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Brief Summary

My laboratory focuses on the biophysical determinants of age-related disorders using a combination of molecular modeling and single-molecule fluorescence. These tools provide a nanoscale lens to study amyloid diseases such as Alzheimer's Disease or Type 2 Diabetes, where promiscuous protein oligomers induce widespread cell death and inflammation. Our use of single-molecule and solution biophysical tools have also enabled us to structurally and functionally compare patient-derived oligomers to lab-derived constructs, which substantively differ from one another. By harnessing the strengths of protein folding simulations (e.g. enhanced-sampling MD) and single-molecule experiments (e.g. FCS or smFRET), we seek to deduce the pathogenic roles of soluble protein oligomers and their contributions to human disease and aging.

Education

PhD Physics, University of Southern California	2013
MS Computer Science, University of Southern California	2012
MA Physics, University of Southern California	2008
BS Physics, San Francisco State University	2006

Experience

Assistant Professor	2019–present
Departments of Pathology and Molecular Biophysics & Biochemistry, Yale School of Medicine	
Associate Research Scientist	2017–2019
Department of Pathology, Yale School of Medicine	
Postdoctoral Researcher	2013–2017
Departments of Physics, Chemistry & Biochemistry, and Materials, UC Santa Barbara	
Graduate/Teaching Assistant	2008–2013
Department of Physics, Information Sciences Institute, USC	
Undergraduate Research Assistant	2003–2006
Department of Physics, San Francisco State University	

Active Federal Funding

1K01AG062752-01 (PI: ZA Levine) 09/01/20–08/31/25
NIH/NIA
Repurposing Prion Proteins as Translational Amyloid-Targeting Therapeutics for Alzheimer's Disease
Role: PD/PI

1R01AG068285-01 (MPIs: ZA Levine, ME Levine) 07/01/20-06/30/25
NIH/NIA
Amyloidogenic Induction of Cellular Senescence in Alzheimer's Disease
Role: PD/PI

1R01AG057912-04 (PI: ME Levine) 09/30/17–05/31/22
NIH/NIA
Molecular Networks Underlying Resilience to Alzheimer's disease among ApoE E4 Carriers
Role: Co-I

Peer-Reviewed Publications (32)

1. Gomes G-N, **Levine ZA**. 2021. Defining the Neuropathological Aggresome Across In-Silico, In-Vitro, and In-Vivo Experiments. Journal of Physical Chemistry B. 125(8), 1974-1996. DOI: 10.1021/acs.jpcb.0c09193 **(Journal Cover)**
2. Gray A, Antevska A, Link, B, Bogin B, Burke S, Dupuy S, Collier JJ, **Levine ZA**, Karlstad M, Do T. 2021. α-CGRP Disrupts Amylin Fibrillization and Regulates Insulin Secretion: Implications on Diabetes and Migraine. Chemical Science. *In Press.* DOI: 10.1039/D1SC01167G
3. Mei Z, Treado JD, Regan L, **Levine ZA**, and O'Hern CS. 2021. Understanding the Native Fluctuations of Protein Cores. Physical Review E. *In Press.*
4. Miazek A, Zalas M, Konstanciuk J, Bogin BA, Grzymajło K, Goszczynski T, **Levine ZA**, Morrow JS, Stankewich MC. 2021. Age-Dependent Ataxia and Neurodegeneration Caused by an αII Spectrin Mutation with Enhanced Calpain Sensitivity. Scientific Reports. 11(1), 1-18. DOI: 10.1038/s41598-021-86470-1
5. Grigas AT, Mei Z, Treado JD, **Levine ZA**, Regan L, O'Hern CS. 2020. Using Physical Features of Protein Core Packing to Distinguish Real Proteins from Decoys. Protein Science. 29. 1931-1944. DOI: 10.1002/pro.3914
6. Mei Z, Treado JD, Grigas A, **Levine ZA**, Regan L, and O'Hern CS. 2020. Analyses of Protein Cores Reveal Fundamental Differences Between Solution and Crystal Structures. Proteins. 1-8. DOI: 10.1002/prot.25884
7. **Levine ZA**, Okada A, Taranishi K, Langen R, Shea JE. 2019. The Mitochondrial Peptide Humanin Targets but Does Not Denature Amyloid Oligomers in Type II Diabetes. Journal of the American Chemical Society. 141 (36), 14168- 14179. DOI: 10.1021/jacs.9b04995. **(Journal Cover)**
8. Wójcik S, Birol M, Rhoades E, Miranker AD, **Levine ZA**. 2018. Targeting the Intrinsically Disordered Proteome using Small Molecule Ligands. Methods in Enzymology. 611, 703-734. DOI: 10.1016/bs.mie.2018.09.036
9. Oi C, Treado JD, **Levine ZA**, Lim CS, Knecht KM, Xiong Y, O'Hern CS, Regan L. 2018. A threonine zipper that mediates protein-protein interactions: Structure and prediction. Protein Science. 27 (11), 1969-1977. DOI: 10.1002/pro.3505.
10. Seo S, Lee DW, Ahn JS, Cunha K, Filippidi E, Ju SW, Shin E, Kim BS, **Levine ZA**, Lins RD, Israelachvili JN, Waite JH, Valentine MT, Shea JE, Ahn BK. 2017. Significant Performance Enhancement of Polymer Resins by Bioinspired Dynamic Bonding. Advanced Materials. 1703026, 1-9. DOI: 10.1002/adma.201703026
11. Sözer EB, **Levine ZA**, and Vernier PT. 2017. Quantitative Limits on Small Molecule Transport via the Electropermeome — Measuring and Modeling Single Nanosecond Perturbations. Scientific Reports. 7 (57), 1-13. DOI:10.1038/s41598-017-00092-0
12. **Levine ZA**, Shea JE. 2017. Simulations of Disordered Proteins and Systems with Conformational Heterogeneity. Current Opinion in Structural Biology. 43, 95-103. DOI: 10.1016/j.sbi.2016.11.006
13. Das S, Lee BH, Linstadt RTH, Cunha K, Li Y, **Levine ZA**, Lipshutz BH, Lins RD, Shea JE, Israelachvili JN, Heeger AJ, and Ahn BK. 2016. Molecularly Smooth Self-Assembled Monolayer for High-Mobility Organic Field-Effect Transistors. Nano Letters. 16 (10), 6709–6715. DOI: 10.1021/acs.nanolett.6b03860
14. **Levine ZA**, Rapp MV, Wei W, Mullen RG, Wu C, Zerze GH, Mittal J, Israelachvili JN, Waite JH, Shea JE. 2016. Surface Force Measurements and Simulations of Mussel-Derived Peptide Adhesives on Wet Organic Surfaces. Proceedings of the National Academy of Sciences of the United States of America. 113 (16), 4332-4337. DOI: 10.1073/pnas.1603065113
15. **Levine ZA**, DeNardis NI, Vernier PT. 2016. Molecular Dynamics Interactions of Phospholipids and Hydrocarbons Between Silicon Electrodes. Langmuir. 32 (11), 2808-2819. DOI: 10.1021/acs.langmuir.5b04090
16. Vernier PT, **Levine ZA**. 2016. Biological Responses. Bioelectrics. Edited by Akiyama H and Heller R. ISBN: 978-4-431-56095-1. Springer. DOI: 10.1007/978-4-431-56095-1.
17. **Levine ZA**, Larini L, LaPointe NE, Feinstein SC, Shea JE. 2015. Regulation and Aggregation of Intrinsically Disordered Peptides. Proceedings of the National Academy of Sciences of the United States of America. 112 (9), 2758-2763. DOI: 10.1073/pnas.1418155112

18. Zerze GH, Mullen RG, **Levine ZA**, Shea JE, Mittal J. 2015. To what extent does surface hydrophobicity dictate peptide folding and stability near surfaces? Langmuir. 31 (44), 12223-12230. DOI: 10.1021/acs.langmuir.5b03814 (***GHZ, RGM, and ZAL share first authorship***)
19. **Levine ZA**, Fischer SA, Shea JE, and Pfaendtner J. 2015. Trp-Cage Folding on Organic Surfaces. The Journal of Physical Chemistry B. 119 (33), 10417-10425. DOI: 10.1021/acs.jpcb.5b04213
20. Shea JE, **Levine ZA**. 2015. Studying the Early Stages of Protein Aggregation Using Replica Exchange Molecular Dynamics Simulations. Protein Amyloid Aggregation: Methods and Protocols (Methods in Molecular Biology). Edited by David Eliezer. ISBN: 978-1493929771. Humana Press
21. Vernier PT, **Levine ZA**, Ho MC, Xiao S, Semenov I, Pakhomov A. 2015. Picosecond and Terahertz Perturbation of Interfacial Water and Electropermeabilization of Biological Membranes. Journal of Membrane Biology. 1-11. DOI: 10.1007/s00232-015-9788-7
22. Kohler S, **Levine ZA**, García-Fernández MA, Ho MC, Vernier PT, Leveque P, Arnaud-Cormos D. 2015. Electrical analysis of cell membrane poration by an intense nanosecond pulsed electric field, using an atomistic-to-continuum method. Transactions on Microwave Theory and Techniques (IEEE), 63 (6), 2032,2040 DOI: 10.1109/TMTT.2015.2418764
23. **Levine ZA**, Venable RM, Watson MC, Lerner MG, Shea JE, Pastor RW, Brown FLH. 2014. Determination of Biomembrane Bending Moduli in Fully Atomistic Simulations. Journal of the American Chemical Society, 136 (39), 13582-13585. DOI: 10.1021/Ja507910r
24. Ho MC, Casciola M, **Levine ZA**, Vernier PT. 2013. Molecular Dynamics Simulations of Ion Conductance in Field-Stabilized Nanoscale Lipid Electropores. Journal of Physical Chemistry B, 117 (39), 11633-11640. DOI: 10.1021/jp401722g
25. Romeo S, Wu YH, **Levine ZA**, Gundersen MA, Vernier PT. 2013. Water influx and cell swelling after nanosecond electropermeabilization. Biochim. Biophys. Acta, 1828(8), 1715-1722. DOI: 10.1016/j.bbamem.2013.03.007
26. Ho MC, **Levine ZA**, Vernier PT. 2013. Nanoscale, Electric Field-Driven Water Bridges in Vacuum Gaps and Lipid Bilayers. Journal of Membrane Biology, 246(11), 793-801. DOI: 10.1007/s00232-013-9549-4
27. Tokman M, Lee JH, **Levine ZA**, Ho MC, Colvin ME, Vernier PT. 2013. Electric Field-Driven Water Dipoles: Nanoscale Architecture of Electroporation. PLoS ONE, 8:e61111. DOI: 10.1371/journal.pone.0061111
28. Vernier PT, **Levine ZA**, Gundersen MA. 2012. Water Bridges in Electropermeabilized Phospholipid Bilayers. Proc. of the IEEE. 101, 494-504. DOI: 10.1109/JPROC.2012.2222011
29. **Levine ZA**, Vernier PT. 2012. Calcium and Phosphatidylserine Inhibit Lipid Electropore Formation and Reduce Pore Lifetime. Journal of Membrane Biology. 245, 599-610. DOI: 10.1007/s00232-012-9471-1
30. Knecht V, **Levine ZA**, Vernier PT. 2010. Electrophoresis of neutral oil in water. Journal of Colloid and Interface Science. 352(2), 223-231. DOI: 10.1016/j.jcis.2010.07.002 **(Journal Cover)**
31. **Levine ZA**, Vernier PT. 2010. Life Cycle of an Electropore: Field-Dependent and Field-Independent Steps in Pore Creation and Annihilation. Journal of Membrane Biology. 236(1), 27-36. DOI: 10.1007/s00232-010-9277-y
32. Vernier PT, **Levine ZA**, Wu YH, Joubert V, Ziegler MJ, Mir LM, Tieleman DP. 2009. Electroporating Fields Target Oxidatively Damaged Areas in the Cell Membrane. PLoS ONE, 4(11), e7966. DOI: 10.1371/journal.pone.0007966

Conference Proceedings and Book Chapters (3)

1. **Levine ZA**. 2017. Lipid Electropore Lifetime in Molecular Models. Handbook of Electroporation. Edited by D. Miklavcic. ISBN 978-3-319-32887-4. Springer. DOI 10.1007/978-3-319-32886-7_86.
2. **Levine ZA**. 2017. Effects of Heterogeneous Membranes and Electrolytes on Electropore Formation. Handbook of Electroporation. Edited by D. Miklavcic. ISBN 978-3-319-32887-4. Springer. DOI 10.1007/978-3-319-32886-7_87.
3. Kohler S., Ho M, **Levine ZA**, Vernier PT, Leveque P, Arnaud-Cormos D, Electrical analysis of cell membrane poration induced by an intense nanosecond pulsed electric field, using an atomistic-to-continuum method. IEEE Microwave Symposium 2014.

Awards & Professional Service

Council Member, IDP Subgroup, Biophysical Society	2021-2024
Information Technology Advisory Committee, Yale University	2020-2021
Yale Pepper Center Career Development Award – REC Fellow	2020-2022
Program Co-Chair, IDP Subgroup, Biophysical Society	2019-2020
Fellow, Branford College, Yale University	Lifetime
XSEDE/NSF Supercomputing Allocation (TG-MCB170142/MCB140122)	2018, 2014
Dow Materials institute and Materials Research Laboratory Fellowship	2015, 2016
Biophysical Society Education Travel Award	2014
Don Eden Award	2005
College of Science & Engineering Student Advisory Board	2005
Golden Key Honor Society	2004

Teaching and Outreach

1.	MBB 275a: Biology at the Molecular Level (Yale)	2021
2.	MBB 302: Principles of Biophysics (Yale)	2021
3.	MBB 364/564a: Light Microscopy (Yale)	2021
4.	C&MP 650/MB&B 676b: Responsible Conduct of Research	2021
5.	MBB 517: Methods and Logic (Yale)	2018, 2019, 2020, 2021
6.	Biophysics instructor at the Telluride School on Theoretical Chemistry	2015
7.	Science instructor for UCSB CNSI Family Ultimate Science Exploration	2015
8.	Outreach volunteer for the MRL Science Teacher Workshop	2014
9.	Education outreach volunteer for the UCSB MRL: Ellwood elementary school	2014
10.	Outreach scientist and speaker for the Santa Barbara Museum of Natural History	2014

Mentoring

During my time at Yale I have mentored 1 postdoc (Gregory-Neal Gomes), 3 permanent graduate students (Bryan Bogin, Matthew Steinsaltz, and Kamila Nurmakova), and 4 undergraduates (Rafi Brent, Scott Taber, Ziyu (Julia) Ding, and Guna Mandava). I have also mentored 9 rotating and temporary students (Raquel Reilly, Zion Perry, Jake Ribich, Liz Li, Joao Victor Gomes, Andy Rodriguez, Paulina Komorek, Jorge Urbina – REU, and Gabrianne Ivey - REU).

Journal Service

1. Reviewer – Science Magazine
2. Reviewer – Biophysical Journal
3. Reviewer – Journal of Physical Chemistry (B/Letters)
4. Reviewer – Soft Matter
5. Reviewer – Journal of Membrane Biology
6. Reviewer – Journal of Colloids and Interface Science
7. Reviewer – Bioelectromagnetics Journal
8. Reviewer – Molecular BioSystems

Invited Talks:

1. **Levine ZA**. 2020. Disordered Protein Aggregates in Human Disease & Aging. MB&B Colloquium. Yale University. New Haven, CT.
2. **Levine ZA**. 2020. Disordered Protein Folding and Solubility as a Determinant of Human Disease. American Physical Society March Meeting. Denver, CO.
3. **Levine ZA**. 2020. Disordered Protein Folding and Solubility as a Determinant of Human Disease. PEB Monthly Seminar. Yale University. New Haven, CT.
4. **Levine ZA**. 2019. Targeting Amyloid Solubility as a Novel Pharmacophore in Cancer and Alzheimer's Disease. Yale Institute for Nanoscience and Quantum Engineering (YINQE) Seminar. Yale University. New Haven, CT, USA.

5. **Levine ZA**. 2019. Disordered Protein Folding and the Thermodynamic Determinants of Amyloid Behaviors. University of Southern California Physics Seminar. Los Angeles, CA.
6. **Levine ZA**. 2018. Intrinsically Disordered Protein Folding and the Thermodynamics of Amyloid Diseases. Physical Engineering Biology (PEB) Seminar. Yale University. New Haven, CT, USA.
7. **Levine ZA**. 2017. Disordered Protein Folding, Aggregation, and Adhesion in Human Disease and Next-Generation Biomaterials. Systems Biology Institute (SBI) Seminar. Yale West Campus. New Haven, CT, USA.
8. **Levine ZA.** 2016. Developing Biologically-Inspired Materials using Atomistic Simulations. UCSF. Department of Preventative and Restorative Dental Sciences Seminar. San Francisco, CA, USA.
9. **Levine ZA**, Okada A, Teranishi K, Langen R, Shea JE. 2016. Reducing IAPP Aggregation with Mitochondrial Humanin Peptides; Results from Simulations and Experiments. Biophysical Society Annual Meeting. Los Angeles, CA, USA.
10. **Levine ZA**, Mullen RG, Shea JE. 2015. Protein folding and assembly on membrane-mimics in constant volume replica-exchange simulations. Invited Speaker for the "Role of Membranes in Amyloid-formation and the Pathogenicity of Amyloid Diseases" platform. American Chemical Society National Meeting. Denver, CO, USA.
11. **Levine ZA**, Larini L, LaPointe N, Feinstein S, Shea JE. 2014. Tau(273-284): A Molecular Dynamics Study of Intrinsically Disordered Protein Conformations in the Presence Of Osmolytes. Biophysical Society Annual Meeting. San Francisco, CA, USA.
12. **Levine ZA**. 2014. The Molecular Symphony of Life. Santa Barbara Museum of Natural History. Santa Barbara, CA, USA.
13. **Levine ZA**, DeNardis NI, Vernier PT. 2013. Molecular Dynamics Interactions of Phospholipids and Hydrocarbons Between Silicon Electrodes. Biophysical Society Annual Meeting. Philadelphia, PA, USA.
14. **Levine ZA**, Vernier PT. 2012. Electropore Dynamics in Time-Dependent Electric Fields. Biophysical Society Annual Meeting. San Diego, CA, USA.
15. **Levine ZA**, Vernier PT. 2011. Temperature Modulation of Phospholipid Bilayer Electropore Creation and Annihilation. Biophysical Society Annual Meeting. Baltimore, MD, USA.
16. **Levine ZA**, Ziegler MJ, Vernier PT. 2010. Life Cycle of an Electropore: A Molecular Dynamics Investigation of the Electroporation of Heterogeneous Lipid Bilayers (PC:PS) In the Presence of Calcium Ions. Biophysical Society Annual Meeting. San Francisco, CA, USA.
17. **Levine ZA**, Vernier PT. 2010. Electropore Life Cycles in Heterogeneous Phospholipid Bilayers in the Presence of Calcium. Bioelectromagnetics Society Annual Meeting. Seoul, Republic of Korea.
18. **Levine ZA**, Vernier PT. Gordon Conference on Bioelectrochemistry. 2010. Lipid Bilayer Electropore Modulation using Calcium, Phosphatidylserine, and Temperature. Biddeford, ME, USA.
19. **Levine ZA**, Wu YH, Ziegler MJ, Tieleman DP, Vernier PT. 2009. Electroporation Sensitivity of Oxidized Phospholipid Bilayers. Biophysical Society Annual Meeting. Boston, MA, USA.
20. **Levine ZA**, Vernier PT. 2009. Increased Susceptibility of Oxidized Phospholipid Bilayers to Electropermeabilization. University of California System-wide Bioengineering Symposium. University of California, Merced, USA.
21. **Levine ZA**, Vernier PT. 2009. Electropermeabilization of Mixed Lipid Bilayers (PC:PS) in the Presence of Calcium. Biomedical Engineering Society Annual Meeting. Pittsburgh, PA, USA.
22. **Levine ZA**, Vernier PT. 2009. Electropermeabilization of Mixed Lipid Bilayers (PC:PS) in the Presence of Calcium. Electroporation-based Technologies and Treatments Workshop. University of Ljubljana, Ljubljana, Slovenia.

Contributed Talks

1. Bogin BA, **Levine ZA**. 2021. Characterizing Structural and Dynamic Features of Soluble IAPP Oligomers. Biophysical Society Annual Meeting. Virtual.
2. Gomes, G-N, **Levine ZA**. 2021. Single-Molecule Characterization of Heterogeneous Soluble Protein Oligomers. Biophysical Society Annual Meeting. Virtual.
3. Treado JD, Mei Z, Grigas AT, **Levine ZA**, Regan L, O'Hern CS. 2020. The Key Differences in Protein X-Ray Crystal and Solution NMR Structures. American Physical Society March Meeting. Denver, CO.
4. Grigas AT, Mei Z, Treado JD, **Levine ZA**, Regan L, O'Hern CS. 2020. Decoy Detection of Computational Protein Designs. American Physical Society March Meeting. Denver, CO.

5. Mei Z, Treado J, Regan LJ, **Levine ZA**, O'Hern CS. 2020. Understanding the Native Fluctuations of Protein Cores. Biophysical Society Annual Meeting. San Diego, CA.
6. Mei Z, Treado J, **Levine ZA**, O'Hern CS, Regan L. 2019. Computational Protein Redesign and Decoy Discrimination. American Physical Society March Meeting. Boston, MA.
7. Tokman M, Lee JH, **Levine ZA**, Ho MC, Colvin ME, Vernier PT. 2014. Electric Field-Driven Water Dipoles: Nanoscale Architecture of Electroporation. Biophysical Society Annual Meeting. San Francisco, CA.
8. Vernier PT, Kohler S, Ho MC, **Levine ZA**, Leveque P, Arnaud-Cormos D. 2013. Toward the physical mechanisms of nanopulse-induced pore formation combining Molecular Dynamics and a 3D electromagnetic tool. Bioelectromagnetics Society Annual Meeting (BioEM). Thessaloniki, Greece.
9. Vernier PT, **Levine ZA**, and Wu YH. 2011. Nanoelectropores in cell membranes and simulated phospholipid bilayers. 21st International Symposium on Bioelectrochemistry and Bioenergetics of the Bioelectrochemical Society. Kraków, Poland.
10. Romeo S, Wu YS, **Levine ZA**, and Vernier PT. 2011. Water influx after nanoelectropermeabilization. International Bioelectrics Symposium. Toulouse, France.
11. JH Lee, **ZA Levine**, PT Vernier, M Tokman, M Colvin. 2010. Electric Field Effects on Water and Water-Vacuum Interfaces in Molecular Dynamics Simulations. Biophysical Society Annual Meeting. San Francisco, CA, USA.
12. Vernier PT, **Levine ZA**, Wu YH, Joubert V, Ziegler MJ, Mir L, and Tieleman DP. 2009. Increased susceptibility of oxidized phospholipid bilayers to electropermeabilization. 20th International Symposium on Bioelectrochemistry and Bioenergetics. Sibiu, Romania

Technical and Computational Skills

Bash/Linux, C, C++, Perl, Python, Java, Fortran, MPI, OpenMP, pThreads, CUDA, Matlab, R, GROMACS, CHARMM, AMBER, NAMD, LAMMPS, COMSOL, SQL, HTML, CSS, XML, Oracle RDBMS. Scientific visualization and image processing using VMD, VisIt, and OpenGL. Experience with UTMOST and BSIM for SPICE modeling.