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Biocomplexity Faculty Search Committee
C/o Prof Rob de Ruyter van Steveninck
Biocomplexity Institute
Indiana University
Swain Hall West 117
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47405-7105

To whomever it may concern:

I am writing in enthusiastic support of Dr. Astrid Prinz's application for a position as an Assistant Professor at your institute. Astrid has been working in my laboratory for a little more than 3 years. I strongly urged her to apply for faculty level positions this year because I believe she is ready to embark on an independent career. The other people in my laboratory were horrified at the idea of Astrid leaving, because she is an integral part of the scientific and intellectual fabric of the laboratory. My postdocs and graduate students respect her enormously, and they turn to her for scientific guidance, help, and advice.

Astrid works very hard and very systematically. Consequently, she has been quite productive in her time here. She is first author on two original papers that have already appeared, she is writing a third as we speak, she is second author on one that should be submitted shortly, and she has been involved in the writing and thinking behind several high-profile review articles. Additionally, she has collaborated with Carmen Canavier's group on a more mathematical project.

Over the years I have worked with a large number of theorists of all kinds. Astrid stands out as being one of the clearest thinking, most disciplined, and most principled among them. In addition to being a theorist, Astrid is a skilled electrophysiologist, and this has shaped the way she approaches her theoretical work. She wants her models to capture the essence of the biological system she is studying, while at the same time appreciating that the utility of theoretical work is that it can reduce the complexity of a problem to a tractable level. Describing Astrid's development of her data base approach to the construction of conductance-based models will allow me to illustrate many of her strengths.

As I am sure you know, developing semi-realistic conductance-based models is both a goal of many neuroscientists (including us) and a fool's errand. It is a fool's errand because it is never possible to measure everything one would want or need to

construct such models, and one is left feeling a hostage to the inadequacies of one's biological data. Nonetheless, even imperfect models can lead to great insight, and certainly allow the formulation of many important and interesting biological questions. At a certain point Astrid wished to construct a model of the pyloric rhythm of the crustacean stomatogastric ganglion. To do so meant developing candidate models of each of the cells. Astrid first spent some time hand-tuning models, starting with others in the laboratory. She quickly became frustrated in so doing because the problem with hand-tuning is that one never knows if one has found the best solution, etc. So, Astrid constructed a data base in which she constructed 1.7 million model neurons, each with 8 different membrane conductances. She used 6 different values of each of the 8 conductances, and then ran all of the model neurons. I might say at this juncture that if she had asked me ahead of time if she should do this, I would have told her she was stark-raving mad. But she ran the first data base simulations in the background on a number of lab computers, and three weeks when she first told me what she had done, I just started laughing because it was so clear it was the right thing to do.

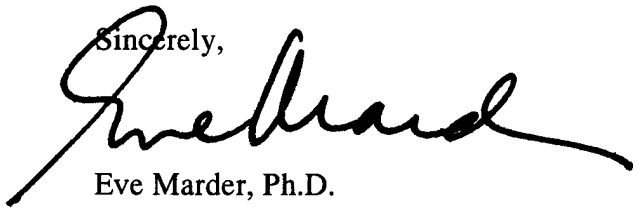
The first paper describing this approach has just been published (Prinz et al., J . Neurophysiol, 2003). In this approach the investigator uses brute force in a non-random fashion to simulate a very large number of possible models, and then the properties of the models are classified and searched to find models with specific attributes. The challenge is not to generate the models, but in designing simple and efficient classification and search algorithms so that the richness of the models' properties can be understood and used. Astrid's care and systematic approaches were crucial in setting us this kind of project. Astrid is now working on a second paper in which she ran 20,000,000 model pyloric circuits. She is now using this data base to extract specific predictions about which synaptic strengths are most crucial for the model's dynamics, and to answer numerous other questions. Already this network model has suggested numerous experiments and data analyses. I think Astrid will be involved in the future with both developing new methods for the construction and analysis of this kind of systematic approach to model building, as well as in using these and other tools for the study of a number of important biological problems.

Astrid is a truly lovely person. She is gracious, kind, and will go to great lengths to help others. She is also incredibly stubborn and determined, while at the same time being humble about her own abilities. She is a born teacher, both one-on-one and in front of an audience. Astrid writes extremely well. She is a delight to coauthor papers with, because she delivers almost perfect and complete versions of manuscripts, but is never defensive if we think the draft needs a different perspective. She took the lead on putting together not only her research papers but also the TINS paper we recently submitted.

Astrid speaks very well, gives excellent seminars, and I am sure she will develop into an outstanding classroom teacher. She has the gift of clarity, and works hard to make theory accessible to all. Astrid also asks very pointed and thoughtful questions in seminars, and her questions are always illuminating to the audience.

Astrid has all of the skills and determination to be an outstanding faculty member and to be consistently productive in both research and teaching. Astrid is likely to always do "grounded theory", where the theory is always well-connected to true biological measurements and principles. As such, she is the ideal theorist for a biology department or neuroscience program unaccustomed to theory, as she has the ability to be the perfect interface and translator between worlds, such as physics (in which she obtained her Ph.D.) and biology.

Sincerely,



Eve Marder, Ph.D.