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

Dear Search Committee,

It is a real pleasure for me to support Dr. Marcos Betancourt for an assistant professorship at your department. Marcos was a very good graduate student at my laboratory. He is a very independent and creative scientist, and his Ph.D. thesis provided several new contributions to the field of protein folding. Although Marcos was at UCSD for several years, he was in my group for only two and half years. Before changing to molecular biophysics, he was working in non-linear physics. Protein folding was an entire new topic for him but, as it can be noticed from our joint papers, he was able to succeed in this very short period. Marcos has both, very good analytical and numerical capabilities, skills extremely necessary for attacking this kind of problems.

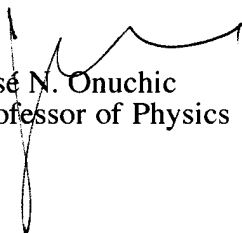
Let me comment on some specific results. In his first manuscript ("Kinetics of Protein-Like Models: The Energy Landscape Factors that Determine Folding," J. Chem. Phys 103, 773, 1995), he performed careful studies in small chains in 2-dimensions. From this analysis several new concepts were obtained. For example, by looking at the infinity temperature limit, he was able to show in a quantitative way that different sequences have different accessibility towards the native configuration. This is a totally geometrical effect and is independent of the choice of potential. On the other end, he defined the concept of "hindering contacts" to quantify "energetic" frustration. Since all the native states for the different chosen sequences have the same energy, one expects that the folding time would be dependent on these "hindering contacts." Larger numbers of them should lead to longer folding times. The results obtained show a overall good agreement, i.e., it can be used to differentiate good sequences from bad sequences. However, when sequences that have similar geometrical effects are used, the agreement is perfect. It was nice to see how he was able to create approaches to separate "geometrical" from "energetic" frustration. We know that one should be careful relating the quantitative conclusions for results in 2-D with real proteins, however the important concepts can be analyzed in this framework. This work has had such an impact that it has almost 100 citations.

After San Diego, he moved to the University of Maryland at College Park with a NSF postdoctoral fellowship. Working with Dave Thirumalai was an ideal postdoctoral choice for him. He was able to apply his ideas to more realistic systems. The connection between simple and realistic models is very important in folding, and Marcos was the ideal person to address this problem. He published great papers addressing folding in vivo and moved also towards creating new methods for protein structure prediction.

He had such a great success with Thirumalai, that Jeff Skolnick hired him as a research scientist in his group. Together they had great success. As you can see from his publications (almost 20 by now), he has focused in two major areas. He is developing simplified protein models that are sufficiently simple to simulate folding events, but are sufficiently accurate to reproduce the native structure without the use of homology modeling. He is also creating better methods for native structure information extraction from threading for native structure prediction applications

Concluding, to support Marcos for this position is a special pleasure for me. Marcos has a solid theoretical formation and he is a very creative and hard worker. In a short time in the field of protein folding during his PhD, he already achieved significant results, and after San Diego his career really took over. He gives good talks and he has been a good TA at UCSD. For this reason, I believe he will be a great teacher. He is a natural person for this job and you will be very fortunate if you can recruit him. Please feel free to contact me if you need any further information.

Sincerely,



José N. Onuchic
Professor of Physics