BIOGRAPHICAL SKETCH

NAME: Lin Li

eRA COMMONS USER NAME (credential, e.g., agency login): LINLI5

POSITION TITLE: Assistant Professor

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Huazhong University of Science & technology (China)	B.S.	05/2005	Applied Physics
Huazhong University of Science & technology (China)	Ph.D.	03/2011	Biophysics
Clemson University (Clemson, SC, U.S.)	Postdoctoral	07/2013	Molecular Biophysics

A. Personal Statement

I am a New Investigator at University of Texas at El Paso. I have solid biophysics and computer science background, which gives me opportunities and skills to develop novel Biology models from the view of Physics, and implement such models into computational approaches. During my Ph.D. career, I have developed software packages such as ASPDock and SRM (Soft Restrict Method). After I joined in Dr. Alexov's group as a Postdoc Fellow in Clemson, I have developed many new algorithms and tools in DelPhi software package, such as Gaussian smooth method, MEMPOT (MEMbrane Potential) and DelPhiForce. My new developments result in three intellectual properties. I have finished varies of projects in which I used numerical approaches to study important biological problems. My research interests include mechanisms of molecular motors' motilities, virus capsid assembly, protein-protein/DNA/RNA interactions, *etc*. Working as computational biophysicist, I have gained rich experience on collaborating with experimental scientists to achieve scientific goals. My expertise and experience show strong evidences of successful achievements for numerical simulations of molecular motors. In the proposed research project, my large-scale simulation package will work with experimental results to reveal the mechanisms of kinesins' binding and motility features at atomic level.

1. **Lin Li**, Li C, Sarkar S, Zhang J, Witham S, Zhang Z, Wang L, Smith N, Petukh M, Alexov E.* ***DelPhi: a comprehensive suite for DelPhi software and associated resources,*** *BMC Biophys*, (2012) May14;4(1):9.
2. **Lin Li**, Chuan Li, Zhe Zhang, Emil Alexov, ***On the Dielectric "Constant" of Proteins: Smooth Dielectric Function for Macromolecular Modeling and Its Implementation in DelPhi****, J Chem Theory Comput*. 2013 Apr 9;9(4):2126-2136.
3. **Lin Li**, Joshua Alper, Emil Alexov, ***Multiscale method for modeling binding phenomena involving large objects: application to kinesin motor domains motion along microtubules***. *Scientific reports.* 2016 Mar 18;6:23249.
4. **Lin Li**, Zhe Jia, Yunhui Peng, Arghya Chakravorty, Lexuan Sun, and Emil Alexov. ***DelPhiForce web server: electrostatic forces and energy calculations and visualization.*** *Bioinformatics* (2017).

B. Positions and Honors

Positions and Employment

2017 – Assistant Professor, Department of Physics, University of Texas at El Paso
2016 – 2017 Research Assistant Professor, Department of Physics and Astronomy, Clemson University
2013 – 2016 Research Associate, Department of Physics and Astronomy, Clemson University
2011 – 2013 Postdoctoral Fellow, Department of Physics and Astronomy, Clemson University
2005 – 2011 Research Associate, Department of Physics and Astronomy, Huazhong University of Science and technology, China

Hornors

2019: NIH BUILDING SCHOLARS Summer Sabbatical Research Award
2019: University Research Incentive (URI) Program Award (University of Texas at El Paso)
2016: FASEB (Federation of American Societies for Experimental Biology) MARC Travel Award
2011: National Scholarship from Ministry of Education of the P.R. China (top 0.2% in China)
2005-2009: Excellent Leader of Student Groups in University in Huazhong University of Science and Technology (4 Consecutive years)
2002: National Scholarship from Ministry of Education of the P.R. China (top 0.2% in China)
2003-2004: Individual Scholarship in Huazhong University of Science and Technology (2 Consecutive years)
2002: The First Prize Scholarship in Huazhong University of Science and Technology

C. Contribution to Science

1. One of my main achievements is the development of new models and algorithms for DelPhi software package, which is very widely used software by many biophysics and biochemistry groups around the world to do the energy calculation for biomolecules. I have successfully developed many new algorithms to improve the performance of DelPhi. These developments result in three intellectual properties. One of the new algorithms is called Gaussian smooth algorithm, which models the protein as inhomogeneous material thus more accurate than the previous algorithms. These novel algorithms improve the accuracy of energy calculations for biomolecules, which is important for protein-protein interactions, protein folding, drug design and many other fields.

   a) **Lin Li**, Li C, Sarkar S, Zhang J, Witham S, Zhang Z, Wang L, Smith N, Petukh M, Alexov E.* ***DelPhi: a comprehensive suite for DelPhi software and associated resources,*** BMC Biophys, (2012) May14;4(1):9.
   b) **Lin Li**, Chuan Li, Zhe Zhang, Emil Alexov, ***On the Dielectric "Constant" of Proteins: Smooth Dielectric Function for Macromolecular Modeling and Its Implementation in DelPhi,*** J Chem Theory Comput. 2013 Apr 9;9(4):2126-2136.
   c) **Lin Li**, Chuan Li, Emil Alexov, ***On the Modeling of Polar Component of Solvation Energy Using Smooth Gaussian-Based Dielectric Function***, Journal of Theoretical and Computational Chemistry, 2014.
   d) **Lin Li**, Arghya Chakravorty, Emil Alexov. **DelPhiForce, *a tool for electrostatic force calculations: Applications to macromolecular binding***, *Journal of Computational Chemistry 38.9 (2017): 584-593*.

2. Another important work of mine is utilizing cutting edge techniques to parallelize computational programs. I worked on parallelizing DelPhi package to be able to perform the energy calculations on super large and complex systems, such as adeno-associated virus, which contains more than a million atoms. Using parallelized DelPhi and hundreds of CPUs, I obtained the periodical and symmetric distribution of electrostatic potential around the entire adeno-associated virus. Such symmetric electrostatic potential distribution indicates that the electrostatic forces play an important role in virus capsid assembly. Those electrostatic features

around the whole capsid of a virus are important to reveal the mechanisms of virus capsid assembly and essential for anti-virus drug design. The parallelized DelPhi is also used on membranes and microtubules, which reveals the electrostatic features of large pieces of membranes and microtubules.

a) Chuan Li, **Lin Li**, Jie Zhang, Alexov E.*, ***Highly efficient and exact method for parallelization of grid-based algorithms and its implementation in DelPhi***, J Comput Chem. (2012)
b) **Lin Li**, Lin Wang, Emil Alexov, ***On the energy components governing molecular recognition in the framework of continuum approaches***, Frontiers in Molecular Biosciences 2 (2015): 5.
c) Roberta Dias[$], **Lin Li[$],** Thereza A. Soares and Emil Alexov, ***Modeling the Electrostatic Potential of Asymmetric Lipopolysaccharide Membranes: The MEMPOT Algorithm Implemented in DelPhi,*** Journal of computational chemistry (2014). **([$] contributed equally)**
d) Chuan Li, **Lin Li**, Marharyta Petukh, Emil Alexov, ***Progess in developing Poisson-Boltzmann equation solvers,*** Molecular Based Mathematical Biology. Volume 1, Pages 42-62

3. I have worked on protein-protein/DNA/RNA interaction for many years. Compared to monomer structures, many complex structures are much more difficult to solve in experiments. However, the complex structures are usually crucial for studying functions of biomoleculs. My main goals are developing new algorithms to improve the protein-protein/DNA/RNA docking methodology and use new algorithms to predict complex structures for protein-protein/DNA/RNA. I have developed a protein-protein/DNA/RNA docking algorithm (ASPDock) to calculate binding free energy of protein-protein and protein-DNA complexes, which improves the accuracy of the complex structure predictions. ASPDock gives very good success rate in a large set of benchmarks. Besides ASPDock, I developed a Softly Restricting Method which uses biological information to enhance the success rate of protein-protein interaction predictions. I also developed a DelPhiForce program, which is able to calculate the binding force between biomolecules. Using ASPDock and Softly Restricting Method, I and my team have participated in two rounds of Critical Assessment of PRediction of Interactions (CAPRI). We got high-quality hits for T40 and T41 and the best LRMSD were 2.35 Å and 1.41 Å, respectively. (ranking 6th in 40+ teams).

a) **Lin Li**, Dachuan Guo, Yangyu Huang, Shiyong Liu, Yi Xiao*, ***ASPDock: protein-protein docking algorithm using atomic solvation parameters model,*** *BMC Bioinformatics*, 2011, 12(1): 36.
b) **Lin Li**, Yanzhao Huang, and Yi Xiao, ***How to Use Not-Always-Reliable Binding Site Information in Protein-Protein Docking Prediction***, PloS one 8.10 (2013)
c) Huang, Yangyu, Shiyong Liu, Dachuan Guo, **Lin Li**, and Yi Xiao. ***A novel protocol for three-dimensional structure prediction of RNA-protein complexes,*** Scientific reports 3 (2013).
d) **Lin Li**, Zhe Jia, Yunhui Peng, Arghya Chakravorty, Lexuan Sun, and Emil Alexov. ***DelPhiForce web server: electrostatic forces and energy calculations and visualization.*** *Bioinformatics* (2017).

4. Another research direction of mine is the study of important biological systems, such as molecular motors. Molecular motors are extremely important proteins, which are involved in various of functions, such as mitotics, organelle transport, cytoskeleton dynamics, cell movements and signal transduction. Dysfunctions of molecular motors lead to many human diseases. I have revealed important fundamental mechanisms of molecular motors. One of my recent studies on dynein-microtubule system demonstrates that the electrostatic force plays significant roles for dynein's binding to microtubule. The structures of dynein and microtubule result to elegant electrostatic interactions which make the dynein binding to microtubule in an accurate and robust way. With experimental evidences, I have also proved that the electrostatic binding energy is strongly related to the dynein's run length and velocity on microtubule. My other recent publications have validated that the interaction between kinesin's motor domain and microtubule is an important factor for molecular motors binding and motility features. My recent data has also revealed that mutations on kinesins causing the electrostatic force changes between kinesins and microtubules are strongly correlated to diseases. All of these findings on molecular motors are novel and exciting. These mechanisms of molecular motors are valuable for human health and fundamental research.

a) **Lin Li**, Joshua Alper, and Emil Alexov, ***Cytoplasmic dynein binding, run length, and velocity are guided by long-range electrostatic interactions*****,** *Scientific Reports 6 (2016).*

b) **Lin Li**, Joshua Alper, and Emil Alexov. ***Multiscale method for modeling binding phenomena involving large objects: application to kinesin motor domains motion along microtubules,*** *Scientific Reports,* 6 (2016): 23249.

c) **Lin Li**, Arghya Chakravorty, Emil Alexov. **DelPhiForce, *a tool for electrostatic force calculations: Applications to macromolecular binding***, *Journal of Computational Chemistry 38.9 (2017): 584-593*.

d) **Lin Li,** Zhe Jia, Yunhui Peng, Subash Godar, Ivan Getov, Shaolei Teng, Joshua Alper, and Emil Alexov. **Forces and Disease: Electrostatic force differences caused by mutations in kinesin motor domains can distinguish between disease-causing and non-disease-causing mutations.** *Scientific Reports* 7 (2017).

Complete List of Published Work in MyBibliography:

https://www.ncbi.nlm.nih.gov/sites/myncbi/1NMpzOw8vZ9QM/bibliography/47532210/public/?sort=date&direction=ascending

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

1SC1GM132043-01 Li (PI) 08/01/2019-07/31/2023
Developing and applying large-scale simulation approach to understand the mechanisms of kinesins' motilities along microtubules
The goal of this study is to develop a large-scale simulation approach to reveal the mechanisms of kinesins' motilities.
Role: PI

Completed Research Support

Department Startup Grant Li (PI) 09/01/2017-08/31/2019
University of Texas at El Paso
Research Start-Up Funds
The purpose of this grant is to help the PI to set up the research lab and support preliminary studies needed to be competitive for extramural research support.
Role: PI