Yale University

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October 20, 2004

Biocomplexity Faculty Search Committee
C/o Professor Rob de Ruyter van Steveninck
Department of Physics
Indiana University
Swain Hall West 117
Bloomington, IN 47405-7105

CONFIDENTIAL

Re: **Recommendation Letter for Dr. Jason Mezey**

Dear Faculty Search Committee,

Jason Mezey has been known to me since he entered Graduate School here at Yale. He did a rotation in my lab working on shark Hox genes, a project that set the stage for a paper that was later published in PNAS (2000, 97: 1655-1660). Then he decided that he wanted to work on a theoretical project and took on the problem of whether one can select for a modular genotype-phenotype map. This is an extraordinarily difficult problem, both conceptually and technically. The fact that in the end we found that the class of models we worked on at the time can not lead to modularity is of no fault of his. As a result of his work we now understand why this was impossible with the models we used. In the course of the work he analyzed the mathematical properties of the model we were using at the time (J theor Biol. 203:163-175 (2000)). In addition, he worked on statistical models for testing for the modularity in QTL data (Genetics, 156:305-311 (2000)).

Even more exciting than his dissertation project is the recent work he has done with David Houle in which he explored the genetic interpretation of Confirmatory Principle Component analysis as applied to genetic correlation matrices. One paper is in print in Evolution (2002, 56:433-440) another one published in Genetics (2003, 164:411-425). The main message of the latter paper is that CPC, if applied to two populations from the same species, can detect modularity in the genotype phenotype map just from comparing the structure of the genetic correlation matrices. This is an entirely unexpected and exciting result. Jason derived the mathematical result for me on the blackboard and I agreed with his conclusions. The basis for this unexpected result is that one considers the genetic covariance matrix of two populations that differ in the distribution of allele frequencies.

If this method can be turned into an effective statistical tool it will have a major impact on evolutionary biology and genetics, since it will allow insights into the structure of the genotype phenotype map that currently are only attainable with very expensive molecular techniques, like QTL mapping. I consider this as the most original and noteworthy result.

Jason is a population geneticist who has an excellent handle on the properties and the dynamics of complex genetic traits. He has mastered both, the modeling of complex traits as well as data analysis, and is thus poised to make important contributions. His work on confirmatory factor analysis further shows that he is brilliant and creative. I strongly and enthusiastically support his application. He has the brain, determination and skills to succeed as an independent researcher. I rank him among the top 10% of graduates from our department, which is blessed with an extraordinary group of talented graduate students.

Sincerely yours,

Günter P. Wagner
Alison Richard Professor of
Ecology and Evolutionary Biology