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Dr. Brun:

I am writing to highly recommend Dr. Yi Jiang, who has applied for a faculty position in your department. I have worked with Dr. Jiang for the past five years on modeling of solid tumors. I would like to provide a little background on myself, briefly describe our joint project and my interactions with Yi, and then provide my assessment of Dr. Jiang's scientific and professional strengths.

I am a biophysicist working with 3-D *in vitro* models of the tumor microenvironment. Our primary system is referred to as a multicellular spheroid, which is a spherical aggregate of tumor cells that mimics the chemical, physiological and therapeutic microenvironment within a solid tumor. We have emphasized experimental measurement of how the cellular microenvironment regulates tumor cell proliferation, metabolism and physiology. I have developed several new methods for analyzing this tumor model system, and applied a variety of measurement techniques including flow cytometry, molecular biology, NMR spectroscopy, proteomics and metabolomics. I also have a long-standing interest in mathematical modeling of spheroids, from a paper published as a graduate student, through several publications with a group at the Mayo Clinic, to the model that was just published with Yi in *Biophysical Journal*.

Yi originally approached me with an idea to simulate the growth of spheroids using the lattice model she had originally developed for cellular pattern development. A weakness in much of the field of tumor modeling is that there is often little connectedness to the actual biology of the system: the majority of tumor models are derived instead from a pre-existing mathematical framework. Dr. Jiang's multiscale approach truly represents a paradigm shift in this field, since each of the three elements is derived directly from biological phenomena. Over the last few years we have expanded this model to include cell-cell interactions, a gene regulatory network controlling proliferation, and a chemical transport component regulating metabolism and viability. This model accurately predicts the growth and development of an avascular tumor from a single cell through growth saturation (~6 orders of magnitude). In addition, the model provides accurate estimates of proliferation, metabolism and cell death under different external growth conditions. As highlighted in an AMS review article, Yi's model is the state-of-the-art in this field. Yi is currently extending our model to the next stage in malignant progression, angiogenesis.

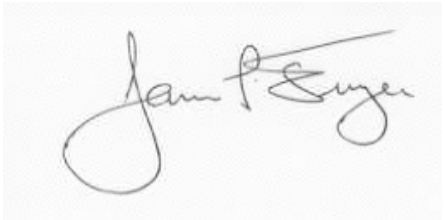
My collaboration with Dr. Jiang has been exciting, both personally and scientifically. In my experience, Yi is one of those rare mathematicians who can truly grasp the experimental details of our biological system. We have spent many hours discussing the intricacies of tumor biology, which has greatly strengthened our work together. Yi is very receptive to challenges to her 'theoretical' concepts when they don't match up with the biological realities, again not necessarily a common trait among theoreticians (in my experience). In addition to being willing to learn from a biologist, she has been an excellent teacher for a long-time experimentalist with little background in mathematics. I think I could actually explain the mathematics of our model, which is due almost entirely to Yi's instruction and guidance. Another of Dr. Jiang's strengths is her ability to combine this biological understanding with an excellent grasp of mathematical modeling, from theoretical development through computer implementation and everything in between. These strengths show in the breadth of her current biological modeling work, which varies from tumors to bacterial aggregation to molecular self-assembly to lipid bilayers. Yi also has a number of non-biological modeling projects, further testimony to her breadth of knowledge and experience. Another scientific and professional strength is Dr. Jiang's excellent leadership qualities: she has been the driving force behind our collaboration and leads several of the other efforts as well. Finally, Yi is extremely dedicated to her work. Bootstrapping off of other projects has funded our tumor modeling collaboration. We have submitted both internal and NIH grant applications, but getting an award in an interdisciplinary area such as this is never easy. Dr. Jiang has persevered despite some discouraging setbacks, and we are submitting a revised NIH application that came very close to funding last time.

Another important application of Dr. Jiang's talents has been in the area of mentorship. Our collaborative project has involved working with several graduate and undergraduate students: the other two authors on our recent paper are students. I have seen Yi's interactions with students first hand, and I have always been impressed. I work with students myself quite a bit, and I have learned a thing or two from Yi. My personal assessment of Yi's strengths in this area are backed up by her being awarded the Outstanding Mentor Award at LANL in 2004; only two staff members from across the entire Laboratory are chosen for this award.

On a more personal side, Yi is an extremely hard-working, energetic and highly intelligent scientist. I have found her to be very easy to interact with, as have all of her colleagues and collaborators. I have been consistently impressed with her willingness to have a spirited discussion without rigorously holding to her original ideas. Her persistence has paid off in our project and has been an inspiration to me and to many of her co-workers and, particularly, her students. I plan to continue my collaboration with Yi regardless of her location, as it is one of the best in my career. I can recommend Dr. Jiang to your group enthusiastically and with no reservations whatsoever.

Please feel free to contact me if I can provide any further information.

Sincerely,



James P. Freyer, Ph.D.

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