Nathan M. Lim

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My research focuses on using molecular simulations for predicting important properties related to pharmaceutical drug design. I am interested in designing methods that utilize high-performance GPU computing and cloud computing resources to accelerate drug discovery. My goal is to develop software that will enable researchers to make rapid and highly accurate predictions of physical properties, such as protein-ligand binding affinities and small molecule solubility.

Education

SEPT 2014 - *PRESENT*

Ph.D. Pharmaceutical Sciences / University of California, Irvine

Ph.D. Candidate, Adviser: David L. Mobley

SEPT 2014 - JULY 2017

M.S. Pharmaceutical Sciences / University of California - Irvine

Adviser: David L. Mobley

SEPT 2010 - JUNE 2014

B.S. Pharmaceutical Sciences / University of California - Irvine

Advisers: David L. Mobley, Thomas L. Poulos

Research Experience

SEPT 2014 - *PRESENT*

Graduate Researcher / Mobley Lab, UCI Dept. of Pharma.Sci.

- Developing a machine learning based approach for predicting ligand binding modes and computing their occupancies to improve efficiency in calculating protein-ligand binding affinities [1]. I manage a team consisting of another graduate and two undergraduates students to test the application of my approach on a large-scale blind fragment screen to *soluble epoxide hydrolase* obtained from *OpenEye Scientific Software Inc*.
- Collaborating with *OpenEye* to develop code that will automatically setup and run molecular dynamics simulations on the cloud using Amazon Web Services [github.com/oess/openmm_orion]
- Co-developed a Python toolkit called BLUES (Binding Modes of Ligands using Enhanced Sampling) which accelerates ligand binding mode sampling during a molecular dynamics simulation in OpenMM [2].
- Used molecular dynamics simulations with alchemical free energy calculations via NAMD to characterize the membrane insertion process of diphtheria toxin [3].
- Designed the mobleylab.org website and deployed on Amazon Web Services through an EC2 instance.

JUN 2015 – AUG 2015

Scientific Developer Intern / Schrödinger, LLC. New York, NY

- Developed an enhanced sampling approach for improving relative protein-ligand binding affinity predictions by accelerating protein motions [4]. I presented my research as a poster at the *Spring 2016 San Diego American Chemical Society* conference and the *Theory and Applications of Computational Chemistry 2016 Seattle* conference.
- Wrote the manual for LigandFEP, a *Schrödinger* toolkit for academics, used to perform free energy perturbation calculations for computing relative protein-ligand binding affinities [5].

JUN 2014 – SEPT 2014

Scientific Developer Intern / Schrödinger, LLC. New York, NY

- Developed a protocol for computing absolute protein-ligand binding affinities using Desmond within the *Schrödinger* application suite.

MAR 2013 – SEPT 2014

Undergraduate Researcher / Mobley Lab, UCI Dept. of Pharma.Sci.

- Developed Python code for performing the statistical analysis and scoring of entries submitted to the blind prediction challenges in SAMPL4 [6, 7].
- Used molecular dynamics simulations with GROMACS to compute hydration free energy calculations for validating automatically planned calculations from our toolkit known as LOMAP [8].

MAR 2013 – JUN 2014

Undergraduate Researcher / Poulos Lab, UCI Dept. of Pharma.Sci.

- Purified and crystallized proteins for characterizing structural features in *bacterial nitric oxide synthase* and assisted in development of an enzyme assay for measuring binding activity and inhibition [9, 10].

Work Experience

MAR 2007 – SEPT 2012

Online Retailer / eBay & Amazon

Self-Employment

- Managed a large online retail store for DVDs, CDs, and video games
- Maintained PowerSeller status with a customer satisfaction rating of 98%
- Packaged and shipped over 20,000 orders

MAR 2008 – DEC 2011

Computer Technician / Reliable Computers

Self-Employment

- Built computers customized according to customer needs and specifications
- Repaired and maintained customer computers by providing training and technical support

Skills

- **Programming languages:** proficient at Python, familiar with Bash
- **Python packages:** OpenMM, OpenEye-toolkits, MDTraj, PyEMMA, MSMBuilder, Scikit-learn, NumPy, Matplotlib, Jupyter Notebooks
- **Software:** Github (with continuous integration), Desmond, NAMD, CHARMM, GROMACS, VMD, PyMOL

Awards

• National Science Foundation Graduate Research Fellowship 2015

• Molecular Sciences Software Institute Phase-I Software Fellow 2018

Publications

1. **Lim, N. M.**; Gill, S.; Bergazin, D.; Nguyen, L. P.; Osato, M.; Mobley, D. L. “Progress on computing fragment binding mode occupancies with BLUES” London, U.K., 2017. Oral presentation at the *miniCUP London 2017*.

2. Gill, S; **Lim, N. M.**; Grinaway, P.; Rustenburg, A. S.; Fass, J.; Ross, G.; Chodera, J. D.; Mobley, D. L. “Binding Modes of Ligands Using Enhanced Sampling (BLUES): Rapid Decorrelation of Ligand Binding Modes Using Nonequilibrium Candidate Monte Carlo” *Submitted to J. of Phys. Chem.* (2017)

3. Kyrychenko A.; **Lim, N. M.**; Freites, J. A.; Nguyen, L. P.; Tobias, D. J.; Mobley, D.L. “Refining Protein Penetration into the Lipid Bilayer Using Fluorescence Quenching and Molecular Dynamics Simulations: The Case of Diphtheria Toxin Translocation Domain” *Submitted to J. Mem. Bio.* (2017)

4. **Lim, N. M.**; Wang, L.; Abel, R.; Mobley, D. L. "Sensitivity in binding free energies due to protein reorganization" *J. Chem. Theory Comput.*, *12*(9), 4620-4631. 2016

5. **Lim, N.** “Molecular Dynamics Ligand FEP Tutorial August 2015” Schrödinger Academy. New York, NY. 2015

6. Mobley, D.L.; Liu, S.; **Lim, N.M.**; Wymer, K.L.; Perryman, A.L.; Forli, S.; Deng, N.; Su, J.; Branson, K.; Olson. A.J. “Blind prediction of HIV integrase binding from SAMPL4 challenge” *J. Comput. Aided Mol. Design*. 28(4):327-345. 2014.

7. Mobley, D.L.; Wymer, K.L.; **Lim, N.M.**; Guthrie, J.P.; “Blind prediction of solvation free energies from the SAMPL4 challenge” *J. Comput. Aided Mol. Design*. 28:135-150. 2014.

8. Liu, S.; Wu, Y.; Lin, T.; Abel, R.; Redmann, J.; Summa, C.M.; Jaber, V.R.; **Lim, N.M.**; Mobley, D.L. “Lead Optimization Mapper: Automating free energy calculations for lead optimization” *J. Comput. Aided Mol. Design*. 27(9):755-770. 2013.

9. Holden, J.K.; **Lim, N.**; Poulos, T.L. “Identification of Redox Partners and Development of a Novel Chimeric Bacterial Nitric Oxide Synthase for Structure Activity Analyses” *J. Biol. Chem.* 289(42):29437-29445. 2014.

10. Holden, J.K.; Kang, S.; Hollingsworth, S.A.; Li, H.; **Lim, N.;** Chen, S.; Huang, H.; Xue, F.; Tang, W.; Silverman, R.B; Poulos, T.L. “Structure-based design of bacterial nitric oxide synthase inhibitors” *J. Med. Chem. 58*(2), pp.994-1004. 2015