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Justin Blau, Ph.D.
Assistant Professor

Department of Biology
1009 Silver Center
Washington Square East
New York, NY 10003-6688

Telephone: (212) 998-8261
Fax: (212) 995-4015

justin.blau@nyu.edu

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Dear Committee,

It is a great pleasure to recommend **Danny Forger** for an Assistant Professor position. Danny moves freely between Math and Biology with great love and enthusiasm for both. Danny is now in my lab as an Alfred Sloan Fellow in Computational Biology, where he is designing experiments based on his models of the circadian clock, and then conducting them himself.

I first met Danny during his Ph.D with Charlie Peskin at Courant in which he modeled the mammalian circadian clock. These clocks drive the daily rhythms in sleep/wake cycles and numerous aspects of physiology that allow an animal to anticipate environmental changes. Danny was a “real” Ph.D. student – he brought the topic of circadian rhythms to Charlie and developed it under Charlie’s guidance. This model was published in PNAS in 2003 and has been praised by many people as accurate, highly detailed and for its attention to experimental results.

Our shared interest in circadian clocks meant that Danny and I ran into each other during his Ph.D. I would typically ask him when his modeling would become “useful” (i.e. predictive not just descriptive). Two days after one of these questions, Danny came to my lab’s weekly meeting, in which we discussed our recent data on a second feedback loop in the *Drosophila* molecular clock. At one point, Danny had a “Eureka” moment and became very excited that this second clock loop could help a clock compensate for temperature changes (i.e. keep running with a 24 hour period in winter and summer). This is an unusual property of circadian oscillators that was observed a long time ago, but for which there is still no convincing molecular explanation. Danny suggested that the second loop had the correct structure to allow temperature compensation – an insight that came straight from his modeling and simulations of feedback loops at different temperatures, and that we had not considered in the lab. I suggested that this could be tested by assaying flies lacking one copy of the second clock loop genes and invited Danny to perform the experiments. Danny accepted the challenge eagerly and spent a lot of time in my lab over the next few months loading flies into glass cuvettes to monitor their circadian rhythms at different temperatures. The results look promising and we plan to write up this “design principle” of the clock soon.

In my lab, Danny has also initiated a number of other projects based on ideas arising from his modeling work. Through one of these, he may be able to explain some experimental observations that my lab has puzzled over for a while – how could a clock lacking one of the second loop components run under light:dark cycles and yet be stopped in complete darkness? Recently Danny has become fascinated by the electrophysiology of pacemaker neurons and has been collaborating with a leading mammalian circadian lab (Chuck Allen in Oregon) to apply some of his experience in modeling and recording electrophysiological rhythms to the circadian system.

These are just a few examples of Danny's intuitive approach to science. It has been exciting and provocative to have Danny in the lab: he does not think in the ways that molecular biologists think, his ideas challenge many of our points of view, and he frequently stresses the need for rigorous mathematical models to understand any genetic network. He has put up with skepticism from many people about the usefulness of modeling in Biology – but he realizes that a working relationship between Math and Biology requires that mathematicians understand how biologists get data *and* that mathematicians must be predictive to be valued by biologists.

I believe that Danny has enough background in Biology and enough brilliance in modeling to succeed in Math-Biology. Danny cares deeply about Math-Biology and is determined that its rigor rises so that modern Biology recognizes the need for Math. He is passionate about his subject and is also able to express himself extremely clearly – I almost understand Math when Danny talks about it! and I am convinced that he would make an inspiring and engaging teacher.

Perhaps the only question is whether Danny is ready to be a PI. Danny has only spent one year as a postdoc. However, he was almost a PI in Peskin's lab – Danny was instrumental in bringing money from DARPA to the lab and he was the one modeling and then presenting at the meetings to the other PIs in the multi-university group. Danny should have no problems funding his work – for example, the Air Force recently invited him to submit a proposal! He was also asked to be part of a group modeling human circadian rhythms for a large NIH grant: he declined because it would detract from his work here. Danny is already invited to give talks regularly – most recently he shared the stage with Dan Gillespie and Tim Elston at the Mathematical BioSciences Institute, and apparently his talk attracted more discussion than those of the other two big names!

In short, Danny would make an excellent colleague. He is almost already a leader in Math-Biology, and should do pioneering work in the field. I certainly suggest that you interview Danny!

Yours sincerely,

A handwritten signature in black ink, appearing to read "Justin Blau", written over a horizontal line.

Justin Blau, Ph.D.