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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

Sub: Dr. Cynthia Gibas

Dear Search Committee,

I have great pleasure in writing this letter on behalf of Dr. Cynthia Gibas (Cindy) who has applied to your Center for a position. It is absolutely certain that it Cindy will be a good recruit for any institution, especially one such as yours, that is focused on research problems related to the large volume of emerging biological data.

Cindy joined my group as a graduate student in 1992 to work on research problems in computational biology. Having had a solid training in her undergraduate and graduate curriculum in biophysical chemistry, she chose to work on research problems that have a very strong tie to experimental biophysical chemistry. I assigned her the problem of calculating pH-dependent properties of amino acid residues in proteins with a view to understanding their structure and function in different solution milieu. Experimentally there are very few proteins where precise pKa values of the individual amino acid residues have been measured and given the importance of titratable residues in catalysis, it seemed an excellent idea to obtain them from computation. This problem has been identified as an important one by scientific stalwarts such as Debye, Onsager and Kirkwood and they have laid the statistical mechanical foundations for computing titration behavior of proteins. However, only recently a detailed atomic-level picture of three dimensional structure of proteins is emerging thanks to crystallography, and numerical computational methods can be used effectively to compute the titration behavior of proteins. Within a short time after starting her research, Cindy obtained a detailed picture of titration behavior of complexation of an antibody-lysozyme complex and this was in excellent agreement with experimental measurements. Further Cindy characterized precisely the role played by localized solvent molecules in modifying the pka values. All of this

work has been published in reputed peer-reviewed journals. After investigating several other biological systems, Cindy wrote her dissertation on the computation of pH-dependent properties of proteins.

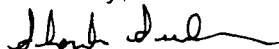
Cindy has a very strong intuition for protein structure. This prompted her to take up my challenge of attempting to design a sequence that would represent a soluble version of a membrane protein. This exercise was more an aid to deriving knowledge-based rules for protein design. Cindy made several constructs which would have putative soluble protein sequence requirements. Her work was published in the journal, "Protein Engineering" and several researchers all over the world have expressed interest in exploring this approach to designing proteins with targeted functionality. More recently, Cindy in collaboration with two other graduate students in my laboratory, has developed novel tools for mining protein structure data to build structural fragment classes. These classes will aid in homology modeling and we are preparing a manuscript that describes the power of fragment-based approaches in protein structure modeling.

Cindy is very helpful to her colleagues. She has worked with a number of graduate students in our laboratory. She has a good facility of scientific expression and was the primary author on an invited review in the "Methods" series.

Cindy joined Virginia Tech a few years ago as a faculty member in biology. She has strived to succeed, but it appears she has been limited by the support she obtained from her Department. She also undertook writing a book, which I am sure detracted her away from more research. As a consequence her scientific productivity has suffered. Nevertheless, she is good faculty material and will do well in a good environment.

In summary, I recommend her to you in the strongest terms and would urge you to consider her for this position. Please feel free to contact me if you have further questions concerning Cindy.

Sincerely,



Shankar Subramaniam