

## Dr. Alan Grossfield

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### Research Interests

- Structure and dynamics of membranes and membrane proteins
- Molecular simulation and statistical mechanics of biological systems
- Physical origins of allosteric regulation of GPCRs
- Mechanisms of antimicrobial lipopeptides and biosurfactants
- Thermodynamics and kinetic properties of  $\alpha$ -synuclein fibrils

### Education and Professional Experience

- Associate Professor, Department of Biochemistry and Biophysics  
University of Rochester Medical Center  
March 2014 – present
- Assistant Professor, Department of Biochemistry and Biophysics  
University of Rochester Medical Center  
October 2007 – March 2014
- Research Staff Member, IBM T. J. Watson Research Center  
Biomolecular Dynamics and Scalable Modeling, Blue Gene Project  
Group Leader: Dr. Michael Pitman  
September 2004 – September 2007  
Molecular dynamics simulations of rhodopsin
- Post-doctoral fellow, Washington University Medical School  
Department of Biochemistry  
Adviser: Dr. Jay Ponder  
May 2000 – August 2004  
Ion solvation thermodynamics, polarizable force field thermodynamics
- Graduate Student, Johns Hopkins Medical School  
Department of Biophysics and Biophysical Chemistry  
Adviser: Dr. Thomas Woolf  
August 1994 – May 2000  
Thesis title: Computer simulation of membrane-protein interactions
- Undergraduate Student, Cornell University  
Physics major, concentration in Biology  
September 1990 – May 1994

### Funding

- NSF MCB-1817862 (sub-contract) Light-Induced Protein Quake of Visual Rhodopsin Investigated by Femtosecond Time-Resolved X-Ray Scattering, 2018–2021

- DOE DE-SC0000235212 (sub-contract), Photosynthesis Protein Collective Vibrations Role in Energy Transfer and Dissipation, 2018–2021
- DOE DE-SC0016317 (sub-contract), “Photosynthesis Protein Collective Vibrations Role in Energy Transfer and Dissipation”, 2016-2017
- NIH GM068411 (administrative supplement to training grant), 2016-2017
- NIH GM095496 (PI), “Multiscale modeling of GPCRs”, 2011-2016
- NIH National Research Service Award (1 F32 NS42975) 2001 – 2004

## Publicly Distributed Software

- LOOS, a C++ library for rapidly implementing new molecular simulation analysis techniques, <https://github.com/GrossfieldLab/loos>
- WHAM, a commonly used implementation of the weighted histogram analysis method for analyzing umbrella sampling free energy calculations, <http://membrane.urmc.rochester.edu/content/wham>
- Contributed to OpenMM: support for SMOG structure-based potentials
- Contributed to WESTPA: support for tcsh
- Contributed to TINKER: Nose-Hoover thermostat, potential smoothing, constant pressure, replica exchange, and principal component analysis

## Service

- Grant reviewing
  - NSF MCB Biophysics (2019)
  - NIH ad-hoc for BBM (2018, 2019)
  - Referee for ANTON grants (2018)
  - NIH study section special interest groups, 2014 (BMCB), 2015 (BPNS)
  - NSF ad-hoc reviewer (2017)
  - DOE ad-hoc reviewer (2017)
- Journal editing and reviewing
  - Editor, Biophysical Journal (starting 1/2018)
  - Editor, Chemistry and Physics of Lipids (2017 - )
  - Referee for Proteins, Biophysical Journal, BBA Biomembranes, Structure, J. Phys. Chem. B, J. of Mol. Biol., J. Mol. Graphics Model., J. Comput. Chem., J. Chem. Phys., Biochemistry, J. Mem. Biol., PLOS, J. Amer. Chem. Soc., J. Med. Chem., PNAS, Nature Chemistry, J. Chem. Theor. Comput. (15-20 papers/year)
- University of Rochester
  - University of Rochester Computational Research Committee, 2009-
  - University of Rochester Medical Center Faculty Council, 2009-2017
  - Education Director, Program in Biophysics, Structural and Computational Biology, 2011-2012
  - Recruiting and Admissions Director, Program in Biophysics, Structural and Computational Biology, 2012-
  - Dean’s Committee on Graduate Admissions, 2012
  - Steering Committee for Ethics Training, 2011-
  - 2 ad-hoc promotion committees

## Teaching

- IND408 (Advanced Biochemistry): protein folding, molecular modeling, 4 lectures/year
- IND501 (Ethical Conduct in Research): small-group discussion leader, 7 meetings/year
- IND509 (Molecular Biophysics): statistical mechanics, molecular modeling, 12-16 lectures/2 years
- IND411 (Structural Biophysics): solid-state NMR, 1 lecture/2 years
- BCH412 (Topics in Macromolecules): membranes, solid-state NMR, ligand-binding calculations (3 lectures/year)
- Teaching awards
  - Outstanding Graduate Student Teacher Award, 2013
  - Teaching Award in Biophysics, 2008, 2009, 2013, 2014, 2016, 2017, 2018
  - Graduate Student Society Mentoring Award, 2019

## Invited Seminars since Fall 2007

- 2019: ACS Spring National Meeting (Orlando), University of Illinois Urbana-Champaign, Biological Membranes and Membrane Proteins (Santa Fe), ACS Fall National Meeting (San Diego), Virginia Tech
- 2018: University of Guelph, State University of New York at Oswego,
- 2017: American Chemical Society National Meeting (San Francisco), University of Pennsylvania, Illinois Institute of Technology, SUNY Brockport
- 2016: University of Vermont, Workshop on Biological Processes: GPCRs, CUNY Graduate Center, University of Akron, Colgate University, University of Maryland, SUNY Geneseo
- 2015: Houghton College, Washington University in St. Louis
- 2014: Gordon Conference on Computational Chemistry, Gibbs Conference on Biothermodynamics
- 2013: University of Illinois Urbana-Champaign, Biophysics Symposium, University of West Virginia, Ursinus College, Wells College, Dept of Chemistry, Telluride Conference on Membrane Protein Folding and Function, Delaware Membrane Protein Symposium, Rochester Institute of Technology, Biophysical Society National Meeting, Subgroup Meeting on Membrane Structure, University of Chicago, University of North Carolina-Wilmington, University of Pittsburgh
- 2012: University of Toronto/Sick Kid's Hospital, Cornell University Biophysics Colloquium, American Chemical Society National Meeting, Arizona State Membrane Biophysics Conference, Membrane Protein Biophysics FASEB Meeting (Snowmass)
- 2011: American Chemical Society National Meeting, University of Southern Florida, Cornell University Dept. of Chemical Engineering
- 2010: SUNY Potsdam, Allegheny College, Wells College, University of Texas-Austin

- 2009: Cornell University Biophysics Colloquium, 31<sup>st</sup> IEEE-Engineering in Medicine and Biology Conference, Biological Membranes and Membrane Proteins: Challenges for Theory and Experiment”, Telluride, University of Minnesota, SUNY Binghamton
- 2008: Cornell High Energy Synchrotron Center, Rochester Institute of Technology, Session Chair, Computational Chemistry Gordon Research Conference, “Fukuoka Symposium on Molecular Soft Interactions at the Biomembrane Interface”, Kyushu University, Fukuoka, Japan, University of Western Ontario
- 2007: “Biological Membranes and Membrane Proteins: Challenges for Theory and Experiment”, Park City, Utah

## **Publications** (Google Scholar h-index=30)

1. Smith, L. G., Tan, Z., Spasic, A., Dutta, D., Salas-Estrada, L. A., Grossfield, A., and Mathews, D. H., **Chemically accurate relative folding stability of RNA hairpins from molecular simulations**, *J. Chem. Theor. Comput.*, 2018, 14, 6598-6612
2. Grossfield, A., Patrone, P. N., Roe, D. R., Schultz, A. J., Siderius, D. W., and Zuckerman, D. M., **Best practices for quantification of uncertainty and sampling quality in molecular simulations**, *Living Journal of Computational Molecular Science*, 2018, 1, 1-24
3. Sur, S., Romo, T. D., and Grossfield, A., **Selectivity and mechanism of fengycin, an antimicrobial lipopeptide, from molecular dynamics**, *J. Phys. Chem. B*, 2018, 122, 2219-2226
4. Salas-Estrada, L. A., Leioatts, N., Romo, T. D., and Grossfield, A., **“Lipids Alter Rhodopsin Function via Ligand-like and Solvent-like Interactions**, *Biophys. J.*, 2018, 114, 355-367
5. Thompson, J. L., Zhao, Y., Stathopoulos, P. B., Grossfield, A., and Shuttleworth, T. J., **Phosphorylation-mediated structural changes within the SOAR domain of STIM1 enable specific activation of distinct Orai channels**, *J. Biol. Chem.*, 293, 3145-31552018
6. Romo, T. D., Lewis, A. K., Braun, A. B., Grossfield, A., and Sachs, J. N., **Minimal nucleation state of  $\alpha$ -synuclein is stabilized by dynamic threonine-water networks**, *ACS Chemical Neuroscience*, 2017, DOI: 10.1021/acschemneuro.7b00171
7. Aytenfis, A. H., Spasic, A., Grossfield, A., Stern, H. A., Mathews, D. H., **Revised RNA dihedral parameters for the Amber force field improve RNA molecular dynamics**, *J. Chem. Theor. Comput.*, 13, 2017, 900-915
8. Lin, D., **Generalized and efficient algorithm for computing multipole energies and gradients based on Cartesian tensors**, *J. Chem. Phys.*, 2015, 143, 114115
9. Lin, D. and Grossfield, A., **Thermodynamics of micelle formation and membrane fusion modulate antimicrobial lipopeptide activity**, *Biophys. J.*, 2015, 108, 750-759
10. Leioatts, N., Romo, T. D., Danial, S. A., and Grossfield, A., **Retinal conformation changes rhodopsin’s dynamic ensemble**, *Biophys. J.*, 2015, 109, 608-617
11. Romo, T. D., Leioatts, N. and Grossfield, A., **Lightweight object-oriented structure analysis: Tools for building tools to analyze molecular dynamics simulations**, *J. Comput. Chem.*, 2014, 35, 2305-2318
12. Lin, D., and Grossfield, A., **Thermodynamics of antimicrobial lipopeptide binding to membranes: Origins of affinity and selectivity**, *Biophys. J.*, 2014, 107, 1862-1872
13. Leioatts, N., Suresh, P., Romo, T. D., and Grossfield, A., **Structure-based simulations reveal concerted dynamics of GPCR activation**, *Proteins: Struct. Func. Bioinf.*, 2014
14. Romo, T. D. and Grossfield, A., **How fast is your camera? Timescales for molecular motion and their role in restraining molecular dynamics**, *Biophysical Journal*, 2014, 106, 2549-2551
15. Romo, T. D. and Grossfield, A., **Unknown Unknowns: the Challenge of Systematic and Statistical Error in Molecular Dynamics Simulations**, *Biophysical Journal*, 2014, 106, 1553-1554, PMC4008789
16. Horn, J. N., Kao, T.-C., and Grossfield, A., **Coarse-grained molecular dynamics provides insight into the interactions of lipids and cholesterol with rhodopsin**, in *Computational Approaches to G Protein-Coupled Receptor Modeling and Simulation in Support of Rational Drug Discovery*, ed. Marta Filizola, *Adv. Exp. Med. Biol.*, 2014, 796:75–94, PMC40344522

17. Leioatts, N., and Grossfield, A. **Molecular dynamics simulations of membranes and membrane proteins**, in *Molecular modeling at the atomic scale - Methods and applications in quantitative biology*, ed. Ruhong Zhou, Taylor and Francis, 2014
18. Leioatts, N., Mertz, B., Martínez-Mayorga, K., Romo, T. D., Pitman, M. C., Feller, S. E., Grossfield, A., and Brown, M. F., **Retinal ligand mobility explains internal hydration and reconciles active rhodopsin structures**, *Biochemistry*, 2013, 53, 376-385, PMC4096112
19. Kimura, T., Vukoti, K., Lynch, D. L., Hurst, D. P., Grossfield, A., Pitman, M. C., Reggio, P. H., Yeliseev, A. A., Gawrisch, K., **Global Fold of Human Cannabinoid Type 2 Receptor Probed by Solid-State <sup>13</sup>C-<sup>15</sup>N-MAS NMR and Molecular Dynamics Simulations**, *Proteins: Struct. Func. Bioinf.*, 2013, 82, 452-465, PMC4071771
20. Horn, J. N., Cravens, A., and Grossfield A., **Interactions between fengycin and model bilayers quantified by coarse-grained molecular dynamics**, *Biophysical Journal*, 2013, 105, 1612-1623, PMC3822635
21. Horn, J. N., Romo, T. D., and Grossfield, A., **Simulating the mechanism of antimicrobial lipopeptides with all-atom molecular dynamics**, *Biochemistry*, 2013, 52, 5604-5610, PMC4030210
22. Seckler, J. M., Leioatts, N., Miao, H., and Grossfield, A. **The interplay of structure and dynamics in the function of HIV-1 reverse transcriptase**, *Proteins: Struct. Func. Bioinf.*, 2013, 81, 1792-1801, PMC3773008
23. Leioatts, N., Romo, T. D., and Grossfield, A., **Elastic Network Models are Robust to Variations in Formalism**, *J. Chem. Theor. Comput.*, 2012, 8, 2424-2434, PMC3424003
24. Olausson, B., Grossfield, A., Pitman, M., Brown, M., Feller, S., Vogel, A., **Molecular dynamics simulations reveal specific interactions of post-translational palmitoyl modifications with rhodopsin in membranes**, *J. Am. Chem. Soc.*, 2012, 134, 4234-4331, PMC3299983
25. Horn, J. N., Sengillo, J. D., Lin, D., Romo, T. D., and Grossfield, A., **Characterization of a potent antimicrobial lipopeptide via coarse-grained molecular dynamics**, *Biochim. Biophys. Acta*, 2012, 1818, 212-218, PMC3694338
26. Romo, T. D., and Grossfield, A. **Block covariance overlap method and convergence in molecular dynamics simulation**, *J. Chem. Theor. Comput.*, 2011, 7, 2464-2472
27. Romo, T.D., Bradney, L.A., Greathouse, D.V., and Grossfield, A., **Membrane binding of an acyl-lactoferricin B antimicrobial peptide from solid-state NMR experiments and molecular dynamics simulations**, *Biochim. Biophys. Acta*, 2011, 1808, 2019-2030
28. Grossfield, A., **Recent progress in the study of G protein-coupled receptors with molecular dynamics computer simulations**, *Biochim. Biophys. Acta*, 2011, 1808, 1868-1878
29. Romo, T. D. and Grossfield, A., **Validating and enhancing elastic network models using molecular dynamics simulations**, *Proteins*, 2011, 79, 23-34
30. Hurst, D. P., Grossfield, A., Lynch, D. L., Feller, S., Romo, T. D., Gawrisch, K., Pitman, M. C., and Reggio, P. H., **A lipid pathway for ligand binding is necessary for a cannabinoid G protein-coupled receptor**, *J. Biol. Chem.*, 2010, 285, 17954-17964, PMID: 20220143
31. Romo, T. D., Grossfield A., and Pitman, M. C. **Concerted Interconversion Between Ionic Lock Substates of the  $\alpha$ 2-Adrenergic Receptor Revealed by Microsecond Time Scale Molecular Dynamics**, *Biophysical Journal*, 2010, 98, 76-84
32. Grossfield, A., and Zuckerman, D. M. **Quantifying uncertainty and sampling quality in biomolecular simulations**, *Annual Reports in Computational Chemistry*, 2009, 5, 23-48, NIHMS155855
33. Khelashvili, G., Grossfield, A., Feller, S. E., Pitman, M. C., and Weinstein, H. **Structural and dynamic effects of cholesterol at preferred sites of interaction with rhodopsin identified from microsecond length molecular dynamics simulations**, *Proteins: Struct. Func. Bioinf.*, 2009, 76, 403-417
34. Romo, T. D., Grossfield, A., **LOOS: an extensible platform for the structural analysis of simulations**, *Proceedings of 31<sup>st</sup> IEEE-Engineering in Medicine and Biology Conference*, 2009, 2332-2335
35. Grossfield, A. **Implicit modeling of membranes**, in "Computational Modeling of Membranes", ed Scott Feller, *Current Topics in Membranes* 2008, 60, 131-157
36. Grossfield, A., Pitman, M. C., Feller, S. E., Soubias, O., and Gawrisch, K. **Internal Hydration Increases during Activation of the G-Protein-Coupled Receptor Rhodopsin**, *J. Mol. Biol.* 2008, 381, 478-486
37. Lau, P.-W., Grossfield, A., Feller, S. E., Pitman, M. C., Brown, M. F. **Dynamic structure of**

- retinal inverse agonist of rhodopsin probed by molecular dynamics**, *J. Mol. Biol.* 2007, 372, 906-917
38. O'Neil, L. L., Grossfield, A., Wiest, O. **Computational Investigation of the Base Flipping of the Thymine Dimer in Duplex DNA**, *J. Phys. Chem. B*, 2007, 111, 11843-11849
  39. Grossfield, A., Feller, S. E., Pitman, M. C. **Convergence of molecular dynamics simulations of membrane proteins**, *Proteins: Struc. Func. Bioinf.*, 2007, 67, 31-40
  40. Martínez-Mayorga, K., Pitman, M. C., Grossfield, A., Feller, S. E., and Brown, M. F. **Retinal counterion switch mechanism in vision evaluated by molecular simulation**, *J. Am. Chem. Soc.*, 2006, 128, 16502-16503
  41. Jiao, D., King, C., Grossfield, A., Darden T. A., Ren, P. **Simulation of Ca<sup>2+</sup> and Mg<sup>2+</sup> solvation using Polarizable Atomic Multipole Potential**, *J. Phys. Chem. B*, 2006, 110, 18553-18559
  42. Grossfield, A., Feller, S. E., Pitman, M. C. **Contribution of omega-3 fatty acids to the thermodynamics of membrane protein solvation**, *J. Phys. Chem. B*, 2006, 110, 8907-8909
  43. Grossfield, A., Feller, S. E., Pitman, M. C., **A role for direct interactions in the modulation of rhodopsin by omega-3 polyunsaturated lipids**, *Proc. Nat. Acad. Sci. USA*, 2006, 103, 4888-4893
  44. Fitch, B. G., Rayshubskiy, A., Eleftheriou, M, Ward, T.J.C., Giampapa, M., Zhestkov, Y., Pitman, M. C., Suits, F., Grossfield, A., Pitera, J., Swope, W., Zhou, R., Feller, S., and Germain. R. S., **Blue Matter: Strong scaling of molecular dynamics on Blue Gene/L**. In V. Alexandrov, D. van Albada, P. Sloot, and J. Dongarra, editors, *International Conference on Computational Science (ICCS 2006)*, volume 3992 of LNCS, pages 846–854. Springer-Verlag, 2006.
  45. Pitman, M. C., Grossfield, A., Suits, F. and Feller, S. E., **Role of cholesterol and polyunsaturated lipids in lipid-protein interaction: molecular dynamics simulations of rhodopsin in a realistic membrane environment**, *J. Am. Chem. Soc.*, 2005, 127, 4576-4577
  46. Fitch, B. G., Rayshubskiy, A., Eleftheriou, M, Ward, T.J.C., Giampapa, M., Zhestkov, Y., Pitman, M. C., Suits, F., Grossfield, A., Pitera, J., Swope, W., Zhou, R., Feller, S., and Germain. R. S., **Blue Matter: Strong scaling of molecular dynamics on Blue Gene/L**. Research Report RC23688, IBM Research Division, 2005.
  47. Grossfield, A. **Dependence of ion hydration on the sign of the ion's charge**, *J. Chem. Phys.*, 2005, 122, 024506-10
  48. Drozdov, A. N., Grossfield, A., and Pappu, R. V., **The role of solvent in determining conformational preferences of alanine dipeptide in water**, *J. Am. Chem. Soc.*, 2004, 126, 2574-2581
  49. Grossfield, A., Ren, P., and Ponder, J. W., **Single ion solvation thermodynamics from simulations with a polarizable force field**, *J. Am. Chem. Soc.*, 2003, 125, 14671-14682
  50. Grossfield, A., and Woolf, T. B., **Interaction of tryptophan analogs with lipid bilayers investigated by molecular dynamics and free energy calculations**, *Langmuir*, 2002, 18, 198-210
  51. Petrache, H., Grossfield, A., Mackenzie, K. R., Engelman, D., and Woolf T., **Modulation of glycoporphin A transmembrane helix interaction by lipid bilayers – molecular dynamics calculations**, *J. Mol. Biol.*, 2000, 302, 727-746
  52. Grossfield, A., Sachs, J. and Woolf, T. B., **A dipole lattice membrane model for protein calculations**, *Proteins:Structure, Function, and Genetics* , 2000, 41, 211-223
  53. Woolf, T. B., Grossfield, A., and Tychko, M., **Differences between apo and three holo forms of intestinal lipid binding proteins seen by molecular dynamics computer calculations**, *Biophys. J.*, 2000, 78, 608-625
  54. Woolf, T., Grossfield, A., and Zuckerman, D., **Electrostatics of membrane systems --- complex, heterogeneous environments**, in *Simulation and Theory of Electrostatic Interactions in Solution*, Pratt, L. and Hummer. G. eds, no. 492 in AIP Conference Proceedings, American Institute of Physics, 1999, 510-532
  55. Woolf, T., and Grossfield, A., and Pearson, J., **Indoles at interfaces: calculations of electrostatic effects with density functional and molecular dynamics methods**, *Int. J. Quant. Chem.*, 1999, 75, 197-206