Anthony Hazel

Graduate Research Assistant
School of Physics
Georgia Institute of Technology
837 State Street
Atlanta, GA 30308
Phone: (407) 530-9608
email: ahazel3@gatech.edu

Education

Ph. D. in Physics
School of Physics, *Georgia Institute of Technology* (August 2012 – December 2018)

Advisor: James C. Gumbart

Thesis: *Using Molecular Dynamics Simulations and Enhanced Sampling Methods to Understand Protein Folding and Assembly at the Outer Membrane of Gram-negative Bacteria*

B. Sc. in Physics and Applied & Computational Mathematics
Department of Physics, *Florida State University* (August 2008 – July 2012)

Advisor: Peng Xiong

Honors Thesis: *Semiconductor Nanostructure-Based Field Effect Transistors for Biosensing Applications*

Research Projects

---

1. *Examining the effects of solvent and polarization on the folding of small peptides.* I studied the folding of model α-helical and β-hairpin peptides by calculating free energy landscapes using replica-exchange umbrella sampling (REUS), incorporating collective variables measuring both structure acquisition and compaction to improve sampling in both the folded and unfolded ensembles. I ran multiple replica molecular dynamics simulations using NAMD and its *colvars* module for both CPUs and GPUs on high performance supercomputing resources such as Titan, Stampede2, and

Bridges. I first generated starting states for REUS simulations using steered molecular dynamics and adaptive biasing forces. I compared multiple CHARMM force fields, including CHARMM36 and CHARMM22* as well as the polarizable Drude model. Examining internal hydrogen bond ordering and backbone hydration I was able to reveal differences in folding mechanisms, such as cooperativity, of α-helices and β-sheets in different environments and the subtle effects of the solvent on the balance of folded and unfolded states. Lastly, using a pertubative WHAM formalism, I was able to efficiently test small tweaks in protein parameters in order improve the Drude model's ability to reproduce experimental folding free energies.

2. *Investigating the* in vitro *and* in vivo *folding pathways of the β-helical passenger domain of the autotransporter, pertactin.*. Building on my work of folding α-helices and β-sheets, I developed a protocol for studying both the concerted *in vitro* and vectorial *in vivo* folding mechanisms of the pertactin β-helical passenger domain. I employed the self-learning umbrella sampling (SLUS) algorithm of Bernèche and coworkers (*J. Chem. Theory Comput.* 2013, 9, 1885–1895) in combination with REUS simulations. High temperature and metadynamics simulations were used to seed the SLUS algorithm. I calculated the folding free energy of isolated "bands" of the helix structure and compared those to the free energy of folding one band on top of another. These simulations show that the helical bands rarely fold in isolation, necessitating the need for a concerted (*in vitro*) or vectorial (*in vivo*) folding mechanism.

3. *Determining the flexibility of the membrane fusion protein, AcrA, from the AcrAB-TolC multidrug efflux pump.* Again employing the SLUS+REUS protocol, I calculated high dimensional free energy landscapes of AcrA using internal angles relating the orientation of its four main structural elements. To accelerate the WHAM calculations, I modified the WHAM code of Alan Grossfield (`http://membrane.urmc.rochester.edu/content/wham`) to incorporate the method of direct inversion in the iterative subspace (Zhang et al., *Mol. Sim.* 42(13), 1079–1089). By comparing the free energy landscapes of free and AcrB-bound AcrA, I was able to deduce the dominant binding mechanism. Comparing AcrA in the two binding sites on AcrB may also reveal information about the ordering or timing of binding events. I also tested the effects of experimentally determined mutations in AcrA on its ability to bind to AcrB. This included running free energy perturbation in several states generated from the REUS simulations as well as states determined from cryo electron microscopy. Lastly, using long equilibrium simulations run in AMBER on GPUs with hydrogen mass repartitioning, I compared the ensemble of states for wild type and mutated AcrA monomers.

Awards/Scholarships

6. Larry S. O'Hara Scholarship (Georgia Tech, 2016-2017)
5. G. F. Amelio Fellowship (Georgia Tech, 2012-2014)
4. President's Fellowship (Georgia Tech, 2012-2016)
3. Magna Cum Laude with Honors (FSU, 2012)
2. Sigma Pi Sigma Physics Honor Society (FSU, 2011)
1. Undergraduate Scholarship (FSU, 2008-2012)

Journal Articles

8. **A. Hazel**, N. Abdali, J. M. Parks, J. C. Smith, H. I. Zgurskaya, and J. C. Gumbart. "Conformational dynamics of AcrA in the free and AcrB-bound states." (In preparation.)
7. C. Balusek, H. Hwang, C. H. Lau, K. Lundquist, **A. Hazel**, A. Pavlova, D. Lynch, P. Reggio, Y. Wang, and J. C. Gumbart. "On the validity of Hydrogen Mass Repartitioning for CHARMM36 membrane systems in NAMD." (In preparation.)
6. M. Bañó-Polo*, C. Baeza-Delgado*, S. Tamborero*, **A. Hazel***, B. Grau, I. Nilsson, P. Whitley, J. C. Gumbart, G. von Heijne and I. Mingarro. "Transmembrane but not soluble helices fold inside the ribosome tunnel." (Accepted for publication on October 30, 2018.) *Nat. Commun.* **These authors contributed equally to this study.*
5. **A. Hazel**, E. Walters, C. Rowley, and J. C. Gumbart. "Folding free energy landscapes of β-sheets with non-polarizable and polarizable CHARMM force fields." (2018) *J. Chem. Phys.*, 149:072317. DOI: 10.1063/1.5025951.
4. J. C. Gumbart, M. Ulmschneider, **A. Hazel**, S. White, and J. Ulmschneider. "Computed free energies of peptide insertion into bilayers are independent of computational method." (2018) *J. Mem. Biol.*, 251(3):345-356. DOI: 10.1007/s00232-018-0026y.
3. S. Hill, E. Nguyen, R. Donegan, A. Patterson-Oraze, **A. Hazel**, J. C. Gumbart, and R. Lieberman. "Structure and misfolding of the flexible tripartite coiled-coil domain of glaucoma-associated myocilin." (2017) *Structure*, 25:1–11. DOI: 10.1016/j.str.2017.09.008.

2. H. Hwang, T. McCaslin, **A. Hazel**, C. Pagba, C. Nevin, A. Pavlova, B. Barry, and J. C. Gumbart. "Redox-driven conformational dynamics in a photosystem-II-inspired β-hairpin maquette determined through spectroscopy and simulation." (2017) *J. Phys. Chem. B*, *121*(15):3536–3545. DOI: 10.1021/acs.jpcb.6b09481.

1. **A. Hazel**, C. Chipot, and J. C. Gumbart. "Thermodynamics of deca-alanine folding in water." (2014) *J. Chem. Theory Comput.*, 10(7):2836–2844. DOI: 10.1021/ct5002076.

Talks

---

4. **A. Hazel**, E. Walters, C. Rowley, and J. C. Gumbart. "How much detail is sufficient? A comparison of non-polarizable and polarizable force fields for protein folding." NAMD Workshop on Computational Biology. Dalian Institute of Chemical Physics, Dalian, CN. July, 2018.

3. **A. Hazel** and J. C. Gumbart. "Using molecular dynamics simulations in the search for new anti-microbial drugs." Microbial Dynamics Seminar. Georgia Institute of Technology, Atlanta, GA. April, 2018.

2. **A. Hazel** and C. Balusek. "The physical mechanisms that drive protein evolution." Georgia Tech PoLS Lunch and Learn seminar. Georgia Institute of Technology, Atlanta, GA. January, 2016.

1. **A. Hazel** and J. C. Gumbart. "Free energies from molecular dynamics simulations." Georgia Tech PoLS Lunch and Learn seminar. Georgia Institute of Technology, Atlanta, GA. August, 2014.

Poster Presentations

---

9. **A. Hazel**, E. Walters, C. Rowley, and J. C. Gumbart. "Folding free energy landscapes of β-sheets with non-polarizable and polarizable CHARMM force fields." 2018 Workshop on Free Energy Methods, Kinetics and MSMs in Drug Design, Boston, MA. May, 2018.

8. **A. Hazel** and J. C. Gumbart. "Flexibility of free and AcrB-bound AcrA in the AcrAB-TolC multidrug efflux pump of *Escherichia coli* determined using 3D PMFs." Biophysical Society 2018 Annual Meeting, San Francisco, CA. February, 2018.

7. **A. Hazel**, E. Walters, C. Rowley, and J. C. Gumbart. "Folding free energy landscapes of β-sheets with non-polarizable and polarizable CHARMM force fields." Biophysical Society 2018 Annual Meeting, San Francisco, CA. February, 2018.

6. **A. Hazel** and J. C. Gumbart. "Examining the stability of β-sheets using the CHARMM drude polarizable force field." iPoLS 2017 Annual Meeting, Paris, France. June, 2017.

5. **A. Hazel** and J. C. Gumbart. "Examining the stability of β-sheets using the CHARMM drude polarizable force field." Biophysical Society 2017 Annual Meeting, New Orleans, LA. February, 2017.

4. **A. Hazel** and J. C. Gumbart. "Comparing in vitro and in vivo protein folding using molecular dynamics simulations." Biophysical Society 2016 Annual Meeting, Los Angeles, CA. February, 2016.

3. **A. Hazel** and J. C. Gumbart. "Computational methods for measuring the free energy of folding in the ribosomal exit tunnel." Biophysical Society 2015 Annual Meeting, Baltimore, MA. February, 2015.

2. **A. Hazel**, C. Chipot, and J. C. Gumbart. "Thermodynamics of folding for deca-alanine in water." iPoLS 2014 Annual Meeting, Munich, Germany. July, 2014.

1. **A. Hazel**, C. Chipot, and J. C. Gumbart. "Thermodynamics of folding for deca-alanine in water." Biophysical Society 2014 Annual Meeting, San Francisco, CA. February, 2014.

Workshops and Summer Schools

---

2. NAMD Biomolecular Dynamics Simulation Workshop. Dalian Institute of Chemical Physics, Dalian, CN. July 9–13, 2018. `https://www.ks.uiuc.edu/Training/Workshop/Dalian2018/`

1. Physics of Living Systems Summer School for Theoretical Biophysics. Los Alamos National Laboratory, Los Alamos, NM. August 8–12, 2016.