Benjamin Andrew Himes

2021 May 13

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Research Outlook

The 3D structure and temporal dynamics of biological macromolecules determine their function. My research ambition is motivated by my day-to-day experience with other macroscopic problems; context matters! It is my goal to develop the tools needed to extend our understanding drawn from reductionist *in vitro* methodologies to the most physiologically relevant environment, the cell.

Education

University of Pittsburgh School of Medicine Thesis: Structure Determination of Heterogeneous Biological Specimens in Crowded Environments	**Molecular Biophysics**	PhD 2018
Pennsylvania State University	**Physics**	BS 2012
Galloup School of Lutherie	**Luthier**	2004

Professional Experience

Bioinformatics Specialist I (Niko Grigorieff)	HHMI RTI UMass Medical	May 2018 – April 2020
Postdoctoral Associate (Niko Grigorieff)	HHMI Janelia Research Campus	May 2018 – April 2020
Independent Graduate Scholar (Niko Grigorieff)	HHMI Janelia Research Campus	July 2017 – May 2018
Physics Teaching Assistant	Pennsylvania State University	Jan 2009 – May 2010

Research Technician	Center for Eukaryotic Gene Regulation (PSU)	May-Aug 2009,10,11

Invited Talks

"Maximizing label-free macromolecular detection in frozen-hydrated cells." *UMassMed RTI wip seminar,* May 2021 MA, USA

"Multi-scale classification of the floppy bits; using biological priors in emClarity." *SBGrid consortium seminar*, January 2021, Virtual, ~130 Attendees
https://www.youtube.com/watch?v=oDAmiq7e9xU

"Accurate solvent contrast in cryo-EM image simulation via coarse-grained all-atom inelastic scattering model for generalizable training in machine learning." *Stanford SLAC ML seminar*, March 2020 CA, USA (Cancelled COVID)

"Revisiting optimal tilt-schemes for enhanced contrast in cryo-ET" *cryoEM Granlibakken conference*, March 2020 CA, USA (Cancelled COVID)

"Making Medicine: investigating sub-cellular organization and structure using cryo-Transmission Electron Microscopy and Gpu-Accelerated Algorithms." *Nvidia GTC*, San Jose, CA, USA 2020 (Cancelled COVID)

"Understanding diagnostics and troubleshooting *in situ* image processing with emClarity."
"An introduction to high-resolution SPA and new features in *cis*TEM 2.0" *54th International School of Crystallography,* Erice Italy, June 2019

"New image processing tools and data collection strategies to get the most out of cryo-TEM", *Special Seminar, NIST Institute for Bioscience and Biotechnology Research,* Rockville MD, USA, May 2019.

"New tools and approaches for improved resolution of cellular 3D cryoEM." *Special Seminar,* Yale School of Medicine, New Haven CT, USA, April 2019.

"Optimizing data collection for cryoEM for 3D structures at better than 1 nm resolution *in situ.*" *Janelia Research Campus Symposium,* Ashburn Va, USA, Jan 2019.

"emClarity: enhanced macromolecular classification and alignment for high-resolution *in situ* tomography." *CCPEM Spring Symposium*, Keele University, UK, April 2018.

"Structural Studies of Chemosensory Arrays Approaching 1 nm Resolution : Challenges & Insights." *Receptor Fest XVIII*, Boulder CO, USA, August 2015

Publications

[¥] - Authors contributed equally
[v] – Corresponding author

1. Lucas BA[¥], **Himes BA**[¥], Xue L, Grant T, Mahamid J, Grigorieff N. Locating Macromolecular Assemblies in Cells by 2D Template Matching with *cis* TEM [Internet]. Cell Biology; 2021 Apr [cited 2021 May 3]. Available from: http://biorxiv.org/lookup/doi/10.1101/2021.04.20.440648 (In review at eLife)

2. Mendonça L, Sun D, Ning J, Liu J, Kotecha A, Olek M, Frosio T, Fu X, **Himes BA**, Kleinpeter AB, Freed EO, Zhou J, Aiken C, Zhang P. CryoET structures of immature HIV Gag reveal six-helix bundle. Commun Biol. 2021 Dec;4(1):481.

3. **Himes BA** [C], Grigorieff N. Cryo-TEM simulations of amorphous radiation-sensitive samples using multislice wave propagation [Internet]. Biophysics; 2021 Feb [cited 2021 May 3]. Available from: http://biorxiv.org/lookup/doi/10.1101/2021.02.19.431636 (In review at IUCrJ)

4. Cassidy CK, **Himes BA**, Sun D, Ma J, Zhao G, Parkinson JS, Stansfeld PJ, Luthey-Schulten Z, Zhang P. Structure and dynamics of the E. coli chemotaxis core signaling complex by cryo-electron tomography and molecular simulations. Commun Biol. 2020 Dec;3(1):24.

5. Gubins I, Xu M, Moebel E, Lai TM, Han X, Terashi G, Kihara D, **Himes BA**, Zhang J, Gao S, Hao Y, Lv Z, Wan X, Yang Z, Ding Z, Cui X, Zhang F. SHREC'19 Track: Classification in Cryo-Electron Tomograms. 2019;6.

6. **Himes BA**, Zhang P. emClarity: software for high-resolution cryo-electron tomography and subtomogram averaging. Nat Methods. 2018 Nov;15(11):955–61.

7. Cassidy CK, **Himes BA**, Luthey-Schulten Z, Zhang P. CryoEM-based hybrid modeling approaches for structure determination. Curr Opin Microbiol. 2018 Jun;43:14–23.

8. Ning J, Erdemci-Tandogan G, Yufenyuy EL, Wagner J, **Himes BA**, Zhao G, Aiken C, Zandi R, Zhang P. In vitro protease cleavage and computer simulations reveal the HIV-1 capsid maturation pathway. Nat Commun. 2016 Dec;7(1):13689.

9. Liu C, Perilla JR, Ning J, Lu M, Hou G, Ramalho R, **Himes BA**, Zhao G, Bedwell GJ, Byeon I-J, Ahn J, Gronenborn AM, Prevelige PE, Rousso I, Aiken C, Polenova T, Schulten K, Zhang P. Cyclophilin A stabilizes the HIV-1 capsid through a novel non-canonical binding site. Nat Commun. 2016 Apr;7(1):10714.

10. Cassidy CK[¥], **Himes BA**[¥], Alvarez FJ, Ma J, Zhao G, Perilla JR, Schulten K, Zhang P. CryoEM and computer simulations reveal a novel kinase conformational switch in bacterial chemotaxis signaling. eLife. 2015 Nov 19;4:e08419.

11. Fu X, **Himes BA**, Ke D, Rice WJ, Ning J, Zhang P. Controlled Bacterial Lysis for Electron Tomography of Native Cell Membranes. Structure. 2014 Dec;22(12):1875–82.

Posters

B.A. Himes, N. Grigorieff. “Improved motion correction for atomic-resolution cryoEM.” *HHMI Science Meeting*, Ashburn VA, October 2017

B.A. Himes, P. Zhang. “Snapshots of Dynamic Molecular Assemblies.” *Murnau Conference – Large Molecular Assemblies*. Murnau Germany, September 2016

B.A. Himes, P. Zhang. “Embracing Sample Heterogeneity in Large Molecular Assemblies.” *Three-Dimensional Electron Microscopy, Gordon research Conference*. Hong Kong, June 2016

B. A. Himes, C. K. Cassidy, F. J. Alvarez, J. Ma, G. Zhao, J. R. Perilla, K. Schulten, and P. Zhang, “CryoEM and computer simulations reveal a novel kinase conformational switch in bacterial chemotaxis signaling.” *Biophysical Society 59th Annual Meeting*, Baltimore, MD, Feb. 2015

Teaching

Lecture for Oxford DTP students Averaging and reconstructing 3D maps in cryo-ET	**Instructor**	April 28 2021
Lecture for UMassMed Graduate students The next revolution will not be purified!	**Instructor**	April 07 2021
emClarity workshop Yale I designed and led this workshop for 40 participants learning to use emClarity in the Yale cryoEM community hosted in the department of Microbial Pathogenesis.	**Instructor**	April 4 2019

emClarity workshop eBic	**Instructor**	April 8-10 2018

I designed and led this workshop for 10 participants learning to use emClarity at the eBIC at Diamond Light Source, Didcot, UK.

Special Topics MBSB: subtopic CryoEM	**Classroom TA**	January – May 2016

(I helped to design the course and led 20 % of the lectures independently)

Pennsylvania State University, Physics dept.	**Laboratory TA**	Three semesters

I also moderate an active mailing list dedicated to cryo-subTomogram averaging and classification as well as a wiki for my software emClarity. I believe it is important to ensure the algorithms I develop are put into practical, and ideally wide-spread, use.

Administrative

Seva work-study program	**Coordinator**	2015 - 2016
PSU chapter of the ASM	**Activities Chair**	2008 - 2009

Formal Languages

C++/C	Expert
Matlab	Expert
Cuda	Expert
Python	Advanced
Bash	Expert
SQL	Intermediate

Natural Languages

Spanish	Advanced
Italian	Intermediate
Mandarin	Elementary

Research Experience

Experimental:

I have a strong background in protein expression and purification, developed over three years spent working on structural studies of nucleosome core particles and chromatin remodeling proteins. While my day-to-day focus could be described more accurately as theory and computation, this wet-lab experience has been vital to my ability to clearly communicate and develop collaborative projects with other structural biologists. I am familiar with modern microscopes, having worked on numerous projects in sample preparation (cryo-Focused Ion Beam Milling) and data collection for low-dose cryo-Electron Tomography (FEI Polara and Titan Krios.)

Theory:

I have developed the software package **emClarity**. This implements a full image processing pipeline using GPU capable functions in Matlab along with core functions written directly in Cuda to implement both classical and novel algorithms, particularly suited to higher dimensional data. I am also developing new algorithms in ***cis*TEM** where one of my main projects has been writing an accurate and efficient image simulator that includes details necessary to study the rate limiting steps in modern cryoEM, particularly radiation damage, local specimen motion, and the complexities due to Ewald sphere curvature and the mixing of noise and signal in crowded and thick specimen.

References

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1. Lucas BA, Himes BA, Xue L, Grant T, Mahamid J, Grigorieff N. Locating Macromolecular Assemblies in Cells by 2D Template Matching with *cis* TEM [Internet]. Cell Biology; 2021 Apr [cited 2021 May 3]. Available from: http://biorxiv.org/lookup/doi/10.1101/2021.04.20.440648

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