



Division of
Basic Sciences

Laboratory of
Experimental and
Computational Biology

Structural
Glycobiology
Section

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Dr. Pradman K. Qasba

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To,

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

Dear Chair,

I am very pleased to write this letter in support of Dr. Kannan Gunasekaran's application for tenure-track faculty position.

Dr. Gunasekaran is a fine computational biologist with potential to make original contributions to the biological research. Dr. Gunasekaran has an excellent understanding of his area of interest. He is very competent in applying a wide range of computational methods, starting from analysis of peptide and protein structures to molecular dynamics simulations, to solve challenging biological problems that are of immense importance. It is extremely hard to find a scientist like Dr. Gunasekaran with his multifarious skills and talent in an important research field. Dr. Gunasekaran possesses overwhelming and extraordinary knowledge in the computational structural biology.

I know Dr. Gunasekaran's previous and present research accomplishments since I work in a research area that overlaps with his research interest. Furthermore, since we have started collaborating on a joint research project, I have come to know his broad and exemplary understanding of the structure and dynamics of proteins. Dr. Gunasekaran got his undergraduate training in Physics from Indian Institute of Technology (IIT), Pawai, Mumbai (called Bombay earlier), India. IITs are the premier undergraduate technology institutes of India, equivalent to MIT or CalTech of US, where student admissions are highly competitive. After having his Masters degree in Physics, he did his Ph.D. from Indian Institute of Sciences (IISc), Bangalore, India, a premier research center in India, where he worked with a research group that has pioneered the work on the conformational analysis of proteins.

Dr. Gunasekaran, during his Ph.D., analyzed the high-resolution protein crystal structure database and showed the presence of conformationally disallowed residues in the crystal structures of proteins. This finding makes a very fine contribution for structure prediction and molecular modeling

of proteins. He has further carried out conformational analysis of protein motifs and developed rules, which can be used in structure prediction, peptide motif design and protein engineering. Since proteins function through their conformation, these aspects have very high impact on understanding how do they act and why. His original works have been published in highly rated journals such as *Journal of Molecular Biology*, *Biochemistry* and *Current Opinion in Structural Biology*. During his postdoctoral research at the University of Massachusetts at Amherst, USA, he has investigated the protein folding mechanism, through theoretical approaches. He developed a method to detect the hydrophobic core in a predominantly beta-sheet rich protein that has a high sequence variability and conserved fold. He was associated with Dr. Lila Gierasch, who is a well-known experimentalist in the field of peptide and protein structural analysis by NMR, and with Dr. Arnold Hagler, who founded Biosym, Inc. (now Accelrys, Inc.).

Dr. Gunasekaran's Ph.D. and post-doctoral work in the University of Massachusetts at Amherst made important contributions in the area of conformational analysis of proteins. The quality and impact of Dr. Gunasekaran's research work is very much evident from the citations (200 plus) that his Ph.D. and post-doctoral works have received internationally.

Since he joined NCI-Frederick (April, 2001), he is exploring the dynamics and functional mechanism of beta1,4 galactosyltransferase protein in collaboration with my group. This protein is a molecular machine involved in synthesis of lactose in breast milk. This collaboration resulted in a combined publication in *Biochemistry*. Significantly, the paper was selected as 'hot article' by the journal and was highlighted in the *Biochemistry* and *ACS* web sites. Through multiple sets of molecular dynamics simulations, he showed that the movement of the functional long loop is modulated by another interacting loop that has multiple conserved glycines, which supported our earlier experimental observations on the protein. Dr. Gunasekaran also continued and extended his molecular dynamic study to investigate the generality of the mechanism in two other proteins that have different folds, sequence and function. This work also resulted in a recent publication in the *Journal of Molecular Biology*.

Dr. Gunasekaran has also been working on many other projects all of which have been very productive. During the last three and half years of stay in NCI-Frederick, he has published several first author and co-authored articles. This is indeed remarkable. Dr. Gunasekaran has been working on disordered or natively unstructured proteins. In an article published in *TIBS*, Dr. Gunasekaran and co-authors proposed that disordered proteins provide a simple solution to having large intermolecular interfaces, but with smaller protein, genome and cell sizes. In a recently published paper in the *Journal of Molecular Biology*, Dr. Gunasekaran elegantly showed that stable protein monomers can be distinguished from the unstable based on the analysis of disordered and ordered protein complexes. He also worked on the amyloidogenic proteins such as gelsolin and beta2-microglobulin and proposed plausible fibril models. All these works point to multifarious skills and talent of Dr. Gunasekaran.

Dr. Gunasekaran possesses strong interpersonal and management skills in addition to his excellent track record of scientific achievements. He is well versed with computer programming as well as development of tools. He is an asset for any organization devoted to drug discovery and

macromolecular sequence, structure, and function analysis. He is exceptionally qualified for the tenure track faculty position. Therefore, I strongly support his application. If you require any additional information please feel free to contact me.



Dr. Pradman K. Qasba, Ph. D.

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