

Chris Neale

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- OBJECTIVE** Postdoctoral fellowship in computational biomolecular dynamics.
- ABILITIES** Exceptional teamwork and leadership abilities, strong capability to design and independently conduct simulation studies, experience writing proposals for competitive computer allocations.
- EDUCATION**
- | | |
|---|----------------|
| PhD Candidate (Biochemistry) University of Toronto | 2005 – present |
| - Advisor: Régis Pomès | |
| - Thesis: Statistical Convergence of Equilibrium Properties from Molecular Dynamics (MD) Simulation | |
| BSc (Biology) University of Waterloo | 1996-2001 |
- RESEARCH EXPERIENCE**
- Statistical convergence of molecular solutes embedded in lipid bilayers.**
- Identified the slow convergence of equilibrium properties during massively repeated umbrella sampling (US) MD simulations of solutes across a lipid bilayer (amino acid side chain analogs and the 13-residue antimicrobial peptide indolicidin).
 - Elucidated the atomistic basis of this slow convergence, establishing the long autocorrelation times of lipid headgroup salt-bridge interactions as a major obstruction to attaining convergence.
- Accelerating convergence in simulations of molecular solutes embedded in lipid bilayers.**
- Evaluated the application of equilibrium replica exchange of restraining potentials or temperatures to the rate at which equilibrium properties attained convergence.
 - Introduced a novel indicator of hidden barriers, free energy maxima in degrees of freedom orthogonal to the predefined reaction coordinate that introduce systematic sampling errors when simulation timescales are not sufficiently large.
- Solvation and binding of the bacterial membrane enzyme PagP by detergents and lipids.** (PagP is an acyltransferase that transfers the *sn*-1 palmitoyl chain of a donor phospholipid to lipid A.)
- Identified the binding route by which the donor acyl-chain enters the binding pocket and constructed ensemble representations of the bound state.
 - Evaluated the solvation of PagP in detergents.
- Early pore-opening kinetics of the bacterial Mg²⁺ transport system CorA.**
- Used massively repeated simulations in the presence and absence of regulatory ions to evaluate the kinetics of pore hydration, which are accelerated in the absence of regulatory ions.
 - Constructed ensembles that represent a more open state of this pore.

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Self-aggregation of detergents.

- Studied the self aggregation of detergents in water during non-equilibrium unrestrained simulations.
- Used double-decoupling free energy simulations to evaluate detergent critical micelle concentration and mean aggregation number.

Describing unfolded states as structural ensembles.

- Invented new algorithms to efficiently select structures from a large conformational pool and construct an ensemble that fits the available experimental data.
- Applied these new techniques to develop an enhanced conformational description of the unfolded state of the 59-residue drkN SH3 domain.

ADDITIONAL RESEARCH CONTRIBUTIONS

- Played a pivotal role in obtaining new computational resources and assisting colleagues to use these resources. This involved identification of national resources and leadership in the process of drafting competitive resource allocation proposals.
- Coordination of local computational infrastructure.
- Beta testing on the SciNet 30,000-core HPC cluster.
- Enhanced group efficiency via automated submission scripts.
- Active contributor to the GROMACS mailing list.
- Wrote the g_spatial GROMACS tool to compute spatial distribution functions.
- Maintain the software suite for the Distributed Replica extended ensemble sampling method.

AWARDS

- Best Student Presentation – High performance computing symposium (National, \$500). 2010.
- Exceptional Trainee Award – Hospital for Sick Children, molecular structure and function (Institutional, \$500). 2008.
- Hospital for Sick Children research training center scholarship (Institutional, \$9,000 per annum). 2007-2011.
- University of Toronto fellowship (Institutional, \$12,000 per annum). 2005-2011.

PUBLICATIONS

1. **C. Neale**, W. F. D. Bennett, D. P. Tieleman, and R. Pomès, “Statistical convergence of equilibrium properties in simulations of molecular solutes embedded in lipid bilayers”, Submitted to J. Chem. Theory Comput. (2011).
2. L. Huynh, **C. Neale**, R. Pomès, and C. Allen, “Computational approaches to the rational design of nanoemulsions, polymeric micelles, and dendrimers for drug delivery”, Nanomedicine, DOI: 10.1016/j.nano.2011.05.006 (2011).

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3. L. Huynh, **C. Neale**, R. Pomès, and C. Allen, "Systematic design of unimolecular star copolymer micelles using molecular dynamics simulations", *Soft Matter*, 6, 5491-5501 (2010).
4. J. A. Cuesta-Seijo, **C. Neale**, M. A. Khan, J. Moktar, C. D. Tran, R. E. Bishop, Pomès, and G. G. Privé, "PagP crystallized from SDS/cosolvent reveals the route for phospholipid access to the hydrocarbon ruler", *Structure*, 18(9):1210-1219 (2010).
5. N. Chakrabarti, **C. Neale**, J. Payandeh, E. F. Pai, and R. Pomès, "An iris-like mechanism of pore dilation in the CorA magnesium transport system", *Biophys. J.*, 98(5):784-792 (2010).
6. S. Rauscher, **C. Neale**, and R. Pomès, "Simulated tempering distributed replica sampling, virtual replica exchange, and other generalized-ensemble methods for conformational sampling", *J. Chem. Theory Comput.*, 5(10):2640-2662 (2009).
7. M. S. Al-Abdul-Wahid, **C. Neale**, R. Pomès, and R. S. Prosser, "A solution NMR approach to the measurement of amphiphile immersion depth and orientation in membrane model systems", *J. Am. Chem. Soc.*, 131, 6452-6459 (2009).
8. **C. Neale**, T. Rodinger, and R. Pomès, "Equilibrium exchange enhances the convergence rate of umbrella sampling", *Chemical Physics Letters* 460, 375-381 (2008).
9. M. A. Khan, **C. Neale**, C. Michaux, R. Pomès, G. G. Privé, R. W. Woody, and R. E. Bishop, "Gauging a hydrocarbon ruler by an intrinsic exciton probe", *Biochemistry* 46, 4565-4579 (2007).
10. J.A. Marsh, **C. Neale**, F.E. Jack FE, WY. Choy, A.Y. Lee, K.A. Crowhurst, and J.D. Forman-Kay, "Improved structural characterizations of the drkN SH3 domain unfolded state suggest a compact ensemble with native-like and non-native structure." *J. Mol. Biol.*, 367, 1494-1510 (2007).
11. M. Tollinger, **C. Neale**, L.E. Kay, and J.D. Forman-Kay, "Characterization of the hydrodynamic properties of the folding transition state of an SH3 domain by magnetization transfer NMR spectroscopy" *Biochemistry*, 45, 6434 -6445 (2006).
12. L.X. Wu, J. La Rose, L. Chen, **C. Neale**, T. Mak, K. Okkenhaug, R. Wange, and R. Rottapel "CD28 regulates the translation of Bcl-xL via the phosphatidylinositol 3-kinase/mammalian target of rapamycin pathway" *J. Immunology*, 174, 180-194 (2005).
13. R. Rottapel, S. Ilangumaran, **C. Neale**, J. La Rose, J.M-Y Ho, M.H-H Nguyen, D. Barber, P. Dubreuil, and P. de Sepulveda "The tumor suppressor activity of SOCS-1" *Oncogene*, 21, 4351-4362 (2002).

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INVITED

ORAL

PRESENTATIONS

1. “Statistical convergence of equilibrium properties from massive sampling”, SHARCNET sponsored Scientific Computing Seminar Series, Oshawa, ON, Canada. April 2011.
2. “Computational Studies of the Solvation and Binding of the Outer Membrane Enzyme PagP by Detergents and Lipids”, Symposium on Membrane Proteins and Molecular Therapeutics supported by the CIHR Strategic Training Programme in the Structural Biology of Membrane Proteins Linked to Disease, Toronto, ON, Canada. June 2007. – I was the only graduate student invited to present at this symposium.

CONTRIBUTED

ORAL

PRESENTATIONS

3. “Computer simulation studies of an antimicrobial peptide and a microbial virulence factor: statistical convergence of equilibrium properties from massive sampling”, Biophysical Society annual meeting, Baltimore, MD, USA. February 2011.
4. “High-throughput computing of protein function for rational drug design”, High Performance Computing Symposium, Toronto, ON, Canada. June 2010. – Best student presentation award.
5. “Solvation and binding of the outer membrane enzyme PagP by detergents and lipids”, Chemical Biophysics Symposium, Toronto, ON, Canada. April 2007.

POSTERS

1. **C. Neale**, N. Chakrabarti, E.F. Pai, and R. Pomès, “Microsecond pore dilation kinetics and hydrophobic gating of magnesium transport in the Cora system”, Biophysical Society annual meeting, Baltimore, MD, USA. February 2011.
2. L. Huynh, **C. Neale**, R. Pomès, and C. Allen, “Rational design of unimolecular star copolymer micelles for drug delivery: molecular dynamics study of solvation, aggregation, and drug binding properties”, Biophysical Society annual meeting, Baltimore, MD, USA. February 2011.
3. **C. Neale**, J.C.Y. Hsu, C. Madill, C.M. Yip, and R. Pomès, “Atomistic mechanisms of host toxicity in antimicrobial peptides”, Canadian Chemistry Conference, Toronto, ON, Canada. May 2010.
4. **C. Neale**, J.C.Y. Hsu, C. Madill, C.M. Yip, and R. Pomès, “Reducing host toxicity in antimicrobial peptides”, Workshop on free energy methods in drug design, Cambridge, MA, USA. May 2010.
5. **C. Neale**, J.C.Y. Hsu, C. Madill, C.M. Yip, and R. Pomès, “Reducing host toxicity in antimicrobial peptides”, Computer Aided Drug Design, Keystone Symposium, Whistler, British Columbia, Canada. April 2010.

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6. **C. Neale**, J.C.Y. Hsu, C. Madill, C.M. Yip, and R. Pomès, “Atomistic mechanisms of host toxicity in antimicrobial peptides”, Chemical Biophysics Symposium, Toronto, ON, Canada. April 2010.
7. **C. Neale**, M.A. Kahn, J.A. Cuesta-Seijo, G.G. Privé, R.E. Bishop, and R. Pomès, “Solvation and binding of the membrane enzyme PagP by detergents and lipids”, Biophysical Society 54th annual meeting, San Francisco, CA, USA. February 2010.

OTHER WORK EXPERIENCE

- Computer Programmer** – Hospital for Sick Children, Toronto, ON 2003-2005
Generation and analysis of structural ensembles that satisfied experimental observations of the unfolded state of an SH3 domain. Invented and implemented a highly efficient Monte-Carlo algorithm for ensemble selection.
- Lab Technician** – Dalhousie University, Halifax, NS 2003-2004
Molecular cloning, eukaryotic cell-death assays, tissue section staining.
- Lab Technician** – Ontario Cancer Institute, Toronto, ON 2001-2002
Creation of hybrid DNA constructs, protein production for antibody generation and NMR, analysis of signal transduction using hybrid FRET constructs and flow cytometry.
- Computer Programmer** – Hospital for Sick Children, Toronto, ON 2001
Enhanced the data-type capabilities of a computer program that creates ensembles of structures representing unfolded protein states.
- Cooperative Placement** – AstraZeneca Pharmaceuticals, Montreal, QC 1999, 2000
Optimized a new protocol for cDNA enrichment of novel GPCR's and analyzed cDNAs for patterns of GPCR abundance by Lightcycler qtPCR.
- Cooperative Placement** – Huntsman Canada, Guelph, ON 1998
Developed new methodology for near-IR approximation of molecular weight.
- Cooperative Placement** – Ontario Cancer Institute, Toronto, ON 1998
Eukaryotic protein expression analysis by flow cytometry.

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TEACHING	Training – Trained colleagues on molecular dynamics simulation and analysis software.	2005-present
	Teaching Assistant – University of Waterloo, Waterloo, ON Prepared and delivered third year histology laboratory tutorials.	2000
SKILLS	Programming	C, bash, gnuplot.
	MD Software	GROMACS, CHARMM, VMD
	Techniques	Umbrella sampling, double-decoupling free energy calculations, replica exchange, simulations involving lipid bilayers, large-scale simulations, evaluating convergence.
LANGUAGE	English, native	

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ACADEMIC REFERENCES

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