Dr. Alan Grossfield

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Current as of: 5/24/17

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

Research Experience and Education

- 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
- Undergraduate Research, Cornell University
  Adviser: Dr. P. A. Karplus
  Summer, 1993
- Visiting Research Student, CIBA-Geigy
  Summers 1990 – 1992

Invited Seminars since Fall 2007

- 2017: American Chemical Society National Meeting, San Francisco, University of Pennsylvania, Illinois Institute of Technology
- 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, 31st 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

Awards and Service

- NIH GM095496, "Multiscale modeling of GPCRs", 2011-2016
- NIH study section special interest groups, 2014 (BMCB), 2015 (BPNS)
- NSF ad-hoc reviewer (2017)
- University of Rochester Computational Research Committee, 2009-
- University of Rochester Medical Center Faculty Council, 2009-
- 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-
- Outstanding Graduate Student Teacher Award, 2013
- Teaching Award in Biophysics, 2008, 2009, 2013, 2014, 2016, 2017
- NIH National Research Service Award (1 F32 NS42975) 2001 – 2004
- 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
- Invited guest editor for special issue of Chemistry and Physics of Lipids
- Acting editor, Proteins: Structure, Function, and Bioinformatics

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
- Added Nose-Hoover, potential-smoothing, constant pressure, replica exchange, and principal component analysis to molecular dynamics package TINKER

Publications

1. Aytenfisu, 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
2. Lin, D., **Generalized and efficient algorithm for computing multipole energies and gradients based on Cartesian tensors**, J. Chem. Phys., 2015, 143, 114115
3. Lin, D. and Grossfield, A., **Thermodynamics of micelle formation and membrane fusion modulate antimicrobial lipopeptide activity**, Biophys. J., 2015, 108, 750-759
4. Leioatts, N., Romo, T. D., Danial, S. A., and Grossfield, A., **Retinal conformation changes rhodopsin's dynamic ensemble**, Biophys. J., 2015, 109, 608-617
5. 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
6. Lin, D., and Grossfield, A., **Thermodynamics of antimicrobial lipopeptide binding to membranes: Origins of affinity and selectivity**, Biophys. J., 2014, 107, 1862-1872
7. Leioatts, N., Suresh, P., Romo, T. D., and Grossfield A., **Structure-based simulations reveal concerted dynamics of GPCR activation**, Proteins: Struc. Func. Bioinf., 2014
8. 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
9. 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
10. 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

11. 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
12. 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
13. 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 13C-,15N-MAS NMR and Molecular Dynamics Simulations**, Proteins: Struc. Func. Bioinf, 2013, 82, 452-465, PMC4071771
14. 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
15. 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
16. 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: Struc. Func. Bioinf., 2013, 81, 1792-1801, PMC3773008
17. 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
18. 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
19. 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
20. Romo, T. D., and Grossfield, A. **Block covariance overlap method and convergence in molecular dynamics simulation**, J. Chem. Theor. Comput., 2011, 7, 2464-2472
21. 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
22. Grossfield, A., **Recent progress in the study of G protein-coupled receptors with molecular dynamics computer simulations**, Biochim. Biophys. Acta, 2011, 1808, 1868-1878
23. Romo, T. D. and Grossfield, A., **Validating and enhancing elastic network models using molecular dynamics simulations**, Proteins, 2011, 79, 23-34
24. 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
25. Romo, T. D., Grossfield A., and Pitman, M. C. **Concerted Interconversion Between Ionic Lock Substates of the β2-Adrenergic Receptor Revealed by Microsecond Time Scale Molecular Dynamics**, Biophysical Journal, 2010, 98, 76-84
26. Grossfield, A., and Zuckerman, D. M. **Quantifying uncertainty and sampling quality in biomolecular simulations,** Annual Reports in Computational Chemistry, 2009, 5, 23-48, NIHMS155855
27. 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: Struc. Func. Bioinf., 2009, 76, 403-417
28. Romo, T. D., Grossfield, A., **LOOS: an extensible platform for the structural analysis of simulations**, Proceedings of 31st IEEE-Engineering in Medicine and Biology Conference, 2009, 2332-2335
29. Grossfield, A. **Implicit modeling of membranes**, in "Computational Modeling of Membranes", ed Scott Feller, Current Topics in Membranes 2008, 60, 131-157
30. 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
31. 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
32. 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
33. Grossfield, A., Feller, S. E., Pitman, M. C. **Convergence of molecular dynamics simulations of membrane proteins**, Proteins: Struc. Func. Bioinf., 2007, 67, 31-40
34. 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
35. Jiao, D., King, C., Grossfield, A., Darden T. A., Ren, P. **Simulation of Ca2+ and Mg2+ solvation using Polarizable Atomic Multipole Potential,** J. Phys. Chem. B, 2006, 110, 18553-18559
36. 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
37. 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
38. 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.
39. 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
40. 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.
41. Grossfield, A. **Dependence of ion hydration on the sign of the ion's charge**, J. Chem. Phys., 2005, 122, 024506-10
42. 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
43. 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
44. 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
45. Petrache, H., Grossfield, A., Mackenzie, K. R., Engelman, D., and Woolf T., **Modulation of glycophorin A transmembrane helix interaction by lipid bilayers – molecular dynamics calculations**, J. Mol. Biol., 2000, 302, 727-746
46. 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
47. 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
48. Woolf, T., Grossfield, A., and Zuckerman, D., **Electrostatics of membrane systems --- complex, heterogeneous environments**, in S**imulation 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
49. 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