

December 3, 2007

Graduate Research Fellowship Selection Committee
National Science Foundation

Dear members of the NSF GRFP committee:

I am extremely pleased to unequivocally support Aaron Goldman's application for a NSF Graduate Research Fellowship. I currently am an Associate Professor in the Department of Microbiology at the University of Washington (UW) and the principal investigator of a Computational Biology research group currently numbering about 30 members (including undergraduate, graduate, and postdoctoral fellows). My group performs state of the art research on the computational modelling of protein and proteome structure, function, and interactions at both the single molecule and the systems/pathways levels and has produced over seventy publications <<http://compbio.washington.edu/cv.html>>.

I have trained more than 50 mentees, many of whom have gone on to independent research positions in academia, industry, and government. We have published nearly eighty papers, more than fifty of which were written by my group. I am also the Chair of the Admissions Committee at the Department of Microbiology, and thus I usually go over nearly 200 applications each year. It is this broader context that I am primarily using to rate Aaron's accomplishments.

Aaron Goldman first came to my group as a rotation student, mostly trained in bench experimental techniques and with little or no computer science or programming experience. In our group, we have developed algorithms to predict "functional signatures" of proteins, i.e., quantifying how every atom in a protein structure (or every residue in a protein sequence) contributes to its function depending on context. For example, the HIV protease in a host cell cleaves a polyprotein, but a small molecule may inhibit or induce cleavage, and the locations of the atoms influential to these processes may be different. Simplistically, a functional signature can be thought of as a "profile" representing the most important functional residues in a protein. Our current functional signature prediction algorithms take into account sequence conservation, evolutionary history, and structure.

Aaron's initial project was to compare the evolutionary lineages of the Hmd class of proteins in the thermophile *Methanococcus maripaludis*. Though he had no previous computer science experience, he designed and implemented his rotation project almost completely on his own and chose to continue to work in my group as a computational biologist. Specifically he was able to visually classify functional signatures of proteins and provided preliminary results that indicated that he could annotate proteins of unknown function, place them in the proper clade in an evolutionary lineage, identify residues most important for protein function, and also use this knowledge for the design of proteins not observed in nature. After his rotation, he continued working on this project and is in the process of rigorously developing a fully automated algorithm that is more complex and accurate (that will also be made available on the Web), the subject of which is detailed in his research application.

The solutions Aaron has come up with are largely a product of his independent work, and his manuscripts are written with very little intervention on my behalf. In this regard, Aaron is the best student I have encountered at any level and stands out at the top in my group. This is due to the fact that he was able to seamlessly transition from bench science into a computational one, acquiring the admiration of members of my group, his fellow classmates, and faculty in both the departments of Microbiology and Astrobiology. Of particular note is that Aaron accomplished these goals within the span of a year.

Besides being an outstanding scientist, Aaron is also actively involved in program and departmental activities. He has been a teaching assistant for multiple undergraduate classes, is running the course website for one undergraduate class, and has been organising our departments student talks, which demonstrates his dedication to education. Without a doubt, Aaron has all the makings of a successful principal investigator. As indicated by his rapid progress thus far, Aaron has a very broad range of knowledge and experience that he instinctively draws upon to find creative solutions to difficult problems, regardless of their nature. He is very productive and is able to balance many obligations at once without difficulty. He is both an independent researcher and a talented communicator, and is the type of student that a faculty member dreams of having work in their group. All of these qualities combine synergistically to make Aaron a clever, capable, and dynamic individual.

For his dissertation, I have given Aaron a challenging topic that will be an essential component of my groups work and will consist of broad impacts and accomplishments in computational biology in the areas of protein and proteome function, interactions, evolution, and design. I am absolutely confident that Aaron will perform outstanding research and my support for his application is unequivocal. A NSF Graduate Research Fellowship would give the freedom for Aaron to pursue highly difficult problems in biology that would be of utility for biologists worldwide, and also assist the career development of this talented young scientist.

Please feel free to contact me if you need further information.

Sincerely,

A handwritten signature in purple ink, appearing to read 'Ram Samudrala', with a horizontal line underneath.

Ram Samudrala