

Department of Biochemistry, Molecular Biology & Cell Biology

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

re: Letter of recommendation for Dr. Michael G. Poirier

## Dear Colleagues:

I write in strong support of Dr. Michael Poirier's application for a faculty position in your department.

Dr. Poirier received his Ph.D. with Prof. John Marko. I have been familiar with his work with Marko from its inception, and, since Poirier joined my lab a year ago, I have gotten an even clearer sense of his accomplishments and potential.

Poirier is responsible for much of the work that came out of Marko's laboratory from the time that Marko began as an Assistant Professor, through 2003. Poirier built the lab, designed and built the instrumentation and learned how to do the experiments – none of these being Marko's personal strengths at the time – and he then carried out a remarkable series of studies on the mechanical properties of chromosomes. His results refute long-held dogma in the field and attracted much attention, including a review in PNAS written by another expert, Prof. Andrew Belmont at U. Illinois, Urbana. From the biological perspective, Poirier's most important paper is the 2002 PNAS paper describing this work. Several of the other papers detail remarkable materials properties of chromosomes. Poirier's work with Marko was largely responsible for Marko's promotion to tenure at U. Illinois, Chicago.

Poirier then spent two years in France, in the lab Didier Chatenay. This was a sophiosticated choice for postdoctoral training. There he began studies of plasmid partitioning, combining microfuidics and quantitative real time imaging of single cells. Again, Poirier developed much of the instrumentation and experimental approaches. He left France (for family reasons) prior to completing this work; this early departure prevented him from completing his project, but was certainly a great benefit to my lab. He returned to France recently for a month to complete work for a paper.

In my lab Poirier has begun building and analyzing experimental model systems with which to investigate mechanisms of chromatin remodeling and regulatory protein binding in reconstituted long chromatin fibers. This represents a major improvement over our existing analyses, which have focused on single nucleosomes; however it also greatly complicates the task of preparing and characterizing the needed DNAs and reconstituted chromatin samples. Poirier made rapid progress on the constructions and has already accumulated substantial data, starting with the simplest case of passive binding of proteins to target sites in a nucleosome that is flanked by chains of nucleosomes on both sides. A related component of this project will use variants of these oligonucleosome constructions to analyze the folded structure of the chromatin fiber itself. This is a topic that has resisted understanding despite decades of analysis by many groups. Poirier has devised a promising approach that will use fluorescence resonance energy transfer to test and distinguish between differing models.

Poirier's longer-term goal is to combine simultaneous measurement of force, displacement, and fluorescence resonance energy transfer, to elucidate the molecular mechanisms of chromatin remodeling machines. My view is that this approach will prove to be mandatory for the analysis not only of chromatin remodeling machines, but also most of the other macromolecular machines in the cell. Poirier is well ahead of the thinking of most others in this regard. I should emphasize that this was his plan, not mine; however, it is clear to me that he is correct.

Poirier takes complete intellectual responsibility for his project, for the design of the experiments, details of the experimental procedures, and the interpretation of the data. Everything that he does is accomplished professionally. I should point out, as well, that I am not the only person at Northwestern who is impressed by Poirier's accomplishments and potential: he was picked as one of Northwestern University's two allowed nominees for the Burroughs-Wellcome Career Award this year. Overall, I consider that Poirier ranks as comparable to the very best one or two postdoctoral fellow to come through our department in my thirteen years at Northwestern. I strongly recommend him to you.

Yours sincerely,

Jonathan Widom