INDIANA UNIVERSITY

DEPARTMENT
OF PHYSICS

November 23, 2004

Biocomplexity Faculty Search Committee,
c / o Prof. Rob de Ruyter van Steveninck,
Department of Physics,
Indiana University,
Swain Hall West 117,
Bloomington IN, 47405-7105

Dear Dr. de Ruyter:

Dr. Arpita Upadhyaya did her Ph.D. research with me in experimental biological physics and I have followed her progress closely ever since.

Arpita was the strongest of my experimentally-focused students and has gone from success to success since her graduation. Her Pappalardo fellowship at M.I.T. is a strong endorsement of her achievements and promise. She is already conducting novel research of the highest caliber—work that will be fundamental to her field. She should definitely be on your shortlist.

Arpita is an outstanding researcher, creative, disciplined, extremely hard working and with an excellent grasp of theory, computation and experimental techniques. Her proposed projects dealing with the mechanisms of force generation by actin at the cell membrane, cell polarity and direction sensing and surface forces in tissues address some of the most important current problems in biological physics. For example, leading edge formation by actin polymerization is the basis of all cell motility, whether chemotactic, haptotactic or due to differential adhesion, and motility is essential to embryonic development, wound healing and cancer metastasis. Despite the extensive simulations and models of Oster, Arkin, Othmer and others, we have little quantitative experimental data on what happens at a leading edge. The development of cell-free assays for the leading edge (*e.g.* by Borissy and Palmer) has provided new impetus for trying to derive a complete model. Arpita's work with van Ourdenaarden has given ample evidence that her ambitious program will be successful. It will genuinely revolutionize the subject.

Arpita commands a great variety of experimental techniques. During her time with me she studied the mechanisms of cell migration in embryonic development. Most of her experiments used random aggregates of cells from various tissues from embryonic chicken. She developed fluorescent staining protocols to label cells and track their motion in aggregates using scanning

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confocal microscopy and studied the diffusion constants and velocity correlations of clusters of cells as a function of cluster size and actin polymerization inhibition. She worked with Prof. Forgacs at Clarkson University to use his microbalance apparatus to measure surface tensions and viscosity in these tissues. She conducted similar studies in *hydra* both at Notre Dame and in the laboratory of Prof. Sawada at Tohoku University, Sendai, Japan, focusing on engulfment in two-dimensional aggregates. She also collaborated with Prof. Sheetz at Duke, using laser tweezers to measure the tension of *in vitro* endoplasmic reticulum-like tubular membrane networks. In her first postdoc at MIT she learned more molecular biological and genetic techniques as well as sophisticated microfabrication and cell culture methods, while her second postdoc has given her a varied array of microscopic techniques to address actin polymerization. I can see a whole series of problems on molecular machines which she might address using her methods.

I am particularly impressed by the coherence of Arpita's research vision, taking force generation from the level of regulation to the level of tissues. Her breadth and focus on fundamental mechanisms is distinctively physical in philosophy and a perfect example of how physicists can make fundamental contributions to both biology and physics. I am certain that Arpita will have no difficulty developing an empty laboratory into a flourishing research program.

Arpita has a strong track record both of collaboration and independence (as you can see from her publication record). She has the tact and interest to reach out across disciplinary barriers to work with biologists, biochemists and medical researchers.

While she has not taught any lecture courses, she did have extensive teaching experience as a student and is a strong, clear and well-organized speaker. I expect she will be a strong teacher as well and be successful in balancing teaching and research commitments. She is patient and generous with her time and will be an excellent mentor for her students. Already as a graduate student, she was crucial to my laboratory in training and supervising more junior graduate students and both term-time and summer undergraduate researchers.

The funding climate for the types of work Arpita is doing is as good as for any current subject. Her combination of techniques and vision seem right on the money. I expect that she will find both NSF and NIH funding rapidly and relatively painlessly. She is an experienced grant-writer, having already helped me on proposals when she was a graduate student.

In hiring Arpita, you will be buying-in to path-breaking research on crucial problems in one of the fastest growing and most exciting areas of physics. Arpita

has the drive and ability for a spectacular career and deserves your full backing. She will amply repay the trust you place in her.

Sincerely,

James A. Glazier
Professor of Physics, Director, Biocomplexity Institute,
Adjunct Professor of Biology and Informatics