BIOGRAPHICAL SKETCH

NAME: Gopinathan, Ajay

POSITION TITLE: Professor

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Indian Institute of Technology	M.Sc	05/98	Physics
University of Chicago	Ph.D.	08/03	Physics
UCSB/UCLA	Postdoctoral	05/06	Biophysics

A. Personal Statement

I am currently Professor and Chair of the Department of Physics and co-Director of the NSF CREST Center for Cellular and Biomolecular Machines (CCBM) at UC Merced. I received my Ph.D in Physics in 2003, from the University of Chicago, working on theoretical studies of colloids, elastic sheets and polymers. Following this, I was a joint postdoctoral fellow at UCLA and UCSB working on biopolymers with a focus on actin dynamics. My current research involves using ***theoretical and computational*** methods to understand biopolymer assemblies, biomechanics and biological transport at the molecular, cellular and multicellular scales. Examples include understanding cooperative behavior in molecular motor-driven intracellular transport; the role of membrane pore geometry and environment in gated transport through nuclear pores; actin based cellular motility; bacterial cell division and collective migration in cellular clusters and differentiating tissue. Our research has been funded by the NSF, McDonnell Foundation, UC MEXUS and via DOE. Honors include being named a Scialog Fellow by RCSA and the Moore Foundation, receiving the James S. McDonnell Foundation 21st Century Science Initiative Award, the George E. Brown, Jr. award, the UC Merced Chancellor's award, the UCM Senate Award for Distinction in Research and being elected a Fellow of the American Physical Society.

B. Positions and Honors

Positions and Employment

2003-2006 Postdoctoral Researcher, Materials Research Laboratory, University of California, Santa Barbara, CA.
2006-2012 Assistant Professor, Department of Physics, University of California, Merced, CA.
2012-2017 Associate Professor, Department of Physics, University of California, Merced, CA.
2017- Professor, Department of Physics, University of California, Merced, CA.
2018- Chair, Department of Physics, University of California, Merced, CA.

Other Experience and Professional Memberships

2016- Director, NSF CREST Center for Cellular and Bio-molecular Machines
2013-2015 Chair, Physics Graduate Group
2015- Editorial Board Member, Nature *Scientific Reports*
2015- Chair, UC Merced Committee on Research
2013 Principal Organizer, Aspen Center for Physics International Workshop on “Functional Biological Assemblies”
1999- Member, American Physical Society
2004- Member, Biophysical Society

Honors

2009	James S. McDonnell Foundation 21st Century Science Initiative Award
2010	George E. Brown, Jr. Award
2010	UC Merced Chancellor's Award
2014	Scialog Fellow – Moore Foundation and Research Corporation for Science Advancement
2017	UC Merced Senate Award for Distinction in Research
2019	Fellow, American Physical Society

C. Contributions to Science

Nuclear pore complexes : Gated transport across the nuclear membrane in cells is facilitated by nuclear pore complexes which are filled with polymeric disordered proteins. The mechanism of operation has been an open question for more than three decades. The prevailing paradigm was that the NPC interiors were unstructured and that the actual sequences of the disordered proteins were irrelevant. Based on the experimental findings of collaborator Michael Rexach (UCSC), our initial calculations indicated that there can be transitions between distinct polymer brush morphologies (open and closed states of the gate) which has led to the development of an experimental data driven theoretical model, "the forest model" or the "copolymer brush gate model" which is fundamentally different from existing models. Along with the experimental results, this hypothesized structure and mechanism was published in Molecular and Cellular Proteomics (2010) and was featured on the cover. We followed up with four more papers expanding on the physics of the gating mechanism. We also showed that the diblock structure necessary for our model was a conserved feature across different NPC proteins from yeast to humans. Our work also resolved many existing controversies, including indicating that results showing internal structure in the NPC which were long regarded as artifacts in the field were actually consistent. Commentaries on our work have been published in Cell: Structure (2010) and also cited in review papers in Nature (2011) and Science (2011) and many more since.

"Interactions between a fluctuating polymer barrier and transport factors together with enzyme action are sufficient for selective and rapid transport through the nuclear pore", S Ro, Ajay Gopinathan, Yong Woon Kim, Physical Review E 98 (1), 012403 (2018)
"*Cooperative interactions between different classes of disordered proteins play a functional role in the nuclear pore complex of Baker's yeast"*, D. Ando, A. Gopinathan, PLoS ONE 12(1): e0169455 (2017)
***"Nuclear Pore Complex Protein Sequences Determine Overall Copolymer Brush Structure and Function",* D Ando, R Zandi, YW Kim, M Colvin, M Rexach, A Gopinathan, Biophysical Journal 106 (9), 1997 (2014)
***"Physical Motif Clustering within Intrinsically Disordered Nucleoporin Sequences Reveals Universal Functional Features"*, D Ando, M Colvin, M Rexach, A Gopinathan, PloS one 8 (9), e73831 (2013)
"A Bimodal Distribution of Two Distinct Categories of Natively Unfolded Structures with Separate Functions in FG Nucleoporins", Justin Yamada; Joshua L Phillips; Samir Patel; Gabriel Goldfien; Alison Calestagne-Morelli; Hans Huang; Ryan Reza; Justin Acheson; Viswanathan Krishnan; Shawn Newsam; Ajay Gopinathan; Edmond Y Lau; Michael Colvin; Vladimir N Uversky; Michael F Rexach, Molecular and Cellular Proteomics 9, 2205 (2010)

Motor driven intracellular transport: Intracellular transport refers to material being transported between various organelles in the cell by means of molecular motors that can walk along cytoskeletal filaments (protein filaments such as actin and microtubules). These motors have the capacity to drag vesicles containing different material along with them to different destinations. In collaboration with K.C. Huang (Stanford), we have built a comprehensive model for the functioning of such motors with the aim of studying collective behavior of groups of motors (special invited issue of Journal of Physics: Condensed Matter (2011)). In a related collaboration with Jing Xu at UC Merced we are working on the unique transport characteristics of teams of kinesin motors and the influence of microtubule defects. Two papers have been published in Biophysical Journal (2016). Another interesting aspect is that the cytoskeletal network is not an ordered array of tracks, but actually has a complex geometry. Furthermore, the filaments that make up the network can be in a continual state of turn- over- shrinking, growing and getting chopped up- all of these processes being controlled by dozens of regulatory proteins. Our aim is to be able to understand how directed transport can take place in such a complex and

dynamic environment and what novel properties such types of transport could possess. Our explicit simulation work (Biophysical Journal (2015)) showed that the topology of the network is a critical determinant of transport and can indeed be optimally tuned for transport as in insulin secretion (Physical Review E, 2019).

"Anomalous intracellular transport phases depend on cytoskeletal network features", Bryan Maelfeyt, S.M. Tabei, Ajay Gopinathan, Physical Review E 99 (6), 062404 (2019)
"Membrane mediated motor kinetics in microtubule gliding assays", J Lopes, DA Quint, DE Chapman, M Xu, A Gopinathan, LS Hirst, Scientific reports 9 (1), 9584 (2019)
"Microtubule defects influence kinesin-based transport in vitro", Winnie Liang, K Faysal, Stephen King, Ajay Gopinathan, and Jing Xu, Biophysical Journal, 110(10), 2229 (2016)
***"Cytoskeletal network morphology regulates intracellular transport dynamics"*, D. Ando, N. Korabel, K.C. Huang, A. Gopinathan, Biophysical Journal, 109(8), (2015)
***"Cooperative protofilament switching emerges from inter-motor interference in multiple-motor transport*", D. Ando, M. K. Mattson, J. Xu, A. Gopinathan, Scientific Reports 4, 7255 (2014)

Cytoskeletal dynamics : Controlling the polymerization activity of cytoskeletal actin network plays an important role in cell motility. Even in the absence of motility, the actin network is not static but evolves via kinetic processes such as actin polymerization, depolymerization, capping, branching and severing which are regulated by various proteins in the cell. In collaboration with Nir Gov, we studied the coupling between actin dynamics and membrane shape and found a unifying picture that predicted the occurrence of both membrane ruffles and incipient filopodia. This formed a seminal work published in Biophysical Journal (2006). We studied the steady-state morphology of such networks and found that for in vivo values of the regulatory protein concentrations, the actin network morphology was maximally sensitive to changes in these concentrations, leading to the conclusion that the actin network system seemed to have evolved to be ultra-responsive to small changes in regulatory protein concentrations. This work was in collaboration with Andrea Liu (UPenn) and her group and published in Physical Review Letters (2007). Along these lines we have done more recent work in collaboration with Jen Schwarz (Syracuse) looking at how filopodial structures (thin needle like protrusions composed of actin bundles) form dynamically in in-vitro conditions from highly branched and dense “dendritic” networks of actin. Our work was able to reproduce many experimentally observed features and formed a comprehensive treatment of the process (Journal of Mathematical Biology (2010)).

“Dynamics of Membranes Driven by Actin Polymerization”, Nir Gov, and Ajay Gopinathan, Biophys .J , 90(2), 454 (2006)
“Branching, Capping, and Severing in Dynamic Actin Structures”, Ajay Gopinathan, J. Schwarz, K.C. Lee and A.J. Liu, Phys. Rev. Lett., 99, 058103 (2007)
"Modeling the formation of in vitro filopodia", K.-C. Lee, Ajay Gopinathan, J. M. Schwarz, (2009), Journal of Mathematical Biology 63(2), 229 (2011)

***"Conformational changes, diffusion and collective behavior in monomeric kinesin based motility"* K.C. Huang, C. Vega and Ajay Gopinathan, Journal of Physics: Condensed Matter, 23 (37), 374106 (2011)

Cell shape: This is a growing field with lots of unanswered questions especially relating to the feedback from mechanics to the biochemistry. We have argued for a new paradigm where the frustration between the chirality of the filament and the local shape of the cell wall with which it interacts makes it a sensitive “ruler” for curvature at scales significantly larger than the filament. Our theoretical work (Soft Matter, 2012, Biophysical Journal, 2016) and more recent experimental collaboration and validation (Nature Communications 2020) contribute to widening perspectives in this field. We also worked on the feedback between stress and growth, with my calculations making specific predictions for different scenarios which could be compared to experimental data from the Huang lab at Stanford (Biophysical Journal,2013). Another project involved looking at how mechanical forces from the environment (such as growth in an elastic medium) could affect the cell wall assembly and bacterial growth. Using finite element simulations we have been able to model the experimental scenario and a paper on this has been published in Molecular Microbiology (2012). Finally our investigations into the force production in the bacterial contractile ring resolved a long-standing puzzle in the field and resulted in an article in the Proceedings of the National Academy of Sciences, USA (2012).

"Chiral twisting in cytoskeletal polymers regulates filament size and orientation", Handuo Shi, David Quint, Greg Grason, Ajay Gopinathan, Kerwyn Casey Huang, Nature Communications 11 (1), 1-12
"Growth of Form in Thin Elastic Structures", Salem Al Mosleh, Ajay Gopinathan and Chris Santangelo, Soft Matter, 14, 8361 (2018)
"Shape selection of surface-bound helical filaments: biopolymers on curved membranes" D. A. Quint, A. Gopinathan and G. M. Grason, Biophysical Journal **111,** 1575 (2016)
"Mechanical Consequences of Cell-Wall Turnover in the Elongation of a Gram-Positive Bacterium", G Misra, ER Rojas, A Gopinathan, KC Huang, Biophysical journal 104 (11), 2342-2352 (2013)
"Measuring the stiffness of bacterial cells from growth rates in hydrogels of tunable elasticity" Tuson Hannah H.; Auer George K.; Renner Lars D.; et al., Molecular Microbiology, 84(5), 874 (2012)
"Conformational collapse of surface-bound helical filaments", David Quint, Ajay Gopinathan and Greg Grason, Soft Matter 8 (36), 9460-9468 (2012)
"Nucleotide-dependent conformations of FtsZ dimers and force generation observed through molecular dynamics simulations" , Jen Hsin, Ajay Gopinathan and K.C. Huang, Proc. Natl. Acad. Sci. USA, 109 (24): 9432 (2012)

Collective behavior and foraging: The emergence of collective phenomena and behaviors from simple individual rules is a recurring theme in biology. We look at a variety of problems involving collective motion of biological entities ranging from cells to organisms. We study swarms of organisms with agent based computer models and have asked how disorder affects swarming - whether the disorder is in the form of fog or obstacles or even variations in behavior among individuals due to disease or evolution or even mechanical failure in robotic swarms. We found that there is a critical amount of disorder that swarms can tolerate beyond which the system is able to self-organize in different ways, including sorting to leave behind defective swarmers, to overcome the disorder. In related work we have also shown that collective foraging can be beneficial. Recently we have discovered that new modes of collective motility enhance robust chemotaxis in migrating malignant lymphocyte clusters (Science Advances 2018)

***"Frustration-induced phases in migrating cell clusters",* Katherine Copenhagen, Gema Malet-Engra, Weimiao Yu, Giorgio Scita, Nir Gov and Ajay Gopinathan, Science Advances, 4 (9), eaar8483 (2018)
"Cell cluster migration: Connecting experiments with physical models", Ajay Gopinathan and Nir Gov, Seminars in Cell and Developmental Biology https://doi.org/10.1016/j.semcdb.2018.09.009 (2018)
" Multifactorial Optimizations for Directing Endothelial Fate from Stem Cells", Drew E. Glaser, William S. Turner, Nicole Madfis, Lian Wong, Jose Zamora, Samuel Reyes, Andrew Burns, Ajay Gopinathan, Kara E. McCloskey, PLoS ONE 11(12): e0166663 (2016)
"Topologically induced swarming phase transition on a 2D percolated lattice", D. Quint, A Gopinathan, Physical Biology, 17,12(4) 046008 (2015)
***"Optimal cooperative searching using purely repulsive interactions",* N. Tani, A. Blatt, D. Quint, A Gopinathan, Journal of Theoretical Biology, 361, 159–164 (2014)
**"Active matter clusters at interfaces.", K. Copenhagen and A. Gopinathan , Front. Mater. 3:13. doi: 10.3389/fmats.2016.00013

** *publications with undergraduate or graduate authors under my primary supervision*