJ**, Lee, AL, Kohen, A. The Effect of the Protein Mass Modulation on Human Dihydrofolate Reductase. *Biochemistry*, 2016, 55, 1100-1106.
12. **Sapienza, PJ**[§], Falk, BT[§], Lee, AL. Bacterial Thymidylate Synthase Binds Two Molecules of Substrate and Cofactor Without Cooperativity. *Journal of the American Chemical Society*, 2015, 137, 14260-14263.
13. **Sapienza, PJ**, Niu, T., Kurpiewski, MR., Grigorescu, A. & Jen-Jacobson, L. Thermodynamic and Structural Basis for Relaxation of Specificity in Protein-DNA Recognition. *J Mol Biol.* (2014), 426, 84-104.
14. **Sapienza, PJ** & Lee, AL. Backbone and ILV methyl resonance assignments of E. coli thymidylate synthase bound to cofactor and a nucleotide analogue. *Biomolecular NMR Assignments*, (2013) doi:10.1007/s12104-013-9482-6.
15. Wang, Z. **Sapienza PJ**, Abeysinghe T, Luzum C, Lee AL, Finer-Moore JS, Stroud RM, Kohen A. Mg²⁺ binds to the surface of thymidylate synthase and affects hydride transfer at the interior active site. *Journal of the American Chemical Society*, 2013, 135, 7583-7592.
16. 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.
17. **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.
18. **Sapienza PJ** and Lee AL. Using NMR to study fast dynamics in proteins: methods and applications, *Curr. Op. Pharmacol.* (2010), 10, 723-730.
19. 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.

20. 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.
21. Stone KM, Townsend JE, Sarver J, **Sapienza PJ**, Saxena S, Jen-Jacobson L. Electron spin resonance shows common structural features for different classes of EcoRI-DNA complexes. *Angew Chem Int Ed Engl.* (2008), 47, 10192-10194.
22. **Sapienza PJ**, Rosenberg, JM, Linda Jen-Jacobson. Structural and thermodynamic basis for enhanced DNA binding by a promiscuous mutant EcoRI endonuclease. *Structure.* (2007), 15, 1368-1382.
23. **Sapienza PJ**, Dela Torre CA, McCoy WH IV, Jana SV, Jen-Jacobson L. Thermodynamic and kinetic basis for the relaxed DNA sequence specificity of "promiscuous" mutant EcoRI endonucleases. *J Mol Biol.* (2005), 348, 307-324.
24. Engler LE, **Sapienza PJ**, Dorner LF, Kucera R, Schildkraut I, Jen-Jacobson L. The energetics of the interaction of BamHI endonuclease with its recognition site GGATCC. *J Mol Biol.* (2001), 307, 619-636.

* Corresponding author

§ Authors contributed equally.