Kannan '**Guna'**sekaran
National Cancer Institute, Frederick MD

December 31, 2004

To
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 Committee Member,

I am writing to apply for the Assistant Professor position in the College of Arts and Sciences at Indiana University, Bloomington. I am currently working at the National Cancer Institute, Frederick. For the past ten years, my research work has focused on computational structural biology and bioinformatics. I believe that my knowledge of protein structures would well complement the existing strengths in the biocomplexity institute. Moreover, I have strong motivation to carry out research in the systems biology area focusing on proteins, such as the natively unstructured synucleins, that are involved in various neurodegenerative diseases.

I have frequently interacted with experimental scientists on research projects aimed at addressing biological questions. My Ph.D. work centered on stereochemistry of polypeptide chains, and developing and applying analysis tools to study protein structures. Specifically, the focus was on stereochemical rules defining motifs, such as β-hairpins and α-helix termination signals, with the aim of providing lessons for *de novo* design and protein engineering.

My post-doctoral work at the University of Massachusetts at Amherst focused on the protein folding problem, and was well tied with the ongoing experimental research in the lab. I applied various computational techniques and developed a method to detect and explore the hydrophobic core that controls folding. At the NCI-Frederick, I studied the "disordered" proteins and functional mechanisms. The current research focus is on the systems biology approach to address how and why some proteins are able to interact with multiple proteins in the protein-protein interaction network map.

I apologize for not making the December 15, 2004 deadline. Please let me know if it would be possible to consider my application at this stage. If I am not too late, I would be happy to request my mentors to send recommendation letters.

I would be glad to discuss further my research background and future research plans. I am grateful for your time and consideration, and look forward to hearing from you. Thank you.

With best regards,

Guna
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Encl: Curriculum Vitae, Research Plan, and Teaching Statement

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Education and Professional Experience:

2003 -	Scientist II (computational)	SAIC-Frederick, Inc., NCI-NIH, Frederick, USA	Computational Biology & Bioinformatics
2001 - 2003	Research Fellow	NCI-NIH, Frederick, USA	Computational Biology
1998 - 2001	Post Doctoral Fellow	University of Massachusetts, Amherst, USA	Computational Structural Biology - Protein Folding
1993 - 1998	Ph. D.	Indian Institute of Science, Bangalore, India	Biophysics - Database Creation & Analyses
1991 - 1993	M. Sc.	Indian Institute of Technology, Mumbai, India	Physics
1988 - 1991	B. Sc.	Bangalore University, Bangalore, India	Physics, Chemistry and Mathematics

Research Summary:

NCI - Research Fellow, SAIC-Inc. - Scientist: Database analyses and molecular dynamics simulations on peptides and proteins probing functional mechanisms ● Analyses of disordered or natively unstructured proteins to query the reason for their large occurrence in the genome and to predict the stable and unstable monomers ● Conservation analyses aimed at recognizing signatures leading to Amyloid disease ● Systems biology approaches to probe the functional sites and predict interacting proteins ● Analysis of central and edge located β-sheet proteins in a network of protein-protein interactions in the context of Amyloid disease

PDF: Extensive study on cellular retinoic acid-binding protein probing the hydrophobic core that controls folding ● Applied various theoretical approaches to study protein folding ● Developed a method to detect conserved network of interactions and hydrophobic core for a given protein family ● Facilitated to initiate a series of experimental research based on the theoretical work ● Developed an algorithm to identify aromatic-aromatic stacking interactions from the Protein Data Bank ● Worked in an experimental group

Ph.D.: Stereochemical analysis on protein structures aimed towards providing lessons for design, engineering and prediction ● Creation of context free non-redundant structural and of function-specific sequence databases for motif analyses ● Extensive programming in C to search and analyze structural motifs ● Application of statistical methods and structural modeling techniques ● Identification of rules for α-helix termination signals and disallowed backbone conformations ● Collaborated with an experimental group

Research Interests:

Elucidating the structure, function, and interaction of proteins of interest ■ Developing binding site, functional mechanism and protein-protein interaction network databases ■ Developing new tools and applying existing methods to specific systems which are of interest to collaborative experimental research ■ Finding new correlations among heterogeneous and large data produced by genome analyses ■ Analyzing, predicting and altering protein function and specificity ■ Protein folding and prediction of structure and function

Publications:

Research Papers:

(1) **K. Gunasekaran**, C. Ramakrishnan and P. Balaram (1995) Stereochemical analysis of the antigenic tip of the V3 loops peptide of HIV-1 gp120. *Int. J. Peptide Protein Res*. **46**, 359-365.

(2) **K. Gunasekaran**, C. Ramakrishnan and P. Balaram (1996) Disallowed Ramachandran conformations of amino acid residues in protein structures. *J. Mol. Biol.* **264**, 191-198.

(3) **K. Gunasekaran**, C. Ramakrishnan and P. Balaram (1997) β-hairpins in proteins revisited: Lessons for De novo Design. *Protein Engg.* **10**, 1131-1141.

(4) **K. Gunasekaran,** H. A. Nagarajaram, C. Ramakrishnan and P. Balaram (1998) Stererochemical punctuation marks in protein structures: Glycine and Proline containing helix stop signals. *J. Mol. Biol.* **275**, 917-932.

(5) **K. Gunasekaran,** L. Gomathi, C. Ramakrishnan, J. Chandrasekhar and P. Balaram (1998) Conformational interconversions in peptide β-turns: Analysis of turns in proteins and computational estimates of barriers. *J. Mol. Biol.* **284**, 1505-1516.

(6) **K. Gunasekaran** (1999) Thesis abstract: Stereochemical analysis on protein structures-lessons for design, engineering and prediction. *The Journal of the Indian Institute of Science* **80**, 485-488.

(7) **K. Gunasekaran**, S. J. Eyles, A. T. Hagler and L. M. Gierasch (2001) Keeping it in the family: Folding studies of related proteins. *Curr. Opin. Struct. Biol.* **11**, 83-93.

(8) **K. Gunasekaran**, B. Ma, B. Ramakrishnan, P. K. Qasba and R. Nussinov (2003) The interdependence of backbone flexibility, residue conservation and enzyme function: A case study on β1,4galactosyltransferase. *Biochemistry* **42**, 3674-4687. (*selected as 'hot article', highlighted in Biochemistry and ACS websites*)

(9) **K. Gunasekaran**, C-J. Tsai, S. Kumar, D. Zanuy and R. Nussinov (2003) Extended disordered proteins: Targeting function, with less scaffold. *Trends in Biochemical Sciences* **28**, 81-85.

(10) H. Benyamini, **K.Gunasekaran**, H. Wolfson and R. Nussinov (2003) Conservation and amyloid formation: A study of gelsolin-like family. *Proteins:Structure, Function and Genetics* **51**, 266-282.

(11) H. Benyamini, **K. Gunasekaran**, H. Wolfson, and R. Nussinov (2003) β2-microglobulin amyloidosis: Conservation analysis and fibril modeling using docking technique. *J. Mol. Biol.* **330**, 159-174.

(12) **K. Gunasekaran**, B. Ma, and R. Nussinov (2003) Triggering loops and enzyme function: Identification of loops that trigger and modulate movements. *J. Mol. Biol.* **332**:143-159. (*highlighted in BioMedNet, and faculty 1000*)

(13) A. Oron, **K. Gunasekaran**, H. Wofson, and R. Nussinov (2003) Computation of electrostatic potentials and their contribution to interactions. *Protocols in Bioinformatics* 8.4.1-8.4.12.

(14) **K. Gunasekaran**, A. T. Hagler and L. M. Gierasch (2004) Sequence and structural analysis of cellular retinoic acid binding proteins reveals a network of conserved hydrophobic interactions. *Proteins:Structure, Function and Bioinformatics* **54**:179-194. (*cover article*)

(15) **K. Gunasekaran**, and R. Nussinov (2004) Modulating functional loop movements: the role of highly conserved residues in the correlated loop motions. *ChemBioChem* **5**:224-230.

(16) **K. Gunasekaran**, B. Ma, and R. Nussinov (2004) Is allostery an intrinsic property for *all* dynamic proteins? *Proteins: Structure, Function and Bioinformatics* **57**:433-443.

(17) H.-H. (Gavin) Tsai, D. Zanuy, N. Haspel, **K. Gunasekaran**, B. Ma, C.-J.Tsai, and R. Nussinov (2004) The stability and dynamics of the human calcitonin amyloid peptide DFNKF. *Biophysical J.* **87**:146-158

(18) **K. Gunasekaran,** C-J. Tsai and R. Nussinov (2004) Analysis of ordered and disordered protein complexes reveals structural features discriminating stable and unstable monomers. *J. Mol. Biol.* **341**:1327-1341 (*corresponding author*)

(19) D. Zanuy, **K. Gunasekaran**, B. Ma, H.-H. Tsai, C.-J. Tsai, R. Nussinov (2004) Insights into amyloid structural formation and assembly through computational approaches. *Amyloid* **11**:143-161

Published Abstracts:

(20) L. M. Gierasch, S. J. Eyles, J. A. Habink, **K. Gunasekaran**, M. Kosinski and K. S. Rotondi (2000) *Biophysical J.* **78**, 129A-129A. The roles of local sequence and global interactions in the folding of a predominantly β-sheet protein.

(21) M.S. Kosinski, J.A. Habink, **K. Gunasekaran** and L.M. Gierasch. (2000) *Biophysical J.* **78**. Dissecting the hydrophobic core of a β-clam protein.

(22) C. M. McIntosh, **K. Gunasekaran**, A. Kapurniotu and L. M. Gierasch. (2000) *FASEB J.* **14**, A1350-A1350. Conformational analysis of a constrained human calcitonin analogue.

(23) **K. Gunasekaran**, B. Ma, B. Ramakrishnan, P.K. Qasba and R. Nussinov (2002) *Biophysical J.* **82**, 2372. Molecular dynamics simulations on β1,4-galactosyltransferase-1: Flexible regions and conserved positions in the ligand binding mechanism.

(24) H. Benyaminy, **K. Gunasekaran**, H. Wolfson, R. Nussinov (2002) *Protein Science*, suppl. 1, **11**, 73. Conservation and amyloid formation: A study of the gelsolin-like family.

(25) **K. Gunasekaran**, B. Ma, B. Ramakrishnan, P.K. Qasba, R. Nussinov (2002) *Protein Science*, suppl. 1, **11**, 137. The interdependence of backbone flexibility, sequence conservation and function in β1, 4-galactosyltransferase.

(26) **K. Gunasekaran**, B. Ma, R. Nussinov (2003) *Biophys J., suppl.* **84**, 12A-13A. Loops that trigger and modulate functions: An evolving common mechanism in enzymes

(27) **K. Gunasekaran**, C-J. Tsai, N. Haspel, S. Kumar H. Wolfson, R. Nussinov (2003) *Biophys J., suppl.* **84**, 163A-163A . Extended disordered proteins: An elegant solution to having large intermolecular interfaces, yet keeping smaller genome and cell sizes

Conference/Symposium Presentations:

(28) S. J. Eyles, J. A. Habink, **K. Gunasekaran** and L. M. Gierasch. Roles of Proline residues in the structure and folding of a β-clam protein. 16th American Peptide Symposium held in Minneapolis, Minnesota, June 26-July 1, 1999.

(29) K. S. Rotondi, **K. Gunasekaran** and L. M. Gierasch. Investigating the role of turns in the folding of a predominantly β-sheet protein. 16th American Peptide Symposium held in Minneapolis, Minnesota, June 26-July 1, 1999.

(30) **K. Gunasekaran**, A. T. Hagler and L. M. Gierasch. Identification of conserved interactions in a predominantly β-sheet protein; Implications for folding studies. 5th Johns Hopkins Protein Folding Meeting held in Berkeley Springs, West Virginia, March 18-21, 2000.

Oral Scientific Presentations:

(1) "Insight into folding and stability of cellular retinoic acid binding proteins through computational approaches" Delivered on July 7th, 2000 at the National Cancer Institute, Frederick, Maryland

(2) "Loops that trigger and modulate functions: An evolving common mechanism in enzymes" Delivered in 47th Biophysical Society Annual Meeting in San Antonio, Texas, March 1-5, 2003.

(3) "Economy of enzyme mechanism: Triggering loops as an evolving common mechanism" Delivered in 48th Biophysical Society Annual Meeting in Baltimore, Maryland, March 1-5, 2004.

Citations: 170 citations as of 24th April, 2004

Teaching Experience:

Teaching Assistant from 1995-1997 for a graduate level course on conformational analysis of peptides and proteins. Given lectures in journal clubs, departmental meetings, lab meetings, and in conferences.

Professional Activity:

Refereed papers for various international journals such as *Proteins: Structure, Function and Bioinformatics, and Protein Engineering Design and Selection*

Honors and Awards:

Junior (1993-1995) and Senior (1995-1998) Research Fellowship award from the Government of India, New Delhi, India

Memberships in American Association for the Advancement of Science, USA and Biophysical Society, USA

Thesis Titles:

Ph. D. – "Stereochemical Analysis on Protein Structures - Lessons for Design, Engineering and Prediction", submitted to Indian Institute of Science, Bangalore, India, in 1997

M. Sc. – "Numerical Approach to Atomic Hartree-Fock Equations and its Applications", submitted to Indian Institute of Technology, Mumbai (Bombay), India, in 1993

Bio-Computations Experience:

Computation skills:

Programming Languages	C, C++, FORTRAN, PERL, BASIC and HTML
Programming Experience	Fifteen years
Operating Systems used	VMS, NOS/VE, Unix - (IRIX, WINIX, AIX, LINUX, SOLARIX, SUN-OS), MS Windows, Mac
Graphics Workstations used	IRIX, INDIGO, ONYX, O2, OCTANE2, SUN-SPARC, IBM
Mainframe Computers used	VAX-88, Cyber, DEC-10000, IBM, CD4360, Power Challenge, SP2, ULTRA-SPARC, ORIGIN2000, Biowulf Clusters @ NIH
System Administrations	Three years in UNIX (LINUX) and three years in IRIX
Application Software/Packages used	MSI (Discover/InsightII), MIDAS, MOPAC, CHARMM, AMBER, CDISCOVER, NAMD, VMD, FASTA, MSP, GCG, XPLOR, MOLSCRIPT, ORTEP, RASMOL, CLUSTALW
Databases used	PDB, SWISS-PROT, Gene Bank, HSSP, DSSP, PROSITE, PFAM, SCOP, DIP, KEGG, GO

Programs developed:

HAIRPIN	C program to identify and classify β-hairpins in protein structures
HELIXP	C program to identify positional preferences of amino acids in helices
HBOND	FORTRAN program for characterization of hydrogen bond types in protein structures
PSEARCH	Knowledge-based search tool in FORTRAN for identification of motifs based on C^{α} positions
SEQHOM	C program for sequence comparison of two PDB entries
FINDSEQ	Sequence pattern search algorithm coded in C
COMPMAP	C program to compare structures based on backbone dihedral angles
CONFPIC	C program to pick residues adopting Ramachandran-disallowed conformation
IDFYSIM	C program to identify the correlated mutational behavior of the interacting amino acids
SEQANAL	C program to tabulate the amino acid replacements in each position of a given sequence from multiple sequence alignment
STACKFIND	C program to identify aromatic-aromatic stacking interactions from protein structures

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References:

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(Ph.D. thesis advisor; Prof. C. Ramakrishnan co-pioneered the work on "Ramachandran Map" for his Ph.D.)

Additional References available upon request