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Systems Biology/Microbiology Faculty Search
Department of Biology
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November 3, 2005

Dear Chair, Systems Biology/Microbiology Faculty Search Committee,

Evaluation of Dr. Guocheng Yuan for a junior faculty position

I mainly know Dr. Yuan from a 1-week stint of teaching he did on a course I co-organize. I have also read his proposal and discussed it with him, and I am familiar with the area of biology he proposes to focus on.

Dr. Yuan volunteered to develop and teach a section on computational methods and use of MATLAB to describe and analyze biological processes. This was part of the MBL physiology course, taught at Woods Hole last summer. His section of the course was a team effort of 4 young scientists, including Dr. Yuan. They developed the material as a team, that included writing guided exercises, and they co-taught it as an intensive 10 hr/day, 6 day unit. I sat in on the development sessions, and kept an eye on the class. Dr. Yuan did a great job. He has an excellent grasp of the math and science, and was full of ideas and examples for how to communicate them. He fit in well with the team, and consistently had a great attitude. He received very good evaluations from the students.

I was impressed with Dr. Yuan's proposal compared to many others I have seen for would-be assistant professors in systems biology. The first biological problem he has chosen to work on, chromatin-based modulation of gene expression, is topical and important. That field is dominated by an attractive hypothesis, Allis' "histone code" model. This dominant model needs to be critically evaluated in light of quantitative data, and I bet it will need to be replaced by new models. Histone modification can be altered by small molecule drugs, and there is a hope that this is an area of cell biology where it will be possible to develop therapeutic drugs that usefully modulate gene expression, for

example in cancer therapy. Success in that area is going to require much better quantitative understanding, and Yuan's proposed research is a step in the right direction.

From my limited acquaintance, I rate Dr. Yuan as a strong candidate for a junior faculty position. His analytic, communication and teaching skills are excellent, and he has identified a very promising area for independent research.

Sincerely,

Timothy Mitchison, PhD

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Dear Search Committee:

Guo-Cheng (GC) Yuan has been a post-doctoral fellow at the Bauer Center since January 2004. Since I was on sabbatical for the first six months of 2004, I know GC more for his considerable accomplishments than from day to day contact with him, and I will leave detailed comments on that area to his post-doctoral mentors, Lani Wu, Steve Altschuler, and Ollie Rando, all of whom were, or still, are fellows at the Bauer Center. In addition, since I am an experimental biologist, I cannot make any assessment of GC's technical skills in mathematics.

The Bauer Center is an interdisciplinary initiative, whose intellectual core is formed by 10 fellows, outstanding young researchers who have been appointed to five-year positions to develop their own, completely independent research program. The fellows come from a diverse set of backgrounds, including genomics, molecular and cellular biology, organismal and evolutionary biology, computer science, mathematics, and physics. Their enthusiasm for interdisciplinary collaboration with other fellows and the faculty in surrounding departments is a key criterion in their selection; all of the fellows are already involved in active collaborations. Their research areas are diverse but interwoven with each other, ranging from computational methods of defining genetic circuits and mathematical modeling to studying the reciprocal interactions between gene expression and organismal behavior in animals and plants. They are described in detail on our web site (http://www.cgr.harvard.edu).

As his mentors will describe in more detail, GC worked on analyzing the data from experiments designed to map the position of nucleosomes (the roughly spherical complex of the core histones, which DNA wraps around) on the chromosomal DNA of the budding yeast. In particular, he developed the Hidden Markov Model that was used to determine the position of nucleosomes based on data from DNA microarrays, and this work earned him first authorship on a paper that recently appeared in Science. This is an important paper for three reasons: it shows that most of the nucleosomes on the yeast genome are positioned at the same point on the DNA in most of the cells in the population (rather than being randomly distributed across a range of similar positions in different cells), it reveals that the transcriptional start sites of most genes are free of nucleosomes, and that statistical analysis

of microarray data can give a detailed and surprising picture of the architecture of chromatin. This paper will be one of the best ten papers published this year on chromatin structure and gene regulation and will rapidly become a classic in the field.

GC has thus already made a large mark on biology, and I expect he will make many more. He is a bright, outgoing, and thoughtful person. When he has spoken at the Bauer lab group meetings, his presentations have been crisp and clear, and when others are speaking, he has asked intelligent and perceptive questions. When he and I have talked, I have been impressed both by his knowledge of biology and his ability to explain mathematical concepts to a naïve but enthusiastic listener. He is a respected and responsible member of the Bauer community, and I imagine that he will make an excellent colleague when he becomes a faculty member.

In summary, GC has already used his mathematical skills to make an important discovery in biology, and the combination of his intelligence and his mastery of both fields ensures that he will make others in the future. I recommend him to you strongly and without reservation.

Sincerely,

A W Murray

Andrew W. Murray
Herchel Smith Professor of Molecular Genetics
Codirector, Bauer Center for Genomic Research
Professor of Molecular and Cellular Biology