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Yves Brun, Systems Biology / Microbiology Faculty Search Department of Biology, Indiana University Jordan Hall 142, 1001 E 3rd St. Bloomington, IN 47405-7005

## Dear Search Committee:

I am writing to recommend Dr. Kurt Thorn for a position in your department as an Assistant Professor. I was Kurt's graduate student advisor at UCSF, and I have followed his progress at the CGR at Harvard.

Kurt is exceptional. He is one of the smartest graduate students that I have encountered at UCSF. I will elaborate on some of his specific abilities below. I anticipate that a barrier for an admission committee will be his publication record. He had two solid papers from graduate school and will have a very strong paper from his Fellow position. However, there will be applicants with more papers and in higher profile journals. Nevertheless, I believe that Kurt will outstrip many "more qualified" applicants in terms of his potential, ability to do creative research, and value that he would add to a department. These qualities will be apparent when you interview him. So I would encourage you to see beyond the sheer number of papers that he has published, pay close attention to his reference letters, and hopefully invite him for an interview so that you can appreciate his potential as an investigator and colleague in your department first hand.

Prior to coming to my laboratory, Kurt already proved himself as a researcher in undergraduate school, having published crystallography studies with Schutt at Princeton and performing several interesting studies with the x-ray source at the Brookhaven laboratories. Clearly, he was a very gifted undergraduate with an unusual propensity for research. In my laboratory, Kurt conducted work on the kinesin processivity, publishing a very nice study with surprising result that a coiled coil adjacent to the motor domain can control kinesin processivity (featured on the cover of JCB). Kurt was even able to design a kinesin that had significantly greater processivity than wildtype kinesin. In this work, Kurt became expert in single molecule fluorescence and protein engineering and molecular biology. However, Kurt did more in our laboratory, nucleating difficult projects that lead eventually led to new research efforts in our laboratory. For example, Kurt built an optical attachment to our total internal fluorescence microscope for simultaneous measurement of two fluorophore to detecting single molecule FRET. This project was started at the end of his time in the laboratory, and was picked up by a postdoctoral who used Kurt's initial prototype to begin this project which led to successful results. In addition, Kurt began our lab's initial work on dynein, which was courageous given the magnitude of difficulty in working with this very large enzyme. Six years later, this project is beginning to yield results, and this project is a legacy of Kurt's pioneering efforts. Moreover, and as a tribute to Kurt's independence, Kurt and another graduate student Andy Bogan developed a computation strategy for identifying sites on protein surfaces that are involved in protein-proteins interactions. This work was conceived of and performed without any guidance (also without any interference) from any UCSF faculty and published in J. Mol. Biol. I cannot think of any other graduates that have had the initiative to develop an entire project on their own in this way.

Kurt's talents were certainly recognized when he was offered a prestigious Fellows position at the CGR at Harvard. Kurt conceived of a project to measure protein-protein interactions through quantitative FRET in living cells. There were many good aspects of this project, but also some down sides. On the positive side, Kurt identified a very important problem and one that represented a completely new direction from his graduate student work. Being very quantitative and rigorous, he was not satisfied until he understood all aspects of making these FRET measurements, at a level that few people have dared to question and investigate. But as a result, this work proved difficult and took a long time to develop technically, hence yielding less biological insight than he would have liked for the time invested. I imagine that his progress on this problem would have been accelerated if he was in an environment where he would have had more input and advice on this problem. From what I gather, he worked pretty much independently on this very challenging problem, and the Murray laboratory and other fellows were working on very different areas. However, his Fellow's work did lead to several achievements. First, he succeeded in deriving a very interesting model for the septin complex, which represents a significant advance on this poorly understood filament complex. Second, he worked out many of the technical challenges in this project, allowing much more rapid progress in subsequent investigations. Thus, I firmly believe that he is in a great position to capitalize on his technical advancements. Measurement of protein-protein interactions in living cells is a critical frontier in systems/cell biology. I think that cytokinesis is a wonderful subject that would benefit from defining protein-protein contacts, especially now that the list of essential genes are now known in several organisms. The cytokinesis field needs to know how these proteins work and interact, and Kurt is in a great position to make important contributions in this area.

Kurt has many outstanding qualities. As I mentioned earlier, he is terrifically smart. It is pleasure to talk science with him. Kurt keeps you on your toes and has great insight. He also is multi-faceted. He is great at structural biology, computation, light microscopy, and molecular/cell biology. Trained as a physicist, he approaches biological problems with very keen physical and quantitative insight. He is very rigorous in experimentation and analysis. Kurt also is very willing to tackle difficult problems, as you can see from my description above.

Kurt also is wonderful person. He is modest, unassuming, kind, and unselfish. He was very liked in my laboratory, and was great citizen. I gather that the same has been true in Harvard. He is very willing to share his time and expertise with others. Perhaps he is a bit "nerdy" (but who am I to talk!), but he has plenty of outside interests and a good circle of friends. He brews great beer. I am confident that he will be similarly well-liked and a great community player as an assistant professor at a University.

In summary, I think very highly of Kurt and feel that he will make a great assistant professor in your department. There are few people with Kurt's intellect, dedication and skills. He has the potential to make important and original contributions in the new era of quantitative biology. He will also make a wonderful colleague and be an inspiring supervisor for graduate students. I think that you will be delighted and impressed with him when you interview him. I am happy to answer any additional questions that you may have.

Sincerely yours,

Ronald D. Vale, Ph.D.

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