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Subject: Recommendation letter for Arpita Upadhyaya

Cambridge, November 28, 2004.

Dear Search Committee,

This letter is in reference to Arpita Upadhyaya who is applying for the position of Assistant Professor at your Department. Arpita is my first post-doc. I was very fortunate to attract Arpita to my new lab at the end of 2000. In the Summer of 2001 Arpita obtained the very prestigious and competitive Papparlardo Fellowship in Physics. Each year the Physics Department at MIT awards about three fellowships to rising stars in Physics. We typically receive about 100 application per year uniformly distributed across the different fields of Physics. The Pappalardo fellow position is similar to the Harvard fellows and the Berkeley Miller fellows. The fact that Arpita obtained this position by competing with talented string theorists, atomic physicists, etc. clearly demonstrates her potential as a young scientist. The fellowship provided Arpita with more scientific freedom allowing her to collaborate with groups inside and outside of MIT. Below I will focus on the work that Arpita performed in collaboration with our lab.

The first major impact that Arpita made involved the development of a new experimental technique that allows quantitative measurements of the mechanical forces generated during actin polymerization. Arpita synthesized phospholipid vesicles that are coated with the protein ActA that she purified from *Listeria monocytogenes*. This protein allows actin filaments to nucleate at the membrane interface. Since the vesicles are flexible objects they can be used as force sensors. By carefully quantifying the shape deformation Arpita deduced the mechanical forces exerted by the polymerizing actin gel. Surprisingly she found that actin can both push and pull on the membrane. Arpita headed all the different aspects of the project. She purified the necessary molecules, she fluorescently labeled the proteins, synthesized the vesicles, performed all the microscopy and data analysis. Together with a graduate student she also development a numerical model that reproduced the dynamics of the vesicle motion. Because of the simultaneous pulling and pushing forces vesicles perform a characteristic stepping motion. Arpita's model provided a convincing argument for the origin of this instability. Arpita's results were published in *PNAS* and received a lot of attention including the Editor's choice in *Science*. Additionally her work let to the invitation to write two reviews for *Current Biology*. One is an extensive overview on biomimetic systems that are used to explore the forces generated during actin polymerization. The second review is a shorter dispatch. She took the lead in both these publications. Arpita is a great writer. She is one of the few students who hands in close to perfect manuscripts. Her work on the vesicles also resulted in an invited talk at the annual meeting of the American Society of Cell Biology. She gave a wonderful presentation.

The second main project that Arpita headed, involved the biomechanical aspects of the contraction of Vorticella. Vorticella is a small organism that lives in ponds and consists of a cell body of about 20 μm that is connected to a slender stalk of about 200 μm. The stalk can contract extremely fast. A full contraction occurs in about 1 ms. Arpita performed high-speed microscopy and was able to attach small beads to the stalk to characterize the local contraction properties. By varying the external viscosity she deduced the force-velocity relation for this biomechanical spring. By carefully tracking beads connected to the stalk she showed that contraction starts at the cell body and propagates down to the base of the stalk. We think that the contraction is initiated due a misbalance between the electrostatic forces trying to straighten the stalk and the entropic tendency to collapse the coil. The manuscript is almost ready to be sent out to *Biophysical Journal.*

The last and most recent project involves the symmetry breaking of a polymerizing actin gel. Based on her earlier work Arpita developed a new method in which giant vesicles (> 10 μm in diameter) are compressed by an external polymerizing actin gel. Arpita found that for small vesicles the initially symmetric actin gel breaks symmetry, resulting in a vesicle that is propelled by the polymerizing actin gel. However big vesicles do not break symmetry and get crushed as a result of the growing gel. She developed a model that involves the mechanical stresses in the gel that build up during polymerization and the stresses in the membrane. We plan to send this work to *Current Biololgy* soon.

In summary I think Arpita is a very talented biophysicist with an extensive expertise in cellular biomechanics. I strongly recommend her for the position of Assistant Professor without any reservations. She is a great experimentalist, she gets things working and has the patience necessary for these difficult experiments. She has an easy-going personality and is pleasant to communicate with. Arpita is very popular among undergraduates and she mentored 5 undergraduates during their senior theses. She will be a great teacher and mentor. She already proved this through her successful collaborations with the MIT undergraduate and graduate students. Her presentations are very clear and her writing skills are excellent. This will come in handy during application for grants. I strongly recommend you to invite Arpita to your Department for a presentation. You will love it. Please let me know if you need any further information.

Sincerely,

Alexander van Oudenaarden
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